

Review of Traditional Chinese Medicine Puerariae Lobatae Radix

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Abstract: Puerariae Lobatae Radix is the dried root of Pueraria lobata (Willd.) Ohwi, which is commonly known as kudzu. It's a traditional Chinese medicine with long history. According to ancient records, the effects of Puerariae Lobatae Radix include relieving muscle fever, raising the sun to stop diarrhea and activating the meridians and collaterals. In modern pharmacology, Puerariae Lobatae Radix has the effect of treating fever, diabetes and other diseases. Traditionally, Puerariae Lobatae Radix is mostly combined with other medicines and given to patients in the form of soup. Nowadays it can be applied in granules, capsules, oral liquids and other dosage forms. Based on the literature review and summarization, the article reviews the research progress of five aspects of the Chinese medicine Puerariae Lobatae Radix, namely chemical composition, extraction process, content determination, pharmacological effect, and preparation process, and gives an outlook and discusses the further development and research direction of Puerariae Lobatae Radix.

Keywords: Puerariae Lobatae Radix, chemical component, extraction process, content determination, pharmacological action, pharmaceutical technology

1. Introduction

With the shift in lifestyle in modern society, the incidence of cardiovascular diseases, metabolic diseases (e.g., diabetes) and neurological disorders has risen significantly, and Pueraria lobata has come into the limelight for its potential therapeutic efficacy in these areas. Pueraria lobata (Willd.) Ohwi is the dried root of Pueraria lobata (Willd.) Ohwi, a leguminous plant, which has the efficacy of relieving muscles and fever, elevating yang and stopping diarrhoea, activating the meridians, and detoxifying alcohol, and is commonly used to treat fever, headache, thirst, and dizziness. The main active components of Pueraria Mirifica are isoflavonoids, especially Puerarin, which also contains triterpenoids, coumarins and other compounds. These constituents have shown significant pharmacological activity in modern studies on the cardiovascular system, nervous system, liver damage, and even in the areas of anti-inflammatory and anti-osteoporosis. Pueraria lobata preparations have evolved from traditional tonics to tablets, capsules, injections, etc., with new microemulsions and nanoformulations. The research involved today mainly focuses on the extraction, content determination and pharmacological effects of the chemical constituents of Pueraria Mirifica. However, existing extraction processes and formulation methods often face the problems of low efficiency and unstable composition, which leads to the limited utilisation of the active ingredients of Pueraria Mirifica in clinical applications. The aim of this paper is to provide a systematic review of

the research progress on five aspects of Pueraria Mirifica: chemical composition, extraction process and isolation and purification, content determination methods, pharmacological effects, and preparation process. By summarising and analysing the existing research results, it reveals the potential and development direction of Pueraria lobata in modern medical applications.

2. Chemical composition

The chemical composition of Pueraria Mirifica contains isoflavonoids, triterpenoids, saponins, alkaloids, coumarins and polysaccharides. Of these, isoflavonoids are the most prominent compounds, including puerarin and its derivatives, such as daidzein, genistein and biochanin A [1].

3. Extraction Process and Purification

3.1. Extraction Process

The optimisation of Pueraria lobata extraction process is a hot research topic in recent years. Liu Xiaofang[1] used Pueraria lobata as raw material to optimize the enzyme-microwave-assisted synergistic extraction of Pueraria lobata using response surface methodology, and found that the best process flow for enzyme-microwave-assisted synergistic extraction of Pueraria lobata using response surface methodology was as follows: microwave power of 450 W, microwave time of 7 s, and the amount of enzyme added was 190 U/g, and the amount of Pueraria lobata leached under these conditions was 8.87 mg/100 g. Huang Qinghua et al.[2] analysed different parts of Pueraria lobata and the distribution pattern of Pueraria lobata content in wastewater during Pueraria lobata extraction by using high-performance liquid chromatography. They analysed the distribution of Pueraria Mirifica in different parts of Pueraria Mirifica and in the wastewater of Pueraria Mirifica powder extraction process, and obtained the optimal process as follows: adsorption time of 90 min, adsorption stirring speed of 150 r/min, and desorption of ethanol concentration of 60%.

3.2. Purification

Xiaohong Shang [3] et al. used UPLC-MS/MS to isolate a variety of nutrients and medicinal components including amino acids, nucleotides, polysaccharides, lipids, and flavonoids from Pueraria Mirifica by crushing, 70% methanol extraction, centrifugation, and 0.22 µm filtration. Limin Qu et al. [4] developed a simple and efficient method based on Cloud Point Extraction, CPE, and High-Performance Liquid Chromatography, HPLC, for the simultaneous separation and purification of the extracts from Pueraria Mirifica. The results of this study were summarized in the following table. A simple and efficient method based on Cloud Point Extraction (CPE) and High-Performance Liquid Chromatography (HPLC) was developed for the simultaneous separation and determination of six isoflavonoids in Pueraria Mirifica samples: puerarin, daidzin, genistein, daidzinin, genistein, and mangostin (puerarin, daidzin, genistein, daidzein, genistin, and formononetin).

4. Determination method of Puerarin content

Puerarin content is the key index to evaluate the qualification of Pueraria lobata, according to the 2020 edition of the National Pharmacopoeia, the content of Puerarin shall not be less than 2.4%. The following introduces the commonly used methods for the determination of Puerarin content in recent years [1].

4.1. High Performance Liquid Chromatography (HPLC) method

Several studies found the performance of different C18 columns in determining the content of Pueraria Mirifica in drugs, and finally the column with the best separation was chosen and the HPLC-DAD method or HPLC method was established. Yalkun[5] et al. chose the CapcellPakC18MGII column with the mobile phase water-acetonitrile, the temperature of the column was 35°C, the flow rate was 0.4 mL/min, and the linear range was 0.05-1.60 mg/mL, $r^2=0.9990$, and the spiked recovery was 99.57% with RSD 0.42%. Yu Jiezhen et al [6] chose AgilentZORBAXSB-C18 column, the mobile phase was methanol-0.1% aqueous phosphoric acid (21:79), the column temperature was 40 °C, the linear range was 0.1583-0.5540 µg/mL, $r^2=0.9994$, the spiked recoveries were 99.69%, RSD 0.42%.

4.2. Ultra performance liquid chromatography (UPLC)

Liu-Ting Wei[7] used a ZORBAXRRHD Eclipse PlusC18 (2.1x50mm, 1.8µm) column, methanol-0.1% formic acid aqueous solution (25:27) as the mobile phase, with the column temperature of 25°C, flow rate of 0.3mL/min, and the double internal standards of umbelliferolide and rutin, to establish a rapid and sensitive UHPLC-MS/MS method for the simultaneous determination of 13 active components of Pueraria lobata in mouse plasma and brain homogenate.

4.3. Thin layer scanning method (TLCS scanning)

Cheng Geng Jinsheng et al [8] spotted samples on silica gel GF254 plate with chloroform-methanol-ethyl acetate-water (14 : 7 : 3 : 1) as the unfolding agent, and used a single-wavelength scanning with a detection wavelength of 254 nm, and the slit width of 6 mm×0.3 mm to determine the content of geranylgeranyl in the thirst-quenching pills, with a good linearity within the range of 2.0-10.0 µg, and the average recovery of 101.1%, RSD= 1.7%. Jin Ying et al [9] spotted samples on silica gel GF254:0.5% CMC-Na (1:4) thin layer plate, chloroform-methanol-ethyl acetate-water (14:6:3:1) as the unfolding agent, the reference wavelength of 370 nm, the determination of the wavelength of 254 nm, determination of geraniol content in Songling haematoxylin capsule, the linearity was good within the range of 0.5-2.5 µg, with an average recovery of 97.93%, RSD=1.25%.

5. Pharmacological Activity

Pueraria lobata, as a traditional Chinese medicine, has various pharmacological effects, with puerarin as the main bioactive component. At the same time, the amino acids and starch in Pueraria Mirifica also have pharmacological activities. Modern pharmacological studies have shown that Pueraria lobata has a protective effect in vivo and in vitro on the cardiovascular system, nervous system, liver injury and inflammation [10].

5.1. Pharmacological effects on cardiovascular system

Puerarin has anti-atherosclerotic effects, with potential clinical applications in regulating blood lipids and reducing inflammation. He GX et al[11] further found that the combination regimen of puerarin combined with α -lipoic acid was remarkable in its efficacy, and was able to effectively improve the levels of blood lipids and oxidative stress indexes of the patients, while maintaining good safety, which has a high value for application. Zhang CM[12] et al. found that Puerarin down-regulated ox-LDL-induced Toll-like receptor 4 (TLR4)-NF- κ B signal transduction pathway in human monocyte cell line-derived THP-1 macrophages, and its anti-atherosclerotic effect was more direct and effective in targeting chronic inflammation itself.

5.2. Pharmacological effects on cerebrovascular system

Studies have shown that Puerarin has neuroprotective effects in a variety of brain disorders. Lubo et al. found that the combination of Puerarin and Naloxone showed enhanced efficacy in the treatment of traumatic cerebral infarction and reduction of intracranial haemorrhage. Puerarin injection was shown to enhance HSP70 expression, inhibit Fas expression, increase erythropoietin activity and Bcl-2 expression, thereby reducing apoptosis in a rat model of focal and global cerebral ischaemia-reperfusion injury [13]. Puerarin can reduce the neurological function damage, inhibit brain oedema, regulate the synaptic plasticity of brain tissues, and restore the curvature of synaptic interfaces in FCI rats, and its mechanism of action may be related to the activation of the SIRT1/HIF-1 α /VEGF signalling pathway [14].

5.3. Anti-osteoporosis effect

Puerarin can prevent osteoporosis and improve bone mass in experimental animals. Some studies suggest that Puerarin can increase alkaline phosphatase and osteocalcin activity, promote type I collagen secretion, up-regulate the expression levels of bone morphogenetic protein 2, Runt-related transcription factor 2, osteoblastin and osteoprotegerin, and promote matrix mineralisation, etc., as well as accelerating the proliferation, differentiation and maturation of osteoblasts [15]. Relevant studies suggest that puerarin may induce osteoblast proliferation and differentiation through NO/cGMP, MEK/ERK, PI3K/Akt, ER, p38MAPK, Wnt/ β -catenin signalling pathways, through NF- κ B/RANKL/TRAFF6/ROS/MAPK/NF- κ B and Akt/LPS signalling pathways inhibition of osteoclastogenesis as well as prevention of osteoclast activation by blocking the integrin β 3-Pyk2/Src/Cbl pathway [16].

6. Moulding process

One of the main components of the Chinese medicine Pueraria Mirifica is Puerarin, due to the poor water solubility of Puerarin and low oral bioavailability, its clinical effects will be limited as a result, so the formulation moulding process of Pueraria Mirifica is crucial for the quality, efficacy and application of the main component Puerarin [17].

6.1. Soup

Pueraria Mirifica Soup is the earliest dosage form of Pueraria Mirifica preparations, and as a standard soup for Chinese medicine tablets, it needs to be prepared according to Chinese medicine theory and clinical application. To ensure the safety of medication and consistent efficacy, the preparation process needs to be appropriately adjusted according to the characteristics of the herbs to optimise dissolution. Zhang Dandan [18], in the HPLC study of the effect of different decoction times of Pueraria Mirifica on the content of puerarin in Shengma Pueraria Mirifica Soup, found that the content of puerarin in Shengma Pueraria Mirifica Soup was relatively highest when Pueraria Mirifica was decocted for 35 min, and that Pueraria Mirifica was used in Shengma Pueraria Mirifica Soup by the special decoction method of 'first decoction', which might have the effect of improving the clinical efficacy.

6.2. Injectables

Puerarin is classified as an intravenous drug in the Biopharmaceutics Classification System due to its low solubility and low permeability, and is widely used in cardiac and cerebrovascular diseases, among others [19]. However, these injections have some side effects and need to be improved. Xu Qiu Zhe [20] selected the pH, activated carbon dosage, antioxidant and sterilisation conditions of

Pueraria Mirifica preparations by comparative method and found that the quality of Pueraria Mirifica injections prepared at pH 7.5, activated carbon and sodium sulphite dosage of 0.5 % each, circulating steam at 110°C, sterilisation for 30 min was stable and controllable.

6.3. Nano-formulations

Puerarin solid lipid nanoparticles are a new type of nano-delivery system, and making Puerarin into solid lipid nanoparticles can improve the bioavailability and prolong the time of circulation in the body, combining the advantages of other dosage forms [21]. Wang YH [22] et al. found that the nanocrystal self-stabilising Pickering emulsion (NSSPE) is a new type of emulsion, using only the nanocrystals of the insoluble drug crystals as stabilisers, NSSPE with Kawakawa oil as the main oil phase could significantly promote the oral absorption of geraniol.

7. Discussion

Pueraria lobata (kudzu), as a traditional Chinese medicine, contains multiple active components such as isoflavones, saponins, and coumarins. Its primary component, puerarin, has demonstrated notable pharmacological activity in the treatment of cardiovascular and neurological disorders as well as osteoporosis. Modern studies indicate that puerarin is effective in areas such as anti-atherosclerosis, liver protection, blood sugar regulation, antioxidation, and estrogen-like effects. However, traditional extraction methods face challenges in efficiency and stability, limiting clinical efficacy. This has led researchers to continually explore optimized extraction methods, such as enzyme-microwave-assisted and ultrasonic extraction, to enhance the purity and efficiency of active components. Additionally, to address the poor water solubility and low oral bioavailability of puerarin, new formulations like nano-preparations and microemulsions have been developed, significantly improving its circulation time and efficacy in vivo.

Future research can focus on the following areas: first, identifying and isolating new active compounds in kudzu through advanced extraction and separation techniques; second, further investigating its mechanisms of action, particularly for its potential in treating chronic diseases like cardiovascular disease and diabetes; and finally, verifying the efficacy and safety of kudzu in various diseases through clinical trials to broaden its range of clinical applications.

8. Conclusions

In conclusion, as a traditional Chinese medicine with multiple pharmacological effects, Pueraria lobata shows broad application potential in modern medicine. Its primary component, puerarin, has significant effects on cardiovascular regulation, neuroprotection, and osteoporosis prevention, with important clinical value in antioxidant, blood sugar-lowering, and estrogen-like actions. With advancements in extraction techniques and formulation processes, the active ingredients of kudzu can be extracted and applied more efficiently and stably; however, further research is needed to optimize extraction efficiency and improve bioavailability. In the future, research should focus on identifying new compounds in kudzu and elucidating their mechanisms of action. Through more in-depth clinical validation, kudzu's application in the prevention and treatment of chronic diseases can be solidly supported, advancing its integration into modern medical practice.

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