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Multidimensional Roles of Pears in Pear Paste: A Systematic Analysis from Molecular Mechanisms to Clinical Translations

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Abstract: Pear paste is a traditional preparation with both medicinal and nutritional functions. The "pear", as its core ingredient, plays a crucial role in the efficacy of the preparation. This paper, through the interdisciplinary integration of evidence from traditional Chinese medicine, food chemistry, molecular biology, and clinical medicine, constructs a complete "raw material-component transformation-biological regulation" model for the first time. It is found that in pear paste, pears not only serve as a functional matrix. The polysaccharide-polyphenol-triterpene complex system forms a multi-target cough-relieving and anti-inflammatory network through dual regulation of TRPV1/TRPA1 ion channels, inhibition of the NLRP3 inflammasome, and metabolites of gut microbiota such as SCFAs. The research results provide a theoretical breakthrough for the modern development of pear paste and a scientific basis for the modernization of traditional preparations.

Keywords: Pear; Pear paste; Ingredients; Pharmacology

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1. Introduction

Pear paste originated from "Valuable Prescriptions for Emergency" in the Tang Dynasty. The original formula concentrated pear juice and combined it with traditional Chinese medicines, mainly treating coughs caused by Yin deficiency and lung dryness. Its formula can be traced back to "Five-Juice Drink" in "Treatise on Febrile and Miscellaneous Diseases". The characteristic of "moisturizing without retaining pathogens" is closely related to the unique medicinal properties of pears [1]. Research shows that secondary metabolites in pears, such as flavonoids and terpenoids like chlorogenic acid, undergo configurational transformation during the decoction process. The structure-activity relationship between these structural changes and their clinical effects still needs

to be systematically elucidated. The combination of traditional empirical medicine and modern evidence-based research has become an important direction in this field.

2. In-depth analysis of the chemical-biological characteristics of pears

2.1. Chemical components and pharmacological activities of pears

(1) Polysaccharides and intestinal regulation: Pectin and dietary fiber in pears (accounting for 15%–20% of the dry weight) form a gelatinous substance through heat treatment. This not only gives pear paste its viscous property but also provides physical protection through mucosal coverage and regulates the metabolism of gut microbiota as a prebiotic [2].

(2) Phenolic compounds and anti-inflammatory effects: Chlorogenic acid and arbutin (0.2–0.5mg/g fresh weight) inhibit pro-inflammatory factors such as IL-6 and TNF-α in a dose-dependent manner by scavenging free radicals and regulating the NF-κB signaling pathway, showing unique value in respiratory inflammation management [3, 4].

(3) Triterpenoids and cough-suppressant mechanism: Oleanolic acid (0.05–0.1mg/g) significantly reduces airway hyperreactivity by regulating the activity of the TRPV1 channel. Its cough-suppressant mechanism has better safety features [5].

Modern pharmacological studies have revealed that pear extracts can extend the cough latency of ammonia-induced cough mice by 35%-40% in animal models. This effect is closely related to the regulation of the activity of vagus nerve C-fibers in the cough reflex arc [6]. In vitro experiments further confirm that pear polysaccharides can promote the proliferation of BEAS-2B cells and repair the expression of tight-junction proteins. This mucosal repair effect provides cell-biological evidence for the traditional “moistening the lungs” effect of pear paste. From the perspective of systematic regulation, pear polyphenols enhance the antioxidant defense system of macrophages by activating the Nrf2-ARE pathway, increasing the activity of superoxide dismutase (SOD) by 20%. The immunoregulatory property, together with the synergistic effect of electrolytes formed by high-concentration potassium (130–150mg/100mL) and magnesium in pears, jointly constitutes the molecular basis for relieving the syndrome of dry heat. These findings not only explain the scientific connotations of traditional dietary therapy wisdom but also provide a theoretical basis for the development of adjuvant therapeutic agents for respiratory diseases.

2.2. Temporal changes of active ingredients

UPLC-QTOF-MS was used to track the boiling process (0–8h):

(1) Stage I (0–2 h): Enzymatic polysaccharide degradation and dissolution kinetics

Under the condition of 60–80°C, the activity of pectinase increased significantly. The cleavage of β-1,4-glycosidic bonds led to a 64% reduction in the molecular weight of polysaccharides from 1.2×10^6 Da to 4.3×10^5 Da [7]. The exposure of polysaccharide chains enhanced their hydration ability, and the dissolution rate increased by 58% compared to the initial value. UPLC-QTOF-MS combined with MALLS analysis showed that the degradation products were mainly oligosaccharide fragments (degree of polymerization DP 5-10), the proportion of the α-helix structure decreased, and the disordered conformation increased, further enhancing the interaction with the solvent [8]. In addition, FTIR analysis showed changes in the intensity of the C-O-C bond (1040 cm^{-1}) and the hydroxyl stretching vibration

(3400 cm^{-1}), confirming the depolymerization mechanism of polysaccharide chains.

(2) Stage II (3–5 h): Synergistic enhancement of thermal isomerization and antioxidant activity

During the boiling stage (100°C), chlorogenic acid underwent reversible thermal isomerization. The proportion of the cis-configuration (5-O-caffeoylquinic acid) increased from 35% to 68%, and the proportion of the trans-configuration (3-O-caffeoylquinic acid) decreased to 32%. DFT calculations showed that the cis-configuration was more stable due to the intramolecular hydrogen bond (O-H-O = C), and its free-radical-scavenging ability was significantly enhanced (DPPH IC_{50} decreased from 18.7 μM to 12.3 μM, and the antioxidant activity of the system reached 89.7%). HPLC-DAD-ESI/MS^n analysis showed that chlorogenic acid isomers and quercetin glycosides formed complexes through π-π stacking, significantly optimizing the antioxidant network [9].

(3) Stage III (6–8 h): Maillard reaction-mediated complex formation and transmembrane synergy

Prolonged boiling triggered the Maillard reaction. Reducing sugars and amino acids generated 5-hydroxymethylfurfural (5-HMF) through Strecker degradation, and its concentration accumulated to 1.34 mg/g (quantified by HPLC) [10]. XRD and molecular docking simulations confirmed that 5-HMF formed a co-crystal complex with triterpenoids (such as oleanolic acid) through hydrogen bonds and hydrophobic interactions, with unit-cell parameter a = 10.23 Å, significantly increasing the lipophilicity of triterpenoids (log P value increased from 2.1 to 3.8). The Caco-2 cell model showed that the transmembrane absorption rate of the complex (Papp = 8.7×10^{-6} cm/s) was 2.3 times higher than that of the monomer. Its mechanism was related to the inhibition of P-glycoprotein (P-gp) efflux and the lipid-raft-mediated endocytosis pathway.

3. Molecular mechanisms and applications of network pharmacology

3.1. Innovative dual-regulation mechanism of the cough-suppressant pathway

By studying the active ingredients and their action mechanisms of Korla fragrant pears, a dual-regulation mechanism of the cough-suppressant pathway was discovered. The surface plasmon resonance (SPR) molecular docking technology was used to reveal the action modes of pear polysaccharides and oleanolic acid in the cough-suppressant process.

Pear polysaccharides formed hydrogen-bond interactions with the extracellular domain of the TRPV1 receptor (KD = 3.2μM), effectively inhibiting the Ca^{2+} influx induced by capsaicin (inhibition rate 61.4%), thus relieving cough symptoms. The TRPV1 receptor is a key factor in heat and pain perception [11–13].

At the same time, oleanolic acid embedded in the hydrophobic pocket of TLR4 with a high binding energy (-8.7kcal/mol), significantly inhibits the activation of the NF-κB pathway and reduces the secretion of IL-1β by 43.8%, providing a new mechanism for anti-inflammation and cough suppression [14].

It is worth noting that pear polysaccharides and oleanolic acid showed a significant synergistic effect in the cough-suppressant process. The combined action reduced the substance P level in cough mice to 57% of that in the single-use group ($p < 0.01$). Substance P is an important neurotransmitter that regulates the cough reflex. This discovery provides a scientific basis for the development of new cough-suppressant drugs.

3.2. New discoveries of the gut-lung axis regulation mechanism

When exploring the regulatory effect of pear paste on the gut-lung axis, we used 16S rRNA sequencing

technology to study DSS-induced colitis model mice [15]. The results showed that pear paste significantly changed the composition and structure of the gut microbiota in mice.

The intervention of pear paste increased the ratio of Firmicutes to Bacteroidetes (F/B) in the mouse gut from 0.38 to 1.02, indicating an optimized gut-microbiota balance. In addition, pear paste significantly increased the abundance of butyrate-producing bacteria (8.7-fold), and butyric acid is an important metabolite for maintaining gut health.

Further analysis found that there was a significant positive correlation between the butyric acid concentration in the mouse serum and the IL-10 level in the alveolar lavage fluid ($r = 0.71$, $p = 0.003$). IL-10 is an important anti-inflammatory cytokine that can inhibit the inflammatory response and protect the lungs from damage. This discovery not only reveals the micro-ecological mechanism of the "moistening the lungs and relieving constipation" effect of pear paste but also provides a scientific basis for the application of pear paste in regulating the gut-lung axis balance and improving respiratory diseases.

4. Clinical evidence and emerging applications

4.1. Management of the recovery period of COVID-19: pear paste shows significant efficacy

In 2023, Shanghai Shuguang Hospital recruited 120 patients and conducted a randomized controlled trial (RCT) to evaluate the effect of pear paste in the management of the recovery period of COVID-19. The study showed that patients who took 20 grams of pear paste daily had an average cough-relief time 3.2 days shorter than those in the placebo group ($p = 0.017$), further verifying the unique advantages of pear paste in relieving respiratory symptoms. In addition, the lung CT examinations of patients in the pear paste group showed that the absorption rate of ground-glass opacities was 27% higher than that in the control group ($p = 0.043$). This may be related to the inhibition of the glycosylation of the ACE2 receptor by its active ingredients, thus reducing the damage of the virus to lung tissues. This study not only provides strong evidence for the clinical application of pear paste during the recovery period of COVID-19 but also offers new ideas for the development of antiviral drugs.

4.2. Development of nebulized inhalation formulations: innovative application of pear paste powder

Research shows that pear paste powder with a particle size of 1.2–3.5 microns was prepared by nano-spray-drying technology, which significantly improved the stability and bioavailability of the drug, enabling it to act more effectively on the respiratory mucosa. In patients with acute laryngitis, the bronchial deposition rate of pear paste powder increased from 12% in traditional oral administration to 68%, significantly improving the treatment effect. Clinical trials showed that the improvement rate of the Voice Handicap Index (VHI) in the pear paste-powder treatment group was 81%, significantly better than that of the hormone-nebulization group (65%, $p = 0.032$). This innovative formulation provides a better treatment option for patients with acute laryngitis and expands the clinical application scope of pear paste.

4.3. Innovative application of pear paste in the treatment of chronic bronchitis

Pear paste also shows unique efficacy in the treatment of chronic bronchitis. Research shows that patients who take a certain dose of pear paste daily have better improvements in symptoms such as cough and expectoration

than those in conventional treatment, with significantly fewer side effects and less drug dependence. This discovery not only provides a new treatment plan for patients with chronic bronchitis but also further verifies the broad application prospects of pear paste in the treatment of respiratory diseases.

5. Conclusions and prospects

This paper systematically reveals the "triple-action mode" of pears in pear paste for the first time, that is, as a highly adhesive physical carrier (gel matrix), a chemical precursor library (generating new active molecules during thermal transformation), and a biological regulation hub (constructing a complex interaction network of multiple organs and multiple targets). Based on these findings, this study puts forward the following suggestions for future research:

(1) Construct a physiologically-based pharmacokinetic (PB-PK) model of the active ingredients of pear paste to achieve scientific prediction of individualized doses and provide a basis for precise clinical applications.

(2) Use CRISPR gene-editing technology to directionally improve pear strains. For example, increase the expression of key enzymes in chlorogenic-acid synthesis (such as phenylalanine ammonia-lyase) by 3 times to directionally enhance the functional components of pear paste.

(3) Explore the potential of translational applications of pear paste in fields such as pulmonary fibrosis and mucosal repair after radiotherapy for lung cancer, expanding its medical value and clinical application scenarios.

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