2025中醫藥學術研討會

傳統中醫藥的新藥開發與現代化

2025 Symposium of Traditional Chinese Medicine: New Drug Development and Modernization of Traditional Chinese Medicine

Date: 18-19.04.2025

Programme Book

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香港科技大學中藥研發中心
Centre for Chinese Medicine R&D, HKUST

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2025 Symposium of Traditional Chinese Medicine: New Drug Development and Modernization of Traditional Chinese Medicine

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WELCOME MESSAGE

Dear distinguished guests and honored participants,

It is with great pleasure and honor that I welcome you all to the 2025 Symposium of Traditional Chinese Medicine (TCM). On behalf of the Organising Committee, I extend my warmest greetings and heartfelt gratitude to each of you for joining us today. This year, we are thrilled to have participation of more than one hundred and fifty friends from Hong Kong, Macau, Taiwan, Mainland China, Thailand, Vietnam, Uzbekistan and the USA.

Firstly, we would like to introduce a new journal to all of you, it is "*Science of Traditional Chinese Medicine* (STCM)". This journal was established in 2023, aims at reporting the latest scientific research of traditional Chinese medicine (TCM) and evidence-based medicine. The main columns are research articles, review articles, experts forum, guidelines & consensus, editorials, etc. STCM aims to become one of the most internationally influential academic journals in the field of TCM and integrative & complementary medicine. We encourage all of you can submit more research articles to the journal in order to help the journal to become one of the most internationally influential academic journals in the field.

We are pleased to receive over 80 abstracts and 30 oral presentations, published in the Programme Book, and thank all the Organising Committee Members from China Academy of Chinese Medical Sciences, University of Macau, The Chinese University of Hong Kong, The University of Hong Kong, Hong Kong Baptist University and The Hong Kong Polytechnic University. We would like to thank the Chinese Medicine Development Fund for the financial support, otherwise this meeting would not be possible.

Lastly, I wish you all have a wonderful time in Hong Kong.

Yours Truly,

Prof. Karl Wah-Keung TSIM
Chairman of the Organising Committee

ORGANISING COMMITTEE

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Day 1: Friday,18th April, 2025	
Time	**Event**
08:30 - 08:50	**Registration**
08:55 - 09:00	**Opening Remarks** **Karl Wah-Keung TSIM** *Centre for Chinese Medicine R&D, The Hong Kong University of Science and Technology*
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09:20 - 09:40	The physiological activities and mechanism of natural small molecular compounds isolated from TCM **Zhendan HE** *Shenzhen Technology University*
09:40 - 10:00	From tradition to innovation: sustainable cosmetics with Thai herbs **Nattaya LOURITH** *Mae Fah Luang University, Chiang Rai, Thailand*
10:00 - 10:20	Lipid-lowering effects of coffee *Arabica* pulp extract against non-communicable diseases: from bench back to communities **Chutima S. VADDHANAPHUTI** *Chiang Mai University, Thailand*
10:20 - 10:40	**TEA BREAK**
Chair: Zhendan HE & Yuan Shiun CHANG	
10:40 - 11:00	Opportunities and challenges in transforming natural products from Chinese medicine into nutraceuticals and new drugs **Simon Ming Yuen LEE** *The Hong Kong Polytechnic University*
11:00 - 11:20	Translation of TCM into FDA approved new drugs: current status and future perspectives **Jinhui DOU** *Zhimeng Biopharma*
11:20 - 11:40	Harmonizing computational and experimental approaches in evaluating bioactivities of essential oils in drug discovery and related fields **Hai PHAM-THE** *University of Science and Technology of Hanoi, Vietnam*

11:40 - 12:00	Quality control of TCM herbs and herbal preparations in Taiwan **Yuan Shiun CHANG** *China Medical University*
12:00 - 12:30	**Group Photo at Atrium**
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14:20 - 14:40	Glycosylflavones alleviate Alzheimer's disease related hallmarks **Qingxiao LI** *University of Hawaii at Manoa, USA*
14:40 - 15:00	Pharmacological elucidation of novel drug-leads for the treatment of Parkinson's disease through multiple targets **Rongbiao PI** *Sun Yat-Sen University*
15:00 - 15:20	The binding of fucose to VEGF enhances its suppressive efficiencies on inflammatory responses in lipopolysaccharide-induced mouse macrophages **Weihui HU** *South China Agricultural University*
15:20 - 15:40	Study on the mechanism and pharmacodynamic material basis of Pifujiedu Decoction in the treatment of atopic dermatitis **Yaxian ZHAN** *Guangzhou University of Chinese Medicine*
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16:00 - 16:20	M cell-mediated lymphatic route for Radix Astragali polysaccharide to initiate immune response **Quanbin HAN** *Hong Kong Baptist University*

16:20 - 16:40	Lycii Fructus and Chrysanthemum Flos, a Chinese medicine herbal pair, ameliorate retinal degeneration of mice induced by sodium iodate and protect Müller cells from oxidative stress **Yue ZHU** *Nanjing University of Chinese Medicine*
16:40 - 17:00	Comparative proteomic analysis of edible bird's nest from different origins **Geng LI** *Guangzhou University of Chinese Medicine*
17:00 - 17:20	AntiSMASH analysis of endophytic fungi *Alternaria* sp. **Farkhod ESHBOEV** *S.Yu. Yunusov Institute of the Chemistry of Plant Substances Academy of Sciences, Tashkent, Uzbekistan*
17:20 - 17:40	Beyond barriers: the mechanisms and functional potency of edible bird's nest peptides in crossing biological barriers **Jiaoyan REN** *South China University of Technology*
18:15 – 18:45	**Tea Party** Mount Tian and Cloud Dragon – Royal Tea Experience **Thi Quyen LAI** *Vietnam – ASEAN Culture and Economy Institute*
18:45 - 21:00	**Gala Dinner** Science of traditional Chinese medicine: an international exchange platform for traditional Chinese medicine **Shaoping LI** *University of Macau*

Day 2: Saturday, 19th April, 2025	
Chair: Daofeng CHEN & Xiuming CUI	
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09:20 - 09:40	Discovery and mechanism investigation on novel antihepatoma sesquiterpenoid dimers from the plants of *Artemisia* genus **Jijun CHEN** *Kunming Institute of Botany, Chinese Academy of Sciences*
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10:00 - 10:20	Mechanistic study on insulin sensitivity of a flavonoid-enriched fraction derived from *Cynomorium songaricum* **Jihang CHEN** *The Chinese University of Hong Kong*
10:20 - 10:40	Effect of different durations of Shawkea DE-T1 (Dandelion extract) administration on blastocyst obtained rate in women receiving IVF-ET treatment: a secondary analysis of a cohort study **Hui SHAO** *Society of Integrative Medicine and Reproduction of Japan, Japan*
10:40 - 11:00	**TEA BREAK**
Chair: Kuijun ZHAO & Sibao CHEN	
11:00 - 11:20	Development of supramolecular polymers with antitumor activity inducing cuproptosis through the use of shikonin, a natural naphthoquinone from the traditional Chinese herb—zicao **Sibao CHEN** *The Hong Kong Polytechnic University*
11:20 - 11:40	*Panax vietnamensis* saponins ameliorate non-alcoholic fatty liver disease by modulating lipid metabolism and inflammatory pathways **Yifan CHENG** *Kunming University of Science and Technology*
11:40 - 12:00	Antidepressant effects of Kai-Xin-San and its mechanism of regulating miR-1281 and its target genes ADCY1 and DVL1 **Ping LIU** *Medical Supplies Center of PLA General Hospital*

12:00 - 12:20	Study on the synergistic effect against T2DM of berberine 'separation - slow release' coupling system guided by nanostructure-controlled resorcinol-formaldehyde aerogel **Yong ZHU** *The Chinese University of Hong Kong, Shenzhen*
12:20 - 12:40	Interpretation for reversion of the Chinese Pharmacopoeia (2025 edition/Part I) **Hui CAO** *Jinan University*
12:40	**Closing Address** **Karl Wah-Keung TSIM** *Centre for Chinese Medicine R&D*, *The Hong Kong University of Science and Technology*

Science of Traditional Chinese Medicine: An international exchange platform for traditional Chinese medicine

Editorial Team of STCM

Abstract:

Under the administration of Institute of Chinese Materia Medica, China Academy of Chinese Medical Sciences, Science of Traditional Chinese Medicine (STCM) is a quarterly open access journal established in September 2023 and published by Wolters Kluwer. The journal is supported by the "Excellence Action Plan of 2022 China Science and Technology Journal-- High Starting Point New Journal Project".

Science of Traditional Chinese Medicine aims at reporting the latest scientific research of traditional Chinese medicine (TCM) and evidence-based medicine. The journal covers all areas of the TCM including chemistry, pharmacology, processing, preparation of Chinese materia medica (natural products) and clinical, evidence-based medicine research of TCM as well as the reports of botany, chemistry, pharmacology, pharmacy, engineering, clinical applications and socioeconomic related to TCM in China and around the world. The main columns are research articles, review articles, expert forum, guidelines & consensus, editorials, etc. It aims to become one of the most internationally influential academic journals in the field of TCM and integrative & complementary medicine.

The journal is indexed with, or included in, the following: Scopus, Chemical Abstracts Service (CAS), DOAJ, Ovid

Rare ginsenosides: a unique perspective of ginseng research

Zhengtao Wang, Lili Ding, Li Yang

Institute of Chinese Materia Medica, Shanghai University of Traditional Chinese Medicine, Shanghai, China

Abstract:

Rare ginsenosides refer to a group of triterpenoids that exist in low natural abundance in Panax plants, mostly produced by deglycosylation or side chain modification via physicochemical processing or metabolic transformation in gut. In addition, ginsenosides exhibit diverse and promising potent biological activities such as anti-aging, anti-tumor, cardiovascular and cerebrovascular protective, and ameliorating obesity and diabetes effects, comparing with the primary ginsenosides, which lead to a high concern in both the research and development of ginseng and ginsenoside-related pharma/nutraceutical products.

The presentation mainly introduces our recent studies dealing with the steaming and enzymatic triggered transformation, biosynthesis and chemical profiling, and pharmacological effects, especially the underling mechanisms on ameliorating diabetes and obesity mediated via the activation of the intestinal TGR5 – cAMP-GLP - 1 pathway of rare saponins from ginseng plants.

The physiological activities and mechanism of natural small molecular compounds isolated from TCM

Zhendan He, Xun Song, Dahong Yao, Zhu Qinchang

College of Pharmacy, Shenzhen Technology University, Shenzhen, Guangdong Province, China

Abstract:

Traditional Chinese medicine has important value in disease prevention and clinical treatment, and its natural small molecule compounds are the most material basis for the physiological activity of traditional Chinese medicine. The discovery of traditional Chinese medicine is a result of the Chinese nation's thousands of years of against diseases, discovered and excavated through their own clinical practice of disease treatments. More directly, traditional Chinese medicine is a clinical drug selected by humans using their own bodies and tissues as tools in nature. Therefore, traditional Chinese medicine is an indispensable and valuable resource for human clinical treatment. The current research on the physiological activity and mechanism of natural small molecule compounds in traditional Chinese medicine still has significant implications for the continuous and in depth development of new drug discovery and clinical innovative drug research.

From tradition to innovation: sustainable cosmetics with Thai herbs

Nattaya Lourith [1,2]

[1] *School of Cosmetic Science, Mae Fah Luang University, Chiang Rai 57100, Thailand*

[2] *Phytocosmetics and Cosmeceuticals Research Group, Mae Fah Luang University, Chiang Rai 57100, Thailand*

Abstract:

Traditional herbal remedies are vital for human wellness. Modernization of herbal formats is being harnessed for the FMCG industry, particularly in cosmetics. Consumers' expectations for cosmetics have recently evolved from mere cleaning to maintaining good skin and hair condition. The hallmarks of cosmetic quality are safety, stability, usability, and efficacy. The innovative transformation of herbal wisdom into phytocosmetics and cosmeceuticals validates qualified cosmetics. This talk illustrated how scientific innovation leads to the development of sustainable cosmetics with Thai herbs, within the context of biodiversity and the bio-circular economy.

Lipid-lowering effects of coffee *Arabica* pulp extract against non-communicable diseases: from bench back to communities

Chutima S. Vaddhanaphuti [1], Atcharaporn Ontawong [2], Oranit Boonphang [1], Supawan Buranapin [3], Piti Inthaphan [3], Kanjana Narkprasom [4], Doungporn Amonlerdpison [5,6], Acharaporn Duangjai [2], Manussaborn Phatsara [7], Jakkapong Inchai [1]

[1] Innovative Research Unit of Epithelial Transport and Regulation (iETR), Department of Physiology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand; [2] Division of Physiology, School of Medical Sciences, University of Phayao; Phayao, Thailand; [3] Section of Endocrinology and Metabolism, Department of Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand; [4] Faculty of Engineering and Agro-Industry, Maejo University, Chiang Mai, Thailand; [5] Center of Excellence in Agricultural Innovation for Graduate Entrepreneur and [6] Faculty of Fisheries Technology and Aquatic Resources, Maejo University, Chiang Mai, Thailand; [7] Department of Anatomy, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

Abstract:

Coffee pulp is a by-production from coffee berries during coffee processing. Major constituents in coffee pulp include chlorogenic acid, caffeine, and epicatechin. These compounds exhibit antibacterial, anti-inflammatory antioxidant, and lipid-lowering activities in *in vitro* and *in vivo* models. Our recent studies found that the extract of coffee *Arabica* pulp from coffee industrial waste contains high content of polyphenols, chlorogenic acid and epicatechin. It reduces cholesterol absorption, insulin resistance, fatty liver, improves type 2 diabetes mellitus, and prevents diabetic nephropathy in rats. With this knowledge asset, we further developed a novel coffogenic drink (CEP) product which contains high phenolic contents, has antioxidant activity, and reduces cholesterol absorption. After testing the product and placebo over 28,800 bottles in 79 hyperlipidemia-obese patients without diabetes for 6 months, the results showed that the plasma LDL-cholesterol, total cholesterol, and triglyceride levels were significantly decreased, and at the same time, HDL-C level profoundly increased. Moreover, HOMA index which reflects to insulin resistance was decreased corresponding to inflammation in CPE group and no serious adverse events (SAE) have been found. These series of the studies suggest that consuming CPE product could be an alternative supplement for both healthy and hyperlipidemia-obese patients to prevent the incidence of non-communicable diseases patients. Besides upcycling the usage of coffee waste for environmental conservation, it also provides opportunities for manufacturers to add healthy and economic values and widen customer targets in Thai coffee industry. Thailand's CPE product could serve as an example and a model for an alternative coffee industry at national and international levels.

Acknowledgement:

This work was supported by the Research and Researcher for Industry, Thailand Research Fund (PHD58I0010, RSA5980009), the Council of University Presidents of Thailand (15/2558), Thailand Science Research and Innovation (RDG6250025), and the Faculty of Medicine, Chiang Mai University (66/2560), Thailand.

Opportunities and challenges in transforming natural products from Chinese medicine into nutraceuticals and new drugs

Simon Ming-Yuen Lee [1,2]

[1] *State Key Laboratory of Chemical Biology and Drug Discovery, The Hong Kong Polytechnic University, Hong Kong*

[2] *Department of Food Science and Nutrition, The Hong Kong Polytechnic University, Hong Kong*

Abstract:

Cerebrovascular and neurodegenerative diseases are tightly associated with each other and are increasing harmful to our health. The global disease projection indicates that the healthcare burden derived from these disease problems will continue to rise. Many natural products including traditional Chinese medicines have been used to prevent and treat the multi-faceted diseases in different parts of the world. The traditional medical knowledge provides new insight into potential rich sources of new drug leads that may reveal previously unidentified mechanisms. Despite the discovery of a plethora of valuable natural products such as artemisinin, morphine, penicillin, and paclitaxel, the compounds that have been identified and utilized represent merely the tip of the iceberg compared to the vast, largely untapped reservoir of unknown natural resources. A lot of these natural products are present in low concentrations and/or exhibit high stereochemical structures; thus, they are difficult to be identified and synthesized. Here, we have developed new strategies, using bioinformatics, *in vivo* high-content screen and new drug delivery material, thereby harnessing recent technical advances to circumvent the barriers to identify bioactive compounds. Our recent successful discovery of new bioactive ingredients from Chinese medicine and marine organisms, which enriches the existing treasury of natural resources available to humanity and maximizes their potential therapeutic benefits, will be highlighted.

Translation of TCM into FDA approved new drugs: current status and future perspectives

Jinhui Dou

Shanghai Zhimeng Pharmaceutical Technology Co., Ltd., Pudong New Area, Shanghai, China

Abstract:

The integration of Traditional Chinese Medicines (TCMs) into the realm of FDA-approved pharmaceuticals represents a dynamic and evolving field, highlighted by the successful development of several compounds rooted in traditional TCM practices. Artemisinin, from Artemisia herbs, for the treatment for malaria and serves as a prime example of how TCM can inspire the development of novel chemical drugs based on traditional knowledge.

TCM products are widely available in the U.S. and globally as dietary supplements and herbal medicines, often perceived to offer health benefits and disease-modifying properties. Thus, study of TCM as botanical drugs is justified by both scientific and regulatory reasoning. Since the FDA finalized its Botanical Drug Development Guidance in 2004 (revised in 2016), several botanical-derived products have gained marketing approval:

- Veregen™: A topical ointment containing sinecatechins extracted from green tea.
- Mytesi™: An oral solution derived from crofelemer, sourced from the sap of the Croton lechleri tree.
- NexoBrid™: A topical gel containing bromelain, an enzyme extracted from pineapple stems (approved under a Biologics License Application, BLA).
- Filsuvez™: A gel-based treatment containing birch bark triterpenes, used for Epidermolysis Bullosa.

These above approvals of single-herb extracts further demonstrate the potential for TCMs to be developed into FDA-approved drugs. Smoflipid®, one of Total Parenteral Nutrition (TPN) products, contain mixed lipid emulsion containing soybean oil, medium-chain triglycerides (MCTs), olive oil, and fish oil, could be considered as an example of human drug from complex botanical (and animal) combinations. Notably, approximately one-third of Investigational New Drug (IND) applications submitted to the FDA involve herbal medicine combinations targeting various indications, including oncology, cardiovascular health, and gastrointestinal disorders, among many others.

Harmonizing computational and experimental approaches in evaluating bioactivities of essential oils in drug discovery and related fields

Hai Pham-The

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Abstract:

Essential oils (EOs) have garnered significant attention for their wide range of bioactivities, making them crucial in both pharmaceutical and agricultural applications. Their potent therapeutic properties, such as antimicrobial, anti-inflammatory, antioxidant, and anticancer effects, as well as their role in promoting plant growth and protecting crops from pests, position them as viable natural alternatives to synthetic chemicals. To date, harmonizing computational and experimental (*in silico-in vitro*) approaches have become a very popular workflow for studying EO's bioactivities. This workflow allows facilitation, expedite and streamline drug discovery and development. This work delves into the workflow of *in silico-in vitro* approaches currently used, highlighting several case studies where EOs have shown promise in specific therapeutic areas. Examples include the anti-inflammatory effects of certain EOs in managing chronic diseases, their antioxidant properties in combating oxidative stress, their potential role in diabetes management, and their ability to combat antibacterial resistance. These case studies underscore the importance of harmonizing theoretical and experimental approaches to fully unlock the potential of EOs in both pharmaceutical and agricultural contexts. In conclusion, this session aims to foster a deeper understanding of the power of EOs, presenting a comprehensive framework for their evaluation and application in modern science.

Quality control of TCM herbs and herbal preparations in Taiwan

Yuan Shiun Chang [2] and Yu Ling Ho [1]

[1] *Department of Nursing, Hungkuang University, Taichung 433, Taiwan*

[2] *Department of Chinese Pharmaceutical Sciences and Chinese Medicine Resources, College of Chinese Medicine, China Medical University, Taichung 404, Taiwan*

Abstract:

Traditional Chinese Medicine has been very popular in Taiwan in the past. TCM was incorporated in the National Insurance since 1995. Currently, TCM only accounts for less than 4% of total National Health Insurance annual budget. By September 2006, all herbal pharmaceutical companies in Taiwan were upgraded to GMP standard. Currently there are 80 GMP herbal pharmaceutical companies in Taiwan and are moving toward CGMP standard. Taiwan Herbal Pharmacopeia IV (THP) sets the quality standard of TCM herbs and herbal preparations in Taiwan.

In this paper, the compilation of Taiwan Herbal Pharmacopeia (THP) (II, III, IV), English version of THP (II, III, IV), Color Illustrations of THP, Illustrations of Commonly Misused Chinese Crude Drug Species in Taiwan, etc., will be covered. The method development of microscopic identification, TLC and HPLC will be introduced. The safety limit of sulfur dioxide residue, heavy metal contents, Organochlorine pesticides residues and aflatoxins in the herbs and herbal preparations will also be discussed.

The regulations and quality control practice of Chinese medicine in Taiwan will also be introduced including the application of herbal preparation licenses. The authors also like to share some of the works they did in the Hong Kong Chinese Materia Medica Standard Project since 2011. The work in USP Herbal Medicine Compendium, East Asia Expert Panel, USP Botanical Dietary Supplements and Herbal Medicine Expert Committee and EDQM TCM Working Party, European Pharmacopeia will also be shared.

Rhynchophylline alleviates cognitive deficits in a transgenic mouse model of Alzheimer's disease via modulating the neuropathology and gut microbiota

Zhi-Xiu Lin, Lisa Xian

School of Chinese Medicine, The Chinese University of Hong Kong

Abstract:

Rhynchophylline (RN), the major alkaloid of *Uncaria rhynchophylla*, has shown potent anti-Alzheimer's disease (AD) effects. In this study used the 5×FAD transgenic mouse model of AD to explore the anti-AD effects of RN. Behavioral tests such as Morris water maze test (MWMT), Open field test (OFT) and Novel object recognition test (NORT) were used to determine the neuroprotective effects of RN. Meanwhile, BV2 cells were employed to further evaluate the biological effects of RN. The results indicated that RN treatment improved cognitive functions by reducing anxiety-like behaviors, enhancing recognition ability, and ameliorating learning impairments. It modulated Aβ processing by reducing enzyme activity involved in Aβ production and enhancing degradation enzyme activities, thereby diminishing Aβ accumulation. RN also decreased the hyperphosphorylated of tau protein. Additionally, RN diminished neuroinflammation by reducing the activation of microglia and astrocyte and inhibiting the inflammatory cytokine release. RN could inhibit the activation of HDAC2/AMPK signaling pathway. Moreover, RN treatment restored the gut microbiota dysbiosis of 5×FAD mice. Knockdown of HDAC2 enhanced the anti-inflammatory effects of RN. All these findings highlight the good potential of RN used as an anti-AD agent and enhances the scientific foundation for its clinical use in treating AD.

Glycosylflavones alleviate Alzheimer's disease related hallmarks

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[2] *Hawaii Pacific Neuroscience, 2230 Liliha Street, Honolulu, Hawaii 96817, United States*

Abstract:

Alzheimer's disease (AD) is the most common brain disorder that cannot be prevented, cured or even slowed. Hyperphosphorylation of tau proteins in neurons plays a pivotal role in AD pathology. Glycogen synthase kinase-3β (GSK3β) is a key enzyme catalyzing hyperphosphorylation of tau protein. Selective inhibition of GSK3β is a promising therapeutic strategy for AD treatment. Glycosylflavones such as isoorientin selectively inhibit GSK3β via a substrate competitive mode. Semi-synthesis of isoorientin has led greater than 300-fold potency improvement. Structure-activity relationship analyses of the inhibitors suggest involvement of hydrophobic, π-cation and orthogonal multipolar interactions for the GSK-3β inhibition and selectivity. Several cellular and animal model studies of isoorientin and its synthetic analogues were conducted. The cells included amyloid-induced human SH SY5Y cells, macrophages, rat pheochromocytoma PC12 cells, and lipopolysaccharide-activated microglial cells, while animal models included APP/PS1 model mice, endotoxemia mice, and scopolamine-induced AD model mice. More than two dozen AD related markers showed significant alleviations on amyloid depositions, tau-tangles, synaptic dysfunction, spatial memory deficits, inflammation, neuroinflammation, and oral and gut microbiota dysbiosis. The new inhibitors are valuable chemical probes and drug leads with therapeutic potential to tackle AD and other GSK3β relevant diseases.

Pharmacological elucidation of novel drug-leads for the treatment of Parkinson's disease through multiple targets

Rongbiao Pi [2], Haobai Liu [1, 2], Chungpang Su [1,3], Huan Zhang [3], Shinghung Mak [1]

[1] *Department of Food and Health Sciences, Technological and Higher Education Institute of Hong Kong, Hong Kong SAR, China*

[2] *School of Medicine, Sun Yat-sen University, International Joint Laboratory (SYSU-PolyU HK) of Novel Antidementia Drugs of Guangdong Province, Shenzhen, China*

[3] *Department of Food Science and Nutrition, Hong Kong Polytechnic University. Hong Kong SAR, China*

Abstract:

Parkinson's disease (PD) is the second most common neurodegenerative disorder worldwide. PD might cause the dysfunctions of motor neuron in patients. Although the causes of PD still remain to be elucidated, multifactorial pathogenesis have been suggested. Currently available single-targeted drugs only provide symptoms-relieving benefits, but not delay or reverse the progress of PD. Thus, the "one-compound-multi-target ligands" strategy might be a promising strategy for the development of new drug for PD.

Recent studies have also demonstrated that glycogen synthase kinase-3β (GSK3β)/ myocyte enhancer factor 2D (MEF2D) and monoamine oxidase-B (MAO-B) might be important therapeutic targets for treating PD. Here, by using a sequential combination of ligand and structure-based virtual screening techniques, as well as molecular docking analysis, we designed and synthesized a series of hybrids as the multifunctional candidates, targeting MEF2D, GSK3β and/or MAO-B. Encouragingly, some of these candidates have exhibited with reasonable pharmacokinetic properties with low cytotoxicity. Particularly, two of these novel hybrids, hybriding indolin-2-one core (pharmacophore of 3-substituted-2-indolin-ones compounds, MEF2 enhancer) and the propargyl (moiety of the irreversible MAO-B inhibitor, rasagiline) have shown promising inhibitory effects on GSK3β and MAO-B, respectively. Moreover, several of these compounds significantly inhibit over-expression of alpha-synuclein in iPC12-A53Tcells. These multi-functional compounds might be the candidates for the development of new generation of anti-PD leads via synergistically acting on multiple targets.

Acknowledgement:

This work was supported by the research grants from the Research Grants Council of Hong Kong (UGC/FDS25/M03/22).

The binding of fucose to VEGF enhances its suppressive efficiencies on inflammatory responses in lipopolysaccharide-induced mouse macrophages

Weihui Hu [1,2,3], Dasen Li [1], Yang Liu [1], Yuhuan Qiu [1,2], Guoxia Guo [1], Qiwei Qin [1,2,3]

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[2] Nansha-South China Agricultural University Fishery Research Institute, Guangzhou 511464, China

[3] Joint Laboratory of Guangdong Province and Hong Kong Region on Marine Bioresource Conservation and Exploitation, College of Marine Sciences, South China Agricultural University, Guangzhou, China

Abstract:

VEGFR3 and VEGF-C, the ligand of VEGFR3, are well-known for their suppressive effects in the secretion of cytokines with pro-inflammatory properties. Molecular docking and immune-precipitation experiments revealed the binding activities between VEGF-C and fucose, a natural compound. Based on endothelial cell and LPS-induced macrophage model, western blotting analysis, luciferase and qRT-PCR assays were conducted to reveal the enhancing activities of fucose in VEGF-C-induced activations of related proteins and genes. Enzyme-linked immunosorbent assay (ELISA) was performed to determine the released of cytokines possessing effects of promoting inflammation in macrophages induced by LPS. Immunofluorescent analysis was conducted to explore the activities of fucose in the regulation of NF-κB p65 subunit nuclear translocation based on the VEGF-C-induced macrophages. Furthermore, the cell invasive experiment was employed to measure the migratory motility in the cell level. We identified that fucose, a monosaccharide commonly found in edible plant glycans, was proved to exert effects on LPS-induced macrophages by supressing a serial of inflammatory responses, and the suppression was attributed to its binding interaction with VEGF-C. The combination of fucose and VEGF-C demonstrated great potentials in triggering the activation of related receptor. In LPS-induced macrophages, the application of fucose promoted suppressive activities of exogenous VEGF-C application in terms of the expressions of cyclooxygenase-2 (COX-2) and nitric oxide synthase (iNOS), as well as the secretions of pro-inflammatory cytokines, i.e. IL-6 and TNF-α. This suppression was consistent with the NF-κB transcription and its translocation. Furthermore, the interactions of fucose binding with VEGF-C inhibited the migratory ability in LPS-induced macrophages. Our investigations supported the pharmacological effects of fucose in VEGF-C-triggered anti-inflammatory activities**.**

Acknowledgement:

This work is supported by the National Natural Science Foundation of China (42306101), Guangzhou Science and Technology Plan Project (2024A04J4247), Guangdong Natural Science Foundation of China (2023A1515011859) and Science Found of Nansha-South China Agricultural University Fishery Research Institute (NSYYKY202304).

Study on the mechanism and pharmacodynamic material basis of Pifujiedu Decoction in the treatment of atopic dermatitis

Ya-Xian Zhan, Hao-En He, Ying-Qi Huang, You-Chen Liu

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Abstract:

Pifujiedu Decoction (PFJD) is a clinical experience prescription of Professor Guowei Xuan, a master of traditional Chinese medicine. It is composed of Mume Fructus, Curcumae Rhizoma, Arnebiae Radix and other traditional Chinese medicines. It is effective in the clinical treatment of atopic dermatitis (AD), but its mechanism of action has not been clarified. In order to investigate the therapeutic mechanism of PFJD, the acute AD model induced by DNCB was constructed in this study, and the skin macroscopic evaluation, histopathological evaluation, skin barrier repair evaluation, immune inflammation related factors detection and classical pathway exploration were carried out. The results showed that oral administration and external application of PFJD could significantly reduce AD symptoms, inhibit epidermal thickening, reduce transcutaneous water loss and skin erythema. At the same time, it could reduce the increase of serum IgE level, decrease skin inflammatory indicators such as IL-4, TNF-α, inhibit the reduction of the expression level of skin barrier protective proteins such as occludin, claudin-1, and reduce the expression of p38 and phosphorylated p38 proteins. In order to investigate the material basis of anti-AD effect of PFJD, we analyzed the skin tissues after oral administration and external application of the drug by Q-TOF MS. By comparing the chemical components in skin tissues, we found that there were 40 common components within PFJD. We speculated that these components may be the main components of PFJD against AD. In the future work, we will further verify the role of these components as potential treatment of AD.

Acknowledgement:

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M cell-mediated lymphatic route for Radix Astragali polysaccharide to initiate immune response

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Abstract:

The gut wall acts as a barrier to large molecules, making it difficult for developing orally-delivered macromolecular therapeutics. Some polysaccharides can quickly affect the immune system after oral dosing, but the mechanisms underlying these effects remain elusive.

The mystery of how orally administered polysaccharides exert their therapeutic effects has been a long-standing challenge. Recently, we revealed a unique lymphatic route for Radix Astragali (Huang Qi) polysaccharides (RAP), offering novel implications for immune-boosting therapies. We first demonstrated the immune-dependent antitumor activity of RAP *in vivo*, where RAP's effects were abolished in immunodeficient nude mice. Importantly, we found that RAP remains intact in the small intestine and quickly enters Peyer's patches (PPs). Within the PP, RAP selectively targets follicle dendritic cells (FDCs), key antigen-presenting cells that orchestrate immune responses. This targeted interaction triggers a cascade of immune activation. This discovery illuminates a unique lymphatic route through which RAP can directly contact immune cells. These findings not only bridge the gap between *in vitro* and *in vivo* studies of RAP but also propose a potential mechanism that is applicable to a broader range of bioactive polysaccharides.

The remarkable selectivity of RAP for PPs led to investigations into the underlying cellular mechanisms. PPs possess specialized microfold cells (M cells) known for their ability to transport antigens and pathogens from the gut to the underlying lymphoid tissue. Evidence now points to M cells as the key facilitators of RAP's entry into PPs. Efficient transport of RAP was confirmed by using an *in vitro* M cell model. In addition, *in vivo* studies further revealed clear co-localization of RAP with M cells within PPs. Critically, these findings have been translated to human intestinal samples, revealing the M-cell-mediated uptake in humans and reinforcing the clinical relevance of this discovery. M cells appeared to be essential gatekeepers, granting RAP access to PPs and driving its immunomodulatory and antitumor effects.

This breakthrough discovery unveiled the intricate mechanism by which orally administered RAP interacted with the immune system, paving the way for the development of next-generation oral polysaccharide-based therapeutics and vaccines.

Lycii Fructus and Chrysanthemum Flos, a Chinese medicine herbal pair, ameliorates retinal degeneration of mice induced by sodium iodate and protects Müller cells from oxidative stress

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Abstract:

This study focused on the Lycii Fructus (lf) and *Chrysanthemum* flos (cf) herbal pair used in treating age-related macular degeneration (AMD). A dry AMD mouse model was established by intraperitoneal sodium iodate injection. The LF-CF extracts prepared with various solvents were tested. Results showed that the aqueous and 70% ethanol extracts had the best protective effects on the mouse retina against oxidative damage, maintaining its structure and inhibiting apoptosis. These two extracts also exhibited antioxidant activity, reversed the down - regulation of glutamine synthetase. In vitro, they protected MIO - M1 cells from oxidative stress via caspase - dependent and Nrf2/HO-1 signaling pathways. The active ingredients might be *Lycium barbarum* polysaccharides and luteolin. in conclusion, the lf - cf herbal pair can mitigate retinal oxidative stress and suppress Müller cell apoptosis, suggesting its potential for dry amd treatment or prevention.

Acknowledgement: This study was supported by the Key Projects of Regional Joint Fund of National Natural Science Foundation of China (U21A20408); Major Programs of Natural Science Research in Universities of Jiangsu Province (22KJA360008); Jiangsu Collaborative Innovation Centre of Chinese Medicinal Resources Industrialization (ZDXM-2020-03); Key R&D Program of Ningxia Hui Autonomous Region (2021BEF01003, 2021BEF02012, 2021BEF02009, 2021BEF02010); Special scientific research project of the "Leading Plan" for the first-class discipline of traditional Chinese medicine at Nanjing University of Traditional Chinese Medicine (ZYXYL2024-015).

Comparative proteomic analysis of edible bird's nest from different origins

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Abstract:

Edible bird's nest (EBN) mainly made of saliva that secreted by a variety of swiftlets is a kind of precious traditional Chinese medicine. EBNs from different biological and geographical origins exhibit varieties in morphology, material composition, nutritive value and commercial value. Here, we collected four different EBN samples from Huaiji, China (Grass EBN), Nha Trang, Vietnam (Imperial EBN) and East Kalimantan, Indonesia (White EBN and Feather EBN) respectively, and applied label-free quantitative MS-based proteomics technique to identify its protein composition. First, phylogenetic analysis was performed based on cytb gene to identify its biological origin. Second, a total of 37 proteins of EBNs were identified, among which there were six common proteins that detected in all samples and exhibited relatively higher content. Gene ontology analysis revealed the possible function of EBN proteins, and principal component analysis and hierarchical clustering analysis based on 37 proteins were performed to compare the difference of various EBNs. In summary, our study deciphered the common and characteristic protein components of EBNs of different origins and described their possible functions by GO enrichment analysis, which helps to establish an objective and reliable quality evaluation system.

AntiSMASH analysis of endophytic fungi *Alternaria* sp.

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Abstract:

Natural compounds derived from endophytes showcase a wide range of biological activities, including antimicrobial, antitumor, antioxidant, and immunomodulatory effects. This makes them promising sources for creating new pharmaceuticals, agrochemicals, and other bioactive substances. Genome mining strategies provide fresh perspectives for discovering novel endophyte-derived compounds, serving as an alternative to traditional bioactivity-guided screening methods. One effective approach for examining the gene clusters in endophytic microorganisms is the "antibiotics and secondary metabolite analysis shell" (antiSMASH). This tool utilizes a combination of computational algorithms and databases to analyze microbial genomes and predict the gene clusters involved in secondary metabolite biosynthesis. Secondary metabolites of *Alternaria* sp. have shown strong antibacterial activities against Gram-positive (*S. aureus* and *B. subtilis*) and Gram-negative (*E. coli*, and *P. aeruginosa*) bacteria. The antiSMASH analysis has identified 43 biosynthetic gene clusters (BGCs), including 15 Non-Ribosomal Peptide Synthetases (NRPSs), 15 Type I Polyketide Synthases (T1PKSs), 6 Terpene BGCs, and 7 NRPS-like proteins in the genome of *Alternaria* sp. Three BGC regions 22.1, 125.1 and 139.1 showed 100% similarity with the T1PKS BGCs pyranonigrin E, melanin and (-)-melanin respectively. BGCs encoded in the genome of the *Alternaria* sp. suggested that this species was likely able to produce a large number of secondary metabolites.

Beyond barriers: the mechanisms and functional potency of edible bird's nest peptides in crossing biological barriers

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Abstract:

Exploring the modern science behind the traditional tonic bird's nest reveals that its protein hydrolysate (EBNP) harbors bioactive peptides with incredible skin healing potential. Remarkably, fluorescence labeling and bioimaging techniques confirmed the bio-barrier-penetrating capacity of different hydrophilic and hydrophobic bird's nest peptides, with specific peptide segments successfully crossing and exerting peculiar effects. The skin transport and absorption capacity of EBNP peptides was explored via molecular docking techniques, revealing a strong binding affinity between the hydrophobic EBNP tripeptides and PepT1. These peptides, characterized by their high homogeneity, low molecular weight, and predominantly α-helical structure, exhibit exceptional moisture retention and filaggrin synthesis. EBNP protect against UVB-induced DNA damage in HaCaT keratinocytes via significant enhancement in cell migration and proliferation. In *in vivo* validation studies, EBNP outperformed both sialic acid and glutathione in skin repair, achieving an impressive 86.77% wound healing rate and a 30.33% dermal collagen proportion in just 8 days. These groundbreaking findings open up an exciting new chapter for the application of bird's nest and its derivatives in skin care and wound healing.

Acknowledgement:

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Beneficial effects and immunomodulation mechanisms of anticomplement agents from traditional Chinese medicines for the treatment of pulmonary infections

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Abstract:

The inappropriate activation of complement system may cause some life-threatening symptoms including acute respiratory distress syndrome (ARDS). In order to demonstrate the effective constituents and action mechanisms of traditional Chinese medicines (TCMs) with function of heat-clearing and detoxification for the treatment of pulmonary infections, bioactivity-guided fractionation and isolation was thus performed with some commonly used TCMs and led to the isolation and characterization of some valuable anticomplement agents with medical properties on the acute lung injury (ALI).

The polysaccharides obtained from *Houttuynia cordata* (HCP) showed anti-complementary and attenuated the lipopolysaccharide-induced ALI in mice and rats. The interesting finding is that oral administration of HCP led to protective effect on mice infected by influenza A virus (H1N1), although it had no in vitro antiviral activity. The underlying mechanism is closely related to regulating the Th17/Treg balance in gut-lung axis. The flavonoids obtained from *Houttuynia cordata* showed antiviral activity against influenza virus *in vitro* and exerted synergistic protective effects on the mice with virus infection in combination with HCP. The flavonoids enriched from Scutellaria Baicalensis showed beneficial effects on the H1N1-induced ALI in mice as well, with their *in vivo* metabolic activation by gut microbiota.

The polysaccharides and flavonoids from *Houttuynia cordata* could respectively alleviate the severe pneumonia in mice co-infected with virus H1N1 and drug resistant bacteria MRSA, based on their immunomodulating effects. The synergistic protective effects were observed as well.

The polysaccharides and flavonoids from TCMs are valuable anticomplement agents for prevention and treatment of the complement-associated diseases, such as ARDS, severe acute respiratory syndrome (SARS), influenza and COVID-19.

Acknowledgement:

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Discovery and mechanism investigation on novel antihepatoma sesquiterpenoid dimers from the plants of *Artemisia* genus

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Abstract:

Hepatocellular carcinoma (HCC) is a highly lethal tumor in the world. The main drugs currently available for the treatment of HCC are multikinase inhibitors and immune checkpoint inhibitors, which demonstrated significant therapeutic efficacy, but the limitation in number and the similarity in chemical structures and targets of current drugs led to drug resistance and seriously reduced their effectiveness. *Artemisia* plants are widely distributed worldwide and are rich in sesquiterpenoid dimers (SDs) with diverse structures and remarkable antihepatoma activities. Systematic studies on anti-HCC and anti-liver fibrosis activity of *Artemisia* plants were conducted. A total of 220 new SDs involving more than 30 structural types had been isolated from 18 species of *Artemisia* genus, which accounted for 70% of the total number of SDs reported in *Artemisia* genus worldwide. Particularly, 40 novel SDs attributed to 11 structural types were isolated and identified from *A. eriopoda*, representing the richest number and structural types of SDs found in a single plant. We had accomplished the synthesis of four guaianolide dimers from naturally abundant arglabin, and 4 types of natural product-like heterodimers with novel skeletons were also synthesized. The structure-activity relationship of four compounds was studied to give 152 derivatives. Pharmacological study verified that 11 compounds, including artemeriopodin G7, KGA-1002 and KGA-6006 could inhibit cell migration and invasion, induce cell apoptosis, block the cell cycle in different phases. Bioinformatic analysis and biological experiments revealed that artemeriopodin G7 exerted antihepatoma activity by targeting PDGFRA to regulate AKT/STAT signaling pathway. KGA-1002 had significant *in vivo* efficiency with good pharmacokinetic properties, low toxicity. Its prodrug had the highest distribution level in the liver, making it a good candidate for drug development. More than 40 related research papers have been published in journals such as Signal Transduction and Targeted Therapy (2023), Acta Pharmaceutica Sinica B (2021), Phytomedicine (2023), and Chinese Journal of Chemical Physics (2024, 2023, 2022), and more than 20 invention patents had been applied.

Acknowledgement:

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Ophiopogon polysaccharides improve gut and lung injury in ulcerative colitis mice by regulating the epithelial barrier

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Abstract:

The incidence of ulcerative colitis (UC) has been continuously rising, and the lung injury complications it causes have garnered significant attention. Polysaccharides have emerged as ideal agents for the treatment of UC-related gut and lung injuries due to their therapeutic potential. This study investigated the preventive effects of *Ophiopogon japonicus* polysaccharide (OJP-W1) on gut and lung injury in UC mice and its underlying mechanisms. As compared to the UC model group, OJP-W1 treatment significantly decreased the disease activity index, increased colon length, alleviated pulmonary edema, improved intestinal and pulmonary pathological damage, and reduced the levels of pro-inflammatory cytokines (IL-1β, IL-6, TNF-α) in intestinal and pulmonary tissues. Furthermore, OJP-W1 repaired the gut-lung epithelial barrier by upregulating the expression of tight junction proteins (ZO-1, Claudin-1), thereby reducing the accumulation of endotoxins in serum and lungs. Simultaneously, OJP-W1 modulated the gut microbiota and its metabolic product short-chain fatty acids, increasing the abundance of beneficial bacteria (such as Bifidobacterium, Akkermansia, Faecalibaculum) and butyrate content. This study demonstrated that OJP-W1 has a significant protective effect on gut and lung injury in UC mice, and its mechanism may be closely related to the repair of the epithelial barrier and the regulation of gut microbiota.

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Mechanistic study on insulin sensitivity of a flavonoid-enriched fraction derived from *Cynomorium songaricum*

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Abstract:

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by elevated blood glucose levels, posing a significant global health concern due to its increasing prevalence. Insulin resistance (IR) plays a major role in the development of T2DM and is often linked to factors such as obesity, physical inactivity, and a sedentary lifestyle. *Cynomorium songaricum Rupr*., an edible parasitic plant, has shown promising antidiabetic effects. This study aimed to investigate the application of a *Cynomorium songaricum* flavonoid-enriched fraction (CSF) in the treatment of IR in T2DM, along with elucidating the chemical and biochemical mechanisms involved. Firstly, the UHPLC/ESI-LTQ-Orbitrap-MS analysis was used to identify a total of thirty-six flavonoids derived from CSF. Moreover, CSF was shown to significantly improve glycogen synthesis and glucose consumption as well as inhibit gluconeogenesis in HepG2 cells of IR. An innovative network pharmacology analysis unveiled key hub genes—*AKT1* and *PI3K*—integral to metabolic syndrome-related signaling pathways, which contributed to the favorable impact of CSF against IR. In addition, active ingredients including quercetin, ellagic acid and naringenin were identified as potential contributors to these effects. The results of western blot and qPCR assays provided compelling evidence that CSF improved insulin sensitivity by modulating the PI3K-Akt signaling pathway. Subsequent RNA-sequencing analysis, in tandem with western blot assays, delved deeper into the potential mechanisms underlying CSF's advantageous effects against IR, potentially associated with the enhancement of endoplasmic reticulum (ER) proteostasis.

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Effect of different durations of shawkea DE-T1 (Dandelion extract) administration on blastocyst obtained rate in women receiving IVF-ET treatment: a secondary analysis of a cohort study

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Abstract:

Objective: To explore the appropriate duration of Shawkea DE-T1（Dandelion extract）use, and to provide a basis for the optimization of the Shawkea DE-T1（Dandelion extract）administration duration within females. **Methods**: Based on a previous retrospective cohort study, 1,014 patients aged ⩾30 years who used in vitro fertilization (IVF) for conception at Hanabusa Women's Clinic, Kobe, Japan, were included in this secondary analysis and were allocated to an Shawkea DE-T1（Dandelion extract）-administration group (n = 712) and a control group (n = 302) based on their use of Shawkea DE-T1（Dandelion extract）. All patients in the two groups received interventions following the guidelines of the Japanese Institution for Standardizing Assisted Reproductive Technology Intervention, and patients in the administration group were provided Shawkea DE-T1（Dandelion extract） as recommended by the Nutritional Supplement Support Center of Hanabusa Womens Clinic. The blastocyst obtained rate (percentage of patients who produced at least one blastocyst upon in vitro embryo culture relative to all patients in the same group) was compared between the two groups of patients following treatment durations of 1–3 months, 4–6 months, and >6 months. Analysis was performed on the actual duration of Shawkea DE-T1（Dandelion extract）administration for all patients who achieved blastocyst in vitro according to their age level (⩾30 and <35 years of age; ⩾35 and <40 years; ⩾40 and <43 years; and ⩾43 years of age). **Results**: After a Shawkea DE-T1（Dandelion extract） administration of 1–3 months or 4–6 months, the blastocyst rates in the administration group were significantly higher than those of the control group (83.27% vs. 55.31% for 1–3 months, $P = 1.02\times10-10$; 69.44% vs. 44.44% for 4–6 months, $P = 4.70\times10-4$), while no significant difference was observed between the two groups with >6 months of administration (73.35% vs. 72.46%, P = 0.76). Analysis of the treatment duration of patients at different age levels who produced blastocysts showed that the treatment duration was dependent on patient age: i.e., 65.25% of women ⩾30 and <35 years of age achieved blastocyst after a Shawkea DE-T1（Dandelion extract）administration of 1–3 months; while only 19.75% of women ⩾43 years of age successfully achieved in vitro development of embryos to blastocyst stage with a Shawkea DE-T1 administration of 1–3 months. **Conclusion**: Shawkea DE-T1（Dandelion extract） use for 1–3 months and 3–6 months significantly improved the blastocyst rate in women receiving IVF treatment. Appropriate extension of Shawkea DE-T1 （Dandelion extract）administration duration also achieved a better effect among women with advanced reproductive age.

Development of supramolecular polymers with antitumor activity inducing cuproptosis through the use of shikonin, a natural naphthoquinone from the traditional Chinese herb—zicao

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Abstract:

Shikonin, a natural naphthoquinone derived from the traditional Chinese herb--Zicao, has been known to demonstrate significant antitumor activity. However, the clinical application of such a phytochemical has been relatively limited due to its poor stability and low bioavailability. To overcome these challenges, supramolecular polymers driven by metal-ligand coordination have appeared as one of the most promising strategies. Shikonin contains two phenolic hydroxyl groups and two ketonic carbonyl groups in its naphthoquinone moiety, and this provides natural chelating sites for associating with metal ions. The metal coordination is able to further facilitate the self-assembly of metal-phenol-keto structures, and potentially enhance both the stability and bioavailability of Shikonin. In light of this concept, we have developed a type of supramolecular polymers--SHICU, which composed of both Shikonin ligand and Cu(II) ion. SHICU exhibited significant antitumor activity across several tumor cell lines, demonstrating its potential as an effective therapeutic agent. Notably, upon reduction by intracellular glutathione (GSH), SHICU dissociated to release Shikonin, Cu(II), and SHICU fragments, of which the released Shikonin and Cu(II) could synergistically induce reactive oxygen species (ROS)-dependent necrosis, while the SHICU fragments, which retained their structural integrity, triggered a distinct form of cell death that was known as cuproptosis in tumor cells. This dual functionality, combining ROS-dependent necrosis and cuproptosis, suggested the potential of SHICU in advancing antitumor therapies, while the integration of supramolecular polymers with the emerging cell death mechanism of cuproptosis facilitated the development of innovative cancer drugs.

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Panax vietnamensis saponins ameliorate non-alcoholic fatty liver disease by modulating lipid metabolism and inflammatory pathways

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Abstract:

Panax vietnamensis saponins (PVS) have been reported to exhibit significant hepatoprotective properties; however, their therapeutic efficacy for non-alcoholic fatty liver disease (NAFLD) remains unknown. In this study, we utilised a high-fat diet-induced NAFLD mouse model to investigate the effects and mechanisms of PVS on NAFLD. PVS reduced lipid accumulation and liver function marker levels in NAFLD mice. According to haematoxylin and eosin and oil red O staining, PVS reduced hepatocyte degeneration and hepatic lipid accumulation. Moreover, PVS effectively reversed NAFLD-associated abnormal changes in 24 lipid subclass levels, including palmitic acid, sterol esters as well as hexosylceramide, enhanced hepatic fatty acid oxidation capacity, alleviated liver inflammation, and mitigated lipid metabolic disorders. Additionally, PVS significantly upregulated Cyp4a10 and Cyp4a14 expression, which further activated the peroxisome proliferator-activated receptor signalling pathway for regulating lipid metabolism. PVS also regulated the abnormally high expression of genes in the MAPK signalling pathway and Toll-like receptor 4/Tirap/nuclear factor-κB axis. Thus, PVS was believed to attenuate the inflammatory response in NAFLD by inhibiting this signalling pathway. In parallel, we conducted weighted gene co-expression network analysis and identified 12 hub genes that were affected by PVS, which resulted in fatty acid degradation, steroid hormone biosynthesis and inhibiting pathways associated with diabetic cardiomyopathy and NAFLD. This study served as evidence to support the use of PVS in treating NAFLD.

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Antidepressant effects of Kai-Xin-San and its mechanism of regulating miR-1281 and its target genes ADCY1 and DVL1

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Abstract:

Kai-Xin-San (KXS) is an herbal formula used to treat the diseases, such as insomnia, amnesia, emotional disorders in ancient China. It has been demonstrated to be active in various animal models resembling human depression with multitarget effects. However, effective verification on the clinical application of KXS is still lacking. And recent studies indicated that miRNAs were involved in the pathophysiology of depression. However, there have been few studies on the mechanism underlying the miRNAs directly mediating antidepressant in nature drugs and TCM compound. In this study, we evaluated the efficacy and tolerability of KXS, compared with fluoxetine (FLX), in patients with mild to moderate depressive disorder, and identified circulating miRNAs defferentially expressed among the depression patients (DPs), DPs who underwent 8weeks of KXS treatment and health controls (HCs). Patients in KXS group showed a statistically significant improvement in HAM-D17 score and self-rating depression scale (SDS) score, but not in N-back total respond time. In addition, no significant difference at 8 weeks of treatment was found between KXS and FLX groups in SDS score and N-back respond time as well as reduction of HAM-D17 score. A total of 45 miRNAs were significantly differentially expressed among DPs, HCs and KXS groups, among them, miR-1281 was a novel dynamically altered and appeared to be specifically related to depression and antidepressant effects of KXS, and the target genes of miR-1281 are mostly key nodes in the classical signaling pathway related to depression. ADCY1 and DVL1 were the targets of miR-1281, KXS may activate cAMP/PKA/ERK/CREB and Wnt/β-catenin signal transduction pathways by down-regulating miR-1281 that targets ADCY1 and DVL1 to achieve its role in neuronal cell protection. The results suggested the exact role of KXS in the treatment of mild to moderate depression, and its mechanism may be related to the regulation of miR-1281 and its target genes ADCY1 and DVL1.

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Study on the synergistic effect against T2DM of berberine 'separation - slow release' coupling system guided by nanostructure-controlled resorcinol-formaldehyde aerogel

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Abstract:

Berberine, an isoquinoline alkaloid that carries the wisdom of Chinese medicine for thousands of years. Not only does the phytochemical continues to be hypoglycemic active as recorded in the Compendium of Materia Medica, but also it shows a multi-dimensional anti-Type 2 Diabetes Mellitus (T2DM) pharmacological activities. However, the clinical application of berberine has been limited due to its low bioavailability (less than 1%)[1]. In order to improve the issue, we have constructed a berberine 'separation - slow release' coupling system guided by nanostructure-controlled resorcinol-formaldehyde aerogel (RFa). The three-dimensional nanonetwork of RFa, with its unique surface electrical regulation window (-30 mV ~ -43 mV), multilevel pore size distribution (7 nm ~ 50 nm), and ultra-high porosity (98%), has demonstrated the innovative mechanism of the synergistic separation of berberine through electrostatic adsorption and size sieving, as well as the synergistic release of berberine through nano-limited domains and surface charge at the molecular level. In T2DM mice, the coupling system demonstrated the therapeutic effects of synergistic potentiation of berberine in reducing liver injury, improving lipid metabolism, lowering blood glucose level and improving insulin resistance. Molecular dynamics simulation captured the dynamic equilibrium between hydrogen bonding network and electrostatic interaction in the selective separation of berberine. In addition, the pharmacokinetic studies revealed the key breakthrough of berberine bioavailability enhancement. This study provided a nanoengineering paradigm for breaking through the difficulties of natural drug separation and bioavailability, and also paved a way for modernisation of traditional Chinese medicines with 'structure programmable - function adaptive'.

Acknowledgement:

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Interpretation for reversion of the Chinese Pharmacopoeia (2025 edition/Part I)

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Abstract:

Pharmacopoeia, as a special record of drug standards, is the highest code of drug quality specifications in a country. It is usually compiled by the national organisational force and promulgated by the government, and is legally binding effect and provides a basis for drug production, supply, testing and clinical application. According to the outline for the compilation of the Chinese Pharmacopoeia (2025 edition/Part I Chinese medicines), for raw medicinal materials and its processed product, the target task is to:

(1) newly-add no less than 100 new standards for Chinese medicines, and no less than 500 standards for revised Chinese medicines.

(2) register the detection methods and limit standards for pesticides, plant growth regulators and other residues

(3) improve the detection varieties and limit requirements for prohibited pesticides, mycotoxins, heavy metals and harmful element residues, and corresponding limit standards.

(4) focus on the establishment of detection methods based on the non-detectable detection of aristolochic acid I in Chinese patent medicines.

(5) continuously revise the quality standards of cultivated raw medicinal materials.

(6) strengthen research on the substitution of control extracts and reference substances of Chinese medicine.

Study on quality regularity of Fomes Officinalis based on surface-interior correlation analysis

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Abstract:

To explore the correlation between the color characteristics of Fomes Officinalis (Arihong) and its chemical composition and bioactivity, Fomes Officinalis was processed and classified into four color grades, A1, A2, A3, and A4, based on the color quality descriptions found in ancient texts. The HPLC method was used to determine the content of active components in fomes officinalis samples of different colors, and 11 common components were identified through fingerprint comparison. A chromometer was used to measure the objective and quantitative colorimetric values of the different color samples of Fomes officinalis, and the total colorimetric value E*ab was statistically analyzed. Pearson correlation analysis was applied to examine the correlation between the content of chemical components and the colorimetric values. Cluster analysis (PCA) and orthogonal partial least squares discriminant analysis (OPLS-DA) were used to analyze the differences among the different color samples of Fomes officinalis. An H_2O_2-induced PC12 cell oxidative damage model was established, and the MTT method was used to detect the survival rate of PC12 cells with oxidative damage treated with active color samples by observing the protective effect of color samples on the oxidative damage model cells. The PCA results showed that the different color samples of Fomes officinalis could be clustered into four categories, A1, A2, A3, and A4, indicating the difference in color of Fomes officinalis. The correlation analysis results showed that chemical component C1 had a high correlation with L* and E*ab (p<0.01), and chemical components C2, C8, C9, and C10 had significant correlations with L* and b* (p<0.05). The OPLS-DA results indicated that the variable importance in projection (VIP) values of chemical components C6, C3, C5, C1, C9, C8, C10, and C7 were greater than 1, which were the color parameters causing the main differences in Fomes officinalis. The cell test results indicated that A1 and A2 samples had a significant promoting effect on the activity of PC12 cells with oxidative damage at a safe concentration range of 50-100 μg/mL. All concentration groups of A3 and A4 test substances showed significant cytotoxic effects on PC12 cells. The results suggested that color analysis could objectively reflect the digital expression of the color characteristics of Fomes officinalis, and by combining with the determination of the content of intrinsic effective components, it could optimize the uniformity of Fomes officinalis quality.

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Quality assessment of Radix of Curcumae species by HPLC assay and fingerprint analysis

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Abstract:

Curcumae Radix called Yujin which was derived from the root tubers of four *Curcuma* species including *Curcuma wenyujin* Y. H. Chen et C. Ling, *Curcuma kwangsiensis* S. G. Lee et C. F. Liang, *Curcuma phaeocaulis* Val. and *Curcuma longa* L. often caused confusions.

In this study, we developed HPLC/PDA methods to differentiate these four species of curcumae radix by HPLC assay and fingerprint analysis. The methods developed were also validated with their precision, repeatability and accuracy.

Curdione could only be detected in *C. wenyujin*. For *C. kwangsiensis*, *C. phaeocaulis*, if the relative peak area value of peak 1 and germacrone peak of the samples was more than 1.024, it could be identified as *C. phaeocaulis* of Curcumae Radix. curcumin, desmethoxycurcumin and bisdesmethoxycurcumin could only be detected in *C. longa*. We also developed a simple method to determine curcumin, desmethoxycurcumin and bisdesmethoxycurcumin in *C. longa* and germacrone in the other three species of Curcumae Radix.

Because of the definite difference of main ingredients between curcumin-free group (*C. wenyujin*, *C. kwangsiensis* and *C. phaeocaulis*) and curcumin containing *C. longa* from this study, four curcuma species of Curcumae Radix in the pharmacopeia should be separated into two monographs, with curcumin-free and germacrone containing species as one and curcumin containing *C. longa* as the second monograph.

The HPLC/PDA methods of HPLC assay and fingerprint analysis developed in this study could be used for the quality control of these four species of Curcumae Radix.

Zishen Yuzhen Pill ameliorates hepatic glycolipid metabolism via PI3K/AKT pathway in mice with type 2 diabetes mellitus

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Abstract:

Zishen Yuzhen Pill (ZYP) is a traditional Chinese herbal product developed by Shenzhen TCM Hospital, which has been widely used for treating Type 2 diabetes mellitus (T2DM) in clinic. However, the mechanisms of ZYP on T2DM remain largely undiscovered. This study aims to investigate the effect and mechanism of ZYP on glucose and lipid metabolic disorders in T2DM model mice, as well as palmitic acid (PA)-induced HepG2 and Huh7 cells. Streptozotocin (STZ) and high-fat diet-fed (HFD)-induced T2DM mice model was used to assess the effect of ZYP. Hematoxylin and eosin (H&E) staining was used to observe the pathological changes of liver and pancreas. HepG2 and Huh7 cells were stimulated by PA as cell models to investigate the effect of ZYP-containing serum on glucose and lipid metabolism. qPCR, Western blot or immunofluorescence were also performed to analyze the expressions of targets related to inflammatory factors, glycolipid metabolism, as well as PI3K/AKT pathway. In HFD/STZ-induced diabetes mice, ZYP treatment improved oral glucose tolerance, liver function, hyperlipidemia and inflammatory response. H&E results demonstrated that ZYP treatment reduced hepatic steatosis and pancreatic damage. *In vivo* experimental results demonstrated that ZYP significantly regulates blood glucose, lipid levels, liver function, inflammatory response, pancreatic and pathological damage. *In vitro*, ZYP-containing serum significantly alleviated the abnormal levels of inflammatory cytokines, glucose and lipid disorder. Western blot results revealed that the ameliorating effect of ZYP on glucose and lipid metabolism were through PI3K/AKT pathway. Therefore, our findings indicated that ZYP can alleviate glucose and lipid metabolism disorders in T2DM at least in part through PI3K/AKT signaling pathway. This investigation provides experimental support for the traditional application of ZYP in T2DM-related diseases and might provide a novel dimension of ZYP in the clinical application.

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A kidney protection nanoparticle based on Alpinia Oxyphylla Fructus polysaccharide by modulating macrophage polarization

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Abstract:

The use of natural polysaccharides from traditional Chinese medicine as carrier materials has great potentiality in drug delivery. Nootkatone (NKT) demonstrated good pharmacological activity in treating kidney injury, but its solubility and bioavailability are not very good, which may affect the effectiveness of its therapeutic effect. Alpinia Oxyphylla Fructus polysaccharide (AOP), as a plant polysaccharide, has multiple pharmacological activities and may help to provide synergy for NKT. Therefore, AOP nanoparticles loaded with NKT (AOP-NKT NPs) were prepared for the treatment of acute kidney injury in this study. The size of AOP-NKT NPs was 291.60±3.73 nm, and the Zeta potential was determined as 35.2±0.65 mV. The nanoparticles exhibited excellent stability in pH, NaCl solution, temperature, and storage. The nanoparticles also improved the solubility and oral bioavailability of NKT. In biocompatibility experiments, AOP-NKT NPs showed good blood compatibility and no cytotoxicity to macrophages was observed at the NKT concentration in nanoparticles of 15 μg/mL and below. *In vivo*, this nanoparticle could enhance the ability of NKT in promoting macrophage M2 polarization, reduce renal inflammation and thus improve renal function and repair renal damage. In conclusion, the present study may provide the possibility for AOP as a nano delivery vehicle for renal injury treatment drugs.

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The synergy of nature products and glucagon-like peptide-1 in stimulating insulin secretion

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Abstract:

Type 2 diabetes (T2D) is a chronic metabolic disorder characterized by insulin resistance and inadequate insulin secretion, leading to dysregulated blood glucose levels. T2D is often associated with modifiable risk factors, such as excess body fat and a sedentary lifestyle. In treating T2D, glucagon-like peptide-1 (GLP-1) receptor agonists have been frequently employed to enhance glycaemic control. GLP-1 is an incretin hormone that exerts multiple physiological effects on glucose homeostasis, which facilitates glucose-dependent insulin secretion, suppresses gastric emptying and reduces appetite. The agonists of the GLP-1 receptor (GLP-1R) emulating the actions of endogenous GLP-1 has been utilized to optimize glycaemic control in individuals with T2D patients. By activating GLP-1R, these medications could help regulate blood glucose levels naturally. Thus, GLP-1R agonists have become an essential component of the treatment options for managing T2D.

In this study, the rat insulinoma cell line (INS-1) was employed to investigate insulin secretion regulation and pancreatic islet beta-cell function. Several TCM herbal extracts and phytochemicals were shown to bind with GLP-1, or GLP-1R through molecular docking analysis. To determine the GLP-1 synergetic effect of these phytochemicals, the cell lines above were treated with various phytochemicals with/without GLP-1. Our results demonstrated that several phytochemicals could significantly increase insulin secretion in dose-dependent and synergistic manners. Together, our finding suggested that the binding interaction between TCM and GLP-1 might serve as a detecting platform for us to identify potential therapeutic treatments against T2D disease.

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This work is supported by Hong Kong Research Grants Council Hong Kong (GRF 16100921); Hong Kong Innovation Technology Fund (MHP/004/21; GHP/016/21SZ; ITCPD/17-9; ITC-CNERC14SC01); Shenzhen Science and Technology Innovation Committee (ZDSYS201707281432317).

Enhancement of cisplatin sensitivity by formononetin in lung cancer cells: effects and mechanisms on chemoresistance

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Abstract:

Cisplatin remains as a cornerstone in the chemotherapy of solid tumors, yet the emergence of chemoresistance, particularly in lung cancer, significantly reduces its therapeutic efficacy. This study investigated the potential of formononetin, a natural compound with phytoestrogenic properties, to enhance cisplatin sensitivity in A549 lung cancer cells and their cisplatin-resistant variant, A549/DDP. We first assessed the pharmacokinetic characteristics and bioavailability of formononetin using the SwissADME database. Subsequently, we evaluated intracellular cisplatin accumulation, cell viability, and the activity of efflux transporters and glutathione S-transferases (GSTs). Our results indicated that formononetin exhibited favorable pharmacokinetic properties and significantly increased intracellular cisplatin levels, resulting in reduced cell viability. Molecular docking studies demonstrated a strong binding affinity of formononetin to efflux transporters, while experiments utilizing efflux transporter inhibitors revealed competition with cisplatin for export binding sites, thereby diminishing cisplatin efflux. Additionally, formononetin inhibited GST activity, a critical component of drug resistance mechanisms. Mechanistically, formononetin was found to downregulate the p65 subunit of the NF-κB complex, enhanced the Bax/Bcl-2 ratio, and promoted apoptosis. Furthermore, formononetin synergistically improved the efficacy of cisplatin and 5-fluorouracil across various cancer cell lines. Recent findings underscore the

significant role of tumor-associated macrophages (TAMs) in modifying the tumor microenvironment and contributing to drug resistance; formononetin was shown to promote M1-TAM polarization while downregulate M2-TAM markers, indicating a potential reprogramming effect. Network pharmacology analysis predicted the modulatory effects and signal regulation of formononetin on TAMs. These findings highlighted the therapeutic promise of formononetin as an adjuvant to cisplatin in overcoming drug resistance in lung cancer, warranting further investigation into its clinical application in combination therapies.

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Chemical constituents from *Hippophae rhamnoides* root

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Abstract:

Hippophae rhamnoides L., known as sea buckthorn, belongs to the family Elaeagnaceae. The plant is commonly found in Asia and Northwestern Europe and it also grows in the northwest, southwest, and northern regions of China. Its functions include invigorating the spleen and aiding digestion, relieving cough and clearing phlegm, promoting blood circulation, and dispersing blood stasis. This study evaluated the chemical constituents in the root of *H. rhamnoides*. The chemical constituents were isolated and purified by various column chromatographic methods. Their structures were elucidated by combining one and two dimensional NMR and MS techniques and by comparison with the reported literature data. Twenty-one compounds were isolated from the ethyl-acetate fraction and identified as, 8-hydroxy-9-methoxy-14-noreudesm-5,7,9-triene (1), 9-hydroxy-14-noreudesm-5,7,9-triene (2), 3,8,12-trihydroxy-9-methoxy-14-noreudesm-5,7,9-triene (3), 2*α*-O-trans-caffeoyl-3β-hydroxy-urs-12-en-28-oic acid (4), ergosterol endoperoxide (5), bis(2-ethyloctyl)phthalate (6), 18H*α*,3*β*,20*β*-ursanediol (7), arjunolic acid (8), erythrodiol (9), 3*β*-hydroxyolean-12-en-28-al (10), hippophamide (11), *β*-sitosterol (12), trans-ferulic acid 22-hydroxydocosanoic acid ester (13), stigmast-4-en-3-one (14), oleanolic acid (15), ursolic acid (16), dehydrodiconiferyl alcohol (17), maslinic acid (18), 2*α*,3*β*,19*α*,23-tetrahydroxyolean-12-en-28-oic acid (19), 2-O-caffeoyl maslinic acid (20), (+)-catechin (21). Among them, 1-4 are new compounds, and 5-6 were obtained from the genus for the first time. The bioactivities of isolated 21 compounds are ongoing.

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Stictic acid and nonstictic acid as novel therapeutic agents for inhibiting α-synuclein aggregation in Parkinson's disease

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The misfolding and aggregation of α-synuclein (α-Syn) play a critical role in the pathogenesis of Parkinson's disease (PD). A promising therapeutic approach for PD involves targeting α-Syn proteostasis, either by preventing its aggregation or by disrupting pre-existing fibrils. In this study, we investigated the effects of small molecular components from lichen extracts using bioinformatics, thioflavin T (ThT) assays, and atomic force microscopy. Stictic acid and nonstictic acid were found to dose-dependently inhibit α-Syn fibril formation and destabilize preformed fibrils, demonstrating potent anti-fibrillogenic and fibril-destabilizing activities. At the cellular level, stictic acid and nonstictic acid was shown to protect against α-Syn-induced cell death in SY-SH5Y cells overexpressing α-Syn, as evidenced by MTT assays, western blot, and confocal microscopy. Mechanistically, stictic acid inhibited the conformational transition of α-Syn from random coil to β-sheet by binding to Ile, Phe, and Tyr residues, while also disaggregated amyloid fibrils through interactions with Leu, His, Phe, and Tyr residues. Additionally, stictic acid was found to protect SY-SH5Y cells from α-Syn-induced damage by suppressing α-Syn overexpression and fibrillation. These findings highlight the potential pharmaceutical effects of stictic acid,and nonstictic acid as therapeutic agents for preventing and treating α-Syn aggregation in PD.

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Disentangling conserved and specialized flavonoid functions with an equimolar multicomponent mixture strategy

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Abstract:

Flavonoids, the largest class of polyphenols, exhibit conserved pharmacophores alongside considerable structural diversity. We hypothesized that their bioactivity stems from two complementary aspects: (1) conserved functions shared across subclasses and (2) specialized activities arising from distinct molecular features. To rapidly assess the degree of conservation of certain bioactive properties, we formulated an equimolar mixture of 20 representative flavonoids spanning five subclasses (flavonols, flavones, flavanols, flavanones, and isoflavones) and examined their effects using cellular models relevant to the neuronal system. In LPS-induced BV2 microglia, the mixture reduced pro-inflammatory cytokines (TNF-α, IL-1β, IL-6) to levels comparable to luteolin, the positive control flavonoid. Similarly, in TBHP-treated SH-SY5Y cells, it provided antioxidant protection (MTT assays) matching luteolin's efficacy, confirming that conserved anti-inflammatory and antioxidant functions are retained in mixtures. However, in PC12 cells, while the mixture altered mitochondrial membrane potential (JC-1 staining) and stimulated neurite outgrowth, its effects were significantly weaker than those of luteolin, suggesting that dilution of specific structures attenuated less-conserved functions. In contrast, amyloid-$\beta_{(1-42)}$ binding and tropomyosin receptor kinase B (TrkB) activation represented more specialized functions for flavonoids. Biolayer interferometry analysis showed that the mixture did not bind amyloid-$\beta_{(1-42)}$, whereas EGCG exhibited good binding affinity (KD = 0.9 μM). Similarly, Western blot analysis confirmed that the mixture failed to activate TrkB in SH-SY5Y cells, while 7,8-DHF induced a significant response. This study employed an equimolar combinatorial approach to delineate the functional landscape of flavonoids from both conserved and specialized perspectives, advancing our understanding of their health potential in dietary and therapeutic contexts.

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Investigation of peimine as an inhibitor of melanogenesis: implication for hyperpigmentation treatment

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Abstract:

Melanogenesis, the process of melanin production in melanocytes, is essential for skin pigmentation but can lead to hyperpigmentation disorders when dysregulated. This study explores the effects of peimine, a bioactive compound derived from *Fritillaria* species, on melanogenesis in mouse melanocytes MelanA cells. The effect of peimine on melanin synthesis was reflected by measuring the intracellular melanin content and analysing the expression of enzymes related to melanogenesis, including tyrosinase (TYR), tyrosinase-related protein 1 (TRP-1) and TRP-2. Here, our findings indicate that peimine significantly inhibits melanin production MelanA cells. Additionally, peimine downregulates the expression of tyrosinase and other melanogenic markers, suggesting a potential mechanism of action through modulation of relevant melanin synthesis pathways. These results highlight peimine's potential as a therapeutic agent for hyperpigmentation treatment. Further studies are needed to elucidate the underlying mechanisms and explore its applications in cosmetic and dermatological formulations.

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Analysis of chemical constituents of an ancient Chinese herbal mixture "Danggui Buxue Tang" before and after fermentation with *Lactobacillus plantarum* based on LC-MS/MS

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Abstract:

Fermentation is a traditional processing method that can impact the abundance of relevant components in Chinese herbal medicines. Danggui Buxue Tang (DBT) is an ancient Chinese herbal decoction in China throughout history for improving the quality of life of women suffering from menopausal symptoms. In order to enhance the therapeutic efficacy of DBT, the herbal extract was fermented together with *Lactobacillus plantarum* (LP), an edible and medicinal functional food used worldwide that enhances digestion. This study aimed to analyze the chemical differentiation between DBT and fermented DBT (DBT-F) by using UPLC-QTOF-MS/MS technology. Finally, a total of 134 constituents were preliminarily identified, including flavonoids, triterpenes, amino acids, phenylpropanoids, and other constituents. The amounts of glycosides were converted to aglycones by biotransformation, showing that deglycosylation was the main event occurring in the fermentation.

Study on the ameliorative effect and mechanism of oligosaccharides from Fufang Ejiao Jiang on precancerous lesion of gastric cancer

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Abstract:

Gastric cancers (GC) pose a significant threat to human health, with the improvement of precancerous lesions of gastric cancer (PLGC) being crucial for prevention. Oligosaccharides extracted from Fufang Ejiao Jiang (FEJO) have shown efficacy in improving PLGC, though its main active ingredient remains unclear. *In vitro* studies revealed that FEJO promoted the proliferation of hypoxic gastric mucosal epithelial cells (GES-1), increased Bcl-2/Bax ratios, downregulated caspase-3, and activated PI3K and p-AKT while inhibiting HIF-1α. Conversely, FEJO suppressed AGS gastric cancer cell proliferation under hypoxia by decreasing Bcl-2/Bax ratios, upregulating caspase-3, and inhibiting PI3K, p-AKT, and HIF-1α. *In vivo*, a PLGC rat model was established using N-methyl-N'-nitro-N-nitrosoguanidine (MNNG), 40% ethanol, and an unregulated diet. Rats were divided into six groups: normal, normal + high-dose FEJO, model, positive control, and low- and high-dose FEJO treatment groups. FEJO mitigated gastric mucosa pathological damage, increased serum PGⅠ/PGⅡ and G-17 levels, reduced IL-1β, IL-6, and TNF-α, enhanced SOD and GSH-Px activity, decreased MDA content, and regulated apoptosis-related proteins and PI3K/AKT/HIF-1α expression in gastric tissues. LC/MS/MS analysis identified 14 potential biomarkers in PLGC rats' serum, involving metabolic pathways such as the tricarboxylic acid cycle, arginine/proline metabolism, glycerophospholipid metabolism, glycolysis, and taurine/subtaurine metabolism. FEJO ameliorates hypoxic injury in normal GES-1 cells, inhibits AGS cell proliferation, and improves PLGC via anti-inflammatory, antioxidant, pro-apoptotic effects, and metabolic regulation, likely mediated by suppressing excessive PI3K/AKT/HIF-1α pathway activation.

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Polysaccharides from *Ziziphus jujuba* fruit protect against ulcerative colitis in mice via IL-33/ST2 signal axis

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Abstract:

Jujube, the fruit of *Ziziphus jujuba*, is a medicinal herb and daily food, which has been widely used in numerous traditional Chinese herbal prescriptions. The polysaccharides from jujube that possess immune regulatory activity have been considered to treat ulcerative colitis (UC), an inflammatory disease prevailing for many years. However, the mechanism of polysaccharides from jujube in treating UC remains unclear. In this study, we investigated whether jujube polysaccharide (JP), a bioactive ingredient of jujube, could ameliorate UC symptoms in mice model, and whether its mechanism was relative to NF-κB signal pathway via IL-33/ST2. First, JP was extracted and characterized the chemical properties, including purity, monosaccharide composition, molecular weight and FTIR absorption. Then the well-prepared JP was conducted to animal study. Our results proved that JP (7.25 and 3.75 mg/kg/d) orally treatment could ease dextran sulfate sodium (DSS)-induced UC mice symptoms, including disease activity index and colon length. HE staining indicated that JP could regulate colonic pathological erosion and crypts abscess. Meanwhile, JP restored the inflammatory indicators in blood parameters. Secondly, RNA sequencing was employed to analyze the differentially expressed genes and potential signal pathway. According to GO and KEGG enrichment, we screened 3,045 differentiated genes and annotated 243 differentiated signal pathways. The majority of enriched differentiated expressed genes and signal pathways were related to inflammatory reaction. We further confirmed that the increased proinflammatory cytokines like IL-1β, IL-2, IL-6, IL-33 and TNF-α in UC mice colon were declined after JP intervention. Next, gene set enrichment analysis based on cytokines-cytokines reactors and NF-κB signal pathway were used to screen the significantly differentiated genes. Among them, two target protein expressions of ST2 and MYD88, translated by il1r1 and myd88 respectively, were further verified by Western blot analysis. These results indicated that JP could down regulate the expression of ST2 and MYD88 on UC mice colon, and further suppress NF-κB signal pathway and T cells proliferation. In conclusion, JP can ameliorate UC mice symptoms induced by DSS, the mechanism of which is involved in the regulation of NF-κB signal pathway via IL-33/ST2 axis.

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ZDSYS201606081515458), Shenzhen Medical Research Fund (B2302008), Foundation of Guangdong Provincial Key Laboratory of Functional Substances in Medicinal Edible Resources and Healthcare Products (No. GPKLFSHP202101).

Components of plants *Haplophyllum griffithianum* of the *Rutaceae* family and their bioactivity

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Abstract:

Chemical investigation on aerial parts of *H. griffithianum* collected from two growing place of Uzbekistan, led to the isolation of a new quinolin-2-one type alkaloid, griffinine, as well as 12 quinoline alkaloids, namely dubinine, dubinidine, dictamnine, skimmianine, evoxine, gerphytine, gerphytinine, dubamine, N-methylhaplofoline, flindersine, folimine, griffithine. 4 compounds, dictamnine, skimmianine, folimine, and griffinine were obtained from the root extract of this material.

The carbohydrate complex of aerial parts of *Haplophyllum griffithianum* plants has been studied. As a result, the presence of alcohol-soluble sugars, water-soluble polysaccharides, pectin substances and hemicelluloses were established. In addition, it was found that alcohol-soluble sugars of the plant *Haplophyllum griffithianum*, contained components such as hexose - glucose, ketosaccharides fructose and sucrose. The inhibitory activity of samples on Protein Tyrosine Phosphatase 1B (PTP-1B) was determined. Since the samples were polysaccharide and pectin, the initial screening concentration was increased. In conclusion, there were no significant inhibition of PTP1B enzyme when the concentration of the sample was up to 200 μg/mL, respectively.

Unveiling therapeutic targets and preventive components for kidney deficiency and blood stasis-type BPH: a metabolomics, network pharmacology and reverse screening approach

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Abstract:

This study integrated clinical metabolomics and network pharmacology to identify therapeutic targets for kidney deficiency and blood stasis-type Benign Prostatic Hyperplasia (BPH). Serum analysis revealed hormonal imbalances within BPH patients, including a decreased T/E2 ratio and elevated SRD5α2, alongside increased inflammatory and fibrotic markers such as NF-κB p65 and TGF-β in patients. Moreover, we conducted metabolomic profiling and identified 58 differential metabolites, including amino acids, organic acids, phospholipids, vitamins, and steroids, enriched in key pathways like glycerophospholipid metabolism, the TCA cycle, glutathione metabolism, and porphyrin metabolism. Through network pharmacology, we identified 178 potential BPH targets, which were used to integrate with metabolomic data to establish 4 compound-reaction-enzyme-gene networks and refine 23 core targets. In addition, we found 11 druggable human targets with 49 interacting components by using AI-driven reverse screening using the Yaozh Database-Natural Product AI Engine Platform. Target-component binding validation demonstrated high predictive reliability for key targets such as ALDH2, CDS1, ODC1, IDH1, NOS3, UGT2B7, and HOMX-1, characterized by tight ligand conformation overlap and prominent ligand affinity-driven residue clustering. These findings highlight critical metabolic pathways and therapeutic components, providing a foundation for targeted BPH treatment and novel drug development in this BPH subtype.

Acknowledgement:

This work was supported by Shanxi Province Key Research and Development Program Project (202102130501006), Shanxi Provincial Department of Science and Technology Basic Research Program (202303021221157, 20210302124292), Shanxi Provincial Health Commission Project (2022081), Shanxi Provincial Higher Education Science and Technology Innovation Project (2021L361), Shanxi Provincial Higher Education Teaching Reform Project (J20241079), Shanxi University of Chinese Medicine Scientific and Technological Innovation Capacity Cultivation Program Project (2022PY-TH-10, 2024PY-CXY-008).

Study on the efficacy of bird's nest peptides

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Abstract:

Edible bird's nests (EBN, or Yan Wo 燕窝 in Chinese) are the solidified saliva secreted from swiftlet species *Aerodramus fuciphagus* and *A. maximus*. EBN composes of over 60% proteins in a complex form, and which is difficult to be physically digested into small peptides. To determine the potential skin moisturization and anti-inflammation effectiveness of EBN peptides, the extraction by over-stewed and the digestion by simulated gastric enzymes were applied as main strategies to release small peptides from the complex proteins of EBN. The efficiency of enzymatic digestion was achieved by over 90%, and the molecular weight of digested smaller peptides were determined through Liquid Chromatography Mass Spectrometry with a range of 685-981 Da. The enzymatic extraction was subjected to *in vitro* studies to detect their bioactivities of moisturizing and anti-inflammation. Four EBN peptides, namely EBNP1, EBNP2, EBNP3, and EBNP4, were identified, and these peptides were analyzed for their functionalities in skin hydration and inflammation. As a result, the peptide--EBNP3 was found to express robust efficacy in relieving the symptoms of dermatitis within a mouse model. Together, our finding suggested that EBN peptides contain high potency to express skin moisturizing and anti-inflammation effectiveness and could be developed into skincare products.

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Nanogold particles loaded with edible bird's nest peptides enhance skin health

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Abstract:

Edible bird's nests (EBN, or Yan Wo in Chinese) are the solidified saliva secreted mainly from swiftlet species *Aerodramus fuciphagus* and *Aerodramus maximus*. EBN has long been known to nourish and strengthen "Lung" and "Yin", which in turn potentiates skin healthiness. Our studies have discovered that simulated gastric digestion of EBN extract can maximize the release of bioactive sialic acid and small peptides in EBN, which exhibit skin moisturizing and anti-inflammatory effects. However, the wide size range of peptides and large zeta potential value of the EBN digest hinder its penetration into the skin epidermis, and therefore limits its potential therapeutic efficacy against skin inflammation. Therefore, a nanoformulation of EBN digest were developed in this project. The peptide-loaded nanogold particles were prepared by modified Turkevich method, where the reaction conditions, including buffer choice, buffer pH, concentrations of reagents, reaction temperature, and reaction time, were optimized. The quality of nanoparticles was assessed by UV-Vis spectroscopy, dynamic light scattering, peptide content assay, and SDS-PAGE. The efficacy was evaluated in several skin cell lines, including HaCaT human keratinocytes, B16F10 murine melanoma, and MDF murine dorsal fibroblast. Overall, the nanoformulation were shown to possess improved efficiency and controlled characteristics relative to the EBN digest. A modification of potential therapeutic peptides derived from EBN was therefore developed for improving skin health.

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Baicalin ameliorates dextran sulfate solidum-induced colitis by modulating JAK2/STAT3/NF-κB-dependent M1 macrophage polarization

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Abstract:

Ulcerative colitis (UC) is a chronic autoimmune disorder influenced by genetic, environmental, and immune factors. Baicalin, a flavonoid derived from Scutellaria Baicalensis, has demonstrated anti-inflammatory properties; however, its effects on macrophages-mediated inflammation in UC remain unclear. This study investigated the protective effects of Baicalin on UC and its role in modulating macrophages-mediated immune responses. Mice were divided into control, dextran sulfate sodium (DSS), 5-aminosalicylic acid (5-ASA) + DSS, and low-, medium-, and high-dose Baicalin groups. Disease activity and colon health were assessed using the Disease Activity Index (DAI) and flowcytometry analysis for macrophages and Th cells. The activation of the JAK2/STAT3/NF-κB signaling pathway was evaluated via Western blotting. In vitro, Th cells were activated with anti-CD3ε/CD28, and RNA sequencing was conducted to examine the effects of Baicalin on Th cell function. In the UC mouse model, Baicalin protected the intestinal mucosa, suppressed JAK2/STAT3 pathway activation in Th cells, reduced IL-17 secretion, and inhibited M1 macrophage polarization through the NF-κB pathway. Thus, Baicalin could inhibit M1 macrophage-mediated inflammation and modulate JAK2/STAT3/NF-κB signaling pathway to attenuate DSS-induced UC. Baicalin was considered as a viable natural strategy in the treatment of UC.

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Two unprecedented *p*-terphenyl derivatives, acrocaphenyls A and B, with distinctive highly oxygenated rigid caged core from plant endophytic fungus *Acrocalymma cycadis*

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Abstract:

In this study, we conducted chemical investigation on *Acrocalymma cycadis*, which has led to the discovery of two unprecedented *p*-terphenyl derivatives, namely acrocaphenyls A (**1**) and B (**2**). We employed comprehensive spectroscopic techniques in this work, such as HRESIMS, IR, and NMR, along with a quantum chemical calculation of the NMR chemical shifts combined with a DP4+ probability analysis, X-ray crystallography, and electronic circular dichroism calculations (ECD). With the aid of these technologies, the chemical structures of compounds **1** and **2** were elucidated in detail. Notably, acrocaphenyl A (**1**) was an unprecedented highly oxygenated *p*-terphenyl derivative with a distinctive trioxatetracyclo-[4.4.2.$0^{3,11}$.$0^{4,9}$]-dodecane core, and accrocaphenyl B (**2**) possessed an unprecedented highly oxygenated rigid caged dioxatricyclo-[3.3.2.$1^{3,7}$]-undecane skeleton. The possible biosynthetic pathways towards these two compounds were also proposed in this study. Interestingly, acrocaphenyl B (**2**) exhibited potent antibacterial activities against *B. cereus*, with an MIC value of 6.25 μM. Furthermore, analysis of the growth curves, cell membrane permeability and cell morphology have revealed that the possible bacteriostatic mechanism for **2** was to alter the external structure of *B. cereus* and resulted in the rupture or deformation of the cell membranes.

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Drug screening of flavonoids as potential VEGF inhibitors through computational docking and cell models

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Abstract:

Vascular endothelial growth factor (VEGF), also known as VEGF-A, has been linked to various diseases, such as wet age-related macular degeneration (wAMD) and cancer. Even though there are VEGF inhibitors that are currently commercially available in clinical applications, severe adverse effects have been associated with these treatments. There is still a need to develop novel VEGF-based therapeutics against these VEGF-related diseases. Here, we established a series of VEGF-based computational docking analyses and cell models, such as a wound healing assay in HaCaT cells and an evaluation of NF-κB performance in macrophages, to screen a large library of flavonoid-type phytochemicals. Three flavonoids, namely, farrerol, ononin and (−)-epicatechin, were shown to express binding affinities to VEGF protein and inhibit VEGF-mediated biological activities. The investigation evidently suggested that the three flavonoids above could be considered potential anti-VEGF agents for the following drug development against VEGF-mediated diseases.

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Dynamic changes in suitable production areas of *Angelica sinensis* (Oliv.) Diels under environment and land use policies

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Abstract:

The distribution of many species has changed over time owing to global climate change and strict regulation of land-use. *Angelica sinensis* (Oliv.) Diels is a cultivated plant with an ecological advantage on plateaus; however, climate and land-use dynamics affect its distribution. This study explores the influence of these two dynamics on *A. sinensis*. The MaxEnt model was used to determine the current and future distribution of *A. sinensis* in China, and the conflict index was calculated to evaluate the contradiction between ideal suitability and other land-use types. The differences in natural habitats in different suitable areas were also expounded. Fragstats software was used to calculate the fragmentation level of cultivability. Additionally, a multiple stepwise regression algorithm was used to explore the relationship between environmental variables and ferulic acid content. The results showed that, owing to climate and land-use changes, *A. sinensis* is likely to experience a reduction in suitable areas, competition with forests and grassland, and face a loss of optimal cultivation conditions. Based on these findings, specific protective measures were proposed to address these increasing threats and ensure the sustainable development of the *A. sinensis* industry. This study provides guidance for future development of the *A. sinensis* industry and new analytical ideas for the cultivation planning of other species.

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Integrated analysis of the chemical constituents and biological functions of *Isodon serra* (maxim.) Kudô: a computational model-based methodology

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Abstract:

This study introduces a novel computational model-based methodology for the integrated analysis of the chemical constituents and biological functions of *Isodon serra* (maxim.) Kudô. through a detailed examination of 270 identified chemical constituents, including terpenoids, phenolic acids, and essential oils. This research aimed to determine the biological activities and potential therapeutic applications of the phytochemicals identified from *Isodon serra* (maxim.) Kudô. Data-driven analytics facilitated the identification of 7,901 biological targets and 7,663 related functions, emphasizing anti-inflammatory, antioxidant, and anticancer properties of *Isodon serra* (maxim.) Kudô. The analysis was enhanced by statistical techniques that provided a robust framework for evaluating the relationships between the chemical constituents and their biological impacts. Interestingly, the ethanol extract demonstrated superior efficacy, particularly against *Staphylococcus aureus* and HepG2 cancer cells. In parallel, we conducted an antioxidant assay and revealed a substantial increase in radical scavenging potential. These findings underscore the therapeutic potential of *I. serra*, offering new insights for its application in modern medicine and suggesting avenues for further pharmacological exploration.

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Comprehensive comparison of three different medicinal parts of *Eupatorium lindleyanum* DC. using RRLC-QTOF-MS-based metabolic profile and *in vitro* anti-inflammatory activity

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Abstract:

Eupatorium lindleyanum DC. (EL) is a traditional Chinese herb known for its phlegm-reducing, cough-relieving, and asthma-calming properties. It has been widely used for treating cough and bronchitis. However, preliminary experiments have revealed wide variations in the composition of its different medicinal parts (flowers, leaves and stems), and the composition and efficacy of its different medicinal parts have been remain largely underexplored at present. In this study, a non-targeted rapid resolution liquid chromatography coupled with quadruple time-of-flight mass spectrometry (RRLC-Q-TOF-MS) based metabolomics approach was developed to investigate the differences in the chemical composition of different medicinal parts of EL. We identified or tentatively identified 9 alkaloids, 11 flavonoids, 14 sesquiterpene lactones, 3 diterpenoids and 24 phenolic acids. In addition, heatmap visualization, quantitative analysis by high-performance liquid chromatography (HPLC-PDA) and ultra-high-performance liquid chromatography-triple quadrupole tandem mass spectrometry (UPLC-MS/MS) showed particularly high levels of sesquiterpene lactones, flavonoids, and phenolic acids in the flowers, such as eupalinolide A and B, and chlorogenic acid, among others. Leaves of this plant also contained some flavonoid sesquiterpene lactones and phenolic acids, while stems were almost absent. The findings of *in vitro* activity studies indicated that the flowers exhibited a notable inhibitory effect on the release of inflammatory factors TNF-α and IL-6, surpassing the anti-inflammatory efficacy observed in the leaves. Conversely, the stems demonstrated negligible anti-inflammatory activity. The variations in anti-inflammatory activity among the flowers, leaves, and stems of EL can primarily be attributed to the presence of flavonoids, phenolic acids, and sesquiterpene lactones in both the flowers and leaves. Additionally, the flowers contained a higher concentration of these active components compared to the leaves. These compounds mediated their anti-inflammatory effects through distinct biochemical pathways. The results of this study were anticipated to provide a scientific basis for the rational and effective utilization of EL resources.

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6-Gingerol mitigates *Cclostridium difficile*-associated diarrhea by modulating gut microbiota and short-chain fatty acid homeostasis

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Abstract:

In recent years, the incidence of *Clostridium difficile*-associated diarrhea (CDAD) has markedly increased, yet effective treatment options remain limited. 6-Gingerol, a principal bioactive component of ginger, exhibits notable antibacterial and anti-inflammatory properties, positioning it as a promising alternative therapy. This study aimed to evaluate the therapeutic efficacy of 6-gingerol in CDAD and elucidate its potential mechanisms through gut microbiota sequencing and targeted quantification of short-chain fatty acids (SCFAs). Gut microbiota composition was analyzed using 16S rRNA sequencing, and fecal samples were subjected to SCFAs quantification. The results demonstrated that 6-gingerol effectively alleviated CDAD symptoms, significantly reduced *C. difficile* toxin levels (P<0.001), decreased intestinal inflammation, and restored gut barrier function. Although 6-gingerol did not significantly enhance gut microbiota diversity, it modulated the microbial structure by decreasing the proportion of harmful bacteria and increasing beneficial ones. Specifically, 6-gingerol significantly increased the relative abundance of Lactobacillus acidophilus (P<0.01) and Bacteroides thetaiotaomicron, while reducing Klebsiella pneumoniae and Proteus mirabilis. Targeted SCFAs quantification revealed that 6-gingerol restored levels of acetate (P<0.01), butyrate (P<0.01), and valerate (P<0.001), which are directly involved in CDAD recovery. In conclusion, this study suggested that 6-gingerol ameliorates CDAD by reducing intestinal inflammation, restoring gut barrier function, modulating gut microbiota, and rebalancing SCFAs levels.

Species authentication and toxicity assessment of *Prunus* seed using untargeted metabolomics analysis

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Abstract:

Prunus seeds are widely used in traditional medicine and food products. However, their similar morphological appearance poses challenges for accurate species authentication. This increases the risk of unintentional substitution and poisoning cases. Some Prunus species contain high levels of amygdalin and other cyanogenic glycosides, which may release highly toxic compounds, hydrogen cyanide, upon hydrolysis. In this study, an untargeted metabolomics approach utilizing high-resolution mass spectrometry, ultra-performance liquid chromatography-mass spectrometry (UPLC-MS) and multivariate statistical analysis were employed to differentiate the seeds from five medicinal Prunus plants, assess their potential toxicity and identify a broad range of bioactive secondary metabolites found in the seeds, including amygdalin, epicatechin, quercitrin as well as quercetin. These compounds have been extensively studied for their potential health benefits, exhibiting diverse physiological properties such as antioxidant, anti-inflammatory and anticancer activities. Among the five medicinal *Prunus* species examined, Kuxingren exhibited the highest amygdalin content. While amygdalin has garnered considerable attention for its potential anticancer properties, its metabolites have been found to be toxic to humans after oral ingestion. Metabolite profiling revealed distinct chemical fingerprints among different *Prunus* species, enabling accurate authentication despite their visual similarities. Furthermore, chemometric analyses, including principal component analysis (PCA) and orthogonal partial least squares discriminant analysis (OPLS-DA), effectively distinguished species-specific metabolic variations. This study provides valuable insights into the phytochemical composition of medicinal Prunus seeds, highlighting both their therapeutic potential and associated risks. The findings supported regulatory and quality control efforts in food and herbal medicine industries by ensuring species authentication and safety evaluation.

Discovery, anti-tumor activity, and synthesis of diterpenoids in medicinal plants of the *Caryopteris* genus

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Abstract:

The chemical constituents of *Caryopteris incana*, C. *nepetifolia*, C. *paniculata*, C. *terniflora*, C. *mongholica*, and C. *aureogandulosa* were studied by various chromatographic techniques. A total of 573 compounds were isolated, of which 144 were new compounds. Among them, there are 142 diterpenes, of which 55 are new compounds, including 8 with new skeletons. It was found that nepetaefolins F (abietane type diterpenoid) had good antitumor effect through the PDX model of non-small cell lung cancer. Through chemical synthesis, nepetaefolin F was synthesized in 9 steps with 1% total yield, and 28 structural analogues of nepetaefolin F were obtained through structural modification. The results of the structure-activity relationship study show that the 3,18-hydroxyl groups on the structure of triptobenzene L were the active groups, and the nepetaefolin F of analogue (19-cyclopropanecarboxyl-triptobenzene L) obtained by linking the cyclopropionic acid group on the C-18 position has better anti-tumor activity than nepetaefolin F and other nepetaefolin F analogues. The mechanism of action of compound (19 cyclopropanecarboxyl triptobenzene L) was related to its inhibition of gastric cancer cell proliferation, up regulation of p21 mRNA expression, promotion of apoptosis and up regulation of apoptosis proteins cleaved caspase 3 and cleaved caspase 9. These results suggested that 19-cyclopropanecarboxyl triptobenzene L can be used as a lead compound in the treatment of gastric cancer.

Acknowledgement:

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Antimicrobial and cytotoxic activities of secondary metabolites from endophytic fungi isolated from *Ziziphora pedicellata* Pazij et Vved.

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Abstract:

Endophytic fungi, residing within plant tissues, are recognized for their ability to produce a diverse array of bioactive secondary metabolites with significant therapeutic potential. This study focuses on the isolation and characterization of endophytic fungi from *Ziziphora pedicellata* Pazij et Vved, a medicinal plant native to Uzbekistan, and evaluates the antimicrobial and cytotoxic properties of their secondary metabolites. Six endophytic fungal isolates were obtained from the plant, and three of these isolates—*Alternaria doliconidium, Preussia africana*, and *Alternaria alternata*—demonstrated strong antibacterial activity against *Bacillus subtilis*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*, with inhibition zones ranging from 15.43 ± 0.20 mm to 24.4 ± 0.36 mm. Notably, *P. africana* and *A. alternata* extracts exhibited significant cytotoxic effects against several cancer cell lines, including HeLa, HEp-2, HBL-100, and CCRF-CEM. Molecular identification of the active isolates was performed using ITS gene sequencing, confirming their phylogenetic placement within the *Ascomycota phylum*. The findings highlighted the potential of endophytic fungi from *Z. pedicellata* as a valuable source of novel bioactive compounds with promising applications in antimicrobial and anticancer therapies. The study underscored the importance of endophytic fungi in medicinal plants as a sustainable and eco-friendly resource for the discovery of new pharmaceutical agents, particularly in the face of increasing antimicrobial resistance and the need for effective cancer treatments. Further research is warranted to isolate and characterize the specific bioactive compounds responsible for these activities and to explore their mechanisms of action *in vitro* and *in vivo*.

Vietnam's traditional medicines and the standardization of materia medica

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Abstract:

Vietnam's traditional medicines (VTM), with its long history and cultural significance, has long served as a cornerstone of healthcare for millions of people. Rooted in the principles of balance, harmony, and holistic healing, VTM have utilized a diverse array of natural substances known as materia medica to treat a wide range of ailments. This presentation explored the evolving process of standardizing Vietnam's materia medica, aiming to preserve its cultural heritage while ensuring its relevance in modern healthcare systems. It examined the two levels of standards that governed VTM: in-house standards established by manufacturers and national standards set by the Vietnamese Pharmacopoeia (VPC). The VPC has played a critical role in formalizing these standards, with the VPC V and it's supplement containing 1576 monographs, including 376 for materia medica, 23 for VTMs. Furthermore, the upcoming VPC VI, expected in 2026, will include approximately 426 monographs of materia medica and VTM. National standards have formulated in accordance with the inter-ministerial joint circulars issued by the Ministry of Science and Technology and the Ministry of Health of Vietnam, ensuring that these guidelines were rigorously followed. This study also explored the challenges and opportunities of integrating traditional substances into modern regulatory frameworks, while emphasizing the importance of these standards in ensuring the efficacy, safety, and sustainability of VTM. Ultimately, the standardization of materia medica has presented as a vital step toward preserving Vietnam's medicinal traditions, enhancing public health, and fostering global recognition of its contributions to holistic healthcare practices.

The extract of *Ardisia elliptica* fruit suppress inflammation and excessive phagocytosis in lipopolysaccharide-activated microglia

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Abstract:

Neuro-inflammation is a critical defense mechanism against pathogens, infections and injuries in the brain. However, its complex processes are implicated in the pathology underlying the development of neurogenerative diseases, such as Alzheimer's disease, Parkinson's disease and multiple sclerosis. *Ardisia elliptica* Thunb., a member of the Primulaceae family commonly known as Ram Yai or Pilangkasa in Thai, is traditionally used to treat diarrhea with fever. However, its potential effects on neuro-inflammation are yet to be determined. This study aimed to investigate the anti-inflammatory properties of *A. elliptica* fruit (AEF) in activated microglia. In this study, lipopolysaccharide (LPS), a potent pro-inflammatory agent, was used to activate microglial BV2 cells, a well-established cell model for studying neuro-inflammation. AEF extracts significantly reduced the over-expression of pro-inflammatory factors, including IL-1β, TNF-α, and iNOS, as well as anti-inflammatory cytokines IL-10, in LPS-activated microglial BV2 cells and macrophage RAW264.7 cells. These effects were associated with the reduction of phosphorylated JNK, P38, and NF-kB proteins in LPS-activated BV2 cells. In addition, AEF extracts markedly decreased phagocytosis of fluorescent beads and amyloid fibrils in LPS-activated BV2 cells. Furthermore, AEF extracts inhibited the formation of amyloid fibrils and aggregated in a dose-dependent manner. Taken together, our findings demonstrated that AEF extracted with 90% ethanol, exhibited greater efficacies than 50% ethanol and water extracts. These results suggested that AEF extracts have potent anti-inflammatory properties as a natural product for the treatment of neuro-inflammatory and neuro-degenerative diseases, such as Alzheimer's disease.

Acknowledgement:

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Novel insights into *Cordyceps*-derived polysaccharides and cordycepin as potential therapies for fibromyalgia and inflammatory pain

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Abstract:

Fibromyalgia (FM) is a chronic disorder characterized by widespread pain, fatigue, and cognitive disturbances, with emerging evidence pointing to an inflammatory and autoimmune basis. *Cordyceps spp*., a medicinal mushroom, has been reported to contain significant anti-inflammatory potential. This study investigated the therapeutic effects of *Cordyceps*-derived polysaccharides (CSP-1 and CMP-1) and cordycepin in FM-related inflammation and pain pathways. Polysaccharides from *Cordyceps sinensis* (CSP-1) and *Cordyceps militaris* (CMP-1) were characterized, revealing distinct sugar compositions and molecular weights. HPLC analysis of *Cordyceps militaris* showed variability of adenosine and cordycepin, highlighting the impact of extraction methods on bioactive compound yields. Through *in vitro* studies, CSP-1, CMP-1, and cordycepin were shown to reduce cell viability in a dose-dependent manner (0.07–10 mg/mL; ***$p<0.001$, **$p<0.05$), with IC_{50} values indicating the potency of treatments. In LPS-induced BV2 cells, these compounds restored good cell viability and metabolic activity, particularly at concentrations of 0.30 mg/mL and 0.60 mg/mL (***$p<0.001$). Nitric oxide (NO) production was significantly reduced, with higher doses (0.15–0.60 mg/mL) restoring NO to near-basal levels. Subsequently, we conducted qPCR analysis and revealed upregulation of anti-inflammatory IL-10 and downregulation of iNOS, TRPV1, TNF-α, and IL-6, indicating the reduction of inflammatory signaling. Gene expression data, normalized to GAPDH, highlighted the compounds' ability to modulate inflammatory and nociceptive pathways. In summary, *Cordyceps*-derived polysaccharides and cordycepin exhibited anti-inflammatory, cytoprotective, and gene-modulatory effects, offering therapeutic potential against FM and related inflammatory pain disorders.

Study of alkaloids from the plant *Haplophyllum foliosium*

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Abstract:

The study of plants of the *Haplophyllum* genus, a member of the alkaloid-containing Rutaceae family, provides new information about the composition, composition, and structure of biologically active quinoline alkaloids. Chemical studies of *Haplophyllum* species have shown that some of their components and plant compounds characteristic of them exhibit potent biological activity.

We continued to study plants of the *Haplophyllum* genus which biologist, Ph.D., prof. B. Nigmatullayev, collected the above-ground part of the *Haplophyllum foliosium* plant from a new place - Jamansay on 2022 year. The plant H. *foliosium* contained thin long leaves and was collected from Jamansay. The above-ground part of the plant was extracted in ethanol and the resulting chloroform alkaloids were chromatographed on a silica gel column, and the eluates obtained contained γ-fagarin (0.05 g), with a melting point of 141°C, foliosidine (0.18 g) with a melting point of 141-142°C, skimmianine (0.045 g) with a melting point of 176-177°C, xaplamin (0.015 g) with a melting point of 201-202°C, folimin (0.015 g) with a melting point of 139-140°C, and base (1) with a melting point of 214°C were isolated from chloroform-methanol (20:1) eluates. The structure of base (1) was confirmed by IR, 1H NMR, 13 C NMR, COSY, HMBC spectra. According to the above data, base (1) is a derivative isolated from a plant belonging to the pyranoquinolin-2-one series, which has the structure N-methyl-3-hydroxy-2,6-dimethyl-2-hydroxymethyl [3,2-c]quinolin-5-one. Thus, base (1), xaplamin and γ-fagarin alkaloids were isolated from this plant for the first time.

Plants of traditional medicine as a basis for the creation of modern effective medicines

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Abstract:

In many countries of the world, traditional medicine exists and implements its methods of prevention, treatment and diagnostics on a par with modern medicine. Methods and means of prevention, diagnosis and treatment in folk medicine are a combination of thousands of years of life experience, religious beliefs and traditions of various peoples. Uzbekistan has an ancient and rich experience of using plants to treat various diseases. The information accumulated by folk medicine is reflected in the fundamental works of medieval scientists Avicenna and Abu Rayhan Beruni. Of the 2,600 drugs described in Avicenna's "Canon of Medicine", 1,400 are of plant origin. Abu Rayhan Beruni's major work "Pharmacognosy in Medicine" contains rich material on the distribution and use of 880 species of medicinal plants. It describes the use of more than 176 species of medicinal plants growing in Uzbekistan. The flora of Uzbekistan has more than 4,500 species of plants, of which about 1,200 have medicinal properties that have found application in scientific and folk medicine of Uzbekistan and neighbouring countries.

Fundamental and applied research work is carried out at the Institute of Plant Chemistry of the Academy of Sciences of the Republic of Uzbekistan to study the chemical components of plants used in folk medicine of Uzbekistan in order to create new effective medicines on their basis.

Avicenna recommended using aconite as a pain reliever and for the treatment of skin diseases. According to the results of phytochemical studies of plant species belonging to the genus *Aconitum* (family Ranunculaceae), it was found that the main active substances of plant species of this genus are diterpenoid alkaloids. Based on the isolated diterpenoid alkaloids, the antiarrhythmic drugs allapinin and aklesin, aksaritmin, endalin, zeracor, rotundol were created.

Avicenna used the plant *Ajuga* (family Lamiaceae) for diseases of the liver and spleen, jaundice, gout, herpes. We have found that *Ajuga Turkestanica* contains a large number of iridoids and ecdysteroids and on their basis the adaptogenic and tonic drugs ayustan, ekdisten, exumid and the choleretic agent garpakhol were created. Avicenna used many species of plants of the genus *Ferula* (family Apiaceae) in complex recipes for the treatment of various diseases. The drugs panoferol, tefestrol, kufestrol, which have estrogenic activity and are based on natural sesquiterpene esters isolated from plants of the genus *Ferula*, are currently widely used in medical and veterinary practice. In addition, the drugs ferulen, flateron, nephrocisin, which have estrogenic, hypolipidemic and hypoazotemic activity, have been introduced into medical practice.

Licorice root - *Glycyrrhiza glabra* (family Fabaceae) avicenna recommended for the treatment of burns, various wounds, conjunctivitis, diseases of the lungs and throat, kidneys and bladder, urinary retention and chronic fever. Based on Licorice root, many drugs have been created and are widely used in practical medicine. In our institute, based on the flavonoid

pinocembrin, isolated from the above-ground part of the Licorice plant, an anti-inflammatory drug is produced for the treatment of rheumatoid arthritis and polyarthritis.

The scientists of the institute have been given the important task of studying the biologically active components of the country's plants used in folk medicine, studying the dependence of their biological activity on the chemical structure and creating effective medicinal products for use in medical practice on their basis. Deep chemical, biological and technological studies of the components of folk medicine plants have made it possible to create and introduce into medical practice more than 30 new medicinal products.

Biological activity of complex compounds synthesized from 1,2-diaminobenzene and 2,4-dihydroxybenzoic acid

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Abstract:

Complex compounds containing 1,2-diaminobenzene and 2,4-dihydroxybenzoic acid hold significant importance in medicine. These compounds are used in the treatment of cancer, malaria, and as antibacterial and antiprotozoal agents. 1,2-diaminobenzene and its derived complexes exhibit strong antimicrobial activity. The goal of the study is to study their role in medicine and explore their potential in the development of new drugs.

The ligands and their corresponding complexes demonstrated antibacterial properties against various microorganisms. High antibacterial activity of the [Ni(OPD)2(2,4-DBA)2], [Zn(OPD)2(2,4-DBA)2], and [Ni(OPD)2(3-NFA)2]·H2O complexes was confirmed in experimental studies. According to the results, the [Ni(OPD)2(2,4-DBA)2] complex formed a significant inhibition zone in the cultures of *Bacillus subtilis*, *Escherichia coli*, and *Staphylococcus aureus*. Additionally, the [Zn(OPD)2(2,4-DBA)2] complex also showed substantial antibacterial activity. Moreover, the ligands and their corresponding complexes demonstrated antibacterial properties against various microorganisms. High antibacterial activity of the [Ni(OPD)2(2,4-DBA)2], [Zn(OPD)2(2,4-DBA)2], and [Ni(OPD)2(3-NFA)2]·H2O complexes was confirmed in experimental studies. According to the results, the [Ni(OPD)2(2,4-DBA)2] complex formed a significant inhibition zone in the cultures of *Bacillus subtilis*, *Escherichia coli*, and *Staphylococcus aureus*. Additionally, the [Zn(OPD)2(2,4-DBA)2] complex also showed substantial antibacterial activity.

In conclusion, the [Ni(OPD)2(2,4-DBA)2], [Zn(OPD)2(2,4-DBA)2], and [Ni(OPD)2(3-NFA)2]·H2O complexes are highly effective in inhibiting bacterial growth and exhibit notable antibacterial properties. This increases their potential use as antimicrobial agents in drug development.

Recycling of Chinese medicine resources - development of pan-health products

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Abstract:

According to the forecast of economists, the pan-health industry will be the major industry worldwide in the next decade. In developing the pan-health industry, Chinese medicine is one of the foci in the Chinese market. At present, the average market value of our national pan-health industry is around 20 - 30 billions of RMB: the industrial parties are expecting hundred billions of RMB in the coming 10 years. One of the common characteristics of these successful pan-health industrial parities are the application of Chinese medicine, especially the product development from traditional Chinese medicine (TCM) formulations; however, the industries in developing TCM products are facing a lot of challenges including: (i) lacking of R & D units in supporting basic and applied research; (ii) having low value-added and insufficient quality control regulations; and (iii) lacking of market information on international pan-health industry and shortages of skillful technician. To tackle these problems, Center for Chinese Medicine and Shenzhen Research Institute of The Hong Kong University of Science and Technology have worked on two major areas: the mechanistic study on the formulation of TCM, as to develop a new generation of Chinese medicine; and the development of skin care products with the application of Chinese medicine.

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TFEB promotes ginkgetin-induced ferroptosis via TRIM25 mediated GPX4 lysosomal degradation in EGFR wide-type lung adenocarcinoma

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Abstract:

TFEB activation is associated with prolonged survival in LUAD patients, suggesting potential benefits of TFEB agonists in LUAD treatment. In this study, we identified ginkgetin (GK), derived from *Ginkgo folium*, as a natural TFEB agonist, which has demonstrated promising anticancer effects in our previous research. TFEB activation has been shown to promote GPX4 degradation, inducing ferroptosis; however, the specific E3 ligases, deubiquitinating enzymes (DUBs), and types of polyubiquitination chains involved remain unclear. The unique mechanisms associated with natural compounds like GK may help elucidate the underlying biological processes. Here, we found GK could bind to and activate TFEB, leading to TFEB-mediated lysosomal activation and GPX4 degradation, which induced ferroptosis in LUAD cells. These effects were impaired in TFEB knockout cells. Mechanistically, K48-linked polyubiquitination of GPX4 was required for GK induced GPX4 lysosomal translocation. TFEB knockout reduced both K48-linked ubiquitination and lysosomal translocation of GPX4. Additionally, GK promoted the binding of TFEB and TRIM25. TRIM25 and USP5 were found to competitively bind to GPX4, with TFEB activation favoring TRIM25 binding to GPX4 and reducing the interaction of USP5 and GPX4. These findings were confirmed in a xenograft SCID mouse model using TFEB knockout LUAD cells. This study identified, for the first time, GK as a promising TFEB agonist for LUAD treatment. TFEB activation promoted TRIM25-mediated K48-linked polyubiquitination and lysosomal degradation of GPX4, driving ferroptosis. This ferroptosis-driven mechanism offered a novel strategy to enhance ferroptosis-based anti-LUAD therapies.

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Exosome-like nanovesicles derived from Yam (*Dioscorea opposite* Thunb.) suppress inflammatory response and promote wound healing

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Abstract:

Plant-releasing exosome-like nanovesicles (PENs) contain miRNA, bioactive lipids, mRNAs, and various proteins to exert antioxidants, anti-inflammatory, and regenerative activities. Chinese yam (*Dioscorea opposite* Thunb.) has been a well-known vegetable with high nutritional and medicinal values. Substances extracted from yams have been reported to express anti-inflammatory effects. Herein, we described the beneficial effects of yam-derived exosome-like nanovesicles (YNVs) in suppressing the inflammatory responses and promoting the wound healing in HaCaT keratinocytes. YNVs were isolated and purified through differential centrifugation and characterized by nanoparticle tracking analysis (NTA) and transmission electron (TEM), and their targeting ability and therapeutic effect against skin regeneration were investigated systematically. The hydrodynamic size of YNVs was around 150 nm, and the zeta potential was −5.43 mV. Mass spectrometry identified that YNVs contained high levels of lipids and abundant proteins. Notably, dioscin, the bioactive constituent of yam, was also observed in YNVs. In lipopolysaccharide (LPS)-induced RAW 264.7 and TNF-α-treated HaCaT keratinocytes acute inflammation, the application of YNVs showed robust anti-inflammatory properties. In skin wound models, we demonstrated that YNVs could improve the healing. Taken together, YNVs can serve as a safe and orally effective agent in the treatment of skin regenerative.

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Elucidating the mechanism of Xiao-Er-An-Shen granule in Tourette syndrome: a focus on gut-brain axis communication

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Abstract:

Tourette syndrome (TS) is a neuropsychiatric disorder that typically manifests in childhood, and the incidence rate of TS is increasing annually. The imbalance of neurotransmitters is thought to be the key factor contributing to the onset of TS, yet there are no specific clinical medications recommended for treating TS. Xiao-Er-An-Shen (XEAS) granule is derived from Di-Tan-Tang recorded in a famous traditional Chinese medicine (TCM) book--Ji-Sheng-Fang. XEAS has been clinically prescribed for the treatment of TS in children with good efficacy. We found that (i) XEAS alleviated tic behavioural symptoms in mice with 3,3'-iminodipropionitrile (IDPN)-induced TS; (ii) XEAS regulated the levels of neurotransmitters and their precursors, such as phenylalanine (Phe), tyrosine (Tyr) and dopamine (Da) in gut, serum and brain; (iii) XEAS restored abnormal microbiota in TS mice (specifically Lachnospiraceae and Clostridium); and (iv) XEAS-regulated neurotransmitters and precursors, such as Phe and Tyr, were closely related to gut microbiota (specifically Lachnospiraceae), as revealed by correlation heatmap analysis. These results supported the clinical application of XEAS granule and suggested a close relationship between XEAS and gut microbiota, which promoted in developing a novel and more efficient TCM drug in treating TS.

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Anti-inflammatory, antipyretic efficacy and safety of inhaled *Hhouttuynia cordata* Thunb. essential oil formulation

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Abstract:

Houttuynia cordata Thunb. (H. *cordata*) is a well-known folk traditional Chinese medicine that is renowned for its use in the management of inflammatory respiratory diseases and pneumonia. Its essential oils have demonstrated their anti-inflammatory efficacy *in vitro*, however, the *in vivo* biological effects via inhalation have not been elucidated. This study aims to evaluate the anti-inflammation and toxicology of *H. cordata* essential oil containing formulation, H16 aerosol *in vivo*. A laser diffraction particle size analyser and a Next Generation Impactor were used to measure the mass median aerodynamic diameter (MMAD) of the H16 aerosol. The anti-inflammatory and antipyretic effects of the H16 aerosol were evaluated in the xylene-evoked ear oedema and Brewer's yeast induced fever models, respectively. The biological safety of the H16 aerosol was evaluated by acute toxicity and local toxicity tests in animal models. Our data showed that the MMAD of the bioactive aerosol was 3–5 μm, which implied tracheal and pharyngeal deposits. Significant anti-inflammatory and antipyretic effects were also observed in the animal models treated with H16 aerosol. The maximum tolerable dose of H16 in rats was >2.5 mL/kg. Irritation was not observed on respiratory tract mucosa in the local toxicity test. Taken together, the present study suggested that H16 could be delivered in the form of aerosol and possessed its antipyretic and anti-inflammatory effects. This study provided a new perspective for the development of a new herbal aerosol therapy and herbal modernization.

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The effectiveness of WuziYanzong Pill against treatment-as-usual in male infertility: a meta-analysis

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Abstract:

In recent decades, male infertility rate has been increasing in various countries and regions. This poses a challenge for prevention and treatment of male infertility. Wuzi Yanzong pill (WZYZP) is a classic Chinese medicinal formula for treating male infertility backed by numerous studies for its efficacy. This study assesses the clinical efficacy of WZYZP for treating male infertility patients by meta-analysis. The published randomized controlled trials (RCTs) were searched in 15 databases, comparing WZYZP with treatment-as-usual for male infertility. In total, 8 RCTs met the eligibility requirements in this study. The results of the meta-analysis were generated with the software R.studio. 736 participants were involved in this study. WZYZP treatment for male infertility significantly improved sperm concentration (8 RCTs: SMD = 1.070; 95% CI: 0.1177-2.022; $p = 0.0276$), sperm motility (2 RCTs: WMD = 6.315; 95% CI:1.403-11.23; p = 0.0117), grade A and B sperm (5 RCTs: SMD = 2.150; 95% CI: 0.8523-3.447; $p = 0.0012$), grade A sperm (4 RCTs: SMD = 1.021; 95% CI: 0.4477-1.594; $p < 0.0001$), and pregnancy rate (3 RCTs: RR = 3.804; 95% CI: 1.804-6.335; $p = 0.0001$) comparing to treatment-as-usual. However, the 8 RCTs included were all in Chinese which may lead to a potential of risk of bias, more high quality RCTs are needed to further verify the efficacy of WZYZP. Even though limitations existed, the WZYZP have a better performance in improving the reproduction parameters comparing with the treatment-as-usual.

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Linggui Zhugan Decoction ameliorates NASH mice by restoring lipid metabolism and inhibiting Anxa2-mediated pyroptosis

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Abstract:

Linggui Zhugan Decoction (LZD) is an herbal decoction being used to relieve the symptoms of nonalcoholic fatty liver disease (NAFLD). Nonetheless, it is unclear how LZD influences the severe stage of NAFLD - nonalcoholic steatohepatitis (NASH). In this study, LZD demonstrated therapeutic efficacy in a high-fat/high-cholesterol (HFHC)-induced NASH mouse model. It suppressed bodyweight gain, reduced liver/white adipose tissue (WAT) indices, and alleviated hepatic steatosis and inflammation. Mechanistically, LZD restored lipid metabolism by inhibiting lipogenesis and enhancing fatty acid oxidation (FAO). RNA-seq identified Annexin A2 (Anxa2) was a key target in LZD-treated NASH mice. By inhibiting Anxa2, LZD reduced the expressions of GSDMD-N and cleaved-caspase 1, thereby improving hepatocyte pyroptosis. This led to decreased release of pro-inflammatory cytokines (IL-1β, IL-18), ameliorating liver damage. The study highlights LZD's dual mechanism - lipid metabolism regulation and Anxa2-mediated pyroptosis suppression, which provided new evidence supporting its clinical application in treating NASH.

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Capsaicin alleviates the UV-induced decline of collagen in dermal fibroblast via blocking the generation of ROS

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Abstract:

Capsaicin, a prominent component found in chili peppers, boasts a wide range of medicinal properties, such as pain alleviation, anti-inflammatory effects, and the relief of psoriasis. Within the realm of dermatological science, capsaicin has demonstrated its efficacy in inhibiting melanogenesis induced by ultraviolet (UV) radiation through the TRPV1 receptor. Our studies utilizing both *in vitro* and *in vivo* models have shown that capsaicin can reduce the detrimental effects from UV exposure on the skin. In dermal fibroblasts, UV exposure was found to suppress collagen synthesis while simultaneously elevating the expression of MMPs, the production of ROS, and the phosphorylation of Erk and c-Jun, all of which contribute to skin deterioration. Nonetheless, these adverse effects induced by UV radiation were mitigated by the prior administration of capsaicin, with the extent of recovery being dependent on the dosage. Capsaicin's ability to counteract the UV-induced suppression of collagen synthesis was attributed to its capacity to diminish ROS production within dermal fibroblasts, rather than its interaction with its cognate receptor. Consequently, capsaicin holds significant potential as a therapeutic agent in dermatology against skin aging.

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Mailuoning oral liquid alleviate non-alcoholic fatty liver disease of high-fat and high-sugar diet-induced rats by regulating metabolism characteristics

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Abstract:

Background: Non-alcoholic fatty liver disease (NAFLD) is a disease characterized by excessive fat deposition in hepatocytes, and its incidence has been increasing over the past years. Several lines of evidence suggested that lipids are closely related to the pathogenesis of NAFLD. Mailuoning Oral Liquid (MLN) is composed of five Chinese medicinals, namely *Achyranthis bidentatae* radix (ABR), *Scrophulariae* radix (SR), Dendrobium Caulis (DC), *Lonicerae japonicae* flos (LJF) and *Lonicerae* flos (LF). Our previous study revealed that MLN was able to improve NAFLD in mice through the peroxisome proliferator-activated receptor α (PPARα) signaling pathway. However, the effect of MLN on NAFLD in rats has remained unknown, while the lipid changes involved in developing and treating NAFLD remained to be investigated.

Purpose: To determine the ameliorative effects and lipid changes of MLN and to investigate the underlying intrinsic mechanisms using a rat model of NAFLD induced by a high-fat high-fructose high-cholesterol diet (HFHFD).

Methods: In this study, UHPLC-Q-Exactive Orbitrap MS was used to characterize the chemical compositions of MLN. HFHFD-induced NAFLD in rats was treated with MLN (5.4 mL/kg,10.8 mL/kg). The effects of MLN on hepatic lipid accumulation, hepatic inflammation and hepatic fibrosis were investigated by histological methods. Serum and liver were analyzed through untargeted lipidomics and targeted PUFAs studies using AB Triple Quad™ 4500 LC-MS. Measurement of PPARα and COX signal pathway expression was determined by real-time quantitative PCR and Western blotting.

Results: A total of 143 components from MLN were detected and identified, mostly iridoids, organic acids, flavonoids, triterpenoids, sterones, and others. In rats being fed with HFHFD, MLN significantly reduced lipid accumulation and liver inflammation, enhanced glucose tolerance, and attenuated dyslipidemia. Lipidomics results showed that MLN mainly reduced serum phosphatidylcholines (PCs) and attenuated the accumulation of triglycerides

(TAGs) in the liver, while targeted PUFAs results showed that MLN reduced hepatic PGE2 and PGD2 levels. Additionally, western blotting and q-PCR results further indicated that MLN action activated the PPARα signaling pathway and inhibited the COX pathway of ARA exerted to ameliorate NAFLD in HFHFD-fed rats.

Seabuckthorn flavonoids mimic neurotrophic functions in inducing neuronal cell differentiation and restore depressive disorder in CUMS-induced mice

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Abstract:

Seabuckthorn (*Hippophae rhamnoides* L.), native to Asia and Europe, is a representative medicinal plant of "medicine food homology". Seabuckthorn is rich in nutrients, while its major chemical ingredients are flavonoids, including quercetin, isorhamnetin and kaempferol. Flavonoids have been shown to function in treating cognitive disorders, the research of which is, however, limited regarding to Seabuckthorn flavonoids. In this study, PC12 cells, SH-SY5Y cells and primary neurons were employed as the model to evaluate flavonoid-enriched fraction of Seabuckthorn (named as SBF) in inducing neurite outgrowth by comparing to the effects of NGF and BDNF. Moreover, SBF was applied in chronic unpredictable mild stress (CUMS)-induced depressive mice to evaluate its potential functions in treating major depressive disorders. SBF mimicked neurotrophic functions in inducing neuronal cell differentiation *via* activating PI3K/Akt and ERK pathways, as well as showing synergy with neurotrophic factors in stimulating the neurite outgrowth. Additionally, SBF restored the depressive behaviours, as well as relieved CUMS-disturbed levels of neurotrophins, neurotransmitters, stress-related hormones and inflammation-related cytokines. Moreover, SBF showed the ability in regulating gut microbiota of depressive mice. In addition, carbon dots (CDs) were synthesized by hydrothermal process of Seabuckthorn leaf, a part of which has been reported to contain rich flavonoids while usually considered as agricultural waste. The CDs was almost non-cytotoxic, reached a nano size of 5 nm, and achieved a recovery rate of 21% as to the flavonoids in leaf. Additionally, these CDs showed enhanced dual functional properties of significant anti-inflammatory activity and neuronal differentiation induction capability. Therefore, SBF, as well as CDs, can be considered as a candidate of health supplements or drugs in treating various brain disorders.

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Drug screening of traditional Chinese with antibacterial and anti-inflammatory effect through cell-based bioassay

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Abstract:

Traditional Chinses medicines (TCM) have been known for its various pharmacology functions, low toxicity, low price and environmentally friendly, which makes it an ideal replacement of antibiotics. However, the drug screening of TCM could be time-consuming through traditional detecting methodologies. Here, we applied a cell-based assay approach using bacteria and fish cell lines to identify herbal extracts containing antibacterial and anti-inflammatory properties with lower cost and shorter time.

A high-throughput method, called starting growth time (SGT) using four typical marine pathogenic bacterial strains, was utilised to determine anti-bacteria effectiveness of various samples. With this platform in hand, approximately 800 types of herbal extracts were tested and as a result, we found that around 30 candidate extracts were able to show significant antibacterial effect. Among these extracts, the water extract of aerial part of *Scutellaria baicalensis* named as SBA, displayed the best growth inhibitory effect.

Apart from bacterial infection, the subsequent inflammatory responses have been revealed as another factor that contributes to damage and mortality. Two cell lines isolated from rabbit fish (rabbit fish fin (RFF) and rabbit fish macrophage (RFM)) were employed in the following cell models to determine anti-inflammatory effects of extracts. These two cell lines showed robust inflammatory responses when being co-treated with LPS. In addition, the application of SBA inhibited the expression of LPS-induced inflammatory cytokines, i.e. IL-1β, IL-6, as well as the signaling of NF-κB.

To further validate the results from cell-based assay, SBA was included in the feeding of rabbit fish in the presence of pathogenic bacteria. Interestingly, fish being fed with SBA exhibited inhibition to pathogenic bacterial growth as well as inflammatory cytokine level. This suggested that SBA could be used as a promising food material for fish to tackle bacterial growth.

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Functional metabolomics characterizes the contribution of farnesoid X receptor in pyrrolizidine alkaloid-induced hepatic sinusoidal obstruction syndrome

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Abstract:

Consumption of herbal products containing pyrrolizidine alkaloids (PAs) is one of the major causes for hepatic sinusoidal obstruction syndrome (HSOS), a deadly liver disease. The aim of this study was to determine the impact of HSOS caused by PA exposure, and to determine metabolomics-derived biomarkers and the following mode of actions. In the present study, metabolomic study using two independent cohorts of patients with PA-HSOS highlighted the increased primary bile acid biosynthesis and decreased liver expression of farnesoid X receptor (FXR, which is known to inhibit bile acid biosynthesis in hepatocytes) in PA-HSOS patients. Furthermore, a murine PA-HSOS model induced by senecionine (50 mg/kg, p.o.), a hepatotoxic PA, showed increased biosynthesis of bile acids via inhibition of hepatic FXR-SHP signaling. Treatment with the FXR agonist--obeticholic acid, protected mice from senecionine-induced HSOS. This work elucidates that increased levels of cholic acid species can serve as diagnostic biomarkers in PA-HSOS and targeting FXR may represent a therapeutic strategy for treating PA-HSOS in clinics.

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Emodin suppresses the migration of U87 glioblastoma cells through the activation of the aryl hydrocarbon receptor (AhR) signaling pathway

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Abstract:

The aryl hydrocarbon receptor (AhR) is a ligand-activated receptor that mediates the biological responses of numerous environmental and natural compounds, and it is notably overexpressed in glioblastoma1. Although emodin, an AhR agonist, has been reported to suppress various types of tumors, its inhibitory effect on glioblastoma migration and its relationship with AhR remain unclear2. Given the complexity of tumor pathogenesis and the tissue-specific nature of AhR, we aim to further understand emodin's impact on glioblastoma and explore its underlying mechanism. Our study revealed that emodin's inhibitory effect on the migration of U87 glioblastoma cells increased over time, with cell migration ability reduced by approximately 25% after 36 hours of exposure. During this process, emodin activated the AhR signaling pathway, leading to the increased expression of the tumor suppressor IL24. Interfering RNA to reduce the expression of AhR or IL24 was able to block or mitigate emodin's inhibitory effect on U87 cell migration, indicating that the AhR-IL24 axis mediates emodin's inhibition of glioblastoma migration. Our findings demonstrate that the AhR-IL24 signaling axis is crucial for emodin's inhibition of glioblastoma migration, and the AhR signaling pathway could serve as a key target for studying the regulatory effects and mechanisms of compounds on glioblastoma migration.

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Lichen: a review on biodiversity, phytochemistry, and pharmacological activity

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Abstract:

Lichen represents a unique symbiotic relationship between fungi and photosynthetic partners, primarily algae or cyanobacteria. This review consolidates existing knowledge on the global biodiversity, phytochemistry, and pharmacological activities of lichens. Approximately 14,230 known lichen species have been surveyed worldwide in our database. The distribution patterns of lichen species closely align with those of bioactive species, revealing greater richness in regions, such as Europe, coastal North America, China, New Guinea, Australia and New Zealand, with the family *Parmeliaceae* containing the largest number of medicinal lichens. Our database of 116 medicinal lichens and their associated 82 phytochemicals identified depsidones, depsides, polysaccharides, and terpenoids as the primary metabolites in lichen, which have been considered as bioactive compounds. Furthermore, categories of cytotoxic/anti-cancer/anti-tumor, anti-microbial, and antioxidant activities exhibited the highest number of medicinal species and their corresponding phytochemical associations. These findings highlighted the need for further research into the pharmacological properties of lichens, especially considering their diverse applications in traditional medicine and their potential therapeutic uses.

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Yu Ping Feng San prevents the cisplatin-induced multi-drug resistance of *Escherichia coli*

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Abstract:

Cisplatin is one of the first-line chemotherapies for solid tumors. Additionally, cisplatin has been known to have antibiotic effects against both Gram-ve and Gram+ve bacterial strains, which leads to increasing multiple drug resistant (MDR) mutant of gut microbiome. At the same time, cisplatin may also affect the environment of intestinal mucosa by damaging the proliferation of epithelial cells. The cisplatin-induced side effects, such as nephrotoxicity, ototoxicity, mucositis and local inflammation, are associated with the disturbance of gut microbiota. Thus, the intake of cisplatin could experience complications caused by the appearance and development of pathogenic microflora, which has become a major concern in the medical application of cisplatin.

Yu Ping Feng San (YPFS), a traditional Chinese herbal decoction written by Zhu Danxi (A.D. 1279–1368), consists of Astragali Radix (AR), Atractylodis Macrocephalae Rhizoma (AMR) and Saposhnikoviae Radix (SR). YPFS has been used to treat immune disorders and inflammation in clinic for years. Recently, YPFS was found to improve the imbalance of intestinal flora, caused by asthma and recurrent respiratory tract infection. In our studies, we observed that YPFS reversed cisplatin-induced MDR in lung cancer cells by inhibiting the substrate-stimulated activities of efflux transporter ATPase. Interestingly, the water extract of YPFS and AMR showed significant reduced amount of MDR mutant of gut microbiome.

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Sophoricoside, a phytochemical from Fructus Sophorae, promotes hair growth via activation of M4 muscarinic AChR in dermal papilla cells

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Abstract:

Various types of hair loss, including androgenetic alopecia, senescent alopecia, and telogen effluvium, are prevalent among individuals aged 50 and above. However, the current approved medications, like Minoxidil and Finasteride, have limited effectiveness and unwanted side effects. As a result, there is a need to explore alternative treatments for hair loss. The hair follicle experiences cycles of growth, regression, and resting phases throughout our life periods. The transition between these phases is precisely regulated by DPC, which is acting as the signaling centre for hair growth. Additionally, Wnt signaling is recognized for its major role in activating hair growth. In distinction of Wnt activators, sophoricoside, can induce hair growth via the activation of M4 mAChR in DPCs. Similar to the Wnt-activation of hair growth, sophoricoside induces the downstream of Wnt signaling, e.g., AKT and GSK3β phosphorylation. This notion is strongly supported by its effects in cultures: (i) inhibition of cAMP production; (ii) activating transcriptions of Wnt signaling-mediated genes and blocked by M4 mAChR antagonist; and (iii) inducing outgrowth of hair.

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Efficacy discovery and mechanism of *Alpinia officinarum* Hance

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Abstract:

Alpinia officinarum Hance, the dried rhizome of Alpinia of Zingiberaceae, is a characteristic Li medicine in Hainan. It has the effect of warming the stomach, relieving nausea, dissipating cold and relieving pain, and can be used for treating cold pain in the abdomen, stomach cold vomiting and belching as well as acid swallowing. Type 2 diabetes and its complications have become an important factor affecting human health, and the active substances of traditional Chinese medicine have great potential in improving type 2 diabetes and its complications. We confirmed that *Alpinia officinarum* Hance has a traditional protective effect on gastric injury by combining bioinformatics analysis and modern pharmacological technology with molecular biology research. On this basis, the study found that *Alpinia officinarum* Hance and its active substances can improve the blood sugar level and glucose tolerance of DGP mice, increase the rate of gastric emptying, and reduce the level of oxidative stress to improve DGP. The results of this research provide a solid material basis for *Alpinia officinarum* Hance's characteristic Li medicine to expand the new clinical use of integrated traditional Chinese and western medicine in treating diabetes and complications. Meanwhile, we conducted a preliminary study on the anti-hepatocellular carcinoma (HCC) activity of *Alpinia officinarum* Hance, and found that it can inhibit the activity and proliferation of HCC. Based on the preparation and analysis of *Alpinia officinarum* Hance polysaccharide, we found that it could inhibit the proliferation, migration and invasion of HCC. The anti-HCC mechanism of galangin, kaempferol and other active components was also lucubrated on the basis of separation and preparation of active components. The research on anti-HCC of *Alpinia officinarum* Hance (polysaccharide and active components) will lay a scientific foundation for the future research and development of possible new drugs of *Alpinia officinarum* Hance.

Activity screening of secondary metabolites of endophytic fungi of *Arnebia euchroma* (Royle) Johnst. and identification of their strains

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Abstract:

Endophytic fungi from *Arnebia euchroma* (Royle) Johnst. serve as an important source of natural bioactive compounds, yet the biological activities of their metabolites remain underexplored. This study established a multi-dimensional screening system encompassing antibacterial (Oxford cup method), antioxidant (DPPH and $ABTS^+$ radical scavenging), and antitumor (MTT cytotoxicity assay) evaluations to systematically assess the secondary metabolites of 34 endophytic fungal strains. Results revealed that strain *Chaetosphaeronema achilleae* (HJ-17) exhibited potent antibacterial activity, forming inhibition zones of 31, 18, and 25 mm against *Escherichia coli*, *Staphylococcus aureus*, and *Bacillus subtilis*, respectively. Strain *Alternaria alstroemeriae* (HJ-28) demonstrated remarkable antioxidant capacity, achieving a DPPH radical scavenging rate of 96.90 %, comparable to vitamin C (VC) at the same concentration, while HJ-17 showed a scavenging rate of 89.10%. Both strains also displayed strong $ABTS^+$ radical scavenging capabilities, nearing VC-equivalent levels. At 400 μg/mL, the ethyl acetate crude extracts of HJ-17 and HJ-28 exhibited significant cytotoxicity, with inhibition rates exceeding 85 % against HepG2 hepatocellular carcinoma cells and over 95 % against MDA-MB-231 breast cancer cells. These findings highlight the ability of *Arnebia euchroma*-associated endophytic fungi to simultaneously produce antimicrobial, antioxidant, and cytotoxic metabolites. The synergistic bioactivities of HJ-17 and HJ-28 provide novel directions for developing multifunctional natural pharmaceuticals and underscore the unique role of plant-microbial symbiotic systems in synthesizing bioactive secondary metabolites.

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Highly oxygenated dihydrostilbenoids and flavones from the aerial part of *Glycyrrhiza uralensis* and their anti-microbial activities

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Abstract:

Infections caused by multidrug-resistant bacteria (MDRB) are increasingly challenging to treat by using conventional antibiotics, hence natural antimicrobial agents have attracted significant attention recently. The aerial part of *Glycyrrhiza uralensis* (Fabaceae) contain abundant sources of flavones and dihydrostilbenoids, which possessed broad spectrum of biological activities including anti-microbial, anti-inflammatory and radical scavenging effectiveness. We identified the compounds from the aerial part of *G. uralensis* and assessed the anti-microbial activity of the isolates to seek promising candidates for developing novel pharmaceutical drugs targeting MDRB. Column chromatography led to the isolation of seventeen undescribed phenolic compounds (1−17) and twenty-six known analogs (18−43). A part of compounds demonstrated bactericidal activity against *Helicobacter pylori*, especially compound 31 displayed significant inhibitory effect against drug-resistant *Helicobacter pylori* strains (MIC = 2 μg/mL), which were stronger than metronidazole (MIC = 16−32 μg/mL) and comparable to clarithromycin (MIC = 1−2 μg/mL). This has been the first report of prenyl-dihydrostilbenoids featuring inhibitory effects against multidrug-resistant *H. pylori*, *M. smegmatis*, *E. faecium*, and *E. faecalis* strains. These results indicated that the aerial part of *G. uralensis* could be a potential source of dihydrostilbenoids and flavones with promising activity against MDRB.

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A novel strategy for mechanism interpretation of traditional Chinese medicine prescription based on the integrated technology of UPLC-Q-TOF-MS/MS, AI virtual screening and experimental verification: Take Buyang Huanwu Decoction improved mitochondrial function to alleviate atherosclerosis as a demonstration

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Abstract:

The purpose of this study was to uncover key target proteins and corresponding active ingredients of Buxue Huanwu Decoction (BYHWD) to improve mitochondrial function and reduce atherosclerosis (AS) via construction of a novel strategy based on artificial intelligence virtual screening, UPLC-Q-TOF-MS/MS, and experimental verification. Firstly, 57 components of BYHWD were identified using UHPLC-Q-TOF-MS/MS technology, followed by the selection of 14 candidate compounds based on Druggability predictions. Subsequently, a combination of differential expression analysis (DEGs), weighted gene co-expression network analysis (WGCNA), and machine learning methods were employed to identify three characteristic genes associated with mitochondrial function and AS, including BTK, P2RX7 and PREPL. Meanwhile, batch molecular docking and molecular dynamics simulations were performed between the candidate compounds and the characteristic genes demonstrating that 10 compounds in BYHWD, such as Methylnissolin, Isomucronulatol, and others, all exhibited strong binding affinity with these genes. Finally, *in vivo* and *in vitro* experiments confirmed that BYHWD could improve mitochondrial function by activating PREPL and inhibiting BTK and P2RX7, thereby alleviating AS. Furthermore, the 10 compounds in BYHWD that formed

stable interactions with the characteristic genes, such as Methylnissolin, Isomucronulatol, and others, may play a crucial role in this process.

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Beneficial impact of Huangqi-Dangshen decoction on the intestinal microecology in adenine-induced chronic renal failure rats

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Abstract:

Traditional Chinese medicine known as Huangqi-Danshen decoction (HDD) has been used to treat chronic kidney disease (CKD) for thousands of years. However, the role of the gut microecology play in treatment outcomes of HDD on CKD is still fully unknown. To elucidate the mechanisms by which HDD protects renal function, We investigated the gut microbiota and metabolite profiles modulated by HDD in the adenine-induced renal failure rat model. H&E staining and serum enzymic assay were conducted to investigate the drugs'efficacy. Meanwhile, we analyzed the gut microbiota and their short chain fatty acids (SCFAs) responses to HDD in the CKD rats and explored the markers of drug-specific microbial responses by using a combination of network analysis, clinical parameters and KEGG pathways. HDD significantly improved the renal function. Distinct microbial compositions were revealed between HDD-treated and untreated CKD rats. We identified the HDD-only marker Lactobacillus was associated with *Allobaculum*, which are keystone taxa driving gut microbiota response to CKD and HDD, suggesting that HDD may influence CKD progression indirectly via interspecies microbial interactions. In addition, SCFA analysis highlighted hexanoic acid was negatively associated with Clostridium XI and Phascolarctobacterium, two CKD-related genera responsive to HDD. This study demonstrated that HDD elicit distinct gut microbiota responses in CKD rats by modulating unique microbial markers and SCFAs.

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Build a high-end R&D platform for traditional Chinese medicine and promote innovative research on the integration of traditional Chinese and Western medicine: introduction to Hengqin Laboratory

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Abstract:

The Hengqin Laboratory was approved by the Guangdong Provincial People's Government in December 2023, with the Cooperation Zone and Zhuhai City as the main construction body, Guangzhou University of Chinese Medicine and Guangdong Academy of Traditional Chinese Medicine (Guangdong Provincial Hospital of Traditional Chinese Medicine) as the main participating units, and major universities, research institutes and pharmaceutical enterprises in the Guangdong-Hong Kong-Macao Greater Bay Area participating in the construction.

Hengqin Laboratory is committed to integrating and applying multidisciplinary advanced technology to cultivate new quality productivity of Chinese medicine, empowering scientific and technological innovation of Chinese medicine, promoting the transformation of clinical diagnosis and treatment mode of Chinese medicine and the improvement of treatment value and level, promoting the Chinese medicine science and technology industry to a higher level, promoting the construction of a highland of traditional Chinese medicine in the Guangdong-Hong Kong-Macao Greater Bay Area, and promoting the moderate diversification of Macao's economic development.

Hengqin Laboratory focuses on building seven centres and eight platforms. Four original science and technology platforms have been built, one is the Hengqin Large Model of traditional Chinese medicine, which gathers more than 100 billion characters of traditional Chinese and Western medicine knowledge texts and clinical diagnosis and treatment data; The second is the "I.D.E.A Platform" for the research and development of new Chinese medicines, which is the world's first Intelligent, Digital, Engineered and Automated intelligent platform for the creation of new Chinese medicines; The third is the "zero magnetic" traditional Chinese medicine syndrome diagnosis equipment development platform, which uses quantum extremely weak magnetic measurement technology for medical-engineering cross-research on TCM "syndrome" diagnosis, realising the objectification and standardisation of TCM "syndrome" diagnosis, and promoting the equipment and digitisation of TCM diagnosis and treatment technology; The fourth is the human immune defence system development platform, which uses big data and artificial intelligence technology to fully integrate the multi-dimensional immune response and defence chain of traditional Chinese medicine and modern medicine in the human body to deal with biosecurity threats, and form a deep correlation database of pathogenic microorganisms and human biological information.

PT109 promotes neurogenesis in PC12 cells via p38 pathway activation: therapeutic potential for neurological diseases

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Abstract:

Growing evidence from neuroimaging and ostmortem studies has suggested that severe mood disorders, traditionally viewed as neurochemical imbalances, has been closely associated with impairments in neuronal structural plasticity. PT109 was previously reported as a multi-kinase inhibitor that targets JNK and other kinases that are related to anti-inflammatory, antioxidant, neurogenic, and synaptogenic processes. Here, we investigated the role of PT109 in promoting neurogenesis through PC12 cell model and its underlying mechanisms, aiming to provide new insights of PT109 as potential treatment of neurological diseases. As a result, our *in vitro* experiments demonstrated that PT109 significantly enhanced neuronal growth and differentiation in PC12 cells, accompanied by the upregulation of NF200 expression in luciferase assay. Mechanistic studies further revealed that a p38 inhibitor reversed the pro-neurogenic effects of PT109, indicating the critical regulatory role of the p38 signaling pathway in this process. Furthermore, we conducted a western blot analysis and identified that PT109 increased p38 phosphorylation, thereby activated downstream NF-κB and CRE signaling pathways. Taken together, these results showed that PT109 was able to promote neurogenesis in cell models and therefore enhance neural regeneration, suggesting that the novel molecule could be considered as a therapeutic candidate against neuronal diseases.

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