

Research Advances on Chemical Components and Pharmacological Activities of Barrenwort

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Abstract. Epimedium is a kind of traditional Chinese medicinal materials, which is regarded as, at present, the one of the most valuable medicinal plants in China. The chemical components of Barrenwort mainly contain flavonoids, phenol glycosides, chromones, phenylethanoid glycosides and steroids, which are verified that they have some effect on central nervous, skeletal system, immune system, reproductive system and cardiovascular system, and have distinct anti-tumor and antioxidant effect in modern pharmacology study. The following is an overview.

Introduction

In ancient China, traditional Chinese medicine has played a key role in the social development, the diagnosis and treatment of people's disease, and the health care, and is the treasure in the traditional culture. Modern medical research has proved that many components in the traditional Chinese medicine have some pharmacological effect, and there is huge development potential^[1]. Epimedium, also known as herba epimedii, is a kind of traditional Chinese medicine and perennial herb, and about 80% of the species are distributed in central China and southeast China^[2]. As early as the Han Dynasty, the relevant statements that "warm, spicy, sweet and fragrant" were made in "Shennong Bencao Jing", and the "Compendium of Materia Medica" of Li Shizhen stated that "Epimedium,, benefit pneuma, strong bones and muscles, nourishing loin and knees, and strong mental and physical". In modern pharmacology, Epimedium has been proved to have multiple effects on the adjustment of immune function and bone metabolism, prevention and treatment of Parkinsonism, anti-tumor and anti-aging, and has a high application value in osteoporosis, cardia-cerebrovascular disease and other diseases. Therefore, Epimedium has huge development value in the field of medicinal food and dietary therapy, which is considered to be, at present, the one of the most valuable medicinal plants in China^[3]. The approved and listed Chinese patent medicine with raw materials of Epimedium, including Kangguzengsheng tablets, Xianlinggubao capsules, Kidney pills, herba epimedii tablets, Yanlingchangchun capsules, Sealpills, Yangchun peroral liquid, Huolisu peroral liquid and herba epimedii beer, has the increasingly expanding market shares. This study is to make summary of research advances on chemical components and pharmacological activities of Barrenwort.

Chemical Components of Barrenwort

Epimedium, widely distributed in East Asia, has a large of species of plants, and is influenced by heat rain and other natural conditions, genetic diversity and other factors. There may exist bigger differences in the chemical components of different barrenwort^[4-5]. On the whole, North Korean Epimedium has better quality and the highest medicinal value in barrenwort. The research on the chemical components of barrenwort is made at home and abroad, and more than one hundred kinds of compounds have been separated, mainly including flavonoids, phenol glycosides, chromones, phenylethanoid glycosides and steroids. Where, the flavonoids compounds have relatively more proportion, and polysaccharide, alkaloid, lignans, terpenoid and other components take the second place, which is also rich in small amount of vitamin C and nutritional ingredient of microelement catheter^[6].

Flavonoids. The flavonoids compounds are the effective chemical components with the most proportion in barrenwort, accounting for around 5% or more. Specifically, the flavonoids compounds contain quercetin, alfalfa, baohuoside I, baohuoside B, baohuoside II, icariin, icarisid C, icarisid I, hyperin, korepimidoside A, epimedokoreanin A-D, ginkgetin, icariin A, epimedin A, epimedin B, and astragaloside. Moreover, Epimedium also has Breviflavone A, Breviflavone B and other minor compounds. The extraction of components is subject to species, natural conditions, processing methods, extraction methods, extraction parts and other factors[7]. The flavonoids compounds are 2- color phenyl ketone derivative compounds with the substituent groups of hydroxyl, methoxyl, carboxymethyl and isopentenyl, which is mainly combined with Glc and Rham in the plants.

Components of Volatile Oil. Currently, the volatile oils of the known epimedium mainly include alcohol, lauric acid, tetradecanoic acid, palmitic acid, linalool, alkyne, phytol, etc..

Lignans. Lignans mainly contain (7R, 8S), 9-dihydroxy-3, 3'-dimethyl oxygen residues-7, (7R, 8S, 8'R) 4, 4', 8', 9-tetrahydroxy-3, (+)-cycloolivil, Epimedium A1, Epimedium A2, etc.. In which, part of compounds have not yet been defined completely.

Steroids. Steroids mainly include daucosterol, maltol, β -sitosterol and so on.

Others. These cover henylethyl alcohol glycosides rhodiola glycosides, nonflavanoids with icariin A5, icariin F, epimedoicarisoside A, non-carbohydrates with icariin F, and other new alkaloids that have been reported by some scholars, but the structural analysis has not yet been made completely and the extraction efficiency is very low.

Research on Pharmacological Activities of Barrenwort

As early as the Han Dynasty, "Shennong Bencao Jing" had recorded that Epimedium has the efficacy of warming kidney and activating yang, and strengthening tendons and bones, and is praised as herba epimedii in the history of medicine. Moreover, in the modern pharmacology, Epimedium has been proved to have multiple effects on the adjustment of immune function and bone metabolism, prevention and treatment of Parkinsonism, anti-tumor and anti-aging. The research is an overview on this.

Influence on the System. (1) Influence on Immune System. In view of "Compendium of Materia Medica" and other records in the history of medicine, Epimedium has the efficacy of activating yang and has immune adjustment ability proved in the modern pharmacology. Meanwhile, the animal experiment has verified that the cellular immunity and humoral immunity of mice can be enhanced after fed with Epimedium, and the pathological research has proved that Epimedium can improve the phagocytosis of phagocyte to inhibit the spread of pathogene, and Epimedium can be applied to cyclophosphamide to enhance the inhibition function of antibody and reduce the cytotoxicity[9]. Moreover, Epimedium can enhance NK cell activity of aged rats and the aged LAK cell killing activity function[10]. The study made by Du Wenjing has shown that icariin can adjust the apoptotic gene glair Bcl-2, improve the apoptotic gene glair MBax, promote the apoptosis reduction in the intrapulmonary eosinophils and reduce EOS infiltration, and inferred that Epimedium can have comprehensive function in chemotactic migration and apoptosis of eosinophils, and a kind of hemameba of eosinophils is widely involved in immunity and general adaptation response[11].

(2) Influence on Skeletal System. The icariin obviously has the function of inhibition of osteoclast differentiation and promotion of bone formation, inhibits the absorption of osteoclastic bones and improve bone density and bone morphology. Chinese materia medica preparation with raw materials of Epimedium, including Kangguzhengsheng tablets, Xianlinggubao capsules all can treat the skeletal hyperostosis. In recent years, there are more and more study on pharmacology function of Epimedium in skeletal system. The result from Zhai Yuankun's study on the influence of icariin and its main metabolite --- icarisid II on the cultivation of the osteogenic differentiation of rat mesenchymal stem cells, has shown that the activity of promotion of osteogenic differentiation of icarisid II mesenchymal stem cells is better, the efficacy can be displayed through the oral medication, and the anti-osteoporosis effect is related with the metabolin components[12]. Mao

Xiangmiao has studied the bone differentiation of Epimedium glycoside supplemented on the promotion of mesenchymal stem cell C3H10T1/2 and analyzed the correlation of the differentiation function and the mitogen-activated protein kinase pathway, and the results have shown that the ossification promotion function of supplemented icariin is obvious, and may be related with activation of P38 and inhibition of EPK protein expression[13]. Liu Bo has made research of the influence of Epimedium on osteoporosis in ovariectomized rats, and the results, after compared with the model group, show that Epimedium can reduce the serum levels of related indicators, improve the serum P, SOD activity and the alkaline phosphatase activity, and enhance the estradiol concentration and the testosterone concentration. The pathological section has shown that the high dose of Epimedium can effectively prevent the trabecular bone exercise and reduce the serious disease risk. As we all know, estrogen has an important protective role, and Epimedium can enhance the gonadal hormone concentrations and eliminate the reactive oxygen, which may be the significant mechanism to prevent osteoporosis[14]. Yang Qianxu has tried to select the active ingredients of inhabitation action of Epimedium for the osteoclast growth, and investigated the influence of all kinds of Epimedium in different producing areas on the preosteoclast through MTT method. The results show that there are obvious differences, and the analysis of model group shows that baohuoside I activity is better[15]. Wang Jianzhong has tried to evaluate the influence of Epimedium on the glucocorticoid-induced avascular necrosis of bone tissue, and adopted muscle injection and intragastric administration methods to conduct the animal experiment, take the femoral head bone tissue to make pathological examination, and extract general RNA to test OPG and RANKL mRNA expression level. The results show that Epimedium group OPG and mRNA expression is lower and prompt that the prevention of hormonal caput femoris necrosis of Epimedium may have relationship with the antagonism cortical hormone[16]. In addition, the biological pharmacokinetics research has shown that secondary indicant and aglycone produced by metabolism after total flavonoids of herba epimedii, icariin, baohuoside I and icaritin absorbed by human body, are the important material basis of anti-osteoporosis of total flavonoids of Epimedium.

(3)Influence on Cardiovascular System. Epimedium glycosides substances have the cardioprotective effects, help to reduce the myocardial oxygen consumption, and ameliorate the myocardial ischemia. Epimedium flavonoids can interdict the adrenergic receptor, selectively block the myocardial β_1 receptor, reduce the myocardial contractility and control the heart rate[17]. Liu Tao has researched the influences of icariin and icarisid on the porcine aorta endothelial cell based on the epidermal growth factor receptor and the porcine aorta endothelial cell, and the results has shown that icariin and icarisid II can do up-regulation PAE and PAE-EGFR cells eNOS expression, enhance the endothelial nitric oxide synthase (NOS) activity, and improve the vascular endothelial function. The function may be related with the activated cell EGF-EGFR signal path[18].

(4)Influence on Reproductive System. Epimedium is a kind of drug with reinforcing kidney and activating yang, and has the enhancement effects of reproductive system function and reproductive endocrine function. The animal experiments have shown that the rat adenohipophysis function and the epididymis quality can be enhanced, and the gonadal hormone concentrations can be adjusted after total flavonoids of Epimedium is fed to the rats.

(5) Influence on Central Nervous System. Epimedium can also effect the central nervous system. Zhong Haibo has made the animal experiment and the study has shown that Epimedium extraction can improve the despair model tail suspension test, force the unceasing swim test, inhibit the activity of monoamine oxide A and monoamine oxide B of mouse brain tissue midbrain from the despair model tail suspension test, and prompt Epimedium has some anti-depression functions. Zhang Yaodong has studied the inhibition effect of icariin on the acetylcholine esterase based on the method of enzyme inhibition dynamics, and the results have shown that Epimedium has some inhibition effects on AChE activity, which has the function mainly through the hydrogen bonding, the intermolecular forces combined with AChE peripheral anion locus action.

Biological Function. (1)Anti-tumor Effect. Epimedium has obvious anti-tumor effect, mainly based on the inhibition of tumor cell reproduction and transfer, and the induction of cell apoptosis, and also can reduce the radiotherapy hazard. Wang Ting has made comparison of 6 kinds of

Epimedium anti-tumor effect, and the result shows that the substitute of flavone 8-bit isoamyl alkenyl is not the decisive factor of anti-tumor activity. Meanwhile, Wang Jie's research has shown that icariin and icaritin all can significantly promote the breast cancer T47D cell proliferation, which may be related with the mediation through the up-regulation of intracellular ER α , ER β protein expression.

(2)Anti-oxidation Effect. Epimedium has obvious anti-oxidation effect to alleviate redox damage. Bao Yu has made comparative study on the antioxidant activity in vitro of icariin and icarisid II, and the result has shown that both can strengthen the anti-oxidation effect, which is related with the functions in eliminating DPPH \cdot , O $_2^{\cdot-}$ and OH \cdot and inhibiting lipid peroxidation.

Summary

The research on chemical components and pharmacological activities of Barrenwort is deeply developing, and the fundamental research chain is basically formed, which covers the extraction and identification of drug activity ingredients, the atlas of medicinal materials and the quality evaluation, the pharmacokinetic study, the correlation research of the effective composition of herbs and the pharmacological effects, the mechanism research on the active ingredient effects of drugs, the clinical pharmacy research and other fields. They all have in-depth development and have achieved many beneficial results. The author believes that, with the increasing deepening on the research, the value of Epimedium medicinal materials will get the maximum development.

References

- [1] H.F. Zhang, X.H. Yang, Y.R. Guo, et al. Present Situation and Prospect of Medicinal Plants Epimedium Resources Sustainable Utilization . Journal of Plant, 2009, 44 (03): 363-370.
- [2] L.N. Guo, Y.H. Ma, W. Zhao, et al. Analysis and Research Advances on Chemical Components of Barrenwort. Chinese Journal of New Drugs, 2013, 22 (08): 919-922+936.
- [3] L.K. Pei, W.H. Huang, T.G. He, et al. Systematic Studies on Quality of Main Species of Herba Epimedii. China Journal of Chinese Materia Medica, 2007, 32 (21): 2217-2222.
- [4] H.L. Bao, L. Chen. Research on Myocardial Mitochondria Oxidative Stress Injury Effect of Anti-diabetic Rats by Icariin. Chinese Journal of Traditional Chinese Medicine, 2011, 36 (11): 1503-1507.
- [5] X. Yu, J. Song, Z.L. Xiong, et al. Simultaneous Assay of Epinedin A, Epimedin B, pimedine C and Icariin in Herba Epimedii by QAMS. Journal of Chinese Materia Medica, 2010, 35 (24): 3310-3313.
- [6] N. Meng, K. Kong, S.W. Li. Research Advances on Chemical Components and Pharmacological Activities of Barrenwort. Journal of Northwest Plants, 2010, 30 (05): 1063-1073.
- [7] F.X. Zhu, Y.G. Zhao, X.B. Jia, et al. Study on Fingerprint of Crude and Processed Epimedium by UPLC-PDA-MS. Acta Chimica Sinica, 2012, 70 (05): 635-642.
- [8] D.W. Zhang, Y. Cheng, J.C. Zhang, et al. Influence of Icariin on Osteoclast Differentiation and Bone Resorption Function. Chinese Pharmacological Bulletin, 2007, 23 (04): 463-467.
- [9] J. Jiang, L. Cui, E. Sun, et al. Material Basis for Anti-osteoporosis Efficacy of Epimedium Flavonoids based on their in Vivo Metabolism. Chinese Herbal Medicine, 2014, 45 (05): 721-729.
- [10] Y.K. Zhai, B.F. Ge, K.M. Chen, et al. Comparative Study on the Osteogenic Differentiation of Rat Bone Marrow Stromal Cells Effected by Icariin and Icariside II. Chinese Herbal Medicine , 2010, 33 (12): 1896-1900.

- [11] W.J. Du, J.C. Dong, C. Cai, et al. Influence of Icariin on Asthma MiceLungs Eosinophils Apoptosis and Bcl-2 and Bax Genes Protein Expression. Chinese Journal of Combining Traditional Chinese and Western Medicine, 2011, 31 (09): 1248-1253.
- [12] Y.K. Zhai, M.G. Wang, Z.Z. Li, et al. Effects of the Serum of Rats Administered Icariin on the Proliferation and Osteogenic Differentiation of rBMSCs in vitro. Journal of Chinese Medicine, 2012, 27 (07): 480-484.
- [13] X.Y. Mao, Q. Bian, Shen Ziyin. Analysis of the Osteogenetic Effects Exerted on Mesenchymal Stem Cell Strain C3H10T1/2 by Icariin via MAPK Signaling Pathway in vitro. Journal of Combining Traditional Chinese and Western Medicine, 2012, 10 (11): 1272-1278.
- [14] B. Liu, R. Zhang, P. Xu, et al. Influence of Epimedium on Osteoporosis in Ovariectomized Rats. Chinese Journal of Experimental Formulas of Chinese Medicine, 2013, 19 (07): 178-181.
- [15] Q.X. Yang, Y.Q. Liu, L. Wang, et al. Bioactive Components Screening in Epimedium for Osteoporosis Treatment by Model Population Analysis. Acta Pharmaceutica Sinica, 2012, 47 (09): 1205-1209.
- [16] J.Z. Wang, H.Y. Gao, K.Z. Wang, et al. Influence of Epimedium on the Glucocorticoid-induced Avascular Necrosis of Bone Tissue OPG/RANKL mRNA Expression. Journal of Southern Medical University, 2011, 31 (10): 1714-1717.
- [17] M. Zhi, J.Y. Cai, D.D. Jiao, et al. Effect of Total Flavonoids of Epimedium on Plasma Levels of TNF- α in Rats with Congestive Heart Failure. Journal of Anhui Traditional Chinese Medical College, 2010, 29 (4): 59-63.
- [18] T. Liu, X.C. Zhan, W.R. Li, et al. Effects of Icariin and Icariside II on eNOS Expression and NOS Activity in Porcine Aorta Endothelial Cells. Journal of Beijing University (Medical Edition), 2011, 43 (04): 500-504.