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Research Progress of the Medicine-food Herbs Against Alcoholic Liver Disease

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Abstract: ***This article analyzes the data from the Special Food Information Query Platform of the Special Food Safety Supervision and Administration Department of the State Administration for Market Regulation, and finds that among the approved health foods in China that have auxiliary protective functions against chemical liver injury, there are 43 medicinal and the medicine-food herbs as raw materials. These traditional Chinese medicines mainly exert protective effects against alcoholic liver injury through mechanisms such as inhibiting free radical release, anti lipid peroxidation, antioxidant stress response, and anti-inflammatory response. Among them, the medicine-food herbs such as kudzu root, lingzhi, goji berry, licorice, reed root, honeysuckle, gardenia, dendrobium and seabuckthorn have been proven to have certain preventive and therapeutic effects. And a review was conducted on the mechanism of action of the medicine-food herbs in the prevention and treatment of alcoholic liver disease at home and abroad in recent years, in order to provide ideas and references for the development of the medicine-food herbs with sobering and liver protecting effects, as well as drugs for the treatment of alcoholic liver disease.***

Keywords: The medicine-food herbs, Alcoholic liver disease, Mechanism, Active ingredient, Research progress**.**

1. Introduction

Alcoholic liver disease (ALD) is a liver disease caused by long-term heavy alcohol consumption. At the initial stage, it usually presents as fatty liver, which can then develop into alcoholic hepatitis, liver fibrosis, and cirrhosis [1]. Alcohol has been recognized globally as a key secondary factor in causing liver cancer and its lethal consequences. According to authoritative data from epidemiological research, the number of liver disease patients induced by alcohol consumption in China has exceeded 60 million. Further statistical analysis shows that about 8% to 20% of individuals who drink excessively for a long time will develop alcohol-related cirrhosis, and among these patients, 2% of cases will progress to hepatocellular carcinoma. This severe situation undoubtedly poses a heavy disease burden on China's public health system [2-4]. At present, the treatment principles for ALD in clinical practice are abstinence from alcohol and nutritional support. The main therapeutic drugs used are hepatoprotective anti-inflammatory drugs, glucocorticoids, etc. Long term use of such drugs may lead to a series of toxic side effects and drug resistance in the body. Research has found that a variety of the medicine-food herbs have significant preventive and therapeutic effects on ALD, and compared to Western medicine treatment, these herbs exhibit a comprehensive advantage of multi-target and multi pathway effects, with minimal side effects and easy acceptance [5]. This article analyzes the current application status of the medicine-food herbs in health foods that have auxiliary protective effects against chemical liver damage through a special food information query platform. It systematically reviews the mechanism of action of medicinal and the medicine-food herbs in the prevention and treatment of alcoholic liver disease at home and abroad in recent years, aiming to provide new ideas and reference for the development of the medicine-food herbs with sobering and liver protecting effects, as well as drugs for the treatment of alcoholic liver disease.

2. Analysis of the Current Status of the Application of Dual-purpose Traditional Chinese Medicine in Health Food with Auxiliary Protective Effects Against Chemical Liver Damage

According to the Special Food Safety Supervision and Administration Department of the State Administration for Market Regulation's Special Food Information Query Platform(http://tsspxx.gsxt.gov.cn/gcbjp/tsspindex.xhtml)As of June 30, 2024, China has approved 244 health foods with auxiliary protective functions against chemical liver injury. Through the advanced search function, enter "health function" as "auxiliary protective function against chemical liver injury", and enter 110 dual-use substances for medicine and food in the "main raw materials" column. After statistical analysis, the following conclusion has been drawn: 43 medicinal and the medicine-food herbs have been used as raw materials for health products with auxiliary protective functions against chemical liver injury (see Table 1 for details).

Table 1: Table of the number of approved traditional Chinese medicine products with auxiliary protective functions against chemical liver injury for both medicinal and edible purposes

Number of products	Name
1~10	Yam, papaya, chrysanthemum, white bean, lily, kelp, sand seed, citron, lotus leaf, radish seed, jujube seed, fresh reed root, Pueraria lobata, Dendrobium officinale, mulberry leaf, sorghum, Polygonatum sibiricum, orange peel, Eucommia ulmoides leaf, seabuckthorn, green fruit, mint, black plum, honeysuckle, cassia seed, angelica sinensis, Codonopsis pilosula, jujube (jujube, black jujube, sour jujube), gardenia, pine pollen, dandelion, American ginseng, chrysanthemum, ginseng
11~20	Huangqi, Yuganzi, Fuling, Hawthorn, Licorice
21~50	Turmeric, goji berries
51~100	Ganoderma lucidum
＞100	kudzu root

3. The Preventive and Therapeutic Effects of the Medicine-food Herbs on Alcoholic Liver Injury

3.1 Pueraria Root

Pueraria lobata is the dried root of the leguminous plant Pueraria lobata (Willd.) Ohwi. Kudzu contains abundant active ingredients, mainly including flavonoids, triterpenoids and saponins, coumarins, organic acids, polysaccharides, alkaloids and other compounds. Modern research has shown that kudzu root can exert protective effects against ALD through mechanisms such as antioxidant stress response, inhibition of free radical release, and anti lipid peroxidation [6]. Wang Shushen [7] established a mouse model of alcoholic liver injury and found that chronic alcohol treatment significantly reduced the levels of glutathione transferase (GST), glutathione (GSH), and total antioxidant capacity (T-AOC) in the liver of mice, while pre-treatment with kudzu root extract effectively increased their levels. This indicates that Pueraria extract has an enhancing effect on the antioxidant capacity of the liver, can antagonize alcohol induced oxidative stress induced liver injury, and has a protective effect on the body. In addition, Pueraria extract can effectively increase the activity of alcohol dehydrogenase (ADH) in the liver of mice with liver injury, reducing the damage of ethanol to the liver. Puerarin is a derivative of isoflavones extracted from the traditional Chinese medicine Pueraria lobata. Its unique mechanism of action in the GSK-3 β/NF - κ B signaling pathway can effectively inhibit the process of liver cell apoptosis and reduce inflammatory reactions, thereby achieving significant relief and positive improvement of liver lesions [8-9]. Research by Li Xue [10] has shown that the active ingredients of Pueraria lobata, puerarin and genistein, can increase the expression of hepcidin by inhibiting the MAPK/ERK signaling pathway, thereby reducing alcohol induced iron overload, liver injury, oxidative stress, and liver cell apoptosis. This is manifested in inhibiting alcohol induced serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST), increasing liver tissue superoxide dismutase (SOD), reducing malondialdehyde (MDA), and iron content levels in alcoholic liver disease mice.

3.2 Ganoderma Lucidum

Ganoderma lucidum is the dried fruiting body of the porous fungi Ganoderma Lucidum (Leyss. ex Fr.) Karst. or Ganoderma sinense Zhao, Xu et Zhang. Research has found that the fruiting body and mycelium of Ganoderma lucidum have good protective effects on liver injury models in ALD rats and mice. Its important pharmacological active ingredients are Ganoderma lucidum polysaccharides and Ganoderma lucidum triterpenoids [11]. Ganoderma lucidum polysaccharides have pharmacological effects such as protecting the liver, anti-inflammatory, and enhancing immunity [12]. Zhao Tingting et al. [13] found that polysaccharides from Ganoderma lucidum mycelium can alleviate ALD by regulating pathways such as NF - κ B or improving gut microbiota composition, improving oxidative stress levels in mouse liver, regulating lipid metabolism levels, and inhibiting inflammatory cytokine levels in mouse liver cells. Ganoderma lucidum polysaccharides can effectively alleviate liver tissue damage and restore liver function by inhibiting the expression of NLRP3 inflammasome in liver tissue, suppressing inflammatory response and liver fat deposition in mice with acute alcoholic liver injury [14]. The active ingredient of triterpenoids in Ganoderma lucidum for ALD protection is mainly ganoderic acid. Ma Bingjun [15] found that ganoderic acid A can significantly reduce the levels of AST, ALT, total cholesterol (TC), triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C) in mouse serum, while increasing the level of high-density lipoprotein cholesterol (HDL-C). At the liver tissue level, ganoderic acid A effectively reduced the levels of reactive oxygen species (ROS) and malondialdehyde (MDA), and enhanced SOD activity and GSH levels, demonstrating its potential for antioxidant stress. Further analysis shows that ganoderic acid A can significantly reduce the levels of inflammatory factors such as interleukin-1 β (IL-1 β), interleukin-6 (IL-6), and tumor necrosis factor - α (TNF - α) in mouse serum and liver tissue, indicating its ability to inhibit inflammatory responses. At the molecular level, ganoderic acid A inhibits the expression of apoptosis related proteins such as TLR4, TLR2, MyD88, NF - κ Bp65, Bax, Caspase-3, Caspase-9, and activates the expression of anti apoptotic proteins such as I κ B α and Bcl-2, revealing its pathway of inhibiting cell apoptosis. In addition, studies have shown that ganoderic acid can also alleviate ALD in mice by regulating gut microbiota disorders [16].

3.3 Fruit of Chinese Wolfberry

Lycium barbarum L. is a dried and mature fruit of the Solanaceae plant Lycium barbarum L. from Ningxia. Goji berries have various chemical components, such as polysaccharides, alkaloids, flavonoids, and carotenoids, which have pharmacological effects such as protecting liver and kidney function, antioxidant, anti fatigue, regulating immunity, anti-tumor, and regulating intestinal microbiota [17] To further investigate the liver protective and sobering effects of goji berries, the research team used an alcohol induced acute alcoholic liver injury mouse model. The experimental results showed that the water extract of wolfberry can significantly regulate the body weight and liver index of mice with alcoholic liver injury, significantly reduce the levels of ALT and AST in serum, and significantly increase the levels of GSH and SOD in the liver. In addition, the extract also showed significant effects on ADH and ALDH, effectively reducing the content of MDA in the liver and significantly improving pathological phenomena such as structural disorder and cell deformation in mouse liver tissue [18]. Wei Fenfen et al. [19] found that Lycium barbarum polysaccharides can significantly reduce serum oxidative markers and increase MDA levels in mouse liver TNF-α、IL-1β、GSH、SOD, Thereby alleviating ALD. In addition, Lycium barbarum polysaccharides can alleviate ALD by regulating the Nrf2/HO-1 signaling pathway, clearing ROS and reactive nitrogen levels, and inhibiting apoptosis. Jia Dongsheng et al. [20] found that anthocyanins from black goji berries also showed significant relief effects on ALD, which includes reducing the activity of ALT and AST in serum, as well as the levels of TNF - α and IL-6, reducing the content of MDA in liver tissue, and increasing the activity of SOD and GSH levels. Black wolfberry flavonoids reduce inflammatory factors related to TNF - α and IL-6 through the NF - κ B

signaling pathway, while promoting the expression of anti-inflammatory cytokine IL-10, effectively alleviating ALD symptoms in mice [21]. In summary, goji berries have shown significant relief effects on ALD through various pathways such as clearing excess free radicals in the body, enhancing antioxidant capacity, inhibiting inflammatory reactions, suppressing lipid peroxidation, and improving lipid metabolism.

3.4 Licorice

Licorice is the dried root and rhizome of the leguminous plants Glycyrrhiza uralensis Fisch, Glycyrrhiza inflata Bat, or Glycyrrhiza glabra L. Modern research has shown that licorice contains various active ingredients such as flavonoids, triterpenoid saponins, and polysaccharides. Among them, the flavonoid compound glycyrrhizin is the main active ingredient in licorice to alleviate ALD. Zhang Fenfen et al. [22] found that glycyrrhizin can effectively increase serum ADH levels and liver ADH and SOD levels in mice with acute alcoholic liver injury by constructing a mouse model. They speculate that this may be related to glycyrrhizin's ability to improve lipid peroxidation, enhance the antioxidant capacity of damaged liver, and reduce inflammatory reactions to a certain extent.

3.5 Reed Root

Reed root is the fresh or dried rhizome of reed Phragmites communis Trin. of the family Gramineae. Modern studies have found that reed root mainly contains compounds such as polysaccharides, organic acids, steroids, terpenoids, and alkaloids, which have pharmacological effects such as antioxidant, anti-inflammatory, and immunomodulatory effects [23]. Rao et al. [24] used rehmannia glutinosa polysaccharide, rehmannia glutinosa pectin and rehmannia glutinosa extract, respectively, as prophylactic drugs for rats for a period of 14 days of administration of treatment, and the results of the experiments showed that, compared to the model group, in the serum of rats in rehmannia glutinosa polysaccharide, rehmannia glutinosa pectin, and rehmannia glutinosa extract groups, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and lactic acid dehydrogenase (LDH), triglycerides (TG) and very low density lipoprotein (VLDL) were significantly reduced. This finding strongly suggests that rutabaga has a significant protective effect against acute alcoholic liver injury in rats, and its potential mechanism of action may be closely related to the antioxidant property of rutabaga and the improvement of hepatic lipid metabolism.

3.6 Honeysuckle

Honeysuckle is a plant in the honeysuckle family, Lonicera japonica Thunb Dried flower buds or newly bloomed flowers, which contain luteolin, hyperoside, and quercetin, have a protective effect against alcoholic liver injury. Liu Chang et al. [25] constructed a rat model of acute alcoholic liver injury and found that honeysuckle water extract can significantly reduce MDA content, thereby inhibiting the response of inflammatory factors. At the same time, the extract can also increase the activity of GSH, SOD, and glutathione peroxidase (GSH Px), effectively inhibit the occurrence of oxidative stress response, and thus have a protective effect on acute alcoholic liver injury.

3.7 Gardenia

Gardenia jasminoides Ellis is a dried and mature fruit of the madder family plant Gardenia jasminoides Ellis. The chemical composition of gardenia is diverse and complex, covering various components such as iridoids, flavonoids, polysaccharides, organic acids, and volatile oils. Among them, geniposide from cyclohexene ether terpenes and geniposide oil from volatile oils have been proven to be key active ingredients in the prevention and treatment of alcoholic liver disease [26]. Specifically, gardenia oil has shown significant effects in responding to acute alcoholic liver injury, significantly reducing the levels of AST, ALT, γ - GT, and TG in mouse serum. This mechanism involves improving the expression pattern of oxidative stress markers in liver tissue, activating the antioxidant enzyme system, and effectively resisting alcohol induced oxidative stress. Meanwhile, gardenia oil can also downregulate the expression of TNF - α, reduce inflammatory response, and have a significant improvement effect on hepatic steatosis and cell death [27]. On the other hand, geniposide also performs well in protecting the liver from alcohol damage. It can effectively reduce the levels of biomarkers such as AST and ALT in the serum of mice with alcohol induced acute alcoholic liver injury. This effect is achieved by increasing the activity of antioxidant enzymes such as GSH and GSH Px in the liver, as well as enhancing the expression levels of CuZn SOD and CAT mRNA and protein, effectively resisting the oxidative stress damage of alcohol to the liver and preventing the occurrence of acute alcoholic liver injury [28]. In addition, studies have further indicated that geniposide can effectively alleviate liver lipid accumulation by promoting the transcriptional activity of peroxisomes and upregulating the expression of nuclear factors 1 α and 4 α in liver cells, significantly improving the histopathological characteristics of alcoholic rat liver tissue and reducing its degree of lipid degeneration and liver injury [29].

3.8 Dendrobium Officinale

Dendrobium nobile Lindl., Dendrobium huoshanense C. Z. Tang et S. J. Cheng, Dendrobium chrysotoxum Lindl., or Dendrobium fimbriatum Hook. are cultivated varieties of orchids in the family Orchidaceae, as well as fresh or dried stems of similar species of the same genus. Research has shown[30] that in a mouse model of chronic alcoholic liver disease, Dendrobium huoshanense can alleviate pathological damage such as hepatic steatosis and hepatic lobular structural disorder, significantly reducing serum ALT, AST, TC, and LDL-C levels, and significantly increasing serum HDL-C levels; The levels of TG, MDA, and inflammatory factors TNF - α, IL-6, and IL-1 β in the liver were significantly reduced, while the activity of SOD was significantly increased. The fresh product of Dendrobium huoshanense can improve the pathological damage of liver tissue in mice with chronic alcoholic liver injury, and its effects are related to regulating lipid metabolism, antioxidant stress damage, and inhibiting inflammatory response.

3.9 Hippophae Rhamnoides

Sea buckthorn is the dried and mature fruit of Hippophaerhamnoides L., a plant in the family Elapidae. Sea buckthorn is rich in ingredients and has a wide range of pharmacological effects, mainly including vitamins, flavonoids, phenolic acids, polysaccharides, etc. It plays an important role in antioxidant, anti-aging, anti-tumor, hypoglycemic, immune regulation, and improving gut microbiota. Tang Weiwei et al. [31] found through research that sulfated seabuckthorn leaf polysaccharides have significant effects, as they can significantly increase the activity of ADH (alcohol dehydrogenase) in intoxicated mice, thereby accelerating the oxidative metabolism of ethanol. At the same time, the polysaccharide can also clear free radicals produced by alcohol metabolism, protect liver cells from alcohol metabolism toxins and free radical damage, and thus play a role in sobering up. In addition, studies have shown [32] that seabuckthorn can significantly reduce the opacity value of the liver in zebrafish models of alcoholic liver injury, effectively improve the problem of liver and yolk sac enlargement, and downregulate the activity values of AST and ALT, improving the enlargement of liver cell nuclei and reducing hepatic tissue fat vacuolar degeneration. From this, it can be concluded that sea buckthorn can improve alcoholic liver injury, and its mechanism may be closely related to improving fatty acid oxidation, cellular metabolism, and inhibiting cell apoptosis.

3.10 Mulberry

Mulberry is the dried ear of Morus alba L., a plant in the mulberry family. Mulberry has the effects of protecting the liver, anti-tumor, anti-inflammatory, and lowering blood sugar. These functions are related to the unique phenolic compounds, polysaccharides, amino acids, minerals, and vitamins found in mulberries [33]. A study has found that mulberry extract can reduce the levels of serum ALT, AST, LDL, total bilirubin (TBIL), and serum cholesterol (CHOL) in mice with chronic alcoholic liver injury. By regulating lipid metabolism, it achieves the goal of anti alcoholic liver injury [34]. Bian Liang [35] confirmed that mulberry polysaccharides have a protective effect on alcohol induced acute liver injury in mice, mainly by regulating lipid metabolism and antioxidant stress damage. Li Wenli et al. [36] found that mulberry anthocyanin extract can reduce liver TC, serum ALT and AST levels in mice, as well as serum endotoxin (LPS) levels, and further improve ethanol induced liver inflammation by reducing IL-1 β, TNF - α, and macrophage chemoattractant protein-1 (MCP-1) levels.

3.11 Hawthorn

Hawthorn is the dried mature fruit of Shanlihong (Crataegus pinnatifida Bge. var. major N.E.Br.) or Shanzha (Crataegus pinnatifida Bge.), family Rosaceae. According to Chang Lulin et al [37], the flavonoids in hawthorn have the ability to reduce the levels of ALT, AST, MDA, and TNF-α as well as increase the activity of SOD, which can effectively alleviate alcoholic liver disease (ALD). The realization of this mechanism is mainly attributed to its reduction of serum free radical levels and inhibition of lipid peroxidation process in mice. On the other hand, hawthorn acid, as an antioxidant, exhibits a variety of biological activities including antioxidant and anti-inflammatory. Studies have shown that hawthorn acid exerts a mitigating effect on ALD by attenuating oxidative stress. A study by Wei Lei et al [38] further confirmed that hawthorn acid was able to reduce the MDA content and simultaneously elevate the GSH content in acute ALD mice, thereby enhancing the antioxidant capacity of the body and achieving the effect of alleviating liver injury. In addition, Yan et al.'s study [39] revealed another mechanism of action of hawthorn acid in alleviating ALD, which is to reduce alcohol-induced acute hepatic oxidative stress and inflammatory stress response by inhibiting CYP2E1 and NF-κB pathways, thus exerting a positive alleviating effect on ALD.

4. Conclusion

In summary, the medicine-food herbs mainly inhibits free radical release, anti lipid peroxidation, antioxidant stress response, anti-inflammatory response, and other mechanisms of action to improve alcoholic liver disease. Dual use traditional Chinese medicine has both medicinal and food properties. After thousands of years of clinical verification, its safety has been confirmed, demonstrating unique advantages and good therapeutic effects. Therefore, it has great potential and development value in the fields of medicine and health products. In depth research on the mechanism of action and clinical application of dual-use traditional Chinese medicine will help enrich the treatment strategies for alcoholic liver disease, improve patients' quality of life, and reduce social burden.

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