

# An Overview of the Pharmacological Studies and Clinical Applications of Chai Hu in Digestive Diseases

Chen Li<sup>1</sup>, Hui Ding<sup>2,\*</sup>

<sup>1</sup>Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China

<sup>2</sup>Shaanxi Provincial Hospital of Chinese Medicine, Xi'an 710003, Shaanxi, China

\*Correspondence Author

**Abstract:** Chaihu was first published in Shennong's Classic of the Materia Medica, and has been used in China for more than 2,000 years. It is derived from the Umbelliferae *Bupleurum Chinese DC* or *Bupleurum scorzonerifolium Willd.* Chaihu is distributed in many parts of China with rich output, among which Shaanxi, Shanxi, Gansu, Guizhou, Sichuan, Hebei, Henan, Hubei and other places as the main producing areas. Chaihu has a long history of application and is one of the oldest and most commonly used Chinese herbal medicine, with high medicinal value. Modern pharmacological studies have found that Chaihu has the ability to protect the liver, protect the gastric mucosa, enhance gastrointestinal motility, inhibit intestinal inflammation, anti-ulcer and other effects. Clinically, Chai Hu and Formulas with Chai Hu as the main herb are widely used in the treatment of digestive disorders, and their efficacy is remarkable. This paper presents a literature review of previous pharmacological studies and clinical applications of Chai Hu in digestive disorders, with the aim of providing a reference for better research on Chai Hu and its applications in clinical practice.

**Keywords:** Chai Hu, Pharmacological effect, Diseases of the digestive system, Literature review.

## 1. Introduction

Chaihu was first published in "Shennong's Classic of the Materia Medica", named Common Gromwell, the Han Dynasty's "Famous Doctors" and the Wei, Jin, and North and South Dynasties' "Wu Pu Materia Medica" called it mountain vegetable, Ru Cao, or Rue Artemisia, and the Tang Dynasty's "Newly Revised Materia Medica" for the first time called it Chaihu, and the "Essence of Materia Medica Pintxed", and called it Chai Cao, and then to the Ming Dynasty, Li Shizhen formally named it Chaihu in his "Materia Medica Compendium", which is in use to the present day [1]. Chaihu in our country are distributed in many places, including Shaanxi, Shanxi, Gansu, Guizhou, Sichuan, Hebei, Henan, Hubei and other places for the main production areas, and Hubei, Henan and Shaanxi provinces at the junction (Zijingguan area) produced by the best Chaihu, such as the "drug out of the production of the identification," said: "produced in Hubei Xiangyang, Xunyang various genera, Zijingguan, Mashangkou and so on for the upper." Chaihu is harvested in spring and fall, impurities and stumps are removed, washed, moistened, cut into thick slices, and dried for use, and different concoctions can be used to achieve different therapeutic effects, such as vinegared Chaihu to enhance the power of liver detoxification, wine Chaihu to enhance the power of ascension and dispersal, and turtle blood Chaihu to nourish the yin and blood to enhance the power of the blood, etc., of which vinegar-roasted Chaihu is commonly used in clinical practice [2].

## 2. Traditional Chinese Medicine's Knowledge of Chai Hu

Chaihu is bitter, flat, slightly cold, non-toxic, and belongs to the liver and gallbladder meridians. Its nature is light, clear and ascending, and it can promote penetration and evacuation, so it can evacuate and reduce fever, treating

externally-induced fever, and combining with *Scutellaria baicalensis* can conciliate Shao-yang, which is the main medicine for treating the evil in Shao-yang, and the exchanges of cold and heat. Such as "Shennong Ben Cao Jing" said: "..... go cold and heat evil gas.....", "Changsha medicinal interpretation" also said: ".....traveling between the exterior and the interior. It is effective in the meeting of the exchange of cold and heat.....". Chaihu can also be used to relieve liver depression, promote the flow of qi and blood, and is often used in the treatment of liver depression and qi stagnation in various diseases. Such as the "theory of medicinal properties" said: "..... declared smooth blood qi", "Shennong Ben Cao Jing" also said: "the main heart and abdomen, to go to the stomach and intestines in the knot gas.....". Chai Hu can also elevate yang qi, treating the symptoms caused by the subsidence of clear yang. "Lei Gong concocted medicinal solution" has said: 'Chai Hu odor rising Yang, can lift the lower yuan Qing Qi upward.....', tonifying the middle and beneficial qi soup, ascending Yang Yi stomach soup and ascending trapping soup are equipped with Chai Hu. Chaihu can also be used to treat malaria, such as in the Chaihu Anti-malaria Soup, in which Chaihu is used as the monarch. There is also Ji Yi Dong Dong's "medicine signs" cloud: "this test all the world so-called malaria, the chest bitter full and thirst, very effective.....".

## 3. Pharmacologic Study of Chai Hu in Digestive Diseases

### 3.1 Effects on the Liver

Yan He and others [3] used intraperitoneal injection of dimethylnitrosamine (DMN) to produce a rat liver fibrosis vascularization model. The SSD group was prophylactically treated with Chaihuisaponin D from day one of modeling. After the control test, it was found that Chaihu Saponin D could significantly reduce the levels of ALT and AST in

serum and the content of HA, LN and IV-C in extracellular matrix of liver in the model group rats. The levels of HA, LN and IV-C in serum and liver tissue were significantly decreased, and the enzyme activity of SOD in liver tissue was increased. It suggests that Chaihu saponin D has hepatoprotective and antifibrotic effects, and its mechanism may be related to the inhibition of lipid peroxidation. Zhu Y and others [4] used intraperitoneal injection of lipopolysaccharide (LPS) and D-aminogalactose 3 lactose (D-GalN) to produce a mouse model of liver injury. The SSA group was treated with Chaihu saponin A from the first day of modeling. In a controlled trial, it was found that Chai Hu Saponin A significantly reduced the levels of MPO, MDA and serum AST in the liver and inhibited the production of pro-inflammatory factors such as TNF- $\alpha$  and IL-1 $\beta$ , and its anti-inflammatory mechanism may be related to the increased ability of LXR $\alpha$  expression. It suggests that Chai Hu Saponin A has a protective effect against liver injury. Chen Y and others [5] used an intraperitoneal injection of carbon tetrachloride (CCL4) to model acute liver injury in mice, and the SSD group was treated with Chaihu Saponin D twenty four hours and half an hour before the start of the CCL4 injection as a prophylactic treatment. In a controlled test, it was found that SSD significantly reduced the levels of MDA and MSP, the mRNA expression of NLRP3, ASC and caspase 1, and the protein expression of caspase 1-P10, NLRP3, ASC, IL-1 $\beta$ , and IL-18, while the activities of SOD, GPX and CAT were increased in rats with acute liver injury. Chaihu saponin D protects the liver by inhibiting oxidative stress and NLRP3 activation of inflammatory vesicles to attenuate the extent of acute liver injury and achieve hepatoprotection.

### 3.2 Effects on the Stomach and Intestines

Xiaobo Sun [6] used Hcl-ethanol gavage to produce a mouse model of acute gastric mucosal injury, and the Chaihu polysaccharide group was treated with Chaihu polysaccharide as a prophylactic treatment fifty minutes before the start of modeling. It was found that the Hcl-ethanol-induced acute gastric mucous membrane injury in mice was effectively inhibited by the controlled test of Chaihu polysaccharide BR-2, indicating that it has a protective effect on the gastric mucous membrane. Shuai Wang and others [7] used anhydrous ethanol gavage to make a model of gastric mucosal injury in rats, and the Chaihu saponin group was treated with Chaihu saponin for intervention on the last day of modeling. After the control test, it was found that the ulcer index and MAD levels of the Chaihu saponin group were lower than those of the model group, and the levels of PGE2, which has a protective effect on the gastric mucosa, and SOD levels were higher than those of the model group. It indicates that Chaihu saponin has a significant protective effect on gastric mucosal damage. Yan Li and others [8] found through experimental studies that Chai Hu Hovenia Combination may enhance gastric emptying and peristaltic propulsion of the small intestine by increasing plasma gastric actin levels, and that the combination can keep plasma gastric actin at a high level. It has been shown that total saponins of Chaihu can both excite isolated guinea pig intestinal smooth muscle and enhance acetylcholine-induced contraction of isolated guinea pig small intestine [9]. Zhou F and others [10] produced a mouse model of colitis by means of sodium sulfate of gluconate (DSS) enemas, which were counter-treated with Chaihu Saponin A

prior to intragastric administration as well as during the administration of sodium sulfate of gluconate. After a controlled test, it was found that Chaihu saponin A significantly reduced the body weight, colon length and disease activity index of the model rats, as well as the level of MPO activity. Levels of the inflammatory cytokines TNF- $\alpha$  and IL-1 $\beta$  were also significantly reduced. Chaihu saponin A significantly reduced LXR $\alpha$  expression, NF- $\kappa$ B activation and I $\kappa$ B $\alpha$  phosphorylation in colon tissues. It suggests that Chai Hu Saponin A has a protective effect against DSS-induced colitis. Haiyan Ma and others [11] produced a rat gastric ulcer model by stress stimulation, ice-vinegar gavage and pyloric ligation, and the administered group was treated with Chaihu saponin for intervention before modeling. It was found that Chaihu saponin significantly decreased the ulcer index, number of ulcers, ulcer area, gastric juice secretion, pepsin activity, and total acidity of gastric juice in the model rats, and increased the PH of gastric juice in the model rats. It indicates that Chaihu saponin has a significant ameliorative effect on gastric ulcer in model rats. Lingbing He and others [12] found that the effective components of Chaihu saponin against ulcer are Chaihu saponin A, D, B2, I, E, prosaikogenin D, F, G, and so on, and there is a correlation between Chaihu saponin and the proliferation rate of human gastric mucosal epithelial cells.

## 4. Clinical Application of Chai Hu in Digestive Diseases.

### 4.1 Gastroesophageal Reflux Disease (GERD)

Kai Wang and others [13] used a randomized numerical table to divide seventy patients with gastroesophageal reflux disease (GERD) of bile-stomach disharmony type into two groups, the treatment group and the control group. Xiao Chaihu Tang with added subtraction (TCM) was given to the patients in the treatment group, and the control group was given patients with esomeprazole enteric-coated capsules. Both groups were observed after four weeks of treatment. The results showed that the total effective rate of the treatment group (85.7%) was significantly higher than the total effective rate of the control group (57.1%),  $P < 0.05$ , and the symptoms of depression and anxiety of the patients in the treatment group were significantly improved. Hongbin Niu [14] randomly divided eighty-four patients with gastroesophageal reflux disease (GERD) into a study group and a control group. Patients in the study group were given the formula of Chai Hu Shuo Liver San plus and minus, and patients in the control group were given morpholine. The course of treatment was two months in both groups. The results showed that the total effective rate in the study group (95.2%) was significantly higher than the total effective rate in the control group (76.2%).

### 4.2 Gastritis

Pu Miao [15] and others randomly divided ninety-four patients with bile reflux gastritis into observation and control groups. The control group was treated with the combination of trimethoprim maleate tablets and ursodeoxycholic acid tablets, and the observation group was treated with the addition and subtraction of Xiao Chaihu Tang on this basis. The course of treatment was three months in both groups. The results

showed that the total effective rate of the observation group (97.87%) was significantly higher than the total effective rate of the control group (74.47%),  $P < 0.05$ . Liansheng Chen [16] randomly divided eighty-six patients with chronic atrophic gastritis with liver-stomach disharmony evidence into a control group and an observation group. The patients in the control group were treated with morpholine, while the patients in the observation group were treated with the addition and subtraction of Chaihu Liver-Sparing Tang. The course of treatment was six months in both groups. The results showed that the total effective rate of the observation group (95.35%) was higher than the total effective rate of the control group (76.74%),  $p < 0.05$ . And the degree of gastric mucosal intestinal epithelial hyperplasia, atrophy and heterogeneous hyperplasia in the observation group were lower than those in the control group,  $P < 0.05$ .

#### 4.3 Peptic Ulcer

Zhenliang Wang [17] used Da Chaihu Tang to treat fifty-three patients with gastric ulcer. Among the fifty-three patients, thirty-eight patients were followed up, of which fifteen patients were cured, seventeen patients had significant effect, three patients were effective, and two patients were ineffective, with an overall effective rate of 94.74%. The total effective rate was 94.74%. And it was found that the decoction of Da Chai Hu Tang could kill *Helicobacter pylori*, increase blood SOD activity, and decrease blood LPO concentration. Fei Wang [18] randomly divided One hundred patients with gastric and duodenal ulcers into a treatment group and a control group. Patients in the treatment group were treated with Xiao Chaihu Tang, and patients in the control group were treated with Omeprazole enteric-coated tablets, aluminum thioglycollate and furazolidone. The course of treatment was six weeks in both groups. The results showed that the total effective rate of the treatment group (92%) was significantly higher than the total effective rate of the control group (84%),  $P < 0.05$ . And the improvement of clinical symptoms was more favorable in the treatment group. Fenqiang Huang [19] randomly divided One hundred and forty patients with ulcerative colitis into an observation group and a control group. On the basis of conventional treatments such as stopping diarrhea and correcting water and electrolyte disorders, the observation group was treated with Chai Hu and Paeonia lactiflora plus and minus formula, and the control group was treated with Liuzasulphadiazine enteric-coated tablets. Compare the results of the two groups after treatment. The results showed that the total effective (97.14%) of the observation group was higher than the total effective rate (87.14%) of the control group,  $P < 0.05$ . The symptom score of the observation group ( $5.61 \pm 2.46$ ) was lower than the symptom score of the control group ( $8.31 \pm 2.66$ ),  $P < 0.05$ .

#### 4.4 Functional Gastroenterology

Renfeng Li [20] conducted clinical observation on fifty-six patients with functional dyspepsia of liver-qi stagnation type, and the patients were divided into the treatment group and the control group by using the randomized numerical table method. Patients in the treatment group were treated with Chaihu Liver-Sparing and Depressant Tang, while patients in the control group were treated with Famotidine tablets. After thirty days of treatment in both groups, the efficacy of the two

groups was compared. The results showed that the total effective rate of the treatment group was 96.43%, and the total effective rate of the control group was 78.57%, compared with the control group, the therapeutic efficacy of the treatment group was more favorable,  $P < 0.05$ . And the treatment group had better symptom improvement and lower incidence of adverse effects. Haisong Jiang [21] randomly divided eighty patients with diarrhea-type irritable bowel syndrome due to liver depression and spleen deficiency into a control group and an observation group. Bifidobacterium bifidum quadruple vivax tablets combined with trimethoprim maleate tablets were given to the control group, and Chai Hu Gui Zhi Gan Jiang Tang was given to the observation group. Comparison of the two groups after treatment. The results showed that the total effective rate of the observation group (95%) was significantly higher than the total effective rate of the control group (67.5%),  $P < 0.05$ . And the degree of symptom improvement and quality of life scores of the observation group were better than those of the control group. Zhaoping Yan [22] used retrospective analysis to analyze the efficacy of thirty-three patients with functional gastrointestinal disorders treated with Chai Hu plus Long Bone Oyster Soup. The patient's course of treatment was one week. Evaluate patient outcomes after treatment. The results showed that after the treatment, the symptoms disappeared in eight cases, partially relieved in fourteen cases, slightly relieved in seven cases, and persisted in four cases, with a total effective rate of 88%; and the anxiety symptoms of the patients were effectively improved.

### 5. Deliberations

The efficacy of Chaihu-like formula with Chaihu as the kingpin in the treatment of digestive disorders, especially for the treatment of digestive disorders accompanied by emotional anomalies, is outstanding and worthy of further popularization and application. There are more abundant reports on pharmacological studies as well as clinical studies on Chai Hu-like formulae, but fewer reports on pharmacological studies on Chai Hu single herb in digestive system diseases. Chinese medicines have more chemical components and complex mechanisms of action, and serum pharmacology and serum medicinal chemistry studies of Chinese medicines are closer to the real process of pharmacological effects of drugs in the body environment. It is conducive to the exploration of the active ingredients and mechanism of action of traditional Chinese medicine, therefore, the research in this direction can be further expanded and deepened in the future, in order to fully elucidate the mechanism of action of Chai Hu in the treatment of digestive disorders, and to provide a more scientific and effective basis for the use of Chai Hu in the treatment of digestive disorders in the clinic.

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