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Review

Niuchangchih (*Antrodia camphorata*) and its potential in treating liver diseases

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ABSTRACT

Niuchangchih (*Antrodia camphorata* (M. Zang & C.H. Su) Sheng H. Wu, Ryvarden & T.T. Chang) is a basidiomycete endemic to Taiwan. It is well known as a Traditional Chinese Medicine (TCM), and Taiwanese aborigines used this species to treat liver diseases and food and drug intoxication. The compounds identified in *Niuchangchih* are predominantly polysaccharides, triterpenoids, steroids, benzenoids and maleic/succinic acid derivatives. Recent research has revealed that *Niuchangchih* possesses extensive biological activity, such as hepatoprotective, antihypertensive, anti-hyperlipidemic, immuno-modulatory, anticancer, anti-inflammatory and antioxidant activities. The fruiting bodies and fermented products of *Niuchangchih* have been reported to exhibit activity when treating liver diseases, such as preventing ethanol-, CCl_4- and cytokine-induced liver injury, inhibiting the hepatitis B virus, ameliorating fatty liver and liver fibrosis, and inhibiting liver cancer cells. This review will address the protective effects of *Niuchangchih* on the pathological development of liver diseases, and the underlying mechanisms of action are also discussed.

Contents

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1. Introduction

The liver is the most important organ in terms of biochemical activity in the human body. The liver has great capacity to detoxify and synthesize useful substances, and therefore, damage to the liver inflicted by hepatotoxic agents has grave consequences (Achliya et al., 2004). Many risk factors, including hepatic viruses, alcohol consumption and chemical agents, have significant impact on the etiologies of liver diseases. Environmental pollution, bad dietary habits, and hepatic viruses have been considered to be the main factors that cause liver diseases (Day and Yeaman, 1994; Szabo, 2003). There are several characteristic pathologies in the livers of patients with liver disease, including fatty liver, hepatitis, liver fibrosis, hepatocirrhosis and liver cancer. Liver fibrosis is the common end stage of most chronic liver diseases regardless of the etiology (Bataller and Brenner, 2005), and its progression leads to liver cirrhosis and liver cancer. Currently, it is believed that the early stage of liver fibrosis can be reversed, while liver cirrhosis cannot. Therefore, preventing and eliminating the bad factors, and ameliorating fatty liver and liver fibrosis, are the most effective methods to prevent the liver from ultimately deteriorating (Freidman, 1993; Brenner et al., 2000). Much progress has been made in the understanding of the pathogenesis of liver diseases, resulting in improved prevention and therapy with promising prospects for even more effective treatments. In view of the severe undesirable side effects of synthetic agents, there is a growing focus on following systematic research methodology and evaluating the scientific basis of traditional herbal medicines that claim to possess hepatoprotective activity (Shahani, 1999; Achliya et al., 2004).

Niuchangchih, also named *Antrodia camphorata* (M. Zang & C.H. Su) Sheng H. Wu, Ryvarden & T.T. Chang, is a fungus that only grows on the brown heartwood of *Cinnamomum kanehirae* Hayata (Lauraceae) in Taiwan (Fig. 1) (Wu et al., 1997). *Niuchangchih* is also called "Niu-chang-ku", or "Chang-chih", in China. "Niu-chang" is the Chinese common name for *Cinnamomum kanehirae* (Bull camphor tree); "ku" in Chinese means mushroom; and "chih" means *Ganoderma*-like fungus. Being a local species, *Niuchangchih* was historically only used in Taiwan by the aborigines as a traditional prescription for the discomforts caused by alcohol drinking or exhaustion. The fruiting bodies of *Niuchangchih* are also used as a Chinese folk medicine for the treatment of liver diseases, food and drug intoxication, diarrhea, abdominal pain, hypertension, itchy skin and tumorigenic diseases (Tsai and Liaw, 1985; Chen et al., 2001a). However, in 1990, *Niuchangchih* was first reported as a new species. In the years since the initial report, *Niuchangchih* has received tremendous attention from the public. Primary investigations have revealed that *Niuchangchih* has extensive biological activities, such as hepatoprotective effects, anti-hepatitis B virus effects, anticancer activity, and antioxidant and anti-inflammation activities (Liu et al., 2007a; Rao et al., 2007).

Fig. 1. *Niuchangchih* fruiting bodies.

Niuchangchih grows at altitudes between 450 and 2000 m in the mountain ranges, and in the counties of Taoyuan, Miaoli, Nantou, Kaohsiung and Taitung. The trophophase of *Niuchangchih* occurs from June to October (Chen et al., 2001b). The fruiting bodies of *Niuchangchih* assume different shapes like the plate-type, the horse's hoof, or the tower shape, which is morphologically similar to *Antrodia salmonea* (vernacularly called Shiang-Shan-Chih), a brown heart rot basidiomata in the empty rotten trunk of *Cunninghamia konishii* Hayata (Lauraceae) (Chang and Chou, 2004). The red to light cinnamon fruiting bodies of *Niuchangchih* are bitter and have a mild camphor scent like the host woods (Chang and Chou, 1995). Chemical ingredients found in *Niuchangchih* include polysaccharides, triterpenoids, sesquiterpene lactones, steroids, phenol compounds, adenosine, cordycepin, ergosterol, etc. (Chang et al., 2005; Lu et al., 2006) The mycelia isolated from the fruiting bodies of *Niuchangchih* form orange red and orange brown to light cinnamon-colored colonies (Chang and Chou, 1995).

In the wild, the fruiting bodies of *Niuchangchih* grow slowly and are hardly noticeable until the host tree falls down. In order to harvest *Niuchangchih* more easily, some people illegally fall the host trees. This illegal felling has severely threatened *Cinnamomum kanehirae* (Chang et al., 2005), and the trees are currently protected by the Taiwan government. However, the wild fruiting bodies of *Niuchangchih* are in great demand and have been sold for about U.S. $15,000 per kg (Wang et al., 2005) due to the efficacies of this fungus. Thus, artificial cultivation was developed as a substitute. Currently, *Niuchangchih* is commercially available in Taiwan in the form of fermented wine or pure cultures in powdered, tablet and capsule form (Cheng et al., 2005b). The mycelia produced by liquid fermentation are innocuous (Lin et al., 2001).

In Chinese folk medicine, the fruiting bodies of *Niuchangchih* are considered to be a potent hepatoprotective remedy. The fruiting bodies and mycelia of *Niuchangchih* have been reported to exhibit the activities of preventing and ameliorating liver diseases, such as preventing ethanol- and CCl_4-induced liver injury, inhibiting the hepatitis B virus, ameliorating fatty liver and liver fibrosis, and inhibiting liver cancer cell growth. This review will address the protective effects of *Niuchangchih* on the pathological development of liver diseases. Most of the data presented here are from in vitro and animal studies, because the efficacy of *Niuchangchih* in preclinical liver diseases is not well documented.

2. Taxonomy

In past years, the taxonomy of *Niuchangchih* has been identified a few times, and several latin names have been suggested to stand as the correct name for the fungus. In 1990, *Niuchangchih* was first identified as a new *Ganoderma* species, *Ganoderma camphoratum*, due to their similar characteristics (Zang and Su, 1990). The generic name, however, was based on a mistake as the type was contaminated by spores of a *Ganoderma* species. Then, Chang and Chou (1995) described the species as *Antrodia cinnamomea* due to its dimitic hyphal system with clamped generative hyphae and ability to cause brown rot. After studying the both types of *Ganoderma comphoratum* and *Antrodia cinnamomea*, these fungi were found to be conspecific. Thus, a new combination, *Antrodia camphorata*, was thought to be more appropriate (Wu et al., 1997). However, given that the host tree of this latter species is *Cinnamomum kanehirae* rather than *Cinnamomum camphora* (L.) Presl., *Antrodia cinnamomea* was suggested again to stand as the correct name for the fungus associated with *Cinnamomum kanehirae* (Chang and Chou, 2004). In 2004, a phylogenetic analysis based on sequence data