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Research Progress on chemical constituents of traditional Tibetan herb Lamiophlomis rotata

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Abstract. Traditional Tibetan herb Lamiophlomis rotata is a traditional medicine with a long history of application. By consulting the relevant research literature of Lamiophlomis rotata, this paper summarizes the research progress of its chemical composition from the aspects of chemical composition, extraction process and quality control, so as to provide reference for subsequent activity research and product development.

Keywords: Lamiophlomis rotata; Tibetan herb; chemical constituents;progress; shanzhiside methyl ester; 8-o-acetyl shanzhiside methyl ester.

1. Introduction

The English name of Duyiwei is Lamiophlomis herb, which is a staple medicine commonly used by Tibetans. It is the dry aboveground part of Lamiophlomis rotata.It is usually harvested, washed and dried in autumn. Its main function is to promote blood circulation, relieve pain, remove blood stasis and stop bleeding. Because of the reliable efficacy of L. rotata and its preparations, it is included in many editions of Chinese Pharmacopoeia. In the Pharmacopoeia, shanzhiside methyl ester and 8-o-acetylgeniposide methyl ester were used as reference materials, and HPLC was used as a means of quality control and evaluation.This paper reviews the research on the chemical constituents of Tibetan medicine Lamiophlomis rotata by consulting relevant literature and hopes to provide a basis for the in-depth research in the future [1].

2. Chemical Compositions

The research on the chemical components of Lamiophlomis rotate began in the 1980s. After many years of experimental research, flavonoids, iridoid glycosides, volatile oils and other components have been isolated from it. The researchers studied the components of the root and aboveground part of Lamiophlomis rotata. This study took the active components of its aboveground part as the object, excluding the underground part.

Liang Chongdong, Zhang Zhaolin et al. first studied the chemical components of Lamiophlomis rotata and obtained luteolin, luteolin-7-o-glucoside, quercetin, quercetin-3-o-arabinoside, apigenin-7-o-neochenpi glycoside, flax glycoside, geniposide methyl ester, 8-o-acetylgeniposide methyl ester and other components[2,3,4].Wang Ruidong et al. isolated luteolin-7-o from the n-butanol part of Lamiophlomis rotata for the first time-[β-D-furan celery sugar(1→6)]-β-D-glucopyranoside. Icariin H1 and three phenylethanol glycosides, forsythoside B, venbascoside and betonyosidesa a, were also obtained from the n-butanol extraction part of the aerial part of Lamiophlomis rotata [5].

Zhang Chengzhong et al. isolated four iridoid glycosides from Lamiophlomis rotata for the first time, namely 7-epiphlomiol (also known as phloyoside I, Chinese Name: Crab glycoside), 8-o-acetylgeniposide methyl ester, geniposide methyl ester and flax glycoside, which were reported that these are the first time to isolate from this genus [6-7].

Zhang Aijun et al. separated the chemical components of Lamiophlomis rotata by chromatography and identified 9 compounds from ethyl acetate, 6,7-dihydroxycoumarin, caffeic acid, 3,4-dihydroxybenzoic acid and apigenin-7-o-β-D-(-6″-p-coumarinyl)-glucoside and syringic acid were isolated from Lamiophlomis rotata for the first time [8].

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Sang Yuli et al. Separated the compounds by polyamide, silica gel and Sephadex LH-20 column chromatography, determined the structure of the compounds by using physical and chemical properties and spectral data, and separated 10 compounds from the ethanol percolated extract of Lamiophlomis rotata. Six flavonoids were separated from the alcohol elution site, which were luteolin (I), quercetin (II), isorhamnetin (III), apigenin-7-o-glucoside (IV), luteolin-7-o-glucoside (V) and icariin (VI); Four compounds were separated from the washed part, which were monolithin a (VII), monolithin B (VIII) β- Sitosterol (IX) and palmitic acid (x). Isorhamnetin and icariin were isolated from Lamiophlomis rotata for the first time [9].

Pan zheng et al. studied the chemical constituents from Lamiophlomis rotata and got ten compounds:decaffeoylacteoside(1),markhamioside A(2),gentioside(3), phloyoside I(4),6-O-acetylshanzhiside methyl ester(5),phlorigidoside C(6) ,7,8-dehydropenstemoside(7),n-hexadecanoic acid (8),β-daucosteol(9),caffeic acid(10)． It is reported that the first three compounds 1-3 were isolated from Lamiophlomis rotate for the first time [10].

Yin Xuefei separated Lamiophlomis rotata by silicagel chromatography, macroporous resin (D101) chromatography,MCI chromatography, semi preparative high performance liquid chromatography (HPLC) and recrystallization.Twenty-five compounds were determined, which were β-Sitosterol(1), verbascoside(2), shanzhiside methyl ester(3), chlorotuberoside(4), 8-epi-7-deoxyloganin (5), salidroside (6), apigenin-7-o-β-D-glucopyranoside (7), luteolin (8), 3,4-dihydroxybenzoic acid (9), caffeic acid(10),CIS 2,4,5-trihydroxycinnamic acid(11),3,4-dihydroxyphenylethanol(12), 2e-4-hydroxyhexenoic acid (13), gentian acid (14), 3β-hydroxy-5α,6α-epoxy-7-megastigmen-9-one(15),loliolide(16),isololiolide(17),luteolin-7-o-β-D-lucopyranoside (18),monosodium glutamate B(19),monosodium glutamateA(20), 7-dihydroxymaganic acid(21),hesperidine(22),monosodium glutamate D(23),monosodium glutamate E(24), monosodium glutamate F(25). Among them, compound 23,compound 24 and compound 25 are new compounds, and compound 6, compound 11-17 and compound 22 are isolated for the first time [11].

3. Extraction Process

Gao Fei et al. Optimized the extraction process of polysaccharide from Lamiophlomis Rotate by response surface methodology.In this study, the crude polysaccharide of Lamiophlomis rotate was extracted by enzymatic hydrolysis. Taking the extraction temperature, extraction time and pH as the influencing factors and the polysaccharide extraction rate as the investigation index, the best influencing factors of polysaccharide extraction rate were selected through single factor investigation. Using response surface design, the optimum extraction process was as follows: extraction temperature 60 ℃, extraction time 60 min, pH 6, and the amount of compound enzyme was 2.0% [12].

Cheng Li-hui took the total flavonoids extraction rate of Lamiophlomis rotata as the investigation index. Firstly, the total flavonoids extraction rates of reflux method, decoction method and ultrasonic method were compared, and then the effects of crushing degree, ethanol concentration, solid-liquid ratio, extraction times and extraction duration on the total flavonoids extraction rate were investigated by single factor. According to the results of single factor experiment, the orthogonal experiment was designed to optimize the best extraction process of Flavonoids from L. rotate by L9(34).The optimum extraction process of total flavonoids in Duyiwei was determined as follows: solid-liquid ratio of 1： 50, ethanol concentration of 80%, reflux extraction for 3 times and reflux extraction time of 25 min [13].

QIU Jian-guo et al. optimized the extraction process of Lamiophlomis rotata. The optimum extraction process was selected by orthogonal test with the yield of total iridoid glycoside,total flavonoids and dry extract as index using the amount of water,extraction times and extraction time as factor. The optimum technology was as follows：adding 26-folds of wate（4-folds of water at the

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first time），extracting for 3 times,1.5h per time,removing impurity at 2-4℃,reducing pressure and drying at 80℃； under the condition, the concentration of total flavonoids was 37.89 μg/ml ,the concentration of total iridoid glycoside was 45.35 μg/ml,and the yield of dry extract was 39.29 %. This optimum technology is stable and reliable,contributes to improve water extraction technology of L. rotate and the quality of related prepated.Qiu Jianguo's research group has carried out the research on the industrial extraction, separation and purification process of different extracts of Lamiophlomis Rotata and the industrial extraction, separation and purification of Total Iridoid Glycosides of Lamiophlomis Rotata, and successfully transformed the experimental results into industrial production [14-16].

TANG Kun et al. optimized processing technology of Lamiophlomis rotate frying with vinegar. With the content of total flavonoids as index,processing method was selected by single factor test,orthogonal test was adopted to optimize processing technology with moistening time,frying temperature,frying time and the amount of vinegar as factors. Stir-baking with vinegar was adopted,the best processing technology was as following: moistened 5 min with 30% vinegar,adjusted temperature to 200 ℃,processing time 15 min [17].

HAO Yan-jun et al. studied the extraction and purification process of the analgesic and hemostatic active part of Lamiophlomis rotata. Determination of the total iridoid glycosides and 8-epideoxyloganic acid were performed by dimethylaminobenzaldehyde method and HPLC respectively.By Using single factor and orthogonal experiments,the best extraction and purification process with macroporous resin was optimized. The best extraction was established as follows: solvent of 60% ethanol,soaking 36 hours,elution volume was 10 times of materials,percolation rate of 5mL·min-1 kg-1. The purification process was as follows: the ethanolic extract should be separated by polyamide.The water elution was separated with XDA-7 macroporous resin and collecting the 30% ethanolic extract [18].

WU Liang et al. et al. investigated the diverse solvent effect on extraction of chemical components from Lamiophlomis rotate.Based on LC-MS/MS technique,and chromatographic peak comparison,potential chemical components screening and partial least squares-discriminant analysis(PLS-DA) were used to establish a quantitation method for simultaneous determination of chlorogenic acid, forsythoside B, verbascoside, luteoloside, quercetin, luteolin and apigenin. According to the results of PLS-DA and quantitative analysis, methanol, water-saturated n-butanol, 75% methanol and 50% methanol showed wider extraction range and higher extraction efficiency to the chemical components of Lamiophlomis rotata. This study offeres references to the extraction technology of Lamiophlomis rotata,and promotes the relative pharmacodynamics study of this medical material [19].

4. Content Determination and Quality Control

The content of luteolin was determined by HPLC. In the previous Chinese Pharmacopoeia, rutin was usually used as the reference substance for content determination. In the subsequent Chinese Pharmacopoeia, HPLC was used to determine the total amount of shanzhiside methyl ester and 8-o-acetylgeniposide methyl ester.

XIE Jun-bo et al. establish a rapid resolution liquid chromatography tandem mass spectrometry (LC-MS /MS) method for determination of luteolin in Herba Lamiophlomis. The method was simple,rapid and accurate and could be used for the determination of luteolin in Herba Lamiophlomis [20].

A capillary electrophoresis (CE) method with large volume sample stacking (LVSS) was developed for simultaneous analysis of four flavonoids luteolin-7-O-glucoside,apigenin,luteolin and quercetin by LUO Mi-na. The detection sensitivity was improved about 300-800 fold. The method was applied to determine four flavonoids in Lamiophlomis rotata successfully . The results demonstrated that it was an easy-to-use method for the analysis of minor flavonoids [21].

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HU Hui-ping et al develop an HPLC method to determine Sesamoside and Phlorigidoside C in Herb Lamiophlomis rotata. The content of C, and the determination of two iridoid components in the aboveground part of Lamiophlomis rotata from 10 batches of different producing areas, comprehensively reflects the quality of iridoid components, and provides a certain reference for establishing the quality control method of iridoid components in Lamiophlomis rotata. The method was rapid and precise, and can be used for controlling the quality of Herb Lamiophlomis rotate [22].

He Yingxia et al. established an HPLC method for the simultaneous determination of forsythoside B, acteoside, luteoloside and Luteolin in L. rotate. The method is accurate, reliable and reproducible [23].

Most of the reports on the quality control of L. rotata are about the determination of 1 or 2 components by HPLC. Zhong Shi-hong et al. established a multi index content determination method of Duyiwei by HPLC, and determined the contents of 7 components, including 2 iridoid glycosides, 2 phenylethanol glycosides, 2 flavonoids and 1 caffeioyl. The seven compounds were well separated with good linear correlations. The mean recoveries of seven compounds were 96.47%-102.2%(RSD 0.70%-2.2%).The established method can comprehensively evaluate the quality of this traditional Chinese herbal medicine, It provides a scientific basis for further improving the quality control standard of Duyiwei and promoting the comprehensive utilization of Duyiwei [24].

In order to shorten the separation time and improve the separation efficiency, Gou Yan-mei et al. used UPLC(ultra performance liquid chromatography) to simultaneously determine eight components: geniposide methyl ester, 8-o-acetylgeniposide methyl ester, flax glycoside, caffeic acid, forsythiaside B, chlorogenic acid, luteolin and ergosterol glycoside, including three iridoid glycosides, two phenylethanol glycosides, one flavone and two caffeioyl glycosides. This method has good specificity and high precision. The effects of different producing areas, different grassland degradation grades and storage time on the content of Lamiophlomis rotata. were also preliminarily analyzed. The results showed that the origin was the main factor affecting the content of the components of Lamiophlomis rotata. At the same time, the results showed that the total content of eight components was the highest in Aba County, Sichuan Province, and the lowest in Maqu County, Gansu Province; The storage time had the greatest effect on the content of flax glycosides, and the content decreased by 23% after one year. The content of other components changed slightly, but had little effect [25].

Jin Guilin et al. Used ultra-high performance confluence chromatography to determine the active components in Lamiophlomis rotate. On the waters acquity UPC column, carbon dioxide and methanol solvent were eluted at a flow rate gradient of 0.7ml/min, and the effective components of Lamiophlomis rotate were successfully separated. The effectiveness of the method was verified by analyzing the precision, repeatability, stability and accuracy of the method. From the perspective of compound separation, supercritical CO2 not only has the diffusion characteristics of gas, but also has the density and fluidity of liquid. Ultra high performance liquid chromatography 3D full wavelength scanning can better determine the content of various chemical components. It is a new drug analysis technology [26].

5. Conclusions

The traditional drugs of ethnic minorities have been paid attention to and the research has been deepened. Tibetan medicine Lamiophlomis rotata is one of them. Lamiophlomis rotata, previously published in the famous Tibetan medical works "four medical classics" and "Yuewang medicine diagnosis", is one of the commonly used herbal medicines of many nationalities such as Tibet and Mongolia [27].It is widely distributed in Qinghai, Tibet, Sichuan and other places in China, and has rich medicinal resources. Clinical application and experimental research show that Lamiophlomis rotata has many effects, such as promoting blood circulation, anti-inflammatory, anti-tumor, improving immunity (modification and evidence, inserting several review articles), and has the

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value of in-depth research and development. At present, the active components of Lamiophlomis rotata have not been fully explored, and the specific components and action mechanism of some functions have not been fully studied. Further in-depth research is needed. In recent years, more and more technologies such as liquid chromatography-mass spectrometry and ultra-high performance confluence chromatography have been used in the quality control of Angelica components. The continuous development of new technologies provides a development direction for future research.

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