

OVERVIEW OF THE POTENTIAL OF TRADITIONAL MEDICINAL INGREDIENTS IN THE TREATMENT OF CHRONIC HEPATITIS

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ABSTRACT

Chronic hepatitis (CH) is a pathology caused by diverse etiologies and can progress to severe complications, including liver cirrhosis and hepatocellular carcinoma. It is also a major contributor to the global burden of disease and mortality, exerting a significant negative impact on the quality of life of millions of people worldwide. Over recent decades, this disease has received increasing scientific attention. Although conventional medicine has developed various pharmacological and non-pharmacological interventions, the currently available treatments still have certain limitations in efficacy associated with adverse effects. In this context, traditional medicine - with a rich diversity of herbal resources and a long-standing tradition - offers a promising therapeutic approach. A Vietnamese herbal formulation, "Misocholic tab", serves as a case study exemplifying the multi-targeted and synergistic principles of traditional medicine. This formulation contains multiple components with complementary pharmacological actions: Anti-inflammatory, hepatoprotective and choleretic effects (Extractum Fel Suillum, Extractum Cynarae Succus); antibacterial properties (Bulbus Allii Sativi) and antioxidant activity (Extractum Cynarae Succus, Bulbus Allii Sativi). This article emphasizes the growing trend toward developing standardized, evidence-based traditional medicinal formulations, which are considered a safe and effective approach to support the comprehensive management of liver diseases.

1. INTRODUCTION

According to the 2019 report "Burden of liver diseases in the world", liver diseases account for approximately 2 million deaths annually, with about 0.1-1.5% of the global population and 7% of the Vietnamese population affected by liver-related conditions [1]. CH is a persistent pathology, characterized by diverse clinical symptoms arising from various etiological factors. Without timely and effective treatment, CH may progress to severe complications, including hepatic cirrhosis and hepatocellular carcinoma.

The pathogenic mechanisms of CH, particularly in the context of oxidative stress, involve multiple biological processes such as hepatocellular necrosis and hepatic fibrogenesis. These mechanisms have been demonstrated to be key contributors to the development and progression of both acute and chronic hepatic injury [1].

In clinical management, lifestyle and dietary modifications remain essential components. In addition, modern medicine has provided several therapeutic options, such as corticosteroid therapy, anticytokine therapy and extracorporeal liver support systems,

that have been demonstrated to have clinical efficacy. However, their long-time use can increase the risk of adverse effects. In this context, the investigation into safe and effective therapies derived from natural medicinal sources has emerged as a promising research direction and is attracting increasing scientific attention.

Vietnamese traditional medicine (VTM) has a rich diversity of herbal resources, supported by a long historical development and a comprehensive theoretical-practical system. Within this theoretical frameworks, CH is classified under the syndromic categories of "Hoàng đản" (jaundice) and "Hiếp thống" (hypochondriac pain) [2], with multiple subtypes of syndrome differentiations. The treatment of traditional medicine not only focuses on detoxification and anti-inflammatory actions, but also emphasizes restoring the balance among the internal organ systems, particularly the Liver – Gallbladder and Spleen – Stomach complexes, which are considered central to the pathology of this condition.

This article aims to provide an overview of the therapeutic potential of VTM ingredients in the management of CH,

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to analyze existing experimental and clinical evidence, and to elucidate the multi-component, multi-target mechanisms of action of the traditional formulation "Misocholic tab."

2. CONCEPTS OF TRADITIONAL MEDICINE REGARDING CHRONIC HEPATITIS DISORDERS

According to traditional medicine, the Liver-Gallbladder system is responsible for the functions of dispersing (so tiet) and regulating (dieu dat), and the dysfunction of this system is closely associated with the pathogenesis of CH. The primary etiological factor is the stagnation of Dampness (thap) in the Middle Burner (trung tieu), which weakens the Spleen-Stomach (Ty-Vi) system, subsequently impairing the dispersing and regulating functions of the Liver-Gallbladder (Can-Dom). As a result, bile fails to follow its normal course, enters the bloodstream, diffuses to the skin and tissues and thereby giving rise to "jaundice" (hoang dan). Furthermore, in traditional medicine, when the ascending-descending dynamics of Liver Qi (Can khi) become dysregulated, disturbances in bile flow, impaired channel patency, the blood stasis may occur, ultimately manifesting as "blood stasis pain" (huyet thong) [2]. Given its complex etiology and pathogenesis, CH is categorized into several major syndrome patterns:

Damp-heat in the Liver and Spleen (Can Ty thap nhiet): this pattern arises from exogenous pathogenic invasion or from improper dietary habits and excessive alcohol consumption, leading to the accumulation of damp-heat in the Middle Burner. This internal retention obstructs the dispersing function of Liver Qi, resulting in bitter taste in the mouth, a feeling of fullness in the chest and hypochondrium, and persistent hypochondriac pain. As outlined above, when the dispersing function of Liver Qi and the transformation of Gallbladder Bile (Dom trap) become impaired, the symptom "jaundice" (hoang dan) can appear on patient.

Liver Constraint with Spleen Deficiency and Qi Stagnation (Can uat Ty hu khi tre): Similar to the aforementioned pattern, this condition arises from similar etiological factors. However, prolonged illness leads to weakening of the Spleen and Stomach, so in addition the aforementioned manifestations, patients may also present with poor appetite, fatigue, and loose stools.

Liver Yin deficiency (Can am thuong ton): This pattern may arise from congenital insufficiency of Yin, but more commonly develops from prolonged illness that depletes of Qi and Blood (khi huyet) or from Spleen deficiency (Ty hu) failing to nourish for blood production. In addition to presentations of jaundice and hypochondriac pain..., patients typically exhibit manifestations of Liver Yin depletion with resultant internal heat, such as heat sensation in the palms and soles, irritability, and dizziness or headache.

Qi Stagnation and Blood Stasis (Khi tre huyet u): This pattern may result from emotional disturbances, internal

injury, or excessive alcohol consumption, which lead to the Liver constraint (can uat) and the internal accumulation of Damp-heat (thap nhiet noi dinh). Patients may have dark or dusky jaundice, emaciation with poor appetite and also be accompanied by the development of collateral circulation.

In treatment, traditional medicine aims to restore the balance within the body. Depending on the specific syndrome pattern, therapeutic approaches may vary, including: clearing heat and draining dampness (thanh nhiet loi thap), tonifying the Spleen and resolving jaundice (kien ty thoai hoang); smoothing the Liver (so can), tonifying the Spleen (kien ty), regulating Qi (ly khi); nourishing Yin and Liver function (tu am duong can); Soothing the Liver (so can), regulating Qi (ly khi), and invigorating blood circulation (hoat huyet).

3. EXPERIMENTAL EVIDENCE ON THE PHARMACOLOGICAL EFFECTS OF TRADITIONAL MEDICINE INGREDIENTS IN THE "MISOCHOLIC TAB" FORMULA

The "Misocholic tab" formulation combines three traditional medicinal ingredients and was developed based on empirical experience in the treatment of hepatic disorders, particularly those corresponding to the Damp-heat in the Liver and Spleen (can ty thap nhiet) pattern. Its therapeutic efficacy derives from the synergistic interactions among its constituent components, whose pharmacological activities have been demonstrated in experimental studies.

3.1. Anti-inflammatory, hepatoprotective and choleretic effects

Artichoke (*Cynara scolymus* L.) use its fresh stems and leaves as medicinal parts, which are typically processed into concentrated extracts. Its principal constituents include polyphenols (comprising phenolic acids and flavonoids) and inulin [3].

According to traditional medicine, artichoke is sweet in flavor and of neutral nature, with the functions of soothing the Liver, benefiting the Gallbladder, and clearing damp-heat (thu Can loi Dom, thanh tiet thap nhiet) [4].

Experimental evidence: In vitro studies have shown that artichoke extract exhibits potent anti-inflammatory effects comparable to indomethacin by inhibiting the production of inflammatory mediators. It also demonstrates hepatoprotective activity, as evidenced by reductions in liver weight and serum liver enzymes, alleviating hepatic lesions, and restoring normal hepatic histological architecture. In addition, it exerts choleretic effects by markedly increasing bile flow.

Pig bile (*Fel Suillum*) is commonly concentrated into an extract and refined using various methods. Its principal components include cholate salts and several biliary pigments including bilirubin [5], [6]

In traditional medicine, pig bile is bitter in flavor and a cold nature with the functions of "thanh nhiet giai doc"

(anti-inflammatory, choleric, and hepatoprotective properties).

Experimental evidence: Several studies have demonstrated that pig bile exhibits anti-inflammatory activity, which is believed to be associated with its ability to reduce vascular permeability, inhibit the synthesis of inflammatory mediators, and scavenge reactive oxygen species while suppressing lipid peroxidation. Regarding its hepatoprotective and choleric effects, bile acids in pig bile facilitate lipid absorption and cholesterol metabolism, increase the intestinal absorption of vitamins, and modulate biliary cholesterol saturation, thereby improving lipid metabolic processes. In addition, an *in vitro* study reported that deoxycholic acid derived from pig bile may modulate uPAR in HepG2 hepatocellular carcinoma cells, thereby inhibiting the metastatic potential of HepG2 cells.

3.2. Antibacterial property

Garlic (*Allium sativum* L.) uses its bulbs as the medicinal parts, which can be processed into various pharmaceutical forms. Garlic is rich in organosulfur compounds, which constitute its primary bioactive components[5],[7].

According to traditional medicine, garlic is pungent in flavor and a warm nature, with the functions of warming the Middle Burner (on trung), dispersing stagnation (hanh tre), detoxifying (giai doc), and eliminating pathogens (sat trung).

Experimental evidence: Studies have shown that garlic exhibits antimicrobial activity in both the gastrointestinal and respiratory tracts, strongly inhibits *Staphylococcus*, *Streptococcus*, *Salmonella typhi*, *Salmonella paratyphi*, and *Shigella* species, primarily due to the actions of allicin.

In addition, pharmacological research has shown that pig bile (*Fel Suillum*) also possesses antibacterial properties, including inhibitory effects against *Staphylococcus aureus* and *Escherichia coli*.

3.3. Antioxidant activity

Shabnam Salekzamani et al. demonstrated that artichoke extract exhibits *in vitro* antioxidant activity by increasing levels of superoxide dismutase (SOD), catalase (CAT), glutathione (GSH), and glutathione peroxidase (GPx), while reducing malondialdehyde (MDA) in the liver and plasma of diseased animals [8]. These effects are attributed to its ability to inhibit lipid peroxidation and scavenge free radicals. Moreover, artichoke extract may also suppress oxidative stress when cells are exposed to toxic agents.

For garlic, its antioxidant effects are attributed to its high phenolic and organosulfur content, which may vary depending on cultivation duration and extraction techniques. Garlic extract, which yields alliin, helps regulate intracellular ROS production by inhibiting mitogen-activated protein kinase activity and suppressing NADPH oxidase 1 [9]. In addition, garlic promotes the activity of antioxidant enzymes, thereby protecting cells against oxidative stress— a key pathological process in CH.

4. PRINCIPLE OF HERBAL SYNERGY AND FORMULATION DESIGN IN THE “MISOCHOLIC TAB” PRESCRIPTION

Artichoke (*Extractum Cynarae Succus*) serves as the chief herb (quan duoc) in the formula. In traditional medicine, it functions to soothe the Liver (thu can), benefit the Gallbladder (loi dom), and clear damp-heat (thanh thap nhiet), thereby exerting anti-inflammatory, hepatoprotective, and choleric effects. According to traditional medical theory, CH is associated with the accumulation of damp-heat in the Middle Burner, leading to Spleen deficiency and stagnation of Liver Qi. Accordingly, artichoke is employed to soothe the Liver and promote bile flow while clearing damp-heat, thus restoring the Liver - Spleen harmony and addressing the underlying cause of the disorder.

Pig bile (*Extractum Fel Suillum*) serves as the deputy component (than duoc) in the formulation, complementing artichoke in addressing the core pathogenic mechanism of the disorder. Characterized by its bitter flavor and cold nature, pig bile is highly effective in clearing heat and detoxifying. By clearing accumulated damp-heat and promoting Gallbladder function, it helps regulate Liver Qi and harmonize the Middle Burner. The combination of artichoke and pig bile produces a synergistic therapeutic effect: while artichoke primarily acts on soothing the Liver, benefiting the Gallbladder, and clearing heat to restore harmony between the Liver and Spleen, pig bile provides potent damp-heat-clearing and detoxifying actions. This complementary interaction enhances the elimination of pathogenic factors and contributes to the re-establishment of balance between the two organs.

Garlic (*Bulbus Allii Sativi*) functions both as an adjunct (ta duoc) and envoy herb (su duoc) within the formulation. It possesses by warming the Middle Burner (on trung), dispersing stagnation (hanh tre), detoxifying (giai doc), and eliminating pathogens (sat trung). As an adjunct herb, garlic works in conjunction with artichoke to enhance antioxidant defenses, a critical process in the pathophysiology of CH, where oxidative stress plays a pivotal role. When combined with pig bile, garlic further strengthens the formulation's anti-inflammatory and antimicrobial activities. In its role as an envoy herb, garlic's warm property and affinity for the Spleen and Stomach meridians help regulate middle burner functions, thereby maintaining internal balance and ensuring the overall coordination and effectiveness of the prescription.

Taken together, the components form a comprehensive therapeutic system that simultaneously targets the underlying pathogenic factors—dampness and damp-heat—while regulating the two principal organs involved in the disease mechanism, the Liver and Spleen. In addition, the formulation may address key clinical manifestations such as jaundice and hypochondriac pain.

5. RESEARCH AND DEVELOPMENT TREND

Research on herbal agents for the treatment of liver diseases has gained increasing attention and is progressing toward an evidence-based scientific approach. The overarching aim is to transform traditional empirical knowledge into standardized pharmaceutical products supported by robust scientific validation and suitable for clinical application.

From empirical experience to scientific evidence: The implementation of experimental research represents an essential key step in the modernization and scientific validation of Traditional Medicine. This study provides preliminary scientific evidence, establishing the theoretical basis and foundational support for subsequent experimental investigations and future clinical trials in humans.

Elucidating molecular mechanisms of action: Modern research extends beyond evaluating macroscopic clinical parameters of CH—such as liver enzymes and hepatic function—to an in-depth exploration of molecular and cellular mechanisms. These include the regulation of oxidative stress in CH, as well as the processes underlying hepatocellular protection and the promotion of tissue regeneration following chronic injury.

Recent studies on CH have focused on elucidating several key mechanisms, including: Antioxidant activity and mitochondrial protection; quantification of pro-inflammatory cytokine expression, such as TNF- α and IL-6; regulation of the gut–liver axis; and inhibition of fibrosis and metabolic stress.

The standardization and development of modern dosage forms: To ensure consistent quality, safety, and therapeutic efficacy, herbal products must be standardized—from raw material cultivation under GACP guidelines to manufacturing processes compliant with GMP standards. The development of modern pharmaceutical dosage forms markedly improves treatment adherence, storage stability, and transportability compared with traditional decoction-based preparation. "Misochoic tab", formulated as a tablet, represents a typical example of this advancement.

Integration of traditional and modern medicine: It is essential to develop integrated treatment guidelines that combine traditional medicine with modern medical approaches to ensure the sustainability and effectiveness of this direction. For example, traditional medicine-based preparations may be used adjunctively with corticosteroid therapy in the management of CH to enhance therapeutic efficacy and potentially reduce corticosteroid-associated adverse effects.

6. CONCLUSION

Chronic hepatitis remains a highly prevalent hepatic disorder that imposes a significant clinical and societal burden, with several therapeutic challenges persisting despite advances in modern medicine. Vietnamese

Traditional Medicine, with its extensive materia medica and well-established theoretical system, offers valuable potential for developing safe and effective adjunctive therapies.

Emerging experimental and clinical studies have increasingly clarified the pharmacological effects of various traditional Vietnamese medicinal substances. Misochoic tab exemplifies a multi-target, synergistic approach that integrates symptomatic relief with interventions directed at the underlying pathogenesis, including clearing damp-heat and regulating Liver–Spleen functions.

In the future, herbal therapies for liver diseases may be further advanced through the systematic integration of traditional medical knowledge with validation derived from modern scientific researching. Through stringent standardization—from cultivation to manufacturing—as well as continued experimental and clinical evaluation, evidence-based traditional formulations have the potential to become safe, effective, and reliable components of integrated treatment strategies, ultimately improving patient outcomes and quality of life.

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