

**The 22nd International Postgraduates Symposium
on Chinese Medicine (IPSCM)**

第二十二屆國際研究生中醫藥研討會

Programme Book

會議手冊

Hong Kong Convention and Exhibition Center
香港會議展覽中心

August 15, 2026 (Onsite & Online Symposium)



Joint-organisers:



WELCOME MESSAGE

Dear participants,

On the occasion of the 22nd International Postgraduates Symposium on Chinese Medicine (IPSCM), on behalf of the Organizing Committee, I would like to extend our warmest welcome and most sincere greetings to all students and friends. Regardless of where you come from or which field you represent, our gathering here today, driven by a shared vision, is the perfect embodiment of the conference's core spirit: “Communication, Collaboration, and Innovation”.

We understand that in an era of rapid change, only through open dialogue and cross-disciplinary collaboration can we push the boundaries of our understanding and generate truly valuable solutions. This conference has provided a platform for graduate students from different research aspects and countries to exchange ideas, and has sparked new inspiration through the exchange of ideas.

We deeply honor to invite more than 100 outstanding young scientists and friends from Hong Kong, Macau, Mainland China, Australia, Bangladesh, Indonesia, Malaysia, Myanmar, Pakistan, Serbia, Singapore, South Korea, Sri Lanka, Thailand, Vietnam, and other countries to present their research findings—including oral and poster presentations. This handbook contains the abstracts submitted by the students to facilitate the academic exchange among students.

As the convener of the Organizing Committee and leader of this year's symposium, I would like to express my sincere appreciation to all members for the time and effort you have devoted to this event. I would like to thank your contributions to this event to make it was able to take place smoothly.

We would like to extend our special gratitude to the MCMIA Foundation, the Hong Kong Trade Development Council, the Chinese Medicine Development Fund, and other supporting organizations and partners. Their collaboration has been instrumental in bringing the 22nd IPSCM to life. We also thank all participating institutions of higher education—your strong support was the foundation for the success of this conference.

I wish this conference complete success! May you all gain insights, connect with like-minded colleagues, and join hands to breathe new life into the development of Chinese Medicine. Thank you once again for joining us, and I hope you all have a fulfilling and wonderful time here!

Yours truly,

Prof. LIN Zhixiu

Convener, Academic Advisory Board of the 22nd IPSCM

Director and Professor, School of Chinese Medicine, The Chinese University of Hong Kong

ACKNOWLEDGEMENTS

The Organizing Committee of the 22nd International Postgraduates Symposium on Chinese Medicine would like to express its sincere gratitude to the following institutions and sponsors for their generous support, which made the successful hosting of this symposium possible (listed in alphabetical order, in no particular order):

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PROGRAMME

Date August 15, 2026

Time:08:30-13:20

Venue: Room N101

Time	Event	
08:30-09:10	Registration	
09:15-09:30	The 22 nd IPSCM Opening Ceremony	
09:30-09:40	“Vincent & Lily Woo Fellowship in Memory of Dr Albert Wong endowed by Vincent & Lily Woo Foundation” Award Presentation Ceremony - Opening Speech by Mr. Harry Yeung Chairman of MCMIA Foundation	
09:40-10:00	Presentations by 2025 Fellowship Recipients (LIN Ting Syuan & ZHANG Xueting)	
10:00-10:13	CHEN Jiayi	Guttiferone K induces apoptosis of quiescent prostate cancer cells via mitophagy-mediated downregulation of MRPS34 <i>School of Pharmacy, Shanghai University of Traditional Chinese Medicine, Chinese Mainland</i>
10:13-10:26	Chae-Yeon Kang	Multi-Target Therapeutic Effects of Coptidis Rhizoma in Obesity, Dyslipidemia, and Type 2 Diabetes: Translational evidence from, In Silico, In Vivo, and Meta-Analysis studies <i>Department of Clinical Korean Medicine, Kyung Hee University, Korea</i>
10:26-10:39	REN Zhengyu	<i>Hericium erinaceus</i> Mycelium Polysaccharide Alleviates Spontaneous Ulcerative Colitis in Monkeys by Enhancing IPA-Mediated Macrophage Efferocytosis via Lysosomal Regulation <i>Institute of Chinese Medical Sciences, University of Macau, Macau</i>
10:39-10:52	LIANG Fuchao	Exosome-Enabled Oridonin-Based Bridged PROTACs for Targeted Androgen Receptor Degradation in Androgenetic Alopecia <i>School of Chinese Medicine, Hong Kong Baptist University, Hong Kong</i>
10:52-11:05	Wan-Jung CHENG	Cytochrome P450 Interactions Between Cardioprotective Chinese Herbal Medicines and Antiretroviral Drugs: A Systematic Review of In Vivo Evidence <i>School of Health and Biomedical Sciences, Royal Melbourne Institute of Technology (RMIT) University, Australia</i>
11:05-11:20	Break & Poster Session (N106-N108)	
11:20-11:33	NG Yan Jie Chester	Herb-Drug Interactions in Integrative Care: From Active Surveillance to Hypersensitivity, Diagnosis, and Policy <i>School of Biological Sciences, Nanyang Technological University, Singapore</i>
11:33-11:46	Tran Thi Hong Ngai	Gastroprotective Effects of Da Khoi Cot, A Traditional Vietnamese Polyherbal Decoction, Against Indomethacin-Induced Gastric Ulcer in Wistar rats <i>Vietnam University of Traditional Medicine, Vietnam</i>
11:46-11:59	LI Xiaofang	Screening and Characterization of a Novel Skeletal Muscle-Targeting Aptamer for Precise Delivery of Triptolide in Traditional Chinese Medicine Therapy of Muscle Inflammation <i>School of Chinese Medicine, The Chinese University of Hong Kong, Hong Kong</i>
11:59-12:12	LIU Feiyang	Pulsatilla Decoction Granules Ameliorate Ulcerative Colitis by Activating the CTCF/VDR/GPX4 Pathway via the Gut Microbiota-C15:0 Axi <i>School of Chinese Medicine, Guangzhou University of Chinese Medicine, Chinese Mainland</i>
12:12-12:25	Aleksandra Mladenovic	Food as Medicine: Traditional Fermented Foods as Dietary Interventions for Neuroinflammation and Healthy Ageing <i>Mladenovic Institute for Biological Research, University of Belgrade, Serbia</i>
12:25-12:40	Break	
12:40-13:00	Award Presentation Ceremony	

Number	Presenter	Title
O-01	CHEN Jiayi <i>Shanghai University of Traditional Chinese Medicine</i>	Guttiferone K induces apoptosis of quiescent prostate cancer cells via mitophagy-mediated downregulation of MRPS34
O-02	Chae-Yeon Kang <i>Kyung Hee University, Korea</i>	Multi-Target Therapeutic Effects of Coptidis Rhizoma in Obesity, Dyslipidemia, and Type Diabetes: Translational evidence from, In Silico, In Vivo, and Meta-Analysis studies
O-03	REN Zhengyu <i>University of Macau</i>	<i>Hericium erinaceus</i> Mycelium Polysaccharide Alleviates Spontaneous Ulcerative Colitis in Monkeys by Enhancing IPA-Mediated Macrophage Efferocytosis via Lysosomal Regulation
O-04	LIANG Fuchao <i>Hong Kong Baptist University</i>	Exosome-Enabled Oridonin-Based Bridged PROTACs for Targeted Androgen Receptor Degradation in Androgenetic Alopecia
O-05	Wan-Jung CHENG <i>Royal Melbourne Institute of Technology (RMIT) University, Australia</i>	Cytochrome P450 Interactions Between Cardioprotective Chinese Herbal Medicines and Antiretroviral Drugs: A Systematic Review of In Vivo Evidence,
O-06	NG Yan Jie Chester <i>Nanyang Technological University, Singapore</i>	Herb–Drug Interactions in Integrative Care: From Active Surveillance to Research, Clinical Practice, and Governance,
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O-09	LIU Feiyang <i>Guangzhou University of Chinese Medicine</i>	Pulsatilla Decoction Granules Ameliorate Ulcerative Colitis by Inhibiting Ferroptosis through Activation of the CTCF–VDR–GPX4 Pathway via the Gut Microbiota–C15:0 Metabolic Axis
O-10	Aleksandra Mladenovic <i>University of Belgrade, Serbia</i>	Food as Medicine: Traditional Fermented Foods as Dietary Interventions for Neuroinflammation and Healthy Ageing
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B-02	YUAN Wenli <i>The Chinese University of Hong Kong</i>	AC01 Enhancing Lymphatic Function and Reducing Inflammation and Fibrosis in Experimental Models of Lymphatic Dysfunction
B-03	LIANG Yuting <i>The Chinese University of Hong Kong</i>	A TCM Herbal Formula Combined with Mechanical Vibration for Managing Sarcopenia
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X-13	WANG Jingwen <i>Shanghai University of Traditional Chinese Medicine</i>	Clinical effectiveness and safety of combined acupuncture-medicine anesthesia for cesarean delivery: a systematic review and meta-analysis
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(B) Biological activities and mechanism study

(C) Clinical trial

(H) Herbal resources

(P) Phytochemistry

(Q) Quality control

(X) Others

Guttiferone K induces apoptosis of quiescent prostate cancer cells via mitophagy-mediated downregulation of MRPS34

藤黄酮 K 调控线粒体自噬下调 MRPS34 诱导静止期前列腺癌细胞凋亡

Jiayi CHEN, Mengfan LIU, Xue JIANG, Zhichao XI, Hongxi XU

School of Pharmacy, Shanghai University of Traditional Chinese Medicine

Background Disease recurrence remains a major clinical challenge in prostate cancer and is frequently associated with metastatic progression and poor prognosis. A subpopulation of chemotherapy-tolerant quiescent cancer cells (QCCs) can survive cytotoxic treatment in a dormant state and subsequently re-enter the cell cycle, thereby driving tumor relapse. Eliminating QCCs before their reactivation may therefore represent an effective strategy for preventing prostate cancer recurrence. Guttiferone K (GUTK), a natural compound isolated from *Garcinia yunnanensis* H. H. Hu, has previously been shown to selectively eliminate QCCs. The underlying mechanism remains unclear. This study aimed to elucidate how GUTK induced death of QCCs and to evaluate its potential as a therapeutic agent for preventing tumor recurrence.

Method Quiescent prostate cancer cell models were established by serum deprivation and contact inhibition. Cell death, apoptosis and mitochondrial membrane potential were evaluated by flow cytometry, JC-1 staining and Western blotting. Proteomic analysis was performed to identify candidate proteins involved in the response to GUTK. The functional role of mitochondrial ribosomal protein S34 (MRPS34) was assessed using lentiviral knockdown and overexpression models in vitro and in a quiescent PC-3 xenograft model. Autophagy and mitophagy were examined using pharmacological modulators, mitochondrial fractionation, Western blotting, immunofluorescence and mito-Keima assays. The anti-recurrence efficacy of GUTK was further evaluated in a docetaxel-treated DU145 xenograft model.

Results GUTK induced mitochondrial membrane depolarization and apoptosis in quiescent prostate cancer cells in a time- and dose-dependent manner, accompanied by increased expression levels of cleaved caspase-9, cleaved caspase-3 and cleaved PARP, as well as reduced Bcl-2 expression. Proteomic analysis identified MRPS34 as a markedly downregulated protein following GUTK treatment. Lower MRPS34 expression was associated with improved patient survival and a reduced risk of recurrence. MRPS34 knockdown enhanced GUTK-induced mitochondrial dysfunction and apoptosis in QCCs, whereas MRPS34 overexpression attenuated these effects. Consistently, MRPS34 knockdown suppressed tumor regrowth in the quiescent PC-3 xenograft model. Mechanistically, GUTK activated autophagy, as indicated by reduced p62 expression. Autophagy inhibitor chloroquine attenuated GUTK-induced MRPS34 downregulation and apoptosis, whereas autophagy inducer Torin-1 enhanced these effects. GUTK also promoted PINK1/Parkin-mediated mitophagy, as evidenced by increased mitochondrial PINK1 and Parkin levels, reduced mitochondrial MRPS34 abundance, decreased expression of MFN1, MFN2 and TOM20, increased mitochondria-lysosome colocalization and enhanced mito-Keima fluorescence signals. Pharmacological inhibition of mitophagy with AC220 attenuated these effects. In the docetaxel-treated DU145 xenograft model, GUTK markedly delayed tumor relapse and significantly prolonged overall survival.

Conclusion GUTK induces apoptosis in quiescent prostate cancer cells by promoting PINK1/Parkin-mediated mitophagy and the associated downregulation of MRPS34. In addition, GUTK suppresses post-chemotherapy tumor recurrence and prolongs survival in vivo. These findings identify mitophagy-associated MRPS34 depletion as a potential vulnerability of QCCs

and support the further development of GUTK as a therapeutic strategy for preventing prostate cancer relapse.

References

1. Xi Z, Yao M, Li Y, et al. Guttiferone K impedes cell cycle re-entry of quiescent prostate cancer cells via stabilization of FBXW7 and subsequent c-MYC degradation. *Cell Death Dis.* 2016;7(6):e2252.

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Multi-Target Therapeutic Effects of *Coptidis Rhizoma* in Obesity, Dyslipidemia, and Type Diabetes: Translational evidence from, *In Silico*, *In Vivo*, and Meta-Analysis studies

黄连对肥胖、血脂异常及 2 型糖尿病的多靶点治疗作用：

基于计算机模拟、体内实验与荟萃分析的转化医学证据

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Introduction Obesity, dyslipidemia, and type 2 diabetes mellitus form an interconnected pathogenic cluster driven by adipose inflammation, disrupted lipid homeostasis, and systemic insulin resistance. Although *Coptidis Rhizoma* (CR) and its primary constituent, berberine, have emerged as promising metabolic regulators^{1, 2} and their cellular mechanisms in obesity-induced inflammation have been previously characterized³, evaluating their comprehensive therapeutic value demands an integrated approach bridging clinical reality with biological plausibility. To address the translational gap of traditional reviews, this study establishes a robust, three-stage framework vertically integrating *in silico* network pharmacology, *in vivo* experimental validation, and a systematic meta-analysis to investigate the multi-target therapeutic effects of CR in metabolic dysfunction.

Methods To achieve this, a comprehensive three-stage methodology was applied. First, an *in silico* network pharmacology approach was applied to identify overlapping targets between berberine and disease-related genes, followed by pathway enrichment and molecular docking analyses. Second, these computational predictions were validated through an *in vivo* experiment using C57BL/6 mice fed a 60% high-fat diet (HFD) for 16 weeks, with oral administration of CR extract (200 or 400 mg/kg/day) or metformin (200 mg/kg/day) during the final 10 weeks. Third, to scale these mechanistic findings into clinical relevance, a systematic review and meta-analysis of 19 randomized controlled trials (RCTs) evaluating CR-containing formulations was conducted.

Results The integrated results systematically demonstrated the multi-target efficacy of CR. Mechanistically, *in silico* network pharmacology identified major common hub targets—including *PIK3CA*, *HTR6*, *JAK2*, *MAOA*, and *PARP1*—directly associated with lipid metabolism, inflammatory signaling, and PI3K-Akt/MAPK cascades, confirmed by stable molecular docking binding affinities. Experimentally, *in vivo* validation proved that CR systematically alleviated HFD-induced dysfunction by suppressing obesity-related phenotypes (body weight, liver weight, fat pad mass), optimizing dyslipidemia (serum cholesterol, free fatty acids), and attenuating glycemic dysfunction (OGTT areas under the curve, fasting insulin, HOMA-IR). Crucially, CR suppressed adipose tissue macrophage (ATM) infiltration, decreasing inflammatory CD11c⁺ M1 ATMs while increasing anti-inflammatory CD206⁺ M2 ATMs, alongside downregulating inflammatory and chemokine genes (TNF- α , F4/80, CCL2, CCL4, CCL5). Clinically, the meta-analysis validated these findings, demonstrating that CR significantly improved key metabolic parameters, highlighted by marked reductions in primary outcomes—body weight, LDL-C, and HbA1c—alongside broader optimizations in overall lipid profiles and glycemic control.

Conclusion This study provides a definitive translational trajectory that moves from virtual screening to preclinical validation, and ultimately to clinical verification. By uncovering the precise molecular rationale of berberine and validating its systemic anti-inflammatory and metabolic efficacy across organismal and clinical levels, this integrated framework firmly establishes the systems-level therapeutic potential of CR. These findings offer robust scientific justification for the clinical application of CR and berberine as multi-target interventions for

complex metabolic disorders.

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***Hericium erinaceus* Mycelium Polysaccharide Alleviates Spontaneous Ulcerative Colitis in Monkeys by Enhancing IPA-Mediated Macrophage Efferocytosis via Lysosomal Regulation**

猴头菇菌丝体多糖调控 IPA-巨噬细胞溶酶体-胞葬轴改善溃疡性结肠炎

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The lack of effective therapies for inflammatory bowel disease (IBD) represents a major unmet clinical need. Most preclinical models rely on chemically induced acute colitis with limited human relevance. Here we utilized a spontaneous ulcerative colitis (UC) monkey model that closely recapitulates human disease, characterized by insufficient macrophage efferocytosis and typical UC-like histological changes in the colon. Serum metabolomics revealed a marked decrease of the gut microbial metabolite indole-3-propionic acid (IPA) in UC monkeys compared to healthy controls, and metagenomics confirmed that IPA-producing *Limosilactobacillus*__t__SGB7095 was also reduced. Remarkably, oral administration of *Hericium erinaceus* mycelium polysaccharide (HMP), a traditional Chinese medicinal fungus-derived polysaccharide, significantly restored IPA levels and the abundance of IPA-producing bacteria.

Mechanistically, although IPA has been previously reported to show therapeutic efficacy via T-cell modulation, our findings challenge this established mechanism. We observed that IPA retained its protective effect in Rag1 knockout (KO) mice, ruling out T-cell dependence. More importantly, IPA efficacy was abolished upon macrophage depletion, identifying macrophages as indispensable. In vitro efferocytosis assays demonstrated that IPA robustly enhanced macrophage efferocytosis by specifically regulating lysosomal function. This finding was further validated in vivo using an efferocytosis-deficient MerTK KO mouse model. Consequently, IPA treatment increased the efferocytosis-driven production of pro-resolution cytokines IL-10 and TGF- β . HMP-conditioned medium (enriched in IPA) recapitulated the efferocytosis-enhancing effect.

Taken together, this study delineates a novel lysosomal-dependent pathway by which a TCM-derived polysaccharide (HMP) boosts endogenous IPA to restore macrophage efferocytosis and intestinal homeostasis in a spontaneous UC model with high human relevance. Our findings lay the groundwork for pioneering therapies targeting the microbiota–IPA–efferocytosis axis in IBD.

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Exosome-Enabled Oridonin-Based Bridged PROTACs for Targeted Androgen Receptor Degradation in Androgenetic Alopecia

基于外泌体递送的冬凌草甲素桥联 PROTAC 用于雄激素受体靶向降解治疗雄激素脱发

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Androgenetic alopecia (AGA) is the most prevalent form of hair loss, yet current therapies remain limited by variable efficacy and poor long-term outcomes¹. Aberrant androgen receptor (AR) signaling in dermal papilla cells drives hair follicle miniaturization and hair cycle dysregulation, but conventional AR-targeted strategies mainly inhibit AR activity rather than eliminate AR protein². Proteolysis-targeting chimeras (PROTACs) represent an emerging strategy for targeted protein degradation, but their unfavorable pharmacokinetic properties and limited bioavailability hinder clinical translation³. Herein, we developed a Chinese medicine-driven, oridonin-derived bridged PROTAC platform and combined it with a mesenchymal stem cell-derived exosome (MSC-Exo) delivery system for targeted AR protein degradation^{4,5}. Through rational molecular design and structure-activity relationship analysis, we established a focused library of oridonin-derived bridged PROTACs and identified OAT-01 as the lead candidate with the most potent AR-degrading activity. OAT-01 was subsequently loaded into MSC-Exo to generate the nanotherapeutic formulation EXO@TAC. EXO@TAC exhibited efficient cellular uptake, sustained release, and prolonged AR degradation. It promoted human dermal papilla cell proliferation, suppressed apoptosis, and restored Wnt/ β -catenin signaling under androgenic stress. In the AGA mouse model, EXO@TAC enhanced hair regeneration, improved follicular architecture, and remodeled the perifollicular microenvironment with a favorable biosafety profile. By integrating traditional Chinese medicine-derived natural products with targeted protein degradation technology, this study provides a novel and mechanistically distinct therapeutic strategy for AGA, with potential translational value for improving long-term disease management and reducing the psychosocial burden associated with hair loss.

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Cytochrome P450 Interactions Between Cardioprotective Chinese Herbal Medicines and Antiretroviral Drugs: A Systematic Review of In Vivo Evidence

心血管保护作用中药与抗逆转录病毒药物的细胞色素 P450 相互作用： 体内研究的系统综述

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Introduction With increasing effectiveness of antiretroviral therapy (ART), people living with HIV are experiencing longer life expectancy alongside a growing burden of comorbidities, particularly cardiovascular disease^{1,2}. Chinese herbal medicine is frequently co-administered in this population; however, potential herb–drug interactions remain a clinical concern due to modulation of cytochrome P450 (CYP450) enzymes, particularly for drugs with narrow therapeutic indices.

Methods A systematic review of in vivo studies was conducted using PubMed, Embase, Scopus, and CNKI up to March 2025. Studies investigating aqueous extracts of six commonly used Chinese medicinal herbs (*Salvia miltiorrhiza*, *Ligusticum chuanxiong*, *Glycyrrhiza uralensis*, *Angelica sinensis*, *Astragalus membranaceus*, and *Atractylodes macrocephala*) were included. Outcomes included CYP450 enzyme activity, protein expression, mRNA expression, and pharmacokinetic parameters. Study quality was assessed using the SYRCLE risk of bias tool. A structured EMS-CI framework was applied to quantify the direction and consistency of CYP450 modulation across heterogeneous datasets.

Results Three consistent CYP450 modulation patterns were identified across studies: neutral, inhibitory-dominant, and induction-dominant profiles. *Salvia miltiorrhiza* demonstrated predominantly neutral modulation across major CYP isoforms. *Ligusticum chuanxiong* showed consistent inhibitory effects, particularly on CYP2B6 and CYP3A4. *Glycyrrhiza uralensis* demonstrated induction-dominant effects. *Angelica sinensis* exhibited mixed modulation across CYP isoforms. *Astragalus membranaceus* and *Atractylodes macrocephala* showed heterogeneous or limited evidence profiles. CYP3A4 and CYP2B6 were identified as the most consistently affected enzymes across all included studies.

Discussion A substantial proportion of antiretroviral agents, including protease inhibitors, boosted regimens, and selected non-nucleoside reverse transcriptase inhibitors, are metabolized via CYP3A4 and CYP2B6 pathways, whereas nucleoside reverse transcriptase inhibitors and most integrase strand transfer inhibitors demonstrate limited CYP450 dependence. The findings demonstrate that herb–drug interactions are not uniform but follow identifiable pharmacological modulation patterns. Application of the EMS-CI framework enables structured comparison across heterogeneous in vivo evidence and supports the development of a pathway-based risk stratification model for predicting herb–drug interactions. This framework may assist in guiding safer co-administration strategies, particularly for drugs with narrow therapeutic indices or high CYP metabolic dependency.

Conclusion Chinese medicinal herbs demonstrate distinct and predictable CYP450 modulation patterns. A pathway-oriented risk stratification approach may improve the safety and precision

of integrating Chinese herbal medicine with antiretroviral therapy in clinical practice.

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Herb–Drug Interactions in Integrative Care: From Active Surveillance to Research, Clinical Practice, and Governance

整合医学中的草药-药物相互作用：从主动监测、研究、临床实践到治理

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The growing global use of herbal medicines alongside conventional Western medicines (WM) has created an urgent need to better understand, detect, and prevent herb–drug interaction-related adverse events. This presentation draws on two of our published studies examining herbal medicine safety from complementary perspectives. The first is a multi-center active surveillance study conducted across Chinese Medicine clinics in Singapore, which found that concurrent Chinese Herbal Medicine (CHM) and WM consumption was common, occurring in 62.65% of screened patients¹. Patients using both CHM and WM were also more likely to report adverse events compared to those using CHM alone, highlighting the importance of structured medication history-taking, active adverse-event screening, and causality assessment in clinical practice. The second paper then examines immediate hypersensitivity reactions to herbal medicines, reviewing IgE-mediated and non-IgE-mediated mechanisms, potential triggers, diagnostic approaches, and regulatory responses². Collectively, these studies show that herb–drug interactions are not only a pharmacological issue, but also a broader clinical and public health challenge. Hence, this presentation will discuss how active surveillance, clinician awareness, pharmacovigilance, and stronger regulation can support safer and evidence-based integration of herbal medicines into modern clinical practice.

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Gastroprotective Effects of Da Khoi Cot, A Traditional Vietnamese Polyherbal Decoction, Against Indomethacin-Induced Gastric Ulcer in Wistar rats

越南传统复方 Da Khoi Cot 对吲哚美辛诱导的 Wistar 大鼠胃溃疡的胃保护作用

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The effective management of gastric ulcers, particularly those induced by non-steroidal anti-inflammatory drugs (NSAIDs), remains challenging due to the adverse effects and relapse associated with conventional therapies. Da Khoi Cot (DKC), a Vietnamese traditional decoction composed of six medicinal herbs, has been used for gastrointestinal disorders, but its efficacy has not been scientifically validated. This study evaluated the gastroprotective effects of DKC in an indomethacin-induced gastric ulcer model in rats. Wistar rats were pretreated orally for 7 days with either DKC (24 or 48 mL/kg/day) or misoprostol (50 µg/kg/day). Gastric ulcers were induced by indomethacin (40 mg/kg). Ulcer severity was assessed macroscopically and histopathologically. MDA, GSH in gastric tissue, TNF-α in serum, as well as AST, ALT, creatinine, and urea levels, were evaluated. DKC at 48 mL/kg/day significantly reduced the ulcer index, and both doses significantly reduced the number of gastric lesions compared to the ulcer control group ($p < 0.05$). Histopathological analysis demonstrated significant improvements in mucosal integrity, with reduced inflammation and hemorrhage. The decoction also produced a marked antioxidant effect, significantly decreasing gastric MDA and increasing GSH levels ($p < 0.05-0.001$). DKC pretreatment also considerably suppressed the indomethacin-induced rise in serum TNF-α ($p < 0.01$). No significant alterations in hepatic or renal function markers were observed. DKC exerts significant gastroprotective effects against indomethacin-induced gastric ulceration while maintaining a favorable safety profile. These results provide the first preclinical evidence supporting DKC's potential as an adjunctive therapy for NSAID-associated gastric ulcers.

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Screening and Characterization of a Novel Skeletal Muscle-Targeting Aptamer for Precise Delivery of Triptolide in Traditional Chinese Medicine Therapy of Muscle Inflammation

新型骨骼肌靶向适配体的筛选与鉴定，及其在中医药治疗肌肉炎症中

精准递送雷公藤甲素的应用

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Skeletal muscle is one of the largest organs in the body and plays critical roles in mechanical activity and metabolism. Chronic myopathies and acute muscle inflammation impose substantial clinical and economic burdens. Although traditional Chinese medicine (TCM) active ingredients, such as triptolide derived from *Tripterygium wilfordii*, exhibit potent anti-inflammatory and immunomodulatory effects on muscle disorders, their clinical application is severely limited by systemic toxicity, non-specific distribution, and insufficient accumulation in skeletal muscle tissues, resulting in suboptimal therapeutic efficacy and dose-dependent adverse effects. These challenges highlight the urgent need for skeletal muscle-specific drug delivery systems to improve the precision and safety of TCM-based therapies.

Aptamers are artificial, short, single-stranded nucleic acids, with unique secondary structures that can recognize and bind to targets. The high specificity, low immunogenicity, and cost-effective synthesis of aptamers make them ideal candidates for skeletal muscle-targeted delivery. In our study, a skeletal muscle-specific aptamer S77 was identified through 14 rounds of cell-SELEX (systematic evolution of ligands by exponential enrichment) against C2C12 myoblasts. After optimization, S77 exhibited a K_d value of 81.54 nM with low cytotoxicity. It effectively bound and internalized into mouse satellite cells, myoblasts, and myotubes.

By integrating S77 with tetrahedral DNA nanostructures (TDNs) as a nanocarrier to load triptolide, the S77-TDN-triptolide system was tested in an LPS-induced acute skeletal muscle inflammation mouse model. Compared with non-targeted formulations, this delivery system significantly decreased the levels of pro-inflammatory cytokines $\text{TNF-}\alpha$ and IL-6, attenuated the decline in forelimb grip strength, reduced muscle histopathological damage, and accelerated tissue recovery.

This study successfully developed a novel skeletal muscle-targeting aptamer S77 with high affinity and specificity. By combining it with TDN nanotechnology for precise delivery

of triptolide, we provide an effective strategy to overcome the limitations of current TCM treatments for muscle disorders, offering a promising platform for safe and efficient precision therapy with strong potential for clinical translation.

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Pulsatilla Decoction Granules Ameliorate Ulcerative Colitis by Inhibiting Ferroptosis through Activation of the CTCF–VDR–GPX4 Pathway via the Gut Microbiota–C15:0 Metabolic Axis

白头翁汤配方颗粒通过调控“肠道菌群–C15:0”代谢轴激活 CTCF–VDR–GPX4 通路

抑制铁死亡改善溃疡性结肠炎

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Background Ulcerative colitis (UC) is a chronic relapsing inflammatory bowel disease with an unclear etiology. Baitouweng Decoction (BTD) has demonstrated definitive therapeutic efficacy in UC. Its granule formulation, Pulsatilla Decoction Granules (PDG), offers advantages in convenient administration, high chemical consistency with standard decoction, and bioequivalence. Accumulating evidence highlights the pivotal role of the gut microbiota and their metabolites in the pathogenesis and resolution of UC¹. Our preliminary research identified the lipid metabolism pathway as a key regulatory axis in BTD-mediated UC treatment, with pentadecanoic acid (C15:0) being the most significantly altered differential metabolite. C15:0 can be synthesized by gut microbiota and may exert protective effects by inhibiting ferroptosis²; however, its precise molecular targets and regulatory mechanisms remain elusive.

Objective This study aims to investigate whether PDG ameliorates UC by modulating the gut microbiota and its metabolite C15:0 to inhibit ferroptosis, and to elucidate the downstream molecular target and regulatory mechanism.

Methods A dextran sulfate sodium (DSS)-induced UC mouse model was established to evaluate the therapeutic effects of PDG. Metagenomic sequencing and gas chromatography-mass spectrometry (GC-MS) were performed to analyze PDG-mediated alterations in key gut microbiota and C15:0 levels. Antibiotic cocktail (ABX) intervention and fecal microbiota transplantation (FMT) were employed to validate the microbiota-dependent action of PDG. The protective effects of *Bacteroides acidifaciens* (B. acidifaciens), *Akkermansia muciniphila* (A. muciniphila), and C15:0 on UC were further assessed, along with the C15:0-producing capacity of these bacterial strains. An erastin-induced ferroptosis model was used to verify the regulatory effect of C15:0 on ferroptosis. Integrative bioinformatics and transcriptomic analyses identified the vitamin D receptor (VDR) as a key target gene, with CTCF predicted as its transcription factor. The functional linkage between CTCF and VDR was established by siRNA-mediated knockdown in NCM460 cells. Efficacy validation was performed in NCM460 human normal colonic epithelial cells using Western blotting (WB), quantitative real-time PCR (qRT-PCR), and immunofluorescence.

Results PDG significantly alleviated DSS-induced colonic inflammation, as evidenced by improved disease activity index (DAI), reduced histopathological damage, and restored intestinal barrier function. Metagenomic sequencing identified B. acidifaciens and A. muciniphila as the core gut microbiota modulated by PDG. GC-MS analysis revealed that PDG treatment significantly increased colonic C15:0 levels, and both bacterial strains possessed the capacity to synthesize C15:0. C15:0 effectively suppressed the release of pro-inflammatory cytokines and inhibited ferroptosis both in vivo and in vitro. VDR was identified and validated as the key target gene, and CTCF was found to specifically bind to the VDR promoter region. Notably, C15:0 treatment significantly upregulated the expression of CTCF, VDR, and its downstream target glutathione peroxidase 4 (GPX4).

Conclusion PDG alleviates UC by enriching *B. acidifaciens* and *A. muciniphila*, thereby promoting the synthesis of their metabolite C15:0. This metabolite, in turn, activates the CTCF-VDR-GPX4 signaling axis, inhibits ferroptosis in colonic epithelial cells, and restores intestinal barrier integrity.

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Food as Medicine: Traditional Fermented Foods as Dietary Interventions for Neuroinflammation and Healthy Ageing

药食同源：传统发酵食品作为针对神经炎症与健康衰老的膳食干预措施

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Background Traditional medical systems have long recognised the therapeutic role of food in maintaining health and preventing disease. Contemporary biomedical research increasingly supports this concept, particularly regarding fermented foods, which contain bioactive metabolites and beneficial microorganisms capable of modulating immune and metabolic functions. Chronic inflammation/neuroinflammation is major drivers of ageing, frailty, cognitive decline, and numerous chronic disorders, underscoring the need for safe, preventive, and sustainable interventions.

Methods We investigated the biological effects of two traditional fermented food products. The first product (FF1), a naturally fermented fruit-based preparation, was evaluated in murine models of lipopolysaccharide (LPS)-induced inflammation and ageing, as well as in a pilot human intervention study. Behavioural, cognitive, and frailty-related outcomes were assessed following prolonged consumption. In parallel, sauerkraut brine (SB), a traditional fermented cabbage product rich in lactic acid bacteria, was examined in acute and repeated models of LPS-induced neuroinflammation in mice, assessing inflammatory, oxidative stress, and behavioural parameters.

Results FF1 significantly attenuated LPS-induced inflammation and improved behavioural and cognitive performance in aged mice. Moreover, three months of FF1 consumption reduced frailty scores in human participants, suggesting beneficial effects on healthspan. SB markedly reduced neuroinflammatory responses, decreasing the expression of pro-inflammatory cytokines in the prefrontal cortex following LPS challenge and preserving antioxidant defences during repeated inflammatory exposure. Behavioural analyses further suggested attenuation of anxiety-like behaviour in SB-treated animals.

Conclusions Two traditional fermented food products demonstrated benefits on systemic inflammation, neuroinflammation, oxidative stress, cognition, behaviour, and frailty. These findings provide experimental and preliminary clinical evidence supporting the concept of “food as medicine” and highlight fermented foods as accessible, culturally rooted, and non-pharmacological interventions for promoting resilience and healthy ageing. The results further illustrate how traditional dietary practices can be integrated with modern evidence-based approaches to support long-term health and disease prevention.

MAD4-LGALS9 signaling promotes atherosclerosis progression through endothelial dysfunction

內皮細胞SMAD4-LGALS9 軸介導內皮功能障礙促進
動脈粥樣硬化的機制研究

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Abstract:

Background: Atherosclerosis is a major global health burden linked to endothelial dysfunction. The SMAD signaling pathway regulates vascular inflammation. Endothelial-specific SMAD4 knockout reduces vascular inflammation in hypertensive mice. However, targeting SMAD4 directly is challenging, so studying its downstream mechanisms is crucial. Galectin-9 (Gal-9, encoded by *LGALS9*) has dual roles in immune modulation. Understanding how SMAD4 regulates LGALS9 in endothelial cells and how the SMAD4-LGALS9 axis affects endothelial function and inflammation stress will provide new insights into AS pathogenesis and therapeutic targets.

Results: Under cardiometabolic risk factors (TNF- α , ox-LDL), the SMAD4-LGALS9 axis is activated in endothelial cells. SMAD4 translocates to the nucleus to promote Gal-9 expression. Dual-luciferase assays confirm SMAD4 directly binds the *LGALS9* promoter to activate transcription. Endothelium removal reduces vascular Gal-9, and TNF- α only enhances Gal-9 in endothelium-intact vessels. Gal-9 treatment impairs endothelial function by upregulating proinflammatory mediators, inducing enrichment of TNF, NF- κ B, NOD-like receptor, and IL-17 pathways as revealed by RNA-seq, increasing ROS generation and monocyte adhesion, and suppressing NO production along with endothelium-dependent relaxation. Antagonizing Gal-9 with lactose or inhibiting its receptor TIM-3 improves endothelial function. Endothelial-specific knockdown of *LGALS9* inhibits HCD-induced atherosclerosis in ApoE^{-/-} mice.

Conclusion: The SMAD4-LGALS9 axis drives atherosclerosis progression through endothelial dysfunction. SMAD4 directly activates LGALS9 transcription. Endothelial-derived Gal-9 promotes vascular dysfunction by exacerbating inflammation, oxidative stress, and monocyte adhesion while suppressing NO. Targeting Gal-9 or TIM-3 effectively restores endothelial function. These findings

may advance the understanding of atherosclerosis pathogenesis and provide a foundation for novel therapeutic strategies.

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AC01 Enhancing Lymphatic Function and Reducing Inflammation and Fibrosis in Experimental Models of Lymphatic Dysfunction

AC01 增強淋巴功能及減少實驗模型中的炎症和纖維化

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Abstract:

Introduction Lymphatic dysfunction is a functional impairment of the lymphatic system which can reduce quality of life (Shih et al., 2009). Our previous studies demonstrated that the traditional Chinese medicine (TCM) herbal extract AC01 has exerted anti-inflammatory and anti-fibrotic activities, suggesting its potential as a therapeutic agent for managing lymphedema.

Methods The raw herbs in the AC01 formula were authenticated according to the Chinese Pharmacopoeia. The anti-inflammatory efficacy of AC01 was evaluated *in vitro* using the murine RAW264.7 macrophage cell line, while its lymphangiogenic and anti-fibrotic functions were examined using human lymphatic endothelial cells (HLECs). *In vivo*: a mouse tail lymphedema model was established in Balb/c mice. **Results** MTT assays demonstrated that AC01 and its components exhibited favorable safety profiles. In the NO assay, NO levels progressively decreased with increasing AC01 concentrations of RAW264.7 cells, compared to the lipopolysaccharide (LPS)-treated cells. Furthermore, AC01 exhibited anti-inflammatory properties in LPS-stimulated RAW 264.7 cells by dose-dependently suppressing the secretion of TNF- α , IL-6, and CCL2. Preliminary results of tube formation and scratch assays In HLECs revealed that AC01 promoted lymphangiogenesis and enhanced cell migration. Preliminary *in vivo* data indicated that AC01 treatment reduced tail volume and alleviated subcutaneous edema compared to the control mice (all $P < 0.05$). **Conclusion** AC01 exhibits significant anti-inflammatory and pro-lymphangiogenic effects, supporting its potential as a novel therapeutic strategy for lymphedema.

Acknowledgement: The study is supported by funding from C.C.Wu Cultural Foundation.

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A TCM Herbal Formula Combined with Mechanical Vibration for Managing Sarcopenia

結合中藥方劑與機械振動治療肌少症

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Abstract

Introduction

Sarcopenia, characterized by age-related loss of muscle strength, mass, and function, is a growing concern due to aging populations. There are currently no approved drugs that specifically target sarcopenia. This study aimed to develop a herbal formula (BCCA01) for its management.

Methods

In vitro: MTT assay assessed cytotoxicity and proliferation. Angiogenesis was evaluated in HUVECs via tube formation and scratch assays. Inflammation was examined in RAW264.7 macrophages by NO and ELISA. Effects on proliferation (BrdU), myotube formation, and ATP were tested in HSkMCs.

In vivo: 6–8 and 8–10-month-old SAMP8 mice received oral BCCA01 for 8 weeks. Grip strength, DXA lean mass, serum biomarkers, and histology/immunohistochemistry were evaluated.

Results

In vitro: BCCA01 was non-toxic up to 2000 µg/ml in all cells. At 250 µg/ml, it enhanced HUVEC tube formation at 8,12,24h ($p<0.0001$), increasing meshes area (13.8-30.8%), nodes (31.8-54.0%), junctions (27.3-42.6%), and total length (10.9-18.7%) at 8 and 12h. Scratch assays confirmed maximal migration at 250 µg/ml. NO decreased dose-dependently, most markedly at 2000 µg/ml. ELISA showed dose-dependent reductions in TNF- α , IL-6, and MCP-1, with IL-6 most reduced. In HSkMCs, BCCA01 (0-200 µg/ml) dose-dependently promoted proliferation. MYOG increased from 25% (day1) to 93.9% (day7). Seahorse assay revealed dose-dependent increases in maximal respiration and spare capacity, supporting BCCA01 as a mitochondrial enhancer.

In vivo: All treatment groups increased grip strength versus control. After 8 weeks, high-concentration BCCA01 plus vibration significantly increased grip strength by 10.4% ($p<0.05$). DXA lean mass, serum biomarkers, and histology/immunohistochemistry analyses are ongoing.

Discussion

BCCA01 enhances mitochondrial function, reduces inflammation, and promotes muscle proliferation *in vitro*. Combined with vibration, it improves grip strength in

vivo, suggesting pharmacological-mechanical synergy.

Conclusion

BCCA01 exhibits anti-inflammatory, pro-proliferative, and mitochondria-enhancing effects. Combined with vibration, it significantly increases grip strength, supporting a dual-mechanism strategy for sarcopenia.

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**Bruceine A induced cuproptosis is a novel strategy to enhance the efficacy of
gemcitabine in the treatment of pancreatic cancer**

**鴉膽子素 A 誘導的銅死亡是一種增強吉西他濱治療胰腺癌療效的新
策略**

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Abstract:

Background: Pancreatic ductal adenocarcinoma (PDAC) has become the third leading cause of cancer-related deaths. Gemcitabine (GEM) is the first-line treatment for PDAC. However, due to its resistance, the therapeutic efficacy is relatively limited^[1]. Therefore, it is an urgent need for new treatment strategies to benefit the patients with PDAC. Bruceine A (BA), a natural compound derived from the seeds of *Brucea javanica*, has garnered attention for its promising medicinal properties, but its efficacy in treating PDAC remains to be elucidated^[2]. Copper (Cu) is an indispensable trace element for the human body. Recent studies have shown that excessive copper can induce conventional oxidative stress responses and trigger cell death through specific mechanisms^[3]. The aim of this study is to investigate whether BA can reduce resistance to GEM therapy in PDAC by affecting cuproptosis, and to elucidate the underlying molecular mechanisms.

Method: Resistant cell lines Capan-2-GR (CR) and Miapaca-2-GR (MR) were established, and the effects of BA on the viability, migration, invasion and cell apoptosis of these resistant cells were assessed. Utilizing Western blot to analysis the expression of proteins associated with cancer cell resistance and cuproptosis. Detection of cellular reactive oxygen species (ROS) levels by flow cytometry. Immunofluorescence assays were used to detect the mitochondrial membrane potential (MMP) and copper ions within the cells. The orthotopic PDAC mouse model were established and administered the treatment for one month. Tumor growth and changes in Ki67 and DLAT expression were evaluated.

Results: BA treatment notably reduced the viability of drug-resistant cells in a concentration-dependent. Compared with the GEM group, the combination therapy group showed a significantly lower IC₅₀ value for drug-resistant cells and a markedly higher drug resistance reversal index. In addition, compared with the GEM group, the combination group suppressed the expression of proteins associated with cell resistance. Moreover, relative to the group receiving GEM alone, the

combination group exhibited notably elevated intracellular ROS levels increased distinctly, and the copper ion fluorescence intensity also raised. MMP indicates that compared with the GEM group, mitochondrial function was impaired after BA administration, and apoptosis increased. Furthermore, combination administration markedly augmented the expression of cuproptosis proteins in contrast to the GEM group. In vivo experiments further confirmed, combination group reduced tumor size and markedly reduced the number of Ki67-positive cells in the tumor tissues.

Conclusion: BA influences mitochondrial status by adjusting copper homeostasis, increases intracellular ROS accumulation, and thereby induces apoptosis, effectively reversing pancreatic cancer resistance to GEM chemotherapy. As a GEM sensitizer, BA holds great potential for use in combination therapy for treating drug-resistant pancreatic cancer.

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**Alkaloids of *Phellodendri Chinensis* Cortex Exerts Uric Acid-Independent
Renoprotection in Uric Acid Nephropathy via the
PFKFB3-Glycolysis-Macrophage Axis**

**黃柏在尿酸性腎病中通過 PFKFB3-糖酵解-巨噬細胞軸發揮非尿酸依
賴性腎臟保護作用**

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Abstract:

Phellodendri Chinensis Cortex (PCC), a fundamental herb for “clearing heat and drying dampness”, has been traditionally employed as a key therapeutic agent for gout and uric acid nephropathy (UAN), owing to its recognized urate-lowering and nephroprotective properties¹⁻². UAN remains a challenging complication of hyperuricemia, with limited therapeutic options that address renal injury beyond lowering serum uric acid³⁻⁴. Current management often fails to halt inflammation-driven kidney damage, highlighting the need for strategies targeting the underlying pathogenic mechanisms⁵. Therefore, this study aims to elucidate the renoprotective efficacy and mechanism of Alkaloids of *Phellodendri Chinensis* Cortex (APC) in UAN.

In our study, the UAN rats model was established to assess the hypouricemic and nephroprotective effects of APC. APC effectively alleviated renal dysfunction and pathological damage independent of its hypouricemic effect, while metabolomic and transcriptomic analyses revealed that APC primarily influences the glycolysis pathway, identifying PFKFB3 as a key target. In vitro, MSU-stimulated THP-1 macrophages treated with APC were used to evaluate glycolytic reprogramming and polarization. Mechanistically, in vivo and in vitro experiments demonstrated that APC directly inhibits PFKFB3 expression, thereby suppressing macrophage glycolytic reprogramming and M1 polarization. The protective effect weakened after PFKFB3 overexpression. Molecular interaction studies revealed that Berberine (BBR), a key component of APC, binds directly to PFKFB3 with high affinity. Furthermore, Mendelian randomization analysis and clinical serum samples corroborated PFKFB3 as a causal risk factor for renal impairment, showing a significant positive correlation with disease severity.

In conclusion, this study reveals a novel therapeutic axis in which APC mediates renal protection through a mechanism independent of uric acid reduction, specifically by targeting PFKFB3 to regulate the macrophage "glycolysis-polarization" axis. Importantly, this work provides the first evidence elucidating glycolytic reprogramming as a key driver in UAN, as well as the regulatory mechanism of APC in this process. Our work provides a potential novel immunometabolism-based therapeutic strategy for UAN patients who respond poorly to existing urate-lowering therapies or present with concomitant gut microbiota dysbiosis.

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**Acetylursolic Acid Attenuates Ferroptosis in Myocardial Ischemia/Reperfusion
Injury by Inhibiting STING-Mediated Autophagic Degradation of GPX4**

**乙酰熊果酸通过抑制 STING 介导的 GPX4 自噬降解改善心肌缺血再
灌注损伤心肌细胞铁死亡的机制研究**

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Abstract:

Myocardial ischemia/reperfusion (I/R) injury remains a major cause of adverse cardiovascular outcomes worldwide. Ferroptosis, an iron-dependent form of regulated cell death, has been recognized as a critical contributor to myocardial I/R injury. This study investigated the protective effects of 3 β -O-acetylursolic acid (AUA) against myocardial I/R injury and explored the underlying mechanisms associated with ferroptosis.

A mouse myocardial I/R model induced by left anterior descending coronary artery ligation and reperfusion was established to evaluate the cardioprotective effects of AUA in vivo. Bioinformatics analysis and molecular docking were performed to identify potential targets of AUA. In addition, the neonatal rat cardiomyocytes (NRCMs) were used to examine the anti-ferroptotic mechanisms of AUA in vitro. A series of experiments, including immunofluorescence staining, cellular thermal shift assay (CETSA), biochemical analyses and Western blotting, was conducted. AUA significantly alleviated myocardial injury and reduced ferroptosis following I/R challenge. Mechanistic studies revealed that AUA suppressed STING-mediated autophagic degradation of GPX4, thereby maintaining GPX4 expression and limiting ferroptotic cell death. Similar protective effects were observed in NRCMs.

In summary, AUA protects against myocardial I/R injury, at least in part, by inhibiting STING-dependent GPX4 degradation and ferroptosis. These findings highlight the therapeutic potential of AUA and identify the STING/GPX4 pathway

as a promising target for the treatment of myocardial I/R injury.

Keywords: Acetylursolic Acid; STING; ferroptosis; Myocardial ischemia/reperfusion

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**Taohong Siwu Decoction Attenuates Post-Myocardial Infarction Myocardial
Fibrosis by Suppressing the PFKP-Glycolysis Axis**

桃红四物汤通过 PFKP-糖酵解轴抑制心梗后心肌纤维化

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Abstract:

Background: Myocardial fibrosis following myocardial infarction (MI) is a key driver of adverse ventricular remodeling and heart failure. Metabolic reprogramming, especially enhanced glycolysis, plays a critical role in cardiac fibroblast (CF) activation and pathological collagen deposition. Taohong Siwu Decoction (THSWD), a classical blood-activating formula, has documented cardioprotective effects; however, whether it modulates CF glycolysis to mitigate fibrosis remains unknown.

Methods: A mouse MI model was established by permanent ligation of the left anterior descending coronary artery. Mice were randomized to receive THSWD (0.75 or 1.5 g/kg/day), captopril (20 mg/kg/day), or vehicle for 28 days. Cardiac function was assessed by echocardiography, and myocardial fibrosis was evaluated by Masson's trichrome staining, immunohistochemistry, and Western blotting for collagen markers. Glycolytic enzymes (PFKP, HK2, PKM2, LDHA) in the infarcted heart were determined. In vitro, primary neonatal rat CFs were subjected to hypoxia (8 h) and treated with THSWD (15, 30, 60 µg/mL). Cell viability, collagen synthesis, and extracellular acidification rate (ECAR) were measured. PFK enzymatic activity and expression of glycolytic enzymes were detected. PFKP was overexpressed via adenoviral vector to test its necessity. Molecular docking assessed the binding potential of THSWD components to PFKP.

Results: THSWD significantly improved left ventricular ejection fraction and reduced ventricular dilation, cardiac fibrosis, and the heart-weight/body-weight ratio compared with untreated MI mice ($P < 0.01$). PFKP, HK2, PKM2, and LDHA were markedly upregulated in the infarcted myocardium, and THSWD

dose- dependently suppressed their expression. In cultured CFs, hypoxia triggered robust collagen I, fibronectin, and α - SMA expression, accompanied by elevated ECAR and PFK activity. THSWD dose- dependently inhibited CF proliferation, collagen deposition, and glycolysis, without affecting cardiomyocyte viability. Adenoviral overexpression of PFKP reversed the inhibitory effects of THSWD on glycolytic flux, PFK activity, and collagen synthesis, confirming PFKP as a critical target. Molecular docking revealed that several THSWD constituents (e.g., nicotiflorin, benzoylpaeoniflorin, paeoniflorin) could occupy the active pocket of PFKP.

Conclusion: THSWD ameliorates MI- induced cardiac fibrosis and dysfunction by targeting the PFKP- mediated glycolysis axis in CFs. This study unveils a novel metabolic mechanism for THSWD in treating post- MI fibrosis and supports its clinical application for ischemic heart disease.

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D2R-PI3K-OCT2 axis underlies the adipocyte uptake of tetrahydroberberine and its therapeutic effect in obesity

四氫小檗堿經 D2R-PI3K-OCT2 軸被脂肪細胞攝取及其治療肥胖症的作用機制

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Abstract:

Obesity arises from an enduring imbalance in energy consumption that culminates in pathological adipose expansion, ectopic lipid deposition, and chronic low-grade inflammation^{1, 2}. Tetrahydroberberine, the principal reductive metabolite of berberine, displays potent lipid-lowering activity and fat targeting^{3, 4}. Nevertheless, the causal link between adipocyte tetrahydroberberine uptake and its anti-obesity efficacy remains undefined. This study investigates the adipocyte uptake of tetrahydroberberine and its anti-obesity effect against MDI-induced adipocyte hypertrophy in 3T3-L1 cells and high-fat diet-induced obesity in C57BL/6J mice. The results demonstrated that tetrahydroberberine reduced body weight, epididymal fat mass, and perirenal fat mass, while ameliorating pathological changes in the adipose tissue of obese mice. Moreover, tetrahydroberberine ameliorated lipid accumulation and suppressed inflammatory responses in both adipocytes and adipose tissues. These effects were associated with the inhibition of the Dopamine receptor D2 (D2R) /Phosphoinositide 3-kinases (PI3K)/ Protein Kinase B (AKT) signaling pathway, which in turn suppressed leptin-mediated expressions of sterol regulatory sequence binding protein type 1c (SREBP-1C) and peroxisome proliferator-activated receptor γ (PPAR- γ). This study also revealed that tetrahydroberberine primarily enters adipocytes via Organic cation transporter 2 (OCT2). More importantly, tetrahydroberberine's inhibition of the D2R/PI3K axis elevated OCT2 expression, enhancing its uptake by adipocytes. Tetrahydroberberine regulated adipocyte uptake through the D2R-PI3K-OCT2 axis while exerting anti-obesity effects. The findings have implications for the mechanism of tetrahydroberberine's anti-obesity effect, which does not neglect the coupling between tetrahydroberberine's adipocyte uptake and its anti-obesity efficacy.

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Elucidating the mechanism of Coptidis Rhizoma bioactive constituent in ameliorating UC comorbid with anxiety/depression through regulating CXCL9 expression via MDC1 non-canonical transcriptional elongation

基于 MDC1 非经典转录延伸功能调控趋化因子 CXCL9 表达探讨黄连药效物质改善 UC 与焦虑/抑郁共病的作用机制

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Abstract:

Ulcerative colitis (UC) is a chronic nonspecific inflammatory bowel disease classified by the World Health Organization as one of the world's refractory diseases [1]. It is characterized by recurrent bloody diarrhea and abdominal pain, and easily precipitates psychiatric symptoms such as anxiety and depression. A multicenter Chinese study involving 2,478 patients with inflammatory bowel disease (IBD) found that over 58.3% exhibited varying degrees of anxiety and depression, respectively [2]. Currently, combining anti-UC agents with anxiolytic/antidepressant medications yields limited overall efficacy[3], and is frequently accompanied by severe adverse effects, representing an unresolved clinical challenge [4]. Therefore, elucidating the molecular mediators and mechanisms underlying the “gut–brain” crosstalk between UC and emotional disorders, and identifying safe and effective therapeutic agents, to have substantial social and economic benefits.

In this study, we employed the classic dextran sulfate sodium (DSS)-induced colitis combined with behavioral screening to select comorbid anxiety/depression-like behaviors mice, and then evaluated the therapeutic efficacy of oxypalmatine (OPAL), an alkaloid of Coptidis Rhizoma (Huanglian). 9.4T structural magnetic resonance imaging (sMRI) was applied to map brain morphological differences. Colonic and blood–brain barrier integrity, systemic inflammatory status, and cerebral endoplasmic reticulum stress were examined by immunofluorescence, transmission electron microscopy (TEM), and Elisa. Colonic whole-transcriptome profiling, RT-qPCR and ELISA were performed to explore the global effect of OPAL, and the most vital role of chemokines in comorbidity of UC. Colonic single-cell RNA sequencing (scRNA-seq) was integrated to delineate how OPAL regulates the source of CXCL9, as well as the regulatory mechanism of it. Surface plasmon resonance (SPR) and co-immunoprecipitation (Co-IP) were

utilized to validate MDC1 as the target protein regulating CXCL9 and to examine its impact on the interaction with RNA polymerase II (RNAPII). Finally, siRNA-mediated MDC1 knockdown in cells, coupled with RNA polymerase II transcriptional inhibitor (DRB) release assays, RT-qPCR, and ELISA, was applied to verify the regulatory effects of OPAL and MDC1 on transcriptional elongation activity.

Our results demonstrated that OPAL ameliorated colonic mucosal injury and systemic cytokines, alleviated anxiety/depression-like behaviors, and sMRI revealed attenuated brain atrophy. OPAL also suppressed neuroinflammation and ER stress. Whole-transcriptome analysis with RT-qPCR and ELISA showed OPAL improved anxiety/depression via chemokine regulation, associated with inhibition of gut-derived CXCL9, thereby blocking gut–brain communication. Colonic scRNA-seq revealed OPAL suppressed CXCL9 release mainly from inflammatory macrophages, linked to non-canonical transcriptional elongation via the MDC1 S/TQ domain. Co-IP and MDC1 knockdown showed OPAL inhibited transcriptional elongation by disrupting RNAPII interaction, reducing CXCL9 pre-mRNA and protein levels, thereby ameliorating UC comorbid with anxiety/depression.

In summary, OPAL, a bioactive constituent of *Coptidis Rhizoma* that modulates the gut-brain axis, targets the MDC1 S/TQ domain to inhibit the transcriptional elongation of CXCL9 in intestinal macrophages, and block the transduction of CXCL9 signaling to the central nervous system, thereby achieving systemic correction of UC comorbid with anxiety and depression.

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**Cyclo(Gly-Tyr) alleviates hypercholesterolemia via modulating gut
microbiota: critical roles and mechanisms of *Bacteroides* and *Akkermansia***

**環 (甘-酪) 二肽通過調節腸道菌羣改善高膽固醇血癥：擬桿菌與阿
克曼氏菌的關鍵作用及機制**

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Abstract:

Hypercholesterolemia is a major risk factor for cardiovascular and cerebrovascular diseases, and the human gut microbiome plays a significant role in its management^{1,2}. Cyclo(Gly-Tyr) (CGY) is a cyclic dipeptide derived from various probiotics, foods, and animals, exhibiting potential lipid-lowering bioactivity^{3,4}. CGY is also a characteristic bioactive dipeptide originally derived from the traditional Chinese medicine (TCM) Squama Manis (pangolin scale), which has been historically used for various medicinal purposes⁵. Given that the source animal is now critically endangered and strictly protected, the development of CGY via chemical synthesis emerges as a promising strategy to replace natural resources while continuing its clinical application. However, its pharmacological activity in lowering cholesterol, along with its effects on the gut microbiota and underlying mechanisms, remains incompletely elucidated.

In this study, CGY was demonstrated to exhibit favorable safety in preliminary acute toxicity studies. CGY was also shown to significantly improve hypercholesterolemia, effectively alleviate liver damage caused by hypercholesterolemia, and restore gut microbiota homeostasis. We have confirmed that CGY can regulate key genes involved in cholesterol synthesis, reverse transport, and bile acid metabolism, such as HMG-CoA reductase (HMGCR), Liver X receptors (LXR), and cholesterol 7- α hydroxylase (CYP7A1), thereby improving abnormal cholesterol metabolism. Pseudo-germ-free experiment and fecal microbiota transplantation (FMT) experiment indicated that CGY's effect on improving dyslipidemia depends on the integrity of the gut microbiota. Notably, CGY enriched *Bacteroides*, promoted the expression of *Bacteroides thetaiotaomicron*-specific sulfotransferase (BtSULT), enhanced the cholesterol sulfonation metabolic pathway, facilitated the conversion of cholesterol to cholesterol sulfate (CS) in the gut, and contributed to cholesterol reduction. Furthermore, CGY enriched *Akkermansia muciniphila* (*A. muciniphila*), promoted

the expression of Mucin 2 (MUC2), and thickened the intestinal mucus barrier, contributing to the cholesterol lowering effect.

These findings reveal the unique mechanism by which CGY ameliorates hypercholesterolemia, provide novel insights into the intervention of lipid metabolism disorders by natural cyclic dipeptides, and offers a practical solution for the conservation of endangered TCM resources.

Acknowledgement:

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Brucea javanica Oil Emulsion Ameliorates Ulcerative Colitis via DNASE2-Mediated Suppression of Cytosolic DNA-Sensing Signaling: Mechanistic Insights and Functional Contribution of Bruceine D

鸦胆子油乳剂通过 DNASE2 介导的胞质 DNA 感知信号通路抑制改善溃疡性结肠炎的机制研究及 Bruceine D 的功能贡献

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Department: ¹ School of Chinese Medicine, Guangzhou University of Chinese Medicine

Abstract:

Background: Ulcerative colitis (UC) pathogenesis involves abnormal cytosolic DNA accumulation, which hyperactivates inflammatory DNA-sensing pathways (e.g., cGAS-STING). DNASE2 is the core enzyme responsible for clearing this DNA. While *Brucea javanica* oil emulsion (BJOE) exhibits significant anti-inflammatory activity, its mechanism in UC remains elusive. This study investigates whether BJOE and its active component, Bruceine D, ameliorate UC by targeting DNASE2 to suppress cytosolic DNA-sensing signaling.

Method: DSS-induced colitis mice were used to evaluate disease severity, barrier integrity, and gut microbiota (16S rRNA). To identify target pathways, LC-MS profiling was integrated with network pharmacology, clinical transcriptomics, and colon proteomics. Mechanisms were validated in DSS-injured NCM460 cells using DNase2 silencing, cellular thermal shift assays (CETSA), molecular docking, and standard molecular analyses.

Results: BJOE significantly improved experimental colitis by reducing DAI scores and tissue damage. It upregulated DNASE2 expression, thereby reducing abnormal cytosolic DNA accumulation and suppressing the activation of the DNA-sensing signaling pathway. Notably, Bruceine D partially recapitulated BJOE's anti-inflammatory effects, confirming its role in modulating DNASE2-related pathways.

Conclusion: BJOE and its core component, Bruceine D, ameliorate ulcerative colitis by upregulating DNASE2 to clear cytosolic DNA and suppress DNA-sensing signaling, offering a promising natural therapeutic strategy for IBD.

Acknowledgement: This study was supported by the National Natural Science Foundation of China (No. 82174045).

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Mechanistic Study of Brusatol Targeting Sucla2 to Regulate Macrophage Polarization for the Treatment of Ulcerative Colitis

鸦胆子苦醇靶向 Sucla2 调控巨噬细胞极化治疗 UC 的机制研究

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Abstract:

Background:

Ulcerative colitis (UC) is a chronic, relapsing inflammatory bowel disease with complex etiology and incompletely defined pathogenesis. Accumulating evidence indicates that intestinal barrier dysfunction and aberrant M1 macrophage activation are crucial contributors to UC initiation and progression. Our previous studies showed that Brusatol, an active constituent of *Brucea javanica*^[1], markedly ameliorates UC symptoms, reduces colonic inflammatory injury, and promotes intestinal mucosal repair, suggesting its therapeutic promise. However, the molecular mechanisms by which Brusatol regulates macrophage polarization and strengthens intestinal barrier protection remain unclear.

Inspired by the modern scientific interpretation of the traditional Chinese medicine function “stopping dysentery,” this study investigated Brusatol in UC intervention with a particular focus on its targeted inhibition of inflammatory M1 macrophage polarization. We aimed to improve the intestinal inflammatory microenvironment and facilitate intestinal barrier repair. To systematically identify and validate Brusatol’s key targets and clarify the underlying mechanisms, proteomics, siRNA-mediated knockdown, surface plasmon resonance (SPR), cellular thermal shift assay (CETSA), and colonic organoid co-culture were applied in an integrated manner. This work seeks to define Brusatol’s therapeutic targets and molecular mechanisms, provide a modern basis for the antidiarrheal effects of *Brucea javanica*, and support Brusatol development as a potential therapeutic agent for inflammatory bowel disease (IBD).

Method:

The therapeutic efficacy of Brusatol in terms of clinical symptoms, histopathology, and intestinal barrier integrity was evaluated using a DSS-induced mouse model. M1 macrophage polarization and inflammatory cytokine levels were measured in both UC mouse models and in vitro macrophage models via Western blot, qRT-PCR, and immunofluorescence. Colon proteomic analysis identified

Sucla2 as a potential target of Brusatol, which was further validated through Sucla2 knockdown, succinylation analysis, and colon organoid co-culture. These findings suggest that Brusatol exerts intestinal protection by modulating macrophage polarization through Sucla2. Furthermore, molecular docking, SPR, CETSA, DARTS, and Co-IP assays confirmed the direct binding of Brusatol to Sucla2 and elucidated the specific mechanism by which it inhibits Sucla2 degradation.

Results:

Brusatol significantly alleviated DSS-induced colitis by improving clinical symptoms and restoring barrier function. Both in vivo and in vitro, Brusatol suppressed M1 macrophage polarization and pro-inflammatory cytokine production. Mechanistically, proteomic and biochemical analyses identified Sucla2 as the direct target of Brusatol. Brusatol binding stabilized Sucla2 protein expression, subsequently reducing protein succinylation and modulating macrophage polarization.

Conclusion:

Brusatol alleviates colitis by directly targeting and stabilizing Sucla2, which inhibits M1 macrophage polarization and restores intestinal barrier integrity. These findings identify Sucla2-mediated macrophage polarization as a novel therapeutic target for inflammatory bowel disease.

Acknowledgement:

This work was supported by the National Natural Science Foundation of China (82174045), the Guangdong Basic and Applied Basic Research Foundation (2021A1515010160, 2021B1515140003, 2024A1515030008), the Shenzhen Science and Technology Program (JCYJ20250604181942056), and the Cultivation Project of Dongguan GZUCM Research Institute (2023PY0101).

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Gut–liver crosstalk mechanism underlying the lipid-lowering enhancement of debitterized Citri Grandis Exocarpium: the pivotal role of the *Akkermansia muciniphila*–indole-3-carboxaldehyde–FXR axis

化橘紅胎“祛苦”炮製品降脂增效的腸-肝對話機制：

Akkermansia muciniphila 介導的吲哚-3-甲醛-FXR 軸驅動作用

Authors: Xiaoya Weng

Department: Guangzhou University Of Chinese Medicine

Abstract:

Objective: Citri Grandis Exocarpium (Huaajuhong), the dried immature outer peel of *Citrus grandis* 'Tomentosa' or *Citrus grandis* (L.) Osbeck, is commonly used for respiratory diseases and was added to the "Medicinal and Food Homologous" catalog in 2024. According to the Compendium of Materia Medica, its efficacy improves with aging. However, natural aging takes five to ten years, and the raw material has a bitter taste, limiting its medicinal and food development[1, 2]. To address this, our team developed a patented technology (ZL 2024 1 0882530.7) [3]that effectively removes bitterness and enhances cough-relieving and lung-protective effects. Currently, Citri Grandis Exocarpium is underexplored for lipid-lowering, and the value of processing technology has been neglected. Therefore, based on the above patent, this study prepares the "bitterness-removed" processed product of immature Citri Grandis Exocarpium (PCG), investigates its lipid-lowering potential, and elucidates its mechanism of action.

Methods: Electronic tongue and artificial sensory evaluation were combined to assess bitterness before and after processing, with HPLC identifying changes in bitter components. High-fat emulsion and high-triglyceride models were used to establish hyperlipidemia in mice. Serum TC, TG, LDL-C, and HDL-C were

measured to verify the lipid-lowering efficacy of PCG. Metagenomics screened for *Akkermansia muciniphila* (A.m). Pseudo-sterile and fecal microbiota transplantation (FMT) experiments verified the microbiota-dependent effects, and qPCR assessed A.m abundance. Metabolomics identified 3-indolecarboxaldehyde (I3A). Animal experiments, qRT-PCR, Western Blot, and molecular docking clarified the key targets.

Results: Electronic tongue analysis showed that PCG exhibited significantly reduced bitterness, with decreased naringin and increased dihydrochalcone. PCG significantly improved serum lipid parameters in hyperlipidemic mice, with better efficacy than the raw product CG. Metagenomics revealed that PCG remodeled the gut microbiota, particularly promoting A.m growth (in vitro experiments confirmed this). Pseudo-sterile and FMT experiments demonstrated that PCG's lipid-lowering effect was gut microbiota-dependent. qPCR showed higher A.m abundance in the FMT-PCG group, and A.m upregulation promoted I3A production. Mechanistic studies indicated that I3A exerted lipid-lowering effects by activating the hepatic FXR receptor.

Conclusion: PCG significantly improves lipid disorders in hyperlipidemic mice by remodeling the gut microbiota, particularly promoting colonization of A.m which promotes 3-indolecarboxaldehyde production. By shifting tryptophan metabolism toward indole compounds, PCG activates the hepatic FXR receptor, exerting lipid-lowering effects. This study provides a new therapeutic target for PCG in improving hyperlipidemia and expands the application prospects of the related patent (ZL 2024 1 0882530.7), offering a scientific basis for functional product development and industrial transformation of PCG.

Acknowledgement:

We would like to express our sincere gratitude to the organizing committee for providing us with the opportunity for academic exchange and presentation. We also

thank Guangzhou University of Chinese Medicine for offering a great scientific research platform, and extend our appreciation to all the teachers and fellow students of the Druggability Research Team for their invaluable guidance and support.

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**Pomegranate ellagitannin improves cholesterol metabolism through
Akkermansia-associated bile acid remodeling**

石榴鞣花单宁通过 *Akkermansia* 相关胆汁酸重塑改善胆固醇代谢

Authors: Tianhui Li^{1,2,4}, Pui Kei Lee^{1,3,4}, Bojian Chen^{1,2,3}, Jie Xiong^{1,2,3},
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Abstract:

Pomegranate (*Punica granatum*) is a medicine-food homologous plant with known metabolic benefits. Among its medicinal parts, the peel is widely used and has attracted research attention due to its rich polyphenol content. Pomegranate ellagitannin (PGET) extract consists of the major bioactive polyphenolic constituent enriched in the peel, i.e., ellagitannins (hydrolysable tannins containing hexahydroxydiphenoyl (HHDP) units on a glucopyranose core). Ellagitannins (ETs) are believed to contribute to the metabolic benefits of pomegranate and have been reported to exert cholesterol-lowering effects. However, due to their poor absorption in the upper intestine, the majority of PGETs enter the lower gut and are subjected to extensive microbial biotransformation to produce bioactive metabolites, primarily urolithins. Emerging evidence suggests that gut microbiota-mediated metabolism of ETs influences metabolic homeostasis through modulation of bile acid composition and metabolic signaling pathways involved in cholesterol metabolism. However, cholesterol-lowering mechanisms of PGET remain poorly understood, particularly the role of gut microbiota and bile acid metabolism. Therefore, this study aimed to investigate whether the metabolic benefits of PGET are mediated via the gut microbiota, its microbial metabolites, or both, and to elucidate the molecular mechanisms with a focus on bile acid metabolism according to our preliminary findings.

To these ends, germ-free mice with a C57BL/6 background colonized with human donor microbiota via fecal microbiota transplantation (FMT) were treated

with PGET or a urolithin mixture for seven weeks. In addition, *in vitro* fermentation assays and a Caco-2 intestinal model were employed to further investigate mechanisms related to bile acid transformation and intestinal farnesoid X receptor (FXR) signaling.

The results showed that seven-week PGET administration significantly reduced plasma total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) levels only in FMT mice with gut microbiota, but not in germ-free mice. In addition, PGET treatment decreased circulating fibroblast growth factor 15 (FGF15) levels and increased hepatic CYP7A1 expression in FMT mice. Targeted metabolomics revealed an altered bile acid profile following PGET treatment, characterized by decreased chenodeoxycholic acid (CDCA) and increased ursodeoxycholic acid (UDCA) and 7-keto-lithocholic acid (7-keto-LCA) levels. Consistently, several bacterial genera enriched by PGET, particularly *Akkermansia*, were positively correlated with UDCA and 7-keto-LCA levels. Furthermore, *in vitro* fermentation suggested that *Akkermansia* may contribute to bile acid transformation from CDCA toward 7-keto-LCA and UDCA. In Caco-2 cells, UDCA and 7-keto-LCA suppressed FXR-FGF19 signaling.

Collectively, these findings suggest that gut microbiota-associated bile acid remodeling contributes to the cholesterol-lowering effects of PGET through modulation of the intestinal FXR-FGF15/19 axis. These findings highlight a potential role of *Akkermansia*-associated bile acid transformation in maintaining cholesterol homeostasis and provide new insights into the mechanistic link between dietary ellagitannins and host cholesterol metabolism.

Investigating Chinese Sweet Tea Leaf Extract as a “Sweet” Remedy for Obesity-Associated Metabolic Disorders

甜茶葉提取物：一種用於肥胖相關代謝紊亂的干預策略

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Abstract:

The escalating prevalence of obesity-associated metabolic disorders, characterized by elevated blood glucose and lipid levels, presents a significant global health challenge. While various interventions exist, primarily lifestyle modification and pharmacotherapy, their efficacy is often limited by low compliance rate and adverse effects¹. Therefore, alternative strategies for long-term metabolic health management are needed. *Rubus suavissimus* leaf, commonly known as Chinese sweet tea, is a traditional Chinese medicinal herb native to southern China. It has been used for millennia as both a medicinal agent and herbal tisane, with non-caloric natural sweetness and purported beneficial effects in metabolic disorders². However, its efficacy and mechanisms by which it alleviates obesity and its complications remain unclear. This study investigated the potential of a *R. suavissimus* leaf extract (RSE) in improving glucose and lipids metabolic disorders associated with obesity. *In vitro* assays revealed that RSE significantly improved glucose-stimulated insulin secretion of INS-1E pancreatic β -cells. Furthermore, RSE potently inhibited key carbohydrate-metabolizing enzymes with an efficacy comparable to acarbose (a blood glucose-regulating drug), potentially limiting digestible carbohydrate metabolism and reducing post-prandial rise in blood glucose. To validate the findings *in vivo*, RSE was administered to male C57BLKS/J-db/db diabetic obese mice for 18 weeks. The results demonstrated that RSE effectively attenuated excessive body weight gain, reduced body fat mass, and lowered circulating total triglycerides and cholesterol levels. In addition, RSE restored structural morphology of pancreas and enhanced glucose tolerance in db/db mice. Metabolomic and transcriptomics investigation further revealed that RSE treatment regulated pathways involving steroid biosynthesis, bile acid metabolism

and lipogenesis. Additionally, RSE favorably modulated the gut microbiota composition by increasing beneficial bacterial groups, such as *Lactobacillus* and *Akkermansia*, while inhibiting obesogenic bacteria. To further determine the roles of gut microbiota in mediating the blood lipid- and glucose-lowering effects, we performed fecal microbiota transplantation (FMT) into germ-free (GF) mice and evaluated RSE in antibiotic-treated mice. Interestingly, the lipid-lowering effect of RSE was abolished while no significant difference was observed in blood glucose homeostasis. This suggests that RSE may exert its metabolic effects via discrete mechanisms, with the lipid modulation being microbiota-dependent while the glucose regulation being microbiota-independent. In conclusion, our study, for the first time, demonstrates the potential of RSE to serve as an alternative dietary remedy for managing obesity and its associated metabolic disorders, and provides translational knowledge for clinical applications.

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**Buyanghuanwu decoction Reduce Fibrosis and Improve Diastolic Dysfunction
in HFpEF mice by regulating p300 through activating the AMPK signaling
pathway**

**補陽還五湯通過激活 AMPK 信號通路調控 p300 減輕 HFpEF 小鼠纖維
化並改善舒張功能障礙**

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Background

Heart failure with preserved ejection fraction (HFpEF) has become the dominant form of heart failure worldwide, driven by population aging and the rising prevalences of obesity, diabetes, and hypertension¹. Cardiac fibrosis is a key contributor to HFpEF pathophysiology². Pathological stimuli promote cardiac fibroblasts (CFs) activation, leading to fibrosis and diastolic dysfunction². Therefore, anti-fibrotic therapies hold promise for the treatment of HFpEF. However, current treatment options for HFpEF are limited, and no effective anti-fibrotic therapies are clinically available. Buyang Huanwu Decoction (BYHWD), a well-known herbal formula with cardioprotective and anti-fibrotic properties, has shown promise in various cardiovascular diseases³, but its potential role in HFpEF remains unexplored. Therefore, this study aimed to investigate the therapeutic effects of BYHWD on cardiac function in HFpEF and explore its potential mechanisms of action.

Methods

A HFpEF mouse model was established using female mice fed a high-fat diet (60% of total calories from fat) combined with the nitric oxide synthase inhibitor L-NAME (0.5 g/L in drinking water) for 12 weeks. Concurrently, HFpEF mice were orally administered BYHWD (0.5 or 1 g/kg/day) or normal saline via gavage over the same 12-week period. Cardiac structure and function were assessed by echocardiography. Histopathological analysis (Masson's trichrome, Sirius Red, and WGA staining), network pharmacology analysis, qPCR, and Western blotting (Collagen I, Collagen III, p-AMPK/AMPK, p300, and acetylated Smad2) were

analyzed. Furthermore, an in vitro model using primary cardiac fibroblasts isolated from neonatal mice was established to evaluate the anti-fibrotic effects of BYHWD.

Results

BYHWD significantly improved cardiac diastolic function and alleviated cardiac fibrosis in HFpEF mice. Network pharmacology analysis suggested that BYHWD exerts anti-fibrotic effects in HFpEF may be mediated, in part, through the AMPK pathway. Consistently, Western blot analysis showed that BYHWD treatment activated AMPK, downregulated p300 expression, and inhibited Smad acetylation, thereby reducing the transcription of fibrosis-associated proteins, such as Collagen I and III. Furthermore, in primary cardiac fibroblasts isolated from neonatal mice, BYHWD effectively inhibited angiotensin II (Ang II)-induced fibroblast activation, as evidenced by reduced α -SMA expression, decreased collagen I/III levels, and inhibition of p300-mediated Smad acetylation. Furthermore, this inhibitory effect was mediated by the AMPK/p300 signaling axis.

Conclusion

In summary, our study demonstrates that BYHWD alleviates cardiac fibrosis and improves diastolic dysfunction in HFpEF mice by activating AMPK and consequently suppressing p300 signaling pathway, highlighting its potential as a therapeutic strategy for HFpEF-associated myocardial fibrosis.

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***In vitro* and *in vivo* investigations on the anti-metastasis and anti-stemness effects of a polysaccharides-rich herbal extract SOL on triple negative breast cancer**

含多糖草藥提取物 SOL 抗三陰性乳腺癌轉移及幹性作用的研究

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Abstract:

Triple-negative breast cancer (TNBC) is widely recognized as one of the most aggressive malignancies¹ due to its high recurrence rate and poor prognosis, which are largely driven by rapid metastasis and the resilience of cancer stem cells (CSCs). Although conventional chemotherapy remains the standard treatment strategy, its clinical efficacy is often limited by severe systemic toxicities and acquired drug resistance². Herbal medicines with low toxicity and multi-target biological activities have attracted increasing interest as potential therapeutic agents³. Hence, this study aims to explore the potential of a polysaccharides-rich herbal extract SOL, in inhibiting TNBC metastasis, and suppressing CSC-like properties both *in vitro* and *in vivo*.

The effects of SOL were assessed using human MDA-MB-231 and murine 4T1 TNBC cells. Using MTT assay, SOL exhibited significant cytotoxicity against MDA-MB-231 and 4T1 cells only at high concentrations (≥ 1600 mg/mL). In MDA-MB-231 cells, SOL altered cell cycle distribution by increasing the G1-phase population and decreasing the S-phase population at concentrations up to 3200 μ g/mL. The colony formation assay further demonstrated that SOL suppressed the long-term proliferative ability of MDA-MB-231 cells. Scratch wound healing and transwell migration assays also showed that SOL markedly suppressed the migratory ability of TNBC cells. To evaluate the effect of SOL on CSC-like properties, ALDEFLUOR assay was conducted in MDA-MB-231 cells. Results showed that SOL decreased the proportion of aldehyde dehydrogenase-positive (ALDH⁺) CSC-like populations.

For *in vivo* studies, an orthotopic 4T1 TNBC tumor-bearing mouse model was

established to explore the anti-tumor and anti-metastasis effects of SOL. Results showed that SOL treatment for 19 days could reduce lung metastasis without inducing weight loss. Furthermore, increased infiltration of CD4⁺ and CD8⁺ T cells were observed in the tumors of SOL-treated mice.

In conclusion, SOL treatment inhibited TNBC cell proliferation and migration, reduced CSC-like populations *in vitro*, and suppressed lung metastasis *in vivo*. These findings suggest that SOL may have potential for preventing TNBC recurrence and distant metastasis. The detailed mechanisms underlying the anti-metastatic and anti-stemness effects of SOL require further investigations.

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**APPL2 Deletion Promotes Neurogenesis and Functional Recovery after
Ischemic Stroke via Regulation of Mitochondrial Dynamics and Function**

**APPL2 通過調節線粒體動態和功能而抑制缺血性中風後神經再生和
功能恢復**

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Abstract:

Ischemic stroke remains a leading cause of disability, and promoting neurogenesis is a critical strategy for long-term functional recovery. While Adaptor protein, phosphotyrosine interacting with PH domain and leucine zipper 2 (APPL2) has been implicated in cell signaling, its role in post-stroke neurogenesis and mitochondrial regulation remains unclear. This study aims to investigate the impact of APPL2 deficiency on neurological function and explore the underlying mitochondrial mechanisms.

Nestin-cre mice and APPL2-flox mice were used to knockout APPL2 in mouse brain. APPL2 conditional knockout (cKO) mice and control littermates were subjected to behavioral tests, including the Morris water maze (MWM), novel object recognition (NOR), open field test (OPT), and rotarod test. Middle cerebral artery occlusion (MCAO) model was performed to assess the effects of APPL2 on post-stroke recovery. Functional recovery was monitored for 28 days, followed by immunofluorescence analysis of neurogenesis in the hippocampal Dentate Gyrus (DG) zone. To investigate the underlying mechanisms, C17.2 neural stem cells (NSCs) were subjected to oxygen-glucose deprivation (OGD) followed by induced differentiation. Mitochondrial function was assessed via mitochondrial membrane potential, mitochondrial superoxide levels, mitochondrial mass, and morphological analysis during differentiation.

Under basal conditions, APPL2 cKO mice exhibited significantly enhanced cognitive function, motor performance, and reduced anxiety-like behavior compared to control mice. Furthermore, after MCAO, APPL2 cKO mice demonstrated superior long-term functional recovery at 28 days, correlated with significantly increased proliferation of neural stem/progenitor cells (NSPCs) and accelerated neuronal differentiation in the hippocampal DG zone. Mechanistically, APPL2 KO significantly accelerated differentiation in C17.2 NSCs after OGD. This was

accompanied by enhanced mitochondrial function, characterized by elevated mitochondrial membrane potential, enhanced mitochondrial superoxide levels, and increased mitochondrial mass. Notably, APPL2 KO C17.2 NSCs maintained a healthier, network-like mitochondrial morphology compared to the fragmented mitochondria observed in controls after OGD.

Our findings demonstrate that APPL2 serves as a negative regulator of neurogenesis. APPL2 deletion confers neuroprotection and enhances post-stroke recovery by optimizing mitochondrial dynamics and function. These results suggest that targeting APPL2 could be a potential therapeutic strategy to boost endogenous neurogenesis and mitochondrial function in ischemic stroke.

***Andrographis paniculata* Suppresses Aggressive Cancer Stem
Cell-Driven Ovarian Cancer Metastasis by Inhibiting SP100 Downstream of
Wnt/ β -Catenin Signaling**

穿心蓮透過抑制 Wnt/ β -catenin 信號傳導路徑下游的 SP100，抑制
由具侵襲性的癌症幹細胞驅動的卵巢癌轉移

Authors: W Yu¹, GGL YUE², CBS Lau^{2,3} and AST Wong^{1,4}

Department: ¹ School of Biological Sciences, The University of Hong Kong; ² Department of Pharmacology and Pharmacy, LKS Faculty of Medicine, The University of Hong Kong; ³ School of Chinese Medicine, LKS Faculty of Medicine, The University of Hong Kong; ⁴ Laboratory for Synthetic Chemistry and Chemical Biology Limited, Hong Kong Science and Technology Parks.

Abstract:

Ovarian cancer remains the most lethal gynecologic malignancy, primarily due to widespread metastasis, frequent recurrence, and therapeutic resistance driven by cancer stem cells (CSCs).¹⁻² Therefore, novel therapeutic target and methods specially toward diminish CSCs are urgently needed. The aqueous extract of *Andrographis paniculata* (APW), a traditional Chinese medicinal herb with known anti-tumor property, exhibited its specificity in targeting cancer stemness-driven malignancies in several squamous cell carcinomas.³⁻⁴ However, its effects on ovarian CSC-associated metastasis and the underlying molecular mechanisms remain poorly understood.

In this study, the effects of APW on CSC-associated aggressiveness in ovarian cancer were investigated. Comparative analyses between CSCs and other less aggressive tumor cells were performed to determine differential sensitivity to APW. A series of *in vitro* functional assays were performed to assess proliferation, adhesion, migration, and stemness-related gene expression at the mRNA level. To elucidate the underlying mechanism, co-immunoprecipitation (co-IP) was used to identify special transcriptional regulators interacting with β -catenin in ovarian CSCs, not in prenatal cancer cells. The *in vivo* therapeutic efficacy of APW was further evaluated in both immunodeficient and immunocompetent mouse models, the latter providing a more physiologically relevant system.

APW preferentially targeted cancer stem cells (CSCs), as evidenced by significantly

lower IC₅₀ values, a more rapid reduction of adhesion capacity and Wnt/ β -catenin expression compared to those in parental cancer cells. APW also markedly suppressed CSC migration, accompanied by downregulation of stemness-associated genes. Mechanistically, SP100 was identified as a novel nuclear transcriptional co-activator that directly interacts with β -catenin in ovarian CSCs to regulate downstream gene expression. Notably, while SP100 directly binds to β -catenin, this interaction is limited in non-CSC cancer cells. Disruption of the β -catenin/SP100 axis by APW led to decreased expression of genes involved in CSC maintenance and metastatic potential. *In vivo*, APW significantly reduced omental tumor burden and mesenteric dissemination in both mouse models.

In conclusion, our findings identify SP100 as a specific mediator of β -catenin-driven transcription in metastatic CSCs and demonstrate that APW selectively targets CSCs by disrupting the Wnt/ β -catenin/SP100 axis. This study highlights the therapeutic potential of *Andrographis paniculata* as a novel strategy for treating CSC-driven ovarian cancer.

Acknowledgement:

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Potential effects of Chinese herbal formula SP on obesity-associated colon cancer through adipocytes–cancer cells interaction

中藥複方 SP 調控脂肪細胞–腫瘤細胞相互作用對肥胖相關結腸癌的潛在作用

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Abstract:

Colorectal cancer (CRC) is a leading cause of cancer-related mortality worldwide¹. Obesity is a significant risk factor for CRC, promoting tumor progression through increased fatty acid availability and pro-tumorigenic signals derived from adipose tissue². However, there are currently no treatments that specifically target on obesity-associated CRC.

The Chinese herb *Patrinia villosa* (Bai Jiang Cao) has long been used in traditional Chinese medicines for treating gastrointestinal disorders and its aqueous extract (PVW) has been shown with anti-CRC activity in our previous study³. On the other hand, *Schisandra chinensis* ethanol extract (SCE) is well known for its lipid-lowering properties in modern pharmacological research. Therefore, we investigated the therapeutic potential of a novel combination of PVW and SCE, designated as herbal formula SP, for obesity-associated colon cancer.

A co-culture system with adipocytes and colon cancer cells was established to mimic the obesity-associated tumor microenvironment. Combination index analysis revealed that PVW and SCE exerted synergistic inhibitory effects on colon cancer proliferation. Formula SP markedly suppressed adipocytes-enhanced CRC cells proliferation, migration, invasion, and epithelial–mesenchymal transition. For the adipocytes, formula SP inhibited preadipocytes differentiation and lipid accumulation. Importantly, formula SP disrupted metabolic crosstalk between adipocytes and colon cancer cells by reducing lipid transfer.

In conclusion, our findings suggest that formula SP exerts synergistic inhibitory effects on colon cancer cell proliferation, suppresses adipocyte function, and disrupts lipid-mediated metabolic interactions between adipocytes and colon cancer cells. This study provides novel scientific evidence supporting the therapeutic potential of formula SP in targeting adipocyte–cancer crosstalk in

obesity-associated CRC. Further animal studies will be conducted to validate the effects of formula SP and to elucidate the underlying mechanisms of action.

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Xanthohumol Alleviates TNF- α -Induced Inflammation in IEC-6 Cells

黃腐酚在腸道上皮細胞炎症中的功能評價

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Abstract:

Inflammatory bowel disease (IBD) is a chronic, relapsing gastrointestinal disorder characterized by a compromised intestinal mucosal barrier and aberrant epithelial cell apoptosis. Current therapeutic strategies for IBD mainly rely on synthetic small-molecule drugs and biologics; however, these conventional treatments are frequently limited by systemic toxicity, high costs, and a risk of long-term side effects. Consequently, traditional Chinese medicine (TCM) has gained increasing attention due to its multi-target efficacy, low toxicity, and suitability for long-term chronic disease management. Xanthohumol (XN), the principal prenylated flavonoid derived from hops (*Humulus lupulus*), a well-known medicinal plant widely utilized in TCM, possesses potent anti-inflammatory and antioxidant properties.

Here, the rat intestinal epithelial cell line IEC-6 was employed to establish a TNF- α -induced inflammation model. Our results demonstrate that XN provides significant barriers and anti-apoptotic protection in TNF- α -challenged cells. Specifically, XN represses the TNF- α -induced transcription of *IL-8*, *IL-6*, *COX2*, and *TNF- α* genes. Mechanistically, XN treatment significantly attenuates phosphorylated p65 levels. Furthermore, XN effectively upregulates the tight junction gene *Occludin* to maintain epithelial integrity. Crucially, XN promotes cell survival by suppressing *Bax/Caspase-3* and enhancing *Bcl-2*. As a bioactive phytochemical derived from an edible TCM, XN offers distinct advantages over conventional synthetic small-molecule drugs, including a superior safety profile and greater suitability for daily dietary intervention in the management of chronic IBD.

Acknowledgement:

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Yu Ping Feng San Prevents the Cisplatin- and 5-Fluorouracil-Induced Multi-Drug Resistance in *Escherichia coli*

玉屏風散預防順鉑及 5-氟尿嘧啶誘導的大腸桿菌耐多藥突變

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Abstract:

Cisplatin and 5-fluorouracil (5-FU) are widely used drugs in first-line chemotherapies for solid tumors. However, they have been proved to have anti-microbial effects on both Gram-ve and Gram+ve bacterial strains, leading to multiple drug resistant (MDR) gut microbiomes. Cisplatin and 5-FU also affect the environment of intestinal mucosa by damaging the proliferation of epithelial cells¹. Cisplatin- and 5-FU-induced side effects, such as nephrotoxicity, ototoxicity, mucositis and local inflammation, are associated with the disturbance of gut microbiota. Thus, the intake of cisplatin and 5-FU should be more likely to the experience of other complications in relating to gut microbiome.

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 Saposhnikovia Radix (SR). YPFS has been used to treat immune disorders and inflammation in clinics for years². Recently, YPFS was found to improve the imbalance of intestinal flora, caused by asthma and recurrent respiratory tract infection. Here, YPFS was shown to reverse cisplatin- and 5-FU-induced MDR in *E. coli*. The induction was due to the regulation of intracellular ROS, cell permeability and depolarization, as well as the induced expression of membrane efflux transporter. The results support the adjacent treatment of the cell is achieved by using YPFS.

Acknowledgement:

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Yu Ping Feng San Prevents the Anti-Cancer Drugs Induced Inflammation in Intestinal Epithelial Cells (IEC-6 Cells)

玉屏風散可預防抗癌藥物誘導的腸上皮細胞 (IEC-6 細胞) 炎症

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Abstract:

The use of chemotherapeutic agents has been shown to elevate proinflammatory factors, leading to intestinal mucositis—a common side effect of chemotherapy that significantly contributes to decreased survival rates in certain treatment settings. However, this clinical problem does not have efficacious interventions. Yu Ping Feng San (YPFS) is an ancient Chinese herbal decoction, as mentioned in the Dan Xi Xin Fa during the Song Dynasty. It comprises Astragali Radix (Huangqi; AR), Atractylodis Macrocephalae Rhizoma (Baizhu; AMR), and Saposhnikovia Radix (Fangfeng; SR) in a formula ratio of 1:2:1.

In this study, we investigated the anti-inflammatory potential of YPFS in the intestinal epithelium in response to chemotherapeutic agents. Utilizing the LPS-induced model on IEC-6 cells, the co-treatment with YPFS demonstrated a reduction in inflammatory cytokines, particularly IL-6, TNF- α , and COX-2. These results confirm that YPFS exerts anti-inflammatory effects in IEC-6 cells under LPS stimulation. Meanwhile, using the same experimental procedure, YPFS also demonstrated an anti-inflammatory effect in a dose-dependent manner under stimulation by doxorubicin, a classical chemotherapeutic agent. To further investigate the effective components of YPFS responsible for its anti-inflammation function, the IC₅₀ values of YPFS and its components (AR, AMR, and SR) were further evaluated.

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Photoprotective and Anti-Inflammatory Effects of Wild Mountain Ginseng Extract Against Ultraviolet-Induced Damage in HaCaT Cells

野山参提取物对 HaCaT 细胞紫外线诱导损伤的光保护及抗炎作用

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Abstract:

Ultraviolet (UV) radiation is a primary environmental stressor responsible for cutaneous photodamage, characterized by accelerated photoaging and chronic photoinflammation. Although *Panax ginseng* is globally renowned for its potent antioxidant and anti-inflammatory properties, the specific protective efficacy of wild mountain ginseng extract (WMGE)—which contains a unique profile of rare bioactive ginsenosides—against UV-mediated cutaneous damage remains to be fully elucidated.

In this study, we evaluated the photoprotective effects of WMGE in UV-irradiated human keratinocyte cell line HaCaT. MTT assay results demonstrated that UV exposure significantly reduced cell viability, which was effectively mitigated by WMGE intervention. Furthermore, qPCR analysis revealed that UV irradiation profoundly up-regulated the mRNA expression of acetylcholinesterase (AChE) and key pro-inflammatory cytokines, including TNF- α , IL-1 β , and IL-8. Crucially, WMGE treatment dose-dependently suppressed the up-regulation of these targets, restoring them toward basal levels. Collectively, these findings demonstrate that WMGE exerts potent anti-inflammatory and cytoprotective effects, highlighting its potential as a natural therapeutic or cosmeceutical ingredient for preventing UV-induced skin damage.

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Anti-Atopic Dermatitis Effects and Mechanisms of Action of Tetramethylpyrazine
川芎嗪对特应性皮炎的疗效及其作用机制
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Abstract: Background: Atopic dermatitis (AD) is the most prevalent allergic inflammatory skin disease, characterized by recurrent eczematous lesions and severe pruritus. Current therapies for AD have limitations, necessitating the development of novel treatments. Tetramethylpyrazine (TMP), an alkaloid derived from <i>Ligusticum chuanxiong</i>, is recognized for its anti-allergic and anti-inflammatory properties. Based on these attributes, we hypothesized that TMP might have potential as an anti-AD treatment. Objectives: This study aimed to: (1) investigate the anti-AD effects and underlying mechanisms of TMP in pharmacological models, and (2) identify novel druggable molecular targets for the treatment of AD. Methods: To investigate the anti-AD effects of TMP, a TNF-α/IFN-γ-treated immortalized human keratinocyte (HaCaT) model was used for in vitro studies. Additionally, a calcipotriol-induced mouse model was employed to assess the anti-AD efficacy of TMP in vivo. Network pharmacology analysis was conducted to predict potential molecular targets of TMP. Clinical datasets, including GSE121212, GSE182740, GSE32924, GSE120721, GSE16161, and GSE193309, were used to identify differentially expressed genes (DEGs) by comparing the skin of healthy individuals with lesional skin from AD patients. The Venny 2.1 web tool was utilized to identify overlapping genes between these DEGs and the predicted target genes of TMP. Results: Our study demonstrated that treatment with TMP at concentrations of 10, 20, and 40 μM significantly attenuated the TNF-α/IFN-γ-induced suppression of HaCaT cell viability. Additionally, TMP showed therapeutic effects in calcipotriol-treated AD mice and TNF-α/IFN-γ-treated HaCaT model, indicating its potential efficacy in vivo and vitro. Through network pharmacology analysis, we identified 165 potential targets of TMP and 2,504 AD-related genes, with 87 overlapping molecules common to both TMP targets and AD-related genes. Additionally, 112 shared DEGs were identified through clinical datasets. We pinpointed several key genes—ITK, LCN2, VEGFA, LCK and AR—as being involved in the anti-AD effects of TMP and the pathogenesis of AD. Notably, while LCK have been previously reported in the context of AD, the roles of ITK, LCN2, VEGFA and AR in AD remain unexplored. Future research is needed to elucidate

the mechanistic contributions of these genes to TMP's anti-AD efficacy.

Conclusions: Completion of this study is expected to generate pharmacological data for developing TMP-based anti-AD medications and discover novel druggable target(s) for treating AD.

Systematic Review of Preclinical Evidence on Antifibrotic Potential of Natural Polysaccharides

天然多糖抗肝纤维化作用的临床前证据系统综述

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Abstract:

Background: Liver fibrosis is a principal driver of morbidity and mortality in chronic liver disease, and there remains an urgent unmet need for effective, approved targeted therapies. Natural polysaccharides—particularly those derived from Chinese medicinal herbs—are promising multitarget candidates rooted in traditional hepatoprotective practice; however, a critical appraisal of their preclinical translatability is lacking.

Objective: To systematically synthesize evidence on the efficacy, mechanisms, and methodological quality of preclinical studies investigating the antifibrotic potential of natural polysaccharides.

Method: Six databases were searched (inception to February 2025) for studies using experimental liver fibrosis models, following PRISMA guidelines. Risk of bias and reporting quality were assessed with the SYRCLE (Systematic Review Centre for Laboratory Animal Experimentation) and ARRIVE (Animal Research: Reporting of In Vivo Experiments) guidelines, respectively.

Results: Eighty-eight studies investigating 44 distinct polysaccharides were included; of these, 75 studies (spanning 36 Chinese medicinal herbs) examined polysaccharides derived from Chinese medicine. A major limitation was the predominant use of the carbon tetrachloride (CCl₄) rat model (54.5%). Despite model homogeneity, polysaccharides showed consistent efficacy: collagen deposition decreased in 92.0% of studies, and serum alanine/aspartate

aminotransferase (ALT/AST) levels were reduced in all studies. Mechanistically, inhibition of the transforming growth factor- β (TGF- β)/Smad pathway (reported in 60.2% of studies) and modulation of the toll-like receptor 4 (TLR4)/nuclear factor- κ B (NF- κ B) pathway (15.9%) were most frequently described. Methodological quality was suboptimal, with unclear allocation concealment (92.0%) and lack of blinding (86.4%) being pervasive.

Conclusion: Natural polysaccharides consistently attenuate experimental liver fibrosis by modulating key fibrogenic and inflammatory pathways, such as TGF- β /Smad. Our review highlights a critical disconnect: demonstrated efficacy is undermined by limited model diversity and poor methodological rigor. Advancing the field requires chemical standardization and Q-marker definition, use of etiologically relevant models, establishment of dose – exposure – response relationships, and strict adherence to SYRCLE/ARRIVE guidelines, with the goal of accelerating antifibrotic clinical translation and laying the groundwork for the standardized development and application of natural polysaccharides within integrative Chinese and Western medicine strategies.

Effects of Sulfur- and Selenium-Containing Miliusane Analogues on Cellular Senescence induction in Triple-Negative Breast Cancer

含硫硒的 Miliusane 類似物對三陰性乳腺癌細胞衰老誘導的影響

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Abstract:

Background & Objective: Triple-negative breast cancer (TNBC) is an aggressive subtype with limited targeted therapeutic options due to lack of ER, PR and HER2 expression, thus contributing to poor prognosis. Inducing stable cellular senescence is emerging as a promising strategy to suppress TNBC cell proliferation and migration without necessarily causing overt cell death. Miliusanes belong to a novel class of anticancer compounds discovered from *Milisia* plants. They have demonstrated potent antitumor effects in various type of cancer cells, including breast cancer¹. This study investigates the induction of cellular senescence by sulfur-and selenium-containing miliusane derivatives to assess their antitumor potential against TNBC². **Methodology:** Two TNBC cell lines were used to assess the cytotoxic, antiproliferative, antimigratory, and pro-senescent effects of natural miliusol, the selenium-containing derivative K1Seb2, and the sulfur-containing K1SS2. Cytotoxicity was quantified using the sulforhodamine B (SRB) assay. Clonogenic survival was evaluated by treating cells with various concentrations of each miliusane compound for 10 days before colony counting. Cell migration was assessed using Transwell chambers, while senescence induction was evaluated in parallel cultures by SA- β -gal staining after 48 h exposure to the miliusanes. **Results:** The IC₅₀ values of miliusol, K1Seb2 and K1SS2 were found to be 1.16, 2.35 and 2.12 μ M for MDA-MB-231 and 0.97, 1.69 and 1.8 μ M for MDA-MB-468, respectively. Additionally, the colony-forming assay demonstrated a significant reduction in colony formation at concentrations of 1 μ M for all three miliusanes, confirming their potency. Moreover, the tested compounds showed significant migration inhibition as compared to control. Likewise, the SA- β -gal staining assay demonstrated that miliusanes increased senescence-associated β -galactosidase activity compared to the control. **Conclusion:** Miliusol and its derivatives K1Seb2 and K1SS2 exhibited potent, dose-dependent cytotoxicity against MDA-MB-231 and MDA-MB-468 cells, with low micromolar IC₅₀ values and marked suppression of clonogenic growth at 1 μ M, indicating strong antiproliferative activity. These miliusane compounds significantly inhibited TNBC cell migration and enhanced

SA- β -gal activity, consistent with robust induction of cellular senescence. Collectively, selenium- and sulfur-containing miliusanes demonstrate promising senescence-inducing and antitumor potential in TNBC cells, supporting their further development as candidates for TNBC therapy. Hong Kong Baptist University's Research Committee, Initiation Grant-Faculty Niche Research Areas (IG-FNRA) 2021/22, Hong Kong (RC-IG-FNRA/21-22/SCM/01), provided support for this project.

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Plant Lignans Target Host-Driven Viral Entry for Broad-Spectrum Antiviral Activity

植物木脂素通过靶向宿主因子抑制病毒进入发挥抗广谱病毒作用

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Abstract:

The persistent threat of viruses to global health stems from their high genetic diversity and rapid mutation rates, highlighting the urgent need for host-directed and broad-spectrum antiviral strategies. A key host factor is v-ATPase, which controls endosomal acidification required by many enveloped viruses for uncoating and infection ^[1]. Although the plant-derived lignan diphyllin is a known v-ATPase inhibitor with potent antiviral activity, its clinical application is limited by significant cytotoxicity ^[2,3]. In this study, we designed and synthesized a library of novel aryl naphthalene lignan (ANL) derivatives using diphyllin as the core scaffold, and evaluated their antiviral efficacy in pseudovirus assays against various viruses. All derivatives exhibited broad-spectrum inhibitory activity, with IC₅₀ values ranging from 0.49 to 3868 nM. Among them, analogue C180A and a corresponding click-chemistry conjugate were the most potent, achieving nanomolar inhibition with the highest selectivity indices. Time-of-addition assays showed that the antiviral effect of the click-chemistry conjugate was most effective during pre-treatment and early infection stages, consistent with interference at viral entry or immediate post-entry steps. This profile mirrors that of diphyllin and supports v-ATPase inhibition as a likely mechanism. Mechanistically, v-ATPase should elevate endosomal/lysosomal pH, prevent pH-dependent viral uncoating, and block infection. To test this, future studies will directly measure endosomal pH, quantify

viral RNA release, and assess functional dependence via v-ATPase subunit knockdowns, as well as evaluate direct target engagement between ANL compounds and v-ATPase subunits using affinity-based assays such as pull-down and MST.

Acknowledgment :

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Polysaccharide-Based Treatment Strategies for Irritable Bowel Syndrome: Targeting the Gut–Brain–Microbiota Axis

多糖類治療腸易激綜合徵的策略：靶向腸–腦–菌群軸

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Abstract:

Background: Irritable bowel syndrome (IBS) is a common disorder of gut–brain interaction with chronic abdominal pain, altered bowel habits and impaired quality of life. Many patients remain symptomatic or cannot sustain long-term drug use despite standard pharmacological and dietary measures, highlighting the need for safe, durable and mechanism-based treatments. Polysaccharide-based strategies—non-starch polysaccharide fibers, prebiotic oligo-/polysaccharides and Traditional Chinese Medicine (TCM) prescriptions with defined polysaccharide fractions—have been proposed as gut–brain–microbiota–targeted treatments.

Methods: We performed a comprehensive literature review (2010–2025) of clinical and preclinical studies in which dietary polysaccharides or TCM-derived polysaccharide fractions were given to IBS patients or IBS-like models, extracting data on symptoms, stool pattern, quality of life, microbiota, barrier function, inflammatory markers and gut–brain-related endpoints.

Results: In clinical studies, soluble fiber preparations such as psyllium and high-specific-volume non-starch polysaccharide products improve stool consistency and composite IBS scores and are used or proposed as first-line nutritional options. Prebiotic formulations in which galactooligosaccharides and related oligo-/polysaccharides are the main functional carbohydrates enrich beneficial genera and reduce pain, bloating and bowel disturbance in subsets of patients, supporting a microbiota-directed functional food strategy. Polysaccharide-rich TCM prescriptions, exemplified by the multi-herb formula Chang-Kang-Fang, further relieve abdominal pain and bowel habits and, in pharmacokinetic work, enhance systemic exposure of co-administered bioactives in a microbiota-dependent manner, underlining the contribution of the polysaccharide fraction¹. In IBS-like models, polysaccharides from *Momordica charantia*, *Atractylodes macrocephala*, *Wolfiporia cocos*, *Cistanches spp.* and Liupao tea reduce diarrhea or constipation, normalize transit and attenuate visceral hypersensitivity, while enhancing short-chain fatty acids and other beneficial microbial metabolite pathways (e.g. indole/tryptophan- and bile-acid-derived), reinforcing epithelial tight junctions and

suppressing mucosal pro-inflammatory cytokines^{2,3}.

Conclusions: Polysaccharide-based nutritional and herbal interventions therefore represent rational, well-tolerated treatment options for IBS that target key elements of the gut–brain–microbiota axis rather than acting as nonspecific bulking agents. Available data support integrating selected soluble fibers, prebiotic polysaccharide formulations and TCM polysaccharide fractions as adjuncts to conventional therapy, while future trials should define structure–dose–response relationships and incorporate microbiome-stratified responder analyses to guide individualized IBS management.

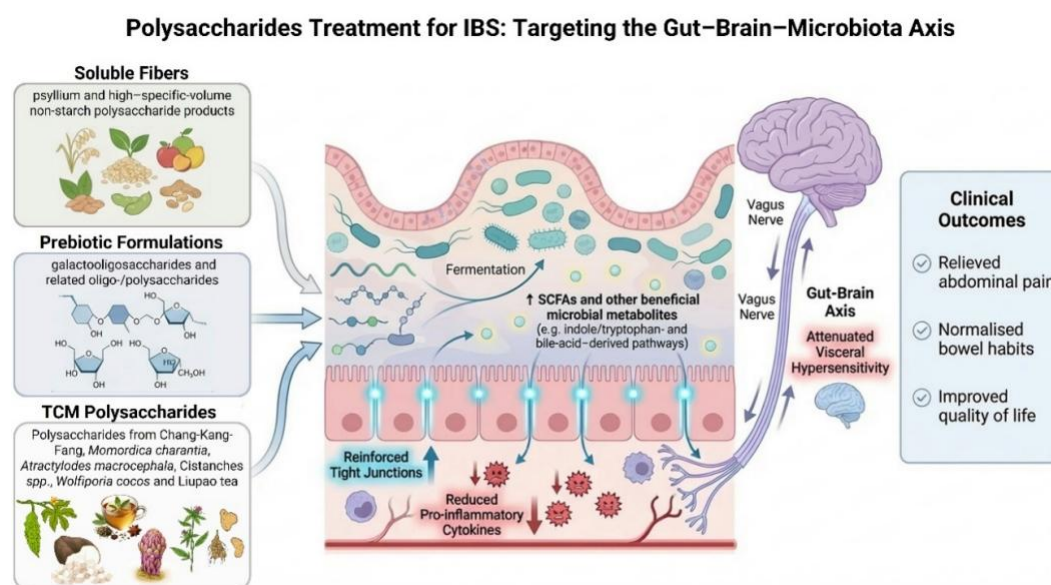


Figure 1. Mechanistic overview of polysaccharide-based treatment strategies for irritable bowel syndrome along the gut–brain–microbiota axis.

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**Taohe Chengqi decoction attenuates metabolic dysfunction-associated
steatohepatitis by suppressing Piezo1/NLRP3 mediated macrophage
inflammation**

**桃核承氣湯通過抑制巨噬細胞 Piezo1/NLRP3 信號通路改善代謝功能
障礙相關脂肪性肝炎**

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Abstract:

Background

Metabolic dysfunction-associated steatohepatitis (MASH) is driven largely by macrophage-mediated inflammation, in which aberrant NLRP3 inflammasome activation plays an important role [1-3]. The mechanosensitive channel Piezo1, highly expressed in macrophages and upregulated in MASH, can trigger NLRP3 activation via Ca²⁺ signaling [4, 5]. Our earlier work showed that macrophage Piezo1 deletion attenuates hepatic fibrosis [6]. Taohe Chengqi Decoction (THCQD)—composed of Taoren (seed of *Persicae Semen*), Dahuang (root of *Rhei Radix et Rhizoma*), Guizhi (twig of *Cinnamomum Cassia*), Mangxiao (*Natrii Sulfas*), and Gancao (root and rhizome of *Glycyrrhizae Radix Et Rhizoma*)—exhibits notable anti-inflammatory activity [7, 8], yet whether it mitigates MASH by targeting macrophage Piezo1/NLRP3 signaling remains unknown.

Purpose

This study aimed to explore the anti-inflammatory properties of THCQD in MASH and to elucidate the potential underlying mechanisms.

Methods and Results

Male C57BL/6J mice were challenged with a methionine-choline deficient (MCD) diet for six weeks to establish a MASH model. During the final four weeks, THCQD or silybin (positive control) was concomitantly administered orally. Our results demonstrated that THCQD treatment significantly alleviated hepatic steatosis,

inflammation, and fibrosis, as confirmed by histological staining and biochemical measurements. To explore the underlying mechanisms, network pharmacology analysis was conducted, which predicted the involvement of the Piezo1/Ca²⁺ signaling pathway in the anti-inflammatory action of THCQD. Subsequent experiments confirmed that THCQD suppressed Piezo1 expression and inhibited Yoda1-induced Ca²⁺ influx in cultured macrophages. Notably, the Piezo1/NLRP3 signaling axis was markedly downregulated in both steatotic livers and activated macrophages following THCQD treatment. To further validate the functional role of macrophage Piezo1, macrophage-specific Piezo1 knockout (*Piezo1^{ΔLysM}*) mice were employed. *Piezo1^{ΔLysM}* mice exhibited attenuated MASH-associated pathology and reduced NLRP3 pathway activation compared to *Piezo1^{fl/fl}* controls. More importantly, the therapeutic effect of THCQD was partially diminished in *Piezo1^{ΔLysM}* mice, confirming the involvement of macrophage Piezo1 in its mechanism of action. Furthermore, molecular docking and surface plasmon resonance imaging (SPRi) indicated that three bioactive constituents of THCQD—glycyrrhizic acid, cynaroside, and quercetin—may directly interact with Piezo1.

Conclusion

These findings indicate that THCQD attenuates MASH-associated hepatic pathology through suppression of the Piezo1/NLRP3 signaling pathway in macrophages. This study demonstrates the beneficial effects of THCQD in preclinical MASH models and supports its further investigation as a potential therapeutic agent.

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**Multi-target Pharmacological Mechanisms and Translational Evidence of
Traditional Chinese Medicine in Hair Follicle Regeneration and Alopecia
Treatment: A Review**

中药促进毛囊再生与治疗脱发的多靶点药理机制及转化证据综述

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Abstract:

Background: Alopecia, particularly androgenetic alopecia (AGA) and alopecia areata (AA), is a common chronic disorder of hair follicles that affects appearance, psychological well-being, and quality of life. Although minoxidil and finasteride are widely used in clinical practice, their long-term application is limited by adverse reactions, incomplete efficacy, and recurrence after discontinuation. Traditional Chinese medicine (TCM) and natural products have attracted increasing attention because of their multi-component, multi-target, and multi-pathway regulatory properties.

Method: This review summarized recent experimental and clinical evidence regarding TCM and natural bioactive compounds in hair growth promotion and alopecia treatment. Evidence from in vitro studies, animal models, and randomized clinical trials was integrated to analyze their effects on dermal papilla cells, hair follicle stem cells, follicular microenvironment, and key signaling pathways involved in hair follicle cycling.

Results: Current evidence indicates that TCM-derived compounds and herbal formulas may promote hair growth through multiple mechanisms. In vitro studies showed that Aconiti Ciliare Tuber extract, catalpol from *Rehmannia glutinosa*, ferulic acid from *Angelica sinensis*, paeoniflorin from *Paeonia lactiflora*, thymol from *Ligusticum chuanxiong*, quercetin, oleanolic acid, and cinnamic acid could enhance dermal papilla cell proliferation, improve mitochondrial function, regulate growth factor secretion, and protect follicular cells against apoptosis, oxidative stress, inflammation, and ferroptosis. Mechanistically, these effects were closely associated with activation of Wnt/ β -catenin, Nrf2/HO-1, ER α /MAPK, SHP2/AKT, OXTR, and Akt/GSK-3 β pathways, as well as inhibition of JAK-STAT signaling and androgen-related mediators. In vivo studies further demonstrated that several herbal extracts and formulas accelerated the telogen-to-anagen transition, increased

hair follicle density, restored dermal thickness, and regulated VEGF, IGF-1, KGF, DKK-1, 5 α -reductase, TGF- β , Bcl-2/Bax, and caspase-related pathways. Moreover, clinical studies of natural product-based preparations, including MK-R7, watercress extract, and Redenyl®, showed potential benefits in improving hair density, hair diameter, scalp inflammation, and local tolerability.

Conclusion: TCM and natural products exhibit promising potential in alopecia treatment by modulating androgen metabolism, inflammatory responses, oxidative stress, apoptosis, ferroptosis, mitochondrial function, and hair follicle regenerative signaling. However, current clinical evidence remains limited by small sample sizes, insufficient long-term follow-up, and inconsistent quality control of herbal preparations. Further standardized pharmacological studies and large-scale randomized controlled trials are required to clarify their efficacy, safety, and clinical application value.

Keywords: Androgenetic alopecia; Hair follicle regeneration; Traditional Chinese medicine; Multi-target pharmacology; Wnt/ β -catenin pathway; Oxidative stress

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**Gut microbiota-derived butyrate mediates the cardioprotective effects of
Modified Taohong Siwu Decoction via the HDAC -PPAR γ axis in macrophages**

**加味桃红四物汤通过调控肠道菌群-丁酸轴诱导修复巨噬细胞表型
转变促进小鼠心肌梗死后修复**

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Abstract:

Background: Modified Taohong Siwu decoction (MTHSWD) has been widely used in clinic to improve cardiac function in myocardial infarction (MI) patients, but its cardioprotective properties and the underlying mechanisms remain undetermined. This study aims to investigate the therapeutic mechanism of MTHSWD in improving post-MI repair from the perspective of regulating intestinal microbiota and metabolites based on the theory of “gut-heart axis”.

Method: The MI model was established in C57BL/6J mice to examine the efficiency of MTHSWD on cardiac function and macrophage phenotypes *in vivo*. Metagenomic sequencing was used to analyze the structure and composition of the gut microbiota after MTHSWD intervention. Targeted metabolomics was used to detect the changes of short-chain fatty acids (SCFAs) contents and metabolism in serum. Fecal microbiota from the MI group and the MTHSWD group were separately transplanted into pseudo-sterile MI mice in order to verify the role of gut flora in the cardioprotective effect of MTHSWD. The direct effects of MTHSWD on SCFA-producing bacteria were assessed using anaerobic culture assays *in vitro*. Sodium butyrate was administrated to MI mice and macrophages (BMDM and RAW264.7) to verify its key intermediating role and to explore its underlying mechanism.

Results: MTHSWD significantly improved the cardiac function, reduce myocardial fibrosis and boost the percentage of cardiac M2 macrophages in mice. Metagenomic data analysis showed that the composition of microbiota among the Sham, MI and MTHSWD-treated group was significantly different. Specifically, MTHSWD markedly enriched SCFA-producing bacteria, especially butyrate producers like *Faecalibacterium prausnitzii*, *Blautia* and *Bifidobacterium*, resulting in a significant elevation of circulating butyrate levels. This microbial-metabolic shift

was essential for the observed cardioprotection, as fecal microbiota transplantation (FMT) from MTHSWD-treated mice and sodium butyrate administration recapitulated the improvements in cardiac function and remodeling. *In vitro*, butyrate directly promoted the polarization of macrophages towards the reparative M2 phenotype. Mechanistically, butyrate acted as a histone deacetylase (HDAC) inhibitor, increasing histone H3K9 acetylation in macrophages. Enhanced H3K9 acetylation at the *Pparg* promoter facilitated transcriptional activation of PPAR γ , a key regulator of alternative macrophage activation, thereby driving the expression of downstream reparative genes and orchestrating macrophage phenotypic transition.

Conclusion: MTHSWD could improve post-myocardial infarction repair and attenuates fibrosis by reshaping the gut microbiota and enhancing microbial butyrate production. Elevated butyrate promotes macrophage reprogramming through histone acetylation-dependent activation of PPAR γ , revealing a microbiota-metabolite-epigenetic axis that links herbal intervention to immune modulation in cardiac repair.

**The “Ruanjian Qingmai” Formula Regulates Macrophage Lipid Metabolism
and Polarization to Treat Atherosclerosis via AMPK-Dependent PPAR γ
Activation**

**軟堅清脈方通過 AMPK 依賴性 PPAR γ 激活調控巨噬細胞脂質代謝及
極化治療動脈粥樣硬化**

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Abstract:

Background: To investigate the inhibitory effects of the Ruanjian Qingmai Formula (RJQM) on plaque formation and macrophage foam cell formation in mice with atherosclerosis (AS), and to elucidate its underlying molecular mechanisms.

Method: A high-fat diet-induced ApoE^{-/-} mouse model was established. Mice were randomly assigned to a wild-type control group, a model control group, and low-, medium-, and high-dose RJQM groups, as well as an atorvastatin group. They were fed the respective diets and received interventions for 12 weeks. Body weight, four lipid parameters, and intima-media thickness of the aortic arch were continuously monitored during the intervention period. After 12 weeks, tissues were collected for gross examination and HE, Masson, and Oil Red O staining of the aortic root. In vitro, oxidized low-density lipoprotein (LDL) was used to induce RAW 264.7 and THP-1 cells as foam cell models. These cells were treated with RJQM-containing serum. Lipid accumulation was observed via Oil Red O staining, and qRT-PCR was used to detect gene expression related to M2 macrophage polarization, inflammatory factors, cholesterol efflux, and fatty acid oxidation. UPLC-MS was used to identify the active components of RJQM in the blood, and core targets and pathways were identified through aortic arch transcriptomic sequencing and network pharmacology. Validation was performed using the PPAR γ agonist rosiglitazone, the antagonist GW9662, and the AMPK inhibitor Compound C; Western blot analysis was used to detect AMPK phosphorylation levels and PPAR γ expression levels.

Results: In the medium- and high-dose RJQM groups, serum total cholesterol and LDL-C levels in mice were significantly reduced; aortic intima-media thickness decreased; plaque area shrank; necrotic core and lipid areas decreased; and collagen ratio and fibrous cap thickness increased. In vitro experiments showed that RJQM-containing serum significantly inhibited foam cell formation, promoted the

polarization of macrophages toward the M2 phenotype, enhanced the expression of anti-inflammatory factors, and upregulated cholesterol efflux and fatty acid oxidation genes, while having no significant effect on genes related to lipid uptake, synthesis, and lipolysis. UPLC-MS identified 10 major bioavailable components. Transcriptomics combined with network pharmacology identified 31 core genes, pinpointing PPAR γ as a key target, which exhibits good binding affinity with the RJQM components hesperetin and kaempferol (<-7 kcal/mol). Functional validation demonstrated that rosiglitazone can mimic RJQM's inhibitory effect on foam cell formation, while GW9662 and Compound C both abolish RJQM's pharmacological effects. Western blot analysis confirmed that RJQM enhances PPAR γ phosphorylation by promoting AMPK phosphorylation.

Conclusion: RJQM effectively inhibits arterial plaque formation and stabilizes plaques in ASO mice. Its mechanism of action likely involves activating the AMPK/PPAR γ signaling pathway, inducing macrophage polarization toward the M2 phenotype, and enhancing cholesterol efflux and fatty acid oxidation, thereby inhibiting macrophage foam cell formation.

Shugan Decoction ameliorates colonic motility dysfunction induced by WAS in rats by inhibiting the tryptophan IDO1/AHR signaling pathway

疏肝饮通过抑制色氨酸 IDO1/AHR 信号通路改善 WAS 诱导的大鼠结肠运动功能异常

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Abstract:

Background: Explore the KYN pathway and key proteins IDO1 and AHR involved in tryptophan (Trp) metabolism to determine whether they are involved in the pathogenesis of diarrhea induced irritable bowel syndrome (IBS-D) in rats induced by water deprivation stress (WAS), and whether Shugan Tang (SGD) treats IBS-D by regulating the Trp KYN pathway.

Method: Network pharmacology and molecular docking were used to screen potential signaling pathways and molecular targets of SGD for IBS-D. SD male rats were divided into Ctrl, WAS, WAS+AHR inhibitor (CH223191), and SGD groups. Daily bowel movements were recorded, and visceral sensitivity was measured via colorectal distension. Colon histopathology was observed by HE staining. Trp-KYN pathway metabolites in colon and hippocampus were detected by UPLC. Expressions of IDO1, AHR, and NMDAR proteins in colon were analyzed by WB, immunofluorescence, and immunohistochemistry.

Results: Network pharmacology and docking suggested that the Trp-KYN pathway and AHR signaling might underlie SGD's therapeutic mechanism. Compared with Ctrl, WAS rats showed increased bowel movements, decreased visceral pain threshold, elevated colon KYN, KYNA, QUIN contents, and upregulated IDO1, AHR, GPR35, NMDAR2B proteins. Hippocampal KYN and QUIN increased, while KYNA decreased; KYN/Trp and QUIN/KYNA ratios rise in both tissues. Compared with WAS, CID123153, CH223191, and SGD groups showed reduced defecation, increased pain threshold, and normal colon mucosa. SGD/CID123153 decreased colon KYN; SGD/CH223191 reduced colon KYNA and QUIN. All three groups downregulated IDO1 and GPR35; CH223191/SGD downregulated AHR. Hippocampal KYN decreased in all three groups; CH223191 reduced QUIN; SGD increased KYNA and decreased QUIN. KYN/Trp and QUIN/KYNA ratios decreased in both tissues.

Conclusion: WAS-induced IBS-D rats exhibit disordered Trp-KYN pathway along the gut-brain axis (GBA). SGD corrects this disorder and improves IBS-D-like symptoms by inhibiting the IDO1-AHR-GPR35/NMDAR2B pathway and restoring abnormal Trp-KYN metabolites and enzyme activity.

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**EC alleviates HFD-induced sarcopenic obesity via Sirt3-mediated
deacetylation of SOD2 at K68**

**EC 靶向 Sirt3 去乙酰化 Sod2 赖氨酸 68 位点缓解由高脂饮食诱导的
肌少性肥胖**

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Abstract:

Background: Sarcopenic obesity (SO) is a metabolic disorder that affects approximately 10–27% of the global elderly population, exhibits a notably higher prevalence among individuals with chronic diseases, and poses an escalating public health burden worldwide. Three incretin mimetics currently approved for obesity treatment—liraglutide, semaglutide, and tirzepatide—are associated with significant gastrointestinal adverse effects and fail to promote muscle gain. Therefore, safe and effective therapeutic agents capable of both reducing fat mass and increasing muscle mass are urgently needed for the management of SO. EC, a flavonoid compound, remains unexplored in the context of SO therapy. Given that mitochondria play a central role in fatty acid oxidation and that mitochondrial dysfunction contributes to lipid metabolic abnormalities and skeletal muscle impairment, targeting mitochondrial function may represent a promising therapeutic strategy for SO.

Method: To investigate the effect of EC on adipogenic differentiation, in vitro experiments were performed using mouse 3T3-L1 preadipocytes and C2C12 myoblasts subjected to the classic cocktail induction protocol. High-content imaging, Western blotting, and qRT-PCR were employed to assess the capacity of EC to reduce aberrant lipid deposition and ameliorate muscle atrophy. Subsequently, C57BL/6J mice were fed a high-fat diet (HFD) for 12 weeks to establish an in vivo model and EC was administered intraperitoneally for 6 weeks. Lipid accumulation was evaluated by CT imaging, and motor function was assessed using behavioral tests, including treadmill and rotarod assays. To explore mitochondrial function under SO conditions, protein levels of Sirtuins, mitochondrial membrane potential (MMP), and reactive oxygen species (ROS) were measured in C2C12 cell lysates. Furthermore, acetyl-proteomics and scRNA-seq were performed on the

gastrocnemius muscle of C57BL/6J mice.

Results: In 3T3-L1 and C2C12 cells, abnormal lipid accumulation during adipogenic differentiation was attenuated by EC, as assessed by oil red O staining. The protein expression of key adipogenic markers, including FASN, ACC, SREBP1, PPARG, ATGL, lipoprotein, and adiponectin, was downregulated by EC. In vivo, adipose tissue accumulation in mice was reduced by EC, as determined by computed tomography (CT) imaging. Moreover, motor function was improved in mice under HFD by EC, as evaluated by behavioral assays (treadmill and rotarod tests). Additionally, ROS levels were decreased, and MMP was enhanced in a cocktail induction model by EC, accompanied by upregulation of the key protein Sirt3, as determined by Western blotting. The K68 acetylation site of SOD2 was identified by acetylproteomics analysis as a critical target in sarcopenia. Furthermore, it was revealed by scRNA-seq that the proportion of inflammatory cells in the HFD mouse model was effectively reduced by EC. Collectively, it was confirmed by experimental validation that Sirt3 expression was significantly upregulated by EC, while the protein level of acetylated SOD2 at K68 was downregulated, thereby improving mitochondrial function.

Conclusion: Sirt3 and acetylation of SOD2 at K68 were identified as key molecular determinants in sarcopenic obesity. EC alleviates HFD-induced sarcopenic obesity via Sirt3-mediated deacetylation of SOD2 at K68.

Xiao-Yao-San suppresses psychological distress-related colorectal cancer metastasis and enhances antitumor immune responses through regulating gut microbiota–bile acid axis

逍遥散调节肠道菌群-胆汁酸代谢抑制心理应激相关肠癌肝转移的作用及机制研究

Authors: Hao Qian¹, Xinxin Hou¹, Ling Zhao¹ and Zhaozhou Zhang^{1,2}

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Abstract:

Background: Psychiatric disorders are recognized as risk factors for tumor progression and metastasis in colorectal cancer (CRC). Xiao-Yao-San (XYS), a traditional Chinese herbal formula with antidepressant properties, has been reported to inhibit CRC growth and modulate gut microbiota. However, its efficacy and underlying mechanisms in preventing metastasis remain unclear.

Methods: The antimetastatic effect of YYS was assessed in a chronic restraint stress (CRS)-induced CRC model. YYS-associated gut microbiota was evaluated using 16S ribosomal RNA (rRNA) sequencing. Peripheral bile acid (BA) profiles were analyzed through targeted metabolomics. Fecal microbiota and commercial bacterial strains were anaerobically cultured to identify bile salt hydrolase (bsh)-expressing bacteria. YYS-mediated antitumor immune responses were determined via flow cytometry, immunohistochemistry.

Results: Administration of dried YYS decoction powder reduced liver metastatic nodules and prevented body weight loss in CRS-induced CRC mice, while also alleviating depressive-like behaviors and lowering serum stress hormone levels. High-dose YYS (2 g/kg/day) produced antimetastatic and antidepressant effects comparable to those of sertraline, although these effects were largely abolished in mice treated with antibiotic cocktails. YYS significantly modulated gut microbiota composition and serum BA profiles, particularly by restoring bsh-expressing bacteria in the cecum and increasing the proportion of free BAs. YYS also reshaped the immune landscape within metastatic foci.

Conclusion: YYS prevents psychiatric disorder-associated CRC metastasis and strengthens antitumor immune responses by regulating bsh-expressing gut bacteria and their derived BA profiles. These findings thus offer a novel mechanistic rationale for the potential use of YYS in treating CRC patients with comorbid psychiatric disorders.

**Stachydrine hydrochloride Protects Against Doxorubicin-Induced
Cardiotoxicity by Stabilizing Optic Atrophy 1 Protein and Preserving
Mitochondrial Integrity**

**益母草水蘇鹼透過穩定視神經萎縮 1 蛋白並維持線粒體完整預防阿
黴素誘導的心臟毒性**

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Abstract:

Background: Doxorubicin (Dox) causes dose-dependent cardiotoxicity (DIC) involving mitochondrial dysfunction and downregulation of OPA1. Stachydrine hydrochloride (Sta), a bioactive alkaloid derived from *Leonurus japonicus*, has demonstrated cardioprotective properties, although its role and mechanism in DIC remain unclear.

Purpose: We aim to evaluate the cardioprotective efficacy of Sta against DIC in vivo and in vitro. Furthermore, we clarify the mechanisms of Sta in DIC and investigate the translational value of Sta in tumor-bearing mice model.

Method: A mouse DIC model was established by intraperitoneal administration of Dox (5 mg/kg weekly for 5 weeks) and further treated with Sta (6 or 12 mg/kg/day,

i.g.) or dexrazoxane. To evaluate the cardiac function, echocardiography, TUNEL assays for apoptosis, and serum biomarkers were performed. In vitro, Dox-induced cardiomyocyte cytotoxicity and mitochondrial function were generated in neonatal rat cardiomyocytes. To further understand the molecular mechanism of STA, bulk and single-nucleus RNA sequencing of cardiac tissues were utilized. Moreover, the direct target of Sta was identified using biotinylated Sta pull-down coupled with LC-MS/MS and validation techniques for molecular docking. OPA1 knockdown (siRNA, AAV9-shRNA) was utilized in functional rescue experiments. Finally, tumor-bearing mice assessed Sta's impact on Dox antitumor efficacy.

Results: We observed that Sta treatment significantly attenuated Dox-induced cardiac dysfunction, pathological remodeling, and cardiomyocyte apoptosis in vivo and in vitro. Both bulk and single-nucleus RNA sequencing revealed that Sta specifically restored mitochondrial pathways in cardiomyocytes. Mechanistically, Sta directly bound to OPA1 protein, thereby counteracting its Dox-induced degradation. Genetic knockdown of OPA1 abolished the cardioprotective effects of Sta. Notably, in tumor-bearing mice, co-administration of Sta did not compromise the antitumor efficacy of Dox while effectively preventing associated cardiac injury.

Conclusion: Sta is a potent natural cardioprotective agent against doxorubicin-induced cardiotoxicity by targeting and stabilizing OPA1, improving mitochondrial fusion dynamics and cardiomyocyte function. To be noticed, Sta does not attenuate the chemotherapeutic efficacy of Dox. These results identify Sta as a promising adjuvant candidate for Dox-based chemotherapy and highlight OPA1 stabilization as a viable therapeutic strategy for mitigating DIC.

**Baohuoside I Alleviates Dexamethasone-Induced Muscle Atrophy by
Targeting FGF21 to Attenuate DNA Damage**

寶藿苷 I 靶向 FGF21 減輕地塞米松致 DNA 損傷引起的肌肉萎縮

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Department: ¹ School of Integrative Medicine, Shanghai University of Traditional Chinese Medicine

Abstract:

Background: Skeletal muscle atrophy is a common pathological phenomenon characterized by decrease of myotube diameter, directly affecting physical activity capabilities or recovery from illnesses, potentially posing a significant social financial burden, and thus needing an effective treatment. Present treatment strategies for skeletal muscle atrophy are limited, which mainly consist of physical exercise, nutritional supplements, and medications. A new strategy needs to be explored. Baohuoside I, a natural compound derived from Epimedium, has the potential to alleviate skeletal muscle atrophy, but its efficacy and the underlying mechanism require further investigation.

Method: To investigate the effect of Baohuoside I in alleviating skeletal muscle atrophy, a dexamethasone-induced muscle atrophy in C2C12 myoblasts was established and treated with this compound. CCK-8 assay was conducted to determine its optimal concentration. Then Giemsa staining, RT-qPCR, Western blot, flow cytometry, and immunofluorescence staining were employed to analyze myofibrillar morphology, assess the expression of genes associated with muscle differentiation or atrophy, detect cell cycle and apoptosis, and visualize γ -H2A.X linked to DNA damage. Thereafter, ChIP-seq was performed to identify target genes, using anti- γ -H2A.X antibodies. Subsequently, C57BL/6J mouse model was established and the treatment for 14 days was administered. Muscle mass was recorded and behavioral experiments were conducted. Morphological analysis including H&E staining was conducted. Total protein was extracted from skeletal muscle, followed by Western blot quantification.

Results: 1 μ M was selected for Baohuoside I treatment based on CCK-8 assay results. At this concentration, Baohuoside I restored C2C12 myotube diameter, along with muscle weight and cross-sectional area recovered in mice. Baohuoside I also restored impaired myotube differentiation, with muscle atrophy markers Atrogin-1, MuRF-1 and Myostatin downregulated and the differentiation markers MyoD, MHC-1 and Myogenin upregulated. In addition, Baohuoside I played a role

in regulating cell cycles and reducing cell apoptosis. Furthermore, immunofluorescence assays revealed lower nuclear γ -H2A.X levels in the Baohuoside I group compared with the dexamethasone group, suggesting DNA damage happened and then improved by Baohuoside I. To define the target of γ -H2A.X involved in DNA damage response, ChIP-seq in C2C12 myoblasts was performed and the results indicated that histone γ -H2A.X bound to 50 genes (49 upregulated and 1 downregulated). Among these genes, FGF21 exhibited distinct enrichment of histone binding, demonstrating the specific interaction between γ -H2A.X and FGF21 and implying that FGF21 may serve as a potential functional target of Baohuoside I.

Conclusion: As in vitro and in vivo experiments confirmed, Baohuoside I significantly alleviated dexamethasone-induced skeletal muscle atrophy. According to the results of ChIP-seq assay, the binding relationship between γ -H2A.X and FGF21 was clarified, with FGF21 preliminarily screened out as the core candidate gene. The existing results suggest that FGF21 represents a potential functional target of Baohuoside I in attenuating DNA damages, providing a direction and experimental basis for subsequent mechanism research.

Effect of Tuina on Hypothalamic Orexin-A Expression and Sleep Behavior in a Rat Model of Primary Insomnia

推拿对原发性失眠大鼠模型下丘脑 Orexin-A 表达及睡眠行为的影响

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Abstract:

Background: Insomnia is a prevalent sleep disorder with limited treatment options due to drug dependence and tolerance^{1,2}. Tuina, a traditional Chinese medicine external therapy, has shown clinical efficacy in treating insomnia, but its central mechanism remains unclear³. The orexin system in the hypothalamus plays a key role in wakefulness regulation⁴. This study investigates whether Tuina alleviates insomnia by modulating hypothalamic Orexin-A expression.

Method: A primary insomnia rat model was established using the modified multiple platform water environment method. Sixty-four Wistar rats were randomly divided into control, model, Tuina, and orexin antagonist (MK-4305) groups. Tuina intervention (abdominal manipulation at CV4, CV15, and GB26, 5 – 7 cycles/min, 10 min/day) was applied for 14 consecutive days. Sleep behavior was assessed using pentobarbital-induced sleep test and open field test. Orexin-A expression in the hypothalamus was detected by immunohistochemistry and real-time quantitative PCR.

Results: Compared with the model group, Tuina intervention significantly shortened sleep latency ($P < 0.05$), prolonged sleep duration ($P < 0.05$), and alleviated anxiety-like behaviors in the open field test. Immunohistochemistry showed that Tuina reduced the number of Orexin-A positive neurons in the hypothalamus, with total staining scores decreasing from 12 (model group) to 9 (Tuina group). qPCR confirmed that Tuina significantly downregulated Orexin-A mRNA expression compared with the model group ($P < 0.05$). Similar to the orexin antagonist MK-4305, Tuina also reduced Orexin-A expression and improved sleep behaviors.

Conclusion: Tuina alleviates insomnia-like behaviors in a rat model of primary insomnia, potentially through downregulating Orexin-A expression in the hypothalamus. This study provides experimental evidence for the central mechanism

of Tuina in treating sleep disorders.

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**Effects of 10.6 μ m Laser Moxibustion and Traditional Moxibustion on
STZ-Induced Diabetic Peripheral Neuropathy in Rats Under Background
Glycemic Control**

**10.6 μ m 激光灸与传统艾灸在血糖控制背景下对 STZ 诱导的糖尿病
周围神经病变大鼠的改善作用**

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Abstract:

Background: Diabetic peripheral neuropathy (DPN) is one of the most common complications of diabetes mellitus (DM) and may continue to progress despite glycemic control. This study aimed to investigate whether 10.6 μ m laser moxibustion and traditional moxibustion could improve or delay the progression of DPN under stable glycemic control.

Method: Male Sprague-Dawley rats were intraperitoneally injected with 1% streptozotocin (STZ) to establish a type 1 diabetes model. Four weeks after model establishment, the rats were randomly divided into five groups (n = 6): blank group, model group, insulin group, insulin + 10.6 μ m laser moxibustion group, and insulin + traditional moxibustion group. After model establishment, insulin glargine was injected daily as background glucose-lowering treatment to better simulate clinical practice. Laser moxibustion and traditional moxibustion were performed bilaterally at Zusanli (ST36), 15 min per side, once every other day, for 2 weeks. Body weight, blood glucose, mechanical pain threshold, thermal pain threshold, sciatic nerve conduction velocity (NCV), sciatic nerve histopathology (HE staining), ultrastructural changes (transmission electron microscopy), intraepidermal nerve fiber density (IENFD) in footpad skin, and ATP content in dorsal root ganglia (DRG) were measured.

Results: Compared with the model group, laser moxibustion and traditional moxibustion significantly increased mechanical pain threshold and thermal pain threshold, increased NCV and IENFD, alleviated pathological and ultrastructural damage of the sciatic nerve, and increased DRG ATP levels. Compared with the insulin group, laser moxibustion and traditional moxibustion further stabilized blood glucose and increased DRG ATP levels.

Conclusion: These results suggest that, on the basis of glycemic control alone, 10.6 μm laser moxibustion and traditional moxibustion can effectively stabilize blood glucose, improve nerve function and mitochondrial energy metabolism, and delay the progression of DPN.

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**HLPP Inhibits White Adipose Tissue Expansion and Promotes Brown
Adipose Tissue Mitochondrial Thermogenesis in diet-induced Obese Mice via
the DUSP4-ERK MAPK Signaling Pathway**

**HLPP 通过 DUSP4-ERK 的 MAPK 信号通路抑制肥胖小鼠白色脂肪增
长并促进棕色脂肪线粒体产热**

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Abstract:

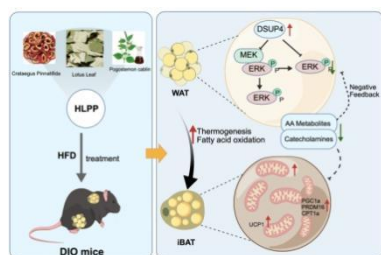
Background: Global obesity prevalence is projected to exceed one billion adults by 2030^[1], with a concomitant rise in related complications such as type 2 diabetes mellitus and cardiovascular diseases. The pathological core of obesity lies in aberrant lipid accumulation driven by disrupted energy homeostasis, with adipose tissue serving as the central regulator of energy storage and conversion^[2]. The herbal formulation HLPP, grounded in the traditional Chinese medicine principles of “resolving food accumulation and guiding out stagnation, resolving phlegm and dispelling dampness,” comprises *Crataegus pinnatifida*, lotus leaf, and patchouli cablin. Although HLPP has demonstrated significant anti-obesity potential, its underlying mechanisms remain to be fully elucidated.

Method: In vivo experiments were performed using a high-fat diet (HFD)-induced diet-induced obesity (DIO) mouse model. Body weight, adiposity index, blood lipids, and liver function were evaluated. Insulin sensitivity was assessed by calculating HOMA-IR and QUICKI. Adipose tissue morphology, as well as gene and protein changes, were analyzed by hematoxylin-eosin staining, qPCR, Western blot (WB), and transmission electron microscopy (TEM). Transcriptomic and metabolite changes in adipose tissue were investigated using transcriptome sequencing and untargeted metabolomics. In vitro experiments employed 3T3-L1 preadipocytes and primary white adipocytes. The effects on adipocyte differentiation and related signaling pathways were examined by Oil Red O staining,

immunofluorescence, and WB.

Results: In vivo studies demonstrated that HLPP significantly suppressed body weight gain and reduced white adipose tissue (WAT) weight in HFD-fed mice. HLPP effectively increased interscapular brown adipose tissue (iBAT) mass, decreased plasma levels of ALT, AST, TG, TC, and LDL-C, markedly reduced insulin resistance (HOMA-IR), and enhanced insulin sensitivity (QUICKI). Histological analysis revealed decreased adipocyte size in both WAT and iBAT, accompanied by a significant increase in the number of brown adipocytes and mitochondria in iBAT. qPCR analysis indicated simultaneous activation of WAT browning and iBAT thermogenic program, with marked upregulation of thermogenic capacity and fatty acid oxidation metabolism. In vitro experiments confirmed that HLPP effectively inhibited white adipocyte differentiation and lipid droplet accumulation. Immunofluorescence showed increased UCP1 expression and mitochondrial content (MitoTracker). Transcriptomic analysis revealed that HLPP upregulated DUSP4, leading to direct inhibition of ERK phosphorylation. Concurrently, metabolomics indicated that metabolic reprogramming reduced upstream activating signals (such as arachidonic acid metabolites and catecholamines). Mechanistic studies demonstrated that, in both WAT in vivo and cell models in vitro, HLPP significantly downregulated the phosphorylation of MEK and ERK in the MAPK pathway. These concerted effects resulted in marked suppression of the MAPK pathway in adipose tissue, thereby inhibiting adipocyte growth.

Conclusion: Compound HLPP effectively ameliorates high-fat diet-induced obesity, dyslipidemia, and insulin resistance. Its mechanism of action may involve upregulation of DUSP4, which directly inhibits ERK phosphorylation, together with metabolic reprogramming that reduces upstream activating signals, thereby negatively regulating the MAPK signaling pathway. This dual mechanism suppresses white adipose tissue expansion and enhances brown adipose tissue mitochondrial function.



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**Baicalein, a natural constituent of *Scutellaria baicalensis*, inhibits Gastric
Cancer Cell Migration and Represents a novel Strategy Against Gastric Cancer
Metastasis**

**黄芩素，一种黄芩中的天然成分，能够抑制胃癌细胞的迁移并为对抗
胃癌转移提供了一种新的策略**

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Department: **Longhua Hospital Affiliated to Shanghai University of Traditional Chinese Medicine; †school of Integrative Medicine SHUTCM, Shanghai University Traditional Chinese Medicine*

Abstract:

Background: Gastric cancer is currently one of the most common and deadly malignant tumors worldwide. Invasion and metastasis are key features of gastric cancer progression and leading causes of postoperative recurrence, poor response to chemotherapy, and reduced overall survival. Classic cytotoxic chemotherapeutics are associated with significant side effects, a high risk of drug resistance, and limited efficacy against metastatic lesions. In contrast, traditional Chinese medicine (TCM) offers advantages such as lower systemic toxicity, multi-targeted anti-metastatic activity, and the ability to reverse drug resistance. Baicalein is a major flavonoid constituent of the traditional Chinese herb *Scutellaria baicalensis*. It has demonstrated anti-proliferative, pro-apoptotic, and anti-metastatic effects in various tumors, however, its impact on gastric cancer cell migration and survival in tumor-bearing animals has not yet been fully elucidated.

Method: AGS and SGC-7901 gastric cancer cells were cultured in vitro. The CCK-8 assay was used to assess the effect of Baicalein on cell viability. The 50% inhibitory concentration (IC₅₀) is determined using the linear interpolation method, and the

formula is $IC_{50} = C_1 + (C_2 - C_1) \times \frac{50\% - I_1}{I_2 - I_1}$; the Transwell assay was employed to evaluate the effect of Baicalein on the migratory capacity of gastric cancer cells; a hematogenous metastasis model of gastric cancer in nude mice was established. Mice were treated with Baicalein, tumor growth was monitored and survival time was recorded to assess its impact on mouse survival. Hematoxylin and eosin (H&E) staining was performed to observe pathological morphology and evaluate lung tumor metastasis.

Results: AGS and SGC-7901 showed a concentration-dependent decrease from 12.5 to 50 $\mu\text{mol/L}$ ($P < 0.05$) in CCK8 assay. The 50% inhibitory concentration (IC_{50}) of Baicalein against SGC-7901 and AGS gastric cancer cells at 48 hours was 102 $\mu\text{mol/L}$ (SGC-7901) and 83 $\mu\text{mol/L}$ (AGS), respectively, indicating that Baicalein significantly inhibited gastric cancer cell viability. Transwell assay demonstrated that at 50 $\mu\text{mol/L}$, baicalein reduced the number of migrating gastric cancer cells by 40.6% in AGS ($P < 0.05$) and 57.4% in SGC-7901 ($P < 0.001$) compared with the untreated group. These results indicate that baicalein inhibits the migration of gastric cancer cells. Macroscopic observation revealed numerous gray-white metastatic nodules on the lung surface of the mice in the model group, some of which were fused. In the treatment group, the number of metastatic nodules was lower, their sizes were reduced, and no fusion was observed. H&E staining further confirmed that tumor cell infiltration in lung tissue was markedly decreased after baicalein administration, and the normal alveolar structure was effectively protected. Kaplan-Meier survival analysis showed that, compared with the untreated mice, the survival curves of Baicalein-treated mice shifted to the right, with a clear separation between the curves. The high-dose Baicalein group prolonged survival by 40%, and the medium-dose group by 20%. These findings indicate that Baicalein can improve survival in gastric cancer-bearing mice.

Conclusion: Baicalein can inhibit gastric cancer cell proliferation, migration, and malignant phenotypes, and prolong survival in tumor-bearing mice. It is expected to become a new type of drug for preventing and treating gastric cancer metastasis.

Acknowledgements

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**Direct Inhibition of Macrophage STING Signaling by Bisdemethoxycurcumin
Ameliorates Myocardial Infarction-Induced Inflammation and Cardiac
Dysfunction**

**双去甲氧基姜黄素直接抑制 STING 信号传导，减弱炎症反应改善心
肌梗死后心脏功能**

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Abstract:

Although macrophages are central to the pathophysiology of myocardial infarction (MI), effective targeted therapies remain elusive. Necrotic cardiomyocytes release cytoplasmic DNA that activates the cGAS-STING axis via IRF3 and NF- κ B, driving type I interferon production, inflammation, and fibrosis, thereby contributing to adverse ventricular remodeling. Pharmacological inhibition of STING mitigates these pathologies and preserves cardiac function^[4]. Bisdemethoxycurcumin (BDMC), a natural anti-inflammatory compound derived from medicinal herbs such as *Curcuma zedoaria*, exhibits therapeutic potential. Here, we investigated whether bisdemethoxycurcumin attenuates post-MI cardiac dysfunction through modulation of the STING pathway.

MI was induced in mice by permanent ligation of the left anterior descending (LAD) coronary artery. Cardiac function was assessed by echocardiography, and collagen deposition was quantitatively analyzed using histopathological staining and immunofluorescence assays. Molecular docking and dynamics simulations were performed to predict the binding interaction between BDMC and STING. Protein expression and phosphorylation levels of the STING pathway were detected via immunohistochemistry and Western blotting. For in vitro mechanistic validation, experiments were conducted using RAW264.7 macrophage cell lines and primary macrophages derived from STING knockout (KO) versus wild-type (WT) mice.

BDMC significantly preserved left ventricular function and elevated ejection

fraction, while concurrently reducing infarct size in the MI mouse model. In vitro, bisdemethoxycurcumin dose-dependently attenuated LPS and c-GAMP-induced hyperinflammatory responses in RAW264.7 macrophages, concomitant with a marked downregulation of STING downstream signaling (e.g., p-TBK1/p-IRF3). Furthermore, molecular docking and dynamics simulations substantiated a high-affinity, stable interaction between bisdemethoxycurcumin and the STING protein.

In summary, BDMC directly targets STING, disrupting the cGAS-STING cascade. This suppresses macrophage-driven inflammation and fibroblast activation, ultimately preserving cardiac function after MI.

Keywords: Bisdemethoxycurcumin; STING; cGAS-STING signaling; Myocardial infarction; Myocardial fibrosis

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Przewaquinone A inhibits neutrophil extracellular trap formation through the Piezo1/Runx1 axis to ameliorate hypertension

**紫丹參甲素通過 Piezo1/Runx1 軸抑制中性粒細胞胞外誘捕網形成抗
高血壓的機制研究**

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Abstract:

Objective: Excessive formation of neutrophil extracellular traps (NETs) is a key pathological driver of vascular inflammation and target organ damage in hypertension^{1,2}. The mechanosensitive ion channel Piezo1 and its downstream transcription factor Runx1 constitute a critical signaling axis regulating NETs generation^{3,4}. Przewaquinone A, a major lipophilic active component of *Salvia miltiorrhiza* (Danshen), exhibits well-documented cardiovascular protective effects. However, whether it exerts antihypertensive effects through the Piezo1/Runx1 axis-mediated inhibition of NETs formation remains unclear. This study aimed to investigate the molecular mechanism by which Przewaquinone A regulates NETs formation via the Piezo1/Runx1 axis to ameliorate hypertension.

Methods: A hypertensive mouse model was established in C57BL/6J mice via subcutaneous infusion of angiotensin II (Ang II) using osmotic minipumps. Mice were administered Przewaquinone A by gavage, and blood pressure was dynamically monitored by the non-invasive tail-cuff method. Cardiac and vascular target organ injury was assessed by echocardiography and histopathology. In vitro, a co-culture system of HL-60-differentiated neutrophil-like cells and HUVECs was established. Sytox Green staining, immunofluorescence, ELISA, qPCR, and Przewaquinone A Western blot were employed to evaluate the effects of Przewaquinone A on Piezo1/Runx1 axis activity, NETs formation, and endothelial inflammation⁵. Surface plasmon resonance (SPR) and molecular docking were performed to analyze the binding kinetics between Przewaquinone A and Piezo1 protein. The pivotal role of the Piezo1/Runx1 axis in mediating the effects of Przewaquinone A was further validated by Piezo1/Runx1 overexpression.

Results: Przewaquinone A significantly reduced systolic and diastolic blood

pressure, attenuated myocardial hypertrophy and aortic fibrosis, and improved endothelium-dependent vasorelaxation in hypertensive mice. Mechanistically, Przewaquinone A suppressed Piezo1 overactivation, attenuated intracellular Ca^{2+} transients, and downregulated Runx1 expression. It markedly decreased NETs markers (CitH3 and MPO-DNA complexes) release and neutrophil infiltration, reduced adhesion molecule expression (ICAM-1, VCAM-1), and restored endothelial NO production. SPR confirmed direct binding between Przewaquinone A and Piezo1 protein. Functional rescue experiments demonstrated that overexpression of Piezo1 or Runx1 partially reversed the inhibitory effects of Przewaquinone A on NETs formation and vascular protection⁶.

Conclusions:Przewaquinone A exerts antihypertensive and target organ protective effects by suppressing the Piezo1/Runx1 signaling axis, thereby blocking NETs formation and attenuating the neutrophil-endothelial positive feedback inflammatory loop⁷.This study elucidates a novel mechanism of Przewaquinone A in hypertension intervention from molecular, cellular, and organismal perspectives, providing potential targets and experimental evidence for the modernization of traditional Chinese medicine and precision prevention of hypertension.

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**Ilex Pubescens Inhibits Ferroptosis post-myocardial ischemia-reperfusion
injury by activating aldehyde dehydrogenase 2**

**毛冬青通過激活 ALDH2 抑制心肌缺血再灌注損傷後的心肌細胞
鐵死亡**

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Hospital of Guangzhou Medical University, Guangzhou, China.*

Abstract:

Background

Ilex pubescens is a traditional Chinese medicine widely used in the treatment of cardiovascular diseases, exhibiting potential anti-inflammatory capabilities in myocardial ischemia-reperfusion injury (MI/RI)¹. Aldehyde dehydrogenase 2 (ALDH2) plays a crucial role in the cascade of events leading to ferroptosis², a form of regulated cell death characterized by iron-dependent lipid peroxidation, which is closely associated with the development and progression of MI/RI³. Although preliminary studies have suggested cardioprotective effects of *Ilex pubescens*, its specific impact on MI/RI and the underlying molecular mechanisms remain unclear and warrant further investigation.

Purpose

This study aims to elucidate the primary mechanism by which *Ilex pubescens* extract (IPES) alleviates ferroptosis following MI/RI, with a particular focus on its regulatory role in the ALDH2 signaling pathway.

Methods

In vivo, a classical myocardial ischemia-reperfusion (I/R) injury model was established in C57BL/6 mice by ligating the left anterior descending coronary artery (LAD) for 30 minutes followed by 24 hours of reperfusion. In vitro, primary cardiomyocytes were isolated from neonatal Sprague-Dawley rats and treated with erastin, a specific ferroptosis inducer, to establish a cardiomyocyte ferroptosis model. To verify whether IPES exerts its anti-ferroptotic effects through ALDH2 activation, the selective ALDH2 inhibitor CVT-10216 was used in intervention experiments, providing both positive and negative validation of the critical role of ALDH2 in this process.

Results

IPES exhibited significant cardioprotective effects. In the animal model, IPES

significantly attenuated cardiac injury induced by I/R, improved cardiac function parameters, and reduced serum levels of cardiac injury-related biomarkers. Meanwhile, IPES treatment markedly decreased inflammatory cell infiltration in myocardial tissue, intracellular reactive oxygen species (ROS) generation, and iron deposition-induced oxidative damage. At the molecular level, IPES significantly downregulated the expression of iron metabolism-related proteins (transferrin receptor 1 (TFR1), ferritin, ferritin heavy chain 1 (FTH1), ferritin light chain 1 (FTL1)) and reduced the concentration of 4-hydroxynonenal (4-HNE), a characteristic metabolite of ferroptosis. Furthermore, IPES inhibited excessive glutathione (GSH) degradation and maintained the normal activity of glutathione peroxidase 4 (GPX4). Notably, IPES significantly upregulated ALDH2 expression levels, highlighting its key role in inhibiting myocardial injury. In vitro experiments further confirmed that IPES effectively protected primary cardiomyocytes from erastin-induced ferroptosis. Moreover, specific inhibition of ALDH2 by CVT-10216 markedly and partially attenuated the cardioprotective effects of IPES, reversely validating the central role of ALDH2 in the anti-ferroptotic mechanism of IPES.

Conclusion

In summary, this study demonstrates that *Ilex pubescens* extract effectively inhibits ferroptosis following myocardial ischemia-reperfusion injury by activating the ALDH2 pathway, providing a solid experimental basis for its potential clinical application in the treatment of MI/RI.

Acknowledgement:

This work was supported by the National Natural Science Foundation of China (Grant No. 82374341, 82374183, 82274246).

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**Dihydrotanshinone I Activates ALDH2 to Suppress Myocardial Cell
Ferroptosis Following Myocardial Infarction**

二氢丹参酮 I 激活 ALDH2 抑制心梗後心肌細胞鐵死亡的研究

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Abstract:

Background

Persistent cardiomyocyte death after acute myocardial infarction (AMI) is the core pathological driver of ventricular remodeling and heart failure. Ferroptosis, an iron-dependent regulated cell death characterized by lipid peroxide accumulation, is critical for AMI-induced myocardial injury. Inhibiting cardiomyocyte ferroptosis is a promising therapeutic strategy to salvage endangered myocardium and optimize AMI prognosis. Myocardial ischemia suppresses aldehyde dehydrogenase 2 (ALDH2) activity, triggering toxic aldehydes and ROS accumulation, aggravating lipid peroxidation and facilitating ferroptosis progression. Dihydrotanshinone I (DHT), a major lipophilic active component of *Salvia miltiorrhiza*, exerts favorable cardioprotective effects. Nevertheless, whether DHT modulates myocardial ferroptosis via targeting ALDH2 remains unclarified.

Methods

In vivo, AMI mouse models were established via left anterior descending coronary artery ligation, and randomly divided into sham, model, low/high-dose

DHT (10, 20mg/kg/d) and captopril positive control groups with 7-day continuous intervention. Cardiac weight index, myocardial histopathological injury, Fe^{2+} level, LDH and ALDH2 activity were detected. Ferroptosis-related proteins (xCT, GPX4, ACSL4) were determined via Western blot and immunohistochemistry. In vitro, neonatal rat cardiomyocytes(NRCMs)were isolated, and CCK-8 assay screened safe DHT concentrations. Erastin was used to construct NRCM ferroptosis model.Cell viability, Fe^{2+} , ROS, mitochondrial membrane potential, oxidative stress indicators and ferroptosis-related proteins were tested.Molecular docking and molecular dynamics simulation verified the binding affinity between DHT and ALDH2.ALDH2 inhibitor CVT-10216 was applied to conduct rescue experiments.

Results

In vivo results demonstrated that DHT elevated LVEF and LVFS, alleviated myocardial inflammatory infiltration and tissue damage, reduced Fe^{2+} and LDH levels, rescued inhibited ALDH2 activity, and upregulated GPX4/xCT expressions (all $P<0.05$). In vitro, 0-1000nM DHT had no cytotoxicity. DHT dose-dependently inhibited Erastin-triggered ferroptosis, reduced oxidative stress and improved mitochondrial morphology ($P<0.05$). DHT possessed strong and stable binding capacity with ALDH2(-8.93 kcal/mol). DHT enhanced ALDH2 activity in a dose-dependent manner, while ALDH2 inhibition partially reversed DHT-mediated cardioprotective and anti-ferroptosis effects($P<0.05$).

Conclusion

DHT ameliorates post-AMI cardiac dysfunction and myocardial damage. It inhibits cardiomyocyte ferroptosis and oxidative stress both in vivo and in vitro. Mechanically, DHT exerts cardioprotective effects by binding and activating ALDH2 to suppress myocardial ferroptosis after AMI.

Acknowledgement:

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Technology Program of Guangzhou(Grant No.2025A03J3833); General Program of Natural Science Foundation of Guangdong Province (Grant No. 2023A1515011090).

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HDAC1 Inhibition by Albiflorin Attenuates Cardiac Fibrosis After Myocardial Infarction *via* Blockade of TGFβR1/Smad2/3 Pathway

芍药内酯苷通过抑制 HDAC1 阻断 TGFβR1/Smad2/3 通路减轻心肌梗死后心肌纤维化

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Abstract:

Background: Myocardial infarction (MI) is a leading cause of cardiovascular death worldwide^[1]. With improved clinical treatments, more patients survive MI but subsequently develop heart failure, in which myocardial fibrosis plays a key role^[2]. Excessive collagen deposition during fibrosis disrupts cardiac structure and function^[3]. HDAC1 is closely linked to organ fibrosis, and its inhibitors exert potent anti-fibrotic effects. Albiflorin, a major active ingredient of Tao-Hong-Si-Wu-Tang, has anti-inflammatory and anti-oxidant properties. This study aimed to explore whether albiflorin relieves post-MI myocardial fibrosis via regulating the HDAC1 pathway.

Methods: A mouse MI model was established by LAD coronary artery ligation. Cardiac function and collagen deposition were assessed via echocardiography, histopathology and immunofluorescence. Molecular docking and dynamics simulated the binding between albiflorin and HDAC1. Immunohistochemistry and Western blot detected pathway activity. In vitro experiments on primary cardiac fibroblasts and HDAC1 overexpression were performed for mechanism verification.

Results: Albiflorin markedly improved left ventricular function in the MI mouse model, reduced myocardial necrotic area, and decreased collagen deposition. At the molecular level, albiflorin down-regulated HDAC1 expression, inhibited the TGF-β1/Smad signaling cascade, and lowered the levels of fibrosis markers including Collagen I/III, fibronectin, and α-SMA. In vitro, albiflorin dose-dependently suppressed TGF-β1-induced proliferation of cardiac fibroblasts, accompanied by reduced expression of cell-cycle proteins CDK4, Cyclin D1, and Cyclin D2. Molecular docking and dynamics simulations confirmed a high-affinity interaction between albiflorin and HDAC1; overexpression of HDAC1 reversed the

anti-fibrotic effects of albiflorin, further validating HDAC1 as a critical target.

Conclusion: Albiflorin directly inhibits HDAC1, thereby disrupting the TGFβR1/Smad2/3 signaling pathway. This leads to inhibition of fibroblast proliferation and collagen deposition, ultimately attenuating myocardial fibrosis after myocardial infarction.

Keywords: Albiflorin; HDAC1; Myocardial Infarction; Myocardial Fibrosis

Acknowledgement:

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Levistolide A ameliorates sepsis-induced cardiac dysfunction by inhibiting ferroptosis via the SIRT1-NRF2 pathway

欧当归内酯内酯 A 通过 SIRT1-NRF2 通路抑制铁死亡改善脓毒症心功能障碍

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Abstract:

Background: Sepsis-induced cardiac dysfunction (SICD) is a life-threatening complication of sepsis, carrying a mortality rate as high as 70%–90%¹, whereas current clinical therapies lack targeted interventions directed at its core pathological mechanisms². Ferroptosis, an iron-dependent form of programmed cell death driven by excessive lipid peroxidation, has been established as a key pathogenic driver of SICD³. The sirtuin 1-nuclear factor erythroid 2-related factor 2 (SIRT1-NRF2) pathway functions as a core regulatory axis governing redox homeostasis and cellular resistance to ferroptosis⁴. Levistolide A (LA), a natural phthalide compound isolated from *Angelica sinensis* with potent anti-inflammatory and antioxidant activities⁵, has an incompletely defined role and underlying mechanism in SICD.

Purpose: This study aimed to investigate the cardioprotective effects of LA against SICD and explore the mechanism by which LA inhibits myocardial ferroptosis via the SIRT1-NRF2 pathway.

Methods: *In vivo*, a murine SICD model was induced via cecal ligation and puncture (CLP). Postoperatively, LA (2, 4 mg/kg) was intraperitoneally administered with dexamethasone as the positive control, followed by assessments of cardiac function, myocardial histopathology, cardiac injury/inflammatory markers, ferroptosis indicators and 72-hour survival rate. *In vitro*, neonatal rat cardiomyocytes (NRCMs) were pretreated with the ferroptosis inducer erastin prior to incubation with gradient concentrations of LA; cell viability, lipid peroxidation, iron metabolism, mitochondrial function and ferroptosis-related protein levels were measured. Bioinformatics analysis, molecular docking and molecular dynamics simulations were performed to predict SIRT1 as the core target of LA; SIRT1 small interfering RNA (siRNA), Western blotting and co-immunoprecipitation (CoIP) were applied to validate the downstream regulatory mechanism.

Results: LA treatment dose-dependently improved cardiac function, alleviated myocardial pathological injury and inflammatory infiltration, reduced serum cardiac injury markers, and significantly elevated the 72-hour survival rate of CLP mice. LA inhibited myocardial ferroptosis, as evidenced by decreased levels of reactive oxygen species (ROS), malondialdehyde (MDA), and ferrous iron, restored glutathione (GSH) content, and modulated the expression of ferroptosis-related proteins. SIRT1 was identified as a hub ferroptosis-related gene in sepsis, and LA bound stably to SIRT1 with a binding energy of -8.07 kcal/mol. Mechanistically, LA activated the SIRT1-NRF2/PGC-1 α pathway and ameliorated mitochondrial dysfunction, while SIRT1 knockdown partially abrogated these protective effects. CoIP assays further confirmed that LA enhanced the protein interaction between SIRT1 and NRF2 and reduced NRF2 ubiquitination in a SIRT1-dependent manner, thereby upregulating downstream antioxidant defense systems.

Conclusion: LA activates the SIRT1-NRF2 signaling pathway to enhance the expression of antioxidant genes, improve mitochondrial function, inhibit myocardial ferroptosis, and ultimately ameliorate sepsis-induced cardiac dysfunction, indicating its considerable therapeutic potential for SICD.

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**Acetylursolic Acid Attenuates Ferroptosis in Myocardial Ischemia/Reperfusion
Injury by Inhibiting STING-Mediated Autophagic Degradation of GPX4**

**乙酰熊果酸通过抑制 STING 介导的 GPX4 自噬降解改善心肌缺血再
灌注损伤心肌细胞铁死亡的机制研究**

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Abstract:

Myocardial ischemia/reperfusion (I/R) injury remains a major cause of adverse cardiovascular outcomes worldwide. Ferroptosis, an iron-dependent form of regulated cell death, has been recognized as a critical contributor to myocardial I/R injury. This study investigated the protective effects of 3 β -O-acetylursolic acid (AUA) against myocardial I/R injury and explored the underlying mechanisms associated with ferroptosis.

A mouse myocardial I/R model induced by left anterior descending coronary artery ligation and reperfusion was established to evaluate the cardioprotective effects of AUA *in vivo*. Bioinformatics analysis and molecular docking were performed to identify potential targets of AUA. In addition, the neonatal rat cardiomyocytes (NRCMs) were used to examine the anti-ferroptotic mechanisms of AUA *in vitro*. A series of experiments, including immunofluorescence staining, cellular thermal shift assay (CETSA), biochemical analyses and Western blotting, was conducted. AUA significantly alleviated myocardial injury and reduced ferroptosis following I/R challenge. Mechanistic studies revealed that AUA suppressed STING-mediated autophagic degradation of GPX4, thereby maintaining GPX4 expression and limiting ferroptotic cell death. Similar protective effects were observed in NRCMs.

In summary, AUA protects against myocardial I/R injury, at least in part, by inhibiting STING-dependent GPX4 degradation and ferroptosis. These findings highlight the therapeutic potential of AUA and identify the STING/GPX4 pathway

as a promising target for the treatment of myocardial I/R injury.

Keywords: Acetylursolic Acid; STING; ferroptosis; Myocardial ischemia/reperfusion

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**Taohong Siwu Decoction Attenuates Myocardial Fibrosis by Promoting
Ubiquitination and Proteasomal Degradation of HDAC1**

**桃紅四物湯通過促進 HDAC1 泛素化及蛋白酶體降解減輕心肌纖維
化**

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Hospital of Guangzhou Medical University, Guangzhou, China.*

Abstract:

Background: Myocardial fibrosis is a key pathological process in the progression from myocardial infarction (MI) to heart failure. Histone deacetylase 1 (HDAC1) is an important epigenetic regulator that promotes cardiac fibrosis by activating pro-fibrotic signaling pathways such as TGF- β and Ang II[1,2]. Previous studies have shown that HDAC1 protein stability is tightly regulated by post-translational modifications, particularly ubiquitination and proteasomal degradation[3]. Taohong Siwu Decoction (THSWD), a classic formula for activating blood and resolving stasis, has demonstrated clinical efficacy in treating ischemic heart disease[4]. However, whether THSWD exerts its anti-fibrotic effects through modulating HDAC1 ubiquitination remains unclear.

Methods: A mouse model of MI was established via left anterior descending coronary artery ligation. Mice were treated with THSWD (low, medium, high doses) or vehicle for 28 days. Cardiac function and fibrosis were assessed by echocardiography and Masson staining. In vitro, primary cardiac fibroblasts (CFs) were stimulated with TGF- β 1 to induce fibrotic activation. Protein and mRNA levels of HDAC1 were detected by Western blot and qPCR. The ubiquitin-proteasome pathway involvement was evaluated using the proteasome inhibitor MG-132. The interaction between HDAC1 and its protective partner MTA1 was analyzed by crosslinking and co-immunoprecipitation (Co-IP) assays.

Results: In the MI mouse model, THSWD treatment dose-dependently improved cardiac function and reduced myocardial collagen deposition. Western blot analysis showed that THSWD significantly decreased HDAC1 protein levels in

both infarcted myocardium and TGF- β 1-induced CFs, whereas HDAC1 mRNA levels remained unchanged, indicating a post-transcriptional regulatory mechanism. Treatment with MG-132 partially reversed this effect, confirming the involvement of the ubiquitin-proteasome pathway. Furthermore, crosslinking and Co-IP assays revealed that THSWD disrupted the HDAC1-MTA1 complex, leading to increased levels of monomeric HDAC1, which is then targeted for ubiquitination and subsequent degradation.

Conclusion: Our findings demonstrate that THSWD attenuates myocardial fibrosis through promoting ubiquitination and proteasomal degradation of HDAC1, mediated by the disruption of the HDAC1-MTA1 complex. This study provides a novel mechanistic insight into the anti-fibrotic action of THSWD and supports its clinical application in treating post-MI cardiac fibrosis.

Acknowledgement:

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**Rosmarinic acid ameliorates endothelial dysfunction and oxidative stress in
HFD/STZ-induced type 2 diabetic mice**

**迷迭香酸改善高脂飲食/鏈脈佐菌素誘導的 2 型糖尿病小鼠的內皮
功能障礙和氧化應激**

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Abstract:

Rosmarinic acid (RA) is a naturally occurring phenolic compound known for its cardiovascular, antioxidant, and anti-inflammatory properties. This study aimed to determine whether RA protects against diabetes-associated endothelial dysfunction and to elucidate the underlying molecular mechanisms. To this end, diabetic mice were induced using a high-fat diet combined with streptozotocin and then treated with RA (100 mg/kg) for eight weeks. In parallel, *ex vivo* mouse aortas and *in vitro* primary rat aortic endothelial cells (RAECs) were exposed to high glucose (HG) conditions.

The results showed that RA treatment significantly restored endothelium-dependent relaxations (EDRs) and reduced oxidative stress in diabetic mouse aortas. Mechanistically, RA activated both the PPAR α /PI3K/Akt/eNOS pathway and the Nrf2/Keap1/HO-1 antioxidant pathway in the aortas and RAECs. The protective effects of RA on endothelial function and oxidative stress were abolished by selective inhibitors of PPAR α , PI3K, Akt, and HO-1, confirming their essential roles.

Collectively, these findings demonstrate that RA alleviates diabetes-associated endothelial dysfunction and oxidative stress through concurrent activation of the PPAR α /PI3K/Akt/eNOS and Nrf2/Keap1/HO-1 signaling pathways.

Acknowledgement:

This work was supported by the Science and Technology Development Fund, Macau SAR (File no. 0002/2025/NRP, 0008/2025/EQP) and the University of Macau.

Rosmarinic acid protects against isoproterenol-induced myocardial infarction in rats

迷迭香酸預防異丙腎上腺素誘導的大鼠心肌梗死

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Abstract:

Myocardial infarction (MI) is one of the major causes of death from cardiovascular diseases (CVD), and current treatments still have limitations. Rosmarinic acid (RA) is a naturally occurring polyphenolic compound, a natural phenolic acid with significant antioxidant, anti-inflammatory, anti-apoptotic, and immunomodulatory effects. We aimed to investigate its protective effects against MI.

A rat model of MI induced by subcutaneous injection of isoproterenol was successfully established. The pharmacological effects of RA were investigated by administering it orally for seven consecutive days. Experimental results suggest that RA may protect against MI via the JAK2/STAT3 pathway. RA inhibits myocardial cell apoptosis through mechanisms such as antioxidant stress (e.g. scavenging reactive oxygen species (ROS), increasing superoxide dismutase (SOD) activity, and reducing malondialdehyde (MDA) levels and lactate dehydrogenase (LDH) levels) and by regulating the Bcl-2/Bax apoptotic pathway, thereby alleviating myocardial ischaemic injury. Meanwhile, RA also effectively improved the levels of cardiac troponin T (cTnT) and Creatine kinase isoenzyme MB (CK-MB), markers of myocardial damage.

This study reveals the role of RA in MI and its potential therapeutic significance, and proposes new therapeutic protocols and pharmacological mechanisms for the treatment of CVD with RA.

Acknowledgement:

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Polysaccharides from *Magnoliae Officinalis* Cortex Ameliorate Ulcerative Colitis via Gut Microbiota-Mediated Restoration of Treg/Th1/Th17 Immune Homeostasis

厚朴多糖通过调节肠道菌群恢复 Treg/Th1/Th17 免疫平衡缓解溃疡性结肠炎

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Abstract:

Ulcerative colitis (UC) is a chronic inflammatory bowel disease characterized by intestinal immune dysregulation and gut microbiota dysbiosis¹. The imbalance among regulatory T cells (Treg), T helper 1 (Th1), and T helper 17 (Th17) cells is critically involved in UC pathogenesis². *Magnoliae Officinalis* Cortex (Houpu) is a traditional Chinese medicine widely used for gastrointestinal disorders³, yet the immunomodulatory mechanisms of its polysaccharides remain unclear.

This study investigated the therapeutic effects of *Magnoliae Officinalis* Cortex polysaccharides (MP) on dextran sulfate sodium (DSS)-induced UC in mice and explored the underlying mechanisms. MP was extracted by hot water extraction and characterized by HPGPC and monosaccharide composition analysis. UC mice were orally administered MP at doses of 200 mg/kg for 5 days. Disease activity index (DAI), colon length, and histopathology were assessed. Treg, Th1, and Th17 cell proportions in colonic lamina propria were determined by flow cytometry. Related cytokines and transcription factors were measured by ELISA and qPCR. Gut microbiota was analyzed by Untargeted/Targeted metabolome and metagenome.

Results showed that MP significantly alleviated DSS-induced colitis, evidenced by reduced DAI scores, preserved colon length, and attenuated histological damage. Flow cytometry revealed that MP promoted Treg differentiation while suppressing Th1 and Th17 responses, thereby restoring the Treg/Th17 and Th1/Th17 balance. Anti-inflammatory cytokines (IL-10) were upregulated, whereas pro-inflammatory cytokines (IFN- γ , IL-17A) were downregulated. Metabolome and metagenome demonstrated that MP restructured gut microbiota composition, increasing beneficial bacteria such as *Lactobacillus* and

Bifidobacterium while reducing pathogenic bacteria. Correlation analysis revealed significant associations between specific microbial taxa and immune cell proportions, suggesting that gut microbiota mediated the immunomodulatory effects of MP.

In conclusion, MP alleviates UC by reshaping gut microbiota to restore Treg/Th1/Th17 immune homeostasis, supporting its potential as a microbiota-targeted therapeutic agent for UC.

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**Acupuncture for constipation-dominant irritable bowel syndrome: a
systematic review and meta-analysis**

針灸治療便秘型腸易激綜合症的系統性回顧與統合分析

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Introduction:

Affecting approximately 3% of the global population, constipation-dominant irritable bowel syndrome (IBS-C) is characterized by abdominal pain, bloating, and hard stools. As an alternative therapeutic approach, the efficacy of acupuncture for IBS-C remains unclear. Therefore, this systematic review with meta-analysis aims to evaluate the clinical efficacy of acupuncture in the treatment of IBS-C.

Materials and Methods:

A systematic search of 7 electronic databases was conducted from inception to August 31, 2025 without language restrictions. Randomized controlled trials (RCTs) comparing acupuncture with pharmacological or non-pharmacological interventions in IBS-C patients were included. Data extraction, risk of bias, and the quality of evidence assessment were performed.

Results:

From 11,116 studies obtained through database search, 14 RCTs (n = 1,078) conducted in China were included, with 6 eligible for meta-analysis. Acupuncture did not demonstrate superiority over pharmacological interventions for improving overall symptom severity (RR = 0.67, 95% CI: 0.23-1.95), or quality of life (SMD = 0.11, 95% CI: -0.27 to 0.48). However, compared with moxibustion, acupuncture significantly improved stool consistency (MD = 1.42, 95% CI: 1.13-1.72). All included studies were rated as having some concerns in risk of bias and moderate to low evidence quality.

Conclusions:

Acupuncture may improve stool consistency compared with moxibustion but does not demonstrate superiority over pharmacological therapies in reducing overall symptom severity or improving quality of life in IBS-C. Current evidence is limited by methodological weaknesses, small sample sizes, and potential biases. High-quality, multicentre, sham-controlled RCTs with standardized outcome measures are needed to establish acupuncture as an evidence-based treatment for IBS-C.

This review is registered on Prospero with the registration number: CRD42024509742.

Acknowledgements:

This study is supported by grant #022448-00001: "Electro-acupuncture for irritable bowel syndrome with constipation: a pilot randomized, double-blinded, sham-controlled trial".

**Effectiveness of 10.6μm CO₂ laser acupuncture for breast cancer-related
lymphedema: a randomized controlled trial**

**10.6μm CO₂ 鐳射針灸治療乳腺癌相關淋巴水腫的臨床療效觀察 :—
項隨機對照試驗**

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Lizhen WANG¹

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Abstract:

Background: The World Health Organization(WHO) reported 2.3 million newly diagnosed breast cancer cases globally in 2022, which ranks as the most prevalent malignancy and contributes to growing postoperative complication risks. Breast cancer-related lymphedema (BCRL) is a stubborn common sequela. Complex decongestive therapy(CDT) serves as major clinical treatment, yet long-term intervention imposes heavy burden on patients¹⁻³. Various treatments are available, while uniform clinical criteria have not been formed⁴⁻⁵.

Traditional acupuncture and moxibustion have been widely used to relieve edema with proven safety. However, such treatments may trigger skin infection on swollen and vulnerable tissue. To overcome these drawbacks and the lack of unified parameters in common laser acupuncture, 10.6 μm CO₂ laser acupuncture was developed. This innovative laser acupuncture shares consistent spectral characteristics with traditional moxibustion, which can effectively simulate its thermal stimulation effect. Acting on acupoints, it improves local lymphatic circulation while retaining the advantages of traditional therapy. Relevant randomized clinical evidence remains insufficient. This study aims to evaluate the clinical efficacy of 10.6 μm CO₂ laser acupuncture in treating BCRL.

Method: In this single-center, open-label, two-arm randomized controlled trial with blinded outcome assessment, 60 female participants diagnosed with unilateral BCRL were randomly assigned (1:1) to receive either laser acupuncture combined with Complete Decongestive Therapy (LA group) or Complete Decongestive Therapy alone (G group) for seven consecutive days. Each LA group session lasted 40 minutes total, consisting of 20 minutes of laser acupuncture followed by 20 minutes of Complete Decongestive Therapy. Laser acupuncture treatment involved

eight acupuncture points with 5 minutes of laser stimulation applied to each point; two laser acupuncture devices were used simultaneously to achieve the 20-minute treatment duration. The G group received 20 minutes of Complete Decongestive Therapy only. The primary outcome was the mean change in circumference difference of the affected arm from baseline to day 7. Secondary outcomes included Visual Analogue Scale (VAS) scores, muscle strength grading, the Functional Assessment of Cancer Therapy – Breast (FACT-B) scale, and the Upper Limb Lymphedema Quality of Life (ULLQoL) questionnaire.

Results: A total of 60 participants (30 per group) completed the trial (July – December 2022). After one week of treatment, both groups had significant reductions in the mean affected limb circumference (both $P < 0.001$), with a mean reduction of 0.82 cm in the LA group and 0.31 cm in the G group; the between-group difference was significant ($Z = -5.791$, $P < 0.001$). The LA group demonstrated significantly greater pain reduction, with median VAS scores decreasing to 0 (IQR, 0-1) versus 3 (IQR, 0-5) in the G group ($P < 0.001$). At 2 weeks post-treatment, both groups showed significant improvements in FACT-B total scores from baseline ($P < 0.001$), with the LA group achieving greater improvement than the G group ($P = 0.017$). At 4 weeks, ULLQOL scores improved significantly from baseline in both groups ($P < 0.001$), with no significant between-group difference ($P = 0.222$). One mild, transient adverse event occurred in each group.

Conclusion: The findings demonstrate that 10.6 $\mu\text{m CO}_2$ laser acupuncture is an effective and safe complementary therapy for managing BCRL, with significant short-term efficacy in reducing arm circumference, relieving pain, and improving quality of life when combined with conventional treatment. This study provides clinical evidence supporting the use of 10.6 $\mu\text{m CO}_2$ laser acupuncture as a valuable adjunctive intervention for breast cancer-related lymphedema.

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**Composition, authentication, and ethnopharmacological rationale of Five
Flowers Herbal Tea in Hong Kong**

香港涼茶的成分、鑒定與民族藥理學依據

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Abstract:

Herbal tea has long been used for preventive and therapeutic healthcare in Hong Kong and South China. Five Flowers Tea is one of the most popular formulations, traditionally used to “clear heat” and “disperse dampness”, that are linked to many summer-related health problems in this hot and humid region. The formula is rich in flavonoids, alkaloids and terpenoids, with reported anti-inflammatory, antiviral, antibacterial, antidiarrhoeal and antioxidant effects. However, the composition of Five Flowers Tea varies widely in the market, raising concerns about consistency of its ethnopharmacological benefits. This study comprehensively analysed the composition of Five Flowers Tea sold in Hong Kong, investigated the rationale behind the herb selection, and evaluated variation and quality across commercial samples.

Thirty-three Five Flowers Tea parcels were collected from grocery stores, herbal retailers, market stalls and Chinese medicine pharmacies in Hong Kong. Macroscopic features (size, texture, colour, organoleptic properties) were documented and compared with the Chinese Pharmacopoeia. DNA barcoding using the *psbA-trnH*, ITS2 and *COI* regions was employed to authenticate herbal components and detect adulterants and insect infestation.

Macroscopic identification revealed 23 herbal species from 18 plant families. The most prevalent herb was *Bombax ceiba*, followed by *Chrysanthemum morifolium*. Only eight samples contained the classical five-flower formula (*B. ceiba*, *Plumeria*

rubra, *C. morifolium*, *Lonicera japonica* and *Sophora japonica*). DNA barcoding identified ten instances of adulteration, including substitution of *L. japonica* by *L. macranthoides*, *Artemisia capillaris* by *Potentilla* species, and *Lysimachia christinae* by *Desmodium styracifolium*. Insect infestation by *Lasioderma serricorne* was confirmed in 12 moist samples.

Five Flowers Tea in Hong Kong shows considerable compositional variation and frequent adulteration, with some samples containing non-traditional or substituted herbs and insect contamination. Macroscopic and molecular authentication methods together provide a robust approach for quality assessment. These findings underscore the urgent need for standardisation and quality assurance of Five Flowers Tea to ensure its safety and the reliable delivery of its traditional health benefits.

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Medical Food Therapy as an Emerging Anti-Aging and Regenerative Intervention

“药食同源”作为一种新兴的抗衰老和再生干预手段

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Abstract:

The convergence of Traditional Chinese Medicine (TCM) and regenerative medicine presents new opportunities to combat age-associated decline through functional dietary interventions. The concept of “Medicine and Food Homology,” which originated from TCM theory, offers a unique framework for developing sustainable, low-toxicity strategies that target degenerative processes central to aging. Across our recent series of reviews, we examined the bioactive compositions and mechanistic pathways of *Crataegus pinnatifida*, *Poria cocos*, and *Atractylodes macrocephala*. We chose to focus on these medicinal foods as they constitute the TCM formula, Zhi Zhu Kuan Zhong capsule, one of our key research interests. For instance, *Poria cocos* polysaccharides (PCP-Cs) exert neuroprotective and hepatoprotective effects through MAPK, AMPK, and NF- κ B modulation ¹; *Crataegus pinnatifida* polyphenols promote mitochondrial homeostasis and cardiometabolic protection ²; and *Atractylodes macrocephala* polysaccharides enhance epithelial regeneration and intestinal barrier integrity via the gut–brain–immune axis ³. In chronic disorders, medicinal food therapy has potential to be continuously incorporated into the diet over long periods, making it a lifestyle-compatible intervention that may support metabolic health and cellular regeneration.

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**The Design and Synthesis of Novel Nitrogen-containing Diphyllin Analogues
as Anti-avian Influenza Virus Agents**

新型含氮山荷葉素類似物作為抗禽流感病毒候選藥物的設計與合成

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Abstract:

Avian influenza viruses (AIVs), commonly known as bird flu, are influenza A viruses that primarily infect birds. Some are zoonotic and can infect humans. They can be classified into low pathogenicity avian influenza (LPAI) and high pathogenicity avian influenza (HPAI) based on disease severity in poultry, with HPAI causing severe disease and high mortality, especially in domestic flocks. Notably, H5N1 strain has caused significant poultry outbreaks worldwide and sporadic human infections since its first emergence in Hong Kong in 1997, and H7N9 has likewise led to poultry outbreaks and human infections since it emerged in China in 2013. H5N1 outbreaks have resulted in the culling of billions of poultry and are associated with high mortality rates among reported human infections. Although WHO and US CDC assess that the current public health risk of HPAs to the general population remains low due to limited human-to-human transmission, recent detections and infections in the US and Europe raised concerns about pandemic potential given the viruses' capacity for rapid evolution.

Diphyllin, a *Justicia* plant-derived aryl-naphthalene lignan (ANL), exhibits potent broad-spectrum antiviral activity, inhibiting vesicular stomatitis virus (VSV), tick-borne encephalitis virus (TBEV), West Nile virus (WNV), Zika virus (ZIKV) and Herpes simplex virus 1 (HSV-1) with submicromolar IC₅₀ values [1,2]. Diphyllin is thus selected as a lead scaffold for structural modification to develop novel anti-avian influenza agents.

Twelve Nitrogen-containing analogues were synthesized and evaluated using the "One-Stone-Two-Birds" pseudovirus assay [3]. Among them, **CN2-f** showed potent antiviral effects against H5N1 and VSV with IC₅₀ values of 119.4 and 103.2 nM, respectively. **CN2-f** also achieved the highest selectivity indices (SIs) of 418.8 and 484.5 against H5N1 and VSV, while **CN1-f** displayed slightly lower SI values. Both **CN1-f** and **CN2-f** exhibited low cytotoxicity (CC₅₀ > 50 μM), highlighting their promise as antiviral candidates. These findings suggest a preliminary

structure-activity relationships (SAR) in which introducing hydrophilic, nitrogen-containing moieties reduces cytotoxicity while maintaining potent antiviral effect.

Acknowledgement:

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***Kluyveromyces marxianus* as a Promising Biocatalyst for the
Biotransformation of Resveratrol to Dihydroresveratrol**

馬克斯克魯維酵母展現將白藜蘆醇生物轉化為二氫白藜蘆醇之潛力

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Abstract:

Resveratrol exhibits broad bioactivity, including cancer chemopreventive effects, but its low bioavailability and poor water solubility limit its clinical translation^{1, 2}. In contrast, its hydrogenated analogues (e.g., dihydroresveratrol) display broader bioactivity spectrum and greater water solubility and are considered promising lead compounds for drug development³. These observations raise a key question: can hydrogenation enhance both the bioactivity and the bioavailability of resveratrol?

To address this question, and given the abundance of resveratrol in grape skins, we sought a microbial biotransformation strategy to convert resveratrol to dihydroresveratrol^{4, 5}. A literature review identified *Kluyveromyces marxianus*, known for its strong coumarin-reducing activity and widespread use in food fermentation, as a promising biocatalyst⁶. We therefore hypothesized that this yeast could efficiently catalyze the hydrogenation of resveratrol to its hydrogenated dihydrostilbenoid analogues.

Preliminary biotransformation experiments were conducted across multiple incubation times. Culture supernatants were extracted and analyzed by QTOF mass spectrometry. A characteristic peak of dihydroresveratrol was detected at 24 h, indicating the biotransformation potential of *K. marxianus*. As dihydroresveratrol is likely a predominantly intracellular product, a substantial fraction of the product may remain within the yeast cells, revealing the need to optimize extraction.

In conclusion, *K. marxianus* demonstrates the ability to convert resveratrol to dihydroresveratrol, offering a potential microbial platform for producing this desired derivative for therapeutic applications.

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Concise Synthesis of Rare Amino Acids in Bioactive Natural Cyclic Peptides

天然活性環肽中稀有氨基酸的簡便合成

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Abstract:

Peptide drugs have attracted considerable attention due to their high bioactivity potency, structural stability, and low toxicity. Bioactive cyclic peptides with unique structures have been discovered in diverse natural sources, including many plants and marine organisms¹. Some cyclic peptides exhibit potent anticancer activity. For example, tamandarin A, first isolated from a Brazilian marine ascidian (family Didemnidae), demonstrated strong cytotoxicity to the pancreatic BX-PC3 cancer cell line with an IC₅₀ value of 1.29 nM². Many of these peptides incorporate rare, and unique amino acids. However, their low natural abundance often limits further development as drug candidates. Although total synthesis provides an alternative supply potential and enables analog generation, progress is frequently hampered by the need to prepare unusual non-proteinogenic amino acid residues through low-yielding, tedious routes, creating a key bottleneck for further development.

This study aims to develop a concise, efficient, and high-yielding synthetic strategy for some sterically crowded and selectivity-unfavorable chiral amino acids. Based on a successful model study, we prioritized the synthesis of the special side chain while ensuring correct stereochemistry. We then employed a S_N2 nucleophilic substitution to construct the key C–C bond, successfully affording the corresponding amino acids. The side-chain precursors bearing the specific chiral functional group were fully characterized by NMR spectrometer.

This practical approach provides a scalable and step-economical route to some rare amino acids, laying a solid foundation for the total synthesis and medicinal chemistry exploration of cyclic peptides as anticancer agents.

Acknowledgements: The work described in this study was financially supported by the Research Grants Council of the Hong Kong Special Administrative Region, China (Project No. HKBU12142016 and HKBU12103021).

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Targeted Isolation and Screening and of Anti-Renal Fibrosis Compounds from *Aquilaria sinensis*

靶向分離與篩選沉香中抗腎臟纖維化活性成分

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Abstract:

Objective: Renal fibrosis is the common pathological process driving the progression of chronic kidney disease (CKD) to end-stage renal disease¹. However, effective FDA-approved therapies for renal fibrosis remain limited. *Aquilaria sinensis* (agarwood), a valuable non-timber forest product widely used in traditional medicine, perfumes, and incense across Japan, Southeast Asia and China. Previous studies have demonstrated therapeutic potential of *A. sinensis* in renal diseases, including diabetic kidney disease and CKD²⁻³. Nevertheless, its anti-fibrotic effects and active constituents have not been reported. Therefore, this study aimed to evaluate the therapeutic potential of *A. sinensis* against renal fibrosis and to identify its bioactive anti-fibrotic compounds.

Methods: *A. sinensis* was extracted using petroleum ether, ethyl acetate, and ethanol, respectively. The chemical profiles of the these extracts were characterized by HPLC-MS analysis. To evaluate their anti-fibrotic activities, TGF- β 1-induced rat renal cells (NRK-49F and NRK-52E) were employed. Cell viability was assessed using the CCK-8 assay, while the expression of fibrosis-related markers (Fibronectin, α -SMA, and collagen I) were determined by Western blotting. Furthermore, a unilateral ureteral obstruction (UUO) mouse model was established to investigate the anti-fibrotic effects of *A. sinensis* *in vivo*.

Results: Cell viability results exhibited that the ethyl acetate and ethanol extracts of *A. sinensis* exhibited lower cytotoxicity than the petroleum ether extract. Among the tested extracts, the ethyl acetate extract showed the most potent anti-fibrotic activity in both TGF- β 1-stimulated NRK-49F and NRK-52E cell models, as evidenced by a greater reduction in fibrosis-related markers. In the UUO mouse model, treatment with the ethyl acetate extract markedly attenuated renal fibrosis, as indicated by improved renal function parameters, including serum creatinine (Cr) and blood urea nitrogen (BUN), together with reduced expression of fibrosis-associated proteins,

including α -SMA, fibronectin, and collagen I. To identify the bioactive constituents responsible for the anti-fibrotic effects, the ethyl acetate extract was further fractionated into 33 fractions using HPLC-guided separation. Bioactivity-guided screening was subsequently performed using the *in vitro* fibrosis models, leading to the three active compounds with potent anti-fibrotic activity.

Conclusion: This study demonstrates, for the first time, the anti-fibrotic efficacy of the ethyl acetate extract of *A. sinensis* in both cellular and animal models of renal fibrosis. HPLC-guided bioactivity screening led to the identification of more than three active compounds responsible for these effects. Collectively, these findings suggest that *A. sinensis* and its bioactive constituents represent promising candidates for the development of novel therapies against renal fibrosis.

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Tryptophan sulfonate: A new chemical marker for accurate and efficient inspection of sulfur-treated herbal medicinal products

色氨酸磺酸鹽：用於精確高效檢測硫磺處理藥材的新型化學標誌物

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Abstract: We identified tryptophan sulfonate as a stable, specific marker for sulfur-treated herbal products using UPLC-QTOF-MS/MS and confirmed it by NMR and synthesis. A sensitive UPLC-QqQ-MS/MS assay was developed and tested on 50 samples, showing better stability and accuracy than traditional sulfite tests. This fast, automated method improves detection efficiency and supports safer regulation of sulfur-treated foods and medicines.

Background: Sulfur treatment, including sulfur fumigation and sulfite additives, is widely used in the herbal medicinal industry for post-harvesting due to its effectiveness and low cost. It helps retain moisture, preserve color, and prevent insect and mold damage. However, concerns have arisen regarding its negative impact on medicinal quality. Sulfite accumulation can lead to respiratory issues upon ingestion and cause irreversible changes in essential metabolites, affecting nutritional value. Long-term consumption may harm liver and kidney functions. Consequently, strict regulations are in place, requiring inspection of treated foods through sulfite assays. Despite being the only available method, it has drawbacks, including potential false positives, instability of sulfite content, and labor-intensive procedures, hindering high-throughput analysis.

Method: Tryptophan sulfonate was identified in sulfur-treated products using UPLC-QTOF-MS/MS. Its identity was confirmed through chromatographic separation, NMR, and chemical synthesis. An assay utilizing UPLC-QqQ-MS/MS was then developed to test 50 commercial food samples for practical inspection.

Results: Fifty commercial food samples were analyzed, demonstrating that tryptophan sulfonate showed greater specificity for sulfur-treated products than sulfites. Stability tests indicated that tryptophan sulfonate remained more stable under heat and during long-term storage. Methodological comparisons revealed that the tryptophan sulfonate assay yielded more robust validation data and was easier, faster, more automated, and environmentally friendly than the sulfite assay. Results suggesting the tryptophan sulfonate assay is more accurate and efficient, making it ideal for inspecting sulfur-treated products, especially in high-throughput screening scenarios.

Conclusion: The new tryptophan sulfonate assay surpasses the sulfite assay in accuracy and efficiency for inspecting sulfur-treated products. These findings

advocate for tryptophan sulfonate as a new indicator, contributing to stricter regulations on sulfur treatment, ultimately ensuring the safety of herbal medicine from production to consumer.

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AI-Assisted Microscopic Identification of Coptidis Rhizoma Powder Based on Deep Learning

基于深度学习的黄连粉末显微特征智能识别研究

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Abstract:

Coptidis Rhizoma is a valuable and commonly used Chinese medicinal material. Its official botanical sources include *Coptis chinensis*, *Coptis deltoidea*, and *Coptis teeta*. After processing into decoction pieces or powder, many macroscopic diagnostic characters are weakened or lost. Microscopic identification remains important for quality control, but conventional examination is highly dependent on expert experience and is inefficient for large-scale screening. This study aimed to develop a deep learning-based strategy for intelligent recognition of diagnostic microscopic features in Coptidis Rhizoma powder.

Our previous work on AI-assisted microscopy has involved model construction for several Chinese medicinal powders, including *Magnoliae Officinalis Cortex*, *Artemisiae Argyi Folium*, *Poria*, *Glycyrrhizae Radix et Rhizoma*, and bran-fried *Atractylodis Rhizoma*. These preliminary studies established a workflow for standardized slide preparation, microscopic image acquisition, feature annotation, model training, and performance evaluation. Based on this workflow, Coptidis Rhizoma powder was selected as the main research object. Key diagnostic microscopic structures, including stone cells, pericyclic fibers, wood fibers, and scaly leaf epidermal cells, were manually annotated according to pharmacopoeial and microscopic identification criteria. A deep learning-based object detection model was then trained and evaluated.

The preliminary model achieved an overall mAP@0.5 of 0.763 for Coptidis Rhizoma microscopic feature detection. Among the annotated features, pericyclic fibers, stone cells, and scaly leaf epidermal cells showed relatively good recognition performance, with AP values of 0.866, 0.819, and 0.791, respectively. Visualization of validation images indicated that the model could locate and classify multiple diagnostic structures in complex powdered microscopic backgrounds.

In the next stage, the dataset will be expanded to include the three official

botanical sources of *Coptidis Rhizoma* and common adulterants or confused species. This study provides a feasible approach for integrating traditional microscopic identification with artificial intelligence and may improve the objectivity, efficiency, and standardization of authenticity evaluation for powdered Chinese medicinal materials.

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Development of a Versatile Flow Chamber for the Simulation of Multiple Hemodynamic Conditions

用于模拟多种血流动力学环境的多功能流动腔系统的开发

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Abstract:

Blood flow–derived mechanical forces, particularly fluid shear stress, are essential regulators of endothelial function and vascular homeostasis. Physiological laminar shear stress promotes endothelial alignment and vascular protection, whereas disturbed or oscillatory flow contributes to endothelial dysfunction and vascular disease. Although numerous in vitro flow systems have been developed, many are limited in their ability to reproduce the diverse and dynamic hemodynamic environments encountered in vivo.

To address this challenge, we developed a novel and versatile flow chamber capable of generating multiple physiologically relevant flow profiles, including laminar, oscillatory, and user-defined flow patterns. The biological performance of the system was evaluated by examining endothelial responses to different hemodynamic conditions. Exposure to distinct flow patterns induced characteristic endothelial phenotypes. Laminar flow promoted cellular alignment in the direction of flow, whereas oscillatory flow produced heterogeneous cellular organization compared with static conditions. Furthermore, transcriptomic analyses revealed clear separation of endothelial responses under different hemodynamic environments, accompanied by distinct gene expression signatures and pathway enrichment profiles.

These findings demonstrate that the flow chamber can reproduce biologically relevant shear stress conditions and elicit characteristic endothelial adaptations at both morphological and transcriptional levels. By providing a controllable, reproducible, and physiologically relevant platform, this system may facilitate mechanistic studies of vascular biology, disease modeling, therapeutic evaluation, and cardiovascular drug discovery.

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Efficacy of Traditional Chinese Medicine Herbal Formulas for Metabolic Dysfunction-Associated Steatotic Liver Disease: A Systematic Review and Meta-Analysis of Reclassified Randomized Controlled Trials

中藥方劑治療代謝功能障礙相關脂肪性肝病療效的系統評價與重新分類隨機對照試驗 Meta 分析

Authors: Wei Song Seetoh¹, Xi Han Aw¹, Goh Xiu Ling Nicole, Yan Zhao¹

Department: ¹ *School of Biological Sciences, Nanyang Technological University.*

Abstract:

Background: Metabolic dysfunction-associated steatotic liver disease (MASLD), previously termed NAFLD and MAFLD, is the hepatic manifestation of systemic metabolic dysfunction and affects approximately 38% of the adult global population^{1,2}. Current management focuses on lifestyle modification and metabolic risk control, while effective pharmacotherapies remain limited³. Given the multifactorial pathogenesis of MASLD, including insulin resistance, lipid dysregulation, inflammation, and fibrosis, multi-target therapeutic strategies may be advantageous. Traditional Chinese medicine (TCM) herbal formulas, characterised by multi-component and system-regulating properties, may serve as a promising intervention to treat MASLD^{4,5}.

Objective: To systematically evaluate the efficacy of TCM herbal formulas for MASLD through meta-analysis of randomised controlled trials (RCTs), with reclassification of NAFLD/MAFLD populations according to MASLD diagnostic criteria.

Methods: PubMed, Embase, Scopus, Web of Science, Cochrane Library, China National Knowledge Infrastructure (CNKI), and WanFang were searched from inception to 11 February 2026. RCTs involving adults with MASLD or reclassifiable NAFLD/MAFLD were included. A random-effects model was used to estimate mean differences (MDs) with 95% confidence intervals (CIs) for various outcomes.

Results: Sixty-three RCTs involving 5,826 patients were included. Compared to controls, TCM herbal formulas significantly improved liver function and glucose and lipid metabolism, regardless of whether they were administered as monotherapy or add-on therapy. TCM treatment resulted in greater reductions in ALT, AST, GGT, ALP, TC, TG, LDL-C, FPG, 2hPG, and HbA1c ($p < 0.05$),

accompanied by a significant increase in HDL-C levels. Furthermore, hepatic steatosis was effectively mitigated, as evidenced by decreases in the controlled attenuation parameter (CAP) and liver fat content scores.

Conclusion: TCM herbal formulas, both as monotherapy and adjuvant therapy, significantly improve hepatic function, steatosis, and systemic metabolic parameters in patients with MASLD. These findings support the clinical utility of TCM's multi-component, multi-target approach in addressing the complex, systemic pathogenesis of MASLD.

Acknowledgement:

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**Development and Comprehensive Multi-Database Validation of an
Interpretable Machine Learning Model for Predicting 28-Day Mortality in ICU
Patients with Staphylococcus aureus Bacteremia**

**基于可解释机器学习模型的 ICU 金黄色葡萄球菌菌血症患者 28 天
死亡率预测模型的开发及多数据库综合验证**

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Department: ¹ *Shanghai University of Traditional Chinese Medicine*

Background: Staphylococcus aureus bacteremia (SAB) in intensive care unit (ICU) patients is associated with high mortality, yet existing risk scores lack pathogen-specific validation. This study aimed to develop and externally validate an interpretable machine learning (ML) model for early prediction of 28-day mortality in ICU patients with SAB.

Methods: Data were extracted from the MIMIC-IV database (internal, n=942) using clinical variables available within the first 24 h of ICU admission. The Boruta algorithm selected core predictors, and five ML models (logistic regression, LASSO, random forest, support vector machine, and XGBoost) were developed. External validation used three independent cohorts: eICU-CRD (n=262), Shanghai General Hospital (n=127), and Shanghai Municipal Hospital of Traditional Chinese Medicine (TCM, n=59). Model performance was assessed by area under the receiver operating characteristic curve (AUC), calibration, and decision curve analysis (DCA). Shapley additive explanations (SHAP) provided interpretability.

Results: The XGBoost model achieved an AUC of 0.782 in the internal test set. In external validation, AUCs were 0.626 (eICU-CRD), 0.703 (Shanghai General Hospital), and 0.732 (TCM Hospital), with an average AUC of 0.711 (range 0.626–0.732). A separate logistic regression model incorporating age, acute kidney injury stage, and alkaline phosphatase (ALP) showed a modest improvement over the SOFA score alone (AUC 0.717 vs 0.669), though inferior to the primary XGBoost model. SHAP analysis identified SOFA score, age, and ALP as the most important predictors, revealing nonlinear threshold effects (such as a U-shaped relationship for sodium). DCA confirmed positive net clinical benefit across a range of threshold probabilities.

Conclusion: The XGBoost model, based on routine clinical variables and validated across multicenter databases, provides moderate predictive performance for 28-day mortality in ICU patients with SAB, albeit with variable generalizability across cohorts. Coupled with SHAP interpretability, it may support early risk stratification, though further prospective validation is warranted.

Keywords: *Staphylococcus aureus bacteremia; XGBoost; 28-day mortality; Intensive care unit; External validation; Shapley additive explanations*

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**Research Hotspots and Frontiers of Tuina and Massage Therapies for
Neuropathic Pain Based on CiteSpace and VOSviewer**

**基于 CiteSpace 和 VOSviewer 的推拿及按摩疗法干预神经病理性
疼痛研究热点与前沿分析**

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Abstract:

Background: Given that Tuina and massage therapies for neuropathic pain has gradually been accepted by clinical pain management fields. However, few bibliometric analyses have been performed on Tuina and related massage therapies for neuropathic pain. Therefore, this study used CiteSpace and VOSviewer to conduct a bibliometric and visualized analysis of this field. The objective of this research was to review this field in recent years and analyze, demonstrate, and evaluate the research status, hotspots and frontiers.

Method: Literature on Tuina and massage therapies for neuropathic pain published from early years to recent years was retrieved from Web of Science Core Collection and China National Knowledge Infrastructure databases. VOSviewer and CiteSpace were utilized to analyze countries, institutions and keyword co occurrence, and to construct bibliometric visualization maps.

Result: A total of 202 relevant studies including 171 English language articles and 31 Chinese language articles were included. The annual number of publications exhibited an upward trend especially after the year 2020. Among them, unspecified journals and China were the most productive journal and country. Beijing University of Chinese Medicine was the leading institution. Regarding authors, unspecified authors published the most articles, while unspecified authors was the most frequently cited. The most highly cited reference was a unspecified study focusing on clinical pain management, lumbar disc herniation, peripheral neuropathy and overall quality of life. Furthermore, keywords such as "neuropathic pain", "traditional Chinese medicine", "peripheral nerve injury" and "activation" were identified as emerging research frontiers for the period from past years to recent years.

Conclusion: In conclusion, this study provides a comprehensive overview and an

in depth understanding of Tuina and massage therapies for neuropathic pain and its emotional comorbidities. The findings highlight that neural injury, inflammatory activation, microglial regulation, central mechanisms, microglial polarization, synaptic plasticity and NLRP3 inflammasome activation are the current research frontiers. We anticipate that this study will not only guide researchers in identifying potential hotspots but also stimulate experimental mechanism research, clinical efficacy studies, neuroinflammation evaluations and traditional Tuina techniques explorations to further advance this field

Potential Application of Single-Cell and Spatial Transcriptomics in Acupuncture Research
on Asthma

单细胞与空间转录组学在针刺治疗哮喘研究中的潜在应用

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Abstract:

Acupuncture is an important intervention in Chinese medicine for asthma and has shown potential advantages in improving airway function, reducing inflammatory responses, and regulating airway resistance ¹. However, the cell-type-specific mechanisms underlying the anti-asthmatic effects of acupuncture remain unclear. Asthma is characterized by chronic airway inflammation, airway hyperresponsiveness, and airway remodeling ². Airway remodeling is not a single inflammatory outcome, but a dynamic pathological process involving epithelial cells, immune cells, stromal cells, and other cell types ^{3,4}.

In recent years, single-cell transcriptomics and spatial transcriptomics have provided new tools for studying airway remodeling in asthma⁵. These technologies can analyze cell types, cell states, spatial locations, and cell-cell communication, and can reveal cellular origins and microenvironmental changes that are difficult to distinguish by conventional pathology, bulk transcriptomics, or single-marker assays⁶⁻⁷. Therefore, single-cell and spatial transcriptomics may provide new opportunities for studying the cellular mechanisms of acupuncture treatment for asthma.

Current studies suggest that airway remodeling in asthma is mainly characterized by airway epithelial reprogramming, increased mucus secretion, amplification of Type 2 inflammation, POSTN-related stromal remodeling, subepithelial fibrosis, and airway smooth muscle thickening³. Its core feature is not the abnormality of a single pathway, but an imbalance in the epithelial-immune-stromal-smooth muscle cell network. Single-cell and spatial transcriptomics can further identify key cell populations involved in these processes, such as mucus-producing epithelial cells, basal cells, ILC2/Th2 cells, macrophages, fibroblasts, and airway smooth muscle cells, and can analyze their interactions in

different spatial regions of the airway.

Previous studies on acupuncture treatment for asthma have mainly focused on inflammatory responses and airway resistance, while cellular-level explanations for structural changes such as epithelial repair, stromal fibrosis, and airway smooth muscle remodeling remain insufficient. In the future, single-cell and spatial transcriptomics can be used to identify key cell populations altered after acupuncture intervention and to analyze whether acupuncture affects epithelial repair, amplification of immune inflammation, stromal fibrosis, airway smooth muscle contraction and relaxation, and cell-cell communication networks.

In summary, single-cell and spatial transcriptomics provide a more refined cellular and spatial perspective for understanding airway remodeling in asthma. Introducing these technologies into acupuncture research on asthma may help identify key cell populations, local microenvironments, and cell-cell communication patterns altered after acupuncture intervention, and may provide a new research path for clarifying the cellular targets and mechanisms of acupuncture against airway remodeling.

Acknowledgement:

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Analysis of the Current Situation of Clinical Trial Registrations of Artificial Intelligence in Traditional Chinese Medicine

中醫藥人工智能臨床試驗註冊現狀分析

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Abstract

Objective To explore the registration status of clinical trials related to artificial intelligence in traditional Chinese medicine (TCM) in China.

Methods Clinical trials of artificial intelligence in TCM registered in the Chinese Clinical Trial Registry and the International Clinical Trial Registry Platform for Traditional Medicine from their establishment to May 31, 2025 were retrieved. Statistical analysis was conducted on information such as registration time, registration regions and institutions, funding sources, research types and designs, blinding methods and sample sizes, research phases, research subjects, classification of artificial intelligence application scenarios, original data sharing and sharing methods, and registration-publication rates.

Results A total of 164 registered studies were included. The top three regions in terms of registration quantity were Shanghai, Beijing, and Zhejiang. The 105 registered institutions were mainly from tertiary hospitals and universities. Regarding research designs, there were 99 interventional studies, among which 80 were randomized controlled trials, and 37 observational studies. Cross-sectional studies were the most numerous, with 14 cases. 29 randomized controlled trials

(35.8%) employed blinding, with sample sizes predominantly ranging from 0 to 100. The diseases studied belonged to 23 disease systems, with the neurological diseases(27 cases) being the most. Artificial intelligence technologies involved 12 specific application scenarios, with intelligent clinical decision support in TCM being the most common, with a total of 79 (48.2%) cases. 45.7% of the studies expressed their willingness to share original data, and the clinical trial public management platform was the most common way for data sharing. Relevant results were published for 4 (2.4%) registered clinical trials.

Conclusion Clinical trials related to artificial intelligence in TCM cover a wide range of diseases, and intelligent clinical decision support is the most important application scenario at present. However, there are problems such as unbalanced distribution of registration regions, low data sharing degree of trial results, and a relatively low registration-publication rate of clinical trials.

Multi-Modal Sensor Fusion for Objective Quantification and Intelligent Recognition of Acupuncture Manipulation

多模態傳感器融合的針刺手法客觀量化與智能識別研究

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Abstract:

Background: Acupuncture manipulation is central to therapeutic efficacy, yet its objective quantification remains a significant challenge in acupuncture research. The standardized evaluation of fundamental techniques lifting-thrusting and twirling along with their reinforcing and reducing variants, is essential for teaching, skill assessment, and mechanistic studies. Current methods lack integrated multimodal sensing capable of synchronously capturing both kinematic and dynamic parameters of needle manipulation.

Method: This study developed an integrated measurement system combining optical positioning and six-axis force/torque sensing for synchronous quantification of acupuncture manipulation. Kinematic and dynamic measurement models were established, and a six-channel wireless force/torque acquisition device was developed. Acupuncture experiments were performed on rat tissues and biomimetic silicone modules, yielding 772 manipulation datasets encompassing lifting-thrusting, twirling, and their reinforcing-reducing variants. Following PCA-based dimensionality reduction, K-means and K-shape clustering algorithms were applied to classify manipulation types and differentiate reinforcing from reducing techniques.

Results: The system achieved synchronous acquisition of kinematic and dynamic parameters at 40 Hz, with positioning accuracy RMS of 0.12 mm and force measurement error under 3.6%. The first two principal components accounted for 61.7% of cumulative variance, corresponding to lifting-thrusting and twirling features respectively. K-means clustering achieved 97.7% recognition accuracy for the two basic manipulation types, while K-shape clustering reached 98.7% accuracy (ARI = 0.949) in differentiating reinforcing from reducing techniques. Notably, the key distinguishing feature between reinforcing and reducing manipulations was the temporal distribution of the operation sequence rather than mechanical amplitude: in

lifting-thrusting reinforcing, the insertion phase was significantly longer than the withdrawal phase; in twirling reinforcing, clockwise rotation was shorter than counterclockwise rotation, with reducing manipulations showing the opposite pattern ($P < 0.001$).

Conclusion: This multi-modal sensing system enables precise synchronous quantification of both kinematic and dynamic characteristics of acupuncture manipulation, and can effectively distinguish basic manipulation types as well as reinforcing-reducing differences based on temporal features. The findings provide a reliable technical platform and experimental basis for the objective evaluation and standardized teaching of acupuncture manipulation.

Massage Therapy Improves Cognitive Impairment in Patients with Autism Spectrum Disorder: A Systematic Review and Meta-Analysis

推拿改善孤独症谱系障碍患者认知障碍：系统评价和荟萃分析

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Abstract:

Objective: To systematically evaluate the efficacy and safety of massage therapy in improving cognitive impairment among patients with autistic spectrum disorder (ASD).

Method: Clinical randomized controlled trials (RCTs) investigating massage interventions for ASD were systematically retrieved from both Chinese and English databases, including PubMed, Web of Science, Scopus, Cochrane Library, CNKI, WanFang Data, VIP, and SinoMed CBM, using computerized search methods. The time frame for the search spanned from the inception of the databases to June 2025, with no restrictions beyond the languages of Chinese and English. The methodological quality of the included studies was assessed using the Cochrane collaboration's tool for assessing risk of bias in randomized trial (RoB1), and a meta-analysis was performed using RevMan 5.3 software.

Result: A total of 754 literatures were retrieved. Based on the inclusion criteria, 722 literatures were excluded. Ultimately, 22 RCTs were included, involving 1,664 children. Meta-analysis results demonstrated that compared with conventional rehabilitation interventions, the combination of massage therapy and rehabilitation significantly reduced the Autism Behavior Checklist(ABC) score [MD=-10.52, 95%CI(-13.16, -7.88), P<0.00001], Childhood Autism Rating Scale (CARS) score [MD=-6.97, 95%CI(-9.38, -4.55), P<0.00001], and Autism Treatment Evaluation Checklist (ATEC) score [MD=-11.27, 95%CI(-13.30, -9.23), P<0.00001], increased the clinical effective rate [OR=3.51, 95%CI(2.46, 5.01), P<0.00001]. Notably, massage therapy showed particular advantages in reducing the ABC score for children with an average age under 5 years [MD=-8.50, 95%CI(-10.02, -6.98), P<0.00001] and the CARS score for children with treatment durations not exceeding 3 months [MD=-3.34, 95%CI(-4.33, -2.35), P<0.00001].

Conclusion: Massage therapy demonstrates a substantial impact on improving

cognitive impairment in individuals with ASD. It is easy to implement, free from pharmacological side effects, and exhibits high patient compliance. As such, it represents a safe and effective intervention approach. Nevertheless, due to the limitations imposed by the quality of existing research, high-quality clinical studies are still required in future investigations to further validate the genuine and objective application value of massage therapy in the rehabilitation of cognitive impairments in ASD.

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A Pose Estimation-Based Action Similarity Assessment System for Liuzijue Qigong: Dataset Construction, Model Optimization, and Reliability Validation

基於姿態估計的六字訣動作相似度評估系統：數據集構建、模型優化與可靠性驗證

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Abstract:

Background: Traditional Chinese exercises (TCEs), such as Liuzijue Qigong, are increasingly used in chronic disease rehabilitation due to their low-cost, location-free nature. However, their large-scale promotion is hindered by the lack of objective, standardized assessment tools; most evaluations still rely on subjective expert judgment and abstract textual descriptions, leading to inconsistent training outcomes. Human pose estimation, particularly the recent RTMPose framework, offers a promising non-invasive and low-cost solution for automated motion analysis. Nevertheless, two critical bottlenecks remain: (1) the absence of a domain-specific dataset that captures the subtle, culturally unique movement patterns of Liuzijue Qigong, and (2) the need for rigorous reliability validation against expert instructors to ensure clinical credibility. To fill these gaps, this study constructs a Liuzijue-specific dataset, fine-tunes the RTMPose model, and validates the system's scoring reliability. The resulting action similarity assessment system offers an objective and scalable solution, advancing the standardization and intelligent development of traditional Chinese exercises.

Method: Real-world videos of six expert instructors and 144 community participants performing Liuzijue Qigong were collected. A dataset of 52,325 manually screened images was constructed following COCO keypoint annotation

standards. The RTMPose-s model was fine-tuned using the AdamW optimizer with a warm-up cosine annealing schedule. Movement deviation was quantified by inferring 3D keypoint displacement angles from 2D estimates. System reliability was evaluated against expert scores using intraclass correlation coefficient (ICC) and Bland-Altman analysis.

Results: On the test set, the fine-tuned model achieved Average Precision (AP) of 91.3% (baseline: 72.1%, +19.2%) and Average Recall (AR) of 92.3% (baseline: 75.0%, +17.3%). The system scores showed excellent consistency with expert evaluations: ICC = 0.97 [95% CI: 0.96–0.98], $P < 0.001$; Bland-Altman mean bias = -0.27 (95% limits: -11.30 to 10.79).

Conclusion: The dataset, optimized model, and validated scoring mechanism provide a reliable foundation for automated Liuzijue Qigong assessment, advancing the objective standardization of traditional Chinese exercises.

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**Integrative Transcriptomics and Machine Learning Uncover Hub Genes
Governing the Oxidative Stress-Immune Inflammation Axis in COPD**

整合转录组学与机器学习揭示慢性阻塞性肺疾病氧化应激-免疫炎症轴的核心调控基因

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Abstract:

Background: Chronic obstructive pulmonary disease (COPD) is a prevalent global respiratory disorder defined by persistent and progressive airflow limitation. Its pathogenesis is critically driven by a self-perpetuating cycle of oxidative stress and immune-mediated inflammation. Although this pathophysiological axis is well-recognized, the specific molecular components that constitute and orchestrate this intricate network, as well as their hierarchical regulatory relationships, remain incompletely understood. This knowledge gap substantially impedes both a deeper comprehension of disease mechanisms and the development of precision-based interventions.

Methods: Transcriptomic sequencing was performed on lung tissues derived from a murine model of COPD and healthy controls. By integrating differential expression analysis, weighted gene co-expression network analysis (WGCNA), and multiple machine learning algorithms (LASSO regression, SVM-RFE, and random forests), we identified core genes implicated in COPD pathogenesis. Their biological functions and interrelationships were characterized using functional enrichment analyses (GO, KEGG, Reactome, WikiPathways) and protein-protein interaction (PPI) network construction. To experimentally validate the bioinformatic findings, an in vitro COPD model was established by exposing MLE-12 alveolar epithelial cells to cigarette smoke extract (CSE). Successful model induction was confirmed via ELISA-detected elevation of pro-inflammatory cytokines and flow cytometric assessment of enhanced intracellular reactive oxygen species (ROS) levels. Subsequently, expression levels of the 12 candidate genes were quantified by qRT-PCR.

Results: Transcriptomic analysis revealed 281 differentially expressed genes between COPD and control groups, which were significantly enriched in pathways related to inflammatory response, oxidative stress, and extracellular matrix organization. Multi-algorithm machine learning cross-validation yielded 12 robust

core genes: Acaa1b, Adh7, Aldh3a1, CpoX, Cyp1b1, Dhfr3, Disc1, Fig4, Flrt2, Gsta5, Igfbp4, and Serpinb1a. These genes are functionally involved in aldehyde detoxification, redox homeostasis, protease inhibition, and cell adhesion. PPI network analysis demonstrated high interconnectivity among these genes, supporting their functional centrality. The combined diagnostic model exhibited excellent discriminative performance (AUC = 0.92, 95% CI: 0.87 – 0.96).

Experimental validation confirmed that the expression of these genes was significantly altered under CSE-induced oxidative stress conditions, consistent with bioinformatic predictions.

Conclusion: This study systematically identifies and validates a panel of key genes that play essential roles within the oxidative stress-immune inflammation interaction network in COPD. These genes collectively form a multidimensional, interconnected molecular regulatory framework, providing a novel molecular roadmap for elucidating the pathological mechanisms underlying COPD. These findings not only advance our understanding of the disease complexity but also establish a theoretical foundation for the future development of diagnostic biomarkers and targeted therapeutic strategies directed at specific molecular nodes.

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Effects of Cervical Jiaji-Point Tuina on Neuropathic Pain in Rats Following Upper Trunk Brachial Plexus Avulsion

颈夹脊穴推拿对臂丛神经上干撕脱伤大鼠神经病理性疼痛的影响

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Abstract:

Background: Neuropathic pain is a common and refractory complication following brachial plexus injury (BPI), severely impairing upper-limb functional recovery and quality of life. Increasing evidence indicates that chronic neuropathic pain involves not only peripheral and spinal sensitization but also maladaptive changes in supraspinal circuits associated with reward, motivation, and affective processing. The nucleus accumbens, a key component of the mesolimbic reward system, has been implicated in the modulation of pain perception and the emotional dimensions of persistent pain. Among the neurochemical systems involved, the endocannabinoid 2-arachidonoylglycerol (2-AG) and the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) are important regulators of neural activity and have been linked to chronic pain-related changes in the brain. Tuina, a traditional non-pharmacological intervention, has demonstrated potential benefits in pain relief and neurological rehabilitation. However, its effects and underlying central mechanisms in neuropathic pain following brachial plexus injury remain insufficiently investigated. Therefore, this study aimed to evaluate the effects of cervical Jiaji-point Tuina on neuropathic pain-related behaviors and on the expression of 2-AG and GABA in the nucleus accumbens of rats with upper trunk brachial plexus avulsion, in order to explore the potential neurochemical mechanisms underlying Tuina-mediated analgesia.

Method: Thirty-two male Sprague – Dawley rats were randomly assigned to four groups (n = 8 per group): Control, Model, Control+Tuina, and Model+Tuina. A neuropathic pain model was established by upper trunk brachial plexus avulsion. Standardized Tuina intervention was initiated on postoperative day 3 and administered once daily for 14 consecutive days. During treatment, Tuina manipulation was applied bilaterally to the cervical Jiaji points corresponding to the C1 – C8 spinal segments. Mechanical hypersensitivity was assessed using von Frey filaments to determine bilateral hind paw withdrawal thresholds (PWTs) before modeling, on postoperative day 3 (before intervention), and on days 1, 3, 7, and 14

after Tuina treatment. Ongoing spontaneous pain was evaluated using the conditioned place preference (CPP) paradigm. In addition, enzyme-linked immunosorbent assay (ELISA) was performed to detect the expression levels of 2-arachidonoylglycerol (2-AG) and gamma-aminobutyric acid (GABA) in the nucleus accumbens. Behavioral and biochemical outcomes were compared among groups.

Results: On postoperative day 3, bilateral hind paw withdrawal thresholds were significantly reduced in the Model group compared with the Control group ($P < 0.05$), indicating successful establishment of the neuropathic pain model. CPP testing further demonstrated ongoing spontaneous pain in model animals ($P < 0.05$). On day 7 after Tuina intervention, significant differences in bilateral hind paw withdrawal thresholds were observed between the Control and Model groups, the Control and Model+Tuina groups, and the Model and Control+Tuina groups (all $P < 0.05$). With prolonged intervention, bilateral hind paw withdrawal thresholds in the Model+Tuina group showed an increasing trend, accompanied by improvements in CPP-related indices. ELISA analysis revealed that the Model group exhibited elevated 2-AG expression and reduced GABA expression in the nucleus accumbens compared with the Control group. After 14 days of Tuina intervention, 2-AG expression in the nucleus accumbens was significantly decreased, whereas GABA expression was significantly increased in the Model+Tuina group compared with the untreated Model group ($P < 0.05$). The most pronounced behavioral and biochemical improvements were observed after 14 days of Tuina treatment.

Conclusion: Cervical Jiaji-point Tuina alleviates mechanical hypersensitivity and ongoing spontaneous pain in rats with brachial plexus avulsion-induced neuropathic pain. These effects may be associated with modulation of endocannabinoid signaling and GABAergic neurotransmission in the nucleus accumbens, suggesting that reward-related neural circuits are involved in Tuina-mediated analgesia.

Keywords: brachial plexus injury; neuropathic pain; Tuina therapy; cervical Jiaji points; conditioned place preference; mechanical allodynia

Analysis of Current Trends in Physical Therapy for Chronic Pelvic Pain and a Discussion on Tuina: A Visualization of Bibliometric Analysis

慢性盆腔痛的物理治疗热点分析与推拿治疗探讨——文献计量可视化分析

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Abstract:

Background:

Chronic pelvic pain (CPP) is a prevalent condition, characterized by persistent or recurrent pelvic pain lasting more than six months. It often involves the urinary, reproductive, gastrointestinal, and musculoskeletal systems and is frequently accompanied by psychological disorders. Physical therapies, including tuina and massage, have emerged as significant non-pharmacological strategies for the management of CPP. The objective of this study was to investigate research trends and significant areas of focus within this field.

Method:

A bibliometric analysis was conducted on 295 publications related to physical therapy and CPP retrieved from the Web of Science Core Collection database (1996–2026). The analysis of publication trends, international collaborations, keyword co-occurrence, research hotspots, and emerging topics was conducted using VOSviewer, CiteSpace, and R software. The potential role of tuina in CPP management was the focus of further discussion, as supported by the bibliometric findings.

Results:

The number of publications on physical therapy for CPP increased substantially after 2014 and reached its peak in 2025. A thorough examination of the extant literature revealed that prominent research topics in this field include "chronic pelvic pain," "massage," "physical therapy," "quality of life," and "low back pain." The research focus has undergone a gradual shift from the control of symptoms to the comprehensive management of comorbidities, rehabilitation, and the enhancement of quality of life. Research focused on massage related interventions has remained a

prominent area of research interest, indicating a growing interest in manual therapies. When considered in conjunction with existing evidence, tuina has the potential to alleviate pelvic pain, improve low back pain and other comorbid symptoms, promote local circulation, and enhance patients' quality of life.

Conclusion:

Research on physical therapy for CPP is growing. It is becoming more focused on a variety of approaches and taking a more comprehensive approach. Tuina is an important traditional Chinese medicine intervention that has shown promise in relieving pain, managing other health problems, and improving quality of life. Future studies should provide stronger evidence from well-designed clinical trials and research on how tuina works to support the use of tuina as part of a comprehensive CPP management strategy.

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**Clinical effectiveness and safety of combined acupuncture-medicine anesthesia
for cesarean delivery: a systematic review and meta-analysis**

**剖腹產手術中針藥複合麻醉的臨床有效性和安全性：系統回顧與薈
萃分析**

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Abstract:

Background: Cesarean delivery (CD) is increasingly common, but perioperative pain and opioid-related adverse reactions remain challenging. Combined acupuncture-medicine anesthesia (CAMA) has been used as an adjunct to conventional anesthesia, yet its efficacy and safety for CD have not been systematically evaluated. This meta-analysis aimed to assess the clinical effectiveness and safety of CAMA during CD.

Method: We searched CNKI, VIP, WanFang, CBM, PubMed, EMBASE, and the Cochrane Library from inception to August 25, 2025, for randomized controlled trials (RCTs) comparing CAMA (any form of acupuncture combined with standardized pharmacological anesthesia) versus the same anesthesia alone in elective CD. Outcomes included anesthesia quality, postoperative pain, ephedrine/opioid use, adverse reactions (nausea/vomiting, chills, hypotension, traction reaction), and neonatal Apgar scores. Meta-analyses were performed using RevMan 5.4.

Results: Twenty-six RCTs involving 2,643 patients were included. Compared with conventional anesthesia alone, CAMA significantly improved the rate of excellent/good anesthesia quality (RR 1.25, 95% CI 1.15 – 1.35), reduced early postoperative pain (0 – 6 h, SMD –0.68, 95% CI –1.22 to –0.15), lowered ephedrine usage (RR 0.61, 95% CI 0.40 – 0.91), and decreased the incidence of nausea/vomiting (RR 0.55, 95% CI 0.43 – 0.71), chills (RR 0.45, 95% CI 0.31 – 0.66), hypotension (RR 0.48, 95% CI 0.28 – 0.80), and traction reaction (RR 0.62, 95% CI 0.51 – 0.76). No significant differences were observed in 1– min or 5– min Apgar scores between groups.

Conclusion: CAMA is a safe and effective adjunctive anesthesia strategy for cesarean delivery. It improves anesthesia quality, alleviates early postoperative pain,

reduces the use of vasopressors and opioids, lowers the incidence of several adverse reactions, and does not compromise neonatal safety. These findings support the integration of acupuncture into perioperative management, especially within enhanced recovery protocols.

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**A Quantitative System for Traditional Chinese Medicine Acupuncture
Manipulation Based on MediaPipe and Sensor Fusion**

基于 MediaPipe 与传感器融合的中医针刺手法量化系统研究

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Abstract:

Background: Acupuncture manipulation is a core technique in acupuncture therapy. Quantitative research on manipulation techniques is essential for standardizing clinical practice, improving therapeutic efficacy, and supporting teaching and inheritance. However, current clinical practice lacks unified operational standards, and traditional transmission based on oral instruction and personal experience is difficult to quantify precisely. This study aimed to develop a quantitative system for acupuncture manipulation to enable multidimensional data acquisition, real-time analysis, and objective evaluation.

Method: Based on acupuncture manipulation theory and quantitative measurement principles, a quantitative platform was established by integrating an acupuncture manipulation parameter measurement device with a real-time posture recognition system. The measurement device used resistance sensors to collect key parameters of lifting-thrusting and twirling manipulations, including amplitude, frequency, displacement, and angle. The posture recognition module was developed using MediaPipe, integrating computer vision and machine learning to capture hand keypoints in real time and analyze joint angles, displacement trajectories, and movement stability. Voice interaction and intelligent question-answering modules were also incorporated to enhance teaching assistance. Manipulation data from physicians and students were collected. SPSS was used to perform t-tests, logistic regression, and receiver operating characteristic curve analyses to screen characteristic parameters and construct a quantitative evaluation model.

Results: The system achieved multidimensional data acquisition and real-time analysis of both single and compound acupuncture manipulation techniques, including lifting-thrusting reinforcing, lifting-thrusting reducing, twirling reinforcing, twirling reducing, Shao Shan Huo “mountain-burning fire”, and Tou Tian Liang “heaven-penetrating coolness”. Significant differences were observed among different techniques in frequency, trendline slope, ascent-to-descent ratio, and cycle variability ($P < 0.05$). The AUC values of the logistic regression models

were all greater than 0.94. The posture recognition module effectively visualized manipulation movements and quantified movement stability. Overall, the system demonstrated good acquisition accuracy, stability, and interactivity.

Conclusion: This study developed a quantitative system that enables synchronized multidimensional data acquisition and analysis of acupuncture manipulation techniques. By incorporating hand posture information, the system addresses limitations of previous studies that focused mainly on needle movement parameters. It provides a scientific tool and data support for objective evaluation, standardized teaching, and clinical standardization of acupuncture manipulation, showing promising potential for practical application.

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