The Chemical Ingredients and Medical Effects of Natural Drugs

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Abstract. Natural medicines have long been used to treat diseases, and in-depth exploration of their components and efficacy is crucial for clinical application. This paper focuses on Sophora japonica (Chinese scholar tree), analyzing its key chemical components, molecular structures, medicinal effects, and current research challenges, while discussing the significance and future directions of natural drug research. It identifies three main components of Sophora japonica: rutin, quercetin, and polysaccharides. Rutin and quercetin, both flavonols with similar structures, differ in efficacy—rutin, with hydrophilic properties, can protect blood vessels and prevent thrombosis, while quercetin is applicable for cancer and tumor treatment; polysaccharides exhibit anti-inflammatory and anti-tumor abilities. The study notes challenges in natural drug research, such as quercetin's low bioavailability, which can be addressed by microfluidic technology and antisolvent precipitation to improve solubility; it also emphasizes strict control of natural drug production steps to enhance quality. Additionally, it points out side effects of natural medicines due to current technical limitations, which reduce their usage rate. This paper deepens understanding of natural medicines and highlights the importance of developing innovative solutions to promote their future application.

Keywords: Flos sophorae; natural medicine; medical effect; rutin, quercetin; polysaccharide.

1. Introduction

Natural medicines, as a traditional means for humans to combat diseases, carry thousands of years of medical practice wisdom. From the earliest existing pharmacological classic in China, the "Shennong Bencao Jing," which systematically recorded 365 types of medicines, to the Ming Dynasty's "Compendium of Materia Medica," which included 1892 natural medicines and detailed their properties, flavors, and effects, the core position of natural medicines such as plant medicine in disease prevention and control has been repeatedly confirmed by history[1,2]. These types of drugs still occupy an irreplaceable position in modern medical systems due to their complex structures and difficult to synthesize multiple chemical components. According to data from the World Health Organization, approximately 80% of the global population relies on natural medicines to maintain their health, with this proportion being particularly prominent in developing countries.[3] At the same time, with the exponential growth of research and development costs for new chemical drugs and the increasingly prominent issue of toxic side effects, mining safe and effective active ingredients from natural medicines has become an important breakthrough in global pharmaceutical research.

In recent years, there has been a trend of integration and innovation in the research of natural medicines both domestically and internationally. The international academic community focuses on verifying the clinical value of traditional Chinese herbs through modern medical methods, particularly emphasizing the research path of combining traditional Chinese and Western medicine. For example, in the case of gastroesophageal reflux disease,[4] researchers have found that natural ingredients such as Artemisia absinthium, Plantago ovata, and curcumin have significant therapeutic effects. In the treatment of ulcerative colitis, a controlled trial of 105 patients showed that Plantago asiatica had comparable relief and maintenance effects to the traditional drug mesalazine, but the former had a lower incidence of side effects. The anti-inflammatory effect of curcumin has also been confirmed through randomized controlled trials, with a significantly lower recurrence rate in the treatment group compared to the placebo group. These studies indicate that the international academic community is focusing on clinical trials to explore collaborative pathways between natural medicines and modern healthcare systems.

Domestic research focuses on the material basis and mechanism of action of natural medicines, and has made significant progress in fields such as anti-tumor, neural regulation, and cardiovascular and cerebrovascular protection[5]. For example, researchers have conducted systematic studies on plants in the family Lamiaceae, including the genera Lycium, Taxus, Wisteria, and Euphorbia. Through separation, purification, and structural analysis, the chemical nature of their anticancer active ingredients has been clarified. At the same time, a complete research system has been established for the antibacterial, anti-inflammatory, and immune regulating effects of natural medicines, from component identification to target validation. Although there are different focuses in domestic and foreign research, they all point to a core issue: the efficacy of natural medicines is closely related to the structural characteristics of their chemical components, and the systematic analysis of this relationship is still a weak link in current research.

Based on this, this paper takes plant medicine as the research object, focuses on the correlation system of "chemical composition structural characteristics pharmacological mechanism" of natural medicine, systematically sorts out the main chemical components of typical natural medicines (such as Sophora japonica), analyzes the chemical structure of its key active ingredients, and elucidates the pharmacological effects corresponding to different components. At the same time, feasible solutions are explored to address the challenges faced in natural medicine research, such as ingredient complexity, pharmacological interference, and bioavailability. This paper aims to provide theoretical basis for the precise development, quality control, and rational clinical application of natural medicines, and promote the modernization and internationalization of traditional natural medicines.

2. The Discovery of Artemisia Annua

The modernization research of natural medicines often follows the core logic of "component identification structure analysis efficacy verification", and the discovery and application of artemisinin is a classic example of this paradigm. [6]In the 1970s, faced with the urgent need for malaria prevention and control and the dilemma of the decline in the efficacy of traditional antimalarial drug quinine, a Chinese research team conducted a systematic study on Artemisia annua using the record of "one grip of Artemisia annua, two liters of water stains" in the ancient Chinese medicine book "Emergency Formula for Elbow Reserve" as a clue. In 1971, Tu Youyou's team first isolated artemisinin from Artemisia annua and determined it to be a sesquiterpenoid lactone containing a peroxide bridge through chemical structure analysis. This unique peroxide bridge structure is the key to its anti malarial activity. The clinical trial completed in 1973 confirmed that artemisinin can rapidly kill the intracellular fission bodies of malaria parasites in red blood cells, and still has high activity against quinine resistant strains, becoming a milestone in global anti malaria treatment.

2.1. Chemical composition and structural characteristics of Sophora japonica flowers

Huai Hua (also known as Huai Mi), as a traditional Chinese medicinal herb, has diverse medicinal effects due to its complex chemical composition, mainly including flavonoids, isoflavones, and polysaccharides. The chemical structure of each component determines its physicochemical properties and biological activity(See Figure 1).

Flavonoids are the characteristic components of Sophora japonica flowers, with the highest proportion, among which rutin (quercetin-3-O-rutinose) content can reach up to 20% [7]. The chemical structure of rutin consists of a quercetin core and a rutin glycosyl group (molecular formula $C_{27}H_{\propto 0}O_{16}$). In its tricyclic system, the A ring is a resorcinol group (providing a metal chelating site), the B ring contains an ortho dihydroxy group (an antioxidant core group), and the C ring is connected to the rutin glycosyl group through glycosidic bonds. This glycosylation modification endows rutin with good water solubility (significantly higher than quercetin) [7]. Technologies such as high-performance liquid chromatography (HPLC) and high-performance thin layer chromatography (HPTLC) can not only accurately determine the content of rutin, but also reveal the

influence of environmental factors (such as soil pH and light) on its accumulation by comparing the differences in the composition of Sophora flowers from different origins.

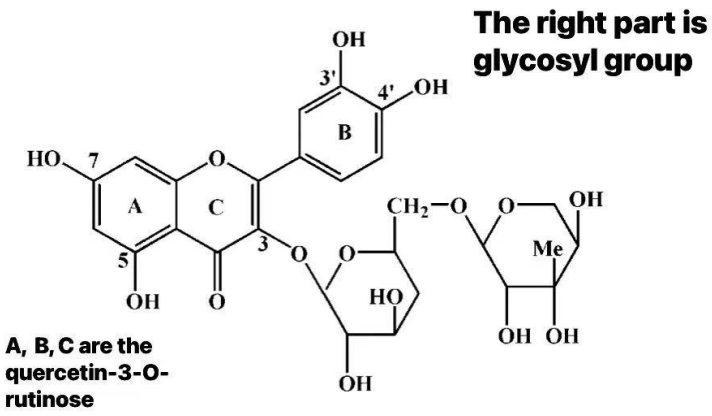

Fig. 1 Chemical structure of rutin [7]

Quercetin, as a glycoside of rutin, belongs to the same class of flavonols. However, due to the lack of rutin glycosylation modification, its structure only retains the tricyclic nucleus, resulting in significantly enhanced lipid solubility and reduced water solubility[8] (See figure 2). This structural difference makes it complementary to rutin in terms of biofilm penetration and target binding. The key difference between isoflavones and flavonoids lies in the B-ring connection position: the B-ring of isoflavones is connected to the C3 position, rather than the C2 position of flavonoids. This isomerization phenomenon leads to significantly different binding specificity with biomolecules such as estrogen receptors, laying the foundation for their selective physiological activity.

Polysaccharides are another important component in Sophora japonica flowers. Sophora japonica polysaccharides (SSP) are water-soluble plant polysaccharides formed by multiple monosaccharides connected by glycosidic bonds to form complex sugar chains. Their structural complexity is reflected in differences in molecular weight distribution (5-50 kDa), monosaccharide composition (glucose, galactose, etc.), and branching degree [9]. Due to the small amount of protein in Sophora japonica, protein impurities need to be removed by Sevag method when extracting polysaccharides, otherwise the purity and efficacy of polysaccharides will be affected by co precipitation [10]. Its hydrophilicity (derived from a large number of hydroxyl groups) determines that the water extraction and alcohol precipitation method is the most suitable extraction process. Although the traditional water extraction and alcohol precipitation method is easy to operate, it has the problems of low extraction rate and long time consumption. In recent years, ultrasound assisted extraction and microwave-assisted extraction techniques have gradually been applied in the extraction of polysaccharides from Sophora japonica. Ultrasonic assisted extraction destroys plant cell walls through the cavitation effect of ultrasound, making polysaccharides more soluble. The extraction rate is 20% -30% higher than traditional methods, and the extraction time is shortened to one-third of the original; Microwave assisted extraction utilizes the thermal and non thermal effects of microwaves to accelerate solvent permeation and solute diffusion, while preserving polysaccharide activity and improving efficiency [11]. The application of these new extraction technologies not only optimizes the preparation process of Sophora japonica polysaccharides, but also provides technical support for their industrial production, which helps to better utilize the medicinal value of polysaccharides.

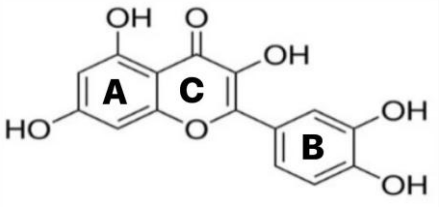

Fig. 2 Chemical structure of quercetin [9]

2.2. The pharmacological mechanism of the main components of Sophora japonica

The pharmacological effects of Sophora japonica are closely related to the structural characteristics of its chemical components. Flavonoids, isoflavones, and polysaccharides work through different molecular mechanisms, reflecting the characteristic of "multi-component synergy" in natural medicine. The pharmacological effect of quercetin is directly related to its "lipid soluble maternal nucleus+phenolic hydroxyl" structure. The ortho dihydroxy group of the B ring can scavenge free radicals (such as $\cdot OH$, O_2^-) through the donor hydrogen atom, while the resorcinol group of the A ring can chelate transition metal ions such as Fe^{2+}, inhibit the Fenton reaction, and thus exert strong antioxidant effects. The 3-hydroxy group has been proven to be a key site for maintaining antioxidant activity [12]. In terms of antibacterial properties, its lipophilicity makes it easy to penetrate bacterial cell membranes, inhibiting the growth of hydrophilic bacteria (such as Escherichia coli) by disrupting cell wall synthesis enzymes (such as transpeptidase), and targeting viruses by binding to proteases (such as influenza virus neuraminidase), blocking their replication [13]. In terms of anti-cancer activity, quercetin can play a role through multiple mechanisms: combining with EGFR on tumor cell surface to inhibit its activation, regulating PI3K/Akt pathway to induce cell apoptosis, and combining with adriamycin can enhance the killing effect on lung cancer, liver cancer and breast cancer cells (MCF-7, MDA-MB-231) [13].

Rutin, due to its hydrophilic nature, is complementary to quercetin in terms of its pharmacological effects. The increase in water solubility makes it easier for it to reach the endothelium of blood vessels through blood circulation, exerting antithrombotic effects by inhibiting platelet aggregation and relaxing vascular smooth muscle; Its metal chelating ability (A-ring) can also reduce oxidative stress in the vascular wall and protect endothelial function. Isoflavones, on the other hand, have the potential to selectively bind to estrogen receptors (ER β) due to the unique location of the B-ring connection, and exhibit potential in regulating endocrine function and improving menopausal symptoms [9]. Isoflavones not only selectively bind to estrogen receptors (ER β) to regulate endocrine function, but recent studies have also found that they have a positive impact on bone metabolism. Due to its structural similarity to estrogen, it can promote osteoblast proliferation and differentiation by acting on estrogen receptors on the surfaces of osteoblasts and osteoclasts, while inhibiting osteoclast activity and reducing bone resorption. Animal experiments have shown that flavonoids extracted from Sophora japonica can significantly increase bone density and reduce the risk of fractures in ovariectomized rats. This discovery provides a new potential drug source for the prevention and treatment of postmenopausal osteoporosis [9].

3. Challenges and Countermeasures in Natural Medicine Research

The pharmacological effects of Sophora japonica polysaccharides are highly correlated with their structural complexity. Polysaccharides from Sophora japonica with a molecular weight of 5-10 kDa can enhance immune function by activating macrophages, promoting the secretion of cytokines such as TNF - α and IL-2, and inducing apoptosis of liver cancer cells by upregulating Bax protein and downregulating Bcl-2 expression. In terms of antioxidant and anti-inflammatory properties, the free hydroxyl groups in its sugar chain can directly clear ROS and inhibit the activation of the NF - κ B pathway, reducing the inflammatory damage induced by porcine circovirus type 2 [14,15]. However, the anti-tumor activity of polysaccharides is significantly influenced by their monosaccharide composition, with components with high mannose content exhibiting stronger activity [11].Although progress has been made in the research of natural medicines such as Sophora japonica, it still faces multiple challenges such as complex composition and limitations in physicochemical properties. Technological innovation and method optimization are needed to break through bottlenecks. At the compositional level, the synergistic or antagonistic effects of flavonoids and polysaccharides in Sophora japonica are not yet clear. For example, the lipid solubility of quercetin and the water solubility of polysaccharides may affect each other's bioavailability; Residual impurities such as proteins and tannins during the extraction process can also interfere with the efficacy evaluation [14].

In terms of physicochemical properties, quercetin has a low oral bioavailability of less than 10% due to its insolubility in water, and undissolved particles can easily irritate the gastrointestinal mucosa [12]. The structural diversity of polysaccharides, such as differences in sugar chain branching, increases the difficulty of standardizing drug efficacy. In addition, environmental factors can cause fluctuations of up to 30% in the rutin content of locust flowers from different regions, seriously affecting the uniformity of quality [7]. Long term use of polysaccharide components may also induce drug resistance in tumor cells [15].

Multi dimensional solutions can be adopted to address the above challenges. By using microfluidic technology and anti solvent precipitation method to prepare quercetin nanocrystals, the increase in specific surface area can increase solubility by 5-10 times, significantly improve bioavailability, and reduce gastrointestinal irritation [16]. By establishing a fingerprint based on HPLC and combining it with an origin tracing system, precise quality control of Sophora japonica can be achieved. Using network pharmacology to construct a "component target pathway" network and analyze the synergistic mechanism between flavonoids and polysaccharides (such as the synergistic effect of quercetin in inhibiting tumor cell proliferation and polysaccharides in enhancing immunity). In the future, further optimization of the physicochemical properties of the components through structural modifications (such as methylation derivatives of rutin) is needed to promote the clinical translation of natural medicines.

4. Conclusion

This paper analyzes the medicinal value of Sophora japonica, clarifying that its core active ingredients are rutin, quercetin, and polysaccharides. Through molecular structure analysis, it was found that although rutin and quercetin belong to the same flavonol group and have similar structures, their pharmacological effects have their own focuses - rutin can enhance vascular function and prevent thrombosis by virtue of its hydrophilicity, quercetin has potential in cancer and tumor treatment, and polysaccharides have dual anti-inflammatory and anti-tumor activities, which together constitute the material basis for Sophora japonica to exert its medicinal value. Although natural medicines represented by Sophora japonica have shown various benefits in disease treatment, current research and application still face significant challenges: the low bioavailability of quercetin can be improved by enhancing its solubility through microfluidic technology and anti solvent precipitation methods; The composition of natural medicines is complex, and strict control of each production process is the key to ensuring drug quality; Meanwhile, the side effects caused by technological limitations have also to some extent affected the actual usage rate of natural medicines. In depth analysis of the chemical composition, pharmacological mechanism, and research bottlenecks of natural medicines (such as Sophora japonica) can not only provide scientific basis for understanding the medicinal nature of natural medicines, but also point out the direction for their subsequent development. In the future, with the continuous emergence of innovative technologies, solutions to the existing problems of natural medicines will gradually improve, which is expected to promote the greater value of natural medicines in clinical treatment and provide more high-quality choices for disease prevention and treatment.

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