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Research and Application Prospect of Active Substances in Houttuynia Cordata

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Abstract: Houttuynia cordata Thunb. is a medicinal and edible herb. It can be used as a snack and also treat many diseases such as pneumonia, influenza, tumors, and so on. It contains volatile oil, flavonoids, alkaloids, polysaccharides, and other active ingredients. In this study, its active ingredients and clinical applications were introduced through comparative analysis and summary of extensive literature. Conclusion: Houttuynia cordata Thunb. has extremely high research potential due to its efficacy in treating various diseases with minimal side effects.

Keywords: Houttuynia Cordata Thunb; Active Ingredients; Extraction Process; Pharmacologic Action; Clinical Application; Toxicity.

1. Introduction

Houttuynia cordata Thunb. is the fresh whole grass or the dried ground part of the Houttuynia plant. In southwest China, such as Yunnan, Guizhou, Sichuan, Chongqing, Houttuynia cordata Thunb. It is commonly eaten in the local area and is widely known as a local flavor snack. It is not only edible, but also can be used in clinical medicine. According to the records in the Mingyi Bielu, Houttuynia cordata was originally named "Ji", also named Zheergen, Stinky grass, etc. It is medicated by the whole herb with roots, which has a pungent nature and a slight cold taste, and enters the lung meridian. It has the functions of clearing heat and detoxing, removing carbo and discharging pus, diuresis and clearing lymph.It is used to treat lung carbo and vomitting pus, phlegm and heat wheezing and coughing, hot lymph, hot dysentery, sore carbo and swelling poison, sore poison, throat milk moth, hemorrhoids and anal prolapse and other diseases.

Today, through the study found that it contains volatile oil (mainly decanoyl acetaldehyde) and flavonoids (quercetin, rutin, etc.), alkaloids (free) core, polysaccharide, organic acid and other active ingredients[1, 2] . These active ingredients play anti-inflammatory,antioxidant, enhance immunity, pharmacological effects. In this paper, the research progress of Houttuynia cordata was summarized from the aspects of chemical composition, extraction method, clinical application, toxic and side effects, and the extraction method was proposed to provide reference for the follow-up research of Houttuynia cordata.

2. Active Ingredients

2.1. Essential Oils

Decanoyl acetaldehyde ($C_{12}H_{22}O_2$), also known as houttuynin, is the major bioactive component of the volatile oil[3]. It exhibits antioxidant, antitumor, immunomodulatory, and antibacterial activities[4]. Methyl nonyl ketone (2-undecanone), a degradation product of decanoyl acetaldehyde, possesses antioxidant[5], anti-inflammatory, antiviral, immunomodulatory, antibacterial, and antitumor properties.

2.2. Flavonoids

Flavonoids are plant secondary metabolites and widely exist in natural plants in the form of free or glycosides combined with sugars. They are a class of polyphenolic compounds with a basic carbon skeleton of C6-C3-C6. They have a wide variety of pharmacological activities, such as anti-oxidation, anti-radiation, anti-tumor and immune-enhancing effects. Among them, they are mainly used in the prevention and treatment of cardiovascular and cerebrovascular diseases and upper respiratory tract diseases [6].

2.3. Alkaloid

According to the literature reports, there are 71 alkaloid compounds identified in Houttuynia cordata, mainly Apophylline-type alkaloids and aristolactams(ALs), which mainly play a physiological role[7] in anti-tumor, anti-virus and liver protection, anti-platelet aggregation.ALs is the primary reduced metabolite generated from AAs in the body, and some subtypes exhibit cytotoxicity, such as aristolactam FII and BIII. Aristolactam FII and aristolactam BIII are cytotoxic (with IC_{50} values of 11.1 and 9.4 $mmol \cdot L^{-1}$, respectively), but they are non-toxic at typical dietary intake levels.[2,28]

2.4. Polysaccharide

The constituents and contents of polysaccharides from Houttuynia cordata polysaccharides were obtained by Toyopearl column chromatography and GC-MS chromatography. The antibacterial effect and the minimum inhibitory concentration of polysaccharides were studied. The results showed that different polysaccharides had different inhibitory effects on different strains, among which HCP1 and HCP2 had stronger inhibitory effects on Staphylococcus aureus. HCP3 showed stronger inhibitory effects on Staphylococcus aureus and Escherichia coli than HCP1 and HCP2.[8]

2.5. Organic Acids

Houttuynia cordata contains organic acids such as chlorogenic acid, phenolic acid, linoleic acid, and 16 kinds of amino[1] acids such as aspartic acid, glutamine, serine,

histidine, etc. It has anti-inflammatory, anti-oxidation, anti-virus and other pharmacological[9] activities.Aristolochic acids(AAs), which has been classified by the World Health Organization as a Group 1 carcinogen due to its irreversible nephrotoxicity.ALs is often used as a biomarker of biological exposure to AAs. However, some researchers have failed to detect AAs I and II in Houttuynia cordata using LC-MS/MS methods.[2,28]

3. Extraction Method

The main component of volatile oil is decanoyl acetaldehyde. According to studies, decanoyl acetaldehyde is easily oxidized and decarboxylated at high temperature, and finally degrades to methyl nonyl ketone[3, 5] . Conventional steam distillation can extract the target substances at high temperature, which is easy to cause the denaturation of the heat-sensitive active components, while supercritical fluid extraction can be performed at low temperature. Therefore, compared with steam distillation, supercritical fluid extraction is easier to protect decanoyl acetaldehyde in Houttuynia cordata from transforming into methyl nonyl ketone, and this extraction method improves the extraction rate of essential oil and increases theutilization rate of raw materials. Zeng Hongyan used supercritical CO_2 extraction method to extract volatile oil, the extraction rate was about 1.76%, the extraction rate of steam distillation method was 0.04%, and the extraction rate of petroleum ether was 0.08%[5]. Zhang Chengcheng optimized the extraction efficiency, and obtained more volatile oil, the extraction rate was about 1.98%[10]. Flavonoids (quercetin, rutin), polysaccharide, organic acid such as polar solute, efficiency of ultrasonic-assisted enzymatic extraction is best[11]. The UAEE method is also carried out in a low temperature environment, which has the ability to protect the function of heat-sensitive substances from inactivation, and is used in combination with enzymatic method to destroy the cell wall of Houttuynia cordata, so that the active substances are more easily dissolved and the yield is improved.

4. Pharmacological Effect

4.1. Anti-inflammatory Effects

Houttuynia cordata extract at the mass concentration of 0.0625-0.125mg/ml could inhibit tumor necrosis factor-α (TNF-α) by about 30%. Houttuyniin injection could inhibit TNF-α and interleukin (IL) -1β and IL-8 in serum. A large number of inflammatory mediators such as cytokines, chemokines and adhesion molecules can be found in atherosclerotic plaques. One study showed that decanoyl acetaldehyde could significantly reduce the levels of TNF-α, IL-1β and IL-6 and increase the level of anti-inflammatory factor IL-10 in rats with atherosclerosis[12] .

4.2. Anti-radiation Effect

Li Zongsheng compared the anti-radiation function of Houttuynia cordata and Leucogen, and found that the comprehensive anti-radiation ability of total flavonoids of Houttuynia cordata was higher than that of Leucogen, which could replace some of the functions of Leucogen. [13]

4.3. Bacteriostatic Effect

Zhang Wei et al. conducted antibacterial effect experiment on different bacteria with volatile oil of Houttuynia cordata.The study shows that the volatile oil of fresh wild purple stem Houttuyniae Houttuyniae has a certain inhibitory effect on beta-hemolytic streptococcus, Staphylococcus aureus and other bacteria, and the maximum inhibitory effect on Staphylococcus aureus is 17.33mm [14].

4.4. Antioxidation Effect

Pearson's study found that polyphenols are the main antioxidant components in Houttuynia cordata. Mei Qianggen et al. found that water extract of Houttuynia cordata has a strong ability[15] to scavengers DPPH free radicals. Houttuynia cordata flavonoids (HCF) can reduce the oxidative stress injury of diabetic mice kidney by reducing the level of malondialdehyde (MDA), increasing the content of glutathione (GSH) and the activities of catalase (CAT) and other antioxidant enzymes. At the same time, HCF can effectively inhibit the expression of inflammatory factors in kidney tissue of diabetic mice. HCF can improve kidney injury and protect kidney function in mice. [16]

4.5. Enhance Immunity

Houttuynia cordata polysaccharides, flavonoids,decanoyl acetaldehyde in Houttuynia cordata have the effect[17] of enhancing the body's immune ability. Shao LAN et al. showed that houttuynia cordata could increase the spleen index of mice and enhance the immunity[18] .

4.6. Anti-virus

The infection capacity of influenza virus decreased 50 times under the direct action of houttuyniin, 800 times under the preventive action, and 25 times[19] under the decanoyl acetaldehyde. Houttuynia cordata could delay the pathological[20] changes of Beijing Ke-61 cells.

5. Clinical Application

5.1. Treatment of Acne

Zhang Naiwen studied the therapeutic effect of houttuynia cordata extract on acne, and the results showed that the Houttuynia cordata extract had a good therapeutic effect [21] on acne.

5.2. Treatment of Respiratory Diseases

Han Ming, the master of traditional Chinese medicine, used houttuynia cordata and other heat-clearing drugs to treat[22] pulmonary nodules. Houttuynia cordata preparation has a good therapeutic effect[23] on a variety of respiratory diseases.

5.3. Treatment of Tumors

One of the main drugs used by Guo Yong in the treatment of lung cancer is Houttuynia cordata. The alkaloids of Houttuynia cordata can inhibit the growth of H460 cells and induce their apoptosis[24]. Shi Haicheng old doctor of traditional Chinese medicine in the treatment of lung cancer early and mid reuse h. cordata with other medicine formula[25] .

6. Toxicity and Adverse Reactions

Li Jie sorted out the toxic substances of Houttuynia cordata and predicted the target information[26] of toxic active ingredients through network pharmacological analysis. Houttuynia cordata injection was often used in clinical practice, but its use was restricted by the state because of its complex composition and unclear allergic source. Main show

is: the skin redness, itching, fever, chills, chest tightness, heart palpitations, anaphylactic shock and other symptoms. Now the use of intramuscular injection, intravenous injection is prohibited. Some people eat fresh houttuynia will have nausea, vomiting and other symptoms. The toxic mechanism of houttuynia cordata is still unclear, which is related to the composition of houttuynia cordata, which is worth studying[27] .

7. Summary

As one of the commonly used medicinal and food homologous plants, Houttuynia cordata is not only used for food, but also can be more used in clinical application. It has great research and development potential. The active substances of houttuynia cordata play a good effect on the health care of the human body and the treatment of diseases. Within the scope of the use of safety, for there is little human liver and kidney damage. A good extraction process can better play the pharmacological effect of the drug itself. The current research did not combine supercritical fluid extraction with ultrasonic enzymatic method. According to the ultrasonic enzymatic method is suitable for the extraction of water-soluble substances and alcohol-soluble substances, the supercritical fluid extraction method is more effective for the extraction of heat-sensitive lipid-soluble substances. In the conception of this study, cellulase was used to destroy the fiber wall of Houttuyniae houttuyniae to promote the dissolution of intracellular active components, then supercritical fluid was used to extract the volatile oil with strong volatility, and finally ultrasonic enzymatic method was used to extract the remaining flavonoids (quercetin, rutin), organic acids, alkaloids and polysaccharides. Ultrasonic enzymatic method was combined with supercritical fluid extraction technology. Because under high-temperature conditions, decanoyl acetaldehyde can be changed into methyln-nonone. The combination of the two methods can not only improve the utilization rate of raw materials, improve economic efficiency, but also protect the core active substances in houttuynia cordata. In this paper, the active substances, extraction methods, pharmacological effects and clinical application of Houttuynia cordata were comprehensively described, aiming to provide theoretical basis for the development of traditional Chinese medicine preparations or products of Houttuynia cordata.

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