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Research Article

Protective Effects of *Dendrobium huoshanense* on Acute Alcohol-Induced Intoxication and Associated Hepatogastric Injury

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Abstract

Background: Acute alcohol-induced intoxication is a dangerous condition caused by excessive short-term alcohol consumption and can lead to a series of liver- and stomach-related injuries. Although studies have shown that *Dendrobium huoshanense* exerts a protective effect against *hepatogastric* injury, the precise mechanisms through which this plant affects acute alcohol intoxication and associated *hepatogastric* injury remain to be fully elucidated. Therefore, this study aimeds to investigate the effects of *Dendrobium huoshanense* on the duration of acute alcohol-induced intoxication and to elucidate the associated protective mechanisms against acute alcohol-induced *hepatogastric* injury. **Methods**: Mouse models of acute alcohol-induced intoxication and acute alcohol-induced *hepatogastric* injury were established by intragastric administration of 53% ethanol at a dose of 15 mL/kg. Before establishing the acute alcoholic hepatic and gastric injury model in mice, each group received the following dose interventions for 14 consecutive days. Three *Dendrobium huoshanense* dosage groups were established at 7.8 g/kg, 3.9 g/kg and 1.95 g/kg. A positive control group was also included and received either Haiwang Jinzun at 3.9 g/kg or omeprazole at 0.026 g/kg. Anti-alcohol effects were evaluated by measuring intoxication latency and duration, conducting histopathology, performing biochemical assays, and analyzing enzyme-linked immunosorbent assay (ELISA) results. **Results**: *Dendrobium huoshanense* could prolong the acute alcohol-induced intoxication latency and shorten the duration of intoxication. *Dendrobium huoshanense* could also increase the levels of alcohol dehydrogenase and aldehyde dehydrogenase, and reduce the ethanol concentration in the liver, indicating that *Dendrobium huoshanense* has an anti-alcohol effect. In addition, *Dendrobium huoshanense* has been shown to possess the capacity to ameliorate the morphological abnormalities observed in hepatocytes and gastric mucosal cells in response to acute alcohol-induced *hepatogastric* injury. *Dendrobium huoshanense* can also alleviate oxidative stress and lipid metabolic disorders in the liver, while concurrently suppressing alcohol-induced inflammatory responses in both the liver and stomach. **Conclusions**: These findings indicate that *Dendrobium huoshanense* has an anti-alcohol effect and can effectively alleviate acute alcohol-induced *hepatogastric* injury.

Keywords: *Dendrobium huoshanense*; acute alcohol-induced liver injury; alcohol use disorder; oxidative stress; inflammation; gastric mucosal injury

1. Introduction

In China, the culture of alcohol consumption has spanned thousands of years of history. Whether at business banquets or gatherings of family and friends, baijiu (Chinese liquor) has been an essential component. Following ingestion, the primary sites of alcohol absorption are the stomach and small intestine, with the majority of its metabolism occurring in the liver [1]. Approximately 90% of ethanol is metabolised in the liver by enzymatic reactions involving alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH), ultimately converting it into carbon dioxide and water for excretion [2]. However, it is important to note that excessive alcohol consumption can have a detrimental effect on the human body, particularly on the liver and the gastric mucosa [3,4].

Consuming more alcohol than your body can handle quickly leads to acute alcohol intoxication. Acute alcohol-induced intoxication is generally hypothesised to progress through three distinct stages. The initial phase is characterised by feelings of elation and heightened excitement, known as the excitement stage. The second stage is the ataxia stage, which is characterised by unsteady gait, limb swaying, slurred speech, and similar symptoms. The third stage is the lethargy stage, during which one person may lose consciousness [5]. Acute alcohol-induced intoxication has the potential to result in coma and multi-organ

damage, including the liver, stomach, and nervous system. As the majority of ethanol is metabolised in the liver, and the first-pass metabolism occurs in the stomach, acute alcohol-induced hepatogastric injuries are the most common alcohol-related diseases in clinical settings. As indicated by statistical data, approximately 5.9% of deaths on a global scale each year are attributable to excessive alcohol consumption, which is equivalent to approximately one death per minute [6].

The pathogenesis of alcohol-induced hepatogastric injury is a highly complex process, with multiple factors contributing to its development and progression [7]. Alcoholic liver injury is primarily associated with the direct toxic effects of ethanol and its metabolite acetaldehyde, as well as oxidative stress and the involvement of inflammatory cytokines [8]. Among these, oxidative stress and inflammation are regarded as the most critical factors in initiating alcoholic liver disease [9]. It has been demonstrated that antioxidant mechanisms provide a protective effect against hepatic injury [10]. Furthermore, additional research confirms that oxidative stress is a key contributor to cellular damage and apoptosis [11]. It has been demonstrated that the metabolism of ethanol accelerates the production of free radicals and depletes endogenous antioxidants, thereby contributing to the development of alcoholic hepatitis and other alcohol-related liver disorders [12,13]. Initially, the condition is characterised by the manifestation of alcoholic fatty liver. In the absence of intervention, the condition has the potential to escalate to more severe liver diseases, including cirrhosis and hepatocellular carcinoma [14]. During the process of alcohol metabolism, the stomach is the first organ to come into contact with ethanol. Due to its lipophilic nature, ethanol readily penetrates the gastric mucosa, inducing direct cellular injury. The impairment of the gastric mucosa also leads to the back-diffusion of hydrogen ions from the gastric juice into mucosal epithelial cells, triggering the release of mediators such as histamine, 5-hydroxytryptamine, and heparin. This results in an increase in mucosal capillary pressure and permeability, causing mucosal congestion, red blood cell exudation, and other damage. In severe cases, the occurrence of gastric perforation is a possibility [15].

At present, acute alcohol-induced intoxication and the associated hepatogastric injury pose a grave threat to public health. In clinical settings, apart from alcohol abstinence and symptomatic treatment, no effective therapy is available. Nevertheless, the attainment of sustained abstinence proves challenging for a significant number of individuals. Furthermore, medications such as antibiotics, non-steroidal anti-inflammatory drugs, remdesivir, tocilizumab, tofacitinib, and dexamethasone may inevitably cause liver changes, which carry risks of adverse effects [16]. Consequently, there is an urgent need to identify natural medicines that can effectively address acute alcohol-induced intoxication and associated hepatogastric injury without causing additional side effects.

Dendrobium huoshanense C. Z. Tang & S. J. Cheng (DHP) is classified within the genus *Dendrobium*, which is itself categorised within the Orchidaceae family. This perennial herb is utilised for both culinary and medicinal purposes. Dendrobium is a traditional Chinese medicinal herb. Research has shown that, in addition to alleviating ethanol-induced liver damage, it can also improve ethanol-induced acute gastric mucosal damage by inhibiting oxidative stress and inflammatory responses [17–19]. Modern research has revealed that DHP contains several bioactive components, including polysaccharides, amino acids, bibenzyls, and flavonoids, each contributing to its hepatoprotective and gastroprotective effects. Among these, polysaccharides are considered the primary active constituents [20,21]. Polysaccharides are defined as natural macromolecular polymers, which are typically formed by the polymerisation of more than 10 monosaccharides through α- or β-glycosidic bonds. These compounds are found in a wide variety of organisms, exhibiting significant anti-tumour properties. Furthermore, they have been shown to mitigate alcohol-induced liver and gastric mucosal damage by modulating oxidative stress and inflammatory pathways [22–25]. Consequently, we hypothesise that *Dendrobium huoshanense* may also protect the liver and stomach by accelerating alcohol metabolism, inhibiting oxidative stress, and suppressing inflammatory responses, thus alleviating the damage caused by alcohol to the body. The present study will entail the execution of experiments to investigate the protective effects of DHP against acute alcohol-induced intoxication and hepatogastric injury, as well as its underlying mechanisms. The present study aims to elucidate the protective mechanisms of DHP against acute alcohol-induced intoxication and associated hepatogastric injury (Fig. 1). The findings will provide new insights for alleviating alcohol-related harm and demonstrating the therapeutic value of DHP.

2. Materials and Methods

2.1 Chemicals and Reagents

Haiwang Jinzun (HWJZ) tablets were purchased from Shenzhen HaiWang Health Technology Development Co., Ltd (King Drink, Guangdong, China). Omeprazole (OME) was bought from Qingfeng Pharmaceutical Group (Bangkaxin, Guangdong, China). Anhydrous ethanol of analytical grade was acquired from Yantai Shuangshuang Chemical Co., Ltd (Shangshuang, Shandong, China). ELISA kits for mice ADH, ALDH, alanine aminotransferase (ALT), aspartate aminotransferase (AST), interleukin (IL)-6, IL-1β, IL-10 and tumor necrosis factor-α (TNF-α), and assay kits for ethanol content, mice triglyceride (TG), cholesterol (TC), malondialdehyde (MDA), superoxide dismutase (SOD), and glutathione (GSH) were purchased from Shanghai Jianglai Biotechnology Co., Ltd. (Jianglai,

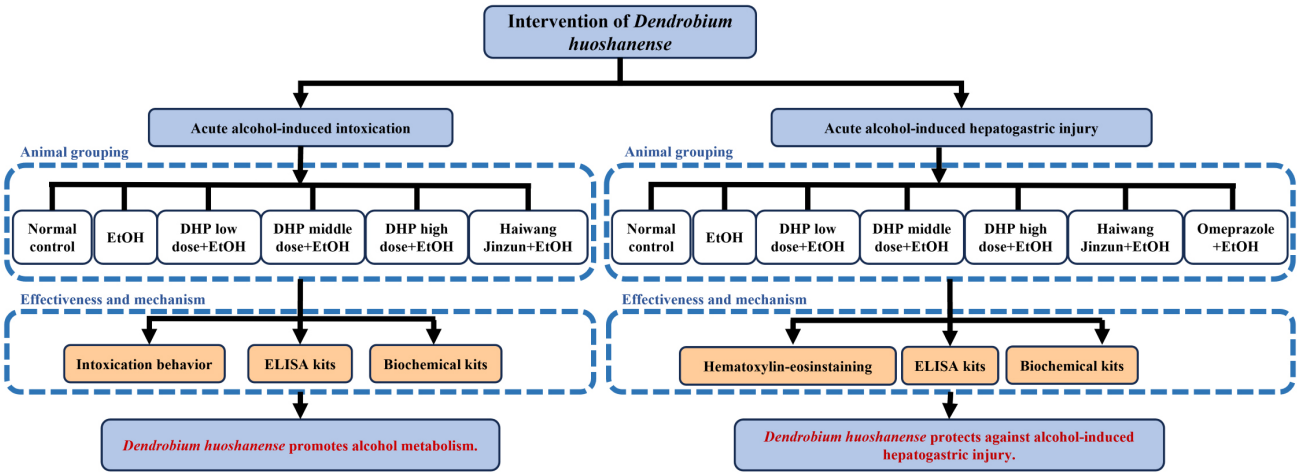

Fig. 1. Schematic diagram of the study design.

Shanghai, China). Xylene was purchased from Tianjin Kaitong Chemical Co., Ltd (Kaitong, Tianjin, China). The hematoxylin staining solution, alcohol-soluble eosin staining solution, and neutral gum were purchased from Anhui Xinle Biotechnology Co., Ltd. (Ebiogo, Anhui, China). Isoflurane was purchased from the manufacturer: Hebei Jinda Fu Pharmaceutical Co., Ltd. (RWD, Hebei, China).

2.2 Preparation of DHP, Haiwang Jinzun, and Omeprazole Solution

The fresh stems of *Dendrobium huoshanense C. Z. Tang & S. J. Cheng* were obtained from the base of Huoshan Changchong Chinese-Herbal Medicine Development Co., Ltd. (Anhui, China) and were identified by Professor Nianjun Yu of Anhui University of Chinese Medicine. About 20 g of fresh DHP stems were weighed, and a fourfold volume of ultrapure water (80 mL) was added. Then, this mixture was homogenised by a wall-breaking machine (MJ-PB13E233, Midea, Guangdong, China). The filtrate was collected and freeze-dried by a vacuum freeze-dryer (LGJ-10, SongyuanHuaxing, Beijing, China). According to the drying rate of 15.91%, the freeze-dried powder was dissolved using ultrapure water, preparing DHP solution with a concentration of 780 mg/mL. HWJZ tablets and OME tablets were ground into a fine powder, and then 1.56 g HWJZ powder and 0.104 g OME powder were individually weighed and dissolved in 40 mL ultrapure water to prepare the HWJZ solution with a concentration of 0.039 g/mL and the OME solution with a concentration of 0.0026 g/mL.

2.3 Animal Experiments

Male SPF-grade ICR mice (20–23 g) were purchased from Henan Sk Bioscience & Technology Co., Ltd (Henan, China). All animal experiments were approved by the Animal Experimental Ethics Committee of Anhui University of Chinese Medicine (animal experimental ethics number: AHUCM-mouse-2023169).

The determination of the dose for acutely alcohol-intoxicated mice was based on the alcohol content of common commercial beverages and relevant literature [26,27]. Five groups of mice (10 mice per group) were administered 53% ethanol solution via gavage at doses of 12 mL/kg, 13 mL/kg, 14 mL/kg, 15 mL/kg, and 16 mL/kg, respectively. The dose required to induce loss of righting reflex without mortality was observed. The experimental results indicated that 15 mL/kg was the optimal dose for inducing intoxication.

To investigate the protective effect of DHP against acute alcohol-induced intoxication, mice were acclimated for 7 days, and then were randomly divided into six groups (10 mice each group): normal control (NC) group, alcohol-induced intoxication model (AIIM) group, HWJZ treatment group (3.9 g/kg) and DHP treatment groups at high dose (DHP-H, 7.8 g/kg), medium dose (DHP-M, 3.9 g/kg) and low dose (DHP-L, 1.95 g/kg). The DHP-L group of mice received an oral gavage dose based on the daily recommended 30 g intake of fresh *Dendrobium huoshanense* in the Chinese Pharmacopoeia. Using an adult body weight of 60 kg as the standard, the equivalent dose for mice was calculated as 1.95 g/kg. Both the NC and AIIM groups received equivalent volumes of saline by oral gavage. Refer to Feng's method [28], thirty minutes after administration, the NC group received saline, while the other groups were administered 53% ethanol (15 mL/kg) by oral gavage. The motor behaviour of mice was recorded, and the degree of intoxication was calculated based on the loss and restoration of the righting reflex. In this calculation, alcohol-induced intoxication latency was defined as the time from oral gavage of ethanol to the loss of the righting reflex, and the recovery time was defined as the time from the loss to the restoration of the righting reflex. Liver samples were collected 2 h after alcohol administration.

To explore the protective effect of DHP on acute alcohol-induced hepatogastric injury, mice were first acclimated for 7 days and then randomly divided into seven

groups (10 mice each group): normal control (NC) group, alcohol-induced hepatogastric injury model (AHIM) group, HWJZ treatment group (3.9 g/kg), OME treatment group (0.0026 g/kg), DHP treatment groups at high dose (DHP-H, 7.8 g/kg)), medium dose (DHP-M, 3.9 g/kg) and low dose (DHP-L, 1.95 g/kg). Equivalent volumes of saline were administered by oral gavage for both the NC and AHIM groups. Refer to Zhang *et al.*'s [29] and Liang *et al.*'s [30] methods, after 14 consecutive days of administration, mice were fasted for 12 h and then administered 53% (v/v) ethanol (15 mL/kg) by oral gavage. Serum, liver, and stomach samples were collected 6 h after ethanol administration.

2.4 Collection of Biological Samples

Mice were anesthetised using a vaporiser for isoflurane (R5835, RWD, Guangdong, China). The procedure was as follows: after removing the mice's whiskers, the mice were placed in an anaesthesia induction box. The isoflurane concentration was set at 3%–5%, and the oxygen flow rate was approximately 1 L/min. Once the righting reflex disappeared, the mice were transferred to the operating table. A mask was used to cover the nasal area, and the isoflurane concentration was reduced to 1%–1.5%, with the oxygen flow rate lowered to 0.2–0.4 L/min to maintain the anaesthesia state. During the blood-collection process, the breathing and muscle relaxation of the mice were closely monitored to prevent excessive anaesthesia, which could lead to mouse mortality. All mice were euthanised by cervical dislocation according to the AVMA Guidelines on Euthanasia (2020). Blood samples were immediately centrifuged at 12,000 rpm for 10 min at 4 °C, and the resulting serum was collected and stored at –80 °C.

The right lobe of the liver and the gastric corpus from three mice per group were fixed in 4% paraformaldehyde for pathological sectioning and staining. Separately, serum, the left lobe of the liver, and dissected stomach tissue from eight mice per group were stored at –80 °C for ELISA and biochemical analyses.

2.5 Biochemical Analyses

To evaluate the protective effect of DHP against acute alcohol-induced intoxication and hepatogastric injury, we analysed a series of biochemical and inflammatory markers according to the manufacturer's protocols using a microplate reader (EnSight, PerkinElmer, Norwalk, CT, USA) and calculated the results according to the standard-curve equation in **Supplementary Table 1** of the **Supplementary Materials**. The measured indicators included hepatic ethanol, ADH, and ALDH levels in acutely intoxicated mice, as well as serum AST and ALT levels, hepatic TG, TC, MDA, GSH, SOD, IL-6, IL-1β, and TNF-α, and gastric IL-6, IL-10, IL-1β, and TNF-α levels in mice with acute alcohol-induced hepatogastric injury.

2.6 Histopathological Study

Liver and gastric tissues were fixed in 4% paraformaldehyde, dehydrated through a graded ethanol series, cleared in xylene, and embedded in paraffin. Sections were cut at a thickness of 5 µm, baked at 66 °C for 20–30 min, and then deparaffinised in xylene (three times, 5 min each). Following rehydration through a descending ethanol series (100%, 95%, and 80%, 3 min each) and a subsequent rinse under running water, the sections were stained with haematoxylin for 2–5 min. This was followed by differentiation in 1% hydrochloric acid, alcohol, and bluing in saturated lithium carbonate solution, with thorough water rinses between each step. After dehydration in 95% ethanol for 2 min, the sections were stained with eosin for a few seconds, followed by dehydration with 95% ethanol (twice, 5–10 min each) and 100% ethanol (twice, 1 min each), and clearing with once phenol-xylene and twice xylene (2 min each) [31,32]. Finally, the sections were mounted with neutral gum and observed under an Olympus microscope (CX41, Tokyo, Japan).

2.7 Statistical Analysis

The data are expressed as mean ± standard deviation (SD). One-way analysis of variance (ANOVA) was performed for statistical evaluation using Prism 9.5 software (GraphPad Software, La Jolla, CA, USA) and SPSS 27.0 software (SPSS Inc., Chicago, IL, USA). p-values less than 0.05 were considered statistically significant ($n = 8$ per group).

3. Results

3.1 The Protective Effect of DHP Against Acute Alcohol-Induced Intoxication

3.1.1 Effect of DHP on the Behaviour of Acutely Alcohol-Intoxicated Mice

To assess the preventive effect of DHP against intoxication, this study used the intoxication latency and intoxication duration as key behavioural indicators. As shown in Table 1, after intragastric administration of ethanol, mice exhibited intoxication latency of 3.27–9.98 min and intoxication duration of 247.73–358.43 min, respectively. Preventive administration of DHP significantly delayed the onset of intoxication and markedly accelerated recovery from intoxication.

3.1.2 Effect of DHP on Alcohol Metabolism in Acutely Alcohol-Intoxicated Mice

In this study, we investigated the protective effect of DHP against acute alcohol-induced intoxication by measuring the levels of ethanol and its metabolic enzymes in the liver. As depicted in Fig. 2, the concentrations of ethanol and its metabolic enzymes in the mice's livers were measured 2 h after alcohol administration. The results showed that compared with the NC group, the AIIM group exhib-

Table 1. Effects of DHP on intoxication latency, intoxication duration, and intoxication rate in acutely intoxicated mice.

Groups	Intoxication (n)	Sober (n)	Intoxication latency (min)	Intoxication duration (min)	Intoxication rate (%)
AIIM	8	0	4.64 ± 2.23	308.38 ± 39.60	100
DHP-L	8	0	8.62 ± 3.58	224.26 ± 33.55***	100
DHP-M	7	1	14.56 ± 9.09***	230.72 ± 31.86***	87.5
DHP-H	7	1	10.17 ± 5.37*	200.83 ± 26.62***	87.5
HWJZ	7	1	11.83 ± 0.97**	193.23 ± 4.36***	87.5

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$ *vs* AIIM group. Eight technical replicates per experiment (n = 8) were adopted, and values were expressed as mean ± standard deviation.

DHP, *Dendrobium huoshanense C. Z. Tang & S. J. Cheng*; AIIM, alcohol-induced intoxication model; L, low-dose; M, medium dose; H, high-dose; HWJZ, Haiwang Jinzun.

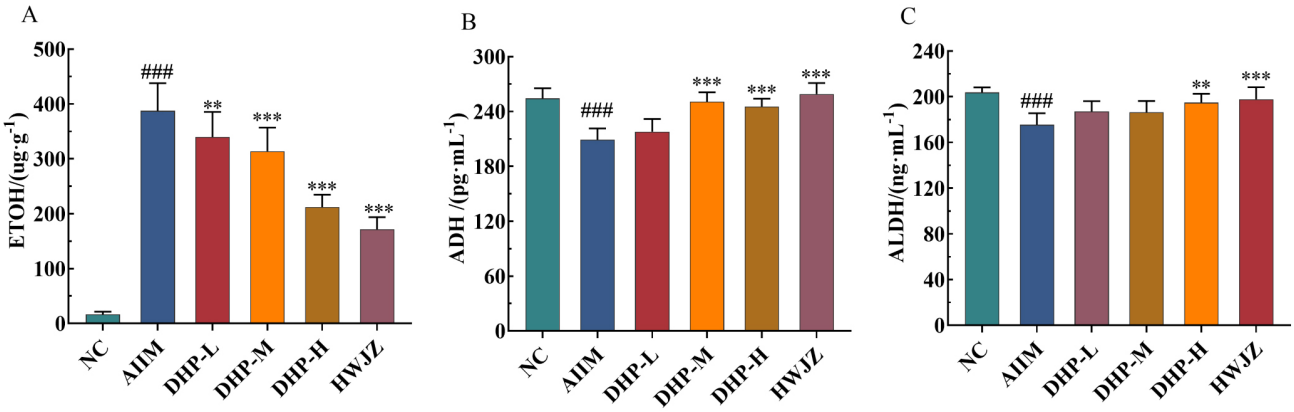

Fig. 2. Effect of DHP on hepatic ethanol (A), ADH (B), and ALDH (C) levels in acutely alcohol-intoxicated mice. $^{###}p < 0.001$ *vs* NC group. **$p < 0.01$, ***$p < 0.001$ *vs* AIIM group. Eight technical replicates per experiment (n = 8) were adopted, and values were expressed as mean ± standard deviation. DHP, *Dendrobium huoshanense C. Z. Tang & S. J. Cheng*; ADH, alcohol dehydrogenase; ALDH, aldehyde dehydrogenase; NC, normal control; AIIM, alcohol-induced intoxication model.

ited a significant increase in hepatic ethanol concentration and a significant decrease in both ADH and ALDH levels, indicating that alcohol markedly impaired the liver's ability to metabolise ethanol. After preventive intervention with DHP, the hepatic ethanol levels in all dose groups decreased compared with the AIIM group, and the activities of ADH and ALDH increased.

3.2 Effect of DHP on Acute Alcohol-Induced Hepatogastric Injury in Mice

3.2.1 Histopathological Analysis of Mice Liver and Gastric Mucosal Tissues

The protective effects of DHP on acute alcohol-induced hepatogastric injury in mice were initially investigated by examining pathological changes in both liver tissue and gastric mucosa. As shown in Fig. 3A, the gastric mucosal structure in the NC group remained intact, exhibiting a pink-coloured surface with smooth folds and no observable congestion, oedema, or damage. In contrast, the AHIM group exhibited severe gastric mucosal injury, characterised by obvious congestion, oedema, dark red discolouration, and the presence of punctate or linear haemorrhages, as well as localised erosion [19]. Pretreatment with DHP or the positive control drug OME significantly ameliorated these pathological changes. Both the OME and DHP groups displayed largely intact gastric mucosal architecture with significantly reduced haemorrhage. The DHP-L group also showed a substantial protective effect, presenting only mild congestion and a lesser overall severity of tissue damage compared to the AHIM group. Haematoxylin-eosin (H&E) staining revealed that the NC group has a well-organised gastric mucosal structure with intact cells, regularly arranged glands and no signs of tissue defect, haemorrhage or inflammation (Fig. 3B). In contrast, the AHIM group showed extensive necrosis and exfoliation of epithelial cells, a large number of red blood cells in the mucosal layer, cellular swelling, and disorganised structure, as well as significant inflammatory infiltration and oedema. Treatment with DHP alleviated these alterations. The DHP-L group showed only focal epithelial necrosis and minimal red blood cell or inflammatory cell infiltration. A more pronounced histological improvement was noted with increasing DHP doses.

As shown in Fig. 3C,D, the liver in the NC group appeared plump and rosy, with a clear structural pattern; hepatocytes were arranged in an orderly, radial pattern around the hepatic sinuses. In addition, hepatocytes appeared plump and intact without signs of degeneration or

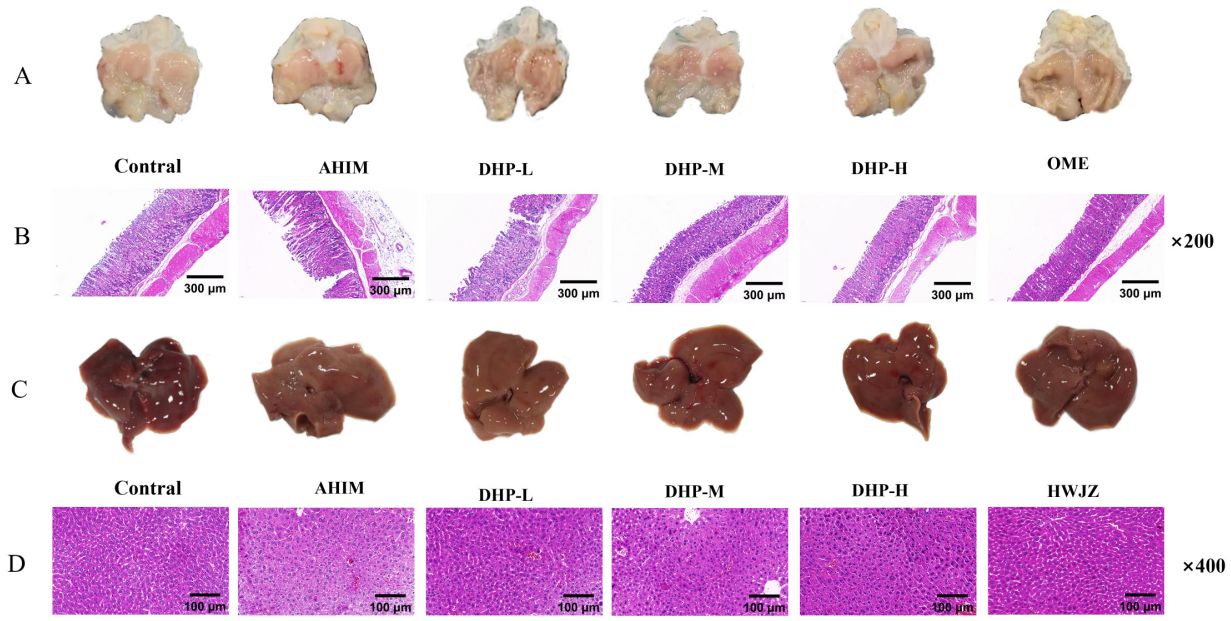

Fig. 3. The protective effects of *Dendrobium huoshanense* on acute alcohol-induced hepatogastric injury in mice. (A) Macroscopic images of the gastric mucosa. (B) Representative microscopic images of the gastric mucosa by H&E staining (200× magnifications). The scale bar: 300 μm. (C) Macroscopic images of the liver. (D) Representative microscopic images of the liver by H&E staining (400× magnifications). The scale bar: 100 μm. H&E, Haematoxylin-eosin.

necrotic cells, and no sinusoidal congestion was observed. In contrast, in the AHIM group, the liver was generally enlarged and pale in colour, exhibited localised congestion, abundant cytoplasmic vacuoles within hepatocytes, disorganised tissue structure, loosely arranged hepatocytes, and occasional focal hepatocyte necrosis, along with pyknotic and hyperchromatic nuclei, though without significant inflammatory cell infiltration. Compared to the AHIM group, the DHP-H group showed no obvious sinusoidal haemorrhage, a well-organised hepatic structure, and no marked necrotic cells or inflammatory cell infiltration. However, both the DHP-L and DHP-M groups still presented minor haemorrhage, scattered focal necrosis, disorganised hepatocyte arrangement with hydropic changes, and occasional fatty vacuoles. These results indicate that DHP confers a protective effect against acute alcohol-induced hepatogastric injury.

3.2.2 Effect of DHP on Serum ALT and AST Indexes in Acute Alcohol-Induced Hepatogastric Injury Mice

As presented in Fig. 4A,B, the serum AST and ALT levels in the AHIM group were significantly elevated relative to the NC group, confirming that alcohol consumption has induced significant hepatocellular injury. All DHP-treated groups exhibited reduced ALT levels compared to the AHIM group, with the DHP-M and DHP-H groups showing notably greater and more consistent reduction. In contrast, the AST levels were significantly reduced only in the DHP-M and DHP-H groups.

3.2.3 Effect of DHP on Liver TG and TC Indexes in Acute Alcohol-Induced Hepatogastric Injury Mice

The significant elevation of the hepatic TG and TC levels in the AHIM group, as opposed to the NC group, is demonstrated in Fig. 4C,D. In contrast, DHP intervention significantly reduced these lipid levels.

3.2.4 Effect of DHP on Liver MDA, SOD, and GSH Contents in Acute Alcohol-Induced Hepatogastric Injury Mice

As shown in Fig. 5A, the AHIM group exhibited a significant increase in hepatic MDA content compared with the NC group, which indicates the successful establishment of acute alcohol-induced liver injury. However, administration of high- and medium-dose DHP significantly reduced hepatic MDA levels in a dose-dependent manner, which demonstrates that DHP effectively attenuates acute alcohol-induced lipid peroxidation and associated liver damage. As depicted in Fig. 5B,C, hepatic GSH and SOD levels were markedly decreased in the AHIM group relative to the NC group, which suggests the rapid depletion of antioxidants after heavy alcohol intake. In contrast, DHP intervention significantly restored GSH and SOD levels, with more pronounced effects observed in the DHP-M and DHP-H groups.

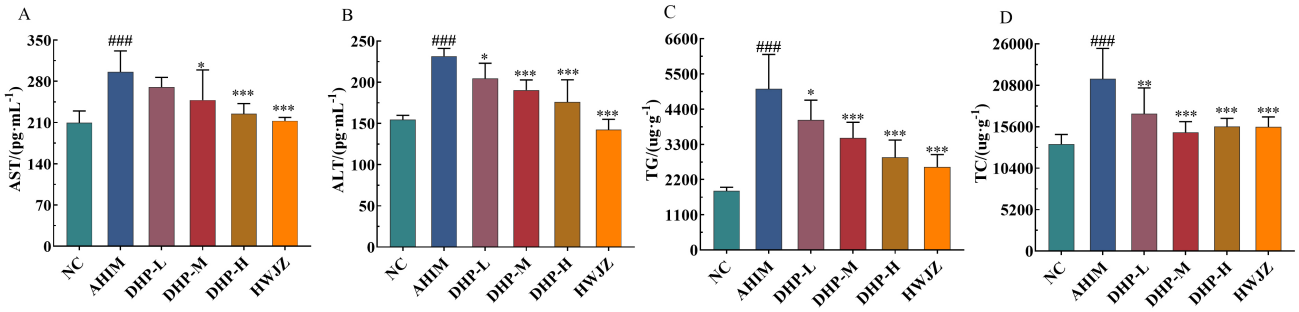

Fig. 4. The impact of DHP on liver and lipid metabolism in acute alcohol-induced hepatogastric injury mice. The serum levels of AST (A), ALT (B), the liver levels of TG (C), and TC (D) were evaluated. $^{###}p < 0.001$ *vs* NC group. $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$ *vs* AHIM group. Eight technical replicates per experiment (n = 8) were adopted, and values were expressed as mean ± standard deviation.

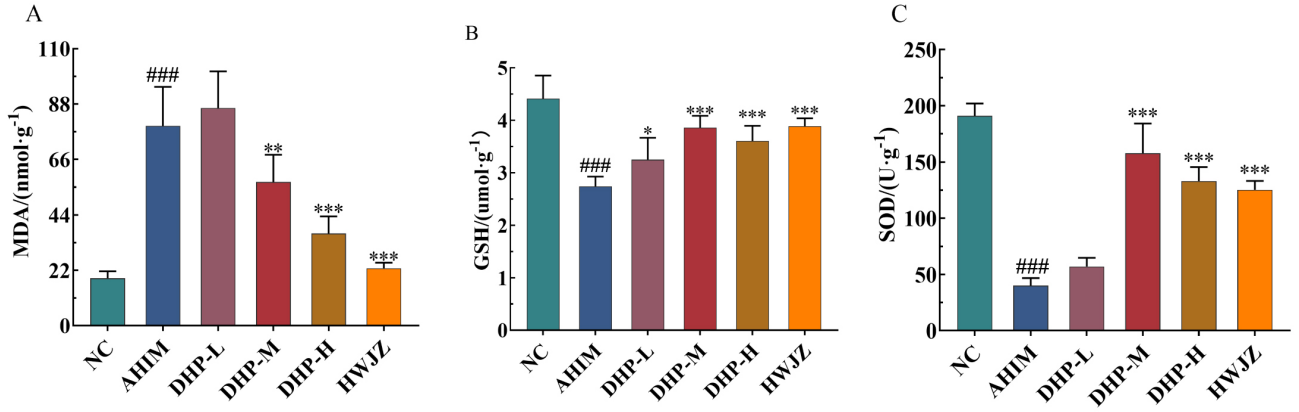

Fig. 5. Effect of DHP on liver MDA (A), GSH (B), and SOD (C) levels in acute alcohol-induced hepatogastric injury mice. $^{###}p < 0.001$ *vs* NC group. $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$ *vs* AHIM group. Eight technical replicates per experiment (n = 8) were adopted, and values were expressed as mean ± standard deviation. MDA, malondialdehyde; SOD, superoxide dismutase; GSH, glutathione.

3.2.5 Effect of DHP on Inflammatory Factors in Liver And Stomach Tissues of Acute Alcohol-Induced Hepatogastric Injury Mice

As illustrated in Fig. 6A–C, the liver IL-6, IL-1β, and TNF-α levels were markedly elevated in the AHIM group compared with the NC group. Conversely, DHP administration effectively reduced the levels of these pro-inflammatory cytokines, with the DHP-M and DHP-H groups showing particularly significant reductions. These results indicate that DHP mitigates alcohol-induced liver inflammation by suppressing the expression of IL-6, IL-1β, and TNF-α, thereby exerting a hepatoprotective effect. As shown in Fig. 6D–G, gastric tissue analysis revealed that the AHIM group had significantly elevated levels of pro-inflammatory cytokines, including IL-1β, IL-6, and TNF-α, and a reduced level of the anti-inflammatory cytokine IL-10 compared with the NC group. Conversely, the administration of DHP reduced the levels of these pro-inflammatory cytokines and increased the levels of anti-inflammatory factors. However, its regulation of the levels of TNF-α in the stomach is not statistically significant.

4. Discussion

Excessive alcohol consumption has been demonstrated to exert a detrimental effect on the human organism and to engender societal instability. The identification of a highly efficacious yet low-toxicity natural medicine is imperative in addressing this issue. In this experiment, we constructed models of acutely alcohol-intoxicated mice and acute alcohol-induced hepatogastric injury mice to verify the protective effects of DHP on hepatogastric damage and its anti-alcoholism efficacy from a more comprehensive perspective.

In order to provide further elucidation on the underlying mechanisms of DHP's protective effects, a histological analysis was performed on gastric and liver tissues. The results demonstrated that DHP effectively alleviated tissue damage induced by acute alcohol exposure. Histological analysis revealed that DHP significantly improved gastric mucosal and hepatocyte structures and reduced inflammatory cell infiltration in a dose-dependent manner. It is noteworthy that the protective effect of high-dose DHP was comparable to that of the positive control group. The results indicate that DHP possesses significant protective

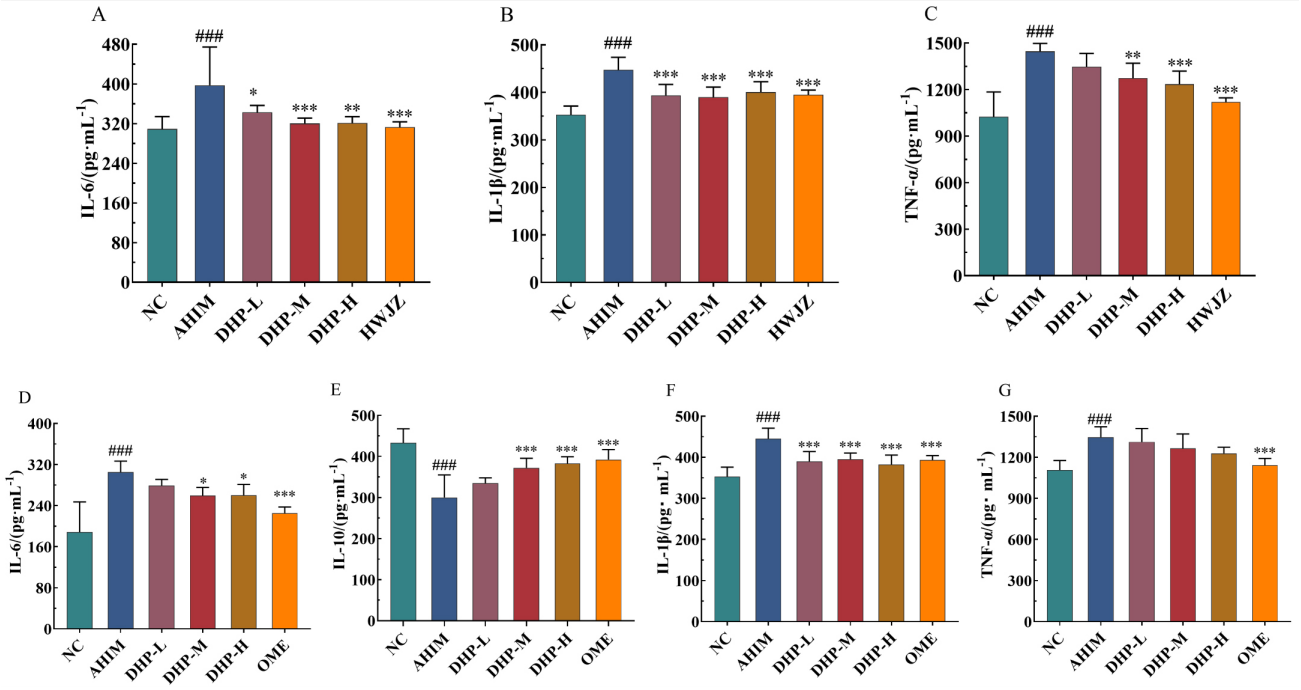

Fig. 6. Effect of DHP on the liver levels of IL-6 (A), IL-1β (B), and TNF-α (C), and the gastric levels of IL-6 (D), IL-10 (E), IL-1β (F), and TNF-α (G) in acute alcohol-induced hepatogastric injury mice. $^{###}p < 0.001$ *vs* NC group. $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$ *vs* AHIM group. Eight technical replicates per experiment (n = 8) were adopted, and values were expressed as mean ± standard deviation. IL, interleukin; TNF-α, tumor necrosis factor-α.

effects on gastric mucosa and hepatocytes, providing morphological evidence for its further development as a hepatogastric protective agent.

In addition to its protective effects on tissues, DHP also significantly mitigates behavioural impairments caused by acute alcohol intoxication. Following substantial ethanol intake, mice exhibit progressive central nervous system depression, leading to a sedated state. The righting reflex test is commonly employed to assess these behavioural changes. This test evaluates an animal's ability to regain its natural posture from a supine position and is a classical method for determining alcohol-induced intoxication levels through reflex competence assessment. The results of the righting reflex test indicate that DHP mitigates alcohol-induced narcosis and promotes recovery by delaying intoxication and shortening the recovery time.

This behavioural recovery improvement is likely due to DHP's modulation of key alcohol metabolism pathways. Alcohol metabolism is predominantly a hepatic process, involving two key enzymes: ADH and ALDH. The initial catalysis of ethanol oxidation to acetaldehyde is initiated by ADH, and this is subsequently broken down by ALDH into carbon dioxide and water. This process has been shown to reduce liver ethanol levels and promote the clearance of alcohol from the body. It has been demonstrated that variations in the activity of ADH and ALDH can directly influence liver ethanol concentrations [33]. The experimental results of this study indicate that DHP can reverse the alcohol-induced reduction in metabolic enzyme levels and promote alcohol decomposition through the restoration of these key enzymes' activity. In summary, the ingestion of DHP has been demonstrated to accelerate alcohol metabolism and alleviate the inhibitory effects of alcohol on metabolic enzymes.

The enhanced alcohol metabolism and reduced ethanol accumulation in the liver contribute to a reduction in alcohol-induced hepatocellular damage, which can be assessed through specific biomarkers. ALT and AST are two major transaminases primarily located within hepatocytes. In the event of hepatic injury, the release of these two enzymes into the bloodstream gives rise to elevated serum ALT and AST levels, which serve as indicators of hepatocellular damage. It is important to note that there is a discrepancy between the subcellular localisations of ALT and AST. ALT is predominantly present in the cytosol, and its elevation is indicative of hepatocellular membrane damage. Conversely, AST is distributed between the cytosol and mitochondria, and its increase signifies injury at the organelle level [34–36]. The present findings are consistent with those of previous studies, which indicate that acute high-dose alcohol induces hepatic injury in mice, with injury extending to the organelle level. The DHP intervention was found to mitigate the damage to both the cell membrane and the intracellular organelles, thereby exerting a substantial dose-dependent protective effect against alcohol-induced liver injury.

In addition to alleviating hepatocellular damage, DHP has also been demonstrated to improve alcohol-induced hepatic metabolic disorders. Among these, abnormalities in lipid metabolism represent one of the earliest and most typical pathological alterations in alcohol-induced liver injury. It is well-established that the primary and earliest hepatic pathological alteration induced by ethanol is steatosis, which involves the excessive deposition of lipid in hepatocytes. Consequently, the quantification of lipid contents, specifically TG and TC, has been identified as a reliable metric for evaluating the severity of alcohol-induced liver damage [37,38]. Bhardwaj *et al*. [39] pointed out that lipids are not only structural components of cell membranes but also key factors driving tumorigenesis and cancer progression. The absorption of lipids plays a significant role in tumour advancement [39], and thus, abnormalities in hepatic lipid metabolism may contribute to the development of hepatocellular carcinoma. The experimental results indicated that DHP could ameliorate alcohol-induced lipid metabolism disorder and exert a protective effect against alcoholic liver injury. This finding is consistent with a previous study, which identified polysaccharides as critical components in suppressing alcohol-induced rises in hepatic TC and TG [19]. The DHP solution utilised in this study is a polysaccharide-rich extract.

In addition to the regulation of metabolism, oxidative stress has been identified as a significant pathway through which alcohol can cause hepatic injury. The protective effect of DHP also extends to modulating this key pathological mechanism. Oxidative stress has been identified as a key pathological mechanism in acute alcohol-induced liver injury. The process of oxidative stress damage is a sequence of events that unfolds in a cascading manner. Initially, the cell's antioxidant capacity is depleted, resulting in the initiation of lipid peroxidation, which in turn attacks cell membranes. This process culminates in the fragmentation of DNA and the subsequent initiation of a cellular programme known as apoptosis [40]. Following ethanol intake, cytochrome P450 2E1 (CYP2E1) activity is significantly induced by elevated ethanol concentrations, whereas ADH activity is not induced. Under this condition, ethanol is predominantly metabolised to acetaldehyde via the CYP2E1 pathway, which generates substantial reactive oxygen species (ROS). The accumulation of ROS not only triggers lipid peroxidation, leading to liver damage, but also reduces the activity of critical antioxidant enzymes such as SOD and antioxidants like GSH [41,42]. MDA, a final product of lipid peroxidation, serves as a direct indicator of the extent of ROS-induced liver damage. Therefore, this study investigated the protective effect of DHP against acute alcohol-induced liver injury by measuring hepatic oxidative and antioxidative parameters in mice [43,44]. Experimental results indicated that DHP promptly enhanced the endogenous antioxidant defence system. Alcohol induced oxidative stress in the mice liver and impaired antioxidant capacity, while DHP pretreatment significantly reduced oxidative products and enhanced antioxidant markers, indicating its protective effect in acute alcohol-induced liver injury by regulating hepatic redox homeostasis.

The oxidative damage and metabolic disturbances induced by alcohol further trigger a systemic inflammatory response [39,45], which constitutes another crucial mechanism in the progression of alcohol-induced organ injury. It is important to note that this inflammatory cascade has the capacity to affect not only the liver but also other organs, such as the stomach. After heavy alcohol consumption, hepatic lipid deposition and oxidative stress activate the inflammatory response, triggering a significant increase in key pro-inflammatory mediators such as TNF-α, IL-6, and IL-1β, which in turn exacerbate liver injury and the inflammatory cascade. Similarly, high concentrations of alcohol directly compromise the gastric mucosal barrier, inducing the rapid production of pro-inflammatory factors, including TNF-α, IL-6, and IL-1β, and inhibiting anti-inflammatory factors like IL-10. This leads to the recruitment and infiltration of neutrophils, thereby worsening mucosal damage [46–49]. The experimental findings are in accordance with those of previous studies, which demonstrated that alcohol consumption results in an elevation of pro-inflammatory factor levels in the liver and stomach tissues. Conversely, DHP intervention has been observed to alleviate the liver and stomach abnormal inflammatory responses caused by alcohol to a certain extent, despite its gastroprotective effect being moderate in comparison to omeprazole.

The results of this study highlight the potential of DHP as a valuable natural product for managing or preventing alcohol-induced hepatogastric injury. The development of the substance as a supplement is a potential treatment option for the long-term management of liver and gastric damage. Despite the encouraging results obtained from this study, it is important to note that there are several limitations that should be acknowledged. It should be noted that all experiments were conducted on male mice, thereby excluding the evaluation of potential sex differences in drug effects. Mechanistic studies have primarily concentrated on acute alcohol-induced hepatogastric injury, while the effects of DHP on chronic hepatogastric injury have not been explored to any great extent. Furthermore, the bioavailability, metabolic pathways, and tissue distribution profiles of DHP warrant in-depth examination.

5. Conclusions

In summary, DHP accelerates the body's metabolism of alcohol by modulating the activity of hepatic ethanol-metabolising enzymes, significantly reducing the duration of intoxication in mice. Furthermore, DHP effectively alleviates acute, alcohol-induced hepatic and gastric damage in mice via several mechanisms, such as improving liver function, balancing hepatic lipid metabolism, regulating oxidative stress levels and inhibiting inflammatory responses in

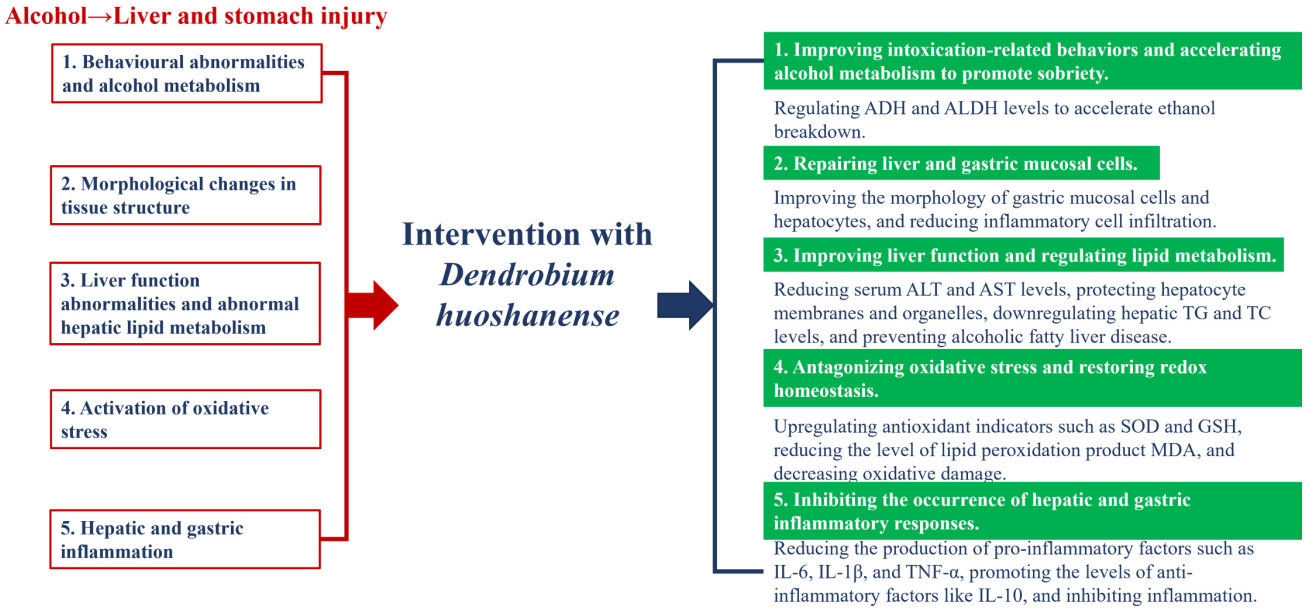

Fig. 7. Protective mechanism diagram of *Dendrobium huoshanense* against acute alcohol intoxication and associated hepatogastric injury.

hepatic and gastric tissues (Fig. 7). This study confirms that DHP is clearly effective in preventing acute alcohol intoxication and acute alcoholic liver and stomach injury. Furthermore, the efficacy of a high DHP dose is comparable to that of the commonly used clinical hepatoprotective drugs omeprazole and Haiwang Jinzun. This research provides experimental evidence for the innovative application of DHP as a hepatoprotective agent for high-risk populations (*e.g.*, chronic alcohol consumers), laying a crucial foundation for its subsequent development and clinical translation.

Availability of Data and Materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

YX, QZ and LH conceived the study and developed the research framework. JH, DP and HX were responsible for designing the experimental protocol. YX, WL and PZ were responsible for conducting the study. HX and DP provided assistance and advice. YX, YG and SJ were responsible for data analysis, whilst DP, SJ, YG and HX were responsible for data interpretation. YX, JH and YG drafted the initial manuscript. QZ, YG and WL revised the content and format of the manuscript. All authors participated in the editing and revision of the manuscript. All authors have read and approved the final draft. All authors were involved in the study throughout and agree to take responsibility for all aspects of the study.

Ethics Approval and Consent to Participate

All the experiments were performed based on the approved animal protocols and guidelines established by the Animal Experimental Ethics Committee of Anhui University of Chinese Medicine (animal experimental ethics number: AHUCM-mouse-2023169). All animal experiments adhere to the 3Rs principle: replacement, reduction and refinement. All animals were treated humanely, and all euthanasia procedures were carried out in accordance with the American Veterinary Medical Association's Guidelines for the Euthanasia of Animals.

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Conflicts of Interest

The authors declare no conflicts of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/IJP49475.

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