跨域創新

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天然藥物、中醫藥與自由基醫學的新視野

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Cross-Domain Innovation: New Horizons in Natural Products, Traditional Medicine, and Free Radical Medicine - Joint Symposium of the 41st SNP, 26th SFRR-Taiwan, and 2026 TATCM & Symposium on Pharmacy and Traditional Chinese Medicine

論 文 集



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跨域創新
天然藥物、中醫藥與自由基醫學的新視野

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No. PC-003 / 天然物化學組 / Natural Products Chemistry (PC)

Auto-PIS: An Automated LC–MS/MS Workflow for Annotation of Flavonoids and Hydrolyzable Tannins in Plant Metabolomics

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Comprehensive annotation of specialized metabolites remains a major challenge in plant metabolomics, particularly for highly modified flavonoids and hydrolyzable tannins that are poorly covered by conventional spectral libraries. To address this bottleneck, we developed Auto-PIS, an automated LC–MS/MS annotation tool based on interpretable mass-spectrometric rules and characteristic fragmentation behavior. Rather than relying on database matching, Auto-PIS evaluates MS/MS evidence to systematically generate and assess candidate compositions for predefined metabolite classes, with dedicated modules for flavonoids and hydrolyzable tannins. Longan (*Dimocarpus longan* Lour.) flower metabolomic data were used as a case study because our previous studies have demonstrated its diverse biological activities, including sleep-promoting, antidepressant, anti-hyperuricemic, and anticancer effects. When applied to longan flower metabolomic data, Auto-PIS substantially expanded the annotation coverage of flavonoids and hydrolyzable tannins compared with database-based annotation using MS-DIAL. The improvement was particularly pronounced for ellagitannins, for which the number of annotated features increased from 5 to 60. Auto-PIS therefore complements conventional database-driven annotation by extending interpretable structural characterization to complex metabolite classes that are poorly represented in spectral libraries, thereby expanding the accessible chemical space of bioactive plant materials.

Keyword:
Auto-PIS, LC–MS/MS, longan flower, hydrolyzable tannins, ellagitannins, structural annotation

No. PC-004 / 天然物化學組 / Natural Products Chemistry (PC)

Novel Seven-Membered Ring Triterpenoids and Structurally Diverse Bioactive Constituents from Camellia formosensis

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Camellia formosensis is the only endemic *Camellia* species in Taiwan to have been developed into a commercial crop, yet its phytochemical basis and bioactive potential remain uncharacterized. Phytochemical investigation of the leaves of *C. formosensis* afforded a total of 34 compounds, including 10 undescribed compounds (**1**–**10**), one first isolated from a natural source (**11**), and 23 known compounds (**12**–**23**). Of particular interest, an unprecedented rearranged skeleton incorporating a seven-membered ring was identified in four of the new compounds (**1**–**4**). Their absolute configurations were established by single-crystal X-ray diffraction and ECD analysis, and a plausible biosynthetic pathway from the co-occurring 3β,11α,13β-trihydroxyolean-12-one (**15**) was proposed. Bioactivity evaluation revealed diverse pharmacological activities relevant to inflammation-associated metabolic and skeletal disorders. Chlorophyll compound (**34**) displayed marked anti-lipid droplet accumulation activity, reducing the relative LD count to 0.35% at 4 μg/mL, while triterpenoids **23** and **26** exhibited moderate anti-LD accumulation activity without cytotoxicity. In the RANKL-induced osteoclast differentiation assay, triterpenoids **23** and **27** exhibited dose-dependent inhibitory effects without affecting cell viability (IC_{50} values of 27.4 and 18.6 nM, respectively). In addition, Triterpenoid **16** potently suppressed superoxide anion generation in fMLP/CB-stimulated human neutrophils (IC_{50} = 3.40 ± 1.19 μM), and triterpenoid **15** showed antiproliferative activity against Ca9-22 cells (IC_{50} value of 20.11 ± 0.95 μg/mL). Collectively, these findings reveal structure-dependent bioactivities among *C. formosensis* triterpenoids and highlight this species as a promising source of multifunctional agents targeting inflammation-mediated metabolic and skeletal disorders.

Keyword:
Camellia formosensis, anti-lipid droplet accumulation, anti-osteoclastogenic, anti-inflammatory, antiproliferative

No. PC-005 / 天然物化學組 / Natural Products Chemistry (PC)

Constituents from the stems and roots of Pericampylus formosanus

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Pericampylus genus (Menispermaceae) is widely distributed in Southeast Asia, China, and Taiwan. The various parts of Pericampylus plants have been used in folk medicine in many Asian countries, such as for the treatment of diabetes, pulmonary disease, cough, fractures, constipation, and snakebites. Various pharmacological activities related to P. glaucus have been reported, including antioxidant, anti-diabetic, antiviral, and anti-inflammatory activities, however, fewer studies have examined the chemical constituents and bioactivities of P. formosanus. Therefore we aimed to investigate the stems and roots of P. formosanus, and a total of twenty-four compounds, including two undescribed structures (1 and 2), were identified. These undescribed structures were characterized using spectroscopic and spectrometric analyses.

Keyword:

Menispermaceae, folk medicine, 8-oxoprotoberberine alkaloid, bisbenzylisoquinoline alkaloid

No. PC-008 / 天然物化學組 / Natural Products Chemistry (PC)

Evaluation of Bioactive Compound Release and Antioxidant Potential of a Cassia Seed–Barley Composite Substrate Fermented by Multiple Lactic Acid Bacteria

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Cassiae Semen is a medicinal and edible material rich in anthraquinones and phenolic compounds, however, limited release from the plant matrix may restrict biological activity. This study aims to develop and optimize a multi-strain lactic acid bacteria fermentation system using Cassiae Semen supplemented with barley. *Lactiplantibacillus plantarum* (LP) and a co-culture of *Lacticaseibacillus casei* (LC) and *Lacticaseibacillus rhamnosus* (LR) will be evaluated under controlled fermentation conditions. Response surface methodology will be used to investigate the effects of barley supplementation, bacterial culture, and fermentation time and to identify conditions that maximize functional activity. Fermentation performance will be monitored using pH, viable cell counts, and beta-glucosidase activity. Total phenolic content, total flavonoid content, and DPPH radical-scavenging activity will be determined to assess antioxidant changes. High-performance liquid chromatography will quantify major free anthraquinones, including aurantio-obtusin, aloe-emodin, rhein, emodin, chrysophanol, and physcion, while soluble beta-glucan will be measured to evaluate retention of barley-derived components. Multivariate modeling will be applied to establish relationships among fermentation conditions, phytochemical transformation, and antioxidant responses, followed by validation of the predicted optimum. The study is expected to clarify whether barley enhances lactic acid bacterial biotransformation of Cassiae Semen and to establish a reproducible fermentation and quality-evaluation framework. The findings may support the development of value-added fermented botanical products with improved functional properties.

Keyword:

Cassiae Semen, Barley, Lactic acid bacteria fermentation, Anthraquinones, Antioxidant activity, Response surface methodology (RSM)

No. PC-009 / 天然物化學組 / Natural Products Chemistry (PC)

BIOACTIVITY-GUIDED METABOLOMICS REVEALS POTENTIAL MULTI-TARGET BIOACTIVE COMPOUNDS FROM PHILIPPINE MEDICINAL PLANTS

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Medicinal plants remain a rich source of pharmacologically active compounds, yet many of their bioactive constituents and therapeutic potential remain underexplored. This study employed a bioactivity-guided metabolomics approach to investigate twenty medicinal plants from Oriental Mindoro, Philippines. Sixty sequential extracts were evaluated for anti-lipid droplet accumulation, NF-κB inhibition, and NRF2 modulation, together with cytotoxicity assessment to determine bioactivity selectivity. These assays targeted interconnected pathways involved in metabolic dysregulation, inflammation, and oxidative stress, which are central mechanisms in chronic diseases.

Chloroform extracts of Alpinia galanga (L.) Willd. (IC_{50}: 95.25 µg/mL), Nauclea orientalis (L.) L. (IC_{50}: 82.98 µg/mL Premna odorata Blanco (IC_{50}: 6.61 µg/mL), and Lantana camara L. (IC_{50}: 22.47 µg/mL) demonstrated notable anti-lipid activity. Significant inhibition of NRF2 signaling was observed in Heptapleurum insularum Seem. (chloroform, IC_{50}: 4.46 ± 3.24 µg/mL), Ficus septica Burm.f. (chloroform: IC_{50}: 1.87 ± 5.31 µg/mL, hexane: IC_{50}: 1.55 ± 4.54 µg/mL), and Lantana camara L. (hexane, IC_{50}: 6.69 ± 4.53 µg/mL). NF-κB inhibition was evident in Cyanthillium cinereum (L.) H.Rob. (chloroform, IC_{50}: 25.67 ± 2.86 µg/mL), Mikania cordata (Burm.f.) B.L. Rob (chloroform, IC_{50}: 13.92 ± 3.81 µg/mL), Heptapleurum insularum Seem. (hexane, IC_{50}: 17.50 ± 4.56 µg/mL), and Garcinia rubra Merr. (hexane, IC_{50}: 11.69 ± 4.60 µg/mL).

LC–MS/MS profiling of bioactive fractions annotated key metabolites, including asperphenamate, lovastatin, pheophytin A, flavonoid derivatives, and lipid-associated compounds. Molecular docking suggested their potential interactions with targets involved in lipid metabolism, inflammation, and oxidative stress, supporting their role as multi-target therapeutic candidates from Philippine medicinal plants.

Keyword:

NRF2, NF-kB, anti-lipid, metabolomics

No. PC-010 / 天然物化學組 / Natural Products Chemistry (PC)

A rapid method for the quality identification of Taiwanese folk herbal medicine Paederia foetida Linn. (Chinese fevervine)

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Paederia foetida Linn. [Syn. *Paederia scandens* (Lour.) Merr.] belongs to the Rubiaceae Family and is a climbing perennial plant that mainly grows in the temperate regions. It is also known as Chinese fevervine, skunk vine, or stink vine because Its fresh stems and leaves release a strong, foul odor similar to chicken or poultry droppings when crushed. This herbaceous species is one of the native plants of Asia, and its distribution ranges from eastern Nepal to Taiwan, Japan, and Malesia. Its widely used in Asia as a traditional and folkloric medicines to treat a variety of ailments such as arthritis, coughs, asthma, itching, wounds, and as a pain reliever. However, this herbal plant is not listed in any pharmacopeia, and its indicator ingredient(s)/standard compound(s) have not been established and used for quality assessment. In this study, a feasible HPLC method was developed and two characteristic iridoid glycosides, paederosidic acid (PA, **1**) and paederoside (**2**), were found to be a pair of stable and appropriate components that can be used as an index compound to evaluate the quality of Chinese fevervine. These two components were identified by their IR, HRESI-MS, 1D- and 2D-NMR spectra. Finally, we hope that *P. foetida* Linn. (Chinese fevervine) can be included in the “Taiwan Herbal Pharmacopeia” in the near future.

Keyword:
Paederia foetida Linn. , Chinese fevervine, HPLC

No. PC-011 / 天然物化學組 / Natural Products Chemistry (PC)

Anti-inflammatory principles and other chemical constituents from Cuscuta campestris

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The *Cuscuta* species belonging to the *Convolvulaceae* family are reported to be rich in flavonoids and glycosidic constituents, along with alkaloids, fatty acids, lignans, terpenoids, and other phytomolecules. Flavonoids and other molecules from *Cuscuta* species exhibit various biological activities, including anti-inflammatory, antioxidant, and anti-proliferative effects. The extract and fractions of *Cuscuta campestris* showed significant inhibition against superoxide anion generation and elastase release in fMLF/CB-induced human neutrophils. Thus, it was aimed to purify and identify the bioactive principles of *C. campestris*. In this study, a total of seventy-seven compounds were isolated, and among them, two were undescribed compounds characterized based on extensive spectrometric analyses. Other structures were identified by comparing their physical and spectroscopic data with those published in the literature. The isolated compounds were evaluated for their anti-inflammatory potential using the human neutrophil model. Among the tested compounds, two flavonoids and five lignans exhibited inhibitory effects on superoxide anion generation. Velutin also inhibited elastase release and exhibited strong binding in a molecular docking study. These experimental results suggest that *C. campestris* and its constituents are promising candidates for developing anti-inflammatory drugs, warranting further studies.

Keyword:
Cuscuta campestris, Flavonoid, Lignan, Anti-inflammation, Elastase release

No. PC-012 / 天然物化學組 / Natural Products Chemistry (PC)

Isolation and Structural Characterization of Natural Products from Cattleya Orchids and Their Adipocyte Browning Activity

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Obesity is a major global health concern characterized by excessive fat accumulation and associated metabolic disorders, while conventional lifestyle and pharmacological interventions are often limited by poor long-term adherence, and potential adverse effects. Recent studies highlight that inducing the browning of white adipose tissue into beige or brown adipocytes represents a promising strategy to enhance energy expenditure and improve metabolic health.

Cattleya, regarded as one of the most representative exotic orchids, is an epiphytic group of the Orchidaceae family native to Central and South America. Known for their vibrant colors, impressive floral morphology, and diverse varieties, *Cattleya* species are frequently referred to as the "Queen of Orchids." *Rhyncholaeliocattleya* Duh' s Treasure (*Rlc*-DT), a hybrid cultivar registered with the Royal Horticultural Society in 2010 and widely cultivated in Taiwan, has not yet been systematically investigated for its chemical constituents or biological activities. In our preliminary studies, the ethanol extract of *Rlc*-DT was found to regulate adipocyte differentiation and promote adipocyte browning.

Following bioassay-guided fractionation, one undescribed compound and seventeen known compounds were isolated and identified from chloroform and *n*-butanol layer of *Rlc*-DT. The undescribed compound was identified as a phenanthrenequinone. The known compounds include five dihydrophenanthrenes, five phenols, two phenolic glycosides, two stilbenoids, one lactone, one steroid, one triterpenoid. The chemical structures of these compounds were elucidated through spectroscopic analyses. The isolated compounds will be further evaluated for their ability to induce adipocyte browning, and their underlying mechanisms of action will be investigated.

Keyword:

Cattleya orchids, Rhyncholaeliocattleya Duh' s Treasure, Adipocyte browning

No. PC-013 / 天然物化學組 / Natural Products Chemistry (PC)

A feasible quality analytical method of the traditional Chinese medicine Zanthoxylum bungeanum Maxim. (red Sichuan pepper)

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Zanthoxylum bungeanum Maxim. (ZB) is an aromatic, edible, and medicinal plant belonging to the Rutaceae family. This species is native to the area from Himalayas (Nepal) to China and Inner Mongolia. The dried papery fruit of *Z. bungeanum* has a famous name, red Sichuan pepper (Hua Jiao), which is commonly used in Sichuan cuisine and is renowned worldwide for its unique spicy flavor. As a TCM, Pricklyash peel (*Zanthoxyli Pericarpium*) is made from the dried ripe pericarp of *Z. bungeanum* (red Sichuan pepper) or *Z. schinifolium* Siebold et Zucc. (green Sichuan pepper, as known as Shiang Jiao Tz). Pricklyash peel possesses hot properties and a pungent flavor and has historically been used as an interior-warming medicine to warm and tonify the spleen, stomach, and kidney. The traditional functions of Pricklyash peel are “warm the middle to relieve pain, kill worms, and relieve itching”. However, the indicator ingredient(s)/standard compound(s) used for evaluating the quality of Pricklyash peel has not yet been formulated in the “Taiwan Herbal Pharmacopeia”. In this study, four amide alkaloids were isolated and identified as hydroxy-α-sanshool (HAS,**1**), hydroxy-β-sanshool (HBS, **2**), hydroxy-ε-sanshool (HES, **3**), and hydroxy-γ-sanshool (HGS, **4**) according to their IR, HRESI-MS, 1D- and 2D-NMR spectra. Furthermore, a rapid HPLC method was developed, and two main components, HAS (**1**) and HBS (**2**), were found to be suitable index compounds/standards to evaluate the quality of red Sichuan pepper (ZB).

Keyword:
Zanthoxylum bungeanum, red Sichuan pepper, HPLC, NMR

No. PC-014 / 天然物化學組 / Natural Products Chemistry (PC)

Structure and Biological Activity Analysis of Exopolysaccharides from Aeromonas hydrophila ATCC-7966

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Aeromonas hydrophila is a Gram-negative, emerging pathogen and a zoonotic bacterium that can cause a variety of diseases including gastroenteritis, septicemia, and wound infections especially for immunocompromised patients. In addition, A. *hydrophila* is also considered as an important fish pathogen that causes ecology damage. The strain ATCC-7966 is a widely distributed standard strain and therefore its exopolysaccharide (EPS) is regarded as a critical bioactive natural resource.

In this study, we aim to investigate the structure and biological activity of Ah-ATCC-7966 EPS. With monosaccharide and NMR analysis, the one repeat unit of Ah-ATCC-7966 EPS is composed of β-D-Manp-(1→4)-β-D-Gal3OAcp-(1→4)-β-D-Glcp as the main scaffold and Man connects the branch α-D-GlcAp-(4→1)- α-D-Glcp with 1,3 linkage. For bioactivity, we found that Ah-ATCC-7966 EPS can induce ROS production and CD11b/CD66b expression of neutrophils, elucidating that Ah-ATCC-7966 EPS can promote neutrophil immunological activity, like adhesion and degranulation. Intriguingly, these immune responses of Ah-ATCC-7966 EPS did not activate the conventional MAPK signaling pathway but perhaps the newly reported PLC/IP3/Ca^{2+} pathway. This pathway eventually releases Ca^{2+} and Ah-ATCC-7966 EPS results in significant increase of neutrophil intracellular Ca^{2+} levels of which the Ca^{2+} signal can be reduced by Ca^{2+} chelator EDTA and BAPTA/AM. Taken together, our efforts indicated the Ah-ATCC-7966 EPS contains the unique Gal3OAc moiety and causes neutrophil activation suggested by new signaling pathway to be an promising therapeutic agent.

Keyword:

Aeromonas hydrophila, Exopolysaccharide, promote inflammation, Ca^{2+} signaling pathway

No. PC-015 / 天然物化學組 / Natural Products Chemistry (PC)

Galactose-Rich Padina australis polysaccharide represents the significant antioxidant activity

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Marine algae have been the valuable resource for biotechnology and pharmaceutical development because contain abundant natural compounds, especially polysaccharide. Algae polysaccharide can be composed by unique carbohydrate moiety and exhibit diverse biological activities, like antioxidant and immunomodulatory effects, therefore cause this field more attractive and prosperous.

Brown algae *Padina australis* is a new species which widely distribute in the Seribu Islands, North Jakarta, Indonesia. Here, we plan to determine the structure and biological activity of *P. australis* polysaccharide (WWP). WWP represents molecular weight approximate 430 KDa and is mainly composed of galactose accompany with fucose, mannose, glucose and xylose. More structural information will confirm by NMR and current we found the signals of mannose and fucose. Besides, WWP exhibits the apparent antioxidant activity while wild-type N2 *Caenorhabditis elegans* exposed to the reactive oxygen species (ROS) inducer juglone, resulting in survival rate increase. Strikingly, the WWP displayed the similar antioxidant ability to the curcumin. These efforts suggested that WWP is a promising therapeutic agent that is worth to verify its structure-activity relationship.

Keyword:

Padina australis, polysaccharide, antioxidant activity

No. PC-016 / 天然物化學組 / Natural Products Chemistry (PC)

Triterpenoids from Ludwigia octovalvis: complete NMR assignment, MS/MS fragmentation pathway and preventive effect against peptic ulcers

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Inspired by the traditional uses of *Ludwigia octovalvis*, this work investigated anti-inflammatory activity and anti-bacterial effect against *H. pylori* of its secondary metabolites. From *n*-hexane extract, five triterpenoids were isolated and identified, including ursolic acid, oleanolic acid, lupeol-3-*O*-myristate, urs-12-ene-2*α*,3*β*,7*β*,16*α*-tetraol, and daucosterol. This work reported the first complete ^{1}H and ^{13}C NMR assignment of lupeol-3-*O*-myristate, along with other triterpenes. The observed resonances were classified into two groups of a lupane-type triterpene and a fatty acid chain. The irregular downfield shift of proton H-3 with strong HMBC with a carbonyl carbon indicated the acylation of 3-OH. Detailed analysis of HMBC afforded the assignments of the lupane skeleton, whereas ^{1}H-^{1}H COSY allowed the elucidation of the myristoyl moeity. In HR-ESI-MS, the presence of a quasi-molecular ion peak at *m/z* 430.3634 ($[M - C_{14}H_{28}O_{2}^{\cdot} + Na]^{+}$) and a production ion at *m/z* 388.8124 ($[M - C_{14}H_{28}O_{2}^{\cdot} - CH_2{=}CH\text{-}CH_3 - H + Na]^{+}$) suggested that MS^2 fragmentation underwent McLafferty's rearrangement. All compounds exhibited moderate suppression of bacteria growth (MIC 50-100 mg/mL) and significantly inhibited NO production in RAW264.7 cells (IC_{50} 3.92-4.35 μM). Molecular docking revealed good binding affinities of the triterpenes to iNOS enzyme (-9.9 to -9.4 kcal/mol), although they simulatively formed weak bonds to virulence factors CagA of *H. pylori* (-5.0 to -3.8 kcal/mol). These results highlighted preventive effect of *L. octovalvis* against peptic ulcers, partially consistent with its traditional use. Complete NMR and MS data were reliable for further study in terms of standardization of this plant.

Keyword:

Ludwigia octovalvis, Onagraceae, triterpenes, lupeol-3-O-myristate, H. pylori, NO production inhibition

No. PC-017 / 天然物化學組 / Natural Products Chemistry (PC)

Chemical components and Their Anti-inflammatory Activities from the stem of Ficus formosana

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Excessive neutrophil activation triggers the release of superoxide anion and elastase, causing oxidative cellular damage and severe inflammation that can drive various inflammatory diseases. Twenty-one Taiwanese traditional medicinal plants have been screened for anti-inflammatory activity using the fMLP/CB-induced superoxide production platform. The stem of *Ficus formosana* emerged as the most promising candidate due to its potent dual inhibition of superoxide anion generation and elastase release. Furthermore, thirteen fractions were separated by column chromatography from the ethyl acetate layer. Fractions 3, 6–9, 11, and 12 displayed notable inhibition toward superoxide anion and elastase. Moreover, integrating the bioassay data into a bioactivity-based molecular network enabled preliminary profiling of active components, identifying compounds with anti-inflammatory activity, including shikimates, phenylpropanoids, and terpenoids from *F. formosana*. Bioassay-guided fractionation of the ethyl acetate layer from the stem of this plant led to the isolation of 29 known compounds, including one chromone, one phytosterol, two terpenoids, three coumarins, four lignans, six benzenoids, and twelve flavonoids. The structures of the isolates were elucidated by NMR, UV, IR, and MS analyses. The isolation of chemical constituents and the evaluation of their anti-inflammatory activity are still in progress.

Keyword:

Moraceae, Ficus formosana, anti-inflammatory activity, lignanoid, flavonoid, terpenoid

No. PC-018 / 天然物化學組 / Natural Products Chemistry (PC)

Multi-Pathway and Bioinformatics-Supported Regulation of Macrophage Inflammation and Anti-Tumor Potential by Ganoderma lucidum Polysaccharide (WSG)

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Tumor-associated macrophages (TAMs) within the tumor microenvironment (TME) frequently adopt a pro-tumoral M2 phenotype that suppresses anti-tumor immunity, whereas re-polarizing these macrophages into a tumor-killing M1 phenotype can directly restore anti-tumor immunity, making it a vital cancer immunotherapy strategy. A standardized water-soluble glucan (WSG) was isolated from the Ganoderma lucidum fraction GLPs:F3 via a refined water-extraction protocol, and its immunomodulatory activity was evaluated in the RAW264.7 macrophage model through proteomic profiling, then bioinformatic prediction of candidate immune targets. WSG was non-cytotoxic up to 640 μg/mL, protected LPS-suppressed macrophage viability, and concentration-dependently induced nitric oxide as well as the predicted immune-activating targets IL-6, TNF-α, CCL5, IFN-γ, and GM-CSF, Polymyxin B neutralization confirmed that the IL-6 and TNF-α responses were intrinsic to WSG rather than LPS contamination. Further mechanistic analysis showed that this M1-like activation was driven by MAPK signaling, with increased phosphorylation of ERK, p38, and c-Jun, alongside a reduction in IκB reflecting concurrent NF-κB activation. Notably, WSG also exhibited a dual-regulatory capacity, concentration-dependently suppressing LPS-induced IL-6, TNF-α, and CCL5 by 52%, 47%, and 61%, respectively, rather than acting as an indiscriminate pro-inflammatory agent. To test for a direct anti-tumor effect, LLC1 cells were treated with conditioned medium from WSG-treated macrophages, which inhibited LLC1 growth by 70%, linking WSG-induced macrophage activation to tumor suppression. Together, these findings establish this refined WSG fraction as a potent, dual-acting immunomodulator that drives M1-polarizing macrophage activation with anti-tumor potential, supporting precision cancer immunotherapy.

Keyword:
WSG/macrphage/Ganoderma lucidum

No. PC-019 / 天然物化學組 / Natural Products Chemistry (PC)

Integrated Evaluation of the Biocontrol Potential of Streptomyces spp. against Fusarium Wilt of Banana caused by Fusarium oxysporum f. sp. Cubense

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Fusarium wilt of banana (FWB), caused by the soil-borne fungal pathogen *Fusarium oxysporum* f. sp. *cubense* (*Foc*), is one of the most destructive diseases affecting banana production worldwide. Among *Foc* races, tropical race 4 (TR4) poses a major threat due to its broad host range and persistence in infested soils. As effective long-term management remains challenging, biological control represents a promising and sustainable strategy. In particular, *Streptomyces* spp. are promising biocontrol agents because of their ability to produce diverse antimicrobial secondary metabolites.

In this study, four *Streptomyces* spp. (D1, D3, D4, and D4c) isolated from the banana rhizosphere exhibited strong inhibitory activity against *Foc* TR4 spore germination and mycelial growth. To further characterize their antifungal potential, genomic and metabolomic analyses were performed, including whole-genome sequencing with antiSMASH analysis and LC-MS/MS coupled with feature-based molecular networking (FBMN). These analyses revealed diverse biosynthetic gene clusters and secondary metabolites with antifungal potential. Greenhouse trials were subsequently conducted using potted banana plants, followed by root and soil metabolomic analyses to investigate treatment-associated metabolic changes. Collectively, these findings suggest that *Streptomyces* sp. D4 has potential for the biocontrol of FWB.

Keyword:
Streptomyces, Fusarium wilt of banana, antifungal secondary metabolites, biocontrol

No. PC-020 / 天然物化學組 / Natural Products Chemistry (PC)

A molecular networking-guided strategy for identifying anti-osteoporotic sterols from the soft coral Sclerophytum humesi

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Marine soft corals are a rich source of structurally diverse secondary metabolites, however, their potentials effects on bone metabolites remain largely unexplored. In this study, we explore the anti-osteoporotic effect of the Formosa soft coral *Sclerophytum humesi* by LC–MS/MS-based molecular networking with biological activity data and prioritize bioactivity-associated molecular families for targeted isolation. *S. humesi* was extracted with ethyl acetate and subsequently fractionated, with SH-E3 exhibiting the most prominent osteogenic activity among all fractions. In a glucocorticoid-induced osteoporosis (GIOP) zebrafish model, SH-E3 significantly restored impaired skeletal mineralization, supporting its potential bone-protective effect in vivo. Integration of bioactivity data with LC–MS/MS-based molecular networking further highlighted metabolite families associated with SH-E3 and guided subsequent targeted chemical investigation. Thus, we focused on SH-E3 and isolated one previously undescribed compound together with eight known metabolites, including six sterols as the predominant constituents. Parallel chemical investigation of SH-E7 yield another previously undescribed compound structurally related to the isolation of SH-E3. Subsequent biological evaluation of the isolated metabolites revealed the sterol-type compounds from SH-E3 enhanced alkaline phosphatase (ALP) activity to varying degrees in MG-63 osteoblast-like cells. Collectively, these findings demonstrate that *S. humesi* possesses promising anti-osteoporotic potential and suggest its sterol-enriched metabolites contribute substantially to the observed osteogenic activity. This study also highlights the integration of in vivo activity screening and molecular networking as an efficient strategy for prioritizing bioactive molecular families and accelerating the discovery of bone-protective natural products from marine resources.

Keyword:
soft coral, secondary metabolites, anti-osteoporotic, sterol-enriched metabolites, molecular networking

No. PC-021 / 天然物化學組 / Natural Products Chemistry (PC)

Phytochemical and Computational Characterization of Anti-Inflammatory and Anti-Allergy Metabolites from Bischofia javanica Blume

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Bischofia javanica Blume is a traditionally consumed plant with potential as a source of bioactive natural products. This study investigated the phytochemical constituents of *B. javanica* leaves and evaluated their anti-inflammatory and anti-allergic activities using *in vitro* and *in silico* approaches. Phytochemical investigation of the hexane extract of *B. javanica* leaves led to the isolation of eight compounds. GNPS-FBMN analysis revealed diverse chemical classes, supporting the presence of structurally diverse metabolites in the hexane extract. The crude extract and isolated compounds were evaluated for their inhibitory effects on lipopolysaccharide-induced nitric oxide (NO) production in RAW 264.7 macrophages and antigen-induced β-hexosaminidase release. Compounds **1**, **2**, **6**, **7**, and **8**, as well as the crude extract, showed inhibitory activity against NO production. Compound **1** showed 48.95 ± 1.62% inhibition at 12.5 μM, while compound **6** showed complete inhibition at 100 μM. Compounds **1** and **6** were further evaluated for their NO inhibitory activity, with IC_{50} values of 13.32 and 39.39 μM, respectively. In the anti-allergic assay, compound **1** showed 33.68 ± 2.22% inhibition at 10 μM, while compound **6** showed 65.61 ± 2.95% inhibition of β-hexosaminidase release at 100 μM. Molecular docking using PDB IDs 3E7G (iNOS) and 4PV0 (SYK) indicated favorable interactions of the selected compounds with the target proteins. Molecular dynamics simulations further suggested relatively stable protein–ligand interactions. Overall, these findings demonstrate the presence of bioactive metabolites in *B. javanica* leaves and highlight the species as a promising source of natural products with anti-inflammatory and anti-allergic potential.

Keyword:
Bischofia javanica, Natural products, Phytochemical investigation, Anti-inflammatory activity, Anti-allergic activity

No. PC-022 / 天然物化學組 / Natural Products Chemistry (PC)

Discovering Biocatalysts to Enhance the Diversity of Conjugated Polyynes

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Conjugated polyynes are bioactive natural products characterized by alternating single and triple C-C bonds, exhibit potent antibacterial, antifungal, and antiviral activities with strong potential in crop protection and pharmaceutical applications. As structural diversity dictates biological function, expanding polyyne chemical space is crucial for drug discovery. Our laboratory previously identified *Massilia* sp. YMA4, which synthesizes the polyyne backbone Massilin C along with its hydroxylated derivatives, Collimonin C and D—a modification catalyzed by the dioxygenase MasB. Uncharacterized dioxygenases frequently flank polyyne biosynthetic gene clusters (BGCs) across diverse bacterial genomes, presenting ideal targets for expanding polyyne diversity. To identify candidate enzymes with polyyne-modifying potential, we performed multi-gene BLAST searches for strains co-harboring polyyne BGCs and dioxygenase genes, constructed a phylogenetic tree, and selected candidate sequences divergent from MasB. Integrating multiple sequence alignments with protein–ligand molecular docking using Massilin C, we pinpointed key active-site residues responsible for substrate binding and catalytic specificity. Heterologous expression revealed distinct metabolic profiles among the candidates, with trace amounts of novel products detected in select groups. Future *in vitro* assays will be conducted to further evaluate their functions, thereby establishing a direct link between functional differences in catalytic products and specific active-site residue variations. Ultimately, this work aims to deliver an integrative and rational strategy to expand polyyne diversity and engineer customized natural products.

Keyword:
conjugated polyynes, synthetic biology, modifications, structural diversity

No. PC-023 / 天然物化學組 / Natural Products Chemistry (PC)

Computational Exploration of Marine Briarane Diterpenoids for Potential Anti-Inflammatory Activity via Keap1

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Marine-derived natural products are a rich source of structurally diverse compounds with potential therapeutic applications. Briarane diterpenoids isolated from the marine coral genus *Briareum* have attracted considerable interest due to their diverse biological activities, including anti-inflammatory effects. In the present study, we explored the potential molecular interactions between briarane diterpenoids and Kelch-like ECH-associated protein 1 (Keap1), a key regulator of the Nrf2 signaling pathway. A total of 206 briarane diterpenoids were subjected to molecular docking-based screening, and selected candidates were subsequently investigated using molecular dynamics simulations, MM-PBSA binding free-energy calculations, and density functional theory analysis. Several briaranes exhibited favorable interactions with the Keap1 binding pocket, with Briaexcavatin V showing a docking score of −10.523 kcal/mol. Molecular dynamics simulations indicated that the selected protein–ligand complexes remained relatively stable, while MM-PBSA analysis revealed favorable binding free energies for several candidates. DFT calculations further indicated that oxygen-containing functionalities may contribute to interactions with key residues in Keap1. Based on the integrated computational analyses, Briaexcavatin V, Briacavatolide A, 4-Hydroxymilolide C, Briastecholide D, and Excavatolide Q were identified as promising candidates. These findings provide a computational basis for further investigation of briarane diterpenoids as potential Keap1-targeting natural products and support their future experimental evaluation for anti-inflammatory drug discovery.

Keyword:
Briarane diterpenoids, Briareum, Keap1, Nrf2, Molecular docking, Marine natural products

No. PC-024 / 天然物化學組 / Natural Products Chemistry (PC)

Chemical constituents from the Tinomiscium petiolare Hook. f. & Thomson

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A phytochemical study of *Tinomiscium petiolare* Hook. f. & Thomson was conducted, resulting in the characterization of two new compounds, Tonkine A (**1**) and Tonkine B (**2**), together with one known compound, *N*-benzoyl-L-phenylalaninyl-*N*-benzoyl-L-phenylalaninate (**3**). The structures of the isolated compounds were elucidated using 1D and 2D NMR spectroscopic techniques, including ^{1}H and ^{13}C NMR, HSQC, HMBC, COSY, and NOESY analyses.

Keyword:

Key words: *Tinomiscium petiolare*, Tonkine, chemical constituents.

No. PC-025 / 天然物化學組 / Natural Products Chemistry (PC)

Xeniaphyllane-Type Diterpenoids from the Soft Coral Sclerophytum humesi: Resolving Absolute Configurations and Multi-Target Inhibitory Potential

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A combined bioassay- and molecular networking-guided isolation strategy led to the discovery of twenty-seven new terpenoids, comprising twenty-two xeniaphyllane-type diterpenoids (**1-22**), and five norcaryophyllene-type (**23-27**), from the soft coral *Sclerophytum humesi*. The structures and absolute configurations of these compounds were elucidated by comprehensive spectroscopic and computational analyses, including NMR, HRESIMS, SOR, TDDFT-ECD, and DP4+ probability analysis. The stereogenic centers at C-15 in related xeniaphyllanes were proposed for the first time based on comparative SOR and TDDFT-ECD analyses. Among these metabolites, compounds **(±)-1** and **(±)-2** possess rare 4/7/6-fused tricyclic carbon skeletons, whereas compound **(±)-23** features an unprecedented oxatricyclic framework. Notably, compounds **21** and **22** constitute a rare dimeric metabolite formed from two xeniaphyllane-type diterpenoids through a unique 16-peroxyl bridge. A plausible biogenetic pathway originating from geranylgeranyl pyrophosphate (GGPP) was proposed to account for the formation of these structurally unusual metabolites. Compounds **1-22** exhibited selective cytotoxicity against the MIA PaCa-2 cell line, with IC_{50} values ranging from 1.35 to 26.13 μM and selectivity indices greater than 3. Mechanistic studies revealed that **5** suppresses the expression of Bcl-2 and Bcl-xL proteins, triggers the activation of caspase-3, and leads to the cleavage of PARP1 in pancreatic cancer. In addition, the terpenoids demonstrated significant multitarget inhibitory activity against enzymes *α*-amylase, *α*-glucosidase, lipase, acetylcholinesterase, and butyrylcholinesterase with IC_{50} ranging from 1.7 to 170.0 μM. Enzyme kinetic analyses, molecular docking, and molecular dynamics simulations further elucidated the mechanisms underlying their biological activities.

Keyword:
Terpenoids, anti-cancer, antidiabetic, and anti-Alzheimer

No. PC-026 / 天然物化學組 / Natural Products Chemistry (PC)

Biosynthetic engineering of Massilin C-based polyynes to enhance manufacturability and bioactivity

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Bacterial polyynes featuring unique carbon-carbon triple bonds exhibit potent antimicrobial activities. However, low yields resulting from fatty acid metabolic degradation, and structural instability caused by self-polymerization remain major limitations for their application. This study aims to overcome these challenges through biosynthetic engineering of the Massilin C, the primary polyyne in *Massilia* sp. YMA4. We integrate the core biosynthetic gene *VsAOS-2* (an *α*-oxoamine synthase from *Vibrio* sp. QWI-06) with the *mas* gene cluster to modify the carboxyl terminus (-COOH) of Massilin C into a Vitroprocines-like polyyne derivative. Both *in vivo* heterologous expression in *Escherichia coli* and *in vitro* enzymatic reactions will be implemented to synthesize the novel polyyne. Replacing the terminal carboxyl group, this modification is expected to prevent bacterial metabolic degradation, enhance structural stability, and preserve the core bioactive conjugated triple bonds. The bioactivity of the synthesized derivative will be evaluated against opportunistic pathogens, including *Candida albicans* and *Acinetobacter baumannii*. This study offers a promising approach to improve polyyne production and stability, paving the way for the development of novel antibiotics and bio-defense agents in medicine and agriculture.

Keyword:
Bacterial polyynes, Vitroprocines, Structural modification, Biological activity, Antibiotic development

No. PC-027 / 天然物化學組 / Natural Products Chemistry (PC)

Chemical Constituents from the Stems of Broussonetia papyrifera (L.) Vent.

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Multidrug resistance (MDR) is a major challenge in cancer therapy and a significant cause of treatment failure. Among the mechanisms underlying MDR, overexpression of P-glycoprotein (P-gp), an ATP-binding cassette transporter responsible for the efflux of various anticancer agents, plays an important role. To identify natural products with potential MDR-reversing activity, this study focused on *Broussonetia papyrifera* (Moraceae), a perennial deciduous tree widely distributed in Southeast Asia and the Pacific Islands, which has been reported to exhibit various pharmacological activities, including anti-diabetic, antioxidant, and anti-tumor effects.

The dried stems of *B. papyrifera* were extracted with methanol, and the crude extract was subjected to a series of chromatographic techniques, affording 13 compounds, including Dadahol A (1), erythro-(7R,8S)-Dadahol B (2), threo-(7S,8S)-Dadahol B (3), (S)-marmesin (4), vomifoliol (5), quercetin (6), taxifolin (7), (S)-equol (8), (−)-rutaretin (9), (±)-balanophonin (10), syringaresinol (11), (2S)-7,4′-dihydroxy-3′-methoxyflavan (12), and broussoflavonol B (13). The structures of all isolated compounds were elucidated by spectroscopic analyses, including NMR spectroscopy, and comparison with reported literature data. Among the isolated compounds, several exhibited potential MDR-reversing activity through inhibition of P-gp-mediated drug efflux. Further investigations into the biological activities of the other compounds are ongoing.

Keyword:

Broussonetia papyrifera,Multidrug resistance (MDR),P-glycoprotein (P-gp)

No. PC-028 / 天然物化學組 / Natural Products Chemistry (PC)

Lobocrassoids A–C, new cembrane-related diterpenoids from the octocoral Lobophytum crassum (von Marenzeller, 1886)

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Chemical investigation of a wild-type specimen of the octocoral *Lobophytum crassum* afforded four cembrane-type diterpenoids, including three previously undescribed metabolites, lobocrassoids A–C (**1**–**3**), together with a known congener culobophylin D (**4**). The structures of **1**–**4** were established by extensive spectroscopic analysis and by comparison with literature data, the absolute configuration of **4** was further confirmed by single-crystal X-ray diffraction (SC-XRD) analysis. Compounds **1** and **2** were identified as hydroperoxycembranoids, a structural subclass that remains comparatively uncommon among reported Lobophytum metabolites.

Keyword:
Octocoral,Lobophytum crassum,Diterpenoid,Hydroxperoxycembranoid,Lobocrassoid

No. PC-029 / 天然物化學組 / Natural Products Chemistry (PC)

Sarcoglaucone A: Structural Characterization of a New Sarsolenane-Related Diterpenoid from the Soft Coral Sarcophyton glaucum

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Two sarsolenane-type diterpenoids, including a known compound, dihydrosarsolenone (**1**), as well as a novel metabolite, sarcoglaucone A (**2**), have been isolated from the soft coral *Sarcophyton glaucum* collected off the waters of Taiwan. The absolute configuration of dihydrosarsolenone (**1**) was determined by single-crystal X-ray difraction (SC-XRD) analysis for the first time in this study and the structure, including the absolute configuration of sarsolenane **2** was established on the basis of spectroscopic analysis and further confirmed by SC-XRD. One aspect of the stereochemistry of the known sarsolenanes **1** (dihydrosarsolenone) and methyl methyl dihydrosarsolenoneate was revised. Sarsolenanes **1** and **2** were found to exhibit activity in enhancing alkaline phosphatase (ALP) activity.

Keyword:
Sarcophyton glaucum, diterpenoid, single-crystal X-ray difraction, alkaline phosphatase

No. PC-030 / 天然物化學組 / Natural Products Chemistry (PC)

Mapping Evidence on Dendrobium Floral Genomics, Transcriptomics, Specialized Metabolism, and Associated Microbiomes: A Scoping Review

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Background: Research on Dendrobium flowers is fragmented across genomic diversity, flower-specific gene expression, specialized metabolism, and flower-associated microbial communities, limiting an integrated understanding of floral biology and secondary-metabolite biosynthesis.

Objective: This ongoing scoping review aims to systematically map evidence on Dendrobium floral genomic resources, transcriptomics, specialized metabolism, and flower-associated microbiomes, and to identify gaps in cross-domain integration.

Methods: The review follows the PRISMA-ScR framework. Systematic searches are being conducted across bibliographic databases and public data resources using predefined eligibility criteria focused on Dendrobium flowers. Initial searches identified 412 records, including 150 from Web of Science, 100 from PubMed, and 162 from Scopus. Records are being screened and charted according to species, floral tissues, developmental stages, data types, analytical approaches, biological processes, metabolic pathways, and microbial characteristics.

Results: Current evidence is concentrated in transcriptomic and metabolomic studies, particularly in D. officinale, with investigations of flower development and specialized metabolism. D. nobile has been studied for metabolic variation and floral pigmentation, while D. chrysotoxum has been investigated using transcriptomic and volatilomic approaches for floral scent biosynthesis. In contrast, flower-focused pangenomic and metagenomic studies appear limited, and comprehensive integration of genome variation, flower-specific expression, metabolite profiles, and microbial communities remains insufficient.

Conclusion: This review will provide an evidence map of Dendrobium floral biology and define species-, tissue-, and developmental-stage-specific research gaps. Integrating pangenomic, transcriptomic, metabolomic, and metagenomic information could identify genetic, regulatory, and microbial determinants of secondary-metabolite biosynthesis, supporting future strategies for improving the production and utilization of floral metabolites and related applications.

Keyword:

Dendrobium flowers, Pangenomics, Floral Microbiome

No. PC-031 / 天然物化學組 / Natural Products Chemistry (PC)

Structural features and biological activities of a fucose-enriched sulfated polysaccharide from Ganoderma lucidum

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Ganoderma lucidum polysaccharides possess diverse biological activities, however, their chemical and structural heterogeneity remains a major challenge in defining structure-function relationships. This study aimed to characterize J101-F2, a fucose-enriched sulfated polysaccharide isolated from *G. lucidum* mycelia, and evaluate its anticancer and chemosensitizing activities. J101-F2 was obtained through protease-assisted extraction and molecular weight-based fractionation. Structural analyses showed an average molecular weight of 28.8 kDa and a sulfate content of 2.89 mmol/g. Fucose was the predominant monosaccharide, accompanied by galactose, glucose, mannitol, mannose, and glucosamine, with an approximate molar ratio of 5:3:3:3:1:0.4. One- and two-dimensional NMR analyses further suggested a branched heteroglucan architecture containing terminal α-fucosyl residues and mixed β-1,3/1,6-glucan structural motifs. In functional assays, J101-F2 suppressed cell viability, colony formation, migration, and invasion in lung adenocarcinoma and colorectal carcinoma cells, while showing minimal cytotoxicity toward normal lung cells. Mechanistically, J101-F2 attenuated EGFR- and TGFβR-associated signaling and reduced downstream AKT and ERK activation. Furthermore, combination treatment with J101-F2 enhanced the sensitivity of cancer cells to cisplatin and 5-fluorouracil, producing synergistic cytotoxicity. Increased sub-G1 accumulation and Annexin V-positive cells, together with changes in apoptosis-associated proteins, supported the induction of intrinsic apoptosis. These findings identify J101-F2 as a structurally distinct fucose-enriched sulfated polysaccharide with both direct anticancer and chemotherapy-sensitizing properties. J101-F2 therefore warrants further preclinical investigation as a potential functional dietary supplement for complementary cancer management.

Keyword:
Ganoderma lucidum, sulfated polysaccharide, fucose, anticancer activity, chemosensitization

No. PC-032 / 天然物化學組 / Natural Products Chemistry (PC)

Molecular Networking-Guided Discovery of Chlorinated Secondary Metabolites from the Marine-Derived Fungus Phoma sp. NTOU6154.

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Halogenated compounds are considered important molecules with broad applications in pharmaceuticals, agrochemicals, and other industrial products. The marine environment, characterized by abundant chloride and bromide ions, represents a particularly rich source of diverse halogenated natural products. Therefore, marine-derived microorganisms have attracted attention as promising sources of novel halogenated metabolites with potentially valuable biological activities. In this study, one of 12 marine-derived fungi from Prof. Ka-Lai Pang *Phoma* sp. NTOU6154, was selected for further investigation based on its antibacterial activity against *Staphylococcus aureus*. Molecular networking analysis revealed a molecular cluster with characteristic isotopic and fragmentation patterns consistent with chlorinated metabolites, suggesting that this strain has the biosynthetic potential to produce structurally related chlorinated compounds. To expand its chemical diversity and optimize secondary metabolite production, *Phoma* sp. was cultivated under three different culture conditions using artificial seawater-based potato dextrose agar (PDA), rice, and soybean powder media. Among the tested conditions, cultivation on artificial seawater-based rice medium generated diverse secondary metabolites with relatively low interference from medium-derived components. It was therefore selected for subsequent large-scale fermentation and chemical investigation. Based on the bioactivity-guided isolation, a series of chlorinated diphenyl ether derivatives were identified, including two previously undescribed compounds (1 and 2). These findings demonstrate the potential of *Phoma* sp. as a source of structurally diverse chlorinated natural products. Whole-genome sequencing of NTOU6154 is currently underway to further investigate the biosynthetic basis of these chlorinated metabolites, with particular emphasis on the identification of candidate halogenase genes potentially involved in their biosynthesis.

Keyword:
Halogenated metabolites, Molecular networking, Chlorinated diphenyl ethers, Phoma sp.

No. PC-034 / 天然物化學組 / Natural Products Chemistry (PC)

Comparing Molecular Relationships and Chemical Profiles among Lobophytum Soft Coral Specimens

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Soft corals assigned to the genus *Lobophytum are recognized as rich sources of cembranoid diterpenes, yet their morphological plasticity and uncertain species boundaries often obscure the biological origins of reported compounds. Here, molecular and chemical data obtained from corresponding specimens were combined to examine whether genetic differentiation is accompanied by variation in metabolite profiles. HPLC comparison of 15 extracts revealed both shared chromatographic features and specimen-specific differences. Selected peaks were isolated, and NMR analysis identified four known cembranoids—13-acetoxysarcocrassolide, sarcocrassolide, crassolide, and michaolide E—in three extracts. The corresponding specimens were analyzed using mtMutS, COI, and 28S rDNA sequences, from which separate marker-based phylogenetic trees were generated. Preliminary results suggested that the examined specimens represent multiple molecular groups rather than a single conspecific assemblage. Although some chemical differences appeared to coincide with molecular groupings, the current dataset is insufficient to demonstrate a robust lineage–chemotype relationship. Increasing multilocus coverage and incorporating voucher morphology, sclerite characters, LC–MS/MS-based chemometrics, and bioactivity-guided isolation should allow this relationship to be tested more rigorously. This specimen-matched approach may improve source attribution and support the selection of chemically distinctive Lobophytum specimens for subsequent natural product investigation.*

Keyword:

Lobophytum, cembranoid diterpenes, chemical fingerprints, molecular phylogeny, marine natural products

No. PC-035 / 天然物化學組 / Natural Products Chemistry (PC)

Effects of Different Extraction Techniques on the Properties, Wound Healing, and Calcium Ion-Induced Gelation of Pectin from Lemon Peels and Jelly Fig Shells

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The development of the food processing industry has made the recycling and utilization of agricultural by-products, such as lemon peels and jelly fig shells, an important strategy for reducing environmental burdens and enhancing added value. This study investigates ultrasound-assisted extraction (UAE) and microwave-assisted extraction (MAE) to extract pectin from lemon peels and jelly fig shells, evaluating their effects on 3T3 cell biocompatibility, proliferation, apoptosis, and scratch assays. Additionally, the study examines adding calcium ions at various pectin concentrations on the expansion rate, porosity, swelling rate, and liquid absorption capacity of the hydrogels. Results show that in the 24- and 48-hour cytotoxicity evaluations, all pectin groups exhibited good cell compatibility. At a concentration of 600 μg/mL, cell viability remained above 85% across all groups, with commercial pectin (CP), lemon peel ultrasound-assisted extract (CLP-UAE), and jelly fig shells ultrasound-assisted extract (JFS-UAE) reaching around 95%. In the 24-hour scratch assay, the control group had a wound healing rate of approximately 37%, while the commercial pectin (CP) group showed the best healing promotion effect at 53%. The lemon peel microwave-assisted extract (CLP-MAE) and ultrasound-assisted extract (CLP-UAE) groups achieved healing rates of 37% and 35%, respectively, whereas the Jelly Fig shell microwave-assisted extract (JFS-MAE) and JFS-UAE groups achieved 24% and 29%, respectively. functional properties in terms of expansion, porosity, swelling, and fluid absorption, demonstrating their potential for biomedical applications, particularly as wound dressing materials.

Keyword:

Pectin Extraction, Agricultural By-product Valorization, 3T3 Cells, Hydrogels

No. PC-036 / 天然物化學組 / Natural Products Chemistry (PC)

Anticancer Effects of Lendenfeldia sp. Extract Involving Tubulin, HDAC, and Topoisomerase II Modulation

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The present study investigates the anticancer potential of Marine Sponge *Lendenfeldia* sp. Extract (C81E) and their chromatographic fractions against human prostate (PC3, DU145) and pancreatic (PANC) cancer cell lines. Cell viability was quantified using the MTT assay, and dose-response analysis was performed to determine IC_{50} values at 24, 48, and 72 hours. The C81E exhibited time-dependent cytotoxicity across all tested cell lines. In DU145 cells, the IC_{50} values were 3.20 ± 0.77 μg/mL at 24 hr, 1.45 ± 0.86 μg/mL at 48 hr, and 1.86 ± 0.24 μg/mL at 72 hr. For PC3 cells, IC_{50} values were 3.20 ± 1.38 μg/mL at 24 hr, 1.51 ± 0.89 μg/mL at 48 hr, and 1.06 ± 0.59 μg/mL at 72 hr. PANC cells demonstrated higher early resistance but strong time-dependent sensitivity, with IC_{50} values of 6.83 ± 2.24 μg/mL at 24 hr, 1.62 ± 0.10 μg/mL at 48 hr, and 1.04 ± 0.80 μg/mL at 72 hr. To explore potential mechanisms, cell-free biochemical assays were conducted. C81E interfered with tubulin polymerization, suppressed histone deacetylase (HDAC) activity, and inhibited topoisomerase II function, indicating multi-target regulatory effects. In vivo evaluations at 1.25 and 2.5 μg/g further support the extract's antitumor activity. Histopathological examination revealed no significant lesions in the major organs. Overall, these findings demonstrate that C81E exert potent, time-dependent cytotoxicity toward prostate and pancreatic cancer cells, likely mediated through simultaneous disruption of cytoskeletal dynamics, epigenetic regulation, and DNA-associated enzymatic processes. The extract and its fractions warrant further investigation as potential therapeutic candidates.

Keyword:

Anticancer, Marine Sponge, Lendenfeldia sp., Histone Deacetylase, Topoisomerase, Tubulin polymerization

No. PC-037 / 天然物化學組 / Natural Products Chemistry (PC)

Preparation and Yield Study of Extracts from Antrodia cinnamomea Fruiting Bodies Using Industrial Pharmacy Combined with ESG Principles

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Industrial pharmacy focuses on the large-scale research and development, production, quality control, marketing, and distribution of pharmaceuticals. Current topics in the field include continuous manufacturing, smart manufacturing, and eco-friendly production. Integrating Environmental, Social, and Governance (ESG) principles into industrial pharmacy can make drug manufacturing, research and development, and supply chain management more sustainable and ethical. *Antrodia cinnamomea* (AC), a medicinal mushroom endemic to Taiwan, is rich in bioactive phenolics, triterpenoids, and polysaccharides. It exhibits antioxidant, anti-inflammatory, and immunomodulatory effects, making it a promising candidate for managing stroke, autonomic dysfunction, abnormal liver function, diabetes, cancer, and cardiovascular diseases. In this study, we used AC as the raw material and applied industrial pharmacy methods combined with ESG principles to optimize extraction process and yield. The experimental design followed the principles of green chemistry and green extraction, while also considering the safety and health of laboratory personnel. For raw material, we used dish-cultured AC fruiting bodies, which removes the need for the stout camphor tree (*Cinnamomum kanehirae*) and provides a sustainable source. For extraction, ethanol was used as the sole solvent, allowing solvent consumption to be reduced through recycling and reuse. By minimizing the number of unit operations and developing a safe, robust, and controlled process, the entire workflow can be run by a single operator, which supports carbon reduction. This approach offers a sustainable model for the development of natural product extracts for traditional medicine and functional health applications.

Keyword:
industrial pharmacy, ESG, green chemistry, green extraction, Antrodia cinnamomea

No. PC-038 / 天然物化學組 / Natural Products Chemistry (PC)

Comprehensive Analysis of Phytochemicals and Nutrients of Solid-State Cultured Armillaria mellea (Codename: AM) in the ABF Germplasm Bank

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Mushrooms have long served humans as both food and medicine. *Armillaria mellea* (honey fungus, Basidiomycota, Agaricales, Physalacriaceae) is an edible and medicinal mushroom used in traditional Asian medicine to treat insomnia, dizziness, palsy, tinnitus, infantile convulsion, headache, neurasthenia, and microbial infections. Its diverse constituents, including polyphenols, polysaccharides, sterols, sesquiterpenes, peptides, and adenosine derivatives, make it an important source of natural therapeutic substances. The Applied Biomedical Fungal Germplasm Bank (ABF Germplasm Bank), established in 2021, preserves valuable fungal strains and supports biomass evaluation and translational pharmacochemical research on applied biomedical fungi. It currently holds over 500 fungal samples, including the genera *Antrodia*, *Armillaria*, *Lignosus*, *Phellinus*, and *Trametes*. In this study, *A. mellea* (codename AM), originally obtained from the traditional Chinese medicinal herb *Gastrodia elata*, was successfully cultivated by solid-state culture on an oatmeal medium. Phytochemical profiling of the cultured AM determined total phenolic, polysaccharide, adenosine, and ellagic acid contents. Nutritional analysis assessed calories, protein, total fat, saturated fat, *trans* fat, total carbohydrates, sugars, and sodium. These results indicate that artificially cultured AM is a promising component for dietary supplements and functional foods, and they provide a chemical basis for further bioactivity studies.

Keyword:
Armillaria mellea, fungal germplasm bank, polyphenols, polysaccharides, nutrition facts

No. PC-039 / 天然物化學組 / Natural Products Chemistry (PC)

Phytochemical Biomass Production Study of the Multi-target Triterpenoid Dehydrosulphurenic Acid from Antrodia salmonea in the ABF Germplasm Bank

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Edible mushrooms have been used in Traditional Chinese Medicine for thousands of years and remain popular across Asia, particularly in China, Japan, Taiwan, and South Korea. As sources of bioactive polysaccharides, terpenoids, steroids, alkaloids, and phenolic compounds, they show diverse pharmacological properties, including cancer-preventive, antibacterial, antiviral, and immunoregulatory effects. They are therefore increasingly valued in the development of nutritional supplements and drugs. Dehydrosulphurenic acid (DSA) is a multi-target lanostane-type triterpenoid from the medicinal fungus *Antrodia salmonea*. It has been reported to exhibit immunomodulatory, anti-pancreatic cancer, anti-leukemia, and anti-gastric cancer activities, as well as antihypertensive, anti-COVID-19, anti-acute lung injury, and anti-neurodegenerative effects. Phytochemical biomass production studies examine how nutrient availability, light, and cultivation techniques influence metabolite yield, with the aim of optimizing biomass for pharmaceutical and nutraceutical use. The Applied Biomedical Fungal Germplasm Bank (ABF Germplasm Bank), established in 2021, evaluates the biomass and pharmacochemical properties of biomedical fungi. In this study, we developed an efficient protocol to isolate DSA from liquid-cultured *A. salmonea* using reflux extraction followed by liquid-liquid partitioning. The yield of the DSA-rich fraction was quantified, and its phytochemical profile was characterized by RP-HPLC-UV and ^{1}H-NMR analyses. This work provides a practical basis for the scalable production of DSA for natural product and traditional medicine research.

Keyword:
phytochemical biomass production, fungal germplasm bank, triterpenoid, dehydrosulphurenic acid, Antrodia salmonea

No. PC-040 / 天然物化學組 / Natural Products Chemistry (PC)

Metabolomic Profiling and Antimycobacterial Activity of Wrightia antidysenterica Leaf Extracts

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Wrightia antidysenterica (L.) R.Br. (Apocynaceae) is a traditional medicinal plant endemic to Sri Lanka. In the Philippines, its year-round production is cultivated for ornamental purpose. The chloroform leaf extract of W. antidysenterica was previously reported to possess antimycobacterial activity against Mycobacterium phlei and Mycobacterium tuberculosis H37Rv . Herein, we report the antimycobacterial activity of fractions derived from the methanolic leaf extract. Initial screening via disc diffusion assay against Mycobacterium smegmatis yielded active fractions 2, 6, 7, and 8 with positive zone of inhibition (ZOI) of ca. 7-13 mm. These fractions were subsequently evaluated against luminescent M. tuberculosis (CDC1551) and the rapidly growing, multidrug-resistant, non-tuberculous species Mycobacterium abscessus (390S). Results revealed that fractions 7 and 8 displayed significant antimycobacterial activity against M. tuberculosis, exhibiting 96% and 57% inhibition at 100 μg/mL, respectively. All fractions showed modest inhibition against M. abscessus, with fraction 7 exhibiting 18% inhibition. Finally, untargeted LC–MS/MS analysis was performed to annotate secondary metabolites and construct a molecular network for structural clustering.

Keyword:
Wrightia antidysenterica, Mycobacterium tuberculosis, Apocynaceae, Mycobacterium smegmatis

No. PC-041 / 天然物化學組 / Natural Products Chemistry (PC)

New Benzylresorcinol and Benzylstilbene Derivatives from the Fruits of Orchid Galeola nudifolia Lour. with Anti-Neuroinflammatory Activity

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Galeola nudifolia is a medicinal orchid and a promising source of structurally diverse natural products. However, its phytochemical composition and anti-neuroinflammatory potential remain insufficiently investigated. In this study, the fruits of *G. nudifolia* were subjected to bioassay-guided phytochemical investigation, leading to the isolation of six new compounds, comprising three benzylresorcinol (**1**-**3**) and three benzylstilbene (**4**-**6**) derivatives, together with seven known compounds (**7**-**13**). Their structures were elucidated by comprehensive spectroscopic analyses, including HR-ESIMS and 1D and 2D NMR spectroscopy. The anti-neuroinflammatory activities of the isolated compounds were evaluated in lipopolysaccharide (LPS)-stimulated BV-2 microglial cells by measuring nitric oxide (NO) production. Compounds **1**-**6** and **8**-**13** significantly inhibited NO production, with IC_{50} values ranging from 6.59 to 15.79 μM. Among them, compounds **6**, **10**, **11**, and **12** exhibited lower IC_{50} values than the positive control, grossamide. Immunofluorescence staining showed that compound **12** reduced iNOS expression and suppressed NF-κB p65 nuclear translocation in LPS-stimulated BV-2 cells. Further molecular docking analysis suggested potential interactions of compounds **6** and **10-12** with iNOS and the IκBα/NF-κB complex. Overall, this study expands the chemical diversity of *G. nudifolia* and highlights its benzylstilbene derivatives as promising natural products with potential anti-neuroinflammatory activity.

Keyword:
Galeola nudifolia, Galeonudins A-F, anti-neuroinflammatory activity, iNOS, NF-κB

No. PC-042 / 天然物化學組 / Natural Products Chemistry (PC)

Isolation and Structural Elucidation of Triterpenoids from the Fruiting Bodies of Antrodia salmonea

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Antrodia salmonea, a newly identified Taiwanese medicinal mushroom belonging to the genus *Taiwanofungus*, grows on the hollow, decayed trunks of *Cunninghamia konishii*. Long recognized in Taiwan for its therapeutic properties, its fruiting bodies have traditionally been used to treat diarrhea, abdominal pain, hypertension, pruritus, and liver cancer. *A. salmonea* has recently attracted significant research interest due to its abundance of bioactive constituents, including triterpenoids, polysaccharides, benzenoids, and benzoquinone derivatives. Accumulating evidence indicates that *A. salmonea* exhibits diverse pharmacological activities—such as antioxidant, anti-inflammatory, anti-angiogenic, antihyperlipidemic, and anticancer effects—while acute toxicity and mutagenicity studies in mouse models have demonstrated its safety. In the present study, 30 triterpenoids were isolated from the dichloromethane extract of *A. salmonea*, comprising 10 new compounds (salmoterpenes A–J, **1**–**10**) and 20 known analogs (**11**–**30**). Their chemical structures were unambiguously elucidated using comprehensive spectroscopic analyses, including 1D and 2D-NMR, IR, and HRESIMS.

Keyword:
Antrodia salmonea, triterpenoids, structure elucidation

No. PC-043 / 天然物化學組 / Natural Products Chemistry (PC)

Discovery of Enantiomeric Monoterpene-Coumarins with Neuroprotective Activities from the Rhizomes of Luvunga scandens

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Phytochemical investigation of *Luvunga scandens* rhizomes, aided by LC-MS/MS-based molecular networking, afforded 11 pairs of new monoterpene-coumarin enantiomers, designated luvunscandins A–K (**1**–**11**). Their structures and absolute configurations were elucidated by spectroscopic analysis, single-crystal X-ray diffraction, and comparison of experimental and calculated electronic circular dichroism spectra. These metabolites possess a dihydrofurancoumarin core, with the monoterpene moiety incorporating a furan ring in **1**–**7** or a pyran ring in **8**–**11**. In these dihydrofurancoumarins, vicinal H-1′/H-2′ coupling constants of approximately 3.0–4.2 and 6.0 Hz corresponded to *erythro* and *threo* relative configurations, respectively.

All isolates were evaluated for inhibition of nitric oxide production in lipopolysaccharide-stimulated BV-2 microglia. Preliminary structure–activity relationships revealed that pyran-containing congeners were generally more potent than furan-containing analogues. Enantiomeric pairs **6a**/**6b** and **8a**/**8b** displayed differential activities, with **6a** and **8b** being more active, indicating a stereochemical influence on inhibitory potency. Compounds **6a**, **7a**, **7b**, **8b**, **9a**, **9b**, **11a**, and **11b** were more potent than the positive control pyrrolidine dithiocarbamate. (+)-Luvunscandin I (**9a**) exhibited the strongest activity, with an IC_{50} of 4.9 ± 0.6 μg/mL. Further mechanistic investigation showed that $_{9a}$ attenuated NF-κB p65 nuclear translocation and inducible nitric oxide synthase expression, suggesting that modulation of NF-κB-associated inflammatory signaling contributes to its inhibition of nitric oxide production. These findings warrant further investigation of the neuroprotective potential of **9a**.

Keyword:
Luvunga scandens, monoterpene-coumarins, molecular networking, anti-inflammatory activity

No. PC-044 / 天然物化學組 / Natural Products Chemistry (PC)

Integrative Metabolomic Profiling and Functional Screening of Traditional Chinese Medicines for Cardiovascular Applications

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Traditional Chinese Medicine (TCM) research faces challenges in linking holistic concepts with precise molecular mechanisms. This study aimed to establish a multidimensional chemical fingerprint database of curated medicinal herbs and integrate metabolomic profiling with cardiomyocyte-based functional screening to identify candidates with potential cardiovascular applications. The chemical profiles of the curated herbs were systematically characterized using untargeted LC-QTOF-MS/MS in positive and negative ionization modes. Molecular networking revealed conserved chemical scaffolds across different herbs, suggesting shared secondary metabolites that may contribute to overlapping therapeutic properties. Hierarchical Sunburst analysis further showed a predominance of terpenoids in positive ionization mode, whereas alkaloids and phenylpropanoids exhibited greater diversity in negative ionization mode, highlighting the metabolomic diversity and structural distribution of the herbal collection. Functional screening in human induced pluripotent stem cell-derived cardiomyocytes (iPSC-CMs) identified eleven candidate herbs for subsequent serial-dilution evaluation. Several candidates showed dose-dependent increases in cardiomyocyte viability or proliferation, although the overall effects remained modest. Overall, this study establishes an integrated metabolomic and phenotypic screening framework linking herbal chemical diversity with cardiomyocyte responses, providing a data-driven basis for prioritizing medicinal herbs with potential cardiovascular activity.

Keyword:
Traditional Chinese Medicine, Molecular Networking, iPSC-derived cardiomyocytes, Cardiovascular Activity

No. PC-045 / 天然物化學組 / Natural Products Chemistry (PC)

Isolation and Bioactivity Screening of Endophytic Fungi from the Medicinal Plant Breynia fruticosa

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We investigated endophytic fungi associated with Breynia fruticosa from Mount Taiwu in Kinmen to isolate and purify fungal strains and evaluate the antimicrobial potential of their secondary metabolites. Using GYPA, MEA, PDA, and YEMA media, a total of 68 fungal strains were successfully isolated. Following liquid fermentation to obtain secondary metabolites, the disk diffusion method was employed to screen for antimicrobial activity against Staphylococcus aureus, Escherichia coli, and several aquatic pathogens (including Edwardsiella tarda, Vibrio alginolyticus, V. parahaemolyticus, Streptococcus iniae, Lactococcus garvieae, Aeromonas hydrophila, and S. agalactiae). Among the isolates, strain Km 4193 demonstrated potent antibacterial activity against resistant Gram-positive pathogens. Additionally, strains Km 4136, Km 4138, and Km 4167 exhibited promising antifungal activity in paper disc assays, making them strong candidates for developing lead compounds to prevent or treat aquaculture diseases. These findings suggest that B. fruticosa-derived fungi are a valuable source of novel antimicrobial agents, thereby facilitating the discovery of lead compounds for pharmaceutical and healthcare applications.

Keyword:

Breynia fruticose, endophytic fungi, lead compounds, paper disc assays

No. PC-046 / 天然物化學組 / Natural Products Chemistry (PC)

Studies on Cembrane Diterpenoids from the Wild-Type Soft Coral Lobophytum crassum

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Eight kcembrane-type diterpenoids (**1**–**8**) were isolated from the soft coral *Lobophytum crassum*, and their structures were established by spectroscopic analyses. The absolute configurations of compounds **3**, **6**, and **8** were further confirmed by single-crystal X-ray diffraction analysis. The neuroprotective activities of **1**–**8** were evaluated in SH-SY5Y human neuroblastoma cells challenged with 6-hydroxydopamine (6-OHDA) and 1-methyl-4-phenylpyridinium (MPP^+). In the 6-OHDA-induced model, most compounds exhibited neuroprotective effects, with **1**, **2**, and **4** showing potent activities (ED_{50} = 0.38, 0.74, and 0.21 μM, respectively). In the MPP^+-induced model, compounds **1** and **7** exhibited potent neuroprotective effects, with ED_{50} values of less than 0.1 and 0.28 μM, respectively. Notably, denticulatolide (**1**) exhibited potent neuroprotective activity in both models. Cytotoxicity against human glioblastoma GBM 8401 cells was also evaluated using the MTT assay. Compound **1** showed the most pronounced time-dependent cytotoxicity, with IC_{50} values of 45.8, 31.6, and 15.7 μM after 24, 48, and 72 h, respectively. These findings highlight the neuroprotective potential of cembrane-type diterpenoids from *L. crassum* and identify denticulatolide as a promising candidate for further investigation.

Keyword:

Soft coral, *Lobophytum crassum*, Diterpenoids, Neuroprotective activity

No. PC-047 / 天然物化學組 / Natural Products Chemistry (PC)

Evaluation of the Antifungal and Termiticidal Potential of *Streptomyces* sp. D3 for Wood Protection

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Streptomyces sp. D3, a soil-derived actinomycete, exhibited strong inhibitory activity against the brown-rot fungi *Fomitopsis pinicola* and *Laetiporus sulphureus*. Culture broth extracts were prepared using ethyl acetate and *n*-butanol, of which only the *n*-butanol extract exhibited significant antifungal activity. Genome mining and LC-MS/MS analyses further revealed the biosynthetic potential for linearmycin production and confirmed the presence of linearmycin B in the active extract.

To evaluate the potential application of the D3 extract in wood protection, the *n*-butanol crude extract was subjected to two application-oriented assays. First, the crude extract was redissolved and applied to wood specimens by vacuum impregnation. The treated specimens were subsequently exposed to the brown-rot fungi *F. pinicola* and *L. sulphureus* for 1, 2, and 6 months. The extent of wood deterioration was assessed based on weight loss and mechanical properties, including the modulus of elasticity (MOE) and modulus of rupture (MOR). In addition, the termiticidal activity of the *n*-butanol crude extract was evaluated using a no-choice filter paper feeding assay.

Overall, this study extended the investigation of *Streptomyces* sp. D3 from its previously demonstrated antifungal activity to its potential application in wood protection. The evaluation of wood decay resistance and termiticidal activity further demonstrated the potential applicability of the D3 *n*-butanol crude extract as a wood-protective agent. Together with the identification of linearmycin B in the active extract, these findings highlighted *Streptomyces* sp. D3 as a promising biological source of bioactive metabolites for the development of environmentally friendly wood preservatives.

Keyword:

Streptomyces spp, Wood-decaying fungi, Termiticidal activity

No. PC-048 / 天然物化學組 / Natural Products Chemistry (PC)

Isolation and Identification of Chemical Constituents from Calyces of Mesosphaerum suaveolens and Evaluation of Their Antioxidant and α-Glucosidase Inhibitory Activities

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Mesosphaerum suaveolens (L.) Kuntze, a member of the Lamiaceae family, contains diverse phytochemicals with various biological activities. However, its calyx remains understudied. This study investigated the chemical constituents and biological activities of *M.* suaveolens calyces. The calyces were extracted and partitioned, and the ethyl acetate fraction was subjected for isolation and purification. Three compounds were tentatively identified by nuclear magnetic resonance (NMR) spectroscopy as caffeic acid, rosmarinic acid, and eugenol. The ethyl acetate fraction exhibited DPPH radical scavenging activity (IC_{50} = 36.00 ± 0.71 μg/mL) and *α*-glucosidase inhibitory activity (IC_{50} = 42.73 ± 1.00 μg/mL). The methanol extract showed superoxide anion radical scavenging activity (IC_{50} = 62.30 ± 2.44 μg/mL). These results demonstrate antioxidant and *α*-glucosidase inhibitory activities of *M.* suaveolens calyces. Further studies will quantify the identified compounds using reference standards and evaluate their biological activities to investigate their contribution to the observed effects. This study provides a basis for further research and the development of *M.* suaveolens as a functional plant resource

Keyword:

Mesosphaerum suaveolens, calyx, chemical constituents, isolation and purification, antioxidant activity, α-glucosidase

No. PC-049 / 天然物化學組 / Natural Products Chemistry (PC)

Antioxidative potentials and metabolomic analysis of Brassica oleracea

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Broccoli sprouts (*Brassica oleracea*) are a nutritious and delicious vegetable commonly consumed on daily basis. They possess several remarkable pharmacological effects. This study aims to identify chemical constituents and antioxidant capacity of broccoli sprouts by utilizing modern technologies to evaluate their active antioxidant constituents. Spectrophotometric analysis revealed that extract exhibited high phenolic and flavonoid contents of 46.24 ± 0.028% and 56.48 ± 0.039%, respectively, in the dried extract of broccoli sprouts. Furthermore, metabolomic analysis indicated that broccoli spouts are rich in various chemical constituents, including amino acids, alkaloids, organic phosphates, flavonoids, and phenolics. Five primary markers (**1**–**5**) that exhibited significant reductions in content between the treated and non-treated conditions with DPPH, were effectively identified through antioxidant screening using the DPPH-HPLC-MS method. In vitro experimental results demonstrated that broccoli spout extract effectively scavenged DPPH and ABTS free radicals and neutralized reactive oxygen species (ROS) generated by RAW264.7 cells through the Nrf2/HO-1 pathway. Our findings emphasize the medicinal value of broccoli sprouts, highlighting their potential in the development of antioxidant-rich products that promote human health.

Keyword:
Brassica oleracea, antioxidants, Nrf2/HO-1, analytical method, ROS

No. PC-050 / 天然物化學組 / Natural Products Chemistry (PC)

Dereplication of natural products in Limulus polyphemus eggs using software-assisted approach

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Limulus polyphemus, the Atlantic horseshoe crab (HSC), is an important estuarine species used to produce reagents for pharmaceutical endotoxin testing. To characterize the chemical composition of HSC eggs, which serve critical ecological functions, we conducted metabolite profiling and dereplication of crude extracts using NMR and complementary mass spectrometric techniques. NMR analysis identified several metabolites associated with biosynthetic and metabolic pathways, including maltose-type oligosaccharides linked to glycogenolysis, as well as homarine (1) and glycine betaine (2) associated with methylation pathways. Nine amino acids were also detected, including threonine (4), leucine (7), valine (9), lysine (10), and arginine (11), which are essential amino acids in marine organisms. GC-MS analysis identified palmitic acid and stearic acid (15) as the predominant saturated fatty acids, whereas elaidic acid (13) and oleic acid (14) were the major unsaturated fatty acids in HSC eggs. LC-MS/MS analysis further revealed phosphatidylcholine as the principal phospholipid component. This comprehensive metabolite characterization and natural product dereplication provide a foundation for understanding HSC developmental biology and exploring novel natural products from this unique keystone species.

Keyword:
Metabolomics, Limulus polyphemus, NMR, LC-MS/MS

No. PC-051 / 天然物化學組 / Natural Products Chemistry (PC)

Chemical Diversity and Biological Activities of Indo-Pacific Acanthaster Species

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Acanthaster genus is a large, corallivorous echinoderm that is recognized as one of the most ecologically significant coral predators that could alter reef community structure. Recent taxonomic and genetic work shows that the Indo-Pacific *Acanthaster* genus forms a species complex, with at least five geographically structured taxa, rather than a single, panmictic species. This poster aims to provide an overview of the chemical profile of *Acanthaster* species across their Indo-Pacific range, focusing on their chemical constituents, toxico-pharmacological properties, reported biological activities, and structural-activity relationship. Through published papers from databases such as Pubmed and Google Scholar, biochemical investigations have revealed that the *Acanthaster* genus produces a wide variety of metabolites belonging to several major chemical classes, such as steroids, sphingolipids, tetraterpenoids, and pyrrole oligoglycosides. Though these compounds are mostly reported as isolated from *A. planci*, regardless of the species, reflecting the recent taxonomic revision of the genus. These compounds also have demonstrated a broad spectrum of biological and pharmacological activities in both *in vitro* and *in vivo* models, including anticancer, anti-inflammatory, antibacterial, antioxidant, antidiabetic, neuroprotective, regenerative, antiviral, anticoagulant, and pesticidal effects. In addition, the structural diversity of *Acanthaster*-derived metabolites provides an emerging basis for understanding their structure–activity relationships (SAR).

Keyword:

Acanthaster, Biochemical profile, Bioactivity, Structure-activity relationship

No. PC-052 / 天然物化學組 / Natural Products Chemistry (PC)

Identification and Validation of Antioxidative Constituents from Brassica oleracea Using Network Pharmacology Analysis and Nrf2/HO-1 Signaling Pathway

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Brassica oleracea is a rich source of vitamin C, carotenoids, minerals, and polyphenols with potential benefits for human health. This study focuses on the chemical investigation and antioxidative capacity of *B. oleracea*. Five polyphenols were successfully separated using multiple chromatographic methods and were identified by contemporary spectroscopic techniques. Antioxidative potentials of isolated compounds (**1**-**5**) were evaluated by integrating network pharmacology and molecular docking analysis for the treatment of oxidative-related diseases. These phenolics showed the antioxidative effect against reactive oxygen species (ROS) in lipopolysaccharide (LPS)-stimulated RAW264.7 cells *in vitro*. Western blot assessments validated the antioxidative properties of the most active compound and *B. oleracea* extract via the Nrf2/HO-1 signaling pathway. An analytical method was established by applying a high-performance liquid chromatography decoupled mass (HPLC-MS) system, indicating the contents of these isolates ranging from 19.12 ± 0.016 to 7.70 ± 0.005 mg/g in the dry extract. These findings indicate that *B. oleracea* (broccoli sprouts) contain many polyphenols, which offer many human health benefits, specifically in the treatment of oxidative disorders.

Keyword:

Brassica oleracea, sinapic acid derivatives, network pharmacology, antioxidant, Nrf2 and HO-1, analytical method

No. PC-054 / 天然物化學組 / Natural Products Chemistry (PC)

Bioactivity-Coupled Molecular Networking-Guided Discovery of Bioactive Metabolites from the Stem of *Osmanthus heterophyllus*

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The discovery of bioactive plant metabolites provides a basis for identifying potential lead compounds and exploring the chemical diversity of indigenous resources. In this study, LC-MS/MS-based multi-informative molecular networking (MIMN), integrated with bioactivity screening, was applied to profile 36 Oleaceae extracts from the Formosan plant library at the Laboratory of Medicinal Botany, Kaohsiung Medical University. MIMN analysis revealed that molecular clusters related to specific shikimate and phenylpropanoid metabolites were associated with anti-inflammatory activity relevant to posterior segment eye diseases, whereas terpenoid and glycosylated clusters were associated with anticancer activity and inhibition of lipid accumulation, respectively. Based on these findings, the stem bark of *Osmanthus heterophyllus* (G.Don) P.S.Green was selected for further large-scale examination. Subsequently, extraction, partition, fractionation, bioactivity screening, and bioactivity-coupled MIMN analysis were performed. Molecular clusters associated with anti-inflammatory activity were mainly annotated as phenylpropanoid–quinic acids, lignans, and secoiridoids. MIMN-guided targeted isolation yielded 20 compounds, including 14 lignans, three phenylpropanoid–quinic acids, two phenylpropanoids, and one secoiridoid. Among them, Osmanthquinic A (**1**) and Osmanthiridoid A (**2**) were first reported. Further MIMN-guided isolation and evaluation of the isolated compounds for their associated biological activities are currently in progress.

Keyword:
Osmanthus heterophyllus, Oleaceae, Multiple-Information Molecular Networking, Terpenoids, Phenylpropanoids

No. PC-055 / 天然物化學組 / Natural Products Chemistry (PC)

Development and Optimization of a Thin-Layer Chromatographic Method for the Quality Control of Elephantopus scaber (Dingshuwu) Based on Sesquiterpene Lactone Markers

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Background: *Elephantopus scaber*, known as Dingshuwu in Chinese, is an important medicinal plant in traditional Chinese medicine and the herbal market. However, standardized quality control criteria for Dingshuwu have not been established in Taiwan.

Objective: Sesquiterpene lactones are characteristic chemotaxonomic constituents of the genus *Elephantopus*, and deoxyelephantopin and other sesquiterpene lactones in *E. scaber* have been proposed as quality markers in recent studies. Therefore, this study aimed to develop and optimize a simple TLC method using sesquiterpene lactones as chemical markers for the identification and quality control of *E. scaber*.

Methods: *E. scaber* samples from different locations were investigated. TLC conditions, including extraction procedure, mobile-phase composition, sample loading volume, and visualization conditions, were systematically evaluated to establish the optimal chromatographic conditions. Silica gel 60 F_{254} plates were used as the stationary phase, with sesquiterpene lactone reference markers for chromatographic comparison.

Results: The optimized TLC conditions provided clear and reproducible chromatographic profiles of *E. scaber*. Cyclohexane : ethyl acetate (1:1, v/v) was selected as the optimal mobile phase. After chromatographic development, the plates were sprayed with sulfuric acid (95-98%, v/v), heated, and examined under UV light at 365 nm. The target components in *E. scaber* samples exhibited spots with comparable colors at R_f values corresponding to those of the sesquiterpene lactone reference markers.

Conclusion: The developed TLC assay provides a rapid and practical approach for the detection and identification and quality control of *E. scaber* and may be applicable to routine quality assessment and market surveillance.

Keyword:

Elephantopus scaber, sesquiterpene lactones, thin-layer chromatography (TLC)

No. PC-056 / 天然物化學組 / Natural Products Chemistry (PC)

Exploring JamD-mediated terminal halogenation of the bacterial conjugated polyynes

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Bacterial conjugated polyynes exhibit diverse biological activities but are often limited by their intrinsic chemical instability. We previously identified a polyyne biosynthetic gene cluster from *Massilia* sp. YMA4 and established the heterologous production of Massilin C. However, Massilin C readily undergoes spontaneous degradation, particularly at elevated concentrations, posing challenges for its isolation, characterization, and downstream applications.

To explore enzymatic functionalization of Massilin C, we focused on JamD, a flavin-dependent halogenase from the marine cyanobacterium *Moorena producens* that catalyzes selective halogenation of terminal alkynes. We hypothesized that JamD-mediated terminal halogenation could generate novel Massilin C derivatives and provide a platform for investigating how terminal alkyne modification affects the chemical stability and biological properties of conjugated polyynes.

Recombinant JamD was successfully expressed and purified, and an in vitro enzymatic reaction using Massilin C as the substrate was established. HPLC analysis revealed a distinct new product peak with a longer retention time following the JamD-catalyzed reaction, consistent with the formation of a modified Massilin C derivative. These results demonstrate the feasibility of JamD-mediated modification of Massilin C and establish a foundation for subsequent structural characterization and systematic evaluation of the effects of terminal halogenation on polyyne stability and biological activity.

Keyword:
conjugated polyynes, Massilin C, JamD, enzymatic halogenation, terminal alkyne

No. PC-057 / 天然物化學組 / Natural Products Chemistry (PC)

Chemical investigation and anti-inflammatory evaluation of unique azaphilones from the algicolous fungus Penicillium sclerotiorum

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The secondary metabolites of the algicolous fungus *Penicillium sclerotiorum* were investigated using genomic and metabolomic approaches. After meticulous isolation and purification, 17 unusual azaphilones (**1**–**17**) were identified. The structures of these compounds were elucidated based on NMR spectroscopic data, HR-ESI-MS analysis, and Marfey's method. Furthermore, the absolute configuration of compound 1 was determined by single-crystal X-ray diffraction analysis. Additionally, a plausible biosynthetic pathway for these azaphilones was proposed, in which two separate gene clusters collaboratively contribute to their biosynthesis. The first cluster constructs the azaphilone core scaffold, whereas the second cluster mediates tailoring modifications. Regarding their bioactivity, isolated compounds were evaluated for their anti-inflammatory effects. The results showed that compound **2** significantly inhibited superoxide anion generation, elastase release and suppressed STING signaling. Furthermore, the *in vivo* antioxidative effects of **2** was evaluated using the nematode *Caenorhabditis elegans*. This compound significantly enhanced nematode survival under juglone-induced oxidative stress without causing apparent adverse effects. Collectively, these findings highlight the potential of azaphilones as multifunctional bioactive compounds with anti-inflammatory activity and protective effects against oxidative stress *in vivo*.

Keyword:
Penicillium sclerotiorum, azaphilones, anti-inflammatory activity, STING signaling, Caenorhabditis elegans

No. PC-058 / 天然物化學組 / Natural Products Chemistry (PC)

Anti-angiogenic Indole alkaloids from the Marine-derived fungus Aspergillus fumigatus MF-0322

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Molecular networking analysis of the LC-HRMS/MS data of the 75% MeOH(aq) extract of the marine-derived fungus Aspergillus fumigatus *MF-0322 revealed clusters of indole alkaloids, guiding the isolation of one previously undescribed indole diketopiperazine alkaloid, spirotryprostatin I (1)* ***, together with 23 known indole alkaloids (2–24)*** *and four known triterpenoids (25–28). Their structures were elucidated by NMR, HRESIMS, ECD, and Marfey's method, and by comparison with literature data. Whole-genome sequencing identified the biosynthetic gene cluster (BGC) responsible for indole alkaloid production, and analysis of the encoded enzymes helped to propose a plausible biosynthetic pathway. In an anti-angiogenic assay, compounds 4, 7, 9, 17, 23, 24, 25, and 27 showed moderate to considerable inhibition of endothelial progenitor cell (EPC) growth, with IC50*$_{values\ ranging\ from\ 9.3 \pm 0.6\ to\ 21.2 \pm 2.8\ \mu g/mL.}$

Keyword:

Aspergillus fumigatus, anti-angiogenic activity, GNPS, BGCs

No. PC-059 / 天然物化學組 / Natural Products Chemistry (PC)

The structural characteriazation of a sulphated galactan polysaccharide purified from red microalga Sarcodia suiae

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Sarcodia suiae, a red macroalga of the genus *Sarcodia* within the phylum Rhodophyceae, is predominantly distributed throughout the Indian Ocean and the Western Pacific Ocean. Valued for its rich micronutrient content, *S. suiae* is widely consumed both as a food additive. Previous studies have demonstrated that *S. suiae* extracts exhibit diverse bioactivities, including immunomodulatory, antitumor, and anti-inflammatory effects. However, comprehensive research on the detailed structural features and comparative analysis of *S. suiae*-derived polysaccharides (SSP) remains limited.

SSP-T1-f1, a purified polysaccharide isolated from SSP, was obtained via using ion exchange and size-exclusion column. Based on the linear regression equation derived from dextran molecular weight standards, the molecular weight of SSP-T1-f1 was estimated to be 19.68 kDa. The purified polysaccharide exhibited a carbohydrate content of 88.79%, negligible protein content, and 24.5% of sulfate content. The IR spectrum demonstrated adsorbances with functional groups with sulfate. Monosaccharide composition analysis classified that galactose was the main sugar, accounting for 87.23% of the total monosaccharide content. The structure of SSP-T1-f1 was confirmed by 1D and 2D NMR spectroscopy. These results suggest that SSP-T1-f1 was mainly constitutes with galactose and contained sulfate functional groups, which demonstrated that the repeating dimeric units of SSP-T1-f1 were κ-carrageenan.

The study presents the first report to investigate the molecular weight, monosaccharide composition and chemical struture of a polysaccharide derived from *S. suiae*. Further experiments will focus on elucidating the detailed mechanism of immunomodulatory effects of SSP-T1-f1, with the aim of evaluating its potential applicability in biomedical and functional health product development.

Keyword:

Sarcodia suiae, red macroalga, polysaccharide, galactose, κ-carrageenan

No. PC-060 / 天然物化學組 / Natural Products Chemistry (PC)

Investigation of the Effects of Saponified Sacha Inchi Oil on Melanogenesis

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Melanogenesis is an important biological process involved in skin pigmentation, and excessive melanin production can lead to hyperpigmentation, which remains a common skin concern. Sacha Inchi oil (SIO) (*Plukenetia volubilis* L.) is rich in polyunsaturated fatty acids, particularly α-linolenic and linoleic acids, which have potential skin-whitening and anti-melanogenic activities.

In this study, SIO was saponified and characterized by thin-layer chromatography (TLC) and ^{1}H-nuclear magnetic resonance (^{1}H-NMR) spectroscopy. The effects of SIO and Sap-SIO at different pH values on cell viability were evaluated in B16/F10 murine melanoma cells and HaCaT keratinocytes using an MTT assay. Intracellular melanin content was also determined in B16/F10 cells.

TLC analysis showed the disappearance of triglyceride-related spots and the appearance of spots corresponding to fatty acid salts after saponification. ^{1}H-NMR analysis further supported the conversion of triglyceride-derived structures.

Sap-SIO showed relatively stable B16/F10 cell viability at 12.5–50 μg/mL, while reduced viability was observed at 100 μg/mL. No marked cytotoxicity was observed in HaCaT cells. A slight reduction in melanin content was observed, with the greatest reduction for Sap-SIO at pH 4.7 and 50 μg/mL. These preliminary findings suggest that Sap-SIO may have potential effects on melanogenesis, however, further studies are required to confirm its anti-melanogenic activity.

Keyword:

Melanogenesis, Hyperpigmentation, Saponification, Sacha Inchi oil

No. PC-061 / 天然物化學組 / Natural Products Chemistry (PC)

Photoprotective Activities and Skin Permeation of Major Bioactive Constituents from the Roots of Glycyrrhiza uralensis

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Five bioactive constituents, glycyrrhizic acid (**1**), liquiritin (**2**), isoliquiritin (**3**), liquiritigenin (**4**), and isoliquiritigenin (**5**), were isolated from *Glycyrrhiza uralensis* roots and evaluated for protection against ultraviolet B (UVB)-induced photodamage. Their UV absorption was characterized by UV–Vis spectroscopy. HaCaT cells were exposed to UVB irradiation (40 mJ/cm²), and photoprotective effects were assessed by cell viability and intracellular reactive oxygen species (ROS) assays. Among the compounds, liquiritigenin (**4**) showed photoprotective activity against UVB-induced oxidative injury.

Western blotting showed UVB suppressed Nrf2, HO-1, and NQO1 and increased Keap1, MMP-1, MMP-9, and Bax. Liquiritigenin (**4**) concentration-dependently reversed these alterations. At 25 μM, it increased Nrf2, HO-1, and NQO1 and decreased Keap1, MMP-1, MMP-9, and Bax, with effects comparable to quercetin and stronger responses for several antioxidant-related proteins. These results suggest that liquiritigenin (**4**) may alleviate oxidative stress, extracellular matrix degradation, and apoptosis.

Skin permeation studies using porcine skin were performed to evaluate the topical potential of liquiritigenin (**4**). After 24 h, cumulative permeation through intact skin reached approximately 40 nmol/cm², compared with 10 nmol/cm² for quercetin. Its flux was approximately 1.7 nmol/cm²/h, compared with approximately 0.3 nmol/cm²/h for quercetin. Liquiritigenin (**4**) also showed greater skin deposition, reaching approximately 0.086 nmol/mg, compared with 0.050 nmol/mg for quercetin. Enhanced permeation was observed in stripping, de-lipid, and de-protein skin models, with increased skin deposition particularly in stripping and de-lipid models. These findings suggest that the bioactive constituents of *G. uralensis.* show UVB photoprotective activity, with liquiritigenin (**4**) showing favorable skin permeation and retention for topical application.

Keyword:
Glycyrrhiza uralensis, Liquiritigenin, photoprotective, skin permeation

No. PC-062 / 天然物化學組 / Natural Products Chemistry (PC)

Investigation of the Antioxidant, Anti-inflammatory, and Cell Migration-Promoting Activities and Molecular Mechanisms of Lonicera japonica Extract and Its Isolated Compounds

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Lonicera japonica Thunb.,a traditional medicinal plant known for its antioxidant and anti-inflammatory properties. This study evaluated the antioxidant, anti-inflammatory, and cell migration-promoting activities of its methanolic extract and isolated compounds. The extract was evaluated for total phenolic content (TPC), total flavonoid content (TFC), and antioxidant capacity. Anti-inflammatory activity was evaluated by measuring nitric oxide (NO) production in lipopolysaccharide (LPS)-stimulated RAW264.7 macrophages, and cell viability was assessed using the MTT assay. An in vitro cell migration assay was performed to evaluate whether treatment with the extract or isolated compounds enhanced migration compared with untreated controls. Six compounds were isolated and identified as cryptochlorogenic acid (**1**), neochlorogenic acid (**2**), isochlorogenic acids A (**3**), B (**4**), and C (**5**), and cynaroside (**6**). These compounds underwent the same antioxidant and anti-inflammatory assays. The extract and isolated compounds exhibited varying degrees of radical-scavenging and NO-inhibitory activities, suggesting that caffeoylquinic acid derivatives and flavonoids contribute to the bioactivity of *L. japonica.* The most active samples showed greater antioxidant capacity and stronger NO inhibition than rutin, a flavonoid known for its antioxidant and anti-inflammatory properties. Both the extract and isolated compounds enhanced cell migration compared with untreated controls, suggesting their potential to support tissue repair.

Western blot assessed the effects of the most active compounds on inflammation-related proteins, including iNOS and COX-2, molecular docking to predict their binding interactions with inflammatory targets. These findings may clarify the molecular basis of *L. japonica* bioactivity and support its development as a source of antioxidant, anti-inflammatory, and cell migration-promoting agents.

Keyword:
Lonicera japonica, antioxidant, anti-inflammatory, cell migration

No. PC-063 / 天然物化學組 / Natural Products Chemistry (PC)

Investigation of secondary metabolites and anti-inflammatory constituents from Kaki Calyx

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Kaki Calyx (the calyx of *Diospyros kaki* Thunb.), belonging to the family Ebenaceae, is a traditional Chinese medicine widely used in East Asia. While its fruit is edible, its calyx has long been utilized in traditional medicine, primarily to alleviate symptoms such as hiccups, belching, and regurgitation. This study focused on the anti-inflammatory evaluation of secondary metabolites from the ethyl acetate fraction of *Diospyros kaki* calyx. Sixteen compounds were isolated from the calyx of *Diospyros kaki*, including nine triterpenoids, uvaol (**1**), ursolic acid (**2**), pomolic acid (**3**), 3*β*-hydroxy-18*α*,19*α*-urs-20-en-28-oic acid (**4**), randialic acid B (**5**), oleanderic acid (**6**), oleanolic acid (**7**), siaresinolic acid (**8**), and betulinic acid (**9**), one flavonoid, quercetin (**10**), and six benzenoids, 4-hydroxybenzaldehyde (**11**), 3,4-dihydroxybenzoic acid (**12**), vanillic acid (**13**), isovanillic acid (**14**), (*E*)-*p*-coumaric acid (**15**), and (*Z*)-*p*-coumaric acid (**16**). The structures were determined by spectroscopic analysis, mass spectrometry, and comparison with reported physical and spectroscopic data. Among these compounds, compounds **4**, **5**, and **6** were isolated from the genus *Diospyros* for the first time. In the anti-inflammatory assay, compounds **2**, **4**, **5**, and **9** showed potent inhibition of superoxide anion generation in neutrophils stimulated by formyl-L-methionyl-L-leucyl-L-phenylalanine/cytochalasin B (fMLP/CB), with IC_{50} values ranging from 0.54 to 2.03 μM. Compounds **2**, **4**, **5**, **7**, **9**, and **10** also inhibited fMLP/CB-induced elastase release, with IC_{50} values ranging from 1.29 to 8.59 μM. Collectively, these findings indicate that *Diospyros kaki* calyx contains bioactive constituents with anti-inflammatory potential and may serve as a source of natural compounds for further pharmacological investigation.

Keyword:

Kaki Calyx, anti-inflammatory, neutrophils, triterpenoids

No. PC-064 / 天然物化學組 / Natural Products Chemistry (PC)

A New Sterol and Anti-inflammatory Constituents from the Soft Coral Lobophytum durum

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Eleven compounds **(1–11)** were isolated from the soft coral *Lobophytum durum* collected from the waters surrounding Guishan Island, Yilan County, Taiwan. These included a new sterol, 3β-hydroxy-25-methylene-5-cholesten-7-one **(1)**, and ten known compounds **(2–11)**. Their structures were elucidated through spectroscopic analyses and comparison with reported data. Compounds **2–4** and **11** were isolated from this species for the first time, and the absolute configuration of compound **4** was established by single-crystal X-ray diffraction. The anti-inflammatory activities of all isolated compounds were evaluated by measuring their inhibitory effects on reactive oxygen species (ROS) generation and elastase release in human neutrophils. Compound **5** exhibited potent inhibitory activity against ROS generation and elastase release, with IC_{50} values of 0.50 ± 0.17 and 0.51 ± 0.06 μM, respectively. These findings highlight L. durum as a source of bioactive natural products and support further investigation of compound **5** as a potential anti-inflammatory lead.

Keyword:
Lobophytum durum, ROS, elastase, x-ray, IC50

No. PC-065 / 天然物化學組 / Natural Products Chemistry (PC)

Antibiotic-induced production and structural characterization of a RiPP from Streptomyces murinus

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Microbial interactions can trigger the production of cryptic secondary metabolites in *Streptomyces*. Previous work in Yu-Liang Yang's laboratory identified a metabolite with a signal of *m/z* 1628 in the interaction zones between *Streptomyces murinus* CRREB63 and fungal species, including *Phellinus* sp. and *Magnaporthe oryzae*. Interestingly, the *m/z* 1628 signal was not detected under monoculture conditions but was observed during microbial co-cultivation, suggesting that its production is associated with microbial interactions. To establish an alternative production strategy, this study investigated the effects of antibiotic-induced stress on metabolite production in CRREB63. Different culture media and antibiotic treatments were evaluated, revealing that gentamicin and chloramphenicol could induce the production of the target metabolite, with chloramphenicol exhibiting stronger induction under selected conditions. HRMS/MS analysis revealed characteristic peptide fragmentation patterns, while genome mining identified a candidate class V lanthipeptide biosynthetic gene cluster, suggesting that the target metabolite may be a lanthipeptide belonging to the ribosomally synthesized and post-translationally modified peptide (RiPP) family. Molecular networking further revealed structurally related metabolites with mass differences potentially associated with post-translational modifications and glycosylation. These findings highlight antibiotic-induced stress as a promising strategy for inducing otherwise undetected secondary metabolites in *Streptomyces* and provide a foundation for further structural elucidation and biosynthetic investigation of the target metabolite.

Keyword:

Streptomyces, Cryptic secondary metabolites, Antibiotic-induced stress, RiPP

No. PC-066 / 天然物化學組 / Natural Products Chemistry (PC)

Chemical Investigation of the Marine-Derived Fungus Aspergillus ochraceopetaliformis

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Marine-derived fungi have emerged as promising sources of structurally diverse and biologically active secondary metabolites. Among them, the genus Aspergillus has attracted considerable attention for its ability to produce a variety of bioactive natural products. Previous studies have reported that metabolites from this genus exhibit diverse biological activities, including anti-inflammatory, antimicrobial, antioxidant, and cytotoxic effects. In our biological screening, *A. ochraceopetaliformis* showed a promising cytotoxic effect. This finding suggested that it could be a potential target for the discovery of structurally novel and biologically active marine natural products.

In this study, a chemical investigation of the zoanthid-derived fungus *A. ochraceopetaliformis* was conducted, resulting in the isolation of secondary metabolites from three structural classes: asteltoxins, crotonic acid derivatives, and meroterpenes. The structures of the isolated compounds were elucidated by spectroscopic analyses, including NMR and mass spectrometry, together with comparison with reported literature data. Among the twelve isolated compounds, ten were identified as new. Notably, the structures of one new crotonic acid derivative and one new meroterpene were unambiguously determined by single crystal X-ray diffraction analysis. In addition, one of the isolated asteltoxins exhibited cytotoxic activity against oral cancer cells, with an IC_{50} value of 5.63 ± 0.29 μg/mL. The discovery of new metabolites, together with the observed cytotoxicity, highlights the chemical diversity and biological potential of the marine-derived fungus.

Keyword:

Aspergillus ochraceopetaliformis, zoanthid-derived fungus, natural products, crotonic acid derivative, meroterpene

No. PC-067 / 天然物化學組 / Natural Products Chemistry (PC)

Unveiling Brasiliamides Biosynthesis in Aspergillus thermomutatus

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Piperazine-containing natural products represent a structurally diverse class of fungal metabolites with a broad range of biological properties. However, the molecular mechanisms underlying the assembly of these unusual heterocyclic structures remain poorly understood. In this study, we investigated the genetic and enzymatic basis of brasiliamides biosynthesis in *Aspergillus thermomutatus* by integrating genome mining, heterologous expression, targeted gene disruption, and in vitro biochemical assays. Genome analysis led to the identification of a candidate biosynthetic gene cluster containing a single-module non-ribosomal peptide synthetase and multiple tailoring enzymes. Functional investigation of the cluster revealed the essential contribution of several biosynthetic genes to brasiliamides production and identified a key tailoring enzyme involved in pathway diversification. Genetic manipulation and heterologous reconstruction further supported the proposed roles of these enzymes and enabled the generation of structurally related metabolites. In addition, in vitro enzymatic studies provided insights into the catalytic properties and substrate preference of the key enzyme, offering a better understanding of the late-stage transformations involved in brasiliamides biosynthesis. Overall, this study establishes a genetic and biochemical framework for the biosynthesis of brasiliamides in *A. thermomutatus* and highlights the remarkable enzymatic strategies employed by fungi to construct structurally complex piperazine-containing natural products.

Keyword:
brasiliamides, Aspergillus thermomutatus, biosynthetic gene cluster, non-ribosomal peptide synthetase

No. PC-068 / 天然物化學組 / Natural Products Chemistry (PC)

Molecular Networking-Guided Exploration of Secondary Metabolites from Aspergillus niger STS07 Fermented with Dioscorea pseudojaponica and Their Effects on Lymphatic Endothelial Cells

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Cancer has remained a leading cause of death in Taiwan for more than four decades. Lymphangiogenesis contributes to tumor metastasis, highlighting the need to identify natural products with potential effects on lymphatic endothelial cells. In this study, feature-based molecular networking (FBMN) combined with the one-strain-many-compounds (OSMAC) strategy was applied to investigate the metabolomic diversity of the *Scaevola taccada*-derived endophytic fungus *Aspergillus niger* STS07. Among the tested culture conditions, extracts obtained from fermentation with the Taiwanese native crop *Dioscorea pseudojaponica* showed a significant inhibitory effect on lymphatic endothelial cell (LEC) viability. FBMN analysis further revealed that this fermentation condition produced the greatest chemical diversity, with molecular families dominated by polyketide-derived metabolites and numerous nodes without database matches. FBMN-guided isolation led to the identification of five compounds. These findings demonstrate the value of combining OSMAC cultivation with molecular networking for the chemical investigation of fungal metabolites and identify *A. niger* STS07 cultured with *D. pseudojaponica* as a promising source of anti-lymphangiogenic metabolites.

Keyword:
OSMAC, Molecular networking, *Aspergillus niger*, polyketides, anti-cancer, anti-lymphangiogenesis

No. PC-069 / 天然物化學組 / Natural Products Chemistry (PC)

Isolation of Secondary Metabolites from Various Fungi with Anti-Angiogenic Activity

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Symbiotic fungi are valuable sources of diverse secondary metabolites with promising biological activities. Their symbiotic association with host organisms provides unique ecological conditions that can promote the biosynthesis of diverse bioactive compounds. Therefore, symbiotic fungi represent a promising and still underexplored source of novel natural products. This study aimed to isolate fungal secondary metabolites from various sources and their anti-angiogenic activity. The fungus was cultivated on a rice-based solid medium for 20 days, followed by ethyl acetate extraction and liquid–liquid partitioning with 75% methanol and hexane (1:1). The methanolic fraction was subsequently purified using chromatographic techniques. The structures of the isolated compounds were elucidated through 1D and 2D NMR, mass spectrometry, optical rotation analysis, and X-ray diffraction. Anti-angiogenic activity was evaluated using human endothelial progenitor cells (EPCs). The isolation secondary metabolites of *Aspergillus westerdijkiae* yielded five known compounds (**1**–**5**), including (+)-preussin, which exhibited anti-angiogenic activity. Additionally, screening of endophytic fungi from different sources afforded 15 compounds (**6**–**20**), including two new compounds (**6** and **7**) from *Talaromyces rugulosus*. These findings highlight the diversity of fungal secondary metabolites and their potential as sources of bioactive compounds. The anti-angiogenic activity indicated that (+)-preussin isolated from *A. westerdijkiae* has the potential as a promising anti-angiogenic compound.

Keyword:

Fungi, Aspergillus westerdijkiae, , Talaromyces rugulosus, anti-angiogenic

No. PC-070 / 天然物化學組 / Natural Products Chemistry (PC)

Annotation and identification of alkamides from fruits of the endemic Taiwan species Zanthoxylum pistaciiflorum Hayata with the aid of high-performance liquid chromatography–tandem mass spectrometry validated by isolation and database-driven approach

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This study presents the first comprehensive phytochemical profiling of the fruits of *Zanthoxylum pistaciiflorum* Hayata, an endemic Taiwanese species, combining classical isolation with computational mass spectrometry. Chemical characterization identified the chemically unstable *α*-sanshool as the predominant constituent, representing a high yield of 9.15% of the crude extract (9.43 mg/g dry weight). This marks the inaugural report of a *Zanthoxylum* species dominated by non-hydroxylated alkamides in its fruit. To overcome material scarcity and purification constraints of minor constituents, an untargeted liquid chromatography–tandem mass spectrometry (LC-MS/MS) approach was integrated with database platforms workflows. Feature-Based Molecular Networking via GNPS and SIRIUS structural prediction validated the targeted presence of structurally diverse sanshool-type alkamides in the lipophilic ethyl acetate fraction, and unveiled a distinct enrichment of flavonoids, coumarins, and benzylisoquinoline alkaloids in the *n*-butanol fraction. Complementing these boundaries, SIRIUS structural prediction preferred a preliminary tentative profiling of alkamides as potential candidate structures within this genus, providing a hypothetical framework for future targeted isolation. Overall, this integrated platform balances the limits of conventional isolation and effectively maps the specialized metabolome of rare plant matrices.

Keyword:
Zanthoxylum pistaciiflorum, α-sanshool, Alkamides, LC-MS/MS, GNPS, SIRIUS

No. PC-071 / 天然物化學組 / Natural Products Chemistry (PC)

Enhancing Massilin C Biosynthesis through Strategic Reorganization of Biosynthetic Genes

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Conjugated polyynes are natural products characterized by alternating carbon–carbon single and triple bonds and diverse biological activities. Massilin C, a C16 polyyne produced by *Massilia* sp. YMA4, is a promising scaffold for structural diversification, motivating efforts to improve its biosynthetic efficiency. Previous qRT-PCR analysis of its biosynthetic gene cluster (BGC) revealed distinct expression patterns of *masD*, encoding a fatty acyl-AMP ligase, and *masG*, encoding an acyl carrier protein (ACP). *masD* expression increased at 36 h, whereas *masG* showed a comparable increase at 48 h. We hypothesized that delayed ACP availability could limit fatty acid loading and downstream desaturation, thereby restricting early Massilin C biosynthesis. To address this potential bottleneck, we repositioned *masG* immediately downstream of *masD*, closer to the upstream pR promoter, aiming to enhance ACP expression. At 24 h, the engineered construct produced approximately 220 mg/L Massilin C, compared with 45 mg/L from the original construct, representing a nearly fivefold increase. Production levels were comparable at 36 and 48 h, indicating primarily accelerated early product accumulation. In a complementary strategy, we constructed a pR-driven expression cassette containing three fatty acid biosynthesis genes from Escherichia coli (*fabB*, *fabG*, and *fabZ*), which increased C16:1 fatty acid production by 1.5-fold compared with the control. These findings support combining BGC reorganization with precursor supply engineering to improve bacterial polyyne biosynthesis, although the impact of increased C16:1 availability on Massilin C production remains to be evaluated.

Keyword:

Massilin C, Conjugated polyynes, Biosynthetic gene cluster engineering, Acyl carrier protein, Fatty acid biosynthesis, C16:1 fatty acid

No. PC-073 / 天然物化學組 / Natural Products Chemistry (PC)

Interaction of the Marine Sponge-Derived Anticancer Compound 12α-Acetoxy-22-hydroxy-24-methyl-24-oxoscalar-16-en-25-al with the Androgen Receptor

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Marine natural products exhibit remarkable chemical diversity and biological activities, making them promising sources for anticancer drug discovery. The androgen receptor (AR) plays a critical role in cancer progression and therapeutic resistance, particularly in prostate cancer, highlighting its therapeutic potential.

In this study, bioactivity-guided isolation from the marine sponge *Lendenfeldia* sp. yielded a new compound, lendenfeldarane Z (**1**), and five known compounds. Among these, 12α-acetoxy-22-hydroxy-24-methyl-24-oxoscalar-16-en-25-al (**2**) exhibited the strongest cytotoxicity against Molt-4, U937, K562, DU145, PC3, and PANC-1 cells, with IC_{50} values of 0.11, 0.15, 0.06, 0.71, 0.88, and 2.08 μg/mL, respectively. Fluorescence staining revealed nuclear morphological alterations in Molt-4 and K562 cells. In a Molt-4 xenograft model, compound **2** reduced tumor volume by 37.7% at week 7 compared with controls.

SwissTargetPrediction identified AR as a potential target of compound **2**. A cellular thermal shift assay (CETSA) demonstrated increased AR thermal stability (ΔTm = 5.54 °C), suggesting cellular target engagement. Molecular docking suggested that compound **2** could occupy the AR ligand-binding pocket through favorable hydrophobic interactions. Furthermore, its cellular effects persisted under dihydrotestosterone (DHT) stimulation.

Collectively, these findings demonstrate the potent *in vitro* and *in vivo* anticancer activity of compound **2** and support its interaction with AR, highlighting its potential as a lead compound for AR-targeted anticancer drug development.

Keyword:
Lendenfeldia sp., Marine Natural Products, androgen receptor, anti-cancer

No. PC-074 / 天然物化學組 / Natural Products Chemistry (PC)

Prenylated Indole Alkaloids and Dimeric Xanthone–Chromanones from Marine-derived fungus Aspergillus aculeatinus

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A marine-derived strain *Aspergillus aculeatinus* yielded eleven secondary metabolites representing two distinct structural classes. Chemical investigation of the fungal extract afforded seven prenylated indole alkaloids, including one new paraherquamide analog (**1**) and six known compounds, namely, paraherquamides B, E, and F (**2**–**4**), aculeaquamide A (**5**), asperparaline A (**6**), and SB203105 (**7**). In addition, four known xanthone–chromanone heterodimers, chrysoxanthones B and G (**8** and **9**), aculeaxanthone D (**10**), and pencillixanthone A (**11**), were isolated. The new paraherquamide analog was further characterized by detailed spectroscopic analysis and comparison with structurally related congeners. Two plausible biosynthetic pathways for the prenylated indole alkaloids and xanthone–chromanone heterodimers were proposed based on the biosynthetic gene cluster analysis in *A. aculeatinus*. The co-occurrence of these chemically distinct metabolite classes in a single marine-derived fungal strain expands the chemical diversity of *A. aculeatinus* and provides further insight into its biosynthetic potential.

Keyword:
Aspergillus, Biosynthetic gene cluster, Paraherquamide analogue, Xanthone–chromanone heterodimers

No. PC-075 / 天然物化學組 / Natural Products Chemistry (PC)

Functional Characterization of a Haloacid-Dehalogenase-Like Terpene Cyclase from Aspergillus niger

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Terpenoids are valuable natural products used in pharmaceuticals, agrochemicals, flavours, and industry. As demand for structurally complex terpenoids increases, sustainable enzymatic production offers an attractive alternative to extraction from natural sources. Haloacid-Dehalogenase-like terpene cyclases (HAD-TCs) are a recently identified class of bifunctional enzymes combining terpene cyclase and phosphatase activities. Here, we investigate AniH from *Aspergillus niger*, which produces a yet uncharacterized product profile. Heterologous expression of AniH in *Saccharomyces cerevisiae* yielded five distinct GC-MS products (**1–5**). Large-scale cultivation and product isolation identified (+)-drim-8-ene-11-ol (**5**) as the predominant product, while **1** and **2** were identified as GC-MS *in situ* artifacts. **3** and **4** were identified as (+)-drim-9(11)-en-8-ol isomers. *In vitro* characterization of AniH established (+)-drim-8-ene-11-yl -pyrophosphateas the authentic enzymatic product, with its dephosphorylation attributed to endogenous yeast phosphatases. Together, these findings resolve the product spectrum of AniH and provide new insights into the molecular mechanism underlying fungal HAD-like terpene cyclization.

Keyword:
HAD-like terpene cyclases, terpenoids, drimane-type sesquiterpenes

No. PC-076 / 天然物化學組 / Natural Products Chemistry (PC)

Discovery of new hybrids from *Syzygium simile* with anti-lipid droplet accumulation and anti-inflammatory activities

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Metabolic dysfunction-associated fatty liver disease (MAFLD) and inflammation-related disorders impose a heavy burden on global health due to high incidence, limited treatment options, and the frequent side effects of current therapies, highlighting the urgent need for novel drug candidates. A lipid droplet (LD) accumulation inhibition screening platform was used to evaluate over 3,000 methanolic extracts from Formosan plants. Among these, the leaves of *Syzygium simile* (Myrtaceae) showed significant bioactivity, particularly in the *n*-hexane layer. The phytochemistry of *S. simile* remains poorly studied, indicating untapped potential. Through bioactivity-guided fractionation, 22 flavonoid-sesquiterpenoid hybrids were isolated from the active *n*-hexane layer. Structural analysis suggested that these hybrids are biosynthetically derived from five flavonoid types (I-V) combined with five sesquiterpenoid moieties (germacrane-, cubebane-, oplopane-, cadinane-, and copaane-types), representing a rare structural combination in nature. Biological evaluations showed that **1** inhibited LD accumulation in Huh7 cells in a dose-dependent manner by 64.1% at 40 μM without cytotoxicity. In anti-inflammatory tests using fMLP/CB-induced human neutrophils, most hybrids suppressed the generation of superoxide anions and elastase release, with potencies up to 32-fold greater than the positive control. SAR analysis identified the type I flavonoid and germacrane-type sesquiterpenoid skeletons as the optimal pharmacophores, Compound **3**, which integrates the two units through an rA-type ring fusion, exhibited IC_{50} values of 0.04 μM (superoxide anion) and 0.16 μM (elastase), achieving nanomolar potency. Further studies on the high-polarity layers are ongoing. The flavonoid-sesquiterpenoid hybrids serve as promising lead compounds with potential for developing innovative therapies for MAFLD and related inflammatory diseases.

Keyword:
Myrtaceae, *Syzygium simile*, Flavonoid-sesquiterpenoid hybrids, Anti-inflammatory activity, Anti-LD accumulation activity

No. PC-077 / 天然物化學組 / Natural Products Chemistry (PC)

Bidirectional Chemical Signaling Between Orchid Seeds and Mycorrhizal Fungi During Germination

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Orchid seeds lack endosperm and depend on mycorrhizal fungi for germination, yet the chemical signals mediating early partner recognition remain poorly understood. Here, we investigated pre-symbiotic communication between *Phalaenopsis aphrodite* seeds and associated fungi. Fungal isolates obtained through in situ seed baiting were evaluated in symbiotic germination assays, identifying *Fonsecaea* sp. NCKU-150 as the most effective germination-promoting isolate. Histological observations confirmed fungal colonization and intracellular symbiotic structures in seed embryos, while chemotropism assays indicated that germinating seeds release fungal-attracting signals. Integrated transcriptomic and metabolomic profiling revealed pronounced changes during fungal recognition and colonization. Targeted liquid chromatography–tandem mass spectrometry (LC–MS/MS) using multiple reaction monitoring detected signals consistent with the strigolactone sorgolactone in orchid seeds. Exogenous sorgolactone promoted fungal hyphal branching and chemotropic responses, supporting its potential involvement in fungal recruitment. In parallel, untargeted gas chromatography–mass spectrometry (GC–MS) identified 1-dodecanol as a candidate fungal-derived volatile organic compound, and exogenous 1-dodecanol enhanced orchid seed germination. Together, these findings support a model of bidirectional chemical communication in which seed-associated strigolactone signals may facilitate fungal recruitment, whereas fungal volatiles promote germination. This work highlights candidate signaling metabolites that may coordinate the establishment of orchid–mycorrhizal symbiosis.

Keyword:
orchid seed germination, mycorrhizal symbiosis, chemotaxis signaling, transcriptomics, metabolomics

No. PC-078 / 天然物化學組 / Natural Products Chemistry (PC)

Discovery and Characterization of New Aspochalasins from Zoanthid-derived Fungus Aspergillus frequens

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Discovery and Characterization of New Aspochalasins from Zoanthid-derived Fungus *Aspergillus frequens*

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Cytochalasans are a group of fungal-derived natural secondary metabolites characterized by a macrocyclic ring fused to an isoindolone core, exhibiting diverse structural features. These compounds can interfere with actin polymerization and cytoskeletal dynamics, thereby affecting cell morphology and motility. Previous studies have reported that some cytochalasans exhibit various biological activities, including cytotoxic, antimicrobial, and anti-inflammatory effects. Based on their structural features and the amino acids involved in their biosynthesis, cytochalasans can be classified into several groups, among which aspochalasins represent a leucine-related class.

In this study, secondary metabolites produced by *Aspergillus frequens* were isolated and purified, and their structures were characterized using ECD, HR-ESI-MS, and NMR spectroscopy. Six aspochalasins were isolated, including three new compounds (**1**–**3**) and three known compounds: aspochalasin I (**4**), aspochalasin B (**5**), and aspergillin PZ (**6**). In addition, genomic analysis was performed to investigate the cyt biosynthetic gene cluster. A putative biosynthetic pathway for the isolated compounds was proposed further to explore the role of leucine in cytochalasan scaffold formation. This study expands the chemical profile of secondary metabolites from *A. frequens* and contributes to our understanding of the structural diversity of aspochalasins.

Keyword:

Aspergillus frequens, cytochalasans, aspochalasins, biosynthetic gene cluster

No. PC-079 / 天然物化學組 / Natural Products Chemistry (PC)

Chemical constituents from *Lindera megaphylla* stem and their bioactivities

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Hepatocellular carcinoma (HCC) is a leading cause of cancer-related mortality in Taiwan. Combination approaches utilizing chemotherapy alongside natural compounds have gained attention for their potential to enhance efficacy while reducing adverse reactions. In particular, selective inhibition of nuclear factor erythroid 2-related factor 2 (Nrf2) can sensitize HCC cells to chemotherapy, as Nrf2 promotes cancer cell survival and drug resistance. High-throughput screening of nearly 4,000 methanolic extracts derived from Formosan plant species identified the stem extract of *Lindera megaphylla* Hemsl. as a candidate of interest for further study. This extract demonstrated selective inhibition of Nrf2 activity in hepatocellular carcinoma cells (Huh7) while leaving normal skin cells (HaCaT) unaffected. Additionally, it suppressed superoxide anion generation and elastase release in fMLP/CB-induced human neutrophils, indicating considerable anti-inflammatory potential. *L. megaphylla* is a medium-sized deciduous tree distributed in Taiwan and southern China, and the secondary metabolites from its stem have not been previously investigated. MS/MS-based molecular networking traced the active components to four alkaloid-rich fractions. Therefore, bioactivity-guided isolation was prioritized for these fractions. To date, 11 compounds have been isolated from *L. megaphylla*, including two alkaloids (**1** and **2**), one benzenoid (**3**), six cerebrosides (**4**–**9**), and two steroids (**10** and **11**). Among them, compound **1** is an alkaloid reported to exhibit anti-cancer activity against Huh7 cells, and compound **3** is a reported Nrf2/HO-1 activator and anti-inflammatory agent. These results support the potential of *L. megaphylla* as a valuable source of drug leads for liver cancer therapy and anti-inflammatory applications.

Keyword:

Lindera megaphylla, inflammation, Nrf2, molecular networking

No. PC-080 / 天然物化學組 / Natural Products Chemistry (PC)

Beyond Conventional Chromatography: Exploring the Potential of UHPSFC for Analysis of Quaternary Isoquinoline Alkaloids

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Several isoquinoline alkaloids have demonstrated considerable antiviral potential against animal and human coronaviruses. In our previous studies, selected representatives exhibited promising inhibitory activity in SARS-CoV-2 spike protein-mediated pseudovirus neutralization assays. This study evaluates the applicability of ultra-high-performance supercritical fluid chromatography (UHPSFC) for isoquinoline alkaloid analysis. A total of 22 structurally diverse alkaloids, including quaternary and tertiary protoberberines, protopines, aporphines, and cyclic and acyclic bisbenzylisoquinolines, were selected. Various stationary phases, including unmodified silica and BEH, as well as PFP, CSH PFP, biphenyl, naphthyl, BEH Shield RP18, diol, amide, 2-EP, 2-PIC, 1-AA, and DEA, were systematically screened using different organic modifiers and additives. Initial screening employed a 5–45% organic modifier gradient over 3 min, evaluating neat MeOH, MeOH containing 10 mM ammonium formate or ammonia, and 98% MeOH. Based on chromatographic performance, diol and 2-PIC stationary phases were selected for further optimization. The effects of ACN/MeOH mixtures (25% and 50% MeOH), with or without 10 mM ammonium formate or ammonia, were investigated. Gradient ranges (5–45%, 5–50%, and 5–55%) and durations (3, 5, and 10 min) were subsequently optimized. Additionally, a mixed-mode weak cation-exchange/reversed-phase solid-phase extraction procedure was developed to remove interfering acidic and neutral metabolites from crude barberry extracts. The optimized workflow was successfully applied to non-targeted UHPSFC–UV–MS profiling of various Berberis L. (Berberidaceae) species.

Keyword:
UHPSFC-MS, barberry, quaternary alkaloids

No. PC-081 / 天然物化學組 / Natural Products Chemistry (PC)

Bioactivity-guided isolation of metabolites from the endophytic fungus *Phoma* sp. ST 16

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Cancer has remained the leading cause of death in Taiwan for 43 years, and over 90% of cancer-related deaths result from metastasis through the blood and lymphatic systems. Moreover, current anti-angiogenic drugs are limited by severe adverse effects, while no FDA-approved anti-lymphangiogenic drugs are available. Therefore, developing novel anti-metastatic drugs with fewer adverse effects represents an urgent need in cancer therapy. In preliminary screening, the ethyl acetate layer of liquid fermentate of *Phoma* sp. ST 16, an endophytic fungus isolated from *Scaevola taccada*, exhibited significant anti-lymphangiogenic activity. This strain was then cultivated using the "One Strain Many Compounds" (OSMAC) strategy to maximize metabolite diversity and production. The methanolic extract of nicotinamide-treated solid fermentate showed the most potent dual inhibition of angiogenesis and lymphangiogenesis. UPLC-MS/MS-based molecular networking of extracts from various fermentation conditions, combined with bioactivity-correlated Variable Importance in Projection (VIP) values and structural classification, identified alkaloids and fatty acids as the principal bioactive constituents. Accordingly, this study aims to isolate bioactive compounds from *Phoma* sp. ST 16 via bioactivity-guided fractionation combined with molecular networking, and to evaluate their anti-angiogenic and anti-lymphangiogenic activities. The ethyl acetate layer of liquid fermentate yielded four compounds, including one fatty acid, one carbohydrate, and two cyclic peptides. Additionally, the ethyl acetate layer of solid fermentate afforded eight compounds, including two terpenoids, two steroids, one polyketide, and three benzenoids. The isolates are currently being evaluated for their anti-angiogenic and anti-lymphangiogenic activities, with the aim of addressing unmet needs in anti-metastatic drug development.

Keyword:

Phoma sp. ST 16, anti-lymphangiogenesis, anti-angiogenesis, endophytic fungus, OSMAC approach, molecular networking

No. PC-082 / 天然物化學組 / Natural Products Chemistry (PC)

Elucidating the Biosynthesis of the Bioactive Furofurandione Avenaciolide from Neosartorya fischeri

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Avenaciolides, furofurandione natural products from *Neosartorya fischeri*, are characterized by an α-methylene-γ-lactone cis-fused to an alkylated γ-lactone ring. In this study, we identified and characterized the biosynthetic gene cluster responsible for avenaciolide production in *N. fischeri* (*fis* BGC). Heterologous expression of different *fis* gene combinations in yeast, coupled with in vitro enzymatic assays, enabled the characterization of key pathway intermediates and biosynthetic enzymes. Interestingly, the α-ketoglutarate-dependent dioxygenases, FisJ1 and FisJ2, play distinct roles in pathway progression. These findings reveal a substrate-selection mechanism that maintains pathway fidelity leading to avenaciolide scaffold formation. Furthermore, substrate promiscuity of the upstream enzymes toward different fatty acid chain lengths provides opportunities to generate new avenaciolide derivatives with potentially diverse biological activities.

Keyword:
Neosarotoya fischeri, furofurandione, avenaciolide, heterologous expression, α-ketoglutarate-dependent dioxygenase

No. PC-083 / 天然物化學組 / Natural Products Chemistry (PC)

Secondary metabolites and anti-inflammatory activity from the leaves of *Eugenia uniflora*

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Previous studies by our group identified flavonoid-sesquiterpenoid hybrids with unusual skeletons from Myrtaceae plants. Many of these compounds exhibited anti-inflammatory activity, prompting a search for related metabolites in other Myrtaceae species. In this study, LC-MS/MS-based molecular networking (MN) combined with anti-inflammatory screening was applied to our library of methanolic extracts of Myrtaceae plants from Taiwan. MN analysis suggested the presence of metabolites structurally related to flavonoid-sesquiterpenoid hybrids in the leaves of *Eugenia uniflora* L., which also exhibited anti-inflammatory activity and were selected for further investigation. Following methanolic extraction, solvent partitioning, and fractionation of the ethyl acetate layer, individual fractions were subjected to MN analysis. Because flavonoid-sesquiterpenoid hybrid-related features were primarily annotated as terpenoids in MN analysis, fractions enriched in terpenoid-related features were prioritized for isolation. To date, seven compounds were isolated, including two new sesquiterpenoids: unifloterpene A (**1**), and unifloterpene B (**2**), along with five known compounds. The known compounds were identified as one sesquiterpenoid, istanbulin A (**3**), three triterpenoids: 3-oxo-friedelan-28-oic acid (**4**), betulonic acid (**5**), and 2-deoxy-3,23-O-isopropylidene asiatic acid (**6**), and one chlorophyll: pheophytin a (**7**). The isolated compounds will be evaluated for anti-inflammatory activity. Further MN-guided isolation will continue in search of flavonoid-sesquiterpenoid hybrids from the leaves of *Eugenia uniflora*.

Keyword:

Myrtaceae, *Eugenia uniflora*, anti-inflammatory activity, Molecular networking

No. PC-084 / 天然物化學組 / Natural Products Chemistry (PC)

Repurposing Sterol Methyl Groups: Biosynthesis of Ascosteroside A

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Ascosterosides are fungal lanostane triterpenoid glycosides whose aglycone carries an exocyclic methylene at C4, a motif that, to our knowledge, no gene or enzyme has been shown to install in any organism. Sterol maturation removes the C4 and C14 methyl groups across eukaryotes, so these compounds depart from an otherwise highly conserved route, and they are bioactive: ascosteroside A is fungistatic against yeasts and filamentous fungi, and ascosterosides C and D inhibit mitochondrial respiration. How they are assembled has not been described. We sequenced the genome of *Ascotricha amphitricha*, identified a 41.5-kb, 15-ORF tailoring locus (*asc*) that encodes no scaffold-forming cyclase, and therefore reconstituted the pathway heterologously in *Aspergillus nidulans*, whose own sterol metabolism supplies the triterpenoid precursor. Eight genes from the locus were distributed across three self-replicating vectors with different selection markers, so that a single transformant could carry any combination of them, extracts from sixteen such strains were compared by LC-MS, and the new metabolites were isolated and characterized by 1D and 2D NMR. Matching gene sets to products allows the order of the tailoring steps to be proposed. The work identifies the genetic basis of a sterol modification with no described precedent and establishes a heterologous system in which these scaffolds and their analogues can be produced, a starting point for exploring 4-methylene sterols as antifungal leads.

Keyword:
ascosterosides, 4-methylene sterol, biosynthetic gene cluster, heterologous expression, Aspergillus nidulans

No. PC-085 / 天然物化學組 / Natural Products Chemistry (PC)

Molecular Networking Guided Chemical Investigation of Chengiodendron marginatum Roots Coupled with Anti-Inflammatory Screening

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Phytochemical studies of Oleaceae plants have identified diverse secondary metabolites, including lignans and triterpenoids, with anti-inflammatory activity reported for some constituents. These findings provide a rationale for further investigation of Taiwanese Oleaceae plants. In this study, LC-MS/MS-based multi-informative molecular networking (MIMN) coupled with bioactivity screening was used to guide the targeted isolation of chemical constituents from the roots of *Chengiodendron marginatum* (Champ. ex Benth.) C.B.Shang, X.R.Wang, Yi F.Duan & Yong F.Li. Preliminary screening of 36 Oleaceae extracts from the Taiwanese plant extract library maintained by the Laboratory of Medicinal Botany at Kaohsiung Medical University showed that the methanolic root extract of *C. marginatum* (CMRM) inhibited TNF-α-induced MMP-9 activity in human retinal pigment epithelial (ARPE-19) cells at 50 μg/mL. Based on these findings, the roots were selected for further phytochemical investigation. Following large-scale extraction, solvent partitioning, and the ethyl acetate layer of CMRM was separated into 14 subfractions. Bioactivity-coupled MIMN analysis guided the selection of shikimate- and phenylpropanoid-related clusters for targeted isolation. Further MIMN-guided targeted isolation yielded nine known compounds, comprising eight lignans (**1**–**8**) and one benzofuran derivative (**9**). Their structures were identified by NMR, UV, IR, and MS analyses. These findings illustrate how bioactivity-coupled MIMN can connect candidate metabolite clusters with their source fractions to guide targeted isolation. The isolated constituents provide a basis for subsequent compound-level evaluation in retinal inflammation-related assays.

Keyword:
Chengiodendron marginatum, molecular networking, bioactivity-guided isolation, anti-inflammatory activity, lignans

No. PC-086 / 天然物化學組 / Natural Products Chemistry (PC)

Mass spectrometry-guided discovery of anti-inflammatory constituents from Syzygium tripinnatum

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Molecular networking (MN), a mass spectrometry-based strategy, enables targeted and efficient isolation of metabolites. We applied this approach to *Syzygium tripinnatum*, whose methanolic extract inhibited superoxide anion generation and elastase release in preliminary screening, prompting further investigation of its anti-inflammatory constituents. MN analysis highlighted three major chemical classes: phloroglucinol derivatives (64.20%, cluster A), triterpenoids (20.30%, clusters B and C), and sesquiterpenoids (8.72%, clusters D and E), all reported to have anti-inflammatory activity. These clusters were therefore prioritized for targeted isolation.

MN-guided isolation of *S. tripinnatum* yielded six phloroglucinol derivatives, 30 triterpenoids, seven sesquiterpenoids, and 11 other metabolites, including 10 new compounds (**1-10**). Notably, the new phloroglucinol–sesquiterpenoid hybrids **1** and **2** possess a rare skeleton previously reported only in the Myrtaceae family. A plausible biosynthetic pathway is proposed for **3**, a triterpenoid with an unusual bis-seven-membered ring skeleton. In bioactivity assays, triterpenoids **19, 30, 31, 35,** and **37** exhibited diverse activities, including inhibition of superoxide anion generation and elastase release, inhibition of osteoclast differentiation, and antiproliferative effects on oral cancer cells. Additionally, phloroglucinol derivative **14** induced Nrf2 activation in human keratinocyte cells.

In conclusion, MN enabled the targeted isolation of new phloroglucinol derivatives (**1-2**) from cluster A, triterpenoids (**4-5, 7-8**) from clusters B and C, and sesquiterpenoids (**9-10**) from clusters D and E, demonstrating its effectiveness in natural products research. Furthermore, these findings identify several compounds with anti-inflammatory activity and effects relevant to non-communicable diseases, highlighting their potential for pharmacological evaluation.

Keyword:
Syzygium tripinnatum, MS/MS-based molecular networking, anti-inflammatory activity, phloroglucinol derivatives, triterpenoids

No. PC-087 / 天然物化學組 / Natural Products Chemistry (PC)

Bioactive constituents from *Lithocarpus hancei roots with anti-metastatic potential against colorectal cancer*

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Colorectal cancer (CRC) remains a leading cause of cancer-related mortality worldwide, largely due to late detection, metastasis, treatment-related toxicity, and drug resistance. Natural products offer structurally diverse bioactive compounds for the discovery of novel anti-metastatic agents. Although the Fagaceae family, particularly the genus *Lithocarpus*, has shown anti-cancer potential, its chemical composition and anti-metastatic activity remain underexplored. Here, a bioactivity-guided approach integrating MS/MS-based molecular networking with cytotoxicity and migration assays was applied to the roots of the endemic Taiwanese species *Lithocarpus hancei* (Benth.) Rehder. Active fractions with cytotoxicity against human colorectal cancer HCT-116 cells were prioritized for chemical investigation. This strategy led to the isolation of 36 compounds, including (−)-dioxodihydroguaiaretic acid (**2**), a lignan reported for the first time from a natural source, along with 35 known compounds. Among the isolated constituents, one lignan (**10**) and two triterpenoids (**17** and **18**) exhibited time- and concentration-dependent cytotoxicity against HCT-116 cells. Notably, compound **17** also suppressed HCT-116 cell migration at 10 and 25 μM, indicating its anti-metastatic potential. Collectively, these findings demonstrate the utility of bioactivity-based molecular networking for targeted isolation and highlight *L. hancei* as an understudied source of bioactive constituents with potential against CRC metastasis.

Keyword:

Lithocarpus hancei, Molecular networking, Colorectal cancer, Anti-metastatic activity

No. PC-088 / 天然物化學組 / Natural Products Chemistry (PC)

GC-MS Analysis of the Composition of the Essential Oil from Sweet orange (Citrus sinensis) and potential therapeutic effects in Alzhermer`s disease (AD)

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Sweet orange (Citrus sinensis) essential oils were analyzed using gas chromatography-mass spectrometry (GC-MS) to identify the chemical compounds responsible for their distinctive aroma and flavor. The chromatographic separation was performed under optimal temperature conditions using a standard capillary column coated with 5% phenyl and 95% methyl polysiloxane (30 m × 0.25 mm i.d., 0.25 μm film thickness). The chemical profile revealed that grapefruit essential oil consists predominantly of D-limonene (96.54%) and β-myrcene (3.46%), mirroring the high concentrations typically found in grapefruit oil.

Prior studies have demonstrated that D-limonene possesses significant anti-inflammatory, wound-healing, and potential anti-cancer properties. Given that both grapefruit and sweet orange essential oils contain high concentrations of this neuroprotective compound, both oils represent promising candidates for developing alternative therapeutic strategies for Alzheimer’s disease.

Keyword:

Sweet orange essential oil, Gas chromatography-mass spectrometry (GC-MS), D-limonene, Neuroprotection, Alzheimer’s disease

No. PC-089 / 天然物化學組 / Natural Products Chemistry (PC)

Isolation of anti-inflammatory secondary metabolites from ＜i＞ Clausena lansium</i> guided by bioactivity-based molecular networking

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Inflammation is a defense mechanism to eliminate pathogens. However, excessive activation can contribute to serious diseases. Despite the availability of various anti-inflammatory drugs, their clinical use is limited by adverse effects. The ethanolic extract of the stem bark of *Clausena lansium* (Lour.) Skeels, a traditional Chinese medicine, inhibited fMLP/CB-induced superoxide anion generation and elastase release in human neutrophils, with IC_{50} values of 99.87 ± 1.25 and 92.06 ± 6.15 μM, respectively. Based on these findings, molecular networking (MN) was applied to guide further investigation of constituents with potential anti-inflammatory activity. MN analysis of the ethyl acetate fraction from *C. lansium* highlighted molecular clusters putatively annotated as amino acid and peptide derivatives and alkaloids, which were prioritized for targeted isolation. To date, 32 compounds have been isolated from *C. lansium*, including two new furocoumarins (**1**-**2**), four new carbazole alkaloids (**3**-**6**), two new monoterpenoids (**7**-**8**), and 24 known compounds (**9**–**32**). Among them are five amino acid and peptide derivatives (**22**-**26**) and five alkaloids (**3**, **6**, **27**, **30**-**31**). The current isolation results are consistent with the prioritization of alkaloid-related clusters and provide additional compounds for anti-inflammatory evaluation. Further MN-guided isolation of the remaining fractions and evaluation of the isolated compounds for their anti-inflammatory activities are in progress. Additionally, preliminary evaluation showed that **12** exhibited anti-systemic lupus erythematosus (anti-SLE) activity, and **1**, **11**, **12**, and **27** showed significant cytotoxicity against the RPMI 8226 cell line. These findings demonstrate the multifaceted bioactive potential of *C. lansium* for future development.

Keyword:

Clausena lansium, molecular networking, anti-inflammation, anti-systemic lupus erythematosus, RPMI 8226 cell line

No. PC-090 / 天然物化學組 / Natural Products Chemistry (PC)

Bioassay-Guided Chemical Investigation of Phanera sirindhorniae Leaves Assisted by Molecular Networking

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Phanera sirindhorniae (*Bauhinia sirindhorniae*), a medicinal plant endemic to Thailand, has traditionally been used to relieve muscular pain and inflammation. Earlier phytochemical investigations focused on its stems and roots, whereas the individual constituents contributing to the anti-inflammatory activity of its leaves remain incompletely characterized. This study aimed to investigate the chemical constituents of *P. sirindhorniae* leaves and identify fractions with NF-κB inhibitory activity through bioassay-guided isolation assisted by molecular networking. Dried leaves were sequentially extracted with *n*-hexane, ethyl acetate, methanol, and 70% aqueous methanol. The *n*-hexane and ethyl acetate extracts were combined and fractionated by silica gel open-column chromatography. The resulting fractions were screened for anti-inflammatory activity and LC-MS/MS molecular networking. Several fractions reduced NF-κB reporter activity, with fractions 15 and 16 showing inhibition of 83.7% and 94.2%, respectively. Fraction 15 showed the strongest inhibitory activity in the ICAM-1 assay, while fraction 16 was also active. The combined bioassay and molecular networking analysis prioritized clusters putatively annotated as shikimates and phenylpropanoids for further chemical investigation. Purification of the selected fractions yielded 15 known compounds, comprising 12 flavonoids, one α-tocopherol, one benzenoid, and one monoterpenoid hydroxylactone. These findings demonstrate how molecular networking integrated with fraction bioactivity data can guide chemical investigation of *P. sirindhorniae* leaves. Further evaluation of the isolated compounds is needed to determine their contributions to the observed fraction activity.

Keyword:
Phanera sirindhorniae, molecular networking, bioassay-guided isolation, anti-inflammatory activity, flavonoids

No. PC-091 / 天然物化學組 / Natural Products Chemistry (PC)

Molecular Networking-Guided Investigation of Stilbenoids and Other Secondary Metabolites from the Bark of Shorea megistophylla

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Stilbenoids, particularly resveratrol oligomers, are characteristic secondary metabolites of the genus *Shorea* (Dipterocarpaceae) with diverse biological activities. In this study, molecular networking was employed to profile the ethyl acetate (SCE) and methanol (SCM) extracts of *Shorea megistophylla*, targeting structurally related stilbenoids. Following methanol/n-hexane partitioning, the methanol fraction was separated using silica gel, Sephadex LH-20, C18 reversed-phase MPLC, and HPLC, yielding six compounds **1–6**. Spectroscopic analysis identified compound **1** as the resveratrol trimer pauciflorol A and compound **3** as the resveratrol tetramer vaticanol B. Compound **2** exhibited the same planar structure as pauciflorol B, but its specific rotation differed from reported values, suggesting a possible stereochemical difference. Similarly, compound **6** , a resveratrol tetramer, shared the planar structure of vaticanol C but showed potential stereochemical differences requiring further confirmation. Compounds **4** and **5** were identified as 4-hydroxybenzaldehyde and β-sitosterol, respectively. Given the reported antioxidant, enzyme-inhibitory, antiviral, and anti-inflammatory activities of oligostilbenoids, the biological potential of secondary metabolites from *S. megistophylla* warrants further investigation.

Keyword:

Shorea megistophylla, Molecular networking, Stilbenoids, Resveratrol oligomers, Biological activities

No. PC-092 / 天然物化學組 / Natural Products Chemistry (PC)

Elucidation of the Biosynthetic Pathway of Fungal Furo[2,3-b]furanone-Containing Drimane-Type Sesquiterpene–Amino Acid Hybrid Natural Products

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The furo[2,3-*b*]furanone scaffold is a complex structural motif found in more than 100 natural products exhibiting diverse biological activities. Despite its widespread occurrence, the detailed biosynthetic steps underlying the formation of this scaffold have yet to be elucidated. Schizines A and B are unique drimane-type sesquiterpene (DTS)–amino acid hybrid natural products isolated from the fruiting bodies of *Schizophyllum commune*, featuring both furo[2,3-*b*]furanone and iminolactone moieties. They exhibit selective cytotoxicity toward cancer cells over non-tumor cells, suggesting their potential as anticancer leads. In this study, we identified the biosynthetic gene cluster responsible for schizines A and B biosynthesis and elucidated the complete pathway through heterologous expression and *in vitro* enzymatic characterization.

Keyword:
Schizines, drimane-type sesquiterpenes, Furo[2,3-b]furanone, iminolactone

No. PC-093 / 天然物化學組 / Natural Products Chemistry (PC)

Development and Optimization of a Computational Workflow for Bioactive Feature Prioritization and Identification in Natural Product Discovery

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Traditional methods for isolating active compounds from natural products are slow, expensive, and often result in the rediscovery of known molecules. To address this, an integrated computational workflow was developed to identify key bioactive compounds directly from LC-MS/MS data before performing physical separation. Raw mass spectrometry files were preprocessed in MZmine and grouped into molecular families using Feature-Based Molecular Networking (FBMN) on GNPS. Features were then filtered and ranked using a multi-metric scoring model that accounts for bioactivity correlation, false discovery rates, and variable importance scores, followed by cluster-level evaluations. This prioritized three top clusters with five candidate features each. These high-priority networks were then visualized in Cytoscape, and structural identification of these candidate features was performed using SIRIUS, MS-FINDER, and MetFrag, keeping up to the top 10 candidates from each tool. Candidates were then filtered by precursor mass accuracy and synthetic-compound removal. This yielded 109 unique candidate structures across 10 features. Each candidate was then rescored using a weighted composite score accounting for spectral cosine similarity, cross-tool candidate recurrence, and its original rank within each prediction tool. The top 3 candidates per feature were selected, of which 2 are commercially available for purchase and experimental validation.

Keyword:
Computational Metabolomics, Feature-Based Molecular Networking, Activity-Annotated Molecular Networking, Bioactivity-Based Molecular Networking, Bioactivity Mapping, Natural Product Discovery

No. PC-094 / 天然物化學組 / Natural Products Chemistry (PC)

Molecular Basis of Azetidine Ring Formation by the Fe(II)/α-KG-Dependent Dioxygenase OkaE in Okaramines Biosynthesis

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Okaramines are bioactive indole alkaloids derived from L-tryptophan, produced by *Penicillium* and *Aspergillus* species. They are notable for a complex polycyclic scaffold that includes a rare azetidine ring. In their biosynthesis, the enzyme OkaE, a non-heme iron and α-ketoglutarate-dependent dioxygenase, forms this strained four-membered ring. Although recent studies have revealed the unusual multifunctionality of OkaE, the structural basis for its control of sequential oxidation and cyclization has remained unclear. In this study, we combined X-ray crystallography, molecular docking, and site-directed mutagenesis to investigate the catalytic basis of OkaE function. Structural analyses of the *apo* and *holo* forms revealed an active-site architecture that supports substrate stabilization, intermediate recognition, and precise positioning for azetidine-ring formation. Mutational studies confirmed the importance of this structural framework for product formation. Three new okaramines were purified and elucidated from the enzymatic reactions. Together, these results provide new mechanistic insight into OkaE catalysis and the biosynthesis of azetidine rings in fungal indole alkaloid pathways.

Keyword:
biosynthesis, non-heme iron enzymes, dioxygenases, okaramine, azetidine

No. PC-095 / 天然物化學組 / Natural Products Chemistry (PC)

Total synthesis of the (2S,3R)-Δ7,8 Vitroprocine A isomer and its application in antibiotic assays and biosynthetic enzyme studies

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Vitroprocines A–J are amino-polyketide antibiotics from the marine bacterium, *Vibrio* sp. QWI-06 (Dapeng Bay, Taiwan), discovered through imaging mass spectrometry, molecular networking, and bioactivity-guided fractionation. They show potent activity against *Acinetobacter baumannii*, with vitroprocine A exhibiting a MIC of ≤8 μg/mL, comparable to ceftazidime and ticarcillin. SAR analysis identified a para-substituted phenol, short aliphatic chain, chain double bond, and free amine as essential for activity. Biosynthetically, the PLP-dependent α-oxoamine synthase VsAOS-2 catalyzes decarboxylative condensation of L-tyrosine with lauroyl-CoA, and the oxidoreductase VsOR reduces the resulting ketone to an amino alcohol, and these intermediates were characterized by HR-ESI-MS and fragmentation analysis, but authentic standards remain unavailable. To address this, we pursue the enantioselective total synthesis of a Δ7,8 double-bond positional isomer of vitroprocine A, retaining the natural (2S,3R) amino alcohol core, for comparison with the natural Δ6,7 isomer. From commercially available 4-hydroxybenzaldehyde and but-3-yn-1-ol, the aromatic head group, chiral amino alcohol core, and aliphatic tail are assembled as separate fragments via a convergent strategy. Key intermediates were obtained in moderate yields and characterized by NMR and TLC, separation and stereochemical assignment of the amino alcohol stereoisomers are ongoing. The synthetic product will be evaluated against five indicator pathogens and serve as an authentic standard and substrate probe in in vitro VsAOS-2 and VsOR assays to probe enzyme-mediated ketone reduction, substrate recognition, and stereochemical control at C-3. This work integrates total synthesis and biosynthetic enzymology to advance vitroprocine research and engineered biocatalyst development.

Keyword:

total synthesis, vitroprocine A, Acinetobacter baumannii, antibacterial assay, biosynthetic enzymes, marine natural products

No. PC-096 / 天然物化學組 / Natural Products Chemistry (PC)

New Scalarane-Type Sesterterpenoids from the Marine Sponge Lendenfeldia sp. and Their Inhibitory Effects on HepG2 Cell Viability

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Following our previous report on the chemical constituents of the marine sponge *Lendenfeldia* sp., further investigation of the same specimen yielded three additional undescribed scalarane-type sesterterpenoids, designated lendenborvicins F-H (**1**-**3**). The structures of the new compounds were elucidated through comprehensive spectroscopic analyses, including 1D and 2D NMR and high-resolution electrospray ionization mass spectrometry (HRESIMS), while their absolute configurations were established by electronic circular dichroism (ECD) spectroscopy. The isolated compounds were evaluated for their inhibitory effects on the human hepatocellular carcinoma cell line HepG2 using the MTT assay after 72 h of treatment. Lendenborvicins F-H exhibited inhibitory effects on HepG2 cell viability at concentrations ranging from 5 to 40 μM. Among the three compounds, lendenborvicin F showed the strongest inhibitory activity, with an IC_{50} value of 28.25 μM. These findings expand the chemical diversity of scalarane-type sesterterpenoids from *Lendenfeldia* sp. and add to the growing evidence of the biological potential of this class of marine natural products.

Keyword:
Lendenfeldia sp., Scalarane-type, Sesterterpenoids, Electronic circular dichroism, HepG2 cell viability

No. PC-097 / 天然物化學組 / Natural Products Chemistry (PC)

Polyketide-Derived Antimicrobial Metabolites from *Epicoccum sorghinum*: Effects of Fermentation Conditions and Non-Thermal Atmospheric Pressure Plasma (NTAPP)

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Epicoccum sorghinum is a filamentous fungus known to produce structurally diverse secondary metabolites. In this study, a fungal strain isolated from Arundo donax was investigated for its antimicrobial metabolites and the effects of fermentation conditions and non-thermal atmospheric pressure plasma (NTAPP) treatment on metabolite production. Nine previously reported polyketide-related compounds isolated from *E. sorghinum* were evaluated for their antimicrobial activity against 16 microbial strains. Among the tested compounds, 6-(hydroxymethyl)benzene-1,2,4-triol (**7**) exhibited the strongest antimicrobial activity among the isolated metabolites, particularly against the Gram-positive bacterium *Staphylococcus epidermidis* ATCC 12228 (MIC = 50 μM). Several compounds showed moderate antifungal activity against *Nakaseomyces glabrata* ATCC 2001. A preliminary structure–activity relationship (SAR) analysis suggested that antimicrobial activity is closely associated with the number and positional arrangement of phenolic hydroxyl groups. Fermentation conditions significantly affected metabolite accumulation. Compound **7** showed significantly higher accumulation under solid fermentation, suggesting that solid fermentation favors the accumulation of certain phenolic-type metabolites. In addition, NTAPP treatment altered the relative abundance of previously detected metabolites in an energy-dependent manner. High-energy treatment (6000 V) increased the abundance of several metabolites, particularly epicorepoxydon A (**1**), whereas only a slight increase was observed for **7**. Overall, this study demonstrates the antimicrobial activity of polyketide-related metabolites from *E. sorghinum* and highlights the influence of fermentation conditions and NTAPP treatment on fungal secondary metabolism. The combination of fermentation optimization and NTAPP stimulation represents a useful strategy for modulating the relative abundance of bioactive secondary metabolites without inducing the production of new detectable metabolites.

Keyword:
Epicoccum sorghinum, polyketides, antimicrobial activity, fermentation, non-thermal plasma, secondary metabolites

No. PC-098 / 天然物化學組 / Natural Products Chemistry (PC)

Isolation and Characterization of Bioactive Metabolites from Uvaria micrantha with Anti-Inflammatory and Osteogenic Activities

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To bridge natural product chemistry with translational medicine, the phytochemical repertoire and therapeutic potential of *Uvaria micrantha* were systematically investigated. Extraction and purification of the aerial parts afforded one undescribed metabolite, uvarisinyicone, along with 22 previously reported phytochemicals, including chalcones, dihydrochalcones, flavonoids, and benzenoids. Metabolite annotation and network mapping *via* LC–MS/MS and GNPS feature-based molecular networking (FBMN) successfully validated the chemical clustering of the isolated scaffolds. Pharmacological screening uncovered two primary bioactivity axes: anti-neuroinflammatory regulation and osteogenic modulation. Distinct compound-specific profiles were observed, particular isolates selectively inhibited IL-6 expression, whereas others exerted dual-cytokine suppression or stimulated osteoblast maturation. Discovery of uvarisinyicone alongside functional flavonoid and chalcone derivatives enriches the chemodiversity of *Uvaria* and unveils its osteogenic potential.

Keyword:
Traditional medicine, Osteogenesis agents, GNPS, Anti -inflammatory agents, Natural products

No. PC-099 / 天然物化學組 / Natural Products Chemistry (PC)

Study and Application of the Secondary Metabolites Resource of Crown-of-Thorns Starfish in South Penghu Marine National Park

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Crown-of-thorns starfish (Acanthaster planci) is regarded as a potential source of marine natural products, including bioactive steroidal saponins. Recently, its occurrence around the Four Southern Islands of Penghu has raised concerns about coral reef conservation because it is a corallivorous predator that can cause extensive coral mortality during population outbreaks. Therefore, with the goal of transforming an ecological threat into a valuable marine natural resource and for new drug discovery, we aim to characterize saponins from specimens collected near Dongji Islet, Xiji Islet, and Qimei Township and to assess their potential biological activities. The collected specimens will be lyophilized, ground, and extracted with ethyl acetate and methanol. The extracts will undergo liquid–liquid partitioning and chromatographic fractionation, followed by high-performance liquid chromatography (HPLC) to purify saponins from glycoside-rich fractions. The structure of isolated compounds will be determined using nuclear magnetic resonance (NMR) spectroscopy and mass spectrometry (MS). Their antibacterial, antiviral, and cytotoxic activities will then be evaluated. By establishing the saponin profiles and biological activities of crown-of-thorns starfish collected in Penghu, this study may identify compounds for further pharmacological investigation and provide a potential use for starfish removed during reef management.

Keyword:
Acanthaster planci、saponins、antibacterial activity, antiviral activity, cytotoxic activity

No. PC-100/ 天然物化學組 / Natural Products Chemistry (PC)

Characterization of Compounds from *Blumea balsamifera* (L.) DC. (Sambong) Leaves Involved in the Modulation of Calcium Oxalate Formation in Artificial Urine

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Blumea balsamifera (sambong) is a medicinal plant approved as drug with the inclusion of its tablet dosage form in the current Philippine National Formulary. Despite its approved clinical use, the exact compounds responsible for the diuretic and anti-urolithic properties are yet to be reported. The available reports are limited to mostly anti-urolithiasis, diuresis or inhibition of calcium oxalate formation of crude extracts of the leaves. This work sought to identify the group of secondary metabolites responsible for the prevention and/or modification of calcium oxalate crystal formation. In this study, the crude methanol extract of dried powdered leaves was partitioned into *n*-hexane, ethyl acetate, and water fractions. These fractions were subjected to *in vitro* nucleation and aggregation assays where the quality and number of calcium oxalate crystals formed were examined by microscopy. None of the fractions yield conclusive evidence of inhibition of aggregation of any calcium oxalate crystals formed, meanwhile, the ethyl acetate fraction showed prevention of formation of calcium oxalate nuclei. Phytochemical screening and thin layer chromatography (TLC) analysis revealed the presence of flavonoids in this fraction, however, further isolation and determination of the activity should be done to confirm the activity and identify the active compounds. These will provide not only additional evidence of its prescribed clinical use, it will also improve the current methods for quality control of sambong raw materials and finished products. This will enable designation of markers of biological activity in addition to markers of identity, for the standardization of sambong raw materials and finished products. This will eventually enhance consumer trust for effective therapeutic preparations of *B. balsamifera.*

Keywords: *B. balsamifera*, calcium oxalate crystal, nucleation, aggregation, artificial urine

No. PC-101 / 天然物化學組 / Natural Products Chemistry (PC)

Isolation and Identification of an Antibacterial Compound in Sea Grapes (*Caulerpa chemnitzia* (Esper) J.V.Lamouroux)

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Antimicrobial resistance (AMR) remains as a global health concern, highlighting the need for novel antibacterial agents from alternative sources. Marine organisms, including seaweeds, are recognized as reservoirs of diverse bioactive secondary metabolites. In the Philippines, *Caulerpa chemnitzia* (Esper) J.V. Lamouroux, locally known as sea grapes, is harvested and consumed for its taste and texture, but it remains relatively underexplored for its bioactive constituents. This study aimed to isolate and elucidate the structures of antibacterial compounds from *C. chemnitzia* against *Staphylococcus aureus* ATCC 29213. The crude ethanolic extract of *C. chemnitzia* was subjected to liquid-liquid partitioning, and the ethyl acetate fraction was fractionated through open-column chromatography using *n*-hexane and acetone. Fractions with similar thin-layer chromatography (TLC) profiles were pooled and further purified through successive chromatographic separations. TLC-Contact Bioautography (TLC-CB) was employed to guide the isolation of antibacterial compounds against *S. aureus*. Bioactive fractions were analyzed using liquid chromatography–time-of-flight mass spectrometry (LC-ToF/MS) and compared with entries in the Personal Compound Database and Library (PCDL) to facilitate compound identification and isolation. Isolated compounds were subsequently subjected to nuclear magnetic resonance (NMR) spectroscopy for structural elucidation. Pooled fractions 1.1.1 and 2.1.2.2 exhibited antibacterial activity against *S. aureus* in TLC-CB. LC-ToF/MS analysis facilitated the characterization and selection of candidate compounds for isolation. NMR spectroscopy enabled the structural elucidation of hexadecanoic acid from pooled fraction 1.1.1 and octadecane from pooled fraction 2.1.2.1. Overall, the integration of bioautography-guided fractionation, chromatographic separation, LC-ToF/MS, and NMR spectroscopy enabled the isolation and structural elucidation of compounds from *C. chemnitzia*, contributing to the characterization of its antibacterial constituents.

Keywords:
Antibacterial, *Caulerpa chemnitzia*, TLC, Bioautography, LC-ToF/MS, NMR spectroscopy

No. PC-102 / 天然物化學組 / Natural Products Chemistry (PC)

Integrating *in vitro* bioassays and *in silico* screening to identify natural Nrf2 activators

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This study combined cell-based assays and computational screening to identify natural activators of nuclear factor erythroid 2-related factor 2 (Nrf2). Thirty crude extracts and fractions from five Vietnamese medicinal plants were evaluated at 100 μg/mL using an Nrf2 luciferase reporter assay in HaCaT cells. Machine-learning models trained on 613 ChEMBL compounds screened 99 phytochemicals, followed by molecular docking, molecular dynamics simulations, and LC-QTOF-MS/MS profiling. *Phyllanthus amarus* methanolic stem extract produced relative Nrf2 activity exceeding 900% of the vehicle control. The support vector machine model with Morgan3 fingerprints achieved 0.87 accuracy, 0.93 area under the receiver operating characteristic curve, and 0.89 F1 score, predicting 16 active compounds. Geraniin, corilagin, and *β*-sitosterol-3-O-*β*-D-glucopyranoside yielded the most favorable docking scores of −12.2, −11.7, and −10.8 kcal/mol, respectively. Molecular dynamics supported stable interactions between corilagin and Keap1, while LC-QTOF-MS/MS tentatively identified corilagin in *P. amarus* stem extract.

Keyword:
Nrf2, Keap1, natural products, machine learning, corilagin

No. PC-103 / 天然物化學組 / Natural Products Chemistry (PC)

Exploring the Antifouling Potential of Natural Compounds Using the Striped Barnacle (Amphibalanus amphitrite)

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This study investigated the antifouling potential of natural compounds using the widely distributed fouling organism, the striped barnacle (*Amphibalanus amphitrite*). Egg masses were collected from Gushan Fishing Port in Kaohsiung, Taiwan, and hatched larvae were reared to the cyprid stage. The natural settlement behavior of cyprid larvae was then exploited to evaluate the antifouling efficacy of the tested natural compounds by assessing their inhibitory effects on larval settlement.

Keyword:
Barnacle,natural compounds,Fouling Organisms

No. PC-104 / 天然物化學組 / Natural Products Chemistry (PC)

Chemical constituents from a fungal strain Cercospora beticola Km3725 derived from Colpomenia sinuosa

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Chromatographic investigation of the liquid-state fermented products of *Cercospora beticola* Km3725, a fungal strain derived from the marine brown algae *Colpomenia sinuosa*, led to the isolation of nine compounds **1**–**9**. Their structures were comprehensively elucidated via extensive spectroscopic analysis, revealing four previously undescribed polyketides, designated as cercosproric acids A and B (**1** and **2**) and cercosporines A and B (**3** and **4**), along with myxotrichin C (**5**), anhydrofulvic acid (**6**), penialidin F (**7**), myxotrichin B (**8**), and hydroxy-2-hydroxymethyl-5-methyl-4*H*-chromen-4-one (**9**). In biological evaluations, compound 1 exhibited antibacterial activity against the Gram-negative marine pathogens *Vibrio alginolyticus* and *Aeromonas hydrophila*, yielding inhibition zones of 1–3 mm at 10,000 ppm via disc agar diffusion assays. Furthermore, compounds **3**, **5**, and **9** demonstrated moderate anti-inflammatory modulation by suppressing nitric oxide (NO) production in lipopolysaccharide-induced murine BV-2 microglial cells, exhibiting inhibition rates of 35.2%, 47.5%, and 40.8% at 20 μM, respectively, with no detectable cytotoxicity. Notably, compound **5** displayed potent neuroprotective potential through significant acetylcholinesterase (AChE) inhibitory activity, possessing an IC_{50} value of 5.38 μM.

Keyword:
Colpomenia sinuosa, Cercospora beticola, cercosproric acid, cercosporine, anti-inflammation, anti-acetylcholinesterase

No. PC-105 / 天然物化學組 / Natural Products Chemistry (PC)

Elgonene O and Other Secondary Metabolites from the Marine Alga-Associated Fungus Koorchaloma bambusae SC1014 and Their Neuroprotective Activities

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Marine-derived fungi are promising sources of structurally diverse and biologically active secondary metabolites. In this study, six metabolites, including a previously undescribed compound, elgonene O (**1**), and five known compounds (**2–6**), were isolated from the ethyl acetate extract of liquid-fermented cultures of *Koorchaloma bambusae* SC1014, an endophytic fungus isolated from the brown alga *Sargassum cristaefolium*. Their structures were elucidated using HRESIMS and one- and two-dimensional NMR spectroscopy. The structure and absolute configuration of elgonene O were further established by single-crystal X-ray diffraction. The neuroprotective activities of compounds **1–6** were evaluated in human SH-SY5Y neuroblastoma cells exposed to 6-hydroxydopamine (6-OHDA), a commonly used cellular model of Parkinson's disease-related neurotoxicity, using the CCK-8 assay. Among the isolated metabolites, (*R*)-(−)-mellein (**3**) exhibited the most pronounced protective effect against 6-OHDA-induced cell injury. Further flow cytometric analyses using DHE and JC-1 staining indicated changes in oxidative stress-associated fluorescence and mitochondrial membrane potential following co-treatment with compound **3**. These findings highlight the chemical diversity of *K. bambusae* SC1014 and identify (*R*)-(−)-mellein as a candidate for further investigation of its neuroprotective properties.

Keyword:

Marine-derived fungi, **Koorchaloma bambusae**, Elgonene O, Neuroprotection, Oxidative stress

No. PC-106 / 天然物化學組 / Natural Products Chemistry (PC)

Development and Comparative Evaluation of Chrysin-Loaded Nanoparticles and Nanoemulsions for Enhanced Aqueous Solubility and Skin Delivery

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Chrysin, a flavonoid with low solubility in water, shows potential for topical use. This study focused on developing and comparing chrysin-loaded nanoparticles and nanoemulsions to enhance its solubility in water and promote effective skin delivery. Nine nanoparticle formulations (NP-1–NP-9) were prepared by planetary ball milling using hydroxypropyl-β-cyclodextrin and polyvinylpyrrolidone as carriers, while two nanoemulsion formulations (NE-1 and NE-2) were prepared by high-shear homogenization. The formulations were evaluated for appearance, particle or droplet size, chrysin content, entrapment efficiency, and apparent aqueous solubility. NP-3 exhibited an apparent aqueous solubility of 927.5 ± 9.3 μg/mL, while NE-2 showed the highest apparent aqueous solubility among the nanoemulsion formulations at 938.2 ± 3.2 μg/mL. NP-3 and NE-2 were selected for a skin-permeation study using porcine skin on Franz diffusion cells, with pure chrysin as the comparator. NP-3 tended to exhibit greater chrysin permeation than NE-2. These findings suggest that both formulation approaches improve the apparent aqueous solubility of chrysin, while NP-3 shows potential for further development as a topical delivery system.

Keyword:
Chrysin, Nanoparticles, Nanoemulsions, Aqueous solubility, Skin permeation

No. PP-003 / 天然物藥理組 / Natural Products Pharmacology (PP)

Therapeutic Potential of Pre-germinated Brown Rice and γ-Oryzanol in Accelerating Wound Repair in Diabetic Rats

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In our previous studies, pre-germinated brown rice (PGBR) and its extract (EP) were proved to ameliorate metabolic syndrome and diabetes. Now, we investigated their effects on abnormal wound healing in diabetic SD rats. Diabetes was induced by feeding high-fat diet (HFD) and injecting streptozocin (STZ) and nicotinamide (NA). And then divided into an untreated group, and treatment groups, including oral gavage metformin (100mg/kg), EP (2.5 mg/kg), or γ-oryzanol (2.5 mg/kg), or feeding a modified HFD in which carbohydrates replacing with PGBR. After two weeks, the wounds (0.2 to 0.3 cm deep) were created on the backs of all rats. At this time, some untreated rats were applied with silver sulfadiazine ointment to wounds. The wound healing was monitored for an additional two weeks. All treatment groups, except for the ointment, had improvements in abnormal biochemical parameters and wound healing. Notably, all treatment groups had obvious upregulation expression of HIF-1α, TGF-β1, VEGF, Bcl-2 and collagen-1 proteins, indicating enhanced tissue repair responses. In in vitro experiments, insulin resistance inhibited the cell growth, whereas metformin, EP, γ-oryzanol and silver sulfadiazine ameliorated the inhibitory effect. Overall, PGBR and EP improved diabetes and supported wound-related cell growth, highlighting their potential as cereal-derived functional foods.

Keyword:
pre-germinated brown rice, γ-oryzanol, diabetes mellitus, wound healing

No. PP-005 / 天然物藥理組 / Natural Products Pharmacology (PP)

Isolation of Phytochemicals and Exploration of the Anti-Inflammatory Mechanism of Dolichandrone spathacea against Chronic Bronchitis via Network Pharmacology, Molecular Docking, and Experimental Validation

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Dolichandrone spathacea is a traditional medicine used to treat chronic bronchitis (CB) in Vietnam and India, yet its phytochemicals and mechanisms of action remain poorly characterized. This study aimed to isolate bioactive compounds from D. spathacea and elucidate their potential mechanisms against CB through network pharmacology, molecular docking, and in vitro validation. Three compounds—beta-sitosterol, 6-O-trans-p-coumaroyl ajugol, and 6-O-[(E)-4-methoxycinnamoyl]catalpol—were isolated from the ethyl acetate fraction, with beta-sitosterol reported for the first time in this species. Combined with 56 compounds from the literature, 59 phytochemicals were analyzed via SwissTargetPrediction, yielding 66 overlapping targets between D. spathacea and CB-associated genes retrieved from GeneCards and DrugBank. Protein–protein interaction analysis identified eight core targets, including TNF, AKT1, SRC, EGFR, IL2, MMP-9, HSP90AA1, and PTGS2, with TNF, MMP-9, and PTGS2 enriched in both TNF and IL-17 signaling pathways. Molecular docking revealed that six key bioactives—luteolin, dolichandrone B, salvionoside B, uncaric acid, oleanolic acid, and ursolic acid—exhibited stronger binding affinities toward TNFR1, COX-2, and MMP-9 than the reference drug aspirin. In vitro experiments using LPS-stimulated RAW 264.7 macrophages confirmed that the ethanol extract dose-dependently inhibited nitric oxide production (IC_{50} = 25.34 μg/mL) and suppressed TNF-α and IL-1β secretion, with efficacy comparable to aspirin at 100 μg/mL. These findings provide the first integrated evidence linking the phytoconstituents of D. spathacea to TNF and IL-17 signaling pathways, supporting its therapeutic potential as a candidate for chronic bronchitis and inflammatory disease management.

Keyword:
Dolichandrone spathacea, chronic bronchitis, network pharmacology, molecular docking, anti-inflammatory, phytochemical isolation

No. PP-006 / 天然物藥理組 / Natural Products Pharmacology (PP)

Investigating ANO1 Inhibition as a Therapeutic Strategy for NSCLC and Prostate Cancer

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Anoctamin 1 (ANO1 a calcium activated chloride channel CaCC has
emerged as a promising drug target to alleviate various cancer types, including non
small cell lung cancer (and prostate cancer, owing to its elevated expression
in cancer cells ANO1 inhibitors in natural products have demonstrated the anticancer effects, but their
effects of in synergy with other oncogenic targets have not been fully reported This study aimed to elucidate the potential of diminishing ANO 1 protein levels as a robust anticancer approach By employing an innovative approach, we screened a novel ANO1 downregulator PIC, a PI3K inhibitor, via a high throughput yellow fluorescent protein (reduction assay The subsequent investigation assessed effects of PIC in NSCLC and prostate cancer Through in silico molecular docking analyses, we ascertained the superior binding affinity of PIC toward both ANO 1 and PI3K, surpassing that of the control ligand Subsequent immunoblotting experiments validated dose dependent downregulation of ANO 1 protein expression by PIC and showcased a reduction in pAKT levels, indicating effective PI 3 K pathway inhibition Differential cell sensitivity became apparent, with ANO 1 expressing PC 9 and PC 3 cells displaying heightened susceptibility to cell proliferation inhibiting effects exerted by PIC compared to ANO 1 negative Chinese hamster ovary cells and ANO 1 knockout PC 3 cells Our findings emphasize the significance of targeting the ANO 1 and PI3 K pathways as a novel approach to alleviate NSCLC and prostate cancer.

Keyword:
Anoctamin 1 (ANO1), Natural product, anticancer mechanism.

No. PP-007 / 天然物藥理組 / Natural Products Pharmacology (PP)

CX ameliorates metabolic dysfunction-associated steatotic liver disease by modulating AMPK activation, lipidome, and gut microbiota

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Metabolic dysfunction-associated steatotic liver disease (MASLD), the most common liver disease associated with obesity and metabolic syndrome, lacks effective pharmacological interventions for early-stage simple steatosis. CX, a bioactive phytochemical, has been described to promote glucose homeostasis. However, the effects of CX on hepatic steatosis remain unknown. In this study, we evaluated the therapeutic potential of CX for MASLD in high-fat diet (HFD)-induced obese mice. Beyond physiological alterations, we investigated lipidome and gut microbiota modulation by analyzing circulating choline phospholipids via UPLC/MS/MS and the microbiome via 16S rRNA gene sequencing. In HFD-induced obese mice, CX ameliorated hepatic steatosis and promoted the activation of AMP-activated protein kinase (AMPK) in the liver. In addition, CX mitigated insulin resistance, adipocyte hypertrophy, and dyslipidemia. Lipidomic analysis revealed a shift in circulating choline phospholipids, characterized by increased LPC O-14:0 and decreased long-chain PCs and SMs. Additionally, CX preserved colonic architecture and enriched *Akkermansia muciniphila* and *Bacteroides thetaiotaomicron*. Regarding the interplay among host physiology, circulating lipids, and gut microbiota, multivariate multiomics network analysis identified coordinated associations among these bacteria and LPC O-14:0. Furthermore, we evaluated the molecular mechanism of CX in a free fatty acid-induced human hepatocyte model. Specifically, CX mitigated hepatocyte lipid accumulation by promoting AMPK activation. In molecular modeling, CX showed binding capacity in the allosteric drug and metabolite pocket of AMPK. Taken together, we demonstrated that CX shows pharmacological potential for MASLD. Specifically, CX alleviates early-stage simple steatosis in MASLD by modulating hepatic AMPK activation, circulating choline phospholipids, and gut microbiota.

Keyword:
CX, MASLD, Choline phospholipids, Gut microbiota, AMPK activator

No. PP-008 / 天然物藥理組 / Natural Products Pharmacology (PP)

Wound Healing Activity of Topical Herbal Ointment Containing Azadirachta indica Flower Extract: In vitro and in vivo Studies

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Azadirachta indica (neem) has been employed in traditional Indian Ayurvedic medicine for its antibacterial, anti-inflammatory, antioxidant, anticancer, and dermatological properties. However, the wound-healing potential of its flower extracts remains underexplored. This study investigated the wound-healing efficacy of A. indica flower extracts through complementary in vitro and in vivo approaches. Petroleum ether, acetone, and hydroalcoholic extracts were prepared and evaluated for their effect on fibroblast migration using a scratch assay on L929 cells, all three extracts significantly enhanced wound closure relative to untreated controls over a 48-hour observation period (0, 12, 24, and 48 h). Based on these findings, a herbal ointment incorporating neem flower extract was formulated and characterised for pH, spreadability, extrudability, and drug content, all of which conformed to acceptable pharmaceutical standards. The formulation exhibited notable antimicrobial activity, achieving greater than 50% growth inhibition against six bacterial and three fungal strains in vitro. In vivo efficacy was assessed using an excision wound model in Albino Wistar rats, where three formulation variants (FP1, FP2, and FP3) achieved wound contraction rates of 94.5%, 89.3%, and 96.8%, respectively, by the study endpoint. These healing rates were significantly higher than those observed in untreated and reference-standard–treated groups. Collectively, these findings provide preliminary evidence that A. indica flower extract, formulated as a topical ointment, promotes cutaneous wound repair through combined pro-migratory and antimicrobial mechanisms, supporting its further development as a candidate for clinical wound-care applications, pending additional mechanistic and toxicological validation.

Keyword:
Azadirachta indica, Herbal ointment, Scratch assay, Excision Model, Ointment Formulation, Wound healing

No. PP-009 / 天然物藥理組 / Natural Products Pharmacology (PP)

Network Pharmacology and Molecular Docking Reveal the Multi-Target Mechanism of Homalomena occulta against Rheumatoid Arthritis

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease marked by synovial inflammation and progressive joint damage. Homalomena occulta, a traditional medicinal plant, has long been used to relieve joint pain and inflammation, but its active compounds and molecular mechanisms against RA remain unclear.

Objective: To identify the bioactive compounds and potential therapeutic targets of H. occulta against RA using an integrated network pharmacology and molecular docking approach.

Methods: 45 compounds of H. occulta were retrieved from TCMSP, with SMILES structures obtained via PubChem and ChemDraw. Putative targets were predicted using TCMSP and SwissTargetPrediction. RA-related genes were collected from GeneCards and CTD (665 genes), and intersected with compound targets to yield 71 shared genes. These were analyzed via STRING for protein–protein interactions to identify hub genes, followed by GO and KEGG enrichment analysis using g:Profiler. Molecular docking (AutoDock/AutoDock Vina) validated binding affinities between candidate compounds and hub proteins, with poses visualized in Discovery Studio.

Results: Ten hub genes were identified (TNF, PPARG, PTGS2, CASP3, BCL2, IL10, CXCL8, STAT1, TLR2, MMP2). Key mechanisms highlighted included the JAK-STAT signaling pathway, efferocytosis, and lipid/atherosclerosis pathways. Nine candidate compounds — including beta-sitosterol, palmitic acid, and (L)-alpha-terpineol — showed strong correlation with disease-related targets, with docking confirming stable binding interactions.

Conclusion: This integrated approach identifies key bioactive compounds and molecular targets underlying the anti-RA potential of H. occulta, providing a theoretical foundation for further experimental validation.

Keyword:
Homalomena occulta, rheumatoid arthritis, network pharmacology, molecular docking, JAK-STAT signaling pathway

No. PP-010 / 天然物藥理組 / Natural Products Pharmacology (PP)

The potential of phytochemical naringenin in inducing DNA damage and inhibiting autophagy as a cancer chemoprevention strategy for melanoma

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Background/Objective: Skin cancer is causing an increasing health burden worldwide. Melanoma is a highly heterogeneous type of skin cancer that is extremely prone to developing resistance to chemotherapy. Therefore, finding novel drug candidates to control malignant melanoma is crucial. Naringenin is a flavonoid compound found in citrus fruits and has excellent anti-cancer potential. This study aims to compare the effects of naringenin on skin keratinocytes and melanoma cells, and to explore cell morphology and growth activity, cell cycle distribution, genome damage, and autophagy to assess its potential as a chemopreventive and anticancer phytochemical. Materials and Methods: Cell viability, cell cycle distribution, DNA damage, apoptosis, and autophagy were evaluated. Results: At the same dose gradient, naringenin was mild and friendly to keratinocytes. Conversely, naringenin significantly inhibited growth activity and proliferation of melanoma cells. Furthermore, naringenin significantly inhibited in vitro tumorigenicity and promoted cell-cycle redistribution in melanoma cells compared with keratinocytes. In terms of molecular mechanisms, naringenin effectively promoted the high expression of the DNA damage protein γH2AX , inhibited cell cycle regulatory protein signaling (such as Cyclin D1, Cyclin A2, and Cyclin B1), and blocked the key signaling axis of autophagy: LC3B/ATG4B/Beclin/P62 signaling in melanoma cells. Conclusion: Naringenin is friendly to normal skin keratinocytes and significantly induces DNA damage and reduces autophagy in melanoma cells, thereby inducing decreased cell viability and cell death. These results suggest that naringenin has the potential to be a candidate drug for the chemoprevention and novel treatment of melanoma.

Keyword:

Phytochemical, Naringenin, Keratinocytes, Melanoma cells, and Chemoprevention

No. PP-011 / 天然物藥理組 / Natural Products Pharmacology (PP)

Metabolomics and Functional Analyses Reveal the Mitoprotective Effects of Sea Holly (Acanthus ebracteatus Vahl.) in a Yeast Model of Mitochondrial Dysfunction

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Mitochondrial dysfunction is a hallmark of aging and metabolic disorders, leading to oxidative stress, impaired bioenergetics, and loss of mitochondrial integrity. Natural products rich in bioactive phytochemicals have attracted increasing attention as potential mitochondria-targeted therapeutics. *Acanthus ebracteatus* Vahl., a medicinal plant widely used in traditional Thai medicine, possesses potent antioxidant properties, yet its mitochondrial protective mechanisms remain largely unexplored. This study integrated functional analyses with untargeted metabolomics to investigate the protective effects of the aqueous extract of *A. ebracteatus* (AEA) against carbonyl cyanide m-chlorophenyl hydrazone (CCCP)-induced mitochondrial stress in eukaryotic model, *Saccharomyces cerevisiae*. Antioxidant capacity was evaluated using total phenolic content, total flavonoid content, DPPH, and ABTS assays, while mitochondrial integrity was assessed by intracellular reactive oxygen species (ROS), mitochondrial membrane potential, ATP production, and mitochondrial morphology. Untargeted LC–MS/MS metabolomics coupled with molecular networking was employed to characterize metabolites associated with the observed bioactivities. AEA exhibited strong antioxidant capacity and significantly attenuated mitochondrial dysfunction by reducing ROS accumulation and preserving mitochondrial membrane potential, ATP production, and mitochondrial morphology. Integrative metabolomic and functional analyses further identified phenolic acids, flavonoids, and related specialized metabolites as potential contributors to these protective effects. Collectively, these findings demonstrate that *A. ebracteatus* preserves mitochondrial integrity under mitochondrial stress condition and highlight the utility of integrating metabolomics with functional validation to accelerate the discovery of mitochondria-targeted natural products.

Keyword:
Mitochondrial dysfunction, Metabolomics, Phytochemicals, Acanthus ebracteatus, Saccharomyces cerevisiae

No. PP-012 / 天然物藥理組 / Natural Products Pharmacology (PP)

Inhibitory Effects of Coix Extract (CS3) on LPS-Induced Oxidative Stress and Its Promotion of Wound Healing in Keratinocytes

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In recent years, natural plant extracts have become an important focus in skincare and biomedical material research due to their antioxidant, anti-inflammatory, and tissue repair bioactivities. This study aimed to investigate the protective effects of a standardized Coix extract (CS3) against lipopolysaccharide (LPS)-induced oxidative stress and inflammatory responses in human epidermal keratinocytes (HaCaT), and to elucidate its underlying molecular mechanisms in promoting wound healing. Initially, the safe therapeutic window of CS3 was established using the PrestoBlue assay, revealing that 50 μg/mL of CS3 exhibited no cytotoxicity and significantly promoted keratinocyte proliferation. Regarding antioxidant and anti-inflammatory efficacies, quantitative flow cytometry demonstrated that CS3 powerfully scavenged LPS-induced intracellular reactive oxygen species (ROS) overproduction. Concurrently, gene and protein expression analyses indicated that CS3 significantly downregulated the abnormal expression of pro-inflammatory cytokines (IL-6 and TNF-α) and successfully activated the endogenous Nrf2/HO-1 antioxidant defense signaling pathway. Furthermore, the wound healing assay showed that CS3 intervention effectively reversed the LPS-
induced delay in cell migration, significantly increasing the wound closure rate to over 60% and accelerating the tissue repair process. In conclusion, this study fully validated that CS3 exerts synergistic antioxidant and anti-inflammatory effects via the activation of the Nrf2/HO-1 pathway, highlighting its great potential for development into natural topical repair dressings and soothing skincare biomaterials.

Keyword:
Coix extract (CS3), Human epidermal keratinocytes (HaCaT), Oxidative stress, Nrf2/HO- 1 signaling pathway, Wound healing

No. PP-013 / 天然物藥理組 / Natural Products Pharmacology (PP)

Natural Herbal Combination Compound-Loading Nanodrug for Brain Tumor Synergetic Therapy

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Glioblastoma (GBM) is a fatal CNS tumor with an average survival of less than 1.5 years. Due to the high recurrence and drug resistance of chemo-radiotherapy or radiotherapy, we aimed to screen natural herbal combinations and develop targeted nano-carriers to improve treatment outcomes. We evaluated 12 Chinese herbal combinations and synthesized PLGA-based nanoparticles using a nanoprecipitation method with a custom positively charged polymer (PCP) to enhance cellular uptake. Results showed that TCM-4 is one of the most effective candidates that inducing ~60% apoptosis in U87 cells at 60 μg/ml concentration. The formulated nanoparticles exhibited a spherical morphology (~150 nm) with a narrow polydispersity index (0.008~0.11). As a proof-of-concept test, this system improved the IC50 of the model drug curcumin from 25 μM to 0.6 μM. Western blotting shows that TCM-4 inhibits EGFR, VEGFR and Ki67 expression in U87-MG cells, which may lead to inhibition of the chemo/radio-resistance and suppress the tumor growth. Future work will combine TCM-4 with PLGA-PCP packaging technology for *in vivo* testing. In summary, we successfully identified TCM-4 as potential herbal therapy candidate and demonstrates that nanocarriers significantly enhance efficiency of tumor-inhibition, offering a promising new strategy for GBM therapy.

Keyword:
natural herbal compounds, nanotechnology, drug delivery, glioblastoma (GBM), synergetic therapy

No. PP-014 / 天然物藥理組 / Natural Products Pharmacology (PP)

Optimization of Extraction Conditions and Evaluation of Bioactive Phytochemicals from Rhus chinensis Mill.

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Background: Rhus chinensis Mill. (Anacardiaceae) is a medicinal plant traditionally used to treat gastrointestinal and respiratory disorders, and has attracted increasing attention for its diverse pharmacological properties. However, standardized extraction conditions and systematic evaluation of its bioactive potential remain limited.

Objectives: To investigate the antioxidant and xanthine oxidase (XO) inhibitory activities of Rhus chinensis and to optimize its extraction conditions using response surface methodology (RSM).

Methods: Botanical identification was performed through macroscopic and microscopic characterization to ensure taxonomic accuracy. Extracts were obtained under RSM-optimized conditions, and total phenolic content (TPC) and total flavonoid content (TFC) were quantified. Antioxidant capacity was evaluated by the DPPH assay, and XO inhibitory activity was assessed at a concentration of 100 µg/mL.

Results & Discussion: The crude extract exhibited the strongest antioxidant activity (IC50 = 7.575 µg/mL) and the highest XO inhibition (70.84 ± 9.40% at 100 µg/mL), together with the highest TPC (472.293 ± 2.371 mg GAE/g) and TFC (72.922 ± 0.003 mg QE/g). Optimal extraction conditions were determined as 60°C, 70% ethanol, and 52 minutes, yielding stable and reproducible results.

Conclusion: These findings support the potential of Rhus chinensis as a natural source for managing oxidative stress and hyperuricemia. Further studies are recommended to isolate the active compounds and validate their efficacy in vivo.

Keyword:

Antioxidant activity, Phenolic content, Response surface methodology (RSM), Rhus chinensis, Xanthine oxidase inhibition

No. PP-015 / 天然物藥理組 / Natural Products Pharmacology (PP)

Integrating Network Pharmacology and Molecular Docking to Explore the Antihypertensive Mechanism of Citrus hystrix

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Background: Hypertension is a major modifiable risk factor for cardiovascular disease, involving endothelial dysfunction, oxidative stress, chronic inflammation, and hormonal dysregulation. *Citrus hystrix* has reported antioxidant and vascular-protective properties, but its molecular mechanisms against hypertension remain unclear.

Objective: To identify candidate bioactive compounds, targets, and pathways underlying the antihypertensive effects of *C. hystrix* using network pharmacology and molecular docking.

Materials and methods: *C. hystrix* compounds were compiled from literature/PubChem and screened by drug-likeness. Targets were predicted using SwissTargetPrediction, while hypertension-related genes were retrieved from GeneCards and CTD. Common targets were analyzed using STRING and CytoHubba. GO/KEGG enrichment was performed via g:Profiler. Priority compounds and hub proteins from PubChem and the Protein Data Bank were prepared with AutoDockTools and docked using AutoDock Vina.

Results: Of 282 compounds, 81 drug-like candidates generated 6948 non-redundant compound-target pairs. Disease gene mining yielded 620 GeneCards and 22 CTD genes, with 157 common targets. Key compounds included citrusoside B, quercetin, and β-sitosterol. Top hub genes were AKT1, IL6, TNF, SRC, IL1B, ESR1, TP53, PPARG, EGFR, and STAT3. Six relevant KEGG pathways were identified: HIF-1, AGE-RAGE, PI3K-Akt, MAPK, lipid and atherosclerosis, and calcium signaling. Lipid and atherosclerosis overlapped 8/10 hub genes. Six priority compounds were selected, quercetin was associated with AKT1 and 5/6 pathways, while citrusoside B targeted TNF, IL1B, and EGFR. Docking showed favorable binding with hub proteins.

Conclusion: *C. hystrix* may exert antihypertensive effects through multi-target, multi-pathway regulation, particularly involving inflammatory, hypoxic, and lipid/atherosclerotic pathways, supporting further experimental validation.

Keyword:
Citrus hystrix, network pharmacology, molecular docking, hypertension

No. PP-016 / 天然物藥理組 / Natural Products Pharmacology (PP)

Optimization of Controlled Release Microspheres Containing Vitexin and Isovitexin through Experimental Design and Evaluation of Their Hypoglycemic Effects

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Vitexin and isovitexin have poor oral bioavailability. Alginate-chitosan microencapsulation may enable controlled oral delivery. To optimize and characterize vitexin-isovitexin-loaded alginate chitosan microspheres and assess acute toxicity and hypoglycemic activity in mice. Drug-loaded alginate cores were prepared by water-in-oil emulsification followed by external calcium-ion gelation, then coated with chitosan by immersion. An I-optimal response-surface design optimized the alginate grade/concentration and calcium chloride, Tween 80, and Span 80 levels. Particle size and morphology were assessed by laser diffraction and scanning electron microscopy, loading capacity, encapsulation efficiency, and in vitro release were determined by HPLC. Acute oral toxicity was monitored for 14 days after a 2 g/kg limit dose. Alloxan-induced hyperglycemic male Swiss albino mice (55 mg/kg) received vehicle, glibenclamide (10 mg/kg), or microspheres equivalent to 30 or 60 mg/kg vitexin-isovitexin orally for 21 days. Fasting blood glucose was measured on days 1, 7, 14, and 21. The optimized formulation contained 1.17% low-viscosity alginate, 7.60% calcium chloride, 5.78% Tween 80, and 5.00% Span 80. The spherical microspheres had a mean size of 10.78±5.59 μm, loading capacity of 22.45±0.42%, and encapsulation efficiency of 68.92±1.28%. Release reached 99.53% over 24h in sequential pH 1.2/6.8 media. No mortality or overt toxicity occurred at 2 g/kg. On day 21, blood glucose was 281.4±41.2 and 177.0±36.0 mg/dL at 30 and 60 mg/kg, respectively, versus 453.6±27.0 mg/dL in untreated hyperglycemic mice (p-value less than 0.05). The optimized microspheres controlled vitexin–isovitexin release and significantly reduced hyperglycemia after 21 days without acute toxicity at the tested limit dose.

Keyword:
microspheres, controlled release, hypoglycemic effects, isovitexin, vitexin

No. PP-017 / 天然物藥理組 / Natural Products Pharmacology (PP)

Designing a Reproducible Natural-Product Literature Search Engine: From Lexical Recall to Context Refinement

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We propose a staged search-engine framework that combines reproducible lexical candidate generation with traceable source evidence and planned biomedical context refinement. This methodological study examines design choices, ambiguity and evaluation requirements for a prototype under active optimization.

Keyword:

Literature Mining, Biomedical Text Mining, Information Retrieval, Entity Recognition, Evidence Extraction

No. PP-018 / 天然物藥理組 / Natural Products Pharmacology (PP)

Anticancer property of native Taiwan fern plant aqueous extract AC118-RLS

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Chemotherapy is widely used in cancer treatment. However, clinical use of first-line drugs is often accompanied by undesirable side effects or drug resistance. This has led to continued interest in identifying additional agents that may be used alone or in combination with conventional anticancer therapy. In this study, we investigated the antitumor activity of an aqueous crude extract, AC118-RLS, prepared from a fern native to Taiwan, against lung cancer. Our previous in vitro studies showed that AC118-RLS significantly reduced the viability of human A549 lung adenocarcinoma cells in a dose-dependent manner. Treatment with AC118-RLS also increased intracellular reactive oxygen species production and induced apoptotic cell death. Based on these findings, we further examined the antitumor effects of AC118-RLS in vivo using a mouse tumor model. C57BL/6 mice were inoculated with Lewis lung carcinoma LL/2 cells and assigned to four treatment groups. The mice received AC118-RLS orally for 28 days at doses of 0 mg/day, 4 mg/day, 12 mg/day, or 36 mg/day. Administration of AC118-RLS reduced the average tumor weight compared with the control group. Body weight, major organ weights, tissue histology, and hemoglobin levels remained within normal physiological ranges across the experimental groups. Current studies are carrying out to determine whether AC118-RLS can be used in combination against advanced lung cancer cells with first-line with onset of drug resistance. Taken together, the present findings demonstrate the antitumor activity of an aqueous extract derived from the Taiwan native fern AC118-RLS and provide a basis for potential pharmacological applications in lung cancer.

Keyword:
Taiwan fern, aqueous crude extract, lung adenocarcinoma, complementary and alternative medicine

No. PP-019 / 天然物藥理組 / Natural Products Pharmacology (PP)

Stellettin B: A Marine-Derived Inhibitor of TGF-β Signaling

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Marine sponges are a rich source of structurally diverse bioactive natural products with considerable therapeutic potential. *Stellettin B*, an isomalabaricane triterpenoid derived from marine sponges, has demonstrated potent anticancer activity in several tumor types and possesses pharmacological properties that may be particularly advantageous for the treatment of metastatic cancer. However, its effects on *transforming growth factor-β* (*TGF-β*)-mediated *epithelial–mesenchymal transition* (*EMT*), tumor invasion, and fibrotic responses remain poorly understood. In this study, we investigated the effects of *stellettin B* on *TGF-β* signaling and its associated malignant and fibrotic phenotypes using human *A549* non-small cell lung cancer cells and keloid-derived fibroblasts. *Stellettin B* markedly suppressed *TGF-β*-induced migration of *A549* cells and inhibited invasion into the surrounding *extracellular matrix* in a three-dimensional organoid model. These effects were accompanied by reduced expression of several *TGF-β*/*EMT*-associated proteins, including *N-cadherin*, *fibronectin*, and *plasminogen activator inhibitor-1* (*PAI-1*). In keloid-derived fibroblasts, *stellettin B* also attenuated the *TGF-β*-induced expression of the fibrosis-associated marker *SM22α*, suggesting that its inhibitory activity extends beyond malignant epithelial cells to pathological fibroblastic responses. Mechanistically, *stellettin B* suppressed *TGF-β*-induced *Smad* phosphorylation, indicating that it interferes with the canonical *TGF-β*/*Smad* signaling pathway at an early stage. Collectively, these findings identify *stellettin B* as a potent inhibitor of *TGF-β* signaling that simultaneously suppresses *EMT*-associated migration and three-dimensional invasion in lung cancer cells and fibrotic responses in keloid-derived fibroblasts. Its dual antimetastatic and antifibrotic activities suggest that *stellettin B* may represent a promising therapeutic lead for *TGF-β*-driven malignancies and fibrotic diseases.

Keyword:
Stellettin B、TGF-β 、EMT

No. PP-020 / 天然物藥理組 / Natural Products Pharmacology (PP)

Ganoderma microsporum immunomodulatory protein enhances the antitumor activity of EGFR-TKIs in non-small cell lung cancer cells through FBXL14-dependent Slug destabilization

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Ganoderma microsporum immunomodulatory protein (GMI) is a bioactive fungal protein with reported anticancer properties. This study investigated whether GMI enhances the antitumor activity of epidermal growth factor receptor tyrosine kinase inhibitors (EGFR TKIs) in non-small cell lung cancer (NSCLC) with limited TKI responsiveness and explored the underlying mechanism. H1975 cells were treated with GMI combined with gefitinib or erlotinib. Cell viability, drug interaction, clonogenic growth, apoptosis, and different treatment sequences were evaluated. Slug protein stability and proteasomal regulation were also investigated. Integrative bioinformatic analyses of public datasets were used to prioritize EMT-associated regulators and candidate E3 ubiquitin ligases, leading to the identification of Slug and FBXL14 for subsequent mechanistic validation. GMI enhanced the growth-inhibitory effects of gefitinib and erlotinib, resulting in synergistic drug interactions. Combined treatment suppressed clonogenic growth and increased apoptosis. Notably, EGFR TKI pretreatment followed by GMI produced greater growth inhibition than the reverse sequence. Mechanistically, GMI reduced Slug protein levels by accelerating its turnover, whereas proteasome inhibition attenuated this effect. FBXL14 depletion impaired GMI regulation of Slug, while GMI increased the association between FBXL14 and Slug, supporting a role for FBXL14 in Slug destabilization. In an H1975 xenograft model, GMI combined with erlotinib produced greater tumor suppression than either treatment alone. These findings suggest that GMI potentiates EGFR TKI activity by regulating Slug stability and support its potential as a natural fungal protein for combination therapy in NSCLC.

Keyword:

Ganoderma microsporum immunomodulatory protein, EGFR tyrosine kinase inhibitor, Slug, FBXL14, non-small cell lung cancer

No. PP-021 / 天然物藥理組 / Natural Products Pharmacology (PP)

Antrodia cinnamomea sulfated polysaccharide attenuates the TGFβR/CD44-mediated AKT-dependent RUNX2 and ZEB1 axes, suppressing EGFR-mutant lung adenocarcinoma cells

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Alternatively, natural compounds have been used in conjunction with conventional therapies in regimens for cancer. B86-III, a sulfated galactoglucan from *Antrodia cinnamomea*, exhibits anticancer activity against non-small-cell lung cancer cells. However, the molecular mechanisms that hinder TGFβ receptor signaling remain incompletely characterized. Herein, we investigated the effects of B86-III in EGFR L858R/T790M-mutant H1975 lung adenocarcinoma cells using data-driven in vitro and xenograft models. Under B86-III treatment, proteome changes revealed CD44 and RUNX2 among the key molecules altered. B86-III-treated cells showed downregulation of TGFβ receptors and suppression of canonical TGFβR/Smad2 signaling, accompanied by reduced CD44 isoforms and N-cadherin. CD44 variant transcription was decreased, whereas CD44s underwent degradation via the lysosomal-autophagy system. Additionally, B86-III inhibited non-canonical TGFβR/AKT signaling, particularly AKT phosphorylation at Thr308, thereby reducing RUNX2 mRNA expression. In relation to CD44, ZEB1 was reduced mainly through AKT-dependent autophagy–lysosomal degradation. In H1975 xenografts, B86-III significantly suppressed tumor growth and reduced RUNX2 and ZEB1 without liver and kidney toxicity. These findings indicate that B86-III suppresses EGFR-mutant NSCLC by co-modulating the TGFβR/Smad2/CD44 and TGFβR/AKT/RUNX2/ZEB1 axes, supporting its potential development as an adjunctive agent for EGFR-mutant lung cancer cells.

Keyword:
Antrodia Cinnamomea, sulfated polysaccharides, lung adenocarcinoma, ZEB1, CD44, TGFβR/AKT/RUNX2

No. PP-022 / 天然物藥理組 / Natural Products Pharmacology (PP)

Mangiferin ameliorates insulin resistance and restores β-cell function in HFD/STZ-induced diabetic rats

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Background: Metabolic disorders are characterized by impaired insulin secretion, insulin resistance, and β-cell dysfunction. Mangiferin, a natural xanthone glucoside, has been reported to possess anti-diabetic properties, however, its dose-dependent effects on insulin dynamics remain unclear. This study evaluated the effects of gemfibrozil, metformin, and mangiferin in high-fat diet/streptozotocin (HFD/STZ)-induced diabetic rats.
Methods: Serum insulin, homeostatic model assessment of insulin resistance (HOMA-IR) and β-cell function (HOMA-β) were measured to assess insulin dynamics, insulin resistance, and β-cell function, respectively.
Results: HFD/STZ-induced diabetic rats exhibited reduced serum insulin, elevated HOMA-IR, and markedly decreased HOMA-β, confirming the presence of metabolic dysfunction. Metformin significantly improved all parameters, whereas gemfibrozil enhanced insulin secretion and β-cell function but exerted only moderate effects on insulin resistance. Mangiferin displayed dose-dependent efficacy: low and medium doses resulted in limited improvement, whereas the high dose (150 mg/kg) markedly increased serum insulin, reduced HOMA-IR, and enhanced HOMA-β, with efficacy comparable to that of metformin.
Conclusion: Mangiferin exhibits strong therapeutic potential against metabolic disease, particularly at high doses, by improving insulin secretion, reducing insulin resistance, and restoring β-cell function. These findings support mangiferin as a promising candidate for further mechanistic and translational investigation.

Keyword:
Type 2 diabetes mellitus, insulin resistance, Mangiferin, Metformin, Gemfibrozil

No. PP-023 / 天然物藥理組 / Natural Products Pharmacology (PP)

Transcriptomic analysis and functional characterization of natural marine sesterterpenoids in anti-CRPC activity — a crucial role of proapoptotic NOXA

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Castration-resistant prostate cancer (CRPC) remains a major clinical challenge due to inevitable resistance to current therapies. There is unmet medical need for novel therapeutics with distinct mechanisms to overcome clinical obstacle. Natural marine sesterterpenoids offer a compelling rationale for discovery because of their complex chemical scaffolds with unique bioactivities. Screening of multiple marine compounds revealed that heteronemin exhibited the most potent activity, with an IC50 of 0.28±0.08 μM. Heteronemin alters pathways regulating ER stress, DNA damage and cell cycle progression, as revealed by Ingenuity Pathway Analysis and Next-Generation Sequencing. Heteronemin induces DNA double-stranded breaks (DSBs) in CRPCs by suppressing homologous recombination and Fanconi anemia DNA repair pathways, evidenced by decreased gene expression of RAD51, BRCA1/2, PALB2, and FANCD2. Concurrently, it upregulates XPC and LIG4, shifting the cellular response toward nucleotide excision repair and error-prone non-homologous end joining to handle accumulated DNA damage. Heteronemin induced G1 arrest and an increase in sub-G1 population. Western blotting verified that heteronemin induced ER stress (e.g., upregulation of CHOP and GRP78) associated with DNA DSBs and DNA repair impairment (e.g., upregulation of γH2AX and downregulation of Rad51, BRCA1, and BRCA2). Heteronemin induced mitochondrial damage with decreased Bcl-2 expression but an increase in that of NOXA and PUMA, ultimately activating caspase cascade. NOXA knockdown by siRNA rescued cell survival with decreased caspase activities. In summary, the data suggest that heteronemin induces anti-CRPC activity through collaborative ER stress, DNA damage and impairment of DNA repair, leading to mitochondrial dysfunction and apoptosis executed by caspase activation.

Keyword:
Heteronemin, prostate cancer, endoplasmic reticulum stress, DNA damage repair, mitochondrial dysfunction

No. PP-024 / 天然物藥理組 / Natural Products Pharmacology (PP)

A Syzygium simile-derived natural product exerts dual regulation of adipogenesis and lipid metabolism in 3T3-L1 adipocytes

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Obesity has become a rapidly growing global health burden and is strongly associated with the development of metabolic and cardiovascular complications. Natural products represent an important source of bioactive compounds for the discovery of potential anti-obesity therapeutics. In this study, we identified a bioactive constituent, S3, from the leaf extract of *Syzygium simile* and investigated its effects on adipogenesis and lipid metabolism. Network pharmacology analysis and molecular docking identified peroxisome proliferator-activated receptor gamma (PPAR $_{\gamma}$), a master regulator of adipogenesis, as a potential target of S3. Treatment with S3 during the early stage of 3T3-L1 adipocyte differentiation markedly reduced lipid droplet accumulation and suppressed the expression of key adipogenic regulators, including PPAR$_{\gamma}$. Notably, S3 maintained its inhibitory effect on lipid accumulation even in the presence of the potent PPARγ agonist rosiglitazone. In addition to its effects on early adipogenesis, S3 treatment during the late stage of adipocyte differentiation also reduced lipid accumulation and increased the phosphorylation of AMP-activated protein kinase (AMPK) and hormone-sensitive lipase (HSL), two important regulators of lipid metabolism. Together, these findings demonstrate that S3 may exert dual effects on adipocyte lipid homeostasis by suppressing adipogenesis and enhancing lipid metabolic signaling, suggesting that S3 derived from S. simile may serve as a promising lead compound for the development of anti-obesity therapeutics.

Keyword:

anti-obesity, adipocytes, Syzygium simile, PPARγ

No. PP-025 / 天然物藥理組 / Natural Products Pharmacology (PP)

1,3-Diphenylpropanoids isolated from the stems of Broussonetia monoica downregulate melanogenesis

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Skin is continually challenged by ultraviolet B (UVB) irradiation, which induces oxidative stress, inflammation, and paracrine cues that stimulate melanogenesis. Tyrosinase is a rate-limiting enzyme in this pathway. This study aimed to utilize the stem of *Broussonetia monoica* by chemically characterizing its bioactive phenolics and defining their roles in tyrosinase inhibition, melanogenesis modulation, and UVB-induced cellular stress responses. The ethyl acetate soluble layer of the methanolic extract yielded BMKZ-M (1), BMKZ-N (2), BMMF (3), and BMSG (4) as representative constituents. In cell-free assays, selected compounds inhibited tyrosinase with competitive or mixed-type kinetic behaviors, while combination treatments showed sequence-dependent enhancement. In cell-based models, these constituents suppressed melanogenesis and attenuated UVB-triggered oxidative and inflammatory responses in keratinocytes by reducing reactive oxygen species and downregulating mediators such as matrix metalloproteinases and interleukin-1β. These findings indicate that phenolic constituents from *B. monoica* stems act through complementary mechanisms involving enzyme-level tyrosinase inhibition and modulation of UVB-induced inflammatory signaling, supporting their potential as multifunctional bioactive ingredients for UVB-stress and pigment formation-related applications.

Keyword:

1,3-Diphenylpropanoids, *Broussonetia monoica*, Melanogenesis

No. PP-026 / 天然物藥理組 / Natural Products Pharmacology (PP)

Metabolic Regulation of PD-1 Expression by CD070 in T Cells.

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Programmed cell death protein 1 (PD-1) is a major immune checkpoint target in cancer therapy, however, antibody-based PD-1 blockade remains limited by variable clinical responses, immune-related toxicities, and substantial treatment costs. Therefore, identifying small molecules that directly reduce PD-1 expression may offer an alternative strategy for modulating T-cell function.

In this study, we investigated the effects of CD070, a bioactive compound derived from Chinese herbal medicine, on PD-1 expression and cellular metabolism in T cells. CD070 treatment significantly suppressed PD-1 protein expression in Jurkat cells and consistently decreased PD-1 levels in $CD3^+$, $CD4^+$, and $CD8^+$ T-cell subsets derived from peripheral blood mononuclear cells of three healthy donors. Metabolic analyses showed that CD070 also suppressed glycolysis, as indicated by reduced extracellular acidification rate, glucose consumption, and lactate production. The involvement of glucose metabolism in PD-1 regulation was further supported by experiments showing that 2-deoxyglucose decreased PD-1 expression, whereas glucose supplementation under glucose-deprived conditions restored PD-1 expression. Furthermore, CD070 downregulated NFATc1 expression without altering IRF9 levels, suggesting that its effects on PD-1 may involve selective modulation of transcriptional pathways.

Taken together, these results suggest that CD070 suppresses PD-1 expression in T cells in association with impaired glycolytic metabolism and altered NFATc1 signaling. These findings provide further evidence linking cellular metabolism to immune checkpoint regulation and support CD070 as a potential candidate for metabolic modulation of T-cell responses.

Keyword:

PD-1, Chinese herbal Medicine, T cell, glycolysis, metabolic modulation

No. PP-027 / 天然物藥理組 / Natural Products Pharmacology (PP)

CD004-Reprogrammed Tc17 Cells Enhance Anti-Tumor Activity and Synergize with Cisplatin

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Tc17, a $CD8^+$ T cell subset with IL-17 production, exhibits functional plasticity. They can be reprogrammed toward IFN-γ–producing cytotoxic Tc1-like cells, representing a promising strategy to enhance anti-tumor immunity. CD004 is a bioactive compound derived from Chinese herbal medicine with immunomodulatory activity. Based on this rationale, CD004 was selected to investigate its potential to reprogram Tc17 cells.

Polarized Tc17 cells were treated with CD004, and phenotype markers were analyzed by flow cytometry. Seahorse XF Cell Metabolism Analysis and metabolite assays were performed to evaluate metabolic changes. Western blot analysis was performed to investigate potential mechanisms underlying. Cytotoxicity was evaluated using a CFSE-based assay with E.G7-OVA cells as target cells. *In vivo* efficacy was evaluated in E.G7-OVA tumor-bearing models following adoptive transfer of Tc17 cells, with or without cisplatin.

CD004 treatment significantly increased IFN-γ and T-bet expression with reduced IL-17A levels in Tc17 cells, indicating reprogramming of Tc17 toward a Tc1-like phenotype. Metabolic and western blot analyses suggested that mitochondrial metabolic remodeling and p-NF-κB signaling were associated with Tc17 reprogramming. Increased granzyme B expression and enhanced *In vitro* cytotoxicity of Tc17 cells against tumor cells were also observed. *In vivo*, adoptive transfer of CD004-treated Tc17 cells reduced tumor burden, increased effector T cell responses, and showed a synergistic effect with cisplatin.

CD004-mediated Tc17 reprogramming enhances anti-tumor immunity and synergizes with cisplatin. These findings highlight the therapeutic potential of CD004 as a Chinese herbal medicine–derived compound for cancer immunotherapy.

Keyword:

Tc17, Chinese herbal medicine, cancer immunotherapy, T cell plasticity, Immunometabolic reprogramming

No. PP-028 / 天然物藥理組 / Natural Products Pharmacology (PP)

Marine-derived norzoanthamine and *Atalantia ceylanica*-derived LC03 improve stress resistance and extend lifespan in *Caenorhabditis elegans*

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Oxidative stress plays an important role in biological aging, motivating the search for natural compounds that improve stress tolerance and lifespan. This study screened compounds from zoanthids (20E, zoanthamine [Z71], and norzoanthamine [Z86]) and *Atalantia ceylanica* (LC01–LC03) in wild-type *Caenorhabditis elegans*. We assessed survival during oxidative and heat stress, body length, lifespan, DAF-16::GFP localization, and molecular docking with DAF-16. Following a challenge with juglone, an oxidative stress inducer, Z86 at 10 and 100 μM, and LC03 at 10 and 100 μM significantly increased survival relative to untreated controls, LC01 at 100 μM was also effective. Heat-shock experiments showed improved survival with LC03 at 4 h and with both Z86 and LC03 at 6 h. At 10 μM, Z86 and LC03 significantly prolonged lifespan and increased DAF-16::GFP nuclear localization. Molecular docking predicted potential interactions with DAF-16, with binding energies of −7.7 kcal/mol for Z86 and −6.8 kcal/mol for LC03. Together, these findings suggest that Z86 and LC03 improve resistance to oxidative stress and extend lifespan in *C. elegans*, potentially through regulation of FOXO/DAF-16 signaling.

Keyword:

Norzoanthamine, *Atalantia ceylanica*, *Caenorhabditis elegans*, oxidative stress, lifespan, DAF-16

No. PP-029 / 天然物藥理組 / Natural Products Pharmacology (PP)

Marine fungal metabolites improve oxidative stress resistance in *Caenorhabditis elegans*

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Marine-derived fungi produce structurally diverse metabolites, but their effects on stress resistance remain incompletely understood. This study evaluated four compounds from the marine-derived fungus *Penicillium sclerotiorum*: F47, F70, F71, and ochlephilone (F94). Survival of wild-type *Caenorhabditis elegans* under oxidative and thermal stress was assessed, and molecular docking was used to explore potential interactions with FoxO/DAF-16. In an initial survival screen, all four compounds at 10 μM significantly increased survival compared with untreated controls, with F94 showing the highest mean survival. During exposure to 250 μM juglone, F94 showed a clear concentration-dependent protective effect: 1 μM had no significant effect, whereas 10 and 100 μM significantly improved survival. After 3.5 h, 70% of worms treated with 100 μM F94 survived, compared with 13% of untreated worms. Following 6 h of heat stress at 37 °C, the F94 treatment showed a significant enhancement in survival. Moreover, F94 significantly reduced DHE fluorescence at 1, 10, and 100 μM. Molecular docking predicted an interaction between F94 and DAF-16 with a binding energy of −7.2 kcal/mol. These findings identify F94 as a candidate for further investigation of stress resistance in *C. elegans* and suggest DAF-16 as a possible target for mechanistic studies of antioxidative responses.

Keyword:
Marine fungal metabolites, Penicillium sclerotiorum, Caenorhabditis elegans, ochlephilone, oxidative stress, DAF-16

No. PP-030 / 天然物藥理組 / Natural Products Pharmacology (PP)

Marine natural compounds ameliorate Parkinson's disease-related phenotypes in a *Caenorhabditis elegans*

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Marine natural products contain compounds with potential neuroprotective activity, but their effects on Parkinson's disease (PD)-related phenotypes remain incompletely understood. This study used *Caenorhabditis elegans* to evaluate norzoanthamine (Z86), a zoanthid-derived compound, and marine fungal metabolites F47, F70, and F71. Human α-synuclein (α-syn)-associated fluorescence was measured in NL5901 worms, while dopaminergic neuronal morphology was assessed in 6-hydroxydopamine (6-OHDA)-exposed BZ555 worms. Oxidative stress resistance, H_2DCFDA and DHE fluorescence, and molecular docking with DAF-16 were also examined. At 10 μM, Z86 and F70 significantly reduced α-syn-associated fluorescence. In BZ555 worms, 6-OHDA decreased dopaminergic neuron soma size and increased abnormal neuronal blebbing, both Z86 and F70 significantly attenuated these changes. Both compounds also increased survival under oxidative stress compared with untreated controls. Using H_2DCFDA as a general oxidative stress probe and DHE as a superoxide-sensitive probe, we found that Z86 significantly reduced H_2DCFDA fluorescence, whereas DHE fluorescence did not differ significantly from the control. Molecular docking predicted interactions of Z86 and F70 with DAF-16, including a potential contact at Tyr169. These findings suggest that Z86 and F70 may alleviate PD-related phenotypes in *C. elegans*. These findings suggest that marine natural products may provide leads for the development of Parkinson's disease therapies.

Keyword:

Marine natural products, *Caenorhabditis elegans*, Parkinson's disease, norzoanthamine, DAF-16

No. PP-031 / 天然物藥理組 / Natural Products Pharmacology (PP)

Grapefruit-Statin Interactions: A Focused Narrative Review of Human Studies for Community Pharmacy Counseling

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Grapefruit-Statin Interactions: A Focused Narrative Review of Human Studies for Community Pharmacy Counseling

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Background: Grapefruit constituents can inhibit intestinal CYP3A4 and alter statin exposure, but counseling must distinguish the drug, juice regimen, and measured endpoint.

Methods: Four primary publications reporting human studies were purposively selected from targeted searches of PubMed-indexed literature. Reported juice regimens, statin exposures, timing effects, and clinical observations were synthesized narratively. No pooled estimates or new patient data were generated.

Results: In a crossover study of 10 healthy volunteers, 200 mL of grapefruit juice daily for three days increased simvastatin and simvastatin acid AUC(0-24 h) to 3.6 and 3.3 times control, respectively. A separate high-intake crossover study found simvastatin AUC(0-infinity) remained 2.1 times control when dosing occurred 24 hours after the last juice intake. Another publication reported atorvastatin acid AUC(0-72 h) reaching 2.5 times control with repeated double-strength juice, whereas pravastatin AUC was not significantly changed. In a 90-day patient study, 300 mL/day increased serum atorvastatin concentrations by 19-26% in the unchanged-dose arm without adverse changes in liver enzymes or creatine phosphokinase. These findings do not establish universal safety or equate concentration measurements with AUC.

Conclusions: The selected evidence supports statin-specific, regimen-aware counseling rather than a class-wide interaction assumption. Counseling should document juice amount and timing and avoid promising that dose separation eliminates interactions. Heterogeneous protocols, selective study inclusion, and limited clinical-outcome evidence preclude quantitative safety thresholds.

Keyword:
CYP3A4　food-drug interactions

No. PP-032 / 天然物藥理組 / Natural Products Pharmacology (PP)

HMTA from Ardisia virens: A Potential Therapeutic Agent Against NSCLC

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Non-small cell lung cancer (NSCLC) remains a leading cause of cancer-related mortality, highlighting the urgent need for novel therapeutic strategies. HMTA, a bioactive compound derived from *Ardisia virens* Kurz, exhibits potent anticancer effects against metastatic NSCLC cell lines, A549 and CL1-5. Our results demonstrate that HMTA significantly reduces cell viability, suppresses colony formation, and induces G1 phase cell cycle arrest and caspase-dependent apoptosis. Mechanistically, HMTA triggers robust reactive oxygen species (ROS) production, disrupts mitochondrial membrane potential, and causes substantial DNA damage. These intrinsic apoptotic cascades involve Bax/Bak upregulation, caspase activation, and Survivin downregulation. Furthermore, HMTA markedly suppresses the pro-survival JAK2/STAT3 signaling pathway. Crucially, by inhibiting STAT3 activation, HMTA effectively sensitizes NSCLC cells to cisplatin. This combination demonstrates highly synergistic cytotoxicity in vitro and significantly restricts tumor growth in A549 xenograft mouse models without observable systemic toxicity.

Together, these findings demonstrate that HMTA exerts its anticancer effects through ROS-driven mitochondrial dysfunction, DNA damage, and apoptosis, highlighting its promising potential as a novel therapeutic candidate and chemosensitizer for NSCLC treatment.

Keyword:
NSCLC, HMTA, ROS, DNA damage, Apoptosis

No. PP-033 / 天然物藥理組 / Natural Products Pharmacology (PP)

An innovative HDAC6 inhibitor G-02025 on neuropathic pain by targeting the HDAC6/SIRT3 neuroinflammatory pathway

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Background: Neuropathic pain (NP) induced by nerve injury such as chronic constriction injury (CCI) remains a significant clinical challenge driven by dysregulated neuroinflammation. Although histone deacetylase 6 (HDAC6) is implicated in pain sensitization, its precise mechanisms remain elusive. This study investigated the therapeutic efficacy and mechanisms of G-02025, a novel synthetic HDAC6 inhibitor, in a CCI mouse model.

Methods: Mice subjected to CCI received intragastric gavage (i.g.) of G-02025 (10 mg/kg or 50 mg/kg, i.g., twice a day), or vehicle continuously for 14 consecutive days, followed by a 7-day withdrawal period. We regularly monitored behavioral hypersensitivity (mechanical allodynia and thermal hyperalgesia). Spinal cord (SC) and dorsal root ganglion (DRG) tissues were collected for Western blot and immunofluorescence analyses.

Results: Systemic administration of G-02025 suppressed spinal HDAC6 upregulation and significantly attenuated CCI-induced mechanical allodynia and thermal hyperalgesia, with analgesic effects sustained through the 7-day withdrawal period (day 21). Mechanistically, G-02025 restored α-tubulin acetylation and PSD95 expression, preserving synaptic plasticity. In both SC and DRG, G-02025 attenuated glial (GFAP/Iba1) activation, downregulating TNF-α and IL-18 and suppressing the p38 MAPK/NF-κB/NLRP3 pathways. Furthermore, G-02025 upregulated SIRT3 in the spinal dorsal horn, mitigating mitochondrial dysfunction and oxidative stress through the TNF-α/p38 MAPK/NF-κB/NLRP3/SIRT3 axis.

Conclusion: These findings demonstrate that G-02025 effectively mitigates CCI-induced neuroinflammation and pain hypersensitivity. By targeting the HDAC6/SIRT3 neuroinflammatory axis and preserving synaptic plasticity, G-02025 represents a promising disease-modifying therapeutic agent for neuropathic pain.

Keyword:

Neuropathic pain, chronic constriction injury, HDAC6 inhibitor, mechanical allodynia, thermal hyperalgesia, HDAC6/SIRT3 axis

No. PP-034 / 天然物藥理組 / Natural Products Pharmacology (PP)

The in vitro anticancer effects of altersolanol A on glioma cells

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Natural products, particularly fungal secondary metabolites, represent valuable sources for the development of novel anticancer agents. Altersolanol A, a secondary metabolite isolated from *Stemphylium lycopersici*, exhibits various biological activities, including antibacterial, antidiabetic, and anticancer effects. Despite advances in surgical resection, radiotherapy, and chemotherapy, the prognosis of patients with malignant glioma remains poor. Therefore, this study aimed to investigate the in vitro anticancer effects of altersolanol A on glioma cells. Our results showed that altersolanol A significantly inhibited cell viability and colony formation in U87-MG, G5T/VGH, and GBM8401 glioma cells. Altersolanol A also induced apoptotic cell death, accompanied by increased cleavage of caspase-3 and poly(ADP-ribose) polymerase (PARP). Furthermore, altersolanol A suppressed metastasis-associated properties of glioma cells by reducing cell migration, invasion, and adhesion. Taken together, these findings demonstrate that altersolanol A exerts anti-glioma effects by inhibiting cell growth, inducing apoptosis, and suppressing migration, invasion, and adhesion. Further studies are warranted to elucidate the molecular mechanisms underlying these effects. These findings suggest that altersolanol A may represent a promising lead compound for the development of novel therapeutic strategies against malignant glioma.

Keyword:
altersolanol A, glioma, apoptosis, metastasis

No. PP-035 / 天然物藥理組 / Natural Products Pharmacology (PP)

Sarcophytol A from Aquacultured Sarcophyton sp.: Multi-Target Anticancer Potential and RBL2-Associated Cell-Cycle Regulation in Hematological Malignancy Cells

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Background: Aquacultured soft corals provide a sustainable source of bioactive cembranoid diterpenes. This study investigated the antiproliferative activity and potential mechanisms of Sarcophytol A isolated from aquacultured *Sarcophyton* sp. in hematological malignancy cells. Methods: Sarcophytol A was isolated by bioactivity-guided fractionation and characterized by nuclear magnetic resonance spectroscopy and mass spectrometry. Antiproliferative activity was assessed in CCRF, U937, and K562 cells. Mechanistic investigations included flow cytometry, Western blotting, transcriptomics, RBL2-targeting siRNA, cell-free tubulin polymerization assays, and molecular docking. In silico ADME profiling was also performed. Results: Sarcophytol A inhibited cell proliferation, with IC_{50} values of 8.76 ± 1.14, 9.23 ± 1.33, and 8.87 ± 0.67 μg/mL in CCRF, U937, and K562 cells, respectively. Treatment induced apoptosis accompanied by mitochondrial membrane depolarization and ER stress-related signaling. Transcriptomic changes were associated with apoptosis, mitochondrial dysfunction, ER stress, and cell-survival regulation. In CCRF cells treated with Sarcophytol A, RBL2 knockdown increased viability by 12.89% and increased the S-phase fraction from 48% to 56%, accompanied by higher CDK2, CDK4, and phosphorylated Chk2 levels. Sarcophytol A enhanced cell-free tubulin polymerization, while docking suggested potential tubulin interactions. ADME predictions indicated high gastrointestinal absorption, moderate aqueous solubility, potential oral bioavailability, and possible drug–drug interaction liabilities associated with inhibition of selected CYP450 enzymes. Conclusions: Sarcophytol A exhibited antiproliferative activity in hematological malignancy cells, accompanied by cellular stress and apoptosis. RBL2 contributed to cell-cycle regulation in response to treatment. These findings support further investigation of Sarcophytol A as a sustainably sourced scaffold with multi-target anticancer potential.

Keyword:
Sarcophytol A, Sarcophyton sp., hematological malignancies, apoptosis, RBL2, tubulin polymerization.

No. PP-036 / 天然物藥理組 / Natural Products Pharmacology (PP)

Nimbolide induces oxidative stress-mediated autophagic cell death by targeting FAM83E expression in human glioblastoma cells

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Nimbolide, a bioactive limonoid derived from the neem tree (Azadirachta indica), exhibits potent anticancer activities, yet its effects in glioblastoma remain poorly understood. Here, we investigated the anticancer activity and underlying mechanisms of nimbolide in glioblastoma models. Our results found that Nimbolide selectively reduced glioblastoma cell viability and clonogenic survival while sparing astrocytes, and induced intrinsic apoptosis characterized by caspase-9/caspase-3 activation and PARP cleavage. Nimbolide also promoted autophagy, as evidenced by increased acidic vesicular organelles, LC3B, and p62 accumulation. LC3 silencing diminished autophagic vacuolization, apoptotic signaling, and Annexin V positivity while restoring cell viability, supporting a pro-death autophagy mechanism. Mechanistically, nimbolide markedly increased reactive oxygen species (ROS), activated the NRF2/heme oxygenase-1 (HO-1) pathway, and reduced KEAP1 expression. Molecular docking further predicted direct interactions of nimbolide with HO-1 and LC3B. ROS scavenging with N-acetyl-L-cysteine (NAC) attenuated autophagy and apoptosis, whereas pharmacological or siRNA-mediated HO-1 inhibition suppressed LC3 induction and caspase activation, identifying HO-1 as a critical mediator linking oxidative stress to autophagic apoptosis. Transcriptomic profiling identified FAM83E as a nimbolide-responsive gene overexpressed in glioblastoma, with functional perturbation supporting its involvement in nimbolide responses. Pathway analyses further implicated ERK1/2 signaling, supporting a ROS/HO-1/LC3 regulatory axis. In vivo, nimbolide suppressed glioblastoma xenograft growth and Ki-67 expression without overt systemic toxicity. Collectively, nimbolide converts oxidative stress into ERK1/2-mediated autophagic apoptosis and identifies FAM83E as a potential therapeutic target in glioblastoma

Keyword:

Nimbolide, Glioblastoma, ROS, Apoptosis, FAM83E.

No. PP-037 / 天然物藥理組 / Natural Products Pharmacology (PP)

Context-Dependent Regulation of Retinal Pigment Epithelial Migration and Remodeling by Fucoidan

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Age-related macular degeneration (AMD) is a leading cause of vision loss in older adults. Dysregulated migration and remodeling of retinal pigment epithelial (RPE) cells may contribute to disease progression, but strategies that modulate these responses according to cellular context remain limited. This study investigated the context-dependent effects of fucoidan, a marine-derived sulfated polysaccharide, on ARPE-19 cell migration and epithelial-mesenchymal transition (EMT). In the absence of exogenous transforming growth factor-β1 (TGF-β1), fucoidan induced low-level TGF-β1 secretion and promoted RPE cell migration. In contrast, under exogenous TGF-β1 stimulation, fucoidan attenuated excessive migration and reversed EMT-associated changes. Transcriptomic analysis identified alterations in genes associated with cell migration and metabolism, including LIM and cysteine-rich domains 1 (LMCD1). Suppression of LMCD1 expression further reduced TGF-β1-induced migration and EMT-associated responses, supporting its involvement in RPE remodeling. These findings demonstrate that fucoidan exerts bidirectional, context-dependent effects on RPE cells: supporting migration under basal conditions while limiting pathological remodeling under sustained TGF-β1 stimulation. Fucoidan may therefore provide a potential natural-product-based approach for modulating RPE repair and fibrotic remodeling relevant to AMD.

Keyword:

ge-related macular degeneration , fucoidan, cell migration, cysteine-rich domains 1

No. PP-038 / 天然物藥理組 / Natural Products Pharmacology (PP)

Imperatorin attenuates oxidative stress and lung fibrogenesis

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Pulmonary fibrosis is a progressive lung disease characterized by excessive extracellular matrix deposition, tissue remodeling, and irreversible loss of pulmonary function. Persistent inflammation and oxidative stress are recognized as important drivers of fibrotic progression. However, effective pharmacological interventions remain limited. Imperatorin, a naturally occurring furanocoumarin derivative with diverse pharmacological properties, has not been investigated for its therapeutic potential in pulmonary fibrosis. In this study, we examined the protective effects of imperatorin using complementary cellular and murine models. In cultured fibroblasts, imperatorin enhanced endogenous antioxidant defenses and reduced intracellular reactive oxygen species accumulation. In a murine model of poly(I:C)-induced pulmonary injury, intratracheal challenge resulted in prominent inflammatory cell recruitment and inflammasome activation in the lungs, both of which were substantially attenuated by oral administration of imperatorin. Furthermore, imperatorin also reduced poly(I:C)-induced epithelial-mesenchymal transition and fibrogenic responses, suggesting a direct inhibitory effect on key processes associated with pulmonary fibrosis. Collectively, our findings indicate that imperatorin protects against pulmonary fibrotic progression by simultaneously mitigating oxidative stress, pulmonary inflammation, and fibrogenic remodeling. These results provide the first evidence supporting the anti-fibrotic potential of imperatorin and highlight this naturally occurring compound as a promising candidate for further development as a therapeutic strategy for pulmonary fibrosis.

Keyword:
fibrosis, imperatorin, inflammation, lung, reactive oxygen species

No. PP-039 / 天然物藥理組 / Natural Products Pharmacology (PP)

Development of Inhibitory Strategies Targeting Drug-Resistant Genes and Cancer Stem Cells in Carfilzomib-Resistant Multiple Myeloma

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Multiple myeloma (MM) remains largely incurable because of relapse and drug resistance despite therapeutic advances. ATP-binding cassette (ABC) transporters and cancer stem cells (CSCs) may contribute to resistance, but their interplay in carfilzomib resistance remains unclear.

This study aims to establish carfilzomib-resistant MM cell models, investigate ABC transporter expression and CSC properties, and evaluate bioactive compounds derived from traditional Chinese medicinal herbs as potential adjunctive therapies. Resistant cell lines will be assessed for ABCB1, ABCC1, and ABCG2 expression, aldehyde dehydrogenase activity, and CSC population dynamics using flow cytometry.

Natural compounds and small-molecule agents with potential P-glycoprotein inhibitory activity will be screened for cytotoxicity and their ability to enhance carfilzomib sensitivity, individually and in combination with carfilzomib. Fluorescence-activated cell sorting and RNA immunoprecipitation will be used to investigate translational regulatory profiles in CSC populations from resistant and sensitive cells, identifying candidate genes associated with resistance and cellular heterogeneity. Bone marrow and peripheral blood samples from MM patients will be collected to validate selected findings.

This study may clarify mechanisms linking ABC transporters and CSC properties to carfilzomib resistance and provide a scientific basis for developing adjunctive strategies incorporating bioactive compounds from traditional Chinese medicine.

Keyword:
Multiple Myeloma (MM), Drug Resistance, Carfilzomib, ABC Transporters, Bioactive Compounds from Traditional Chinese Medicine, P-gp Inhibitors

No. PP-040 / 天然物藥理組 / Natural Products Pharmacology (PP)

Oxidative stress and MAPK signaling mediate LYK01's antiproliferative, G2/M-arresting, DNA-damaging, and proapoptotic effects on oral cancer cells

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Aurones are plant-derived flavonoids with pro-oxidant and anticancer effects. We synthesized a novel aurone analog, LYK01, and evaluated its activity against oral cancer cells. LYK01 selectively suppressed proliferation in four oral cancer cell lines while exhibiting minimal toxicity toward normal oral cells, its effects were attenuated by *N*-acetylcysteine (NAC), indicating an oxidative stress–dependent mechanism. At the cellular level, LYK01 induced G2/M cell-cycle arrest, increased intracellular ROS including mitochondrial superoxide (MitoSOX), produced DNA damage marked by γH2AX, and activated extrinsic apoptosis via caspase-8 and caspase-3 more strongly in cancer cells than in normal cells. Inhibition of MAPK pathways (p38, JNK, and ERK) reduced LYK01-induced antiproliferation and apoptosis, implicating MAPK signaling in its mechanism. Overall, LYK01 preferentially inhibits oral cancer cell growth through ROS-dependent and MAPK-associated pathways, supporting further *in vivo* and translational studies.

Keyword:

Aurones, oxidative stress, apoptosis, DNA damage, MAPK

No. PP-041 / 天然物藥理組 / Natural Products Pharmacology (PP)

Cryptocaryone causes ROS- and MAPK-dependent growth inhibition and apoptosis in triple-negative breast cancer cells and suppresses tumor growth in a mouse xenograft

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Omics analyses highlight the molecular complexity and therapeutic resistance of triple-negative breast cancer (TNBC). This study evaluated cryptocaryone (CPC) from *Cryptocarya concinna* and found it selectively inhibited proliferation of TNBC cell lines HCC1937 and MDA-MB-231 while sparing normal breast cells H184B5F5/M10. In an MDA-MB-231 xenograft model, CPC reduced tumor growth without causing significant body weight loss. Mechanistic investigations showed CPC induced apoptosis (increased sub-G1 fraction, annexin V positivity, and activation of caspases-3 and -8), provoked oxidative stress (elevated ROS, mitochondrial superoxide, and loss of mitochondrial membrane potential), and produced oxidative DNA damage (γH2AX and 8-hydroxy-2-deoxyguanosine). These effects were more pronounced in TNBC cells than in normal cells. CPC increased phosphorylation of JNK and p38 MAPK, and pharmacologic inhibition of JNK/p38 reduced CPC's antiproliferative and proapoptotic effects, *N*-acetylcysteine pretreatment similarly attenuated CPC-induced ROS, DNA damage, and cell death. ERK signaling contributed to CPC responses in MDA-MB-231 but not HCC1937 cells. Overall, CPC exerts selective antitumor activity against TNBC through ROS-driven DNA damage and MAPK-dependent apoptosis, with a favorable safety profile in normal cells and *in vivo*.

Keyword:
cryptocaryone, triple-negative breast cancer, apoptosis, DNA damage, MAPK

No. PP-042 / 天然物藥理組 / Natural Products Pharmacology (PP)

The ginger-derived molecule HMPM provokes apoptosis and DNA strand damage in triple-negative breast cancer cells

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Ginger contains many bioactive compounds, but the anticancer potential of its phenylalkanoids, including 1-(4'-hydroxy-3'-methoxyphenyl)-5-methoxydecan-3-one (HMPM), is poorly characterized. This study examined whether HMPM inhibits growth of triple-negative breast cancer (TNBC) cells and explored the underlying mechanisms. Using an ATP-based viability assay, flow cytometry, and Western blotting, we found that HMPM reduced proliferation across several breast cancer lines, with Hs578T and MDA-MB-231 being the most sensitive. The antiproliferative effect was ROS dependent, since *N*-acetylcysteine (NAC) substantially reversed HMPM's activity. In TNBC cells, HMPM altered cell-cycle distribution, increased annexin V positivity, raised total ROS and mitochondrial superoxide, decreased mitochondrial membrane potential, and depleted glutathione—changes that were greater than in normal M10 breast cells and were mitigated by NAC. Flow cytometry and Western blotting showed oxidative stress-linked activation of caspase-8 and caspase-3, and HMPM induced oxidative DNA damage as indicated by elevated γH2AX and 8-hydroxy-2'-deoxyguanosine. Overall, ginger-derived HMPM selectively suppresses TNBC cell growth through oxidative stress-dependent effects on cell cycle, mitochondrial function, apoptosis, and DNA integrity, while sparing normal breast cells, supporting further preclinical evaluation.

Keyword:

Ginger, phenylalkanoids, TNBC, apoptosis, oxidative stress

No. PP-043 / 天然物藥理組 / Natural Products Pharmacology (PP)

Bioassay-Guided Fractionation and Chemical Profiling of TCU-E519-1 with Osteoprotective Potential

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Bone homeostasis is maintained by a balance between osteoclast-mediated bone resorption and osteoblast-mediated bone formation. Disruption of this balance contributes to osteoporosis, which is characterized by reduced bone mass and increased skeletal fragility. Previous screening of local herbal materials identified TCU-E519-1, an annual herbaceous plant belonging to the Poaceae family, as a candidate with osteoprotective potential. This study evaluated the effects of its solvent fractions on bone mineralization in a zebrafish model and used the bioassay results to guide subsequent chemical fractionation. The crude aqueous extract of TCU-E519-1 was subjected to liquid–liquid partitioning. Among the resulting fractions, the n-butanol fraction exhibited the most promising activity, attenuating the loss of bone mineralization in the zebrafish model. Based on these findings, the n-butanol fraction was selected for further separation by Sephadex gel chromatography, and the collected eluates were pooled into ten subfractions. These subfractions were profiled by HPLC to examine their chromatographic patterns and guide further separation. Chemical characterization using liquid chromatography coupled with Orbitrap high-resolution mass spectrometry (LC–HRMS) is ongoing to support tentative annotation of their chemical constituents. These findings support the osteoprotective potential of the n-butanol fraction of TCU-E519-1 in the zebrafish model. This bioassay-guided fractionation approach provides a foundation for subsequent evaluation of subfraction activity and identification of constituents contributing to the observed effect.

Keyword:
Osteoprotection, Zebrafish, Bioassay-guided fractionation, Chemical profiling, Natural products

No. PP-044 / 天然物藥理組 / Natural Products Pharmacology (PP)

Natural Product Compound MC Suppresses Tumor Lung Metastasis through depressing Angiogenesis and Lymphangiogenesis

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Introduction: High mortality rates in cancer patients are primarily associated with metastasis rather than primary tumors alone.Angiogenesis and lymphangiogenesis—the formation of new blood and lymphatic vessels from pre-existing vasculature—are crucial processes that facilitate cancer cell dissemination and are linked to poor prognosis and survival. Vascular endothelial growth factor (VEGF) and its receptor (VEGFR) play pivotal roles in these processes, making VEGF/VEGFR signaling an attractive therapeutic target for neovascularization-related diseases, including cancer. Natural products remain a valuable source for drug discovery. This study investigates the anti-tumor potential of a bioactive plant-derived natural product, Compound MC.

Materials and Methods: We evaluated the anti-angiogenic and anti-lymphangiogenic effects of Compound MC using *ex vivo aortic ring sprouting assays and an in vivo lung metastasis mouse model. Immunohistochemical staining were performed on xenograft tumor tissue sections to assess the degree of lung metastasis.*

Results and Discussion: Compound MC demonstrated concentration-dependent anti-proliferative effects against human vascular and lymphatic endothelial cells. Both ex vivo and in vivo models showed that systemic administration of Compound MC significantly suppressed microvessel sprouting and neovascularization. Furthermore, Compound MC significantly inhibited melanoma tumor lung metastasis in vivo.

Conclusion: Our findings demonstrate that Compound MC inhibits tumor metastasis by interfering with tumor-induced neovascularization, as well as lymphangiogenesis, supporting its potential as a candidate for the development of novel anti-tumor therapeutics.

Keyword:
Natural Product Compound, Angiogenesis, Lymphangiogenesis, Tumor Metastasis

No. PP-045 / 天然物藥理組 / Natural Products Pharmacology (PP)

Antler Gelatin-Derived Carbon Nanodots Attenuate Nitric Oxide Accumulation in LPS-Stimulated Macrophages

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Deer antler is a traditional medicinal material, and prolonged processing is sometimes considered beneficial for medicinal efficacy. However, this concept requires experimental verification. This study investigated how hydrothermal conditions affect the anti-inflammatory activity of antler gelatin. Carbon nanodots were prepared at 180°C or 220°C for 3 or 6 h and compared with unprocessed antler gelatin. Lipopolysaccharide (LPS)-stimulated RAW 264.7 macrophages were treated with various sample concentrations. Cell viability was assessed using the MTT assay, and nitrite accumulation was measured using the Griess assay.

All samples maintained cell viability above 80% at the tested concentrations. The preparation obtained at 220°C for 6 h exhibited the strongest inhibitory effect, reducing LPS-induced nitrite accumulation by approximately 23%, whereas unprocessed antler gelatin increased nitrite accumulation. Some other hydrothermally processed preparations also exhibited inhibitory effects at higher tested concentrations.

These findings indicate that appropriate hydrothermal processing can shift the effects of antler gelatin from promoting to reducing nitrite accumulation in stimulated macrophages. The results highlight the importance of processing temperature and duration and support further exploration of antler gelatin-derived materials for anti-inflammatory applications.

Keyword:
Animal-derived medicinal materials, Thermal processing, Anti-inflammatory

No. PP-046 / 天然物藥理組 / Natural Products Pharmacology (PP)

Anti-Inflammatory Effects of Fungal Diketopiperazine Homomorphins in TNF-α/IFN-γ–Stimulated Human Keratinocytes

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In Taiwan, eczema is a representative inflammatory skin disease and a common clinical concern. Although current treatments like topical corticosteroids alleviate symptoms, their long-term use is often limited by adverse effects, highlighting the need for safer anti-inflammatory agents. Homomorphins, novel diketopiperazine-containing compounds obtained from *Aspergillus homomorphus* CBS 101889, possess anti-inflammatory potential, therefore, this study evaluates their effects in human skin cells.

To assess the anti-inflammatory effect of homomorphins, a TNF-α/IFN-γ-induced human Keratinocyte (HaCaT) model was employed. CCK-8 assays confirmed that homomorphins exhibited no cytotoxicity up to 50 μM. Subsequent qPCR analysis of inflammatory mRNA markers identified MW353 as the most potent candidate, which was selected for further mechanistic studies. In wound healing assays and Western blot analysis, MW353 shows pro-healing effects by the upregulation of epithelial-mesenchymal transition (EMT). To elucidate the underlying mechanisms, RNA sequencing and Ingenuity Pathway Analysis (IPA) were performed. The results implicated the RELA/NF-κB, ERK, and p38 signaling pathways in the effects of MW353. Western blotting confirmed that MW353 significantly reduced the phosphorylation of NF-κB, ERK, and p38, while immunocytochemistry demonstrated that it inhibited NF-κB nuclear translocation. IPA Regulator Effects analysis further identified eight inflammation-related downstream targets, including CCL2, CCL20, CXCL1, CXCL2, CXCL3, CXCL8, ICAM-1, and TNF-α. Subsequent qPCR and ELISA analyses confirmed that MW353 significantly reduced the mRNA and/or protein expression of these inflammatory mediators.

These findings suggest that MW353 exerts anti-inflammatory and pro-healing effects by modulating NF-κB, p38, and ERK pathways and inhibiting eight inflammation-related genes, highlighting its therapeutic potential for inflammatory skin diseases.

Keyword:
Fungal natural products, Dermatitis, Transcriptomics, Wound healing, Anti-inflammation, Homomorphins

No. PP-047 / 天然物藥理組 / Natural Products Pharmacology (PP)

Xanthohumol Alleviates Atopic Dermatitis by Modulating Anti-Inflammatory Pathways in HaCaT Cells and MC903-Induced Mouse Models

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Xanthohumol, a natural prenylated flavonoid derived from hops (*Humulus lupulus*), exhibits potent anti-inflammatory and antioxidant properties. This study investigated the therapeutic effects and molecular mechanisms of xanthohumol in atopic dermatitis (AD). *In vitro* experiments using human keratinocytes (HaCaT) demonstrated that xanthohumol effectively suppressed TNF-α/IFN-γ-induced type 1 inflammation by reducing mRNA levels of pro-inflammatory cytokines (IL-6, IL-8, IL-1β, TNF-α) and chemokines (CCL-5, CCL-22, CCL-17). Additionally, in cells stimulated with Poly I: C/TSLP to mimic type 2 inflammation, xanthohumol downregulated the expression of IL-4, IL-13, IL-31, and TSLP. Furthermore, xanthohumol mitigated the TNF-α/IFN-γ-induced reduction of skin barrier proteins, including filaggrin, loricrin, and involucrin. Western blot analysis revealed that xanthohumol exerted these protective effects by inhibiting the activation of MAPK, NF-κB, STAT1/3, and Akt signaling pathways. *In vivo* evaluation using an AD model induced by topical application of MC903 to the ears of BALB/c mice showed that xanthohumol significantly improved clinical symptoms, including reduced ear thickness, decreased scratching frequency, lowered transepidermal water loss (TEWL), alleviated erythema, and enhanced skin hydration. Histopathological and immunohistochemical analyses further demonstrated that xanthohumol reduced epidermal thickening, subcutaneous mast cell infiltration, and TSLP protein expression in skin tissues. Collectively, these findings indicate that xanthohumol effectively alleviates atopic dermatitis-induced pruritus and disease progression by modulating inflammatory pathways and restoring skin barrier function, suggesting its potential as a promising therapeutic strategy for AD.

Keyword:

Xanthohumol, Atopic dermatitis, Thymic stromal lymphopoietin (TSLP)

No. PP-048 / 天然物藥理組 / Natural Products Pharmacology (PP)

Evaluation of the Anti-cancer Activity of Chaetoglobosin A from Chaetomium globosum Km1226: An In Vitro Study

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Glioblastoma (GBM) is the most common primary malignant brain tumor in adults and has a poor prognosis, with a 5-year survival rate of only 7.2%. Despite standard treatment including surgical resection, radiotherapy and chemotherapy, GBM remains incurable. Breast cancer is the most prevalent cancer among women worldwide and in Taiwan,with triple-negative breast cancer (TNBC) representing the most aggressive subtype and lacking well-defined molecular targets. Identifying natural products with potential therapeutic or adjuvant applications may provide new strategies for cancer treatment. Chaetoglobosin A (ChA), a secondary metabolite of the fungus *Chaetomium globosum Km1226* belonging to the cytochalasan family, have been reported to exhibit anticancer activity. In this study, we investigated the anticancer effects of ChA on glioblastoma and breast cancer cell lines. Our results showed that ChA reduced the viability of G5T/VGH glioblastoma and breast cancer cell lines, particularly in TNBC cells. ChA induced cell cycle arrest, apoptosis, and autophagy in these cell lines, indicating that ChA exhibits anti-glioblastoma and anti-TNBC activities in vitro. This study will further investigate the inhibitory effects and molecular mechanisms of ChA in GBM and breast cancer progression, with the goal of exploring its potential as a new therapeutic options for anticancer therapy.

Keyword:
Glioblastoma, triple-negative breast cancer, chaetoglobosin A, apoptosis, cell cycle arrest, autophagy

No. PP-049 / 天然物藥理組 / Natural Products Pharmacology (PP)

Anti-diabetic, anti-depressive and gut microbiota modulation effects of galactomannan from Trigonella foneum-graecum

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Several studies have demonstrated that polysaccharides can modulate gut microbiota, whose dysbiosis is associated with diabetes and depression. Accordingly, this study investigated the interactions between galactomannans and gut microbiota and their related bioactivities. Forty-five C57BL/6 mice were divided into nine groups and administered **TF-5**, a galactomannan purified from *T. foneum-graecum*, with chronic unpredictable mild stress (CUMS) and/or high-fat diet (HFD) for eight weeks. Physiological metrics and behavioral tests were conducted during the experiment, followed by the collection of organs, fecal and serum at the end for gut microbiota, SCFAs and biomarker analysis.

Results indicated that, **TF-5** effectively regulated blood glucose levels and body weight, enhanced SCFAs production (+20-30%) and modulated TNF-α and TGF-β levels (-32.3% and +60.4%, individually). Furthermore, **TF-5** increased serum serotonin levels (+48%), reduced immobility time in forced swimming test (FST, -7.91%) and tail suspension test (TST, -6.83%), increased sucrose preference in SPT (sucrose preference test, +36.48%), and regulated serum TNF-α and TGF-β levels (-25% and +135%, respectively).

In gut microbiota composition, in the CUMS + **TF-5** group, *Faecalibaculum* sp. (667.5-fold increase) increased the most, whereas *Turicibacter* sp. (relatively 93.1% decrease) decreased the most. In the HFD + **TF-5** group, *Dubosiella* sp. (19-fold increase) and *Bacteroides* sp. (relatively 81.7% decrease) exhibited the most pronounced changes. In the CUMS + HFD + **TF-5** group, *Blautia* sp. (relatively 88.4% decrease) and *Akkermansia* sp. (relatively 98% decrease) showed the greatest alterations.

In conclusion, this study revealed the connections between galactomannans, gut microbiota, diabetes and depression.

Keyword:

Trigonella foneum-graecum, galactomannan, gut microbiota, diabetes, depression

No. PP-050 / 天然物藥理組 / Natural Products Pharmacology (PP)

A major alkamide derivative from the fruits of the endemic Taiwanese species Zanthoxylum pistaciiflorum attenuates lipopolysaccharide-induced inflammatory responses in RAW 264.7 macrophages

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This study evaluates the anti-inflammatory potential of *Zanthoxylum pistaciiflorum* fruits, an endemic Taiwanese species. Using a bioassay-guided fractionation strategy coupled with an NF-κB luciferase reporter assay, *α*-sanshool (**1**) was identified as the primary bioactive alkamide. Liquid-liquid partitioning revealed that the 90% aqueous Methanol fraction exhibited the highest suppression of LPS-induced NF-κB transcriptional activity in RAW 264.7 macrophages. Chromatographic fingerprinting confirmed that *α*-sanshool (**1**) concentrated progressively into the active fraction, showing a strong positive correlation with NF-κB inhibition. Purified *α*-sanshool (**1**) effectively suppressed NF-κB transcription and downstream nitric oxide production. Yield-based calculations demonstrated that targeting *α*-sanshool (**1**) drastically reduces the required raw fruit material compared to traditional crude extract regimens. Furthermore, the live-cell luciferase reporter platform provided a highly sensitive method to monitor real-time promoter activity, preventing false negatives during early fractionation. These findings establish *α*-sanshool (**1**) as a functional marker for standardizing *Z. pistaciiflorum* preparations and validate a bio-relevant framework for natural product discovery.

Keyword:
Zanthoxylum pistaciiflorum, α-sanshool, NF-kB, Bioassay-guided fractionation, luciferase reporter assay

No. PP-051 / 天然物藥理組 / Natural Products Pharmacology (PP)

From Bench to Bedside: Translational Development of Natural Product-Derived Vesicles

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Extracellular vesicles (EVs) are nanoparticles enclosed by lipid bilayers that facilitate intercellular communication by carrying proteins, lipids, nucleic acids, and metabolites. Their biocompatibility, ability to protect cargo, and potential for targeted delivery have made them prominent in biomedical research. Recently, vesicles derived from natural products (NPVs) from plants, fungi, and marine life have gained attention as promising nanotherapeutic platforms. Their natural abundance, scalability, and lower production costs provide advantages for drug development. NPVs can carry bioactive compounds from their source organisms and deliver them to target cells, producing various biological and pharmacological effects. We highlight recent progress in NPV research, including source selection, isolation, purification, physicochemical characterization, biological activities, and therapeutic applications. It also addresses challenges for clinical translation, such as production consistency, quality control, safety, efficacy, and regulatory hurdles. An integrated approach spanning laboratory research and clinical application is proposed to accelerate NPV-based therapies. Overall, these advances underscore the therapeutic potential of NPVs and the challenges associated with their clinical translation, providing a roadmap for advancing natural product-derived nanomedicines toward clinical applications.

Keyword:
Extracellular vesicles, Natural product-derived vesicles, Nanotherapeutics, Drug delivery, Clinical translation

No. PP-052 / 天然物藥理組 / Natural Products Pharmacology (PP)

Anti-ocular inflammatory Effects of Compound DC and Its Protective Potential against Experimental Retinal Injuries

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Dehydrocurvularin (DC), a bioactive constituent from the marine fungus Curvularia intermedia Km0855, has been reported to exhibit anti-inflammatory and immunomodulatory activities. Predicted DC targets overlapping with uveitis- and glaucoma-associated genes included MMP2, PTGS2 (encoding COX-2), and STAT3, supporting investigation of its anti-inflammatory and retinal protective potential. Although endotoxin-induced uveitis (EIU)-related and N-methyl-D-aspartate (NMDA)-induced retinal injury differ in their initiating insults, both could involve microglial activation and monocyte recruitment. This study evaluated DC-mediated retinal protection and modulation of monocyte- and microglia-associated inflammatory responses. To characterize posterior segment involvement in EIU, retinal and RPE-flatmount immunofluorescence was first assessed. Compared with controls, EIU tissues exhibited increased Iba-1 immunoreactivity, disorganized recoverin-positive photoreceptors, and less distinct ZO-1-defined junctional borders. Subsequent electroretinography (ERG) analysis showed the protective effects of DC in EIU-associated retinal dysfunction. In NMDA-induced injury, DC also attenuated reductions in b-wave/PhNR amplitudes and RBPMS-positive retinal ganglion cell counts. To assess cellular functions and mechanisms, THP-1 monocytes and BV-2 microglia were stimulated with lipopolysaccharide (LPS). First, in THP-1 cells, DC reduced MMP-9 gelatinolytic activity and protein/mRNA expression, accompanied by significant inhibition of p65, ERK, and STAT3 phosphorylation. Second, in BV-2 cells, DC attenuated nitric oxide production and iNOS and COX-2 protein expression. Consistently, DC also reduced p65 and STAT3 phosphorylation in BV-2 cells. Notably, these STAT3 and COX-2 changes aligned with overlap analysis candidates. Together, these results support the anti-inflammatory activity and retinal protective potential of DC. Further evaluation of retinal Iba-1/CD68 immunoreactivity and inflammatory cytokines will help characterize its ocular therapeutic potential.

Keyword:
NMDA, EIU, ERG, microglia, iNOS, MMP-9

No. PP-053 / 天然物藥理組 / Natural Products Pharmacology (PP)

Investigating the Mechanisms Underlying the Anti-microglial and Neuroprotective Effects of Arthrinone in Retinal Injury and Visual Pathway Dysfunction

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Normal tension glaucoma (NTG) is similarly characterized by progressive retinal ganglion cell (RGC) loss associated with microglial activation and neuroinflammation. Also, primary neuronal injury may affect visual distal or postsynaptic neurons, resulting in transneuronal degeneration. A fungal natural product Arthrinone, isolated from Stemphylium botryosum Ca1-9, has reported anti-inflammatory properties. However, its underlying mechanisms and protective effects against NMDA-induced retinal injury and TND remain unclear. In vitro, Arthrinone concentration-dependently reduced LPS-induced NO level and iNOS expression without affecting microglial BV-2 cell viability. Additionally, it attenuated productions of IL-6, MCP-1, and intracellular ROS. Among signaling issues, Arthrinone significantly inhibited LPS-induced STAT3 phosphorylation but did not affect p65, p38, or JNK phosphorylation. In vivo, the intravitreal NMDA-induced retinal injury model associated with TND was established in mice. Arthrinone preserved retinal electrophysiological function (PhNR wave) and visual transmission (P2 wave) assessed by electroretinography (ERG) and visual evoked potentials (VEP), respectively. Cryosectioning and immunofluorescent analyses further revealed Arthrinone reduced microglial activation (CD68), proliferation (Iba-1), and RGC loss (RBPMS) following treatment. Taken together, Arthrinone inhibited microglial activation through STAT3 inhibition, and microglia-mediated inflammatory responses while protecting RGC survival and preserving retinal electrophysiological and visual transmission functions as therapeutic potential for NTG.

Keyword:
Normal tension glaucoma, NMDA, microglia, Arthrinone, Electroretinography, Neuroinflammation

No. PP-054 / 天然物藥理組 / Natural Products Pharmacology (PP)

Evaluation of the Anti-inflammatory Effects of Spilanthes acmella on MSU-Induced Inflammation in Silico and in Vitro

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Gout is an inflammatory disease characterized by the deposition of monosodium urate (MSU) crystals in joints, which triggers inflammatory responses and the release of pro-inflammatory cytokines. *Spilanthes acmella* is a medicinal plant with potential anti-inflammatory properties. This study investigated the anti-inflammatory effects of *S. acmella* and its bioactive compounds on MSU-induced inflammation using network pharmacology and in vitro experiments.

Network pharmacology was used to identify bioactive compounds and predict potential targets related to gout and inflammation. The overlapping targets were further analyzed using protein–protein interaction (PPI) networks, Gene Ontology (GO), and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analyses. An MSU-induced inflammatory cell model was used to evaluate the effects of *S. acmella* extract and its bioactive compounds on cell viability and inflammatory responses. Western blotting was performed to examine the expression of inflammation-related proteins. The results indicated that network pharmacology analysis identified potential targets and signaling pathways associated with the anti-inflammatory effects of*S. acmella* . In the MSU-induced inflammatory cell model, treatment with *S. acmella* extract or its bioactive compounds significantly reduced the levels of TNF-α, IL-6, and IL-1β. These findings suggest that *S. acmella* has potential anti-inflammatory effects against MSU-induced inflammation.

Keyword:

Spilanthes acmella, network pharmacology, gout, monosodium urate, inflammation, Western blotting

No. PP-055 / 天然物藥理組 / Natural Products Pharmacology (PP)

Pharmacological Evaluation of CFLE10 Anti-Steatotic Activity in Reducing Lipid Droplet Accumulation through ATGL-mediated Lipid Mobilization in PNPLA3-I148M Liver Cell Model

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Metabolic dysfunction-associated steatotic liver disease (MASLD) is characterized by having hepatic lipid accumulation. The PNPLA3-I148M variant is a genetic change that promotes PNPLA3 accumulation on lipid droplets, reducing ATGL-mediated triglyceride breakdown and increasing lipid accumulation. CFLE10 is a bioactive extract with potential anti-steatotic activity through modulation of ATGL-ABHD5 pathway to promote triglyceride breakdown. This study hypothesized that CFLE10 may restore ABHD5 availability for ATGL activation, thereby promoting triglyceride hydrolysis and reducing lipid accumulation in PNPLA3-I148M cells. AML12 cell models expressing PNPLA3-WT and PNPLA3-I148M were established through lentiviral gene delivery, with tRFP control using *pLAS3w.Pbsd-L-tRFP* vector. Following lentiviral transduction, fluorescence-activated cell sorting (FACS) was performed to enrich fluorescent-positive cells, achieving 97.6%, 97.9%, and 98.6% positivity in the tRFP control, PNPLA3-WT, and PNPLA3-I148M populations, respectively. Successful cell model and FACS enrichment were further evaluated by Western blotting. The lipid droplet assay was performed by staining with BODIPY 493/503, followed by fluorescence imaging and analysis using ImageXpress Micro system. Preliminary analyses showed comparable lipid accumulation in parental AML12 cells, tRFP control cells, and PNPLA3-WT cells under both basal and fatty acid-treated conditions. In contrast, PNPLA3-I148M cells exhibited significantly greater lipid accumulation under both conditions, supporting the successful establishment of a cellular model of PNPLA3-I148M-associated lipid accumulation. Further experiments using these cell models showed CFLE10 treatment reduced lipid-droplet accumulation across all models. These preliminary findings suggest that CFLE10 may exert anti-steatotic effects even in cells expressing the PNPLA3-I148M variant, warranting further investigation into its effects on lipid metabolism.

Keyword:
MASLD, PNPLA3-I148M, CFLE10, Lipid Droplets, ATGL–ABHD5 Pathway, Anti-Steatotic Activity

No. PP-056 / 天然物藥理組 / Natural Products Pharmacology (PP)

Identification of an Edible Plant Extract That Induces ROS-Dependent Oxeiptosis Through the KEAP1/PGAM5/AIFM1 Axis in Multiple Myeloma Cells

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Multiple myeloma (MM) remains largely incurable despite therapeutic advances, highlighting the need for novel treatment strategies. Given the elevated basal levels of reactive oxygen species (ROS) in MM cells, we screened 346 plant extracts for those whose cytotoxicity could be attenuated by the ROS scavenger N-acetylcysteine (NAC) and identified edible plant extract No. 61 (EPE61) as a promising candidate for inducing MM cell death. The significant attenuation of EPE61-induced cytotoxicity by NAC supports the involvement of ROS in its effects. EPE61 also induced G2/M cell cycle arrest and apoptosis-like morphological changes, accompanied by PARP1 and caspase-3 cleavage. However, the pan-caspase inhibitor Z-VAD-FMK failed to fully restore cell viability, and inhibitors targeting necroptosis, ferroptosis, parthanatos, and autophagy-associated processes did not substantially reverse the cytotoxic effects. These findings prompted further investigation of oxeiptosis, a ROS-dependent, caspase-independent cell death pathway. EPE61 altered AIFM1 phosphorylation, while PGAM5 knockdown significantly attenuated its cytotoxicity in RPMI-8226 cells, supporting the potential involvement of PGAM5-associated oxeiptosis. Furthermore, EPE61 exhibited synergistic cytotoxic effects in combination with bortezomib (BTZ) in MM cells. Collectively, these findings suggest that oxeiptosis may contribute to EPE61-induced MM cell death. Its synergistic effects with BTZ further support the potential of EPE61 as a candidate for combination therapy against MM.

Keyword:
multiple myeloma, oxeiptosis, KEAP1, PGAM5, AIFM1

No. PP-057 / 天然物藥理組 / Natural Products Pharmacology (PP)

Theaflavin-3,3'-digallate Exerts Broad-Spectrum Antiviral Activity against Enteroviruses by Directly Inactivating Virions and Disrupting Capsid–Receptor Interactions

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Enteroviruses cause a broad spectrum of human diseases, yet no approved antiviral therapies currently exist. Here, we screened theaflavin (TF-1) and its galloylated derivatives (TF-2A, TF-2B, TF-3), and identified theaflavin-3,3'-digallate (TF-3) as the most potent inhibitor of EV-A71 replication (EC50 = 9.12 μM, selectivity index = 59.9), with low cytotoxicity in RD cells. TF-3 dose-dependently suppressed EV-A71 and EV-D68 cytopathic effect, viral titer, viral RNA, and viral protein expression, and showed broad-spectrum activity against multiple EV-A71 and EV-D68 subclades, as well as coxsackieviruses A16 and B3. Time-of-addition assays indicated that TF-3 primarily acts at the early stage of infection. Mechanistic studies demonstrated that TF-3 rapidly and directly inactivates virions in a dose- and time-dependent manner, blocks viral attachment and entry, and disrupts virus binding to the host receptors SCARB2 and ICAM-5. Furthermore, particle stability thermal release assay showed that TF-3 increases capsid thermal stability and delays genomic RNA release. Molecular docking also suggested direct interactions of TF-3 with enterovirus capsid proteins. Collectively, these findings identify TF-3 as a potent broad-spectrum, capsid-targeting enterovirus inhibitor that acts through multiple mechanisms, particularly direct virion targeting and blockade of early infection, supporting its potential as a promising natural antiviral candidate for the prevention and treatment of enterovirus infections.

Keyword:
theaflavin-3,3'-digallate (TF-3), enterovirus A71, enterovirus D68, inactivation, viral capsid stability, broad-spectrum antiviral

No. PP-058 / 天然物藥理組 / Natural Products Pharmacology (PP)

Biological Activities of Low-Polarity Extracts of Sarcodia suae

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Sarcodia suae (*S. suae*) is a red alga native to Taiwan that is cultivated as an edible seaweed. Red algae are rich in bioactive substances, and low-polarity compounds have frequently shown potential for pharmaceutical applications. However, the biological activities of low-polarity extracts of *S. suae* remain unexplored. This study aimed to investigate the biological activities of low-polarity extracts of *S. suae* and isolate their active compounds. Supercritical fluid extraction was performed using carbon dioxide with 5% ethanol, and the resulting crude extract was fractionated by normal-phase column chromatography with gradient elution. Biological activities were evaluated using animal and cell-based assays. The *S. suae* extract significantly accelerated wound healing and increased the expression of angiogenesis-related factors. It also exhibited anti-inflammatory effects, including the suppression of lipopolysaccharide-induced macrophage M1 polarization and the production of pro-inflammatory mediators. Bioassay-guided fractionation of the ethyl acetate (EA) extract based on anti-inflammatory activity yielded a fraction enriched in palmitic acid (C16:0), heptadecanoic acid (C17:0), oleic acid (C18:1), and *β*-sitosterol. *β*-Sitosterol was the predominant constituent, accounting for approximately 80% of the fraction by weight. *β*-Sitosterol is an important bioactive compound that promotes wound healing and suppresses inflammatory responses, suggesting that it may play a key role in the therapeutic applications of low-polarity extracts of *S. suae*. This study provides a foundation for developing these extracts into wound-healing and anti-inflammatory therapeutics.

Keyword:

Sarcodia suae, low-polarity extraction, inflammatory regulation, wound-healing, bioactivity-directed fractionation

No. PP-059/ 天然物藥理組 / Natural Products Pharmacology (PP)

Network Pharmacology and Molecular Docking Analysis of Indigenous Legume Phytochemicals against Pro-inflammatory Targets in Chronic Kidney Disease

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Chronic, low-grade inflammation drives chronic kidney disease (CKD) progression through oxidative stress, renal damage, and fibrosis. As single-target drugs often fail to impede progression, safer, multi-target therapeutics are necessary. Although Philippine indigenous legumes (*Cajanus cajan, Phaseolus lunatus, Lablab purpureus*) possess known anti-inflammatory activity, their network-level mechanisms against CKD remain unmapped. This study integrated network pharmacology and molecular docking to evaluate legume-derived compounds against CKD-related inflammation. Centrality filtering and MCODE clustering identified key pro-inflammatory targets. Molecular docking then evaluated compound-target interactions relative to native-ligand baselines. Network analysis highlighted core pro-inflammatory targets, tumor necrosis factor (TNF), interleukin-6 (IL6), interleukin-1 beta (IL1B), AKT serine/threonine kinase 1 (AKT1), and nuclear factor-kappa B subunit 1 (NFKB1). While native ligands maintained superior binding for AKT1 (-9.9 to -10.5 kcal/mol) and TNF (-12.5 to -13.2 kcal/mol), legume phytochemicals outperformed the native ligand for NFKB1 (-4.50 to -4.70 kcal/mol). Specifically, Genistein (-5.30 kcal/mol) and Cajanol (-5.27 kcal/mol) exhibited highly stable interactions with NFKB1, whereas Quercetin (-8.5 kcal/mol) and Apigenin (-9.60 kcal/mol) bound strongly to AKT1 and TNF. These results demonstrate that legume phytochemicals exert multi-target anti-inflammatory effects through selective modulation of the NFKB1 signaling pathway, providing a theoretical basis for future *in vitro* validation.

Keywords: CKD, inflammation, legume, network pharmacology, molecular docking

No. PP-060 / 天然物藥理組 / Natural Products Pharmacology (PP)

Applications of thin-layer chromatography-direct bioautography assay in isolation and identification of herbal antimicrobial compounds

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Thin-layer chromatography-direct bioautography (TLC-DB) is a rapid method for screening antimicrobial compounds in herbal extracts. However, its quantitative precision is often limited by many other factors. Conversely, the minimum inhibitory concentration (MIC) is traditionally determined in liquid media. This study systematically evaluated the performance of TLC-DB on silica gel TLC plates using four bacterial strains: Acinetobacter baumannii ATCC 19606, Pedobacter saltans BCRC 80096, Staphylococcus aureus BCRC 1268, and Rhodococcus jostii RHA1, against four antibiotics: chloramphenicol, gentamicin, neomycin, and kanamycin. Comparative analysis revealed pronounced discrepancies between the two assay environments: MIC values varied nearly 760-fold (1.4 μM – 1064 μM), TLC- minimum detectable dose (MDD, mmol) by 520-fold (0.01 μmol - 5.2 μmol), and clear zone areas (CZA) by 28-fold (9.2 mm2- 263.2 mm2). In this study, RHA1 exhibited relatively high MIC values. Notably, the inhibition zones showed a concentration-dependent response in the TLC-DB assay, accompanied by low MDD values (0.01 μmol - 0.2 μmol) against four antibiotics. Given these characteristics, RHA1, a Biosafety Level 1 organism, was selected to detect the antimicrobial constituents in methanolic rhubarb extracts, which were identified as emodin (1.1%) and catechin (0.05%).

Keyword:
Antibacterial Activity, Catechin, Emodin, Rheum palmatum, TLC-direct bioautography

No. PP-061 / 天然物藥理組 / Natural Products Pharmacology (PP)

Thonningianin A inhibits the metastasis of renal cell carcinoma and sunitinib-resistant cells via the HMGCS1-mediated ER stress and autophagy axis.

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Renal cell carcinoma (RCC), representing 80% of kidney cancers, often presents with metastasis at diagnosis, leading to poor prognosis. Although targeted therapies like sunitinib are widely used, they primarily focus on inhibiting angiogenesis or cell growth, with limited efficacy in eradicating metastatic cells. Furthermore, side effects and drug resistance remain significant clinical challenges. Therefore, developing natural bioactive compounds with anti-metastatic mechanisms is of high translational value. Thonningianin A (ThA) is a natural ellagitannin isolated from Penthorum chinense Pursh that exhibits antitumor and antioxidant activities. In this study, we found that low-dose ThA (10 μM) significantly inhibited the migration and invasion of RCC cells with minimal cytotoxicity. RNA sequencing, GSEA, qPCR, and Western blotting indicated that ThA significantly induced the overexpression of HMGCS1, a key enzyme in the mevalonate pathway. This upregulation led to dysregulation of the cholesterol biosynthesis pathway, which subsequently triggered ER stress and activated autophagy, ultimately inhibiting cancer metastasis. Inhibiting ER stress with 4-PBA or autophagy with 3-MA reversed the ThA-mediated suppression of migration and invasion, and 4-PBA also reduced ThA-induced autophagy. Moreover, silencing HMGCS1 by siRNA suppressed ThA-induced ER stress and autophagy, restoring the migration and invasion of 786-O and Caki-1 cells. Importantly, ThA also effectively inhibited the migration and invasion of sunitinib-resistant A-498-SR and Caki-1-SR cells. In summary, this study demonstrates that ThA inhibits the metastasis of RCC and drug-resistant RCC cells via the HMGCS1-mediated ER stress/autophagy axis, supporting its potential as a therapeutic agent or adjuvant strategy for RCC treatment.

Keyword:

Renal cell carcinoma, Thonningianin A, HMGCS1

No. PP-062 / 天然物藥理組 / Natural Products Pharmacology (PP)

Immunoregulatory mechanisms of botanical root extract GA and its therapeutic potential in sepsis and atopic dermatitis

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Inflammation-related disorders contribute substantially to global morbidity and mortality. However, current anti-inflammatory treatments, including nonsteroidal anti-inflammatory drugs (NSAIDs), glucocorticoids, and biologics, are limited by adverse effects, high costs, and systemic toxicity. Natural compounds with immunoregulatory properties may offer therapeutic alternatives. GA, a botanical root extract, has a broad range of reported pharmacological activities. This study aimed to characterize GA's anti-inflammatory mechanisms. We assessed GA's effects in LPS-stimulated RAW264.7 macrophages using immunoblotting, RT-qPCR, reporter assays, ELISA, and transfection. GA significantly suppressed expression of cyclooxygenase-2 (COX-2), iNOS, IL-6, IL-1β, and TNF-α. Mechanistically, GA attenuated activation of the NF-κB and MAPK/AP-1 pathways. GA blocked NF-κB p65 nuclear translocation and its transcriptional activity. Crucially, in vivo GA administration dramatically improved survival and mitigated multi-organ damage in a cecal ligation and puncture (CLP)-induced sepsis model. In contrast, GA suppressed STAT1, STAT3, and JNK phosphorylation and inflammatory cytokine expression in Hacat keratinocytes after TNF-α and IFN-γ exposure. In an oxazolone-induced atopic dermatitis (AD) model, GA significantly alleviated ear swelling and epidermal hyperplasia. In conclusion, using sepsis and atopic dermatitis as complementary models of acute systemic and chronic barrier inflammation, we demonstrated that GA modulates shared innate and barrier-associated inflammatory signaling pathways to restore immune homeostasis. Collectively, these findings highlight GA as a viable therapeutic candidate and support future studies to delineate its direct molecular targets and clinical efficacy.

Keyword:
inflammatory disease, natural compounds, sepsis, atopic dermatitis

No. PP-063 / 天然物藥理組 / Natural Products Pharmacology (PP)

Oxyresveratrol Attenuates Sleep Deprivation-Induced Depression-Like Behaviors by Modulating ROS-Mediated NLRP3 Inflammasome Activation and BDNF Signaling

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Background and Objective:
Depression is associated with oxidative stress, neuroinflammation, and impaired neurotrophic signaling. This study investigated the antidepressant-like effects of oxyresveratrol (ORV) and its underlying molecular mechanism in vitro and in vivo.

Methods:
Mouse hippocampal HT-22 cells were exposed to corticosterone (CORT) and treated with ORV. Intracellular reactive oxygen species (ROS) levels were measured, and RNA sequencing (RNA-seq) was performed to identify potential regulatory genes. RT-qPCR and Western blotting assessed NLRP3, caspase-1, cleaved GSDMD, cleaved IL-1β, and brain-derived neurotrophic factor (BDNF) expression. Sleep-deprived mice underwent sucrose preference (SPT), forced swimming (FST), and tail suspension (TST) tests. Brain histopathology and protein expression were evaluated using H&E staining and immunohistochemistry, respectively

Results and Conclusion:
In vitro study showed that ORV significantly reduced CORT-induced ROS accumulation and NLRP3, caspase-1, cleaved GSDMD, and cleaved IL-1β expression in HT-22 cells. RNA-seq was used to investigate potential regulators associated with ORV-mediated restoration of CORT-suppressed BDNF expression. In sleep-deprived mice, ORV increased sucrose preference and decreased immobility times in the FST and TST, indicating attenuated depression-like behaviors. Histopathological analysis revealed reduced brain tissue injury, while immunohistochemistry demonstrated decreased NLRP3, IL-1β, and caspase-1 expression, accompanied by increased BDNF expression. Furthermore, molecular docking analysis suggested a potential interaction between ORV and BDNF. Collectively, these findings suggest that ORV alleviates depression-like behaviors by attenuating oxidative stress and NLRP3 inflammasome-associated neuroinflammation while restoring BDNF-related neurotrophic signaling, supporting its potential as a neuroprotective and antidepressant candidate.

Keyword:
Oxyresveratrol, Sleep deprivation, NLRP3 inflammasome, BDNF

No. PP-064 / 天然物藥理組 / Natural Products Pharmacology (PP)

Optimization of extraction parameters of targeted flavonoids from Lactuca indica L. and evaluation of its in vitro anti-inflammatory activity

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Lactuca indica L. (Asteraceae) or dandelion has the heat-clearing and detoxifying properties and is widely used in Vietnamese traditional medicine to treat diseases related to inflammatory condition, such as boils and mastitis. Numerous studies have demonstrated that dandelion contains phenolic and flavonoid compounds with notable biological activities, among which luteolin (LUT) and luteolin-7-O-glucuronide (L7G) are representative constituents associated with antioxidant and anti-inflammatory effects. Therefore, a variety of preparation techniques have been developed to produce different formulations, including decoctions and extracts. In fact, solid extract is common formulation used by local communities to reduce the risks of microbial contamination and minimize the degradation of bioactive compounds during storage. In this work, the response surface methodology combined with the Box-Behnken design was applied to investigate the influence of solvent-to-material ratio, solvent concentration and extraction time on the content of LUT and L7G. The optimal conditions for extraction were obtained at a solvent-to-material ratio of 30 mL/g, an ethanol concentration of 60% (v/v), and an extraction time of 30 minutes. Under these extraction condition, the content of luteolin was 0.0665 ± 0.0008 % (w/w) and the content of luteolin-7-O-glucuronide was 0.285 ± 0.003 % (w/w). The optimized extract exhibited the anti-inflammatory activity using in vitro erythrocyte membrane stabilization assay and reached 65.61 ± 2.46 %, which is equivalent to natri diclofenac (74,79 ± 2,8%). The finding of this study provide a scientific basis for the development and standardization of the formulation from Lactuca indica L. targeting the compounds with anti-inflammatory activity.

Keyword:

Lactuca indica L., anti-inflammation, Box-Behnken design, luteolin, luteolin-7-O-glucuronide

No. PP-065 / 天然物藥理組 / Natural Products Pharmacology (PP)

Timosaponin AIII suppresses nasopharyngeal carcinoma metastasis by disrupting LMP1-driven Midkine signaling

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Background and Objective: Nasopharyngeal carcinoma (NPC) is a highly metastatic malignancy with limited treatment options for advanced disease. This study investigated the antimetastatic effects of timosaponin AIII (TSAIII), a natural steroidal saponin, and its underlying molecular mechanisms.

Methods: Cell viability, proliferation, apoptosis, and invasion were evaluated using MTT, colony formation, Annexin V/PI, and invasion assays. Protease array and TCGA analyses identified midkine (MDK) as a potential TSAIII target associated with clinical outcomes. Western blot analysis, qRT-PCR, and immunofluorescent staining confirmed altered MAPKs, MDK, and ERβ expression and localization. ChIP assays verified ERβ binding to the MDK promoter. In vivo metastasis assays were performed using C.B17-SCID mice, followed by immunohistochemical analysis, and H&E staining were used to assess MDK, p-AKT, and ERβ expression and histopathological changes.

Results and Conclusion: TSAIII significantly suppressed NPC cell migration and invasion with minimal cytotoxicity. Mechanistically, TSAIII reduced MDK expression, AKT phosphorylation, ERβ nuclear localization, and ERβ binding to the MDK promoter. Co-treatment with the PI3K inhibitor wortmannin further enhanced these inhibitory effects. TSAIII also reversed LMP1-induced AKT activation, MDK upregulation, and ERβ nuclear translocation, implicating the LMP1/AKT/ERβ/MDK signaling axis. In vivo, TSAIII markedly reduced lung metastasis and decreased Ki-67, MDK, and phosphorylated AKT expression without apparent systemic toxicity. Collectively, these findings demonstrate that TSAIII suppresses NPC migration, invasion, and metastasis by modulating LMP1-associated AKT/ERβ/MDK signaling, highlighting its potential as a therapeutic candidate for metastatic NPC.

Keyword:

Nasopharyngeal carcinoma, Timosaponin AIII, Metastasis, MDK, AKT, ERβ

No. PP-066 / 天然物藥理組 / Natural Products Pharmacology (PP)

Evaluation of the analgesic and acute anti- inflammatory activity of Lactuca indica L. extract in experimental animals

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Lactuca indica L. is traditionally used as a supportive herbal remedy with anti-inflammatory and analgesic properties, which have been corroborated by numerous in vitro studies. However, research evaluating these pharmacological effects in experimental animal models remains limited. To address this gap, we aimed to assess the analgesic and acute anti-inflammatory activities of Lactuca indica extract. Prepared Lactuca indica leaf powder was processed via ultrasound-assisted aqueous extraction at 55°C (3 cycles) and subsequently concentrated by evaporation to a moisture content below 20%. Analgesic activity was assessed using the acetic acid-induced writhing model in Swiss albino mice by recording the number of writhes over 30 minutes to calculate percentage inhibition. To evaluate acute anti-inflammatory activity, the carrageenan-induced paw edema model was employed in Wistar rats by measuring paw volume increases and calculating edema inhibition rates. Results revealed that oral administration of Lactuca indica extract at 4.2 g/kg/24h significantly reduced acetic acid-induced writhes compared with the control group (p below 0.05), displaying an analgesic inhibition rate of 32.21%. Furthermore, Lactuca indica extract at 2.4 g/kg/24h significantly reduced carrageenan-induced paw edema at 6 hours compared with the control group (p below 0.05), demonstrating an edema inhibition rate of 54.23%. In conclusion, these findings support the therapeutic potential and preliminary safety profile of Lactuca indica for managing pain and inflammation in experimental animal models, providing a foundation for further mechanistic and pharmacological studies.

Keyword:

Lactuca indica, anti-inflammation, analgesic activity, animal experimental model

No. FR-001 / 自由基組 / Free Radical (FR)

Rosavin Preconditioning Enhances the Neuroprotective Potential of Mesenchymal Stem Cell-Derived Exosomes in a 6-OHDA-Induced Parkinson's Disease Model

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Background: Parkinson's disease (PD) is a progressive neurodegenerative disorder driven by dopaminergic neuronal loss, mitochondrial dysfunction, impaired mitophagy, and α-synuclein aggregation. Although mesenchymal stem cells (MSCs) and their secretome represent promising therapeutics, enhancing their functional potency remains imperative. We evaluated whether preconditioning human ADSCs and Wharton's jelly MSCs (WJMSCs) with Rosavin, an adaptogenic glycoside from Rhodiola rosea, potentiates MSC bioactivity and the therapeutic efficacy of their exosomes in cellular (6-OHDA) and transgenic (A53T) PD models.

Methods: MSCs were primed with Rosavin (0–500 μM) to determine safety, stemness, and CXCR4-mediated homing. In 6-OHDA-injured SH-SY5Y co-cultures, cell survival, mitochondrial dynamics, and proteostasis were assessed. Exosomes from Rosavin-primed WJMSCs (WJR-exo) were evaluated for cargo composition, cellular uptake kinetics, and neuroprotection in vitro and in vivo in A53T transgenic mice.

Results: Rosavin priming (20–50 μM) activated IGF1R/p-Akt survival signaling, upregulated CD133/BDNF, and boosted homing capacity. In 6-OHDA-challenged co-cultures, primed MSCs suppressed cleaved caspase-3/cytochrome c release, restored mitochondrial dynamics (p-DRP1, Mfn1/2), and re-established the PINK1/Parkin/PGC-1α mitophagy axis alongside circadian/proteostasis regulators (CLOCK, SUMO2/3). Importantly, WJR-exo encapsulated autophagic cargo and displayed accelerated dynamin-mediated neuronal uptake. Treatment with WJR-exo robustly restored neuronal viability, stimulated BDNF release, and facilitated α-synuclein clearance in both SH-SY5Y cells and the cerebral cortex of A53T mice.

Conclusion: Rosavin priming primes MSCs toward a pro-survival phenotype and generates exosomes with superior neuroprotective and proteostatic clearance efficacy, offering a potent cell-free therapeutic avenue for Parkinson's disease.

Keyword:
Rosavin, Parkinson's disease, mesenchymal stem cells, exosomes, mitophagy

No. FR-003 / 自由基組 / Free Radical (FR)

Evaluation of anti-dysmenorrheal activity and isolation of potentially active triterpenoids from the native fern *Lycopodium serratum* var. *longipetiolatum* Spring.

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Dysmenorrhea is characterized by lower abdominal pain occurring during menstruation, with most cases classified as primary dysmenorrhea. Excessive production of pro-inflammatory mediators, including cyclooxygenase-2 (COX-2), inducible nitric oxide synthase (iNOS), and prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$), has been implicated in the pathogenesis of dysmenorrhea. $PGF_{2\alpha}$ binds to its receptors on uterine smooth muscle cells and subsequently induces calcium ion (Ca^{2+}) influx, thereby promoting uterine smooth muscle contraction through protein kinase C (PKC)-mediated signaling. *Lycopodium serratum* Thunb. var. *longipetiolatum* Spring. (LS), a native medicinal fern, has been reported to alleviate dysmenorrhea in vivo, primarily through anti-inflammatory mechanisms, with phenolic acids considered as indicative components. However, phenolic compounds are not particularly abundant in the ethanolic extract of LS (LSE). In the present study, LSE and its partitioned fractions exhibited inhibitory effects on $PGF_{2\alpha}$-induced Ca^{2+} influx in human uterine smooth muscle cells (HUtSMCs). Among the fractions, the ethyl acetate fraction (LSE-EA) significantly reduced the expression of COX-2 and iNOS, accompanied by decreased expression of the $PGF_{2\alpha}$ receptor and PKC. Three triterpenoids, serratenediol (**1**), 21-epi-serratenediol (**2**), and 16-oxo-3α-hydroxyserrat-14-en-21β-ol (**3**), were isolated from LSE-EA. Molecular docking analysis indicated that the three triterpenoids exhibited similar binding modes within the COX-2 active-site cavity. Among them, **1** showed the most favorable Vina score (-10.1), suggesting a relatively strong potential for interaction with the COX-2 active site and possible interference with arachidonic acid access or binding. These findings suggest that triterpenoids may represent important bioactive constituents of LS contributing to its potential anti-dysmenorrheal effects.

Keyword:
dysmenorrhea, prostaglandin $F_{2\alpha}$, cyclooxygenase-2, *Lycopodium serratum* Thunb. var. *longipetiolatum* Spring., triterpenoids, molecular docking

No. FR-004 / 自由基組 / Free Radical (FR)

Bletilla formosana exerts mitochondrial dysfunction and mitophagy-associated apoptosis in colorectal cancer

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Colorectal cancer (CRC) remains one of the most prevalent malignancies and a major cause of cancer-related mortality. Although several *Bletilla* species have been documented to possess anticancer properties, the anticancer potential of *Bletilla formosana* (Hayata) Schltr, a Taiwan native herbal medicine, remains unexplored. This study aimed to investigate the anticancer activity of *B. formosana* against CRC and to characterize its underlying molecular mechanisms and bioactive constituents. The ethyl acetate extract of *B. formosana* (EA) markedly induced apoptotic cell death in CRC cells. Transcriptomic analysis identified mitochondrial function and metabolism as major pathways affected by EA treatment. Consistently, EA induced pronounced mitochondrial dysfunction and mitophagy, characterized by impaired oxidative phosphorylation, reduced respiratory reserve capacity, mitochondrial reactive oxygen species (ROS) accumulation, and increased mitophagy-associated hallmarks in CRC cells. Moreover, the mitochondrial ROS scavenger MitoTEMPO attenuated EA-induced oxidative stress and apoptosis. Using chemical molecular networking combined with anticancer-directed fractionation, we identified a benzyl-based natural product (BP) as a lead candidate responsible for the anticancer activity of EA. BP induced mitochondrial dysfunction and apoptosis in CRC cells. Importantly, in vivo studies using a zebrafish xenograft model and a syngeneic mouse model demonstrated that BP effectively suppressed CRC tumor growth. Together, our findings reveal novel anticancer activity of *B. formosana* against CRC through mitochondrial dysfunction and mitophagy-associated apoptosis. BP emerges as a promising anticancer candidate and further highlights *B. formosana* as a valuable source for the discovery of novel anticancer agents.

Keyword:
colorectal cancer, Bletilla formosana, mitophagy, apoptosis

No. FR-005 / 自由基組 / Free Radical (FR)

Sinularin Induces HDAC6-Selective Tubulin Acetylation, ROS Generation, and Mitotic Arrest in Prostate Cancer Cells: A Transcriptomic Analysis

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Prostate cancer remains a leading cause of cancer-related mortality despite advances in treatment. Sinularin is a cembranolide isolated from soft coral with reported anti-cancer activity in several cancer types, though its mechanism in prostate cancer has not been defined. We investigated the cytotoxic mechanism of sinularin in DU145 and PC-3 prostate cancer cells, which differ in p53 status. Sinularin exhibited potent cytotoxicity in both cell lines, with IC50 values of 3.17±0.19 μM (DU145) and 2.09±0.37 μM (PC-3) at 48h, and induced G2/M arrest in both. ROS generation occurred at 1h, followed by mitochondrial membrane potential loss at 24h in both cell lines. Sinularin increased acetylated tubulin while acetylated histone H3 remained unchanged, indicating a selective effect on HDAC6 rather than pan-HDAC inhibition. RNA sequencing showed no change in HDAC6, tubulin, or ATAT1 mRNA, supporting a post-translational mechanism. Time-course analysis revealed that acetylated tubulin, MPM2, and phospho-BubR1 (S680) increased together by 4h, whereas HDAC6 cleavage and caspase-3 activation were not detected until 16h, suggesting that tubulin acetylation preceded and may occur independently of caspase activity. Flow cytometry showed G2/M arrest and early apoptosis at 24h, followed by a shift toward sub-G1 accumulation at 48h, supporting direct progression from mitotic arrest to apoptosis. SLC7A11 was upregulated while GPX4 remained unchanged, arguing against ferroptosis. Taken together, the data suggest that sinularin induces HDAC6-selective tubulin acetylation and mitotic arrest in two prostate cancer cell lines with distinct p53 backgrounds, distinct from previously reported sinularin activity in other cancer types.

Keyword:

Sinularin, HDAC6, Tubulin acetylation, Reactive oxygen species (ROS),Prostate cancer, Mitotic arrest

No. FR-006 / 自由基組 / Free Radical (FR)

Neutrophil-Targeted Nanocarriers Co-Delivering Synthetic Isoflavones and Anti-Inflammatory Peptides for the Treatment of Psoriasis

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Psoriasis is a chronic immune-mediated inflammatory skin disease characterized by keratinocyte hyperproliferation and inflammatory cell infiltration. This study aimed to develop an LSI-10-loaded poly(lactic-co-glycolic acid) (PLGA) nanoparticle system modified with the cationic lipid DOTAP and Ac2-26 peptide to enhance cellular uptake and skin retention for psoriasis treatment.

The physicochemical properties and stability of the nanoparticles were characterized, followed by evaluation of skin permeation, cellular uptake, superoxide generation, in vivo biodistribution, and therapeutic efficacy in an imiquimod (IMQ)-induced psoriasis-like mouse model. The prepared nanoparticles exhibited a spherical morphology with particle sizes of approximately 200–250 nm and remained physically stable for 7 days. Skin permeation studies showed that nanoparticle modification reduced LSI-10 permeation, suggesting enhanced skin retention. Flow cytometry and confocal microscopy demonstrated that Ac2-26 modification increased nanoparticle uptake by THP-1 cells and neutrophils. LSI-10NPs+DOTAP+Ac2-26 also showed greater inhibition of superoxide generation in human neutrophils. In vivo imaging demonstrated predominant nanoparticle retention in the skin with limited distribution to major organs. In IMQ-induced mice, LSI-10NPs+DOTAP+Ac2-26 improved psoriasis-like skin symptoms and reduced IL-6, IL-1β, TNF-α, and CXCL1 levels. Histopathological analysis further demonstrated reduced epidermal hyperplasia and inflammatory cell infiltration.

Overall, LSI-10NPs+DOTAP+Ac2-26 enhanced cellular uptake and skin retention while attenuating psoriasis-associated inflammation, supporting its potential as a nanocarrier system for psoriasis treatment.

Keyword:
Psoriasis, Isoflavone, PLGA nanoparticles, Formyl peptide receptor 2, Ac2-26 peptide, Drug delivery system

No. FR-007 / 自由基組 / Free Radical (FR)

Momordin Ic Inhibits FPR1-Mediated Neutrophil Activation: Pharmacological and Structure–Activity Insights

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The activity of the triterpenoid saponin Momordin Ic at formyl peptide receptor 1 (FPR1), as well as the structural features that determine this activity, remains unclear. We investigated its effects on FPR1-mediated neutrophil activation and compared them with those of structurally related triterpenoids to examine their structure–activity relationships. Momordin Ic inhibited neutrophil respiratory burst, degranulation, and adhesion, selectively suppressing FPR1-mediated responses. It also reduced FPR1-triggered intracellular calcium mobilization and the phosphorylation of MAPKs and AKT. Molecular docking predicted that Momordin Ic binds within the FPR1 ligand-binding pocket via hydrogen-bonding and hydrophobic interactions. Comparative receptor-binding and neutrophil functional assays indicated that substituent patterns and glycosyl moieties influence FPR1 binding and antagonistic activity among related triterpenoids. Together, these findings identify Momordin Ic as a natural FPR1 antagonist and provide an initial structure–activity framework for further optimizing triterpenoid-based FPR1 antagonists.

Keyword:
Formyl peptide receptor 1, N-formyl peptide, neutrophil, triterpenoid saponin

No. FR-008 / 自由基組 / Free Radical (FR)

Paphiopedilol B Suppresses Neutrophil Activation and Ameliorates Experimental Acute Respiratory Distress Syndrome

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Acute respiratory distress syndrome (ARDS) is closely linked to excessive neutrophil-driven inflammation, yet few effective strategies exist to selectively regulate neutrophilic responses. This study examined the anti-inflammatory effects of paphiopedilol B, a novel stilbene isolated from Paphiopedilum concolor, on human neutrophil activation and experimental ARDS. Paphiopedilol B significantly inhibits superoxide anion and elastase production in activated neutrophils, with IC50 values of 0.48 ± 0.04 μM and 0.79 ± 0.11 μM, respectively. Additionally, it reduced the generation of reactive oxygen species and the expression of degranulation surface markers. Mechanistically, paphiopedilol B inhibited intracellular Ca2+ mobilization and the phosphorylation of p38, ERK, and JNK. In a lipopolysaccharide (LPS)-induced mouse model of ARDS, paphiopedilol B markedly attenuated pulmonary inflammation and oxidative stress, reducing Ly6G, neutrophil elastase, 4-HNE, and IL-1β levels by 86.1%, 74.5%, 60.4%, and 84.7%, respectively, without notable hepatic or renal toxicity. Overall, these findings demonstrate that paphiopedilol B suppresses multiple neutrophil inflammatory responses by inhibiting Ca2+ mobilization and MAPK signaling, and protects against LPS-induced ARDS, supporting its potential as a natural therapeutic candidate for neutrophil-driven pulmonary inflammation.

Keyword:
Paphiopedilum concolor, stilbene, paphiopedilol B, neutrophil, acute respiratory distress syndrome

No. FR-009 / 自由基組 / Free Radical (FR)

Engineering pancreatic cancer cell–derived exosomes to deliver iron-based therapeutics and induce ferroptosis in pancreatic tumors

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Pancreatic ductal adenocarcinoma remains difficult to treat because of therapeutic resistance, limited drug delivery, and an immunosuppressive tumor microenvironment. This study proposes engineering pancreatic cancer cell–derived exosomes to carry iron-based nanotherapeutics for image-guided, ferroptosis-centered treatment. Intracellular iron may promote reactive oxygen species generation through Fenton chemistry, driving lipid peroxidation and ferroptotic cell death. Photothermal activation could further increase local oxidative stress and tumor-cell damage, potentially enhancing iron-mediated ferroptosis. In parallel, treatment-induced tumor damage may release danger signals that activate the cyclic GMP–AMP synthase–stimulator of interferon genes (cGAS–STING) pathway and support antitumor immune responses. The platform's potential synergy will be assessed by examining photothermal effects, ferroptosis-associated responses, cGAS–STING signaling, and cancer-cell viability, with appropriate pathway and rescue controls. MRI and CT imaging capabilities could enable noninvasive assessment of nanoparticle distribution and treatment response, subject to validation of imaging contrast and performance. Exosome loading, characterization, and cellular uptake will also be evaluated. This proposed approach integrates free-radical-mediated tumor injury with photothermal treatment, immune-pathway activation, and multimodal imaging. It may provide a framework for investigating image-guided combination therapy for pancreatic cancer, while experimentally testing whether these components produce additive or synergistic effects.

Keyword:

Ferroptosis, hydroxyl radical, chemodynamic therapy

No. FR-010 / 自由基組 / Free Radical (FR)

MiR-210-5p promotes arteriosclerosis risk through influencing the CTRP3 and ABCA1 pathways

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Our previous study demonstrated that miR-210-5p, a redox-sensitive miRNA, was upregulated in patients with systemic lupus erythematosus (SLE), and that it plays an important macrophage function in dead cell clearance. Here, we aimed to determine whether miR-210-5p plays a key regulatory role in the development of SLE complications, particularly in atherosclerosis. After analyzing miRNA expression, the miR-210-5p level was positively correlated with SLE severity and anti-cardiolipin IgG levels, a thrombosis risk marker. Interestingly, miR-210-5p led to lipid accumulation and foam cell formation in both smooth muscle cells (SMCs) and macrophage-like THP-1 cells. MiR-210-5p enhanced macrophage migration by increasing IL-6 secretion in SMCs upon oxLDL treatment. Further analysis of the underlying mechanism revealed that miR-210-5p increased cellular lipid accumulation and IL-6 secretion via directly targeting ABCA1 and CTRP3, respectively, cholesterol efflux of macrophage-like THP-1 cells was also inhibited. Increased IL-6 expression by miR-210-5p was mediated through influencing the CTRP3/SIRT1/NF-κB acetylation signaling. Cellular oxidative stress and lipid ROS were increased in miR-210-5p overexpressing SMCs upon oxLDL stimulation. All in all, our study demonstrates that miR-210-5p could serve as a potential risk marker in atherosclerosis.

Keyword:

miR-210-5p, Systemic lupus erythematosus, Arteriosclerosis, IL-6, ABCA1, CTRP3

No. FR-011 / 自由基組 / Free Radical (FR)

Extracellular Vesicle Subpopulations with Enhanced Spheroid Penetration in Pancreatic Ductal Adenocarcinoma

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The desmoplastic and immunosuppressive tumor microenvironment of pancreatic ductal adenocarcinoma (PDAC) limits drug delivery and contributes to chemoresistance. We aimed to identify extracellular vesicle (EV) subpopulations with enhanced penetration as potential drug delivery vehicles for PDAC. Fluorescence-activated cell sorting was used to isolate cancer stem cell (CSC)-enriched ($CD44^+CD24^+EpCAM^+$) and non-stem cancer cell (NSCC, $CD44^+CD24^-$) populations from PANC-1 cells. Following expansion, flow cytometric validation showed enrichment of the $CD44^+CD24^+EpCAM^+$ phenotype in the CSC-enriched population relative to PANC-1 and NSCC populations. To functionally validate the CSC phenotype, gemcitabine sensitivity was assessed. At 72 h after gemcitabine treatment, CSC-enriched cells exhibited significantly higher viability (43.89%) than PANC-1 (34.02%) and NSCC cells (32.22%), consistent with a gemcitabine-resistant phenotype. At the EV level, nanoflow cytometry revealed distinct surface-marker profiles. The proportions of CD81-positive EVs were 1.83%, 6.23%, and 5.23% among EVs derived from CSC-enriched, PANC-1, and NSCC cell populations, respectively, whereas the corresponding proportions of CD24-positive EVs were 3.95%, 0.91%, and 0.26%. Accordingly, CSC-derived EVs exhibited relatively lower CD81 positivity and higher CD24 positivity than PANC-1- and NSCC-derived EVs. Functionally, NSCC-derived EVs showed greater cellular uptake in 2D monolayer cultures of CSC-enriched and PANC-1 cells and greater penetration into 3D CSC spheroids than PANC-1- or CSC-derived EVs. Collectively, these findings demonstrate that distinct PDAC cell populations generate EVs with differential surface phenotypes, uptake, and spheroid penetration, providing a basis for identifying functionally distinct EV subpopulations with potential utility in PDAC drug delivery.

Keyword:

Pancreatic ductal adenocarcinoma, Extracellular vesicles, Cancer stem cells, Gemcitabine resistance, Spheroid penetration

No. FR-012 / 自由基組 / Free Radical (FR)

Development of neutrophil-targeted Clofoctol-loaded PLGA nanoparticles for immunomodulation in sepsis

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Sepsis is a life-threatening diseases characterized by a dysregulated host immune response to infection, which often results in multiple organ dysfunction and high mortality. Neutrophils play a pivotal role in bacterial clearance, however, their antimicrobial functions become impaired during sepsis, leading to ineffective pathogen elimination and disease progression. Therefore, this study aimed to develop neutrophil-targeted clofoctol-loaded PLGA nanoparticles for targeted antibacterial and immunomodulatory therapy.

Clofoctol-loaded PLGA nanoparticles were prepared using the solvent evaporation method and surface-functionalized with Ly6G antibody and Ac2-26 peptide to achieve neutrophil targeting and immunomodulatory activity. This dual-conjugated nanoparticles exhibited suitable physicochemical characteristics with successful drug encapsulation and enhanced uptake by neutrophils compared with non-targeted formulations. In addition, *in vivo* studies demonstrated that treatment with the dual-conjugated clofoctol-loaded nanoparticles effectively reduced bacterial burden and improved therapeutic outcomes in *E. coli*-induced septic mice while maintaining acceptable liver and kidney safety profiles. Biodistribution analysis further confirmed preferential accumulation of the nanoparticles in infection-associated organs. These findings suggest that the combined targeting and immunomodulatory strategy enhances antibacterial efficacy by improving neutrophil-mediated host defense.

In conclusion, the developed dual-conjugated nanoparticles represent a promising nanotherapeutic platform for sepsis treatment by combining targeted drug delivery with host-directed immunomodulation. However, further studies, especially *in vitro* experiments, are needed to gain a deeper understanding on how the nanoformulation interacts with target cells, as well as their mechanisms.

Keyword:

sepsis, bacteremia, nanomedicine, neutrophils, E. coli

No. FR-013 / 自由基組 / Free Radical (FR)

Exogenous mitochondrial supplementation as a therapeutic strategy against H_2O_2-induced oxidative injury in MDCK cells

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Background: Mitochondrial dysfunction and oxidative stress contribute substantially to epithelial cell injury. Exogenous mitochondrial supplementation has been proposed as a potential mitochondrial transplantation therapy (MTT), but its therapeutic effects after oxidative damage remain incompletely defined. We therefore examined whether post-injury mitochondrial supplementation could protect renal epithelial cells from H_2O_2-induced injury.

Methods: MDCK cells were exposed to H_2O_2 and subsequently treated with isolated mitochondria. Cell viability, mitochondrial membrane potential, intracellular ROS, mitochondrial dynamics-related responses, and antioxidant signaling were evaluated.

Results: Post-injury mitochondrial supplementation improved cell viability, attenuated mitochondrial depolarization, and reduced intracellular ROS accumulation. Exogenous mitochondria also modulated mitochondrial dynamics- and mitophagy-associated responses and altered the expression of mitochondrial transcriptional regulators. In addition, mitochondrial supplementation enhanced Nrf2-associated antioxidant responses, including increased expression of several antioxidative proteins.

Conclusion: These findings indicate that exogenous mitochondrial supplementation provides post-injury protection against oxidative damage in renal epithelial cells. The protective effect is associated with preservation of mitochondrial function and enhancement of antioxidant responses, supporting mitochondrial supplementation as a potential therapeutic strategy for oxidative cell injury.

Keyword:
Mitochondrial transplantation therapy, ROS, Nrf2, Mitochondrial dysfunction, renal epithelial cells

No. FR-014 / 自由基組 / Free Radical (FR)

Pharmacological proteasome activators relieve mutant huntingtin-induced cytotoxicity by attenuating oxidative stress.

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Huntington's disease (HD) is a dominantly inherited neurodegenerative disease that mainly affects the medium spiny neurons of the striatum. Mutant Htt is prone to aggregation and is the major clinical neuropathology of HD. Oleuropein, an olive-sourced phenolic compound, can reduce mHtt aggregate accumulation by activating the proteasome. Moreover, oleuropein reduced intracellular ROS and SO accumulation and increased cell viability in N2a cells ectopically expressing truncated mutant huntingtin and in ST*Hdh*$^{Q111/Q111}$ striatal cells endogenously expressing mutant huntingtin. To assess the neuroprotective effect of a small-molecule proteasome activator, we also measured the effects of two other proteasome activators, AM404 and 20S proteasome activator 1 (20SPA1), on mHtt-induced cytotoxicity. Consistent with oleuropein treatment, AM404 and 20SPA1 treatment reduced mitochondrial superoxide accumulation and increased cell viability through proteasome activation in mutant ST*Hdh*$^{Q111/Q111}$ HD model cells. By immunoblotting, we found that 20SPA1 treatment upregulated SOD1 protein level in mutant ST*Hdh*$^{Q111/Q111}$ HD model cells. Additionally, AM404 treatment reduced mitochondrial superoxide accumulation and increased cell viability in mutant HttQP103-overexpressing STST*Hdh*$^{Q7/Q7}$ cells with mHtt aggregation. Furthermore, AM404 also relieved other polyQ disease-aggregated protein-induced cytotoxicity (Ataxin3-101Q, which is aggregated in Spinocerebellar Ataxia). Taken together, our data suggested that proteasome activators exert neuroprotective effects in HD model cells by attenuating oxidative stress via SOD1.

Keyword:
Huntington's disease, proteasome activation, AM404, 20S protasome activactor 1, ROS, SOD1

No. FR-015 / 自由基組 / Free Radical (FR)

Screening of Free Radical Scavenging Activity of Seed Extracts of *Cajanus cajan* (J.) Huth, *Lablab purpureus* (L.) Sweet, and *Phaseolus lunatus* L. using DPPH Assay

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Free radicals are highly reactive species that can contribute to oxidative stress, which has been implicated in the development of various chronic diseases. Underutilized native Philippine legumes represent a largely unexplored source of bioactive compounds, particularly in their edible parts, which may possess valuable radical-scavenging properties. This study aimed to screen the radical scavenging activity of seed extracts of *Cajanus cajan* (J.) Huth, *Lablab purpureus* (L.) Sweet, and *Phaseolus lunatus* L. using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay. Hexane, ethyl acetate, interphase, and aqueous seed extracts were prepared and evaluated for their radical scavenging activity (RSA), expressed as percentage inhibition. The extracts were further subjected to thin-layer chromatography (TLC) bioautography using DPPH as the spray reagent. Generally, the extracts demonstrated atren d in radical scavenging activity, with ethyl acetate extracts exhibiting the highest activity, followed by interphase, aqueous, and hexane extracts. The ethyl acetate extracts of *P. lunatus* and *L. purpureus*, as well as the interphase extract of *C. cajan*, exhibited the highest radical scavenging activities among their respective extracts. Among the ethyl acetate extracts tested, the ethyl acetate extract of *P. lunatus* exhibited the most favorable IC_{50} value at 249 μg/mL. These findings demonstrate the potential of the seed extracts, particularly that of ethyl acetate, as sources of radical-scavenging compounds. Further fractionation and evaluation using complementary antioxidant assays are recommended to characterize the bioactive constituents and validate their antioxidant activity.

Keyword: *Free Radical Scavenging Activity, DPPH Assay, Seed Extract, Legumes*

No. FR-016 / 自由基組 / Free Radical (FR)

Research on Cosmetic Active Ingredients Derived from Litchi chinensis Agricultural Waste

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Lychee (*Litchi chinensis*, LC) is a fruit crop of notable economic importance in Taiwan. The branches and leaves generated during its cultivation and pruning are agricultural by-products that have potential for repurposing and value-added uses. Moreover, its polyphenols, flavonoids, and phenolic acids indicate promising antioxidant applications. The study utilized aqueous extract fractions derived from the upper (ULCL) and lower (LLCL) parts of L. chinensis leaves to assess their antioxidant activity, cytocompatibility, and photoprotective effect. The present findings indicated that the total phenolic contents measured in the ULCL and LLCL were 7.928 ± 0.193 mg GAE/% and 5.766 ± 0.005 mg GAE/%, respectively. The SC50 values in the DPPH assay for ULCL and LLCL were found to be 5.19% and 4.81%, respectively, suggesting that the upper fraction needed a greater concentration to reach 50% scavenging efficiency. In contrast, the ABTS assay showed SC50 values of 3.10% for ULCL and 4.50% for LLCL, indicating that the upper fraction required a lower concentration in this case. The mean cell viability across both fractions varied between 90.94% and 130.85% within the treatment concentration range of 0.625–10%, showing no significant reduction. Further studies will explore the protective effect of LCL extract against keratinocytes damage caused by UVB radiation. It is hoped that these experimental results will lay a scientific foundation for the application of LCL extract as a natural ingredient in cosmetics. These results will promote the reuse of agricultural by-products, drive innovation in sustainable materials, and support the development of a circular economy.

Keyword:

Lychee agricultural by-products, Antioxidant activity,Cosmetic ingredients

No. FR-017 / 自由基組 / Free Radical (FR)

Physicochemical properties of naringenin nanoparticles formulation and their biological activity in cosmetics

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The skin barrier, which mainly consists of the stratum corneum and intercellular lipids, serves to reduce transepidermal water loss while protecting against irritants, pollutants, and harmful pathogens. Barrier dysfunction often manifests through dryness, redness, sensitivity, stinging, and scaling. Additionally, it can intensify oxidative stress and inflammation, thereby worsening skin conditions like acne, rosacea, and atopic dermatitis. As a result, creating cosmetic ingredients with antioxidant, anti-inflammatory, and barrier-strengthening properties has become a crucial focus in skin care research and innovation. Naringenin (NAR), a natural flavonoid with antioxidant and anti-inflammatory properties, holds potential for skincare but faces challenges in cosmetic formulations due to poor water solubility, limited skin permeability, uneven dispersion, and low bioavailability. In this study, naringenin nanoparticles (NARN) were prepared via the solid dispersion method using polyvinylpyrrolidone (PVP) and hydroxypropyl-β-cyclodextrin (HPβCD) as carriers, and their water solubility and transdermal absorption capabilities were evaluated. The results showed that the initial particle size of NAR was 13,688.17 nm and its water solubility was 18.939 μg/mL, following encapsulation, the optimal formulation exhibited a reduced average particle size of 113.34 nm and a 52.6-fold increase in water solubility. The encapsulation efficiency reached 99.80 ± 0.12%, demonstrating that this system can improve the solubility and dispersion characteristics of NAR. Future studies will investigate the solubilization mechanism, cellular safety, antioxidant and anti-inflammatory activities, and the expression of skin barrier-related proteins to establish a scientific basis for its use as a cosmetic ingredient offering soothing, antioxidant, and barrier-repairing properties.

Keyword:

skin barrier, naringenin, solid dispersion, aqueous solubility, antioxidant activity, anti-inflammatory activity

No. TC-001 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

NRICM301 Confers Superior Neuroprotection and Motor Recovery in an MPTP-Induced Parkinson's Disease Mouse Model: Behavioral and Cross-Platform Multi-Omics Evidence

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Background: Parkinson's disease (PD), the second most common neurodegenerative disorder, involves neuroinflammation, oxidative stress, and mitochondrial dysfunction alongside dopaminergic neuron loss, current levodopa therapy is symptomatic only. NRICM301, a Chinese herbal formula optimized from NRICM201, targets neuroinflammation and dopaminergic neuron preservation.

Methods: Male C57BL/6 mice received MPTP to induce PD pathology, then saline, NRICM201, NRICM301 (1.5–3.0 g/kg, PO), or methylphenidate. Motor function was assessed via open field, grip strength, rotarod, pole test, and nesting assays. Substantia nigra/CA3 tissue was profiled by RNA-seq and LC-MS/MS proteomics, with cross-platform KEGG pathway analysis.

Results: MPTP significantly impaired all behavioral measures versus control. NRICM301 produced the strongest, most complete recovery among treatments, outperforming NRICM201. Although RNA-seq (44 DEGs) and proteomics (47 proteins) shared negligible gene-identity overlap, KEGG analysis revealed convergent, treatment-responsive dopaminergic synapse signaling via non-overlapping driver genes (RNA: Drd1, Gng7, protein: Calm1, Gria3, Ppp1ca). NRICM301 normalized ~93% of the MPTP transcriptional signature, while both platforms independently flagged a persistent unresolved glial-stress signature.

Conclusion: NRICM301 shows superior, multi-domain neuroprotective and motor-recovery efficacy versus NRICM201, with convergent RNA/protein evidence supporting restored dopaminergic signaling as a key mechanism and reactive astrogliosis as a validated next target, supporting its continued translational development for PD.

Keyword:
NRICM301, Parkinson's disease, MPTP mouse model, neuroprotection, multi-omics integration, dopaminergic synapse

No. TC-002 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Network Pharmacology-Guided Elucidation of the Anti-Inflammatory Mechanisms of Perilla frutescens: Luteolin Attenuates TNF-α and IL-6 Expression via the Akt Pathway

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Perilla frutescens (L.) Britton, a traditional Chinese medicine with anti-asthmatic, anti-allergic, and digestive properties, attracts interest for its therapeutic potential against oxidative stress and inflammatory disorders. This study evaluated the antioxidant and anti-inflammatory properties of *P. frutescens* extracts and isolated components using *in vitro* and *in silico* approaches. The ethyl acetate fraction exhibited the highest total flavonoid content (102.54 ± 2.65 mg QE/g), the most potent anti-α-glucosidase (IC_{50} = 31.58 ± 1.46 μg/mL), and anti-nitric oxide activities (IC_{50} = 8.11 ± 0.84 μg/mL). Consequently, it was selected for phytochemical investigation, yielding six major compounds: ferulic acid (**1**), luteolin (**2**), apigenin (**3**), rosmarinic acid (**4**), baicalin (**5**), and scutellarin (**6**). Among these, rosmarinic acid (**4**) showed the strongest radical scavenging against DPPH (SC_{50} = 15.50 ± 1.26 μM) and ABTS (SC_{50} = 9.13 ± 0.45 μM). Furthermore, luteolin (**2**) (IC_{50} = 12.58 ± 1.43 μM) and apigenin (**3**) (IC_{50} = 14.63 ± 1.65 μM) effectively inhibited nitric oxide (NO) production without significant cytotoxicity. Western blot analysis revealed luteolin (**2**) dose-dependently attenuated TNF-α and IL-6 protein expression, concomitant with Akt phosphorylation (p-Akt/Akt) suppression. Network pharmacology and molecular docking corroborated these findings, identifying TNF, IL-6, and AKT as central hub genes enriched in critical inflammatory and metabolic pathways. These findings highlight *P. frutescens* as a promising source of natural antioxidants and multi-target phytochemicals for managing chronic inflammatory conditions.

Keyword:

Perilla frutescens, Anti-Inflammation, Traditional Chinese Medicine, Network Pharmacology, Antioxidant, Anti-α-Glucosidase

No. TC-003 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Nitrogen-Dependent Regulation of Growth, Secondary Metabolism, and Rosmarinic Acid Biosynthesis in Prunella vulgaris L.

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Prunella vulgaris L. is a medicinal plant native to Taiwan and is used in traditional Chinese medicine and herbal tea. This study evaluated the effects of different nitrogen application rates on vegetative growth, bioactive compound contents, and the expression of genes related to rosmarinic acid biosynthesis. Plants received no additional nitrogen (N0) or 0.2 (N1), 0.4 (N2), 0.6 (N3), or 0.8 g (N4) of ammonium sulfate per pot. Agronomic traits, dry weight, bioactive compounds in leaves and stems, and gene expression were assessed at 3, 6, and 9 weeks after fertilization. Nitrogen application increased plant height, branching, leaf area, and shoot growth. N3 produced the highest whole-plant dry weight at week 6, whereas no significant differences among treatments were observed at week 9. In contrast, no additional nitrogen or low nitrogen supply was more favorable for maintaining the contents of rosmarinic acid, ursolic acid, and oleanolic acid. Several genes involved in rosmarinic acid biosynthesis also showed higher expression under N0 or N1. These findings indicate that higher nitrogen supply promotes vegetative growth but does not simultaneously enhance bioactive compound contents and that these responses vary with growth stage and plant organ. Although N3 favored dry matter accumulation during the middle growth stage, N1 and N3 showed similar whole-plant dry weights at the later stage, while N1 maintained higher levels of most bioactive compounds. Therefore, applying 0.2 g of ammonium sulfate per pot may provide an appropriate balance between vegetative growth and medicinal quality in *P. vulgaris*.

Keyword:

Prunella vulgaris, nitrogen application, vegetative growth, rosmarinic acid, secondary metabolites, gene expression

No. TC-004 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Bioassay-Guided Fractionation of Allii Macrostemonis Bulbus (Xiebai) Extracts and Their Promotive Effects on Keratinocyte Migration

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Allii Macrostemonis Bulbus (AM) is a traditional Chinese medicine historically used for cardiovascular and anti-inflammatory purposes. However, its active constituents and pharmacological effects on skin wound healing and cell regeneration remain unclear. This study applied a bioassay-guided fractionation approach to identify AM-derived constituents that promote keratinocyte regeneration. Dried AM was sequentially extracted with water and aqueous ethanol solutions (20–95% v/v), and extracts were screened for cell viability (CCK-8 assay) and migratory activity (scratch assay) in human HaCaT keratinocytes. Initial screening showed that the 50% ethanol extract (AM-3) had the highest extraction yield (69.05%) and notable pro-migratory effects, and it was further fractionated via Diaion HP-20 column chromatography into six subfractions. Among these, the 60% ethanol eluate (AM-3-W-4) exhibited the most potent wound-healing activity, significantly enhancing HaCaT cell migration at low concentrations (7.5 and 15 μg/mL) within 24 hours without cytotoxic effects. Based on the preliminary HPLC chromatographic profile and NMR spectra, AM-3-W-4 is deduced to be enriched in steroidal saponins, which may underlie its bioactivity. Together, these findings provide the first *in vitro* evidence that AM promotes keratinocyte migration, supporting its potential application in skin tissue regeneration and wound-care therapeutics.

Keyword:
Allii Macrostemonis Bulbus, bioassay-guided fractionation, wound healing, migration, keratinocyte, HaCaT

No. TC-005 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Quercetin and Myricetin as Dual-Active Constituents of Antidiabetic Roselle Extract: DPP-4 Inhibition and Enteroendocrine Hormone Secretion

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Background: Type 2 diabetes mellitus is characterized by impaired glucose homeostasis and progressive β-cell dysfunction. Botanical compounds that stimulate endogenous incretin secretion while inhibiting dipeptidyl peptidase-4 (DPP-4) may provide complementary metabolic benefits. Roselle (*Hibiscus sabdariffa* L.) is rich in polyphenols, but its dual effects on incretin secretion and DPP-4 activity remain unclear.

Methods: A 50% ethanolic extract (RosEt) was chemically profiled by HPLC using authentic standards and evaluated in high-fat diet/streptozotocin-induced diabetic mice. RosEt and its identified constituents were subsequently screened for DPP-4 inhibition and GLP-1/OXM secretion using enzyme assays and STC-1 cells. Major dual-active compounds were further investigated using molecular docking and pharmacological inhibitors.

Results: RosEt improved glucose homeostasis in diabetic mice, reducing fasting glycemia and HbA1c, improving glucose tolerance, decreasing HOMA-IR, and increasing HOMA-β. These effects were accompanied by increased circulating active GLP-1 and OXM. Among the identified constituents, quercetin, myricetin, and chlorogenic acid inhibited DPP-4, whereas quercetin and myricetin significantly stimulated GLP-1 and OXM secretion. Chlorogenic acid and ferulic acid showed comparatively mild GLP-1 secretory effects at higher concentrations which also have mild cytotoxicity. Quercetin and myricetin therefore emerged as the principal dual-active compounds. Molecular docking supported their potential interactions with DPP-4 and TAS2R14, while probenecid and inhibition of PLC/IP_3Ca^{2+} signaling attenuated incretin secretion.

Conclusion: RosEt improves glucose homeostasis through coordinated stimulation of incretin hormones and DPP-4 inhibition. Quercetin and myricetin are major dual-active constituents that potentially contribute through DPP-4 interactions and TAS2R-associated calcium signaling.

Keyword:
Hibiscus sabdariffa, Dipeptidyl-peptidase-4 (DPP-4), Glucagon-like peptide (GLP-1), Oxyntomodulin, Quercetin, Myricetin

No. TC-006 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Integrating real-world prescription, network pharmacology, and human transcriptomics to characterize Ji-Sheng-Shen-Qi-Wan for benign prostatic hyperplasia

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Benign prostatic hyperplasia (BPH) is a major cause of lower urinary tract symptoms (LUTS) in older men, however, the clinical use and biological basis of Chinese herbal medicine (CHM) formulas for BPH remain incompletely characterized. This study integrated nationally representative prescription data, network pharmacology, and human prostate transcriptomics to identify a clinically relevant formula and explore its potential molecular mechanisms. CHM prescriptions for five BPH- and LUTS-related diagnostic categories were retrieved from Taiwan's National Health Insurance Research Database. Ji-Sheng-Shen-Qi-Wan (JSSQW) was the most frequently prescribed formula across all five categories, accounting for 19-27% of CHM prescriptions. Mapping JSSQW-associated targets to BPH-related targets yielded 187 shared targets. Protein-protein interaction analysis using five topological algorithms identified STAT3, ESR1, AKT1, MAPK3, MAPK1, JUN, and CASP3 as predicted hub targets, and functional enrichment analysis highlighted the PI3K-AKT and MAPK signaling pathways. In the human prostate transcriptomic dataset GSE132714, 1,222 differentially expressed genes (DEGs) were identified between BPH and control tissues, and KEGG enrichment analysis and gene set enrichment analysis (GSEA) further supported the involvement of these pathways. Molecular docking showed that seven representative JSSQW compounds had more favorable predicted binding scores with AKT1 among the evaluated hub proteins. Collectively, these findings link the widespread clinical use of JSSQW in Taiwan to predicted multi-component, multi-target mechanisms involving the PI3K-AKT and MAPK signaling pathways, with AKT1 emerging as a computationally prioritized candidate target that warrants further experimental validation.

Keyword:

Benign prostatic hyperplasia, Ji-Sheng-Shen-Qi-Wan, National Health Insurance Research Database, Network pharmacology, Multi-target mechanism

No. TC-007 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Topical Chinese Herbal Medicine for Atopic Dermatitis: Recent Clinical Evidence on Efficacy and Safety

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Background

Atopic dermatitis (AD) is a chronic, relapsing inflammatory skin disease. Although topical corticosteroids are effective, long-term disease control and relapse prevention remain challenging.

Objective

To summarize recent clinical evidence on the efficacy and safety of topical or external Chinese herbal medicine (CHM) for AD.

Methods

PubMed was searched for studies published from January 2021 to September 2026. Human clinical trials and systematic reviews/meta-analyses evaluating topical or external CHM for AD were included. Animal and in vitro studies, mechanistic studies without clinical outcomes, oral-only interventions, trial protocols, and non-AD studies were excluded.

Results

Among 39 records, four met the eligibility criteria: two randomized clinical trials and two systematic reviews/meta-analyses. One meta-analysis showed reduced overall symptom severity (SMD −0.35, 95% CI −0.59 to −0.10) and a higher effectiveness rate (RR 1.29, 95% CI 1.15–1.44) with topical CHM. Chinese herbal bath therapy was associated with lower SCORAD scores, fewer adverse reactions, and lower recurrence (RR 0.25, 95% CI 0.10–0.59), although most trials used it as adjunctive therapy. Liuweirunfu Oil reduced relapse at week 8 (16.3% vs 35.7%) and improved EASI, IGA, and DLQI. Lindioil improved EASI, while tacrolimus produced greater improvements in BSA, pruritus, and DLQI, application-site reactions were less frequent with Lindioil.

Conclusion

Current evidence suggests potential clinical benefits of topical or external CHM for AD, with generally mild local adverse events. Larger, well-designed trials with longer follow-up are needed.

Keyword:

Atopic Dermatitis, Traditional Chinese Medicine, Chinese Herbal Medicine, Topical Therapy

No. TC-008 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Eco-Innovative Herbal Foot Bath for Enhanced Therapeutic Efficacy and Carbon Reduction

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Traditional Chinese herbal foot baths are widely adopted for daily preventive healthcare, blood circulation promotion, and adjuvant therapeutic wellness. However, conventional production and consumption patterns impose significant environmental burdens, while traditional non-woven fabric bags often restrict the extraction and dissolution efficiency of active medicinal compounds due to material barrier constraints. This study aims to integrate scientifically concentrated herbal powder with polyvinyl alcohol (PVA) water-soluble film technology, evaluating not only its life cycle carbon footprint (CFP) based on ISO 14067 but also focusing on breakthroughs in medicinal efficacy and pharmacological active compound release rates. The results demonstrate that compared to conventional coarse-ground herbs with PP non-woven bags, the innovative water-soluble film solution enhances the extraction and release efficiency of effective active compounds by over 25%, realizing an overall carbon reduction rate of 38.03%. Key reduction and pharmacological pathways include: leveraging industrial-scale water extraction concentration and the instant dissolution characteristics of the PVA film to ensure complete release of active constituents while optimizing use-phase water temperatures (streamlining from 45.00°C to 40.00°C), thereby reducing heating energy by 56.28 g CO_2e / pack, and eliminating high-moisture herbal residue disposal and non-woven incineration at the consumer end by centralizing residue valorization at the manufacturing plant. This study confirms that bridging traditional medicine extraction technologies with water-soluble biomaterials successfully balances high pharmacological active release with green circular economy principles, offering a high-efficiency transition pathway with strong clinical and market potential for the natural medicine and healthcare sector.

Keyword:

Keywords: Active compound extraction, Polyvinyl alcohol water-soluble film, Herbal foot bath, Therapeutic efficacy, Life cycle carbon footprint

No. TC-009 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Utilization of Traditional Chinese Medicine Across Disease Categories in Taiwan: A Descriptive Analysis of National Health Insurance Data

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Background: Traditional Chinese Medicine (TCM) has been reimbursed under Taiwan's single-payer National Health Insurance (NHI) since 1995. Although TCM is widely used, recent disease-specific utilization and its scale relative to Western medicine have rarely been summarized together.

Methods: We conducted a descriptive analysis using Taiwan's National Health Insurance Research Database (NHIRD). Indicators included TCM outpatient use, patient numbers by ICD-10 chapter, condition-specific TCM use, workforce, and NHI expenditure. No individual-level data were accessed.

Results: TCM outpatients increased from 5.34 million in 2015 to 7.12 million in 2024 (+33%). The leading disease categories in 2024 were respiratory diseases (1.96 million, 27.5%), musculoskeletal and connective tissue disorders (1.87 million, 26.3%), and digestive diseases (1.44 million, 20.2%). TCM use was reported in 46.3% of patients with allergic rhinitis, approximately 30% of adult patients with cancer, and 22.5% of pediatric patients with cancer. The 2024 TCM outpatient budget was NT$32.3 billion, approximately one-fifth of the Western medicine primary-care budget. Practicing TCM physicians increased from 8,037 in 2024 to 8,234 in 2025. Between 2019 and 2024, home-based TCM care increased from approximately 600 to more than 100,000 visits.

Conclusions: TCM represents a substantial component of healthcare utilization within Taiwan's NHI, particularly for respiratory, musculoskeletal, and digestive conditions, with an expanding role in home-based and cancer care.

Keyword:

Traditional Chinese Medicine, National Health Insurance, health services utilization, Taiwan

No. TC-010 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Development of a Thin-Layer Chromatography Method to Identify a Concentrated Chinese Medicine of Qing-Fei-Tang

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Qing-Fei-Tang (QFT) is derived from Zeng-Bu-Wan-Bing-Hui-Chun (Supplement of Recovery from All Ailments). This formula clears the lungs, resolves phlegm, and suppresses cough, and it is included as a standard TCM formula in the Taiwan Herbal Pharmacopeia (Fourth Edition). Concentrated Chinese medicine, as a modernized dosage form, is commonly prepared as granules, which improves convenience for storage and clinical use. This study developed a thin-layer chromatography (TLC) identification method for ten herbal components in QFT, including Glycyrrhizae Radix et Rhizoma, Angelicae Sinensis Radix, Scutellariae Radix, Platycodonis Radix, Citri Reticulatae Pericarpium, Mori Radicis Cortex, Gardeniae Fructus, Armeniacae Semen Amarum, Schisandrae Chinensis Fructus, and Zingiberis Rhizoma Recens. The method utilized a QFT standard decoction, a QFT blank decoction, reference medicinal herbs, and chemical reference substances. The developed method successfully confirmed the herbal identity of ten commercial concentrated QFT preparations sourced from different manufacturers in Taiwan. The National Research Institute of Chinese Medicine, Ministry of Health and Welfare, reviewed the methodology, and three validated collaborative laboratories verified the protocol. The established TLC method provides a reliable quality-control tool for concentrated QFT preparations and helps ensure public medication safety.

Keyword:

Qing-Fei-Tang, thin-layer chromatography, qualitative analysis

No. TC-011 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Safety Reporting and Assessment of Chinese Herbal Formulas for Liver Cirrhosis: A Review of Randomized Controlled Trials

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Objective: To review safety reporting in RCTs of Chinese herbal medicine for liver fibrosis and cirrhosis published from 2021 to 2025.

Methods: PubMed and Chinese databases were searched for human RCTs evaluating Chinese herbal medicine in liver fibrosis or cirrhosis. Search terms covered herbal medicine, liver disease, RCTs, and safety outcomes. Data on AEs, SAEs, AE types, relatedness, severity, hepatic and renal function, and treatment discontinuation or withdrawal were descriptively analyzed.

Results: Five RCTs involving 1,624 participants were included. Most reported AEs and liver biochemical parameters, but reporting varied for SAEs, relatedness, severity, renal function, and AE-related discontinuation. Differences in safety definitions, reporting formats, and follow-up limited comparisons.

Conclusion: Recent RCTs provide descriptive safety information on Chinese herbal medicine for liver fibrosis and cirrhosis. Standardized safety definitions and reporting methods are needed to improve comparability and support future evidence synthesis.

Keyword:
Chinese Herbal Medicine, Liver Fibrosis, Liver Cirrhosis, Safety Reporting, Adverse Events

No. TC-012 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Authentication of Commercial Polygoni Multiflori Caulis (Ye-Jiao-Teng) in Taiwanese Market Using a PCR-RFLP Assay Reveals Widespread Adulteration by Pleuropterus angulatus

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Background: Polygoni Multiflori Caulis (PMC, Ye-Jiao-Teng), the dried stem of *Pleuropterus multiflorus* (PM), is a traditional Chinese medicine primarily used to treat insomnia and rheumatic arthralgia. However, the morphological similarity between PM and *Pleuropterus angulatus* (PA) may result in substitution or admixture in commercial PMC products, potentially compromising their efficacy and safety.

Objective: This study used a PCR-RFLP assay to assess the authenticity of commercial PMC products sold in the Taiwanese herbal market.

Methods: Thirty commercial PMC samples were collected from herbal stores in northern, central, and southern Taiwan. Total DNA was extracted, and the chloroplast *trnL-trnH* region was amplified. The amplicons were double-digested with BseNI and XbaI to differentiate PM from PA according to species-specific restriction patterns.

Results: PCR-RFLP analysis identified PA alone in 26 of 30 commercial samples (86.67%), while the remaining four samples (13.33%) contained both PM- and PA-specific restriction fragments. No sample contained PM alone, PA was detected in every sample examined.

Conclusion: The predominance of PA and the scarcity of authentic PM in commercial PMC products indicate a serious authenticity problem in the Taiwanese market, highlighting the need for strengthened quality control and market surveillance.

Keyword:

Polygoni Multiflori Caulis, Pleuropterus multiflorus, Pleuropterus angulatus, adulteration, PCR-RFLP, market survey

No. TC-013 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Wound-healing effects of Jinchuang ointment in Hansen's disease: suppression of macrophage inflammation and promotion of skin cell migration

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Jinchuang ointment (JCO) is a traditional Chinese herbal formulation used to promote wound healing. Patients with Hansen's disease frequently develop neuropathy-associated chronic wounds, but the mechanisms underlying its wound-healing effects remain unclear. This study investigated the effects of JCO on macrophage-mediated inflammation, fibroblast migration, and wound healing in patients with Hansen's disease. In human Detroit 551 skin fibroblasts, JCO increased cell viability by 5-20% and enhanced migration by 20-35%, accompanied by increased phosphorylation of EGFR, ERK1/2, Akt, FAK, and Src. The anti-inflammatory activity of JCO was evaluated in LPS-stimulated RAW 264.7 macrophages. JCO reduced NO production and TNF-α and IL-6 secretion. It also decreased COX-2 and iNOS protein expression, restored IκBα levels, and suppressed LPS-induced phosphorylation of p38, JNK, and ERK1/2. Without LPS, JCO slightly increased TNF-α secretion to below 0.1 ng/mL. To examine the effect of soluble factors released by JCO-treated macrophages on fibroblast-mediated wound repair, Detroit 551 fibroblasts were exposed to macrophage-conditioned medium (CM). CM from JCO-treated macrophages increased fibroblast wound closure from 60% to 80-95%. Furthermore, recombinant TNF-α enhanced fibroblast migration without affecting cell viability, demonstrating its pro-migratory activity. In an exploratory clinical study (JCO, n=14, control, n=6), daily topical application of JCO reduced wound area by over 50% within one month, and all treated ulcers healed within 14-83 days. Overall, JCO may promote wound healing by stimulating fibroblast migration, modulating macrophage–fibroblast communication, and suppressing excessive LPS-induced inflammation. This finding supports the therapeutic potential of JCO for chronic wounds associated with Hansen's disease.

Keyword:

Hansen's disease, Jinchuang ointment, Wound healing

No. TC-014 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Herbal Acupoint Injection as a Complementary Therapy: Neuroprotective Effects of Ginkgo Compound Extract in Experimental Autoimmune Encephalomyelitis

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Background: Multiple sclerosis (MS) is an autoimmune central nervous system (CNS) disorder marked by demyelination and progressive neurological dysfunction, with limited disease-modifying options. Integrating bioactive natural compounds with meridian-based delivery via herbal acupoint injection offers a complementary strategy that combines plant-derived extracts with acupoint-targeted stimulation.

Objective: To evaluate the therapeutic efficacy and immunoregulatory mechanisms of acupoint injection with a Ginkgo-derived compound extract (GB) in a mouse model of experimental autoimmune encephalomyelitis (EAE).

Methods: EAE was induced in C57BL/6 mice, and the treatment group received GB acupoint injection at defined acupoints. Clinical severity and body weight were monitored throughout the study. Spinal cord tissue was collected for H&E staining to assess inflammatory infiltration, and flow cytometry was performed on brain and spleen tissue to characterize immune cell populations, comparing local CNS and systemic responses.

Results: GB acupoint injection significantly attenuated clinical severity and preserved body weight relative to EAE controls. Histology showed reduced inflammatory infiltration in spinal cord sections from GB-treated mice versus controls. Flow cytometry revealed a selective reduction in specific CNS immune cell populations, while splenic composition did not differ between groups, indicating a CNS-restricted effect rather than systemic immunosuppression.

Conclusion: GB acupoint injection appears to exert neuroprotective effects by limiting immune cell infiltration and inflammation in the CNS, supported by histological and flow cytometric evidence. These findings support incorporating natural compound-based acupoint injection into complementary approaches for autoimmune neurological disorders, aligning with the integration of natural products and traditional therapeutic modalities.

Keyword:
Ginkgo Biloba, Chinese Herbal Medicine, Multiple Sclerosis, Experimental Autoimmune Encephalomyelitis, Acupoint injection

No. TC-015 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Herbal Medicine for Sjögren's Disease: A Scoping Review of Preclinical Evidence

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Background: Sjögren's disease (SjD) is a chronic autoimmune disease affecting the exocrine glands, particularly the salivary and lacrimal glands. Although traditional medicines have been widely studied for SjD, the scope of the available evidence remains unclear. This study aimed to map the preclinical evidence on the effects of medicinal plants, natural compounds, and herbal formulas on SjD.

Methods: A scoping review of preclinical studies evaluating plant-derived interventions for SjD was conducted by searching PubMed, Scopus, Web of Science, and Embase. Data were synthesized by intervention type, experimental model, outcomes, and proposed mechanisms of action.

Results: Eighty studies were included: 46 on natural compounds, 29 on herbal formulas, and 5 on medicinal plants or plant-derived preparations. Of 75 studies with *in vivo* experiments, 56 (74.7%) used NOD mice or NOD-derived strains. Research focused mainly on the salivary glands and secretory function, while lacrimal glands and dry eye manifestations were less studied. Commonly assessed outcomes included secretory function, glandular damage and inflammation, immune response, and epithelial function. Proposed mechanisms centered on inflammatory signaling, adaptive immunity, epithelial secretory function, oxidative stress and mitochondrial function, cellular homeostasis, and the gut microbiota.

Conclusion: Preclinical evidence on natural products in SjD is rapidly accumulating, showing effects across multiple pathogenic processes. However, the evidence relies heavily on NOD mouse models, focuses primarily on salivary gland manifestations, and lacks consistent mechanistic validation, lacrimal gland involvement also remains understudied. Future research should diversify experimental models, broaden disease manifestations assessed, and strengthen mechanistic validation before clinical translation.

Keyword:
Sjögren's disease, Herbal medicine, Natural compounds, Preclinical, Scoping review

No. TC-016 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Quantitative Dendritic Morphology as a Screening Platform for Natural Products and Traditional Chinese Medicine

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Traditional Chinese medicine (TCM) contains diverse bioactive constituents that may regulate inflammatory and immune responses. However, the complex, multi-component nature of TCM
makes objective evaluation of its cellular effects challenging. We hypothesized that quantitative
dendritic morphology could provide a rapid phenotypic screening layer, followed by independent
immune-function assays to establish biological relevance.
We established a dendritic cell-based screening platform to evaluate Huang Lian Chieh Dwu (HLCD) and related bioactive constituents. Cells were exposed to different concentrations of HLCD or selected tetracyclic isoquinoline-related compounds, followed by standardized microscopic imaging and quantitative image analysis. Morphological parameters included dendrite length, dendrite number, total dendritic extension, branching complexity, cell area, perimeter, aspect ratio, and circularity. Dose-dependent morphological profiles were generated to
identify treatment-associated cellular phenotypes.
Different stimuli induced distinct and concentration-dependent remodeling of dendritic cell cellular architecture. Dendrite length and total dendritic extension were particularly sensitive parameters, enabling rapid discrimination among treatment conditions. Dendritic number and branching complexity further characterized structural remodeling, whereas cell area and shape descriptors provided complementary measures of cellular morphology.
Importantly, morphological changes were not interpreted as direct evidence of immune activation. Instead, dendritic morphology was used as the first-line screening readout, allowing
compounds and concentrations with distinct phenotypic responses to be prioritized. Selected conditions can subsequently be evaluated using independent immune-function endpoints, including dendritic-cell activation or maturation markers and inflammatory or regulatory mediator production.
This two-stage strategy provides a simple, quantitative, and scalable approach for screening TCM-derived natural products and identifying candidates for subsequent functional immunological validation.

Keyword:
Dendritic cell morphology, Quantitative image analysis, Immunomodulation,traditional Chinese medicine, bioactive compounds.

No. TC-017 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Baihe Extract Attenuates PM2.5-Induced Airway Inflammation and Mucus Hypersecretion in BEAS-2B Cells

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Background:
Fine particulate matter (PM2.5) induces oxidative stress, inflammation, and mucus hypersecretion in airway epithelium, contributing to chronic respiratory disease. Baihe (*Lilium spp. bulb), a traditional Chinese medicine used to moisten the lung and relieve cough, may have protective effects against PM2.5-induced airway inflammation.*
Methods:
Human bronchial epithelial BEAS-2B cells were used to evaluate the effects of Baihe extract on PM2.5-induced airway injury. Cytotoxicity was assessed by MTT assay. Cells were pretreated with Baihe extract and exposed to PM2.5 (50 μg/mL). The effects on IL-6, IL-1β, and MUC5B were evaluated using flow cytometry, ELISA, and immunofluorescence staining.
Results:
Baihe extract showed no significant cytotoxicity up to 750 μg/mL, whereas cell viability decreased at 1 mg/mL. PM2.5 increased IL-6-positive cells from 3.16% to 11.42%, while Baihe extract (100 μg/mL) reduced this to 8.30%. Baihe extract (250 μg/mL) also attenuated PM2.5-induced IL-1β secretion and suppressed MUC5B expression.
Conclusions:
At non-cytotoxic concentrations, Baihe attenuated PM2.5-induced inflammatory and mucus responses in airway epithelial cells, suggesting its potential as a component of multi-herb formulations for lung-clearing and phlegm-resolving applications.

Keyword:
Baihe, PM2.5, airway inflammation, MUC5B, BEAS-2B cells

No. TC-018 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Sarcodia suae Polysaccharides Modulate Macrophage Polarization toward an M1-like Phenotype

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Sarcodia suae is a red alga endemic to Taiwan with reported immunomodulatory activity. However, the effects and underlying mechanisms of *S. suae* polysaccharides (SSP) on macrophages remain unclear. In this study, SSP was prepared by hot-water extraction followed by ethanol precipitation, and its immunomodulatory effects were evaluated in THP-1-derived macrophages and RAW 264.7 cells. Cell viability, NF-κB signaling, nitric oxide (NO) production, cytokine secretion, and M1-associated gene expression were assessed using the MTT assay, Western blotting, the Griess assay, enzyme-linked immunosorbent assay (ELISA), and quantitative PCR, respectively. SSP showed no significant cytotoxicity and induced an M1-like phenotype in THP-1-derived macrophages. SSP treatment increased p65 phosphorylation, suggesting activation of the NF-κB signaling pathway, accompanied by increased iNOS protein expression and NO production. Furthermore, SSP promoted the secretion of pro-inflammatory cytokines and upregulated M1-associated genes at the mRNA level. These findings demonstrate that SSP induces M1-like macrophage polarization, suggesting its potential as a natural immunomodulatory agent.

Keyword:

Sarcodia suae, polysaccharides, immunomodulation, macrophage polarization, NF-κB pathway

No. TC-019 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Anti-cancer effect of Guizhi-Fuling Wan on urothelial carcinoma via macrophages

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The traditional Chinese herbal formula Guizhi-Fuling Wan (GFW) is a classic blood-activating and stasis-resolving formula. Previous reports demonstrated that GFW triggers apoptosis in bladder cancer cells and attenuates tumor growth in a mouse orthotopic bladder tumor model. This study aimed to investigate whether the anti-cancer effects of GFW could produce by the interaction between urothelial carcinoma cells and tumor-associated macrophages.

First, cytotoxicity assays showed that 4 mg/mL GFW extract had some cytotoxic (cell viability about 60%) on 5637 urothelial carcinoma cells, but not on M0 macrophages. Notably, after incubation at 37 degree for 24 hours, GFW extract didn't exhibit cytotoxicity toward 5637 urothelial carcinoma cells. Therefore, concentration of 2 and 4 mg/mL were selected for study the interaction between macrophages and 5637 cells. In Transwell migration assay using 5637, M2 macrophages conditioned medium alone exhibited migration inhibition effect, whereas conditioned medium from GFW-treated M2 macrophages further enhanced the inhibition of 5637 cell migration. It suggests that some factors of M2 conditioned medium were changed by GFW, which plays a role on 5637 cell migration inhibition. On the other hand, both of M1 and M2 conditioned medium decreased 5637 cell viability, GFW-treated conditioned medium didn't change it. For macrophage polarization analysis, GFW-treated M2 macrophages showed increased expression of the M1 marker TNF-α and decreased expression of the M2 marker MRC1.

Overall, these findings suggest that GFW may inhibit bladder cancer cell proliferation and may also suppress M2 macrophage polarization, thereby affecting the interaction between macrophages and bladder cancer cells.

Keyword:

Guizhi-Fuling Wan, urothelial carcinoma, macrophages

No. TC-020 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

The Usefulness of Botanical Supplement Ganwei for Metabolic DysfunctionAssociated Steatotic Liver Disease: A Randomized, Placebo-Controlled Trial

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Metabolic dysfunction-associated steatotic liver disease (MASLD) lacks effective therapies. Glycine N-methyltransferase (GNMT), an essential hepatic metabolic regulator, represents a promising therapeutic target for MASLD. Previously, we identified the natural polyphenol 1,2,3,4,6-penta-O-galloyl-β-D-glucose (PGG) as a potent GNMT enhancer. To evaluate the therapeutic efficacy of Ganwei—a PGG-contained botanical supplement developed via a highthroughput screening platform for GNMT activation—we conducted a 6-month, randomized, placebo-controlled trial in 64 MASLD patients assigned (1:1:1:1) to Ganwei alone, metformin alone, combination therapy, or placebo (NCT06244550). Ganwei was certified as a "Health Food" by the Taiwan FDA in 2023 and is formulated with herbal extracts from Schisandra chinensis, Punica granatum, and Paeonia lactiflora. The primary outcomes of hepatic steatosis and stiffness were assessed using FibroScan (CAP and kPa). Secondary outcomes included safety, quality of life (SF-36), and pharmacogenomic analysis (GNMT rs10948059). At 6 months, Ganwei monotherapy significantly attenuated hepatic steatosis (CAP, $p = 0.03$) and stiffness (kPa, $p = 0.048$), outperforming placebo on a 6-point steatosis scale (1.1 ± 1.8 vs. 0.1 ± 0.7, $p = 0.036$) without drug-related adverse events. Notably, treatment efficacy was markedly conducted in patients harboring the T allele of GNMT rs10948059 (C/T and T/T vs. C/C: 2.8 ± 1.9 vs. 0.5 ± 1.3, p less than 0.05), indicating a promoter-activity-dependent treatment response. Ganwei also improved physical, emotional, and general health domains in the SF-36 survey (p less than 0.05). In conclusion, Ganwei represents a safe, effective botanical candidate for MASLD via GNMT induction.

Supported by National Science and Technology Council (115-2321-B-005-009).

Keyword:
Natural products, Botanical supplement, Ganwei, GNMT inducer, MASLD, Pharmacogenomics

No. TC-021 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Divergent Peripheral Metabolic and Cerebral Amyloid Imaging Responses to a GLP-1 Receptor Agonist in a Preclinical Study

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Background: Metabolic dysfunction is associated with neurodegenerative disorders and may influence therapeutic responses. Glucagon-like peptide-1 receptor agonists (GLP-1RAs) have attracted interest for their potential metabolic and neurological effects. However, improvements in peripheral metabolic parameters may not necessarily correspond to changes in cerebral amyloid-related imaging signals. This study examined the effects of a GLP-1RA on peripheral metabolic and cerebral imaging outcomes under experimental conditions involving metabolic dysfunction and amyloid pathology.
Methods: Animals exhibiting metabolic abnormalities and amyloid-associated pathology were treated with a GLP-1RA. Untreated disease-model animals and reference controls were included for comparison. Metabolic outcomes were assessed using body weight, fasting glucose, insulin, homeostatic model assessment of insulin resistance (HOMA-IR), glycated hemoglobin (HbA1c), and glucose tolerance measurements. Cerebral amyloid-related imaging signals were evaluated using ^{18}F-florbetaben microPET.
Results: GLP-1RA treatment attenuated body weight gain and reduced fasting glucose, insulin, HOMA-IR, and HbA1c compared with untreated disease-model animals. However, glucose tolerance remained impaired. Despite these improvements in peripheral metabolic parameters, cerebral ^{18}F-florbetaben signals showed limited responses across the assessed brain regions.
Conclusion: Treatment with a GLP-1RA improved several peripheral metabolic abnormalities without corresponding changes in cerebral amyloid-related imaging signals under the conditions examined. These findings highlight the potential dissociation between peripheral metabolic efficacy and cerebral amyloid-related responses, suggesting that metabolic improvements alone may not adequately predict central therapeutic outcomes.

Keyword:
GLP-1 receptor agonist, insulin resistance, metabolic dysfunction, florbetaben, amyloid imaging, neurodegeneration

No. TC-022 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Anti-inflammatory Effects and Mechanisms of CWTZ Ethanolic Extract and Its Active Constituent in Human Neutrophils

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Poor responsiveness to corticosteroid therapy in patients with severe asthma remains a major clinical challenge. Oxidative stress, elastase release, and neutrophil extracellular trap (NET) formation resulting from excessive neutrophil activation are closely associated with airway remodeling and chronic inflammation. This study aimed to investigate the inhibitory effects of the traditional Chinese medicine CWTZ and its active constituent on inflammatory responses in human neutrophils and to elucidate the underlying molecular mechanisms, thereby evaluating their potential as therapeutic candidates for severe asthma. An ethanolic extract of CWTZ (CWTZ-95E) was prepared, and its chemical composition was analyzed using ultra-high-performance liquid chromatography–tandem mass spectrometry. Human neutrophils were used as an experimental model, chemiluminescence assays, flow cytometry, and Western blotting were performed to assess anti-inflammatory effects and intracellular signaling mechanisms. The results demonstrated that CWTZ-95E significantly inhibited the respiratory burst, degranulation, and NET formation in human neutrophils. Chemical analysis identified sinapic acid as a major active constituent. This study is the first to demonstrate the inhibitory effects of CWTZ on inflammatory responses in human neutrophils and elucidate the associated molecular mechanisms, providing an experimental basis for the further development of natural product-derived therapeutic candidates for severe asthma with poor responsiveness to corticosteroid therapy.

Keyword:

Degranulation, neutrophilic inflammation, neutrophil extracellular traps, respiratory burst, severe asthma

No. TC-023 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Tung-Yi Fang Inhibits HER2-Low Breast Cancer Cell Growth and Modulates the Macrophage Proteome

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Introduction

Tung-Yi Fang (TYF) has shown antitumor activity against triple-negative breast cancer. Its effects on HER2-low breast cancer and macrophages remain unclear.

Aim

To evaluate TYF-induced changes in breast cancer cell growth, cytokine secretion, and the macrophage proteome.

Methods

HER2-low breast cancer cells were assessed using crystal violet staining and cytokine arrays. TYF-treated RAW264.7 macrophages underwent proteomic profiling followed by Gene Ontology and KEGG enrichment analyses.

Results

TYF inhibited breast cancer cell growth and reduced angiogenin secretion. In macrophages, proteomic analysis revealed increased abundance of proteins associated with mitochondrial oxidative phosphorylation and decreased abundance of those involved in ribosome biogenesis and cell-cycle regulation.

Conclusion

TYF suppresses HER2-low breast cancer cell growth and alters macrophage metabolic pathways at the proteomic level. These findings support further investigation of its effects on tumor–macrophage interactions.

Keyword:

Tung-Yi Fang, HER2-low breast cancer, angiogenin, macrophages, proteomics

No. TC-024 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Genetic-Level Comparison and Identification of Two Distinct Agarwood Varieties

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Agarwood is a valuable resinous product of Aquilaria trees, characterized by its distinctive aroma. This study aimed to compare the genetic and transcriptomic characteristics of Aquilaria sinensis (AS) and Aquilaria crassna (AC) and develop molecular methods for species identification. Under identical plant tissue culture conditions, AC exhibited a more intense aroma than AS. RNA sequencing (RNA-seq) was performed to identify differentially expressed genes and associated metabolic pathways. The results revealed distinct transcriptomic profiles, with AC showing greater activation of pathways potentially associated with agarwood aroma compound biosynthesis. To facilitate species discrimination, four DNA barcode regions (ITS1, ITS2, matK, and trnH) were compared, revealing six nucleotide differences in the matK region. Based on these variations, specific primers were designed for loop-mediated isothermal amplification (LAMP) and high-resolution melting (HRM) assays. In conclusion, this study integrates transcriptomic analysis and DNA barcoding to characterize genetic differences between AS and AC and establish molecular approaches for species identification. These findings provide a foundation for investigating species-specific aroma-related metabolism and support the authentication and quality control of agarwood-producing plant materials.

Keyword:

Agarwood, Aquilaria sinensis, Aquilaria crassna, RNA-seq, DNA barcoding, LAMP, HRM

No. TC-025 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Exploiting Pulsatilla chinensis–Driven Histone H3 Cleavage for NF1-Associated Cancer Therapy

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Malignant peripheral nerve sheath tumors (MPNSTs) are highly aggressive soft-tissue sarcomas that frequently arise in individuals with neurofibromatosis type 1 (NF1). Germline loss of NF1, together with secondary genetic alterations, drives hyperactivation of downstream RAS signaling cascades. Despite advances in targeted therapy, drug resistance and poor clinical outcomes remain major challenges, underscoring the urgent need for new mechanistic strategies and therapeutic candidates. To identify alternative treatment strategies, we systematically screened a library of traditional herbal medicines and bioactive natural extracts against NF1-deficient tumor cell lines. Phenotypic and molecular responses were characterized using cell viability assays, Western blotting, and high-throughput transcriptomic profiling. The screen identified a crude extract of Pulsatilla chinensis (PC) as a potent suppressor of the proliferation and survival of NF1-mutant tumor cells. Notably, PC treatment induced robust cell death accompanied by a distinct pattern of site-specific histone H3 clipping, directly linking chromatin-directed proteolysis to its cytotoxic activity. Transcriptomic analysis further revealed widespread dysregulation of gene networks associated with cell survival, stress response, and NF1-related tumor biology. These findings suggest that PC acts through distinct, multi-targeted mechanisms rather than relying solely on conventional inhibition of kinase cascades. Collectively, our results identify Pulsatilla chinensis as a promising natural-product-derived therapeutic candidate for MPNSTs and highlight histone H3 clipping as a novel molecular hallmark of its action. This study provides a strong rationale for isolating the principal bioactive constituents of PC, investigating the functional impact of H3 clipping on chromatin dynamics, and evaluating its therapeutic potential in vivo.

Keyword:
Pulsatilla chinensis, Histone Cleavage, NF1-Associated Cancer

No. TC-026 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Mass Spectrometry-Based Profiling and Anti-Non-Small Cell Lung Cancer Potential of Plant Essential Oil-Derived Sesquiterpenes

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This study explores the anti-tumor potential of plant essential oil-derived sesquiterpenoids, including caryophyllene, humulene, elemene, and germacrene. Utilizing advanced gas chromatography-mass spectrometry (GC-MS) for precise profiling, extensive literature confirms that these natural compounds effectively induce endogenous apoptosis in non-small cell lung cancer (NSCLC) cells, block cell cycle progression, and significantly inhibit tumor invasion and metastasis. These therapeutic effects are primarily mediated through the precise regulation of key intracellular signaling networks, such as the p53/Bcl-2/Bax pathways. By modulating these critical cascades, sesquiterpenoids demonstrate distinct therapeutic advantages characterized by multi-target action and remarkably low toxicity to normal tissues compared to conventional chemotherapy. In addition to reviewing established mechanisms, this paper examines how structural variations among these sesquiterpenoids influence their pharmacological efficacy, therapeutic performance, and bioavailability. Consequently, essential oil-derived sesquiterpenoids represent highly promising candidates for development into novel, low-toxicity chemotherapeutic agents or adjuvant therapies. This comprehensive analysis consolidates current experimental evidence, addresses the challenges regarding their chemical formulation and targeted delivery, and highlights future research directions required to fully translate these plant-derived compounds from laboratory settings into clinical oncology practice. Ultimately, this work provides a framework for integrating natural sesquiterpenoids into advanced, multi-targeted therapeutic strategies to overcome drug resistance and improve overall patient outcomes in modern oncology.

Keyword:

Sesquiterpenoids, Mass Spectrometry (GC-MS), Non-Small Cell Lung Cancer (NSCLC), Endogenous apoptosis, Signaling pathways (p53/Bcl-2/Bax), Multi-target therapy

No. TC-027 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Characteristics of Herb-Induced Liver Injury Reported Through the Taiwan Adverse Drug Reaction Reporting System for Herbal Medicine from 2001 to 2025

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Background: Herbal prescription is a mainstay of Traditional Chinese Medicine (TCM) treatment. In Taiwan, it is increasingly co-prescribed with Western medicine. However, reports of herb-induced liver injury (HILI) have raised safety concerns. We, therefore, analysed HILI cases reported to the Taiwan Adverse Drug Reaction Reporting System for Herbal Medicine (TADRRS-HM) to describe their characteristics.

Methods: We reviewed 48 suspected HILI cases reported to TADRRS-HM from 2001 to 2025. Suspected products were classified by ingredient, functional category, and causality classified by WHO-UMC and Naranjo algorithm. Peak ALT, ALP and total bilirubin (TBil) were also analysed.

Results: Most patients (62.5%) were female with median age of 53 years, and men were generally older than women (median age=70 years, p=0.008). The most frequently suspected single herbs were Huang Qin (*Scutellaria baicalensis* Georgi, 8) and He Shou Wu (*Polygonum multiflorum* Thunb., 5), the most frequent formula was Xiao Chai Hu Tang (4). Overall, Huang Qin was present in half of all cases (24/48). Heat-clearing (33%) and harmonizing (23%) products were most common. Median peak ALT was 398 U/L, 36.2% of patients had ALT ≥20×ULN. 78.3% of those with TBil data had TBil ≥2×ULN. He Shou Wu cases had higher median peak ALT than other cases (1895 vs 324 U/L, p=0.031).

Conclusion: Huang Qin was the most frequent signal, while He Shou Wu was linked to the most severe injury and the most consistently probable causality. As spontaneous reports are subject to under-reporting, future studies should determine causality and identify risk factors in real-world settings.

Keyword:

Liver Injury, Herbal Medicine, Herbal-Induced Liver Injury, Adverse Drug Reaction, Hepatotoxicity, Traditional Chinese Medicine

No. TC-028 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Morphological Identification and Chemical Analysis for Quality Assessment of Abri Mollis Herba

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Abri Mollis Herba , derived from the climbing plant *Abrus pulchellus* subsp. *mollis* (Hance) Verdc. (Fabaceae), is frequently used as a substitute for or mixed with Abri Herba . A preliminary survey of the Taiwanese herbal market identified 18 of 20 batches marketed as Abri Herba as Abri Mollis Herba, whereas only two batches were identified as Abri Herba, indicating that Abri Mollis Herba predominated among the surveyed samples. However, Abri Mollis Herba is not included in the Taiwan Herbal Pharmacopeia (THP), the Chinese Pharmacopoeia (CP), or the Hong Kong Chinese Materia Medica Standards. HPLC analysis revealed distinct chemical fingerprints between the two herbal materials. Schaftoside was detected in Abri Mollis Herba but not in Abri Herba. Quantitative analysis further showed that abrine contents in Abri Herba were 10–20 times those in Abri Mollis Herba. Macroscopic and microscopic examination revealed differences in trichomes on the abaxial leaf surface: Abri Herba exhibited short, appressed trichomes, whereas Abri Mollis Herba had long, soft trichomes. These findings establish baseline data for the morphological identification and chemical characterization of Abri Mollis Herba and provide a scientific basis for considering its inclusion in the THP.

Keyword:

Abri Mollis Herba, *Abrus pulchellus* subsp. *mollis* , Abrine, Schaftoside, Quality Assessment

No. TC-029 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

HPLC Fingerprinting and Aloin Quantification of Commercial Aloe in Taiwan

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Aloe is traditionally used in Chinese medicine for its laxative, liver fire-clearing, and antiparasitic effects. Three commercial forms are available in the Taiwanese herbal market: Old-Aloe (OA), New-Aloe (NA), and calcined-Aloe (CA). OA has a yellowish-brown surface with a slight greenish tint and a waxy fracture, whereas NA is dark green with a glassy fracture. The other CA is charcoal-black to dark brown, lustrous, lightweight, and friable. According to the Taiwan Herbal Pharmacopeia (4th), Aloe consists of the extract of dried leaf juice from *Aloe vera* or *Aloe ferox* (Liliaceae), with an aloin content of at least 16.0%. This study aimed to characterize the chemical profiles and aloin contents of commercial Aloe in Taiwan. Twenty batches were collected in Taiwan herbal market and provisionally classified according to product labeling and macroscopic characteristics as OA (n = 10), NA (n = 7), and CA (n = 3). HPLC analysis revealed distinct fingerprints between OA, NA and CA. Aloins A and B were the major constituents of OA, with combined contents of 19.8–34.7%, compared with 3.9–23.5% in NA and below 0.1% in CA. SK5, one of the samples, initially classified as NA by its appearance, exhibited an HPLC fingerprint and aloins content consistent with OA, highlighting the limitations of macroscopic classification. These findings reveal substantial chemical variation among commercial Aloe forms and suggest that processing, particularly calcination, may contribute to reduced aloin content. HPLC fingerprinting combined with aloins quantification provides a scientific basis for the differentiation and quality assessment of commercial Aloe.

Keyword:

Aloe, *Aloe vera*, *Aloe ferox*, Aloins, Macroscopic identification, HPLC fingerprinting

No. TC-030 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Comparative Analysis of Commercial Gleditsiae Fructus and Gleditsiae Fructus Abnormalis by Morphological Identification, TLC/HPLC Analysis

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Gleditsiae Fructus (GF) and Gleditsiae Fructus Abnormalis (GA) are derived from the mature and infertile fruits of *Gleditsia sinensis* Lam., respectively. Both are traditionally used to resolve phlegm, open the orifices, dissipate nodules, reduce swelling, dispel wind, and eliminate parasites, although their clinical applications differ. GA primarily used to dispel wind-phlegm and open the orifices, whereas GF is used to treat damp-phlegm, wheezing, cough, and constipation, and is applied externally to reduce swelling and promote pus discharge. This study aimed to investigate the availability and labeling of these two herbal materials (GF and GA) in the Taiwanese market and assess their quality through macroscopic and microscopic identification, TLC, and HPLC analyses. The market survey revealed limited availability of GF and identified some products containing GA that were labeled and sold as GF. TLC and HPLC methods were established using echinocystic acid and oleanolic acid as reference compounds, and their contents were quantified in 10 batches of each herbal material. In the samples of GA, echinocystic acid and oleanolic acid contents ranged from 1.012% to 1.241% and from 1.302% to 1.592%, respectively. GF showed greater batch-to-batch variability in echinocystic acid (0.457–1.767%) and oleanolic acid (0.394–0.955%) contents, indicating limited consistency in chemical quality. These findings provide a scientific basis for the identification and quality control of Gleditsiae Fructus (GF) and Gleditsiae Fructus Abnormalis (GA).

Keyword:

Gleditsia sinensis, Gleditsiae Fructus, Gleditsiae Fructus Abnormalis, Echinocystic acid, Oleanolic acid, Chemical analysis

No. TC-031 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Investigation of the Commercial Hoveniae Semen by Microscopic Morphology, TLC and HPLC Analysis

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Hoveniae Semen is widely used as a food supplement and traditional medicine in Taiwan, Japan, China, and Korea. Pharmacological studies have reported its antidiabetic, antioxidant, antiadipogenic, antifatigue, antiallergic, neuroprotective, and hepatoprotective activities. According to the Taiwan Herbal Pharmacopeia (4^{th}), Hoveniae Semen consists of the dried mature seeds of *Hovenia acerba* Lindl., *H. dulcis* Thunb., or *H. trichocarpa* Chun & Tsiang, all belonging to the family Rhamnaceae. To investigate the the botanical origins of commercial Hoveniae Semen in Taiwan and develop analytical methods for species differentiation and quality assessment. Twenty commercial batches were collected from herbal stores across northern, central, and southern Taiwan. Their botanical origins could not be determined by macroscopic or microscopic examination. HPLC fingerprints were established, and the major constituents were characterized. TLC and HPLC analyses using the developed methods identified 10 batches as H. acerba and 10 as *H. dulcis*. Hovenitin I was detected in *H. dulcis* but not in *H. acerba*, suggesting its potential as a chemical marker for differentiating the two species of Hoveniae Semen. Dihydromyricetin content was also quantified in all 20 batches. These findings provide a scientific basis for the authentication and quality evaluation of Hoveniae Semen.

Keyword:

Hoveniae Semen, Hovenia acerba, Hovenia dulcis, HPLC, TLC, Dihydromyricetin

No. TC-032 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Isolation of Root Constituents and Comparative Profiling in Stems of Kleinhovia hospita L. to Assess Substitution Potential

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Kleinhovia hospita L. (Malvaceae) is a Thai medicinal plant traditionally used to relieve muscle pain and allergies. Because roots are predominantly utilized in traditional formulations, persistent root harvesting threatens the sustainability of natural plant populations. To evaluate whether the aerial stem can serve as a viable alternative to the root, this study investigated and compared their chemical constituents and chromatographic profiles. Dried root and stem materials were sequentially extracted by Soxhlet extraction using hexane, ethyl acetate, and methanol. The root ethyl acetate extract was fractionated by medium-pressure liquid chromatography (MPLC), yielding two isolated compounds: paprazine (also known as N-p-trans-coumaroyltyramine) (**1**) and oleanolic acid (**2**) . Ethyl acetate extracts from both plant parts were analyzed by high-performance liquid chromatography (HPLC) at 10 mg/mL and compared against the isolated markers based on retention times and peak UV profiles. The root and stem extracts shared at least seven major peaks at retention times of 16.0, 24.0, 32.0, 34.0 (**1**) , 43.0, 49.0, and 52.0 (**2**) min. Peaks at 16.0 and 49.0 min exhibited higher intensities in the stem extract, whereas the remaining peaks were more abundant in the root extract. Paprazine (**1**) (34.0 min) and oleanolic acid (**2**) (52.0 min) were present in both extracts, with higher concentration observed in root extract. These findings demonstrate substantial chromatographic similarities and confirmed shared chemical constituents between the root and stem, supporting further pharmacological evaluation of the stem as a sustainable alternative plant part.

Keyword:
Kleinhovia hospita L., triterpene, phenolic amide, HPLC analyses, Thai traditional medicine

No. TC-033 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Effects of Drying Conditions on the Physicochemical Characteristics and Bioactive Compounds of Ginger

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Ginger is widely used as a food ingredient and traditional herbal material, and its quality and bioactive compounds may be affected by drying conditions. This study investigated the effects of drying temperature and time on the physicochemical characteristics and bioactive compounds of dried ginger. Fresh ginger samples were dried at 50, 65, and 80°C for 12, 16, and 20 h, resulting in nine drying conditions. Moisture content and color characteristics (L^*, a^*, and b^* values) were evaluated, while high-performance liquid chromatography (HPLC) was used to analyze 6-gingerol and 6-shogaol. Moisture content decreased with increasing drying temperature and duration. The recorded moisture contents ranged from 8.76% to 56.37% at 50˚C, 4.56% to 6.00% at 65˚C, and 4.51% to 5.76% at 80˚C. Color measurements showed variation among drying conditions. Across the nine treatments, mean L^* values ranged from 60.09 ± 0.25 to 69.32 ± 2.61, mean a^*values ranged from −0.16 ± 0.20 to 1.88 ± 0.83, and mean b^* values ranged from 8.19 ± 4.10 to 12.35 ± 3.67 (mean ± SD, n = 3). HPLC analysis showed differences in 6-gingerol and 6-shogaol among the drying conditions. These findings indicate that drying temperature and time affected the moisture content, color characteristics, and bioactive compound contents of dried ginger.

Keyword:
ginger, drying conditions, 6-gingerol, 6-shogaol, moisture content, color characteristics, HPLC

No. TC-034 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Evaluating the Protective Effects of a Traditional Chinese Medicine Against Combined Polystyrene Microplastic and DEHP Exposure in a Drosophila Model

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Polystyrene microplastics (PS-MPs) and di(2-ethylhexyl) phthalate (DEHP) may induce oxidative stress and impair physiological function. Alisma Rhizoma (AS), a traditional Chinese medicine with reported antioxidant properties, was investigated for its protective effects against PS-MPs and DEHP co-exposure in male Drosophila melanogaster. Oxidative stress resistance was evaluated by survival following paraquat exposure, and locomotor function was assessed using a climbing assay. Compared with the control group, flies co-exposed to PS-MPs and DEHP (D+M) exhibited significantly reduced survival under paraquat-induced oxidative stress and impaired climbing performance. High-concentration AS supplementation significantly improved survival, while medium- and high-concentration AS supplementation significantly improved climbing performance. These findings suggest that AS may alleviate oxidative stress susceptibility and locomotor impairment associated with PS-MPs and DEHP co-exposure. Further studies are warranted to elucidate the underlying protective mechanisms .

Keyword:
Traditional Chinese Medicine；Polystyrene microplastics；Di(2-ethylhexyl) phthalate (DEHP)；Oxidative stress；Drosophila melanogaster；Locomotor function

No. TC-035 / 傳統中醫藥暨替代醫學組 / TCM and Complementary Medicine (TC)

Anti-Dengue Bioactive Constituents from the Traditional Chinese Medicinal Plant Cremastra appendiculata

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In traditional Chinese medicine, dengue fever is categorized as "Wenbing" (warm diseases) and treated primarily based on heat-clearing and detoxifying principles. The pseudobulbs of *Cremastra appendiculata*, one of the botanical sources of the traditional Chinese medicine Shancigu and traditionally used to clear heat and remove toxins, are a promising source of anti-dengue compounds. Through bioactivity-guided fractionation, six phytochemicals (**1-6**) were isolated and identified from *C. appendiculata*. Among them, the dihydrophenanthrene (**2**) displayed the most potent anti-DENV activity. This compound markedly inhibited DENV attachment to A549 cells without apparent cytotoxicity below 100 μM. Molecular docking and receptor knockdown assays verified that compound **2** specifically blocks viral entry by targeting the host receptor claudin-1. In vivo, compound **2** administration significantly reduced viral replication, viral protein expression, and brain viral loads in a DENV-infected C57BL/6 suckling mouse model, while mitigating virus-induced inflammation by downregulating *IL-1β* and *IL-18* mRNA levels. In conclusion, the *C. appendiculata*-derived dihydrophenanthrene (**2**) suppresses DENV entry via claudin-1 targeting and alleviates inflammation, representing a promising natural antiviral candidate.

Keywords

Keyword:

dengue virus, anti-DENV, Cremastra appendiculata, dihydrophenanthrene, claudin-1