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• Review

Traditional Chinese medicine for treatment of liver diseases: progress, challenges and opportunities

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ABSTRACT: Traditional Chinese medicine (TCM) is commonly used in treating liver diseases worldwide, especially in China. The advantages of using TCM for treatment of liver diseases include: protecting hepatocytes, inhibiting hepatic inflammation and antifibrosis in the liver. In this article, we introduce TCM herbal preparations from the Chinese materia medica (such as Fuzheng Huayu) that are typically used for the treatment of liver diseases. Literature surrounding the mechanisms of TCM therapy for treatment of liver diseases is presented and discussed. We propose that side effects of herbal compounds are often under-appreciated, and that more care should be taken in the prescription of potentially hepatotoxic medicines. Further, to deepen the understanding of TCM mechanisms, new techniques and methodologies must be developed. Future studies will lead to the enhancement of clinical outcomes of TCM. As complementary and alternative therapies, TCMs will play an expanding role in the future of liver disease treatment.

KEYWORDS: medicine, Chinese traditional; drugs, Chinese herbal; liver diseases (TCM); liver cirrhosis; hepatoprotective drugs; hepatotoxicity; reviews

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1 Introduction

In China, traditional Chinese medicine (TCM), especially traditional Chinese patent medicine, has been, and continues to be widely used to treat various diseases. Even during the severe acute respiratory syndrome (SARS) outbreak in 2003, TCM, combined with Western medicines were used to control and eventually halt the spread of the disease. Compared with Western medicine alone, patients receiving treatment with Western medicine and TCM had reduced hospital stays, pneumonia duration and mortality. Early

TCM treatment can also decrease glucocorticoid dosage needed in the treatment of SARS^[1]. Before Western medicine was introduced into China, the Chinese health care system mainly depended on TCM. Although TCM does not treat specific conditions, it treats patterns of illness such as those associated with infectious diseases^[2–4], cardiovascular and cerebrovascular diseases^[5–11], respiratory diseases^[12–14], digestive diseases^[14–16], urinary diseases^[17–19], reproductive diseases^[20] and blood system diseases^[21], as well as fractures^[22], trauma^[23], ear, nose and throat diseases^[24,25], skin diseases^[26] and mental disorders^[27]. TCM can improve the clinical symptoms, reverse some pathological changes and restore

the body's normal physiological function. Since Western medicine was introduced into China in the 16th century CE, most diseases listed above are treated mainly with Western medicinal interventions. Gradually, TCM has become an alternative medicine rather than mainstream medicine. Even so, TCM therapy still has its advantages in some medical fields where Western medicine has not been as effective, such as in liver diseases. This review will introduce TCM in the treatment of liver diseases.

2 TCM therapy has advantages in liver diseases

Liver diseases are mainly classified into viral hepatitis, nonalcoholic fatty liver, alcoholic liver disease, autoimmune liver disease, schistosomiasis liver disease, drug-induced liver injury, hereditary liver disease, liver cirrhosis due to various causes and diverse liver tumors. TCM is widely applied in the treatment of liver diseases in China by both Chinese medicine doctors and Western medicine doctors because its ability to protect hepatocytes, inhibit hepatic inflammation and reduce fibrosis in the liver. In recent years, the application of TCM in liver cancer treatment has been increasingly widespread^[28,29]. It has been confirmed that TCM can not only reduce the toxic side effects of chemotherapy or radiotherapy, but also inhibit tumor growth and increase survival of patients with tumors^[30]. Although TCM has many uses in treating liver diseases, it cannot replace other treatment methods such as antiviral drugs, hormones, schistosomicide, surgical operation and transplantation.

TCM can be applied to treat diseases in one of the two ways: treatment based on *disease differentiation* or *syndrome differentiation*^[31]. For the disease differentiation approach, Western medicine methods are typically employed to diagnose specific liver diseases. Subsequently the appropriate TCM formula or patent drug is selected to treat the disease according to TCM's characteristics and advantages. The evaluation of the curative effect is based on the recovery of liver function or improvement in pathological changes. In the *syndrome differentiation* approach, TCM diagnosis of a patient's symptoms and signs is used to determine to which syndromes the patient belongs. The appropriate TCM formula or patent drug is then chosen to treat that TCM syndrome. The evaluation of the curative effect depends on the relief or elimination of the symptoms and signs. It is believed that the combination of two kinds of therapies can obtain greater curative effects for liver diseases^[32].

3 Chinese materia medica is frequently used to treat liver diseases

In acute stage of liver diseases, liver inflammation is prominent. Materials listed in the Chinese materia medica,

especially those for heat-clearing and detoxifying, are often applied to protect the liver, inhibit inflammation, decrease activity of serum transaminase and reduce serum bilirubin^[32]. Meanwhile according to the symptoms and signs of each patient, a matching therapy, such as adjusting yin and yang, invigorating qi and blood, soothing the liver, regulating qi, clearing heat and removing dampness, is also applied.

In the chronic stage of liver diseases, the symptoms of the disease are more complicated. Treating the source of the disease (*i.e.*, the virus) is one important and necessary approach. Western medicine does well in inhibiting the viruses that cause hepatitis B (HBV) and hepatitis C (HCV). TCM has little effect in inhibiting the virus, but works well to protect liver function, inhibit inflammation, decrease activity of serum transaminase, reduce serum bilirubin, lower lipid levels^[33], promote diuresis^[34] and relax the bowels^[35]. Depending on the stage of liver disease progression, or different syndrome classifications, TCM can be used to adjust yin and yang, invigorate qi and blood, soothe liver, regulate qi, clear heat and remove dampness^[36-38]. Zhang *et al*^[39] summarized and provided a critical meta-analysis of randomized controlled trials (RCTs) of TCM formulations for the treatment of chronic hepatitis B (CHB) that were reported in China from 1998 to 2008. The results showed that (i) TCMs (TCM formulations alone or in combination with interferon (IFN) or lamivudine (LAM)) had a greater beneficial effect than IFN ($P=0.0003$) and slightly better effect than LAM ($P=0.01$) on normalization of serum alanine aminotransferase; (ii) TCMs had a similar beneficial effect on antiviral activity when used in conjunction with IFN or LAM for CHB, which was evidenced by the reduction of serum HBeAg and HBV DNA; (iii) Treatment with TCMs in conjunction with IFN or LAM resulted in improved liver function.

When the liver tissue is damaged, its repair is accompanied by the formation of an extracellular matrix, also known as fibrosis. Fibrosis is the common pathological process of many liver diseases, and is also reversible. Antifibrotic effects are an important component in the treatment of various chronic liver diseases^[40]. One famous hepatologist, Professor Hans Popper, once said, "Anyone who can stop or delay liver fibrosis would be able to cure most chronic liver diseases"^[41]. The focus of Western medicine scientific and medical research has been on discovering targets for antifibrotic therapy, and developing customized multi-drug regimens^[42].

According to the TCM theory, diseases of liver Zang will transmit to the spleen Zang, thus in the course of treatment, the spleen Zang should be strengthened before it is impaired. If the liver disease has been long-standing, kidney yin should be evaluated during the treatment because the liver Zang and kidney Zang are derived from the same source. In clinical practice, symptoms and signs of spleen-qi deficiency

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