

A Study on the Progress of Astragalus-Coptis Chinensis Medicinal Pair in the Treatment of Diabetes Mellitus

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Abstract: *According to the relevant studies in recent years, it was found that astragalus - Coptis Chinensis drug pair and its analogous formula have a broad prospect for the treatment of type 2 diabetes mellitus (T2DM). Pharmacological studies have shown that Coptis Chinensis possesses the pharmacological activities of antimicrobial, anti-inflammatory, anti-tumor, lipid regulating, hypoglycemic, anti-arrhythmic, and antioxidant activities[1], and Astragalus possesses the effects of enhancing the function of the immune system, antimyocardial ischemia, bi-directional regulation of blood pressure, anti-tumor, anti-aging, hypoglycemia, and protection of metabolic tissues (liver and kidneys, etc.) [2] [3], the use of Astragalus and Coptis Chinensis pairs has demonstrated significant multiple effects. Specifically, this combination not only effectively reduces blood glucose levels, but also significantly enhances the body's sensitivity to insulin, thus helping to improve the phenomenon of insulin resistance and further enhance the overall health status of patients [1][2][3]. This paper analyzes and researches the research progress of astragalus-Coptis Chinensis medicinal pair and its analogous formulae in the treatment of type 2 diabetes mellitus and the improvement of its complications through the collation and summarization of the literature, in order to lay a certain theoretical research foundation for the clinical diagnosis and treatment of type 2 diabetes mellitus by astragalus-Coptis Chinensis medicinal pair and its related formulae, prevention of diabetes mellitus complications, and rational use of medicines in diabetes mellitus clinical treatment.*

Keywords: Astragalus-Coptis Chinensis and its analogous formulas; Diabetes mellitus; Diabetic complications; Research progress.

1. Introduction

Diabetes mellitus, as a metabolic disease characterized by chronic hyperglycemia [4], its prevalence has increased with the improvement of the standard of living, and adults suffering from impaired glucose tolerance (IGT) are also showing a rising trend. Currently known diabetes complications are more varied, under the influence of long-term hyperglycemia can be involved in macrovascular and microvascular lesions, damage to multiple organs and systems of the human body, seriously reducing the quality of life of patients. Combining Chinese and Western medicine to prevent and treat diabetes and its complications is a new trend in modern times to improve the quality of life of diabetic patients.

The pathological basis of type 2 diabetes mellitus (T2DM) is insulin resistance (IR) and decreased insulin-producing ability of pancreatic islet β cells. T2DM belongs to the category of "consumptive thirst" in Chinese medicine theory, which is a chronic disease that is bound to be weak. Long term illness leads to deficiency, and prolonged consumptive thirst will inevitably damage the spleen and stomach, causing weakness and abnormal circulation, resulting in this disease. And with the changes in modern people's dietary structure and lifestyle habits, they tend to indulge in fatty, sweet, and thick flavors, eat more and exercise less, which can easily lead to disharmony between the spleen and stomach in the middle burner, inability to transport food and water, internal obstruction of phlegm and dampness, and prolonged stagnation of heat. The core pathology is Yin deficiency as the root cause and dry heat as the symptom, with heat as the main characteristic manifestation in most cases [6]. As early as in the "Huangdi's classic on medical" there is a record of

consumptive thirst due to heat, Wang Bing note said, this disease in the spleen, splenosis heat, then this is the "Dan spleen", the addiction to fat, sweet and thick food and easy to generate internal heat, people in the fullness of the fullness of the day, the spleen and stomach is difficult to transport, the earth and wood suppression, long time depression and heat [7]. And Professor Wei Junping and others believe that "dampness and heat theory" is more in line with the etiology of diabetes mellitus, pathogenesis characteristics, newly diagnosed T2DM patients with dampness and heat mostly [8]. And "Suwen - assessment of heat disease On the" cloud: "where the evil is, its qi must be deficient", the onset of consumptive thirst is also related to the evil ambush, and some studies have shown that qi deficiency diabetes patients accounted for a relatively high proportion of the nine Chinese medicine physique [9]. Combining the above viewpoints with the characteristics of "the three types of diabetes", the treatment of consumptive thirst is to clear heat and moisten dryness, nourish yin and promote the production of fluids; at the same time, taking into account the identification of the lungs, stomach (spleen), kidneys and other internal organs of the treatment, and reasonably applying medicines to activate blood circulation and eliminate blood stasis, clearing heat and removing toxins, nourishing yin and warming yang, and benefiting the qi and strengthening the spleen. The combination of Astragalus and Coptis Chinensis can strengthen the spleen, benefit the qi and clear heat, and studies have shown that the pair of Astragalus and Coptis Chinensis can regulate blood glucose and lipids, and play a positive role in the state of disorders of glucose and lipid metabolism [10].

2. Astragalus

Astragalus, formerly known as Huangqi, is the long of tonic

medicine, classified as the top grade, is one of the ten famous Long medicine, belongs to the dual-use of the bulk of the Chinese herbal medicine [11], from ancient times to the present day is widely used, the "Jingui Yaolue" in the seven parties containing astragalus [12], and at the same time, in the treatment of a variety of diseases in modern traditional Chinese medicine is also applied to the great number of applications. The 2020 edition of Chinese Pharmacopoeia records that the effects of Astragalus are to replenish qi and promote yang, consolidate the surface and stop sweating, promote diuresis and reduce swelling, generate fluid and nourish blood, promote stagnation and paralysis, support the toxin and expel pus, and converge the sores and promote the growth of muscle [13].

2.1 Active Components of Astragalus and Pharmacological Effects of Its Active Components

In recent years, studies have shown that Astragalus has a variety of chemical components, of which polysaccharides, flavonoids, and saponins are its main chemically active components [14]. According to a large number of literature searches show that the main pharmacological effects of Astragalus are extensive, mainly focusing on the regulation of body immunity, antioxidant, anti-tumor, cardiovascular protection, promotion of body metabolism, hypoglycemia, diuretic and swelling [15].

2.2 Research on the Treatment of Diabetes Mellitus with Astragalus

Astragalus, as the most qi tonic, has been widely used in the prevention and treatment of diabetes mellitus and its related complications, and has significant therapeutic effects. In modern clinical and pharmacological experiments, the main active ingredients in Astragalus have been proved to be able to prevent and control the clinical symptoms of diabetes mellitus and improve the complications of diabetes mellitus, and its active ingredients can stimulate the pancreas to secrete insulin in order to achieve the purpose of lowering blood glucose [16]. Song Jia further confirmed through clinical observation that astragalus has a positive effect on promoting insulin secretion hormone and insulin resistance in patients [17]. Astragalus polysaccharide can promote 3T3-L1 preadipocyte lipocalin expression and regulate GLUT4 protein expression by activating the AMPK pathway, up-regulating hepatic adenylate-activated kinase α , phosphorylated adenylate-activated enzyme α , and promoting glucose uptake, enhancing insulin sensitivity, as well as alleviating the insulin resistance state [18] [19]. Wu Dong et al. explored the effect of astragalus polysaccharide on kidney injury in diabetic rats, and the results showed that the serum inflammatory factor content of diabetic nephropathic rats was reduced, glomerular cell apoptosis was reduced, and kidney function was restored in rats, and kidney tissue injury caused by STZ was improved, and this effect was related to the inhibition of the PI3K/AKT signaling pathway [20]. Some studies have shown that astragalus polysaccharide can also improve glomerulosclerosis caused by diabetic complications [21]. Astragaloside can reduce the quantitative level of 24h urinary protein and improve renal damage in rats with diabetic nephropathy, and it further attenuates endoplasmic reticulum stress by modulating the IRE-1 α signaling pathway, thereby

ameliorating foot cell damage in diabetes [22]. In addition astragaloside may also protect renal function by affecting the eNOS/NO pathway [23]. Hu Yaling concluded that astragaloside regulates autophagy by affecting the SIRT1/NF- κ B signaling pathway, which ultimately affects renal interstitial fibrosis through anti-inflammatory effects [24]. Astragalus flavonoids can play a role in preventing and controlling diabetes by increasing ADPN (lipocalin) activity, effectively improving body weight as well as blood glucose in diabetic mice, and also have a role in preventing apoptosis of pancreatic islet cells, which has a benign effect on lowering the blood glucose of diabetic patients [25][36]. In addition, some studies have shown that astragalus flavonoids in diabetic rat models can inhibit oxidative stress in the dorsal root ganglion tissue of diabetic rats, reduce the occurrence of apoptosis, and reduce the level of p38, p-p38 protein expression, which has a significant effect on the peripheral nerve damage induced by diabetes mellitus [27][28].

3. Coptis Chinensis

Coptis chinensis, buttercup perennial herb. According to Danxi, there is an excess of gas that is fire, which is divided into several categories. Also described in the "Justice of the Materia Medica": *Coptis chinensis* belongs to the big bitter cold, big cold overheat, big bitter and dry, the fire of the five viscera and six bowels can be cured at the same time. The 2020 edition of the Chinese Pharmacopoeia [13] recorded that *Coptis chinensis* belongs to the heart, spleen, stomach, liver, gallbladder and large intestine meridians, and has the efficacy of clearing away heat and drying dampness, and removing fire and detoxifying toxins.

3.1 Active Components of Coptis Chinensis and Pharmacological Effects of Its Active Components

Coptis chinensis contains lignans, phenolic acids, volatile oils, a variety of alkaloids, polysaccharides, flavonoids, and steroids [29]. Modern pharmacological studies have found that the main pharmacological effects of *Coptis chinensis* and its active ingredients include anti-inflammatory effects, inhibition of *Helicobacter pylori* positivity, antidiarrheal, hypoglycemic, relief of myocardial ischemia, hypolipidemic, and inhibition of cancer cell proliferation. Alkaloids are *Coptis chinensis* and its important active ingredients, including berberine (C₂₀H₁₇NO₄), epiberberine-containing berberine (C₂₀H₁₉NO₄), flavonoids (C₁₉H₁₃NO₄), and barmatine (C₂₁H₁₅NO₄), etc. [30]. *Coptis chinensis* has a wide variety of active ingredients and a wide range of effects, which makes it a typical bulk herb.

3.2 Studies on the Treatment of Diabetes Mellitus by Rhizoma Coptidis

Studies have shown that *Coptis chinensis* and its concomitants can be used through multiple pathways and links in order to achieve the effects of lowering blood glucose, lowering blood lipids, and improving the symptoms associated with diabetic patients [31]. Meanwhile, the clinical use of hypoglycemic drugs (e.g., biguanides, sulfonamides) in combination with *Coptis chinensis* will significantly improve its clinical efficacy and alleviate the side effects caused by the drugs [36]. *Coptis chinensis* also has therapeutic effects on diabetic

peripheral neuropathy while lowering glucose and lipids [32]. Studies have demonstrated that the alkaloids of *Coptis chinensis* can exert their antioxidant effects by increasing the SOD activity and decreasing the mALB and MDA content as well as the AR activity [33]. Berberine can regulate the p38MAPK signaling pathway and effectively improve insulin resistance [34]; Li et al. [35] showed that berberine can promote the phosphorylation of adenylate-activated protein kinase (AMPK) and regulate the expression of LDL receptor to regulate the homeostasis of plasma cholesterol, which is important for diabetic hyperlipidemia and diabetic obesity [36]. Berberine has significant efficacy in diabetic nephropathy, which can inhibit podocyte apoptosis through inhibiting the JAK2/STAT3 signaling pathway, as well as inhibit the activation of renal myofibroblasts to improve renal tubulointerstitial fibrosis [37] [38]; the anti-inflammatory effect of berberine [39] can improve glomerular sclerosis in diabetic nephropathy by inhibiting the activity of inflammatory mediators in the body and decreasing the expression of inflammatory factors in the kidney sclerosis, which has a non-negligible important value for the prevention and treatment of diabetic kidney disease. Coptisine can reduce the level of serum TNF- α in rats, so it can be used to improve the inflammatory response in diabetic kidney disease [40].

4. Astragalus-Coptis Chinensis Type Formula

Studies have shown [41] that the *Astragalus* -*Coptis chinensis* pair is widely used clinically in the treatment of diabetes mellitus and its complications. *Astragalus* and *Coptis* have been widely used in the treatment of type 2 diabetes and its complications, respectively, and many modern practitioners have used the *Astragalus*-*Coptis chinensis* pair in the treatment of type 2 diabetes with high frequency, including the classic formula *Angelica Liuhuang* Decoction.

4.1 *Angelica Liuhuang* Decoction

Angelica Liuhuang Decoction, studies have shown that *Angelica Liuhuang* Decoction flavored with western medicine and hypoglycemic drugs together with the treatment of diabetic lower limb vascular lesions (qi and yin deficiency, stasis and heat mutual conjugation certificate) has a better therapeutic effect, can significantly improve the symptoms of diabetes mellitus patients, and at the same time can be used for the treatment of diabetic nephropathy, which can improve the renal function [42][43]. *Angelica Liuhuang* Decoction for the treatment of diabetes mellitus with yin deficiency and dryness heat type, its prescription is characterized by nourishing blood and yin and diarrhea and fire, while taking into account the benefit of qi and solidifying the surface, the main adjustment of diabetic patients with yin deficiency and internal heat of the body, this formula treatment with the body, the symptoms and the root cause of the disease. *Angelica Liuhuang* Decoction [44] can significantly alleviate the sweating symptoms of diabetic patients with yin deficiency and internal heat syndrome, such as palms and feet and profuse sweating after activities. The formula also has good efficacy in treating peripheral neuropathy such as itchy skin in diabetic patients, and it can reduce blood glucose and glycosylated hemoglobin levels and blood lipid levels of patients while treating itchy skin [45].

4.2 *Huanglian WenDan* Decoction Combined with *Shuilu Erxian* Decoction Plus and Minus

Huanglian WenDan decoction combined with *Shuilu Erxian* decoction plus and minus is the empirical formula used by Prof. Ma Juli in the treatment of diabetic nephropathy with spleen and kidney deficiency and damp-heat obstruction, the following is a typical medical case.

Li, male, 65 years old. First visit to the clinic. Dry mouth and thirst for 20 years, accompanied by foamy urine for 3 years. Dry mouth and thirst without obvious triggers, so he went to the hospital, diagnosed as "type 2 diabetes mellitus", 3 years ago, conscious of the increase in urine foam, in the local hospital to check the urine routine and urine nephropathy series results show that the increase in urinary protein, the patient complained of a dry mouth, thirst, fatigue, morning puffiness of the eyelids bilaterally, urinary foamy, Frequent urination, increased nocturia (more 4-5 times/day), dry stools, red tongue with yellow greasy coating, fine pulse; plain fasting blood glucose 8-9 mmol/L, postprandial blood glucose 10-12 mmol/L, poor glycemic control; blood pressure 175/95 mmHg; glycosylated hemoglobin 6.5%; urine routine results: urine glucose (+), urine protein (++) , and urine protein (++) . Urine protein (++) , urine ketone body (-), occult blood (+); 24 h urine protein quantitative 4.984 g/24 h. Western medicine diagnosis: type 2 diabetes mellitus diabetic nephropathy (IVstage); traditional Chinese medicine diagnosis: thirst, spleen and kidney deficiencies, dampness-heat obstruction. Treatment: clearing heat and dampness, strengthening the spleen and kidneys, the formula selected *Huanglian WenDan* decoction combined with *Shuilu Erxian* decoction plus reduction: *Coptis chinensis* 6g, Bamboo Shavings 10g, *FaBanxia* 10g, *Chenpi* 10g, *Zhishi* 15g, *Poria* 15g, *Cicada Flower* 8g, *Astragali* 20g, American ginseng 10g, raw rhubarb 15g, *Rosa Laevigata Michx* 15g, *Gorgon fruit* 15g, licorice 6g, *Cangzhu* 12g, *Plantago Ovatae* 15g. 10 dosage, 1 dose per day, divided into 2 times, boiled water to serve. 10 doses, 1 dose per day, divided into 2 times, water decoction, the patient was advised to continue oral hypoglycemic, antihypertensive drugs, diabetic diet, regular testing and recording of blood glucose, blood pressure.

Second diagnosis: dry mouth, thirst has improved, urine foam reduced, eyelids without swelling, stool without obvious abnormalities, thin yellow tongue, urine routine: urinary protein (+), urinary ketone bodies (-), urinary occult blood (+); 24h urinary protein quantitative 3.5g/24h. Above to go to the *Poria*, add 10g of *Qiancao Charcoal*.

Third diagnosis: dry mouth, thirst improved, foamy urine basically disappeared, thin white tongue coating, pulse fine string. Urine routine examination was not obvious abnormality; 24h urine protein quantitative 2.57g/24h. Adjusted to oral Bering capsule taking, regular review.

5. Conclusion

Astragalus -- *Coptis Chinensis* medicine on the intervention of type 2 diabetes mellitus presented as a multi-target effect, the two together can significantly improve the clinical evidence of diabetes mellitus patients, the treatment of diabetes mellitus in the clinic should be from a variety of aspects of the intervention, will be strictly diabetes mellitus

diet, appropriate physical exercise, pay attention to the combination of Chinese and Western medicine treatment methods, to give full play to the unique advantages of the Chinese medicine, more comprehensive and effective treatment of diabetes mellitus, to lay the foundation for the modernization and development of Chinese medicine to provide a scientific basis for its effectiveness. The modernization of Chinese medicine lays the foundation for the development of diabetes and provides a scientific basis for its efficacy.

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