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Therapeutic and Preventive Effects of Astragalus on Diabetes and Its Complications

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Abstract. Diabetes mellitus is a chronic illness that is one of the complications that have a severe effect on the quality of life of patients, as well as a lack of curative medications. Astragalus, a traditional qi-tonifying herb found in Chinese medicine has exhibited special merits in diabetes and the complications associated with diabetes. This paper is a systematic review of chemical compounds of Astragalus and how it works to suppress diabetic complications. The key bioactive agents of Astragalus are Astragalus polysaccharides, Astragalus saponins, and Astragalus flavonoids, which have therapeutic effects driven by the following four mechanisms:(1) regulating the homeostasis of blood glucose: enhancing insulin sensitivity and optimality of gut microbiota structure; (2) antiinflammatory effects: blocking the NF- 0 signaling pathway, inhibiting the expression of pro-inflammatory factors of TNF- 0 and IL-6, and reducing The clinical data demonstrated that repeated use of the formulations of the Astragalus compound, including Huangqi Gegen Tang (Astragalus and Kudzu Decoction), can increase the therapeutic effect under the conventional treatment considerably. Nevertheless, most available literature relies on animal models, which do not contain a high-quality level of clinical evidence, and other aspects, e.g., the quality of Astragalus and individual treatment plans, are still to be enhanced. The next step should be to prove its effectiveness in terms of multicenter clinical trials, put in place quality control measures, and enhance the modernization and clinical use of Astragalus in the prevention and treatment of complications in diabetes, thus offering new information on the integrated traditional Chinese and Western medicine practice.

Keywords: astragalus, diabetes, astragalus polysaccharides, astragalus saponins, astragalus flavonoids

1. Introduction

Diabetes mellitus is a chronic disease that is associated with hyperglycemia caused by absolute or relative insulin deficiency and impaired insulin use, posing a serious health burden in the world. It is estimated that there are about 537 million cases of adult-based diabetes worldwide [1]. The multiple chronic complications that hyperglycemia causes make it its main clinical challenge, such as diabetic nephropathy, lower extremity vascular disease, foot ulcers, and cardiomyopathy. These complications cause such terrible consequences as amputation, heart attack, and serious psychological stress that predetermines the necessity of the development of effective approaches

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towards the postponement of the disease process and maintenance of the functioning of the organ. As much as the oral hypoglycemic agents provide quick treatment response, the side effects of this treatment as liver and kidney damage, hypoglycemia, and gastrointestinal discomforts as well as their inability to respond individually to treatment regimens limit its use which is often seen as the inability to respond to the treatment needs on an individual basis. Thus, the issue of new and also complementary interventions is especially vital to investigate in modern diabetes treatment.

As research continues to be done, the gap in the current method of Western medicine is becoming clear, the practice of the traditional Chinese has become a more promising trend in intervention. Traditional Chinese medicine considers diabetes to be an Xiao Ke (wasting-thirst syndrome) the pathogenesis of which is mainly explained by the deficiency of Yin and the dry heat. Astragalus (Huang Qi) also has the benefits of tonifying Qi and warming Yang, solidifying the exterior to prevent sweating, stimulating the generation of fluids and nourishment of blood, moving stagnation and unblocking obstructions, expelling toxins and draining pus and astringing sores and tissue regeneration [2]. It may be used to enhance the treatment of diabetic patients by increasing the control of blood glucose levels, decreasing the urinary protein levels as well as decreasing the edema and hence helping in the treatment of diabetes as well as its complication. Meanwhile, Astragalus has the capability of controlling the immune system, increasing the resistantibility of the body, therefore, enhancing the microcirculation and immune activity of patients, and invalidating, curing and treating diabetic complications [3]. The review of the Astragalus and its relationship with diabetic complications is, however, lacking in any detailed review. This article shall briefly outline the key medicinal constituents of Astragalus, expound on its action mechanisms against diabetes and diabetes related complications, and investigate the current state of use of Astragalus in the management of diabetic complications

2. Primary components and pharmacological action of astragalus

The plant known as Astragalus belongs to the family Fabaceae and the roots of it are used to make astragalus, the dried root of the plant. It is reputed as having the effects of strengthening qi and raising yang, solidifying the exterior to prevent sweating, stimulating the generation of fluids and feeding the blood, moving qi and clearing up blockages, expelling toxins and drainage of sores and stimulating tissue growth. It can be used to relieve fatigue, thirst, excessive sweating and prone to common colds. Such activities are mainly due to its key active ingredients, astragalus polysaccharides, astragalus saponins as well as astragalus flavonoids.

2.1. Astragalus polysaccharides

The most active substances in the herb are astragalus polysaccharides. These polysaccharides are structurally composed of sugar molecules like hexuronic acid, glucose, fructose, rhamnose and arabinose and have a wide range of biological activities. It is their significant antioxidant effect which allows them to counteract the harmful radicals and lowers oxidative stress and cellular damage. At the same time, they are shown to have great immunomodulatory effects through the activation of important immune cells contributing to the body defenses against the pathogens. Other possible biological applications are the anti-aging and anti-tumor effects, as well as the positive effects on the metabolic health, like the ability to reduce blood glucose and lipid concentration in the body. Critically, studies identify certain therapeutic effects in managing diabetes; these polysaccharides have been noted in lowering urinary protein levels which are assigns some protective effects on the kidneys that may be of use in reversing diabetic nephropathy. They also

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affect the symptoms through their anti-inflammatory effects, which is possible by the inhibition of the pro-inflammatory substances.

2.2. Astragalus saponins

Another group of significant active constituents in Astragalus, the second in abundance is saponins, second to that of polysaccharides. They have a high level of benefit on metabolic and cardiovascular conditions on their therapeutic profile. One of the key mechanisms is the increase in the level of insulin secretion and the responsibility to enhance the sensitivity of tissues to insulin directly resulting in the decrease of the level of the glucose in blood, which is an essential effect in diabetes treatment. These compounds also decrease blood cholesterol and triglycerides in addition to glycemic control, and this prevents the deposition of the lipids on the arterial walls. This lipid-controlling effect is crucial to prevent the atherosclerosis progression, which highlights the role of cardiovascular-protecting effects of Astragalus saponins.

2.3. Astragalus flavonoids

The astragalus also has different flavonoids, which play a major role in its medicinal properties due to antioxidant, antiflammation, as well as the possible antitumor effect. The compounds that fall under this category are flavones, isoflavones and isoflavanes. Their primary activity entails free radical scavenging with an aim of reducing oxidative cell damage. They are also useful during inflammation by inhibiting the action of the inflammatory cells as well as lowering the formation of the inflammatory signaling molecules. All these flavonoids, along with the polysaccharides and saponins, combine to create the widespread medicine of Astragalus in traditional Chinese medicine.

3. The action mechanisms in diabetic complications therapy

The mechanism of action of Astragalus in treatment of diabetes and complications is much associated with these active components especially with polysaccharides and flavonoids. They appear to act along several fronts: controlling the level of sugar in the blood, lowering the inflammation, protecting the cells that produce insulin in the pancreas, and promoting the condition of other body systems such as the heart, brain, and liver.

3.1. Regulation of blood glucose

Management of blood sugar is central to diabetes management. Astragalus polysaccharides have been causing attention on how they affect glucose metabolism particularly in case of circumstances such as the high fat diets that interfere with a normal balance. The diets may lead to high sugar levels, as they lead to insulin insensitivity of the body and inflammation. It demonstrates that mice that had a high-fat diet were administered astragalus polysaccharides. The results revealed that these mice possessed low levels of blood sugar significantly than mice who were on a high-fat diet alone [4]. The gut microbiome was later identified via further research [5]. These polysaccharides appeared to support good bacterial and discourage bad bacteria. This change in the composition of the gut bacteria is believed to be among the ways through which the body is better able to respond to glucose. Overall, astragalus polysaccharides can probably contribute to normalizing blood sugar due to a combination of actions, including the effects on the insulin sensitivity, the effect on the fat metabolism, and the effect on the gut bacteria that can alleviate the symptoms and prevent certain diabetic complications.

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3.2. Anti-inflammatory

An overactivation of the inflammatory factors is also a decisive determinant in the pathogenesis and course progression of diabetic peripheral neuropathy. The model of the Wang study was to separate 68 diabetic peripheral neuropathy model rats into a normal group, a model group (gavaged with saline) and an intervention group (gavaged with Huangqi Jian Pill). The findings revealed that Huangqi Jian Pill was effective in reducing the quantity of serum TNF- -alpha and IL- 6 in rats, suppressing NF- - - B expression in the sciatic nerve tissue as well as in enhancing indicators of blood glucose and nerve conduction velocity [6].

The previous research clarifies the anti-inflammatory action of Astragalus: persistent elevation of blood glucose is capable of triggering inflammatory cytokine cascades including the NF-kB which increases the release of pro-inflammatory cytokines like TNF- kappa, IL-6, and IL-1 beta in large amounts. These include such factors as causing oxidative stress, disruption of neurotrophic factor expression and destruction of theneurovascular barrier, which eventually result in neuropathy. NF-KB signaling pathway can be inhibited by inclusion of Astragalus polysaccharides which inhibits transcriptional activation of pro-inflammatory factors, and also by Astragalus saponins and flavonoids which inhibits the activation of such inflammatory cells as macrophages which release several inflammatory mediators. This reduces inflammatory injury of nerve tissue and reduces neuropathic symptoms [7].

3.3. Preservation of pancreatic 8 cells

Normal glucose metabolism cannot be completed without pancreatic 2-cells since it is only these cells in the body that can produce insulin which is the most important hormone in the body that regulates the level of glucose in the blood. Astragalus provides protective effects on the pancreatic 8-cells during diabetes and diabetes complications treatment. It has been discovered that astragalus polysaccharides could prevent the pathological alteration in diabetic rats, including islet cell reduction, degranulation, amyloidosis, and atrophy. They also raise the fasting insulin level and early-stage secretion of insulin indicating that astragalus polysaccharides have a protective effect on islet cell function. In addition to this, Wang also examined the regulation influences of other active constituents of Astragalus on insulin. The study of the 36 diabetic mice was randomly split into four groups of model, Astragalus, Astragalus flavonoid and Astragalus polysaccharide group. There was model establishment and gavage intervention of all the groups. Observations of the body weight, blood glucose, and the islet cell count were done in the four groups after the treatment. The findings revealed that Astragalus, and its active constituents had a good therapeutic impact on diabetic mice, which had a significant effect on the levels of blood glucose and pancreatic 8 cells. It has been established by validation that astragalus flavonoids had a closer and stronger effect in depressing the diabetic mouse model than astragalus polysaccharides. They had successfully lowered the blood glucose level and weight as well as insulin and adiponectin concentrations and subsequent suppression of apoptosis of pancreatic islet cells [6].

These results indicate that Astragalus helps to manage the level of blood glucose and retards diabetic complications because it preserves the structure and functioning of pancreatic 2-cells and promotes normal insulin secretion. Conservation of pancreatic 8 cells does not only play a vital role in the regulation of blood glucose but is also an important approach in the prevention and delay of the onset of diabetic complication like vascular, neurological and kidney diseases.

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3.4. Impairments on cardiovascular, cerebral, and hepatic systems

Astragalus also affects the cardiotonic properties particularly that it improves the myocardial contraction and diastolic functions. The article established that Astrazalus combined with puerarin will enhance the myocardial cell status of diabetic model mice, prevent the ultrastructure of cardiomyocytes, endoplasmic reticulum stress, and cardiomyocyte apoptosis [8]. Such is possibly one of the possible mechanisms of preventive and treatment of diabetic cardiomyopathy (DCM). Also, astragaloside IV could prevent cardiomyocytes in ischemic and hypoxic conditions, inhibit inflammation of myocardial fibrosis and hypertrophy, enhance the myocardial contractile function, ameliorate the diastolic dysfunction, prevent or remedy the dysfunction of vascular endothelial, and induce angiogenesis and thereby lower the risk of cardiovascular complications.

With respect to hepatic protection, Astragalus was also found to prevent the liver glycogen depletion. Research has shown that selenium is a trace element that is rich in Astragalus and has the ability to offer protection to hepatocytes through increasing the action of glutathione peroxidase among others. A study was conducted on animals that showed that the alcohol-treated mice that were gavage fed with two different doses of honey-processed Astragalus showed a 59% lowering of the content of triglycerides (TG) in the blood after four weeks with a reduction in serum and hepatic total cholesterol (TC) and free fatty acids (FFA) levelling off by at least 25.9. Liver tissue pathological examination also greatly improved which indicates its possible role in eliminating the risk of hepatic complications [9].

Beause of its therapeutic role, Astragalus is commonly used with other drugs in order to improve the clinical effect. As an example, in the management of chronic heart failure, there has been established evidence of additional benefits of cardiac functioning, reduction of myocardial remodelling, and in certain studies even better results with a combination of Astragalus injection with the conventional medications used in the West like angiotensinconverting enzyme inhibitors.

4. Clinical applications of astragalus

These pharmacological activities are clinically translated into compounds and herb pairs, which are highly targeted. As an illustration, 80 patients were grouped, whereby the treatment group was administered with a modified Astragalus and Pueraria Decoction with traditional therapy. The study demonstrated that the effective rate in the treatment group was 90 percent, which is much higher than the 62.5 percent rate in the control group and this confirms that the formulation is very effective in the treatment of diabetes and its associated complications [10].

Since the therapeutic effect of each particular single herb is often limited, in the clinical practice, Astragalus is commonly used in the form of a synergistic formula. Astragalus is also paired with such herbs as Angelica sinensis (Danggui), Pueraria (Gegen), or Dioscorea (Shanyao). Classical formulas that have been formed like Fangji Huangqi Tang, Buyang Huanwu Tang and Huangqi Tang also show exhaustive systems of treatment, which exploit its characteristics.

Nevertheless, the use of Astragalus in the treatment of diabetes is not entirely unlimited. To begin with, depending on the geographical origins and methods of processing, the quality of the herb, and hence the amount of its active ingredients, can fluctuate considerably, which confirms the absence of standardized quality criteria and specifications of the dosage. Second, the creation of individual treatment regimens depending on the syndromes or complications in particular patients is one of the areas that still need improvement. Lastly, Astragalus can only be used as a supplementary agent and not a substitutionary factor to other normal pharmacological treatments because of its regularly mild and slow effect.

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5. Conclusion

Long-established in the history of medicine as a tonifying herb, astragalus is currently widely used to treat diabetes and complications. The major constituents that are active in it are astragalus polysaccharides, astragalus saponins, and astragalus flavonoids. Astragalus is a potent strategic intervention in the pathogenesis of diabetic complications because it has anti-inflammatory, immunomodulatory, blood glucose homeostatic, and organ-protective effects. But the existing literature focused is supported by the cellular or animal model and does not involve large-scale and long-term follow-up randomized control trials. This hinders its use in the clinics. The directions to be followed in future research are as follows: first, the need to clarify the multi-target effects of the active ingredients of Astragalus and furnish decent evidencebased medical data on the effect of Astragalus by conducting large-scale, multicentric clinical trials;second, the need to develop a standardized system of quality control of Astragalus and to work out the individualized regimes of treatment on the basis of the differentiation of TCM-syndromes and modern biomarkers. In these attempts, it is possible to promote the contemporary coagulation and the hospitality of Astragalus in the treatment of diabetes.

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