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Update in the therapeutic role of Complementary and Alternative Medicine (CAM) in peptic ulcer

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Abstract

Peptic ulcer disease (PUD) is still a global health problem, and *Helicobacter pylori* infection is identified as the principal causative factor. While these are effective, the conventional pharmacological treatments are usually accompanied by side effects, the development of antibiotic resistance, and limited access in some cases. As a result, Complementary and Alternative Medicine (CAM) has become a promising complementary or alternative intervention for PUD. The objective of this systematic review was to assess the therapeutic value, safety, and constraints of CAM interventions for peptic ulcer disease. An extensive systematic review was performed using the PICO format and reported following guidelines, including Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Literature searches were conducted in multiple databases, including the Cochrane Library, Embase, MEDLINE, and the Complementary Medicine Database and included papers from 2000 to 2024. Herbal treatment, complementary medicine, and alternative medicine were the search terms. Available full-text studies had a focus primarily on CAM interventions for PUD. Data were tabulated and synthesized to summarize therapeutic mechanisms, safety profiles, and limitations of the studies. A total of 134 studies met the inclusion criteria, including randomized controlled trials ($n \approx 45$), observational studies ($n \approx 30$), systematic reviews and meta-analyses ($n \approx 20$), and preclinical experimental studies ($n \approx 39$). Herbal medicine was studied the most in CAM. There were agents such as *Nigella sativa*, licorice, turmeric, Aloe vera, and ginger, with gastroprotective, Antioxidant, and anti-*H. Pylori* effects. Probiotics and acupuncture were supportive, too. Compared to conventional therapies, CAM therapy caused fewer adverse effects. Some drawbacks included heterogeneity in herbal preparations, no standardized dosing, small patient populations, and limited large-scale clinical trials. In PUD management, CAM therapies, especially herbal medicines and probiotics, are of significant use as adjunctive drugs. Although both safety and affordability seem good, the overall evidence base is still moderate to low. Standardized preparations and good multicenter randomized controlled trials should be studied further to aid clinical utilization.

Keywords Herbal medicine; peptic ulcer, Complementary medicine, Probiotics, Liquorice, Pharmacognosy

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Introduction

Peptic ulcer disease (PUD) is a chronic, recurrent manifestation involving different patterns of gastric and duodenal ulcers [1]. Gastric and duodenal ulcers differ in their location, structure, and mucosal response. Indeed, gastric ulcers rarely penetrate the muscle wall, are typically benign, originate from a normal-appearing mucosa, respond well to acid-suppressive therapies, and are usually due to nonsteroidal anti-inflammatory drugs, alcohol consumption, tobacco use, or *Helicobacter pylori* infection. In contrast, duodenal ulcers are located in the upper gastrointestinal tract, penetrate the muscle wall, and are generally small and recurrent. This type of ulcer is often associated with acid-related ulcers or duodenal bulb ulcers [2].

Treatment for peptic ulcers should attempt to achieve long-term relief, rapid healing, and prevention of complications and recurrence. According to the American College of Gastroenterology (ACG) Guidelines, the most effective eradication therapy for *H. Pylori* usually involves triple or quadruple therapy [3](Table 1). Besides the treatment for eradication of *H. Pylori* infections, pharmacological treatment was the main therapeutic strategy. The acid secretion control through the use of proton pump inhibitors (PPIs), H2-receptor blockers, mucosal protective agents (e.g., sucralfate) and anti-cholinergic agents is the standard pharmacological therapy for peptic ulcers. Although effective, the long-term use of these drug classes can lead to treatment-related morbidity such as diarrhea and magnesium and vitamin B12 deficiencies [4–6]. Recently, the development and use of complementary and alternative medicine (CAM) for the treatment of peptic ulcers have received increased attention [7–9]. The growing interest in CAM is partly due to dissatisfaction with conventional biomedicine, the belief that CAM is more wholesome, and the increasing popularity of self-medication [10].

CAM represents a diversified set of healthcare practices, beliefs, and therapies, many of which have been researched minimally or not at all. Approaches considered part of CAM range from very simple dietary or lifestyle changes to extremely complex systems of law and

philosophy, such as Chinese medicine and traditional healing among indigenous peoples. Many local medicinal plants have been widely used by the indigenous people to treat this gastrointestinal disorder, along with certain unconscious habits involving dietary style and lifestyle. People from different cultural backgrounds and rural communities have developed various folk suggestions and practices to manage PUD. For instance, Ayurveda and various Indian folk medicinal plants are widely accepted and practiced by a large section of the population, even during the modern era of biomedicine [12–15].

PUD has remained a major health problem since antiquity, and different communities have developed their own folk remedies and practices to treat this condition. Since the majority of these mantras and plants have never been documented scientifically, the present study aimed to scientifically investigate some folk remedies and practices for the management of PUD. This review also examines the role of herbal medicine as an alternative treatment for PUD conditions, which is characterized by its low cost, wide availability, and lower side effects.

Methodology

A scoping review was carried out to chart the scope and character of the evidence base for Complementary and Alternative Medicine (CAM) treatments for peptic ulcer disease (PUD). The review was guided by the Population, Intervention, Comparison, and Outcome (PICO) approach to frame the research question and was reported based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guidelines. A scoping review design was chosen as there was no quantitative synthesis or meta-analysis because of the diversity of study designs, CAM interventions and outcomes reported. Search Strategy. The literature search included multiple search packages across a variety of academic databases (MEDLINE, Embase, Cochrane Library, and Complementary Medicine Database). The search focused on publications from January 2000 to December 2024. Terms included the use of Boolean operators (AND/OR); combinations of the following were added: “peptic ulcer disease,” “*Helicobacter pylori*,” “herbal treatment,” “complementary medicine,” “alternative medicine,” and “CAM therapies.” Eligibility Criteria. Eligibility criteria were the submission of Articles that met the following inclusion criteria:

Inclusion criteria: Full-text articles in English; CAM interventions used for PUD were predominantly addressed; randomized controlled trials, observational studies, systematic reviews, and experimental animal studies were included. Exclusion criteria: Abstract-only articles, editorials, commentaries, case reports without intervention

Table 1 Eradication therapy for *H. Pylori*-induced peptic ulcer according to American college of gastroenterology (ACG) guidelines [11]

Eradication regimen protocol	Medications	Duration
Clarithromycin triple therapy	Clarithromycin + amoxicillin (or metronidazole) + PPI (omeprazole)	14 days
Bismuth quadruple therapy	Bismuth subsalicylate + metronidazole + tetracycline + PPI (omeprazole)	10–14 days

data, and non-CAM or PUD-focused studies. Data Extraction and Screening.

Two independent reviewers screened titles and abstracts for relevance, and full texts were then compared to the inclusion criteria. The same reviewers independently extracted data, including study characteristics, CAM interventions, outcomes, and quality-related parameters. Disagreements are addressed in a discussion, and a third reviewer was called upon for advice when consensus was not achieved.

Data synthesis

Data was thematically analyzed, and thematic analysis of the extracted data was used to identify repetitive therapeutic mechanisms, safety profiles, and methodological limitations across CAM modalities in terms of safety/approaches. The findings were analyzed descriptively, and presented in tabular form to identify evidence trends, gaps in research and trends over time. Doing so enabled the review to contribute to and to update the existing knowledge at the time and evaluate the progress in CAM research for PUD in the last 20 years.

Results

Traditional pharmacologic treatments available for peptic ulcer disease (PUD) are scarce and have been linked with significant side effects and lack of efficacy in some persons. As a result of that, complementary and alternative medicine (CAM) therapies have been studied worldwide. The literature reviewed described a diversity of herbal and alternative therapies, including *Pistacia lentiscus* (mastic gum), *Nigella sativa*, licorice, aloe species, turmeric, propolis, ajwain, flaxseed, sea buckthorn oil, wild carrot essential oil, artichoke leaf, okra-derived components, and various culinary herbs [16–21]. Because of great heterogeneity in interventions and study designs, the results were reported narratively and categorized in terms of CAM type, mechanisms, and evidence. Herbal medicine was found to be the most studied method. Clinical evidence—although largely restricted to small and short-term trials—observed the gastroprotective and anti-*Helicobacter pylori* activities of *Pistacia lentiscus*, licorice, *Nigella sativa*, aloe species, turmeric, and propolis. Numerous other herbal preparations were backed by preclinical evidence from in vitro and animal models. CAM therapies have various beneficial effects on different pathways, including inhibition of *H. Pylori*, Antioxidant and anti-inflammatory properties, improving gastric mucosal defence, and modulation of gastric acid secretion. Nevertheless, the strength of evidence is overall hampered due to our reliance on experimental models, heterogeneity of herbal formulations, and constraints of high-quality randomized controlled trials.

Probiotics

Probiotics, defined as live microorganisms that confer health benefits to the host when consumed in adequate numbers, have emerged as an exciting area of research for the prevention and treatment of peptic ulcers. The use of probiotics in gastrointestinal diseases, particularly for the treatment of acid peptic disease, inflammatory bowel disease (IBD), infectious diarrhea, and antibiotic-associated diarrhea, has been supported in recent evidence-based analyses. The Food and Drug Administration (FDA) has removed the requirement for premarket approval for certain probiotics, and probiotics are generally regarded as safe in healthy adults. Proposed mechanisms involve competitive inhibition, leading to colonization resistance, and alteration of *H. Pylori* adhesion, which inhibits gastric mucosal colonization. Probiotic strains also secrete bactericidal metabolites that damage *H. Pylori* cell walls and stress-inducing compounds that exacerbate pathogenicity. Probiotics may improve the integrity of the intestinal mucosal barrier, decrease intestinal permeability, increase mucus secretion, and have various protective effects [22–24]. Supplementation of Lactobacilli, Bifidobacteria, and fermented dairy products such as yogurt containing live bacteria has been widely used to restore normal microbiota. Increased ingestion of these products has demonstrated protective effects against *H. Pylori*, with randomized controlled trials suggesting an extra cytoprotective effect from probiotics like Misoprostol, sucralose, and Omeprazole [25–27]. Results from a few undersized trials suggest that probiotics may be a safe adjunct strategy for eradication therapy with promising beneficial effects. Controlled trials assessing the efficacy of probiotic consumption in adults infected with *H. Pylori* have yielded promising results.

Probiotic supplementation has significantly increased the eradication rate when used adjunctively with standard triple and quadruple regimens, with up to a 48% reduction in adverse events, most commonly diarrhea, nausea, and abdominal discomfort. Probiotics are considered valid adjuvants to standard *H. Pylori* eradication regimens [22–24]. Despite promising preclinical efficacy, methodologies and results of such studies must comply with strict evaluation criteria if probiotics are to be considered an effective adjuvant in standard triple *H. Pylori* eradication therapy. A probiotic formulation administered during and after a 14-day standard *H. Pylori* eradication treatment with omeprazole, clarithromycin, and amoxicillin was found to be effective, reducing the number of subjects with side effects. Lactobacillus-containing yogurts were also added to the regimen and increased treatment success and reduced side effects [28–33].

Licorice root extract

Licorice root, recognized for its culinary and therapeutic applications, has potential against peptic ulcers and *H. Pylori* infections [34–37]. Licorice, or *Glycyrrhiza glabra*, has been used in traditional Chinese medicine for more than 2000 years. Its main active component is glycyrrhetic acid (GA), which is regarded as an effective antiulcer agent. GA is a potent inhibitor of 11-hydroxysteroid dehydrogenase type 2 (11b-HSD2) in the kidney and colon and exerts its activity in ulcer healing through the enhancement of gastric mucus gel-layer thickness [38–40]. Glycyrrhizin and 18 beta-glycyrrhetic acid promote prostaglandin E2 and mucus output while suppressing acid secretion. Glycyrrhizin pre-treatments curtail necrosis in ethanol-exposed rats and bolster intracellular GSH levels. In vitro, Glycyrrhizin hampers early glycoprotein and protein synthesis processes, inhibiting *H. Pylori* adhesion to gastric epithelium while promoting beneficial bacteria attachment. This agent also enhances the antibacterial activity of clarithromycin, inducing apoptosis in *H. Pylori*. Glycyrrhizin's effects could be harvested via food supplements or nutraceuticals, utilizing its derivatives that lack its pathological side effects. Licorice-containing herbal medicines (e.g., Chai Hu Shu Gan San) have proven efficacy against gastritis/ulcers in pre-clinical and clinical studies. More well-designed clinical trials pertaining to gastritis/ulcer treatment are needed to explore licorice's therapeutic potential further [41–43].

Acupuncture

Acupuncture is an ancient art and medical science that originated in China more than 2000 years ago. It postulates that each individual possesses an invisible energy or life force called “Qi” (pronounced “chee”) that travels the body in channels called meridians. There are more than 300 acupuncture points located along meridians where the energy can be accessed. Health exists when the Qi is in balance and free to flow through the body [44]. Disease develops when there is an imbalance of energy or if the energy is blocked, causing insufficient flow. Acupuncture restores balance and health by manipulating the energies within the body. The insertion of needles into acupuncture points modulates the nervous system, enhances local blood flow, alters hormone levels, and strengthens the immune system. Acupuncture has been used for a variety of ailments, including pain, nausea, headaches, and asthma.

Most studies on acupuncture and peptic ulcers have investigated its effect on ulcers caused by NSAIDs. A clinical study showed a positive effect of acupuncture on gastric ulcers in patients following treatment with phenylbutazone, an NSAID and another study showed it is effective in preventing aspirin-induced gastric mucosal injury [45–51].

Although acupuncture is considered a very safe intervention when performed by well-trained and skilled healthcare professionals, it is not completely without risks. A prior security study on acupuncture practice has demonstrated that the frequency of severe unexpected events associated with acupuncture is very low, and the majority of severe adverse events that have been reported are actually easily anticipated by the clinician [52–54]. The complications observed, from the mild to the severe, include nausea, prolonged muscle soreness, hemorrhage, fainting, pneumothorax, spinal cord injury, unconsciousness, and other discomfort [54–56].

Aloe Vera (*Aloe barbadensis*)

Aloe Vera (AV) is the most widely cultured and used species of the Aloe genus in traditional and complementary medicine. The leaves contain a clear, accountable gel layer that consists mainly of polysaccharides and anthraquinones. The gel also contains electrolytes, cell proliferation-promoting factors (hormones), vitamins, and antitoxins that play a role as immunity enhancement agents. The polysaccharides respond to cellular stress, thus showing anti-inflammatory effects, preventing peptic ulcer development [57–59]. AV can counteract peptic ulcer development induced by necrotizing agents, ethanol, and stress [60, 61]. Other therapeutic activity of the whole AV is mediated by its Antioxidant, anti-inflammatory, immunostimulatory, immunomodulatory, healing-stimulating, promoting cytoprotective effects and suppressing the other layer's active compounds' toxicity [62].

On the other hand, the anthraquinones present are aloin and emodin, which have strong laxative effects. The process of decolorizing whole leaf aloe vera to eliminate the insecticidal toxic anthraquinones, aloin and emodin, generates Aloe vera gel. Adverse effects include hepatitis, allergy, and acute contact dermatitis. It is not safe for lactating, pregnant mothers, and children less than 12 years old. Care should be taken so that the Aloe vera preparation is free from anthraquinones, i.e., processed to remove the toxic portion of the plant (anthraquinones) [62–64]. It is also associated with side effects such as stomach cramps and diarrhea. The suggested mechanism for the observed effect was damage to the epithelium, including the enteric nervous system. Increased contractile activity involving changes in the response to the neurotransmitters acetylcholine and barium chloride has been observed in smooth muscles obtained from the human colon [65, 66].

Turmeric (*Curcuma longa*)

Curcuma longa, or turmeric, originating from the ginger family Zingiberaceae, a widely recognized herb in traditional medicine, has been a prevalent traditional

medicine used in a range of inflammatory and gastrointestinal disorders, such as digestive disorders and liver diseases. The traditionally known risk associated with turmeric is peptic ulcer [36, 67]. Gastrointestinal secretions and counterproductive stimuli are diminished by the administration of turmeric, which contributes to stabilization of the external gastric mucosal layer and healing of the inner lining of the conveyed diverticulum [68–74].

In addition to its efficacy, curcumin and its derivatives, including one of its primary actives, demethoxycurcumin, have demonstrated seasonal allergenicity, including asthma, allergic rhinitis, and skin reactions such as dermatitis upon contact with the skin due to cell infiltration in an IL-4 and IL-5-cell-dependent Th2 response in bronchoalveolar cells. Because few adverse studies are available, the potential toxicity of these findings is not currently known [75–77]. Besides that, the curcuminoids, including desmethoxycurcumin, demethoxycurcumin, bisdemethoxycurcumin, or their combination, have been reported to inhibit P-450 enzymes, CYP2C9, and CYP3A4 [78, 79].

Gummi mastic from pistacia lentiscus

Gummi mastic (GM) from *Pistacia lentiscus* L., which is found in Mediterranean countries, has been reported to have anti-ulcer activity and, in general, a protective effect on gastrointestinal disorders. *Pistacia lentiscus* L. (Anacardiaceae) is a small to medium-sized tree or shrub. It is ecologically adapted to a dry, arid, semi-dry environment. The GM has been extensively studied for its beneficial properties. The antimicrobial, Antioxidant, and anti-inflammatory effects of mastic have been related and supported [80]. The clinical studies and the tradition of use indicate that GM has a laxative effect and is used to protect against stomach ulcers and achieve relief from their symptoms [81–83]. With regard to its role as an anti-ulcer, the majority of the research has focused on its antimicrobial and anti-inflammatory properties. Indeed, the activity investigations carried out by many researchers have verified the therapeutic protocols of traditional medicine.

Vitamin A combination with honey and yolk egg

Researchers have demonstrated that Vitamin A can play a significant role in peptic ulcer prevention and treatment. Vitamin A, known for its role in maintaining healthy epithelial tissues, has been shown to have protective effects on the gastric mucosa. It helps in maintaining the integrity of the stomach lining, which is crucial in preventing ulcer formation and aiding in ulcer healing [84]. In addition to Vitamin A, honey and egg yolk have been traditionally used for their therapeutic benefits. Honey has been reported to have antimicrobial and

anti-inflammatory properties, which can contribute to the healing of gastric ulcers. Similarly, egg yolk provides essential nutrients that support overall gastrointestinal health [85, 86]. The combination of Vitamin A, honey, and egg yolk may offer a synergistic approach to managing peptic ulcers by leveraging their individual properties to enhance gastric mucosal protection and promote healing.

Egyptian Nigella sativa clove smoking

Nigella sativa and Clove (also known as black cumin) offer significant therapeutic benefits in managing peptic ulcers, with oral administration being the preferred and more studied method. Both have demonstrated efficacy in reducing ulcer severity and promoting healing through their anti-inflammatory and antioxidant properties. Clove contains eugenol, a compound with potent anti-inflammatory, Antioxidant, and antimicrobial effects. Eugenol can help in reducing gastric mucosal damage, preventing ulcer formation, and promoting healing [87, 88]. *Nigella sativa* also contains thymoquinone, which has shown significant anti-inflammatory, Antioxidant, and antimicrobial properties. These properties are believed to contribute to its potential in healing peptic ulcers by reducing inflammation, oxidative stress, and bacterial infection [89, 90].

Ajwain seeds or seed extracts combination with curd

Ajwain seed or ajwain seed extract combination with Curd (yogurt): Ajwain seeds, also known as *Carum copiticum*, contain an active compound, thymol, that is a proven anti-ulcer and antimicrobial agent. It is widely known in traditional medicine. In a study, the use of jamun seeds, jeera, etc., is developed through yogurt formulations, which are essential due to their unique health benefits. Ajwain is one such traditional seed that is explored for its combination of benefits with yogurt. Jamun seeds were explored and have been developed through yogurt formulations, such as in a recent innovation [91]. When ajwain seeds are used alone, they have a potent anti-ulcer activity, and when they are combined with yogurt, they are considered an innovative solution to treat peptic ulcers without the current pharmaceutical conventional drug [92, 93].

Egyptian gum acacia

Traditional medicine has used Egyptian gum acacia in the treatment of peptic ulcers [94]. The medicinal property of this molecule is related to its ability to stimulate the proliferation of the surface layer of the gastrointestinal mucosa. Previous studies indicated that Acacia honey has potent anti-inflammatory and antioxidant effects and led to a reduction in secondary complications caused by acetic acid-induced colitis in the rat. Previous investigations

revealed that Acacia should exert its curative function through an increase in factors directed towards epithelial cell migration and proliferation, together with thrombin growth factors. It leads to the migration of epithelial cells from the base of the lesion and proliferates them in a disorganized way. The development of natural antisecretory drugs has not been successful yet. Acacia serves as a membrane stabilization factor of lipid bilayers at the time of ischemia. The digestive and ulcer protective activity of the aqueous extract with the lipid moiety of gum Acacia has been elaborated in the above context. The inhibition of 15-hydroxyprostaglandin dehydrogenase is an indirect anti-inflammatory action that retards the healing of a peptic ulcer. Sudanese Acacia also serves as the n-alkalin, which is generated through the food source. These are said to have nitrogen-fixing bacteria useful for crop growth. Furthermore, the bioactive components of Acacia are used as medicinal agents. With this background, the present study aimed to assess the gastroprotective effect of Acacia in three different models of acute and chronic ulceration in rats [95–97].

Dill seeds

Anethum graveolens L. (Apiaceae) is an annual herb cultivated throughout Europe and Asia for fresh leaf and dried seed production. The plant contains a volatile oil, protein, fatty acids, and phenolic compounds as the main components [98]. The medical properties of *A. graveolens* have been recognized for a long time. Dill water infusion is used to calm babies worldwide. Dill seed extracts are found to be effective in treating diarrhea, peptic ulcers, and stomach spasms. This property of the plant is linked to its anti-*H. Pylori* activity is performed through the enzyme urease. In this study, the crude extract of *A. graveolens* showed an effective bactericidal killing through anti-*H. Pylori* examination's light microscopy study. The treatment adversely impacted the bacterial morphology, causing cellular damage that ultimately resulted in the death of the bacteria. *A. graveolens* has been studied for its potential effects on aggressive factors in the pathogenesis of acute gastric ulceration [99]. The hydroalcoholic seed extracts of the plant can help in preventing ethanol-induced peptic ulcers in rats by reducing LES pressure and gastroesophageal pressure wave amplitudes in the ethanol model. Inflammation and oxidative stress are considered critical in the pathogenesis of ulcer diseases. The Antioxidant and anti-inflammatory essential oil from the seeds of *A. graveolens* may participate in the protection of the gastric mucous membrane, suggesting a possible role in its traditional uses. Active compounds in dill include monoterpenes (like carvone and limonene), flavonoids, fatty acids, and fiber. Dill has been investigated for numerous potential benefits, including slowing the progression of atherosclerosis, decreasing oxidation of

LDL cholesterol, reducing blood sugar, behavioral calming for hyperactive children, diarrhea control, stomach soother, and antifungal activity [100, 101].

Coriander seeds

Coriander seeds are commonly used in culinary and medicinal practices [102]. They are known for their potential health benefits, including anti-inflammatory, Antioxidant, and antimicrobial properties. Coriander seeds contain compounds such as linoleic acid, linalool, and other antioxidants that may help reduce inflammation and oxidative stress, which are involved in the pathogenesis of peptic ulcers. A study demonstrated that coriander seed extract could mitigate oxidative stress and inflammation in ulcer models, suggesting its potential in managing peptic ulcers [103]. It also has a good gastroprotective effect. Studies have shown that coriander seeds can provide gastroprotective effects. An experimental study found that coriander seed oil reduced ulcer index and gastric acid secretion in rats, supporting its traditional use for ulcer management [104].

Asafetida (*Ferula assa-foetida*)

Asafetida, derived from the resin of the *Ferula* plant, has been traditionally used in various cultures for its digestive benefits. Asafetida has shown potential in treating ulcers due to its anti-inflammatory and antimicrobial properties. A study investigated the effects of asafetida on ulcer models and found it significantly reduced ulcer severity and improved mucosal healing [105]. The herb is traditionally used to alleviate digestive disorders, including ulcers. It has been reported to reduce flatulence and gastrointestinal discomfort, which might indirectly benefit ulcer patients by improving overall digestive health [106].

Mustard seeds (*Brassica* spp.)

Mustard seeds are known for their culinary uses and potential medicinal properties, including anti-inflammatory and antioxidant effects. Mustard seeds contain compounds like sinigrin that exhibit anti-inflammatory properties. Research has shown that mustard seeds can help alleviate symptoms associated with peptic ulcers by reducing inflammation in the gastric mucosa [107]. Mustard seeds have been traditionally used to soothe digestive issues. A study highlighted the potential of mustard seeds in reducing gastric acid secretion and ulceration, suggesting a protective role in ulcer management [108].

Ginger (*Zingiber officinale*)

Ginger has been widely studied for its potential benefits in the treatment and prevention of peptic ulcers. Here is an overview of its role: Ginger contains bioactive compounds such as gingerol and shogaol, which

have strong anti-inflammatory properties. These compounds inhibit the production of pro-inflammatory cytokines and enzymes, thereby reducing inflammation in the gastric mucosa. Studies have shown that ginger extract can reduce inflammation and inhibit the expression of inflammatory markers in ulcer models [109, 110]. It acts as a potent antioxidant, scavenging free radicals and reducing oxidative stress. This helps protect the gastric mucosa from damage caused by oxidative stress and enhances ulcer healing. Animal studies have demonstrated that ginger supplementation increases the levels of antioxidant enzymes and reduces oxidative damage in the stomach lining [111]. Ginger enhances gastric mucus production and increases the gastric mucosal defense mechanisms. It also modulates gastric acid secretion and improves the integrity of the gastric mucosal barrier. Clinical trials and animal studies indicate that ginger can prevent and ameliorate gastric ulcers induced by various ulcerogenic agents such as NSAIDs and ethanol [111].

Ginger has been shown to possess antimicrobial properties that can inhibit the growth of *H. Pylori*. In vitro studies have revealed that ginger extracts can reduce the viability of *H. Pylori* and prevent its adhesion to the gastric epithelium [112]. Ginger has analgesic properties that can alleviate pain associated with peptic ulcers. Its compounds may act on the central nervous system to reduce pain perception. Some studies have reported that ginger can reduce pain and discomfort in ulcer patients, although more clinical trials are needed to confirm these findings.

Sea Buckthorn Oil (SBO)

Sea buckthorn (*Hippophaë rhamnoides* L.) is a source of oil from both pulp and seed. The pulp oil is more widely used in dietary supplements, while the seed oil has been found to exhibit more therapeutic activity. The sea buckthorn oil (SBO) is considered a superfruit, famed for its multiple positive health effects, including its potential to provide relief for gastrointestinal problems [113, 114]. The antiulcerogenic potential of SBO was demonstrated in animal models, where the administration of SBO for 14 days showed a decrease in the ulcer score, granulation tissue, and an increase in collagen content compared to the control group [115]. The mechanisms operating for these properties were demonstrated for both oils by increasing gastric wall mucus secretion, antioxidant activity, inhibiting lipid peroxidation, upregulation of VEGF2, and epidermal growth factor-induced PI3-Kinase/Akt signaling.

It was also shown that the oil has potential as a coating for preventing erosion of ulcerated sites in the stomach in a time-dependent mode. Regarding humans, these results are in line with those from small-scale gastric tolerance tests or those confirming the beneficial effects of SBO in reducing the symptom severity in peptic ulcer patients.

Since remedies of plant origin are very popular among people worldwide, and many choose natural remedies as a way to alleviate the symptoms of various medical conditions, plant-based products that contain SBO could be useful to individuals who suffer from ulcers to boost normal therapy [116]. However, everyday consumption of SB products (even consuming 4000 mg of SBO three times a day for up to four months) is generally recognized as safe and may increase the possibility of peptic ulcer development. Table 2 provides an overview of the various CME options for peptic ulcers, highlighting their main components, mechanisms, and adverse effects.

Discussion

Peptic ulcer disease presents significant challenges for clinicians due to its potential to severely impact the lives of those affected and its contribution to increased healthcare costs. Biomedical research has made significant strides in managing the disease, particularly since the bacterial cause of ulcers has been identified. This scoping review investigates the current evidence on complementary and alternative medicine (CAM) for peptic ulcer management. The review highlights probiotics, licorice root extract, and acupuncture as effective CAM treatments for peptic ulcers [10, 126]. These findings suggest that CAM can be beneficial for ulcer patients. However, some CAM therapies may have significant toxicity and side effects, so their use should be approached with caution, especially for mild or uncomplicated cases. It is crucial to consider potential interactions with conventional treatments. CAM is frequently utilized for peptic ulcers, particularly in cases that are refractory or relapsing, or in patients using nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, H2-receptor antagonists (H2RAs), proton pump inhibitors (PPIs), or those with stress-induced ulcers. Open communication between healthcare providers and patients about CAM use is essential.

Additionally, validating CAM resources with a healthcare professional can enhance the effectiveness of treatment choices by weighing the benefits and risks. Potential risks of adverse effects from traditional and herbal medicines are a key safety concern, particularly for patients with chronic, inflammatory conditions and prolonged low stomach acid. Figure 1 illustrates the different CME options available for peptic ulcer management, highlighting their mechanisms of action. Each option works through specific pharmacological pathways to reduce gastric acid secretion, protect the gastric mucosa, or eradicate *H. Pylori*.

Herbal medicine is increasingly recognized as a viable option for treating gastric ulcers. Recent studies indicate that herbal treatments are not only cost-effective but

Table 2 Summary of different CME options used for peptic ulcers, highlighting their key components, mechanisms, and side effects

CME	Active Components	Treatment/ Effect Mechanisms	Potential side effects	FDA Approval Status	References
Probiotics	<i>Lactobacilli</i> , <i>Bifidobacteria</i> , fermented dairy products	Inhibits <i>H. Pylori</i> adhesion, improves intestinal mucosal barrier, and decreases adverse events from ulcer medications	Mild Gas & Bloating	Yes, commonly approved as dietary supplements.	[22–27]
Licorice Root Extract	Glycyrrhetic acid (GA), Glycyrrhizin	Enhances mucus gel-layer thickness, inhibits <i>H. Pylori</i> adhesion, promotes ulcer healing.	Hypertension, Hypokalemia, and Edema.	Yes, but with specific dosage and usage guidelines.	[34–40].
Acupuncture	Needle insertion at acupuncture points	Modulates nervous system, improves local blood flow, hormone levels, and immune response.	Bruising: Minor bruises at needle sites; Dizziness: Lightheadedness; Infection: Rare risk at insertion sites	Regulated as a medical procedure.	[45–51]
Aloe Vera	Polysaccharides, anthraquinones (toxic if not processed)	Anti-inflammatory, immunomodulatory, and enhances mucosal protection.	Diarrhea: Abdominal discomfort, Hepatotoxicity if not processed correctly	Yes, but must be processed to remove anthraquinones.	[62–66]
Turmeric	Curcumin, demethoxycurcumin	Anti-inflammatory, reduces gastric mucosal damage, promotes healing	Nausea, diarrhea, Allergic Reactions: Rash or itching; Risk of Bleeding	Yes, widely approved as a dietary supplement.	[67–74]
Gummi Mastic	Masticadienonic Acid/ Masticin/ Mastin / Flavonoids	Antimicrobial, anti-inflammatory properties. Protects against ulcers, relieves symptoms and inhibits the growth of <i>H. pylori</i>	Gas, bloating; Allergic Reactions: Rare	Yes, widely approved as a dietary supplement.	[80–83].
Vitamin A + Honey + Egg Yolk	Vitamin A (epithelial protection), honey (antimicrobial, anti-inflammatory), egg yolk (nutrients)	Enhances gastric mucosal protection, aids ulcer healing	Vitamin A Toxicity: High Allergic Reactions: Rare, but possible to honey or egg yolk	Vitamin A and honey are approved; egg yolk is not typically used in supplements.	[85, 86]
Egyptian Nigella sativa and Clove	Thymoquinone (Nigella sativa), Eugenol (Clove)	Reduces inflammation, oxidative stress, and bacterial infection, promotes ulcer healing.	Gastrointestinal Irritation: Nausea, stomach upset; Allergic Reactions: Skin rash or itching.	Yes, available as dietary supplements.	[87–90]
Ajwain Seeds + Curd	Thymol (Ajwain seeds)	Anti-ulcer and antimicrobial activity, combined with yogurt for enhanced therapeutic effects.	Gas, bloating; Allergic Reactions: Rare to Curd or ajwain.	Ajwain seeds are approved; Curd not typically used in supplements.	[92, 93]
Egyptian Gum Acacia	Polysaccharides (arabinogalactan)/ Tannins/ amino acids, including proline, leucine, and lysine.	Stimulates epithelial cell proliferation and membrane stabilization. Reduces complications, aids in mucosal healing, protective against ulcers	Bloating or gas, Allergic Reactions: Rare but possible.	Yes, available as dietary supplements.	[94–97]
Dill Seeds	Volatile oil, thymol, phenolic compounds	Anti- <i>H. Pylori</i> activity reduces oxidative stress and inflammation, protective against ulceration.	Nausea, stomach upset, Allergic Reactions: Rare; Skin rashes	Yes, available as dietary supplements.	[99–101]
Coriander Seeds	Contains linoleic acid and antioxidants,	Anti-inflammatory and Antioxidant reducing oxidative stress and inflammation.	Stomach upset in some cases. Allergic: Rare, skin rash or itching;	Yes, available as dietary supplements.	[102–104].
Asafetida	Resin from the Ferula plant	Anti-ulcer Activity improves mucosal healing.	Gastrointestinal Issues: Bloating, gas; Allergic Reactions: Rare but possible.	Yes, available as dietary supplements.	[105, 106].
Mustard Seeds from Brassica spp	Sinigrin	Anti-inflammatory properties. Gastroprotective effects. Reduces gastric acid secretion and ulceration	Nausea, abdominal pain; Allergic Reactions: Rare	Yes, available as dietary supplements.	[107, 108].
Ginger	Gingerol, shogaol.	Ginger enhances gastric mucus production and increases the gastric mucosal defense mechanisms. It also modulates gastric acid secretion and improves the integrity of the gastric mucosal barrier.	Gastrointestinal Distress: heartburn, diarrhea, Blood Thinning Effects. Potential Uterine Contractions: could be a concern during pregnancy Allergic Reactions: Rare	Yes, available as dietary supplements.	[109–112].

Table 2 (continued)

CME	Active Components	Treatment/ Effect Mechanisms	Potential side effects	FDA Approval Status	References
Sea Buckthorn Oil (SBO)	Omega Fatty Acids and Vitamin A	Increased gastric wall mucus secretion Antioxidant activity Inhibition of lipid peroxidation Upregulation of VEGF2 Epidermal growth factor-induced PI3-Kinase/Akt signaling	Gastrointestinal Distress: Nausea, abdominal pain; Allergic Reactions: Rare but possible.	Yes, available as dietary supplements.	[113–116].
Slippery Elm	Mucilage, tannins	Forms a protective layer over the mucous membranes.	Mild Digestive Issues: Gas, bloating; Allergic Reactions: Rare but possible.	Yes, recognized as safe.	[117, 118]
Marshmallow Root	Mucilage, flavonoids	Soothes and protects the gastrointestinal lining.	Mild Digestive Issues: Bloating, gas; Allergic Reactions: Rare but possible.	Yes, used as a dietary supplement.	[119]
Gotu Kola	Triterpenoids, asiaticoside	Supports wound healing and gastrointestinal lining repair.	Mild Allergic Reactions: Rash, itching; Gastrointestinal Issues: Nausea, upset stomach.	Yes, available as a dietary supplement.	[120]
Hawthorn	Flavonoids, procyanidins	Supports gastrointestinal health through antioxidant effects.	Gastrointestinal Issues: Nausea, abdominal discomfort; Dizziness: Rare.	Yes, used as a dietary supplement.	[121]
Peppermint	Menthol, menthone	Provides relief from gastrointestinal discomfort and spasms.	Gastrointestinal Issues: Heartburn, nausea; Allergic Reactions: Rare.	Yes, approved as a dietary supplement.	[122]
Fennel Seeds	Anethole, fenchone	Reduces inflammation and aids digestion.	Mild Digestive Issues: Gas, bloating; Allergic Reactions: Rare	Yes, available as a dietary supplement.	[123]
Astragalus	Polysaccharides, saponins	Supports immune function and aids in ulcer healing.	Mild Digestive Issues: Nausea; Allergic Reactions: Rare	Yes, used as a dietary supplement.	[124]
Psyllium Husk	Soluble fiber	Promotes regular bowel movements and reduces irritation.	Mild Digestive Issues: Bloating, gas; Allergic Reactions: Rare	Yes, widely used as a dietary fiber supplement	[125]

also safe and effective compared to conventional medications. Herbal medicines contain bioactive compounds such as flavonoids, terpenoids, and tannins, which have demonstrated anti-ulcer properties [127]. Research into herbal plants with anti-*H. Pylori* activity also shows promise in reducing gastric inflammation and preventing pre-cancerous changes associated with *H. Pylori* infection [128]. Conventional treatments often fail to provide complete relief, leading to relapses, which open the door for integrating conventional therapies with alternative approaches for better management. Various complementary medicine systems offer different principles and recommendations for managing ulcers. For instance, combining oral herbal tablets with Ranitidine has shown to enhance therapeutic effects, achieving higher cure rates and lower recurrence compared to conventional single-drug treatments [129]. CAM therapies are often used for chronic conditions when conventional medicine does not offer an immediate cure. However, patients should not discontinue conventional treatments without consulting their healthcare provider, as CAM therapies alone do not cure diseases, as noted by the World Health Organization (WHO). While the paper suggests various CAM options for peptic ulcer management, treatment

should be tailored to the ulcer's stage and the individual patient's needs.

Perspectives on CAM in peptic ulcer therapy and research gaps

Recent evidence suggests that complementary and alternative medicine (CAM) therapies can be as effective as conventional treatments for peptic ulcer disease (PUD) and often present fewer adverse effects [130–132]. This is especially relevant in light of current challenges in PUD management, including antibiotic resistance and concerns over the long-term safety of proton pump inhibitors [133, 134]. Herbal medicines such as *Bryophyllum pinnatum*, *Curcuma longa*, and *Glycyrrhiza glabra* have demonstrated mucosal protective, Antioxidant, and anti-*H. pylori* effects in both experimental and clinical studies [132, 135]. Likewise, probiotics show promise as adjuvants to standard eradication regimens by improving eradication rates and reducing treatment-related side effects, although findings remain inconsistent across trials [134, 136, 137].

Despite encouraging outcomes, major barriers hinder the clinical adoption of CAM in ulcer therapy. Issues such as extract standardization, variability in phytochemical

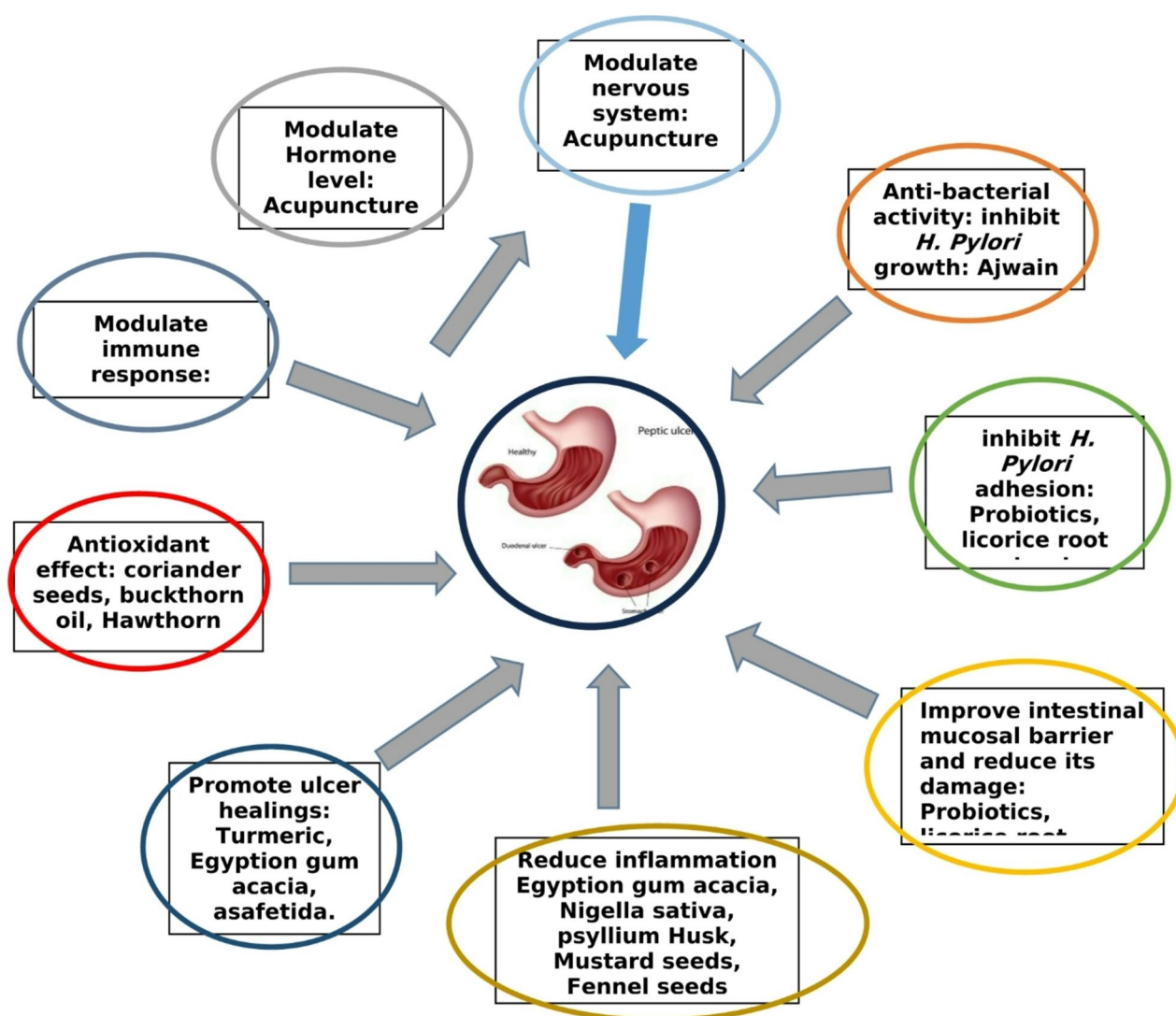


Fig. 1 Overview of different CME options for peptic ulcers, showing their mechanisms of action

content, dosage optimization, and limited large-scale randomized controlled trials restrict translation into practice [138, 139]. Moreover, the lack of robust regulatory frameworks and pharmacovigilance raises concerns regarding herb–drug interactions and product safety.

Practical implications of these findings include the potential to provide clinicians, policymakers, and patients with evidence-based CAM options that are cost-effective and accessible, particularly in low-resource settings [131]. However, further research—especially mechanistic studies and multicenter clinical trials remains essential to establish the therapeutic efficacy, safety, and long-term outcomes of CAM in peptic ulcer management [133, 136].

Authors' contributions

Laila Matalqah: writing—review and editing, supervision, validation, data curation, visualization; Sina Matalqah: Writing- original draft,

Conceptualization, validation; Abdel Rahman Al Tawaha: Writing- Reviewing and Editing, validation, data curation, visualization; Ekaterina Kozuharova: Writing- Reviewing and Editing, validation, data curation, visualization; Lujain Radaideh: Writing- original draft, Reviewing and Editing, validation, data curation, visualization; Qasim Mhaidat: Writing- original draft, Reviewing and Editing, validation, data curation, visualization; Tabark Al-khader: Writing- original draft, Reviewing and Editing, validation, data curation, visualization; Arun Karnwal: Writing- original draft, Reviewing and Editing, validation, data curation, visualization; Natalia Nesterova: Writing- original draft, Reviewing and Editing, validation, data curation, visualization.

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