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# Research progress on the treatment of peptic ulcers with cuttlefish bone

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**Abstract.** Peptic ulcer is a common disease of the digestive system, referring to a defect in the gastrointestinal mucosa that usually extends beyond the mucosal muscular layer. Globally, both its incidence and recurrence rates are relatively high, severely affecting patients' quality of life. The typical symptom of peptic ulcer is upper abdominal pain, which belongs to the category of "stomach pain" in traditional Chinese medicine. Long-term use of therapeutic drugs such as proton pump inhibitors and $H_2$ receptor antagonists brings drawbacks. The emergence of Helicobacter pylori resistant strains and the increasing elderly population, together with more frequent use of anti-inflammatory, analgesic, and antithrombotic drugs, make the prevention and treatment of PU more difficult. At present, traditional Chinese medicine has definite efficacy in treating gastrointestinal ulcers. Among them, cuttlefish bone has a clear therapeutic effect on peptic ulcers, with the functions of astringing to stop bleeding, consolidating essence to stop leucorrhea, neutralizing gastric acid to relieve pain, and absorbing dampness to heal sores. This paper analyzes the reliability of cuttlefish bone in treating peptic ulcers from the perspectives of clinical application, clinical trials, and laboratory research, aiming to provide a reference for the clinical use of medications in peptic ulcer treatment.

**Keywords:** peptic ulcer, gastric ulcer, duodenal ulcer, cuttlefish bone, research progress

## 1. Introduction

Peptic ulcer (PU), as a common disease of the digestive system, refers to a defect in the gastrointestinal mucosa that usually extends beyond the mucosal muscular layer, with gastric acid and pepsin playing a key role in its pathogenesis. Typically, PU refers to gastric ulcer (GU) and duodenal ulcer (DU) [1]. Globally, both the incidence and recurrence rates of PU remain relatively high, severely affecting patients' quality of life [2]. Clinical research by Li Haiyan [3] showed that PU patients with H. pylori infection have relatively low levels of self-care ability. Related epidemiological surveys indicate that approximately 10% of the population develop PU at some point in their lives [4]. One study revealed that between 1990 and 2021, the global incidence and prevalence of PU showed an increasing trend, with men exhibiting higher incidence, prevalence, and mortality rates than women [5]. Over the past 30 years, with the development of treatment drugs such as proton pump inhibitors (PPIs) and $H_2$ receptor antagonists, the prevalence of PU and the incidence of its complications have significantly decreased. However, these treatments cannot completely prevent recurrence nor fully cure the disease. Clinical trials have demonstrated that long-term use of PPIs can raise gastric pH, increasing the opportunity for bacterial overgrowth, particularly of Clostridioides difficile. At the same time, the risks of other diseases, such as chronic kidney disease, gastric cancer, and community-acquired pneumonia, are also increased [6]. Although a causal relationship between the occurrence of these diseases and PPI use has not been fully established, vigilance is still required. Infection with Helicobacter pylori, as a major pathogenic factor of PU, has received increasing attention in recent years, while the emergence of resistant strains has become a new challenge [7]. In recent years, the increased use of anti-inflammatory, analgesic, and antithrombotic drugs in elderly patients has led to a higher incidence of related PU [1]. The aggravation of population aging in China further highlights the need to pay more attention to PU in the elderly. Therefore, the prevention and treatment of PU is becoming increasingly challenging.

The typical symptom of PU is upper abdominal pain, which falls under the category of "stomach and epigastric pain" in traditional Chinese medicine [8]. With the clinical efficacy of traditional Chinese medicine (TCM) treatment, based on the concepts of holism and syndrome differentiation, being increasingly recognized, more and more clinicians have actively studied

TCM formulas and single herbs, achieving certain academic results. This paper focuses on the research progress of cuttlefish bone in the treatment of PU.

## 2. Records in ancient texts

Cuttlefish bone, also known as Haipiaoxiao, Wuzeigu, Wuzeiyu Gu, Moyu Gu, or Moyu Gai, is the dried internal shell of needle-free or Sepia species in the family Sepiidae [9], and it occupies a unique position in traditional Chinese medicine. With the accumulation of clinical experience, practitioners have found that cuttlefish bone plays an important therapeutic role in the treatment of PU, and it has been frequently recorded in classical texts. Li Zhongzi of the Ming Dynasty wrote in Leigong Paozhi Yao Xing Jie: “Treats fright qi entering the abdomen, abdominal pain around the navel.” Huang Yuanyu of the Qing Dynasty recorded in Yuqiu Yaojie: “Stops vomiting, uterine bleeding, abnormal vaginal discharge… contracts sores and dries pus.” These records indicate that ancient practitioners recognized the efficacy of cuttlefish bone in relieving abdominal pain, stopping bleeding, and promoting the healing of sores. According to the Chinese Materia Medica textbook under the National 14th Five-Year Plan, cuttlefish bone is described as salty and astringent in nature, warm in property, and associated with the spleen and kidney meridians. It exhibits significant therapeutic effects in various diseases and shows good efficacy in the treatment of PU, being able to neutralize acid and relieve pain, significantly alleviating discomfort caused by excess gastric acid; it can also reduce dampness, promote ulcer healing, and improve local moist ulcerative symptoms [10]. Therefore, the clinical experience of using cuttlefish bone in PU treatment has continued from ancient times to the present, making it an important traditional Chinese medicine in clinical PU therapy.

## 3. Modern research on the treatment of peptic ulcers with cuttlefish bone

### 3.1. Clinical experience

In recent years, with the increasing application of data mining in the analysis of medical case records, more and more medication patterns have been discovered, including data mining studies on cases of PU. Zhang Xiaobin et al. [11] included a total of 296 prescriptions and 164 Chinese medicines for the treatment of DU using data mining, and found that among the most frequently used Chinese medicines, cuttlefish bone ranked second. Zhao Shuang [12] applied data mining to focus on regional differences in DU treatment between the north and south, finding that Haipiaoxiao (cuttlefish bone) ranked third among high-frequency drugs for DU treatment. The frequency of its use in the south was lower than that in the north, but the dosage used in the south was higher. Regarding case analysis of specific experts, results show that multiple nationally recognized traditional Chinese medicine (TCM) masters exhibited a preference for using cuttlefish bone in the treatment of PU. Xu Youyu [13] conducted data mining on Professor Zhou Zhongying’s PU treatment cases. Among 79 initial prescriptions, 144 Chinese medicines were used, with cuttlefish bone ranking fifth in usage frequency. Zhou Guancheng [14] conducted data mining on Professor Shan Zhaowei’s gastric pain cases and found that Haipiaoxiao was one of his commonly used medicines for treating mucosal injuries. Professor Ge Huinan is skilled in using Haipiaoxiao and other Chinese medicines to achieve acid suppression, gastric protection, and repair promotion in PU treatment [15]. It can be seen that cuttlefish bone demonstrates significant clinical efficacy in the treatment of PU and has been consistently recognized by numerous experts.

### 3.2. Clinical efficacy studies of cuttlefish bone formulations

Clinical studies of compound medicines with cuttlefish bone as a primary component have further confirmed its efficacy. Qin Jiemei et al. [16] conducted a randomized study in which patients with PU were divided into a treatment group and a control group. The treatment group received oral Zhuangyao Yuxie San (Ulcer Powder), while the control group was treated with oral omeprazole capsules, clarithromycin tablets, and metronidazole tablets. The results showed that the efficacy of the traditional Chinese medicine formulation was comparable to that of Western medicine, confirming the effectiveness of Zhuangyao Yuxie San in PU treatment. Other studies include Xie Youliang et al. [17], who conducted clinical trials on Jiawei Wubei San (containing 15 g cuttlefish bone); Liu Daoxi [18], who studied Weiyu Ning Tang (containing 12 g cuttlefish bone); and Wang Zhensheng [19], who analyzed 60 PU cases treated with a self-formulated Haibei Muli San (containing 187 g of finely powdered Haipiaoxiao). All these studies concluded that formulations containing cuttlefish bone produced favorable therapeutic effects in PU patients. However, to date, there is still a lack of clinical studies specifically investigating the efficacy of cuttlefish bone as a single-agent treatment for PU.

### 3.3. Experimental studies

Wang Yaoyu [20] published an article in Zhongyi Zazhi in 1954, reporting that more than thirty cases demonstrated the efficacy of cuttlefish bone in treating GU and DU. However, due to the limitations of research methods and equipment at that time, Wang Yaoyu's study remained at the level of clinical experience and was not explored in depth. With the development of the times and scientific progress, an increasing number of scholars have focused on the mechanisms of cuttlefish bone in PU treatment. Cuttlefish bone mainly contains calcium carbonate, accounting for 80%–85% of its composition, and also contains mucilage 10%–15% and shell keratin 6%–7% [21]. One of the important causes of PU is excessive gastric acid secretion [1]. Therefore, the main component of cuttlefish bone, calcium carbonate, can neutralize gastric acid. Fang Erli et al. [22] found that cuttlefish bone can neutralize gastric acid, thereby increasing cAMP content in gastric tissue and promoting the synthesis of $PGE_2$ in the gastric mucosa, exerting protective effects on cells and ultimately achieving the prevention and treatment of GU. Similarly, cuttlefish bone can prevent indomethacin-induced GU in a dose-dependent manner [23]. Zhang Zhengli et al. [24], through animal experiments, found that the mechanism of cuttlefish bone is related to its dosage. In the experiment, high, medium, and low doses of cuttlefish bone were 6.4, 3.2, and 1.6 g/kg, respectively. The results showed that the medium- and high-dose groups increased the hexosamine content in the gastric mucus layer, mainly by enhancing the protective function of the gastric mucus barrier, thereby protecting the gastric mucosa. The low- and medium-dose groups could reduce the synthesis and secretion of $PGE_2$ in the gastric mucus layer, thereby reducing damage to the gastric mucosa caused by aggressive factors. Cuttlefish bone polysaccharides, an active component extracted from cuttlefish bone, were used to pretreat mice, which were then administered anhydrous ethanol via gavage. It was found that this active component could raise gastric pH in mice, increase local gastric blood flow, reduce oxidative damage to gastric mucosal cells, and enhance gastric mucosal tissue function, allowing the gastric mucosa to resist exogenous irritants [25]. One of the important clinical features of PU is bleeding [1], and cuttlefish bone has hemostatic effects. Wang Jinsong et al. [26] experimentally found that cuttlefish bone significantly shortened coagulation and bleeding times, a property closely related to its effects on coagulation factors and platelets. Based on the confirmed clinical efficacy of cuttlefish bone in PU treatment, Jin Ling et al. [27] conducted in vitro experiments using 0.1090 mol/L hydrochloric acid to simulate gastric acid, and calculated that a daily oral dose of more than 3 g of cuttlefish bone could treat general GU, gastritis, and hyperacidity. However, this does not correspond with the dosage recommendation of 5–10 g provided in the Pharmacopoeia of the People's Republic of China [9], and the effectiveness of this experimental conclusion in vivo remains to be verified.

## 4. Conclusion and outlook

With the advent of PPIs and $H_2$ receptor antagonists, many PU patients have benefited; however, with social development and the increased use of other medications, new problems have emerged. Therefore, treatment of PU cannot remain stagnant, and it is still necessary to actively seek more effective therapeutic drugs. Cuttlefish bone, as an animal-derived traditional Chinese medicine, can be used to treat PU in digestive system diseases, and its favorable clinical efficacy is increasingly recognized by TCM clinicians. Its main components, such as calcium carbonate and cuttlefish bone polysaccharides, can neutralize gastric acid, increase gastric pH, inhibit the production of substances that damage the gastric mucosa, promote the generation of substances that protect the gastric mucosal barrier, and exert hemostatic effects, thereby achieving the therapeutic goal of PU. However, at present, clinical trial studies on cuttlefish bone as a single-agent medicine are still lacking. Its therapeutic efficacy and potential toxic or adverse effects as a single herb remain uncertain, and further research is therefore required.

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