



Research Progress of Chaihu Shugan San in the Treatment of Non-alcoholic Fatty Liver Disease

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Abstract: Non-alcoholic fatty liver disease (NAFLD) belongs to the categories of "flank pain" and "liver fetish" in traditional Chinese medicine. The causes of NAFLD are complex, such as obesity, type 2 diabetes, hyperlipidemia, hypothyroidism, hypopituitarism, sleep apnea syndrome, polycystic ovary syndrome, sexual dysfunction, acanthosis nigricans, vitamin D deficiency and osteoporosis. The causes of NAFLD are very complex, such as obesity, type 2 diabetes. With the development of Chinese society and the further improvement of people's living standards in recent years, people's daily life, working style and diet structure have also changed. The incidence of NAFLD is increasing rapidly, and it has become a common disease in the world, posing a serious threat to our health and affecting our daily life. Traditional Chinese medicine emphasizes a holistic approach and treatment based on syndrome differentiation, with multiple channels, multiple aspects, multiple levels, multiple perspectives, and minimal side effects. It has a considerable therapeutic effect in the treatment of NAFLD. This article aims to organize and summarize the research literature on Chaihu Shugan San in the treatment of NAFLD in recent years, providing reference for further clinical research and application of Chaihu Shugan San in the treatment of NAFLD.

Keywords: Chaihu Shugan San; NAFLD; research progress

1. Brief introduction

Non alcoholic fatty liver disease (NAFLD) refers to a clinical pathological syndrome characterized by diffuse accumulation of fat in liver cells, in addition to alcohol consumption, viruses, and other clear causes of liver damage. It includes simple fatty liver and its evolved fatty hepatitis, cirrhosis, liver fibrosis, and liver cancer[1]. Now this disease has become the largest chronic liver disease in China. Recently, it has been reported that the overall prevalence of NAFLD among adults in China has reached 29.88%[2]. NAFLD not only affects the liver, but also affects extrahepatic diseases such as cardiovascular and cerebrovascular diseases, endocrine related diseases, kidney diseases, etc. At the same time, research shows that NAFLD can also significantly increase the incidence rate of gastrointestinal malignancies[3]. At present, the specific treatment plan for NAFLD in Western medicine is not yet clear. On the basis of daily interventions such as controlling dietary intake and appropriate exercise, liver protection drugs or insulin resistance drugs are added. However, the clinical efficacy is not ideal and the side effects are obvious. Therefore, how to effectively treat NAFLD and improve the quality of life of NAFLD patients is also one of the current research hotspots. Among numerous traditional Chinese medicine prescriptions, Chaihu Shugan San has shown good efficacy in treating NAFLD and alleviating disease progression. The following is a review of research literature on Chaihu Shugan San's treatment of NAFLD in recent years.

2. Research status of Chaihu Shugan San in the treatment of NAFLD

2.1 The Origin and Development of Chaihu Shugan San

Chaihu Shugan San, a traditional Chinese medicine prescription name, comes from the Jingyue Quanshu. It is composed of seven traditional Chinese medicines: Chenpi, Chaihu, Chuanxiong, Xiangfu, Zhike, Shaoyao, and Licorice. It is a qi regulating agent with the effects of soothing the liver, regulating qi, promoting blood circulation, and relieving pain. Indicating liver qi stagnation syndrome. Pain in the rib cage, chest tightness, easy breathing, emotional depression, irritability, or belching, bloating in the epigastric region, and pulse strings. Clinically, it is commonly used to treat patients with liver stagnation and qi stagnation, such as chronic hepatitis, chronic gastritis, and intercostal neuralgia. There is no disease name related to NAFLD in medical records related to traditional Chinese medicine, but there are many records of this disease and similar diseases such as "flank pain", "liver stagnation", "accumulation", "liver distension", "liver fetish", "jaundice", etc[4]. Traditional Chinese medicine believes that the etiology of NAFLD is often due to overeating fatty, sweet,

and thick flavors, as well as poor mood leading to liver dysfunction, spleen dysfunction, and stagnation of blood stasis. For this disease, treatment mainly focuses on soothing the liver and regulating qi, strengthening the spleen and nourishing qi[5]. Therefore, Chaihu Shugan San has been applied in the treatment of NAFLD.

2.2 Research progress on the treatment of NAFLD with Chinese Chaihu Shugan San

Domestic scholars have explored the therapeutic mechanism and efficacy of Chaihu Shugan San on NAFLD through clinical trials, animal experiments, network pharmacology, and other research methods.

Luo Mingchi[6]selected 160 clinical NAFLD patients and divided them into two groups for clinical experimental research. The therapeutic effect of Chaihu Shugan San was significant. Research has shown that Chaihu Shugan San can significantly alleviate clinical symptoms in NAFLD patients, significantly reduce liver function indicators such as ALT, AST, and TBIL levels, improve liver function, and alleviate or eliminate liver inflammation; TC and TG were significantly reduced, improving the patient's lipid metabolism disorder. Clinical studies have shown that Chaihu Shugan San is an effective formula for treating NAFLD and is worthy of promotion and application.

Tan Xiyang[7]used network pharmacology technology to screen the main components of Chaihu Shugan San, explore the key targets, pathways, and mechanisms of action of Chaihu Shugan San in the treatment of NAFLD, and combine experimental data from historical research literature to verify relevant drug disease targets. Existing research has explored the AMPK signaling pathway, TNF signaling pathway, PI3K-Akt signaling pathway, PPAR signaling pathway, and Jak STAT signaling pathway. In summary, Chaihu Shugan San and its effective ingredients intervene in NAFLD through multiple targets, and throughout the entire treatment process, they exert therapeutic effects through multiple pathways. These studies provide new insights into the mechanism of Chaihu Shugan San in treating NAFLD.

Li Qin et al.[8]believe that NAFLD is mostly a syndrome of deficiency and excess, and its etiology and pathogenesis are spleen deficiency, liver depression, phlegm dampness, and blood stasis. We should start by regulating the liver and spleen organs, soothing the liver and relieving depression, regulating qi and strengthening the spleen, and removing blood stasis and phlegm. Chaihu Shugan San has significant therapeutic effects on NAFLD of liver depression and spleen deficiency type. Su Wei[9] found that the application of Chaihu Shugan San to NAFLD patients has an effective rate of over 70% and can effectively reduce blood lipid levels in NAFLD patients.

2.3 Research progress on the treatment of NAFLD with overseas Chaihu Shugan San

Overseas scholars have proposed that Chaihu in Chaihu Shugan San can reduce serum ALT, AST indicators, and TG levels, increase antioxidant substances in liver tissue, and protect the liver by inhibiting lipid peroxidation, eliminating excess free radicals, and reducing inflammatory reactions. It can also be achieved by inhibiting hepatic stellate cells (HSCs) and nuclear transcription factors- κ B (NF- κ B) Activity, exerting anti liver fibrosis effects[10], Xiangfu ethanol extract has the effect of reducing serum glutamate pyruvate transaminase and transaminase[11], thereby improving liver function and reducing liver inflammation.

With the development of science and technology and the improvement of research methods, overseas scholars have made new progress in the treatment of NAFLD with Chaihu Shugan San. Many clinical experiments and pharmaceutical studies have confirmed the effectiveness of Chaihu Shugan San in treating NAFLD. Research has shown that the main effective chemical components of Chaihu Shugan San are quercetin, kaempferol β -Glutininsterol, naringin, etc. β -Sitosterol has a positive effect on lipid metabolism[12] and is currently commonly used in the treatment and prevention of NAFLD. Naringin belongs to the class of dihydroflavonoid compounds and has a wide range of pharmacological effects, including anti-inflammatory, antibacterial, lipid-lowering, antioxidant, anticancer, and anti-tumor effects. It has a positive effect in the treatment of inflammation induced NAFLD. Huan Nie et al.[13]found that after intervention with Chaihu Shugan San to treat NAFLD, the NAFLD rat model showed improvement in body weight, liver tissue pathology, serum and liver lipids. The main component of Chaihu Shugan San, limonene, also has a certain effect in regulating metabolic syndromes such as lipid metabolism disorders and hyperglycemia[14], which can alleviate the resistance of NAFLD rats induced by high-fat diet and N-nitrolevoarginine methyl ester[15].

3. Research concept

3.1 Research Plan

The samples selected for the research on the treatment of NAFLD with Chaihu Shugan San in China are based on traditional Chinese medicine diagnostic criteria, TCM disease classification, and dialectical syndrome classification, as well as the gender, age, symptoms, course, severity, and tongue coating pulse of NAFLD patients. For example, a scholar studied the treatment of liver

depression and spleen deficiency syndrome in NAFLD with Chaihu Shugan San. For example, chest and rib distension, abdominal distension, poor appetite, sticky stools, dry and bitter mouth, hiccup, belching, good rest, chest tightness and vomiting, dizziness and dizziness, pale red tongue, thin and white coating, and thin pulse string; NAFLD patients with liver depression and spleen deficiency syndrome were included in the study sample. Selecting samples based on the diagnostic criteria of traditional Chinese medicine and the classification of traditional Chinese medicine diseases and dialectical syndromes can better identify suitable research subjects and facilitate the smooth progress of the experiment. And the gender, age, and other aspects of NAFLD patients also reflect the overall concept, personalized characteristics, and treatment principles of traditional Chinese medicine. The samples selected for the research on the treatment of NAFLD with overseas Chaihu Shugan powder mainly include NAFLD patients and animal models. The study subjects of clinical trials are patients diagnosed with NAFLD, aged 18-60 years old, who did not receive drug treatment before inclusion in the study, comply with the principle of informed consent, and are not limited to gender, disease course, or other aspects. Patients with inconsistent disease duration and disease severity were also included in the study. According to statistics, the gender ratio in clinical trials is 60% for males, 40% for females, 80% for patients aged 18-60, and 20% for patients over 60. In addition, the clinical diagnostic criteria for NAFLD are based on the Diagnosis and Treatment Guidelines for Non alcoholic Fatty Liver Disease. NAFLD belongs to a type of fatty liver, which is classified into mild, moderate, and severe fatty liver based on fat infiltration. In terms of animal experiments, rats were mostly selected, and a high sugar and high-fat diet was used to induce a rat model of NAFLD. The rats were randomly divided into a normal group, a model group, an experimental group, and a control group. The therapeutic effect of Chaihu Shugan San on NAFLD was observed through different intervention measures.

3.2 Main research plan

The research on the treatment of NAFLD with Chaihu Shugan San mainly relies on clinical trials, animal experiments, network pharmacology, and other research methods. The clinical trial is mainly a randomized controlled trial, comparing Chaihu Shugan San with commonly used drugs. Compare the therapeutic effects of Chaihu Shugan San with commonly used drugs by evaluating quality of life, liver inflammation, and other factors. In a clinical trial involving 80 NAFLD patients[16], Chaihu Shugan San was compared with the commonly used drug polyene phosphatidylcholine capsules. It was found that Chaihu Shugan San can improve the clinical symptoms and signs of NAFLD patients, as well as alleviate the inflammatory response of NAFLD patients. In addition, Chaihu Shugan San is more effective in improving liver function, regulating blood lipids, and has higher safety than Polyene Phosphatidylcholine Capsules. Animal experiments were conducted using rat models to evaluate the therapeutic effect of Chaihu Shugan San on NAFLD through various biochemical indicators and morphological changes in liver tissue. A study found[17] that the NAFLD rat model was divided into a normal control group, a model group, a Dongbao Gantai positive control group, and a high, medium, and low dose group of Chaihu Shugan San. The control group and model group were given corresponding doses of physiological saline by gavage, while the Dongbao Gantai positive control group was given methionine by gavage. The high, medium, and low dose groups of Chaihu Shugan San were given gavage at different doses. The experimental results showed that Chaihu Shugan San can significantly reduce blood lipids, liver lipids, and FFA levels in the blood of NAFLD model rats, significantly increase the content of HDL-L in the blood, and effectively improve lipid metabolism in the body, thereby achieving a lipid-lowering effect. Chaihu Shugan San can significantly reduce liver cell steatosis and damage, effectively lower enzymes to protect the liver, improve liver function, and effectively reduce the number and degree of liver cell damage. In addition, Chaihu Shugan San can enhance the liver's ability to clear lipid peroxidation products and reduce the degree of lipid peroxidation damage.

3.3 Research Results

Based on research on the treatment of NAFLD with Chaihu Shugan San both domestically and internationally, it has been shown that Chaihu Shugan San does have significant therapeutic effects and unique advantages in the treatment of NAFLD. Chaihu Shugan San can effectively reduce patient blood lipid levels, improve lipid metabolism, reduce liver fat content, improve liver function, and has high safety. In traditional Chinese medicine, Chaihu Shugan San has the effects of soothing the liver, relieving depression, promoting qi circulation, and relieving pain. Therefore, Chaihu Shugan San can also delight patients and improve their quality of life.

4. Research prospects and challenges of Chaihu Shugan San in the treatment of NAFLD

4.1 Limitations of current research

As an effective prescription in traditional medicine, Chaihu Shugan San has been extensively studied in terms of its pharmacological effects and mechanisms. The treatment of diseases such as NAFLD, depression, Alzheimer's disease, and functional dyspepsia has been confirmed through numerous experimental studies. However, there is a lack of multicenter and

large-scale experimental research. The specific mechanism of Chaihu Shugan San in reducing liver inflammation still needs further investigation, and further research is needed on the effective parts and pharmacokinetics of Chaihu Shugan San. In existing research, there is a lack of unified standards for the dosage and treatment process of Chaihu Shugan San. The dosage and treatment process used in the study may vary greatly, so it is necessary to standardize the formula of Chaihu Shugan San to better play a role in the treatment of NAFLD.

4.2 Future research planning

In future research, the application scope, mechanism of action, and limitations of the active ingredients in Chaihu Shugan San will be analyzed, and its therapeutic value in NAFLD will be comprehensively analyzed from multiple perspectives. At present, most of the research on Chaihu Shugan San still focuses on the basic theoretical exploration of its formulation and modern basic pharmacological research. In the future, a series of innovative technologies such as proteomics research, traditional Chinese medicine supramolecular theory, and network pharmacology can be combined to provide more authoritative, systematic, and scientific theoretical basis for the treatment of liver diseases with Chaihu Shugan San.

5. Conclusion

In recent years, in the research on the treatment of NAFLD with Chaihu Shugan San, it has been found that the most commonly used method is a sample control experiment, which mainly involves comparing a clinically commonly used drug for treating NAFLD with Chaihu Shugan San. The clinical efficacy of Chaihu Shugan San is evaluated based on different doses and drugs of the sample. Experiments have shown that Chaihu Shugan San has a significant therapeutic effect on NAFLD, effectively lowering enzymes to protect the liver and improving liver function, with high safety and efficacy. However, the specific mechanism of Chaihu Shugan San in treating NAFLD still needs further research, which can provide more authoritative, systematic, and scientific theoretical basis for Chaihu Shugan San in the treatment of NAFLD.

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