Traditional Persian topical medications for gastrointestinal diseases

Laleh Dehghani Tafti 1, Seyyed Mahyar Shariatpanahi 1, Mahmoud Mahdavi Damghani 1, Behjat Javadi 2,*

1 Department of History and Civilization of Islamic Nations, Mashhad Branch, Islamic Azad University, Mashhad, Iran
2 Department of Traditional Pharmacy, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

ABSTRACT

Drug delivery across the skin is used for several millennia to ease gastrointestinal (GI) ailments in Traditional Persian Medicine (TPM). TPM topical remedies are generally being applied on the stomach, lower abdomen, lower back and liver to alleviate GI illnesses such as dyspepsia, gastritis, GI ulcers, inflammatory bowel disease, intestinal worms and infections. The aim of the present study is to survey the topical GI remedies and plant species used as ingredients for these remedies in TPM. In addition, pharmacological activities of the mentioned plants have been discussed. For this, we searched major TPM textbooks to find plants used to cure GI problems in topical use. Additionally, scientific databases were searched to obtain pharmacological data supporting the use of TPM plants in GI diseases. Rosa × damascena, Pistacia lentiscus, Malus domestica, Olea europaea and Artemisia absinthium are among the most frequently mentioned ingredients of TPM remedies. β-arsonic, amygdalin, boswellic acids, guggulsterone, crocin, crocetin, isomasticadienolic acid, and cyclotides are the most important phytochemicals present in TPM plants with GI-protective activities. Pharmacological studies demonstrated GI activities for TPM plants supporting their extensive traditional use. These plants play pivotal role in alleviating GI disorders through exhibiting numerous activities including antispasmodic, anti-ulcer, anti-secretory, anti-colitis, anti-diarrheal, antibacterial and anthelminthic properties. Several mechanisms underlie these activities including the alleviation of oxidative stress, exhibiting cytoprotective activity, down-regulation of the inflammatory cytokines, suppression of the cellular signaling pathways of inflammatory responses, improving re-epithelialization and angiogenesis, down-regulation of anti-angiogenic factors, blocking activity of acetylcholine, etc.

Introduction

The evidence of herbal medicines dates back over 5,000 years. The application of medications to the skin to cure illnesses is a practice that has been utilized by humankind for thousands of years and has included the application of poultices, oils, gels, ointments, pastes, and lotions (1). Skin which is known as the largest organ of the human body plays important role in drug delivery. Three important modes including topical, regional and transdermal are used for delivery of various dosage forms. Topical delivery is used mainly to directly affect cutaneous disorders while regional delivery requires deeper penetration than topical delivery and is used to alleviate disease symptoms in deep tissues such as muscles and vasculature joints, beneath or near the site of application (2). Regional delivery is also applied to reduce drug toxicity, as it is established that systemic delivery, can produce inadequate doses of the drug in target tissue, as well as toxicity in healthy tissue. Transdermal delivery is applied to the skin to achieve systemically active levels of the drug to cure systemic disease (2-4). Transdermal delivery has also several advantages over other routes of administration. It is used to bypass hepatic first-pass effect and other variables associated with the gastrointestinal (GI) tract such as pH and gastric emptying time that can prematurely metabolize or degrade drugs. Moreover, transdermal systems also are non-invasive and can be self-administered. They also improve patient compliance and would cause fewer systemic adverse effects (5-7). Particularly, transdermal administration of medicines has been shown to reduce GI tract related side effects (8).

Drug delivery across the skin is used for several millennia to ease GI ailments in various traditional medicine systems. In Traditional Persian Medicine (TPM), which is based on quadratic elements (9), a majority of GI remedies are being applied to skin and mostly aimed at regional and/or transdermal delivery (10). These remedies are especially administered for the treatment of gastric weakness and dyspepsia, gastritis,
loss of appetite, belching, GI ulcers, colitis, intestinal worms and infections (11, 12). Several medicinal plants, animal products and minerals generally in compound formulations have been recommended to cure these conditions. The recommended formulations are in the forms of poultices, lotions, ointments, rubbing oils, baths, etc. A number of papers have already well studied the medicinal plants used for the treatment of some GI diseases especially peptic ulcer in view of TPM (13, 14). However, there is not any scientific study to specifically survey topical remedies used to alleviate GI problems. Therefore, here we present an overview of the topical GI remedies in TPM and the plant species used as ingredients for these remedies. In addition, relevant pharmacological activities of the mentioned plants in GI tract have been discussed.

Materials and Methods

Firstly, we searched major TPM textbooks to find medicinal plants used for the treatment of GI problems in topical use. These books included Al-Hawi fi’t-Tebb (Comprehensive Book of Medicine) by Razi (865-925), Canon of Medicine by Ibn Sina (980-1037), Ferdows al-Hekmah fi’t-Tebb (Paradise of Wisdom on Medicine) by Tabari (9th century), Konnash fi’t-Tebb by Kashkari (9th, 10th century), Hedayat al-Mota’allemin fi’t-Tebb (An Educational Guide for Medical Students) by Akhawayni (10th century), and Qarabdin-e-Kabir by Aqili-Khorasani (16th-17th century). The search was performed using a software namely Jameel al-Tibb containing a majority of TPM books. Afterwards, the scientific names of the retrieved plant names were authenticated using botanical textbooks, including the Dictionary of Medicinal Plants (15), Qamus al-qanun fi’t-tibb (16), Illustrated polyglottic dictionary of plant names in Latin, Arabic, Armenian, English, French, German, Italian, and Turkish languages (17), Encyclopedia of Medicinal Plants: Arabic-English-French-German-Latin (18) and Tafsir kitāb Diyasquiridis (Explanations of Dioscorides’ Book) (19).

The scientific names were then entered as key terms for the second search. ScienceDirect, PubMed, Scopus, and Google Scholar databases were searched to obtain pharmacological data supporting the use of TPM plants in GI diseases using the following keywords: Gastrointestinal diseases, peptic ulcer, anti-secretory, gastro-protective effects, anti-inflammatory effects, antibacterial, Helicobacter pylori, anti-diarrhea, colitis, etc. Different steps of the present research are illustrated schematically in Figure 1.

**Figure 1. Different steps of the present research**

The use of topical remedies is probably coeval with the appearance of medical knowledge. In TPM, topical medications are almost as applicable as internal formulations (20). In GI problems, topical remedies mostly in the forms of poultices or zemad, ointments or marham, baths or notul, lotions or tali and compresses or kemad, are being applied on the stomach area, lower abdomen, lower back and liver.

Poultices are topical preparations usually containing whole fresh medicinal plants or herbal powders occasionally in mixture with herbal distillates, infusions or oils. These dosage forms are directly applied to the skin near the affected area (12).

Herbal oils are common ingredients of topical remedies. In TPM, herbal oils are mostly extracted by maceration method through which the flowers and other herbal tissues are soaked in a base oil (commonly olive, almond or sesame oils), then filtered (12). This process is repeated several times to obtain rich herbal oils containing essential oils and other lipophilic phytchemicals. Traditional ointments are defined as mixtures of herbal or animal oil and bees wax as a base for bioactive herbal extracts and powders (21). The hydrophobic nature of ointment bases offers an improved percutaneous absorption of herbal extracts. Ointment bases influence drug bioavailability due to their occlusive properties of the stratum corneum, which increases the flux of drug across the skin.
Moreover, they affect drug dissolution and drug partitioning within or from the ointment to the skin (2). Oleo-gum-resins such as mastic, olibanum, guggul, opobalsam, etc. which are rich sources of essential oils are important ingredients of TPM cutaneous GI formulations (12). A number of essential oils have been reported to exert GI protective activities (22, 23). Terpenes, the primary constituents of the essential oils obtained from many types of plants and flowers have been shown to have percutaneous permeation through the intact skin (24). Moreover, some terpene-containing essential oils such as fennel oil, peppermint oil, cardamom oil and sweet basil oil are capable of accelerating the percutaneous absorption of co-administered drugs probably due to the increased skin vehicle partitioning by the oils (25). Various sesquiterpenes have also been found to enhance percutaneous penetration of the drugs possibly by disrupting the intercellular lipid bilayers in the stratum corneum, thus improving co-administered drugs diffusivity, and/or increasing drug partitioning. Some other phytochemicals present in TPM formulations such as fixed oils and fatty acids, aloe juice and α-tocopherol also have percutaneous penetration enhancing effects (26). Thus, these phytochemicals exert multidimensional activities in TPM topical remedies. For instance, the presence of aloe juice in a multi-herbal preparation not only offers multiple GI activities such as anti-ulcerogenic, anti-H. pylori, anti-diarrheal, anthelmintic and anti-ulcerative colitis (UC) effects (27-31), but also act as a base or carrier and penetration enhancing agent for other ingredient of the preparation (26).

TPM cutaneous GI formulations aimed at developing percutaneous absorption and deposition of bioactive phytochemicals as well as offering higher regional concentrations than systemic administration at the same total body exposure to the drug. Cutaneous application of these formulations along with oral preparations offers a multifaceted therapeutic strategy for the treatment of GI diseases.

**TPM recommended medicinal plants for topical use in gastrointestinal diseases**

Around 60 plant species from 34 families have been frequently noted in TPM textbooks to be topically active in the treatment of GI diseases. Most of these species belong to the Apiaceae (eight species) and Rosaceae (four species) families. *Rosa × damascena* Mill. flowers, *Pistacia lentiscus* L. oleo-gum-resin, *Malus domestica* Baumg. fruits, *Olea europaea* L. fruit oil and aerial parts of *Artemisia absinthium* L. are among the most frequently mentioned herbal ingredients of TPM-recommended remedies. A wide spectrum of GI diseases including GI ulcers, gastric inflammations and swellings, diarrheal illnesses caused by gastric dysfunction, bacterial infections and intestinal problems such as inflammatory bowel disease (IBD) and colitis has been traditionally treated by a combination of internal and topical medications (16, 20, 32). Medicinal plants used to alleviate or cure GI diseases and their TPM information are listed in Table 1.

| Scientific names | Family | Traditional names | Plant part | Medicinal uses | References |
|------------------|--------|-------------------|------------|---------------|------------|
| *Acorus calamus* L. | Acoraceae | Vaj | Rhizome | Gastritis, vomiting caused by yellow bile | (10, 21, 32) |
| *Aloe spp.* | Asphodelaceae | Sabr | Dried sap | Stomach weakness, loss of appetite, cholera | (10, 21, 32) |
| *Althaea officinalis* L. | Malvaceae | Khatmi | Flowers, seeds | Gastritis, stomach swelling, gastric abscess | (10, 11) |
| *Amygdalus communis* L. var. *dulcis* | Rosaceae | Badam talkh | Seeds | Stomach swelling and inflammation | (32) |
| *Anethum graveolens* L. | Apiaceae | shebet | Seeds, leaves | Gastritis, stomach swelling, Nausea and vomiting, IBD | (10, 11, 20) |
| *Apium graveolens* L. | Apiaceae | Karafs | Seeds | Stomach swelling | (20) |
| *Aquilaria agallocha* Roxb. | Thymelaeaceae | Ood | Stem wood | Loss of appetite, diarrheaa, digestive aid, stomach tonic, cholera | (10, 20, 21, 32) |
| *Artemisia absinthium* L. | Asteraceae | Afsantin | Aerial parts | Stomach weakness, stomach swelling and pain, gastric abscess, vomiting, diarrheaa, intestinal worms | (10-12, 20, 21, 32) |
| *Boswellia spp.* | Burseraceae | Kondor | Oleo-gum-resin | Stomach weakness, gastritis, Stomach swelling, loss of appetite, diarrheaa, intestinal worms | (10-12, 20, 21, 32) |
| *Brassica oleracea* L. | Brassicaceae | Kalam | Leaves, seeds | Gastrointestinal swellings, colic, hemorrhoids | (10, 21, 32) |
| *Carum carvi* L. | Apiaceae | Zireh | Fruits | Stomach weakness, gastric swellings, flatulence | (10, 20, 21) |
| *Carum copticum* Benth. & Hook.f. | Apiaceae | Zenyan | Fruits | Gastric swellings | (20) |
| *Cissus quadrangularis* L. | Vitaceae | Hamama | Berries | Stomach weakness, gastric swelling caused by phlegm | (10-12, 21) |
| Latin Name | Family | Common Name | Part Used | Uses |
|------------|--------|-------------|-----------|------|
| *Cistus ladaniferus* Curtis | Cistaceae | Ladan | Sap | Stomach weakness, gastric swelling, gastric trauma, bulimia, diarrhea, diarrhea caused by stomach coldness and weakness | (10-12, 20, 21, 32) |
| *Commiphora mukul* Engl. | Burseraceae | Moql'araq | Oleo-gum-resin | Stomach weakness, distention and swelling, belching, intestinal ulcers, IBD, hemorrhoids | (10-12, 20, 21) |
| *Commiphora opobalsamum* Engl. | Burseraceae | Balsan | Oleo-gum-resin | Stomach weakness, distention and coldness, gastritis | (10, 11, 21) |
| *Costus speciosus* (J.Koenig) Sm. | Costaceae | Qost | Rhizome | Stomach coldness, diarrhea, colic | (11, 12, 32) |
| *Crocus sativus* L. | Iridaceae | Zaafaran | Stigma | Cold stomach, gastric distension and swelling, gastritis, nausea, vomiting, diarrhea | (10-12, 20, 21, 32) |
| *Cucurbita pepo* L. | Cucurbits | Kudu | Fruits, seeds, peel | Gastric weakness in pregnancy, hot and dry stomach, gastritis, heart burn, peptic ulcer, nausea, thirst, diarrhea | (10, 20, 21, 32) |
| *Cupressus sempervirens* L. | Cupressaceae | Sarv | Berries, leaves | Gastric weakness, swelling and distension, cholera, intestinal ulcers, rectal prolapse | (10, 11, 21, 32) |
| *Cydonia oblonga* Mill. | Rosaceae | Beh | Fruits, leaves, oil | Poor digestion, nausea, vomiting, gastritis, heartburn, diarrhea, flatulence, cholera | (10, 20, 21) |
| *Cymbopogon schoenanthus* (L.) Spreng. | Poaceae | Ekarher | Roots, flowers | Gastric weakness, swelling and distension, diarrhea | (20, 21, 32) |
| *Cyperus rotundus* L. | Cyperaceae | Soad | Rhizome | Stomach weakness, coldness and swelling, dyspepsia, gastritis, nausea, vomiting, diarrhea | (10-12, 20, 21, 32) |
| *Dorema ammoniacum* D. Don | Apiceae | Oshq | Oleo-gum-resin | Stomach weakness, coldness, swelling and hardness, gastritis, belching, gastric abscess | (10, 11, 21, 32) |
| *Eugenia caryophyllata* Thunb. | Myrtaceae | Milkhak | Flowers | Dyspepsia, stomach weakness, severe nausea, diarrhoea, cholera | (11, 20, 21, 32) |
| *Foeniculum vulgare* L. | Poaceae | Razianeh | Fruits | Hard swelling of stomach | (20) |
| *Glossostemon bruguieri* Desf. | Poaceae | Razianeh | Roots | Hard swelling of stomach | (10, 11) |
| *Hordeum vulgare* L. | Poaceae | Zo | Roots, fruits | Stomach swelling, gastritis, peptic ulcer, nausea, thirst, chronic diarrhea, grippe, flatulence, rectal prolapse, anal fissure | (10-12, 20, 21, 32) |
| *Hyoscyamus niger* L. | Solanaceae | Bangdanek | Seeds, leaves, flowers | Diarrhea, intestinal ulcers, hemorrhoids pain and inflammation, anal fissure, colic | (10, 12, 21, 32) |
| *Iris florentina* L. | Iridaceae | Irka | Rhizome | Chronic vomiting, belching, hemorrhoids | (21, 32) |
| *Lawsonia inermis* L. | Lythraceae | Hana | Leaves, flowers, oil | Coldness of stomach, belching, gastritis, IBD, anal fissure, colic | (10, 21) |
| *Linum usitatissimum* L. | Linaceae | Katan | Seeds | Gastritis, gastric hard swelling, vomiting, chronic diarrhea, flatulence, IBD, colic, ileus, hemorrhoids | (10-12, 20, 21, 32) |
| *Malus domestica* Baumg. | Rosaceae | Seeb | Fruits, fruits oil | Gastric hard swellings, gastric trauma, stomach weakness, pain and inflammation, loss of appetite, intestinal worms, nausea, cholera, chronic diarrhea | (10, 11, 20, 21, 32) |
| *Matricaria Chamomilla* L. | Asteraceae | Babuneh | Flowers | Gastric hard swelling, burning and inflammation, flatulence, belching | (10, 11, 20, 21, 32) |
| Plant Name | Family | Part Used | Mode of Use | Conditions |
|------------|--------|-----------|-------------|------------|
| Viola odorata | Violaceae | Aerial parts | Gastrointestinal weakness, vomiting, diarrhea, swelling, pain, flatulence | (11, 20, 21, 32) |
| Myristica fragrans | Myristicaceae | Aerial parts | Gastrointestinal weakness, vomiting, diarrhea, swelling, pain, flatulence | (10, 32) |
| Nardostachys jatamansi | Fabaceae | Aerial parts | Gastrointestinal weakness, vomiting, diarrhea, swelling, pain, flatulence | (21) |
| Valeriana celtica | Caprifoliaceae | Aerial parts | Gastrointestinal weakness, vomiting, diarrhea, swelling, pain, flatulence | (10-12, 21) |
| Trigonella foenum-graecum | Fabaceae | Seeds | Gastrointestinal weakness, vomiting, diarrhea, swelling, pain, flatulence | (11, 20, 21) |
| Tragopogon pratensis | Asteraceae | Aerial parts | Gastrointestinal weakness, vomiting, diarrhea, swelling, pain, flatulence | (21) |
| Tragopogon graminifolius | Asteraceae | Aerial parts | Gastrointestinal weakness, vomiting, diarrhea, swelling, pain, flatulence | (10, 11, 20, 21, 32) |
| Valeriana celtica | Caprifoliaceae | Rhizome | Gastrointestinal weakness, vomiting, diarrhea, swelling, pain, flatulence | (10, 12, 20, 21, 32) |
| Viola odorata | Violaceae | Seeds | Gastrointestinal weakness, vomiting, diarrhea, swelling, pain, flatulence | (10, 11, 20, 21) |
Pharmacological activities of TPM recommended GI plants

Pharmacological GI activities of TPM recommended medicinal plants have been shown by a large number of in vitro and animal investigations as well as some clinical trials.

Mastic gum (oleo-gum-resin from *Pistacia lentiscus* L.) as one of the most emphatic TPM recommended GI plants has been found to exert anti-*Helicobacter pylori* activities *in vivo* (33). In a randomized clinical trial (RCT) in 148 patients with functional dyspepsia, administration of 350 mg mastic gum three times daily for 3 weeks significantly improved symptoms of functional dyspepsia when compared to placebo (34). Mastic gum decreased histological damage in trinitrobenzene sulfonic acid (TNBS)-induced colitis, regulated oxidant/antioxidant balance and modulated inflammation (35). It improved the clinical features of Chron’s disease (CD)(36). Additionally, mastic gum exhibited antibacterial activity against *Escherichia coli*, *Staphylococcus aureus*, and *Bacillus subtilis* (37).

*Artemisia absinthium* L. another important GI active TPM plant could induce a significant decrease in volume of gastric juice, acid output and peptic activity in rats. It also decreased the ulcer index significantly (38). In a 6 weeks controlled clinical trial in patients with CD, administration of *A. absinthium* improved symptoms of CD by increased production of pro-inflammatory cytokines such as TNF-α (39). *A. absinthium* also exhibited anti-inflammatory, antinociceptive, anhelminic activities properties and antibacterial activities against GI pathogens (40-42).

Olive oil has traditionally been applied to relieve gastric pain and inflammation, dyspepsia, abdominal pain caused by flatulence, bulimia, hiccups, nausea and vomiting, cholera, IBD and hemorrhoids (11, 20, 32). Odabasoglu et al demonstrated that olive oil could prevent the indomethacin-induced gastric damages in rats, enhanced the efficacy of indomethacin for reducing carrageenan-induced paw edema and exerted anti-inflammatory activity against paw edema (43). In a human study, a 30-day olive oil containing diet resulted in attenuating gastric secretory function, suppression of serum gastrin and higher levels of peptide YY in patients with gallstones (44). Olive oil also exhibited strong anti-*H. pylori* activity, decreased acid secretion in the GI tract and reduced the size of peptic ulcers (45).

Additionally, olive oil phenols inhibited the NF-κB driven transcription in a concentration-dependent manner supporting its use in gastric inflammation (46).

Guggul gum (oleo-gum-resin from *Commiphora mukul*) has been widely applied in TPM to alleviate stomach distention and swelling, belching, intestinal ulcers, IBD and hemorrhoids (10, 21). In a randomized controlled trial in 99 patients with hemorrhoids, administration of 3 g/day guggul gum for 4 weeks decreased flatulence, dyspepsia, gastro-esophageal reflux, and colonoscopic grading scores significantly compared to control. The rate of constipation, and proctorrhagia were also significantly improved after 4-week follow-up (47). Guggulsterone, a steroid found in guggul gum, exhibited anti-inflammatory activities in mouse models of colitis by targeting lamina propria T cells (48). In addition, guggulsterone significantly increased apoptosis in HT-29 cells through activating caspases-3 and -8. It decreased cIAP-1 and 2, and Bcl-2 levels and increased the levels of truncated Bid, Fas, p-c-Jun, and p-JNK. The size of HT-29 xenograft tumors in guggulsterone-treated mice was significantly smaller than control group (49).

Pharmacological activities of other TPM GI recommended plants are shown in Table 2. Most of the mentioned plants exhibited various GI activities which support their extended application in TPM. Nonetheless, the majority of studies have investigated the effects of internal administration of the plants and there is scarcity in studies dealing with their topical application as it is recommended in TPM. Therefore, future studies are needed to elucidate GI effects of TPM plants in topical use. Interestingly, some of the mentioned plants like saffron are traditionally used in depression, tension, anxiety and insomnia even in topical use (21, 50, 51). These effects can exert additional relieving effects on stress-related GI diseases such as peptic ulcers, IBD, etc.

Essential oils from aromatic plants have components with antibacterial activities. Cinnamaldehyde, thymol analogues, geraniol, menthol and carvacrol are examples of these components which mostly derive from terpenes and terpenoids (52, 53). Topical use of plants containing antibacterial essential oils may reduce bacterial pathogens in GI track especially in the intestines. Interestingly, phenolic monoterpenes and phenylpropanoids (typically showing strong antimicrobial activities) in combination with other components were found to increase the bioactivities of these mixtures which support the application of the combination of herbal oils in TPM (12, 54). It is well-established that the combination of phenolics such as thymol and carvacrol, with monoterpenes alcohols like eugenol produced synergistic effects on several microorganisms. There are some generally accepted mechanisms of antimicrobial interaction that produce synergistic effects. These mechanisms include the sequential inhibition of a common biochemical pathway, inhibition of protective enzymes of microorganisms; and the use of cell wall active agents to enhance the uptake of other antimicrobials (54). Polyphenols have been found to exhibit numerous beneficial activities in the gastrointestinal tract, including antiinflammatory, anti-ulcer, anti-secretory, anti-colitis, anti-diarrheal, and anti-oxidative stress properties (55). For instance, flavonoids and other phenolic compounds such as flavone, quercetin and naringenin which are present in many TPM plants have
been found to be effective in inhibiting the growth of the microorganisms (56). In addition, a number of polyphenolic compounds including oleuropein, cinnamic acid, baicalein, rutin, quercetin, and tephrosin have been reported to exhibit anti-ulcerogenic activity with a good level of gastric protection (57). Generally, polyphenols possess anti-ulcer activities through improving cytoprotection, re-epithelialization, angiogenesis, and neovascularization which are mediated by the up-regulation of tissue growth factors, PGs, and vWF/ factor VIII complex, together with the down-regulation of anti-angiogenic factors. Moreover, polyphenols have been shown to suppress vascular permeability and leukocyte-endothelium interaction mediated by the down-regulation of cellular and intercellular adhesion agents. Polyphenols can pailate inflammatory responses and down-regulate pro-inflammatory cytokines within mucosal ulcers by inhibiting intracellular signaling pathways of the inflammatory process (ERK, JNK, and MAPK), as well as modulating intracellular transcriptional factors (55). Besides their action as gastroprotectives, flavonoids also can be alternative agents for alleviating peptic ulcers associated with *H. pylori* (58).

Alkaloids have been also isolated from a number of TPM recommended plants. Isocorydine alkaloid found in some *Aquilaria spp.* which are used in TPM GI remedies exhibited spasmolytic effects and weak gastric H/H+-K+-ATPase activity (59). Tropane alkaloids such as atropine and scopolamine which are found in Solanaceae family are used to block the muscarinic activity of acetylcholine showing anti-secretory and antispasmodic effects in the treatment of peptic ulcer, gastroenteritis, and spastic colitis (60). Anthocyanins also possess beneficial activities in the management of many GI disorders such as IBD by alleviating oxidative stress, exhibiting cytoprotective activity, down-regulating the inflammatory cytokines and suppressing cellular signaling pathways of inflammatory responses (61). Gastrointestinal activities of a number of phytochemicals present in TPM plants have been shown in Table 2. As seen in Table 2, several phytochemicals from TPM plants have been found to be effective in GI ailments. β-asarone from *Acorus calamus* L. (potent anthelmintic, anti-amoeobic and antibacterial activities), amygdalin from *Amygdalus communis* L. var. *dulcis* (anti-gastric ulcer activity), boswellic acids from *Boswellia serrata* (gastric ulcer protective effect, protecting the colonic mucosa against tissue injury, and reducing colitis activity), guggulsterone from *C. mukul* (anti-inflammatory, apoptogenic properties in colon cancer cells), crocin from *Crocus sativus* L. (inhibiting the growth of colorectal cancer cells), crocetin (ameliorating UC and anti-*H. pylori* effects), isomasticadienolic acid from *P. lentiscus* (Reducing *H. pylori* colonization), and cyclotides from *Viola odorata* L. (anti-gastrointestinal nematodes) are among the most GI bioactive phytochemicals. Accordingly, above-mentioned compounds are potential active principles with GI tract actions as well as good candidates for future pharmacological and clinical studies and developing new GI protective medicines.

**The most emphatic TPM topical GI formulations**

Numerous multi-herbal topical formulations are used in TPM for the treatment of GI diseases. Some of these formulations have been frequently mentioned in many TPM textbooks indicating their extensive effectiveness and safety in traditional medicine observations. The following formulations are examples of the most frequently applied topical TPM formulations for the treatment of GI ailments.

A topical preparation containing *Valeriana celtica* L., mastic oil, aloe sap and verjuice is recommended to apply on stomach area to relieve gastritis and gastric burning and discomfort. As seen in Table 2, some of the ingredients of this remedy have been found to be strongly GI-protective supporting their use in TPM. A poultice consist of barley flour in combination with diverse gastroprotective anti-ulcer plants such as pureed quince, squash, purslane, mastic, sandalwood powder, *etc.* has also been frequently used to alleviate gastric inflammation, pain and burning (10, 21). An ointment containing *Commiphora opobalsamum* Engl. oleo-gum-resin, aloe and bees wax is used to relieve symptoms of gastritis (10). Another well-experienced topical prescription for gastric discomfort, nausea and vomiting is a mixture of crushed squash, purslane, barley flour and vinegar (10).

Rubbing a mixture of rose oil and mastic oil on stomach has been frequently recommended for terminating prolonged episodes of hiccups (21). A poultice containing olibanum, mastic gum, agarwood, sweet flag, pomegranate flowers, quince juice and wine is noted in many TPM books for the treatment of poor appetite (10, 21).

An ointment containing guggul gum in mixture with dill and fenugreek seeds, henna leaves, olive oil and rose oil has been used as a potent remedy to alleviate IBD symptoms (10).

The above-mentioned prescriptions along with many other TPM remedies as invaluable sources of experienced traditional knowledge offer new horizons for future studies to find bioactive phytochemicals and develop new phytopharmaceuticals and therapeutic strategies for the treatment of GI diseases.

**Conclusion**

With around 60 different plant species from 34 families frequently used in hundreds of recipes of TPM for topical application to cure a wide variety of GI ailments, we can conclude that these plants (in simple use or in combination recipes) can be
potential alternatives are generally applied in forms of poultices, ointments, baths and lotions on the stomach area, lower abdomen, lower back and liver to achieve regional and/or systemic delivery of the plant’s biologically active compounds. β-asarone from *A. calamus*, amygdalin from *A. communis* L. var. *dulcis*, boswellic acids from *B. serrate*, guggulsterone from *C. mukul*, crocin and crocetin from *C. sativus*, isomasticadienolic acid from *P. lentiscus*, and cyclotides from *V. odorata* are among the most important phytochemicals present in TPM plants with GI protective activities. These phytochemicals along with many other bioactive compounds play pivotal role in alleviating GI disorders through exhibiting numerous activities including anti-spasmodic, anti-ulcer, anti-secretory, anti-colitis, anti-diarrheal, antibacterial, anthelmintic, anti-inflammatory and anti-oxidative stress properties. Several mechanisms underlie these activities including the alleviation of oxidative stress, exhibiting cytoprotective activity, down-regulation of the inflammatory cytokines, suppression of the cellular signaling pathways of inflammatory responses, improving re-epithelialization, angiogenesis, and neovascularization mediated by the up-regulation of tissue growth factors, PGs, and vWF/factor VIII complex, together with the down-regulation of anti-angiogenic factors, blocking muscarinic activity of acetylcholine (resulting in antispasmodic effects), etc. TPM topical GI remedies commonly contain a combination of herbal powders, oils, oleo-gum-resins and extracts which may have synergistic effects with different mechanisms. Mastic gum, aloe, absinthe and olive oil are the most frequent herbal ingredients of TPM GI recipes. Although pharmacological investigations well support the use of TPM plants, data on topical application of these plants are scarce. Accordingly, there is a need to investigate pharmacological activities, clinical efficacy, pharmacokinetic aspects as well as possible skin reactions and other adverse effects of recommended plants in topical use. In conclusion, TPM topical GI remedies, the mentioned medicinal plants and their active compounds are useful pharmacological tools to discover new active principles with GI tract actions.

Table 2. Gastrointestinal activities of TPM-recommended plants for topical use and their main phytochemicals

| Scientific name | Common name | Extract/phytochemical/plant part | Pharmacological activities | Model | Reference |
|-----------------|-------------|---------------------------------|---------------------------|-------|-----------|
| *Acacia arabica* (Lam.) Muhl. ex Wild. | Gum arabic tree | Gum arabic-supplemented oral rehydration solution | Anti-diarrhea | *in vivo* | 62 |
| *Acorus calamus* L. | Sweet flag | Crude extract/n-hexane fraction | Spasmolytic activity by inhibition of spontaneous and high K+-induced contractions through Ca²⁺-channel blockade in the isolated rabbit jejunum preparation | *ex vivo* | 63 |
| *Aloe vera* | Aloe | Aqueous extract of leaves of *A. ferox* Mill | Improving intestinal motility, increasing fecal volume in loperamide-induced constipation, Inhibitory effects on colorectal prostaglandin E2 and interleukin-8 production | *in vitro* | 27 |
| *Althea officinalis* L. | Marshmallow | Hydro-ethanolic extract of aerial parts | Antibacterial against *Escherichia coli* | *in vitro* | 30 |
| *Amygdalus communis* L. var. *dulcis* | Bitter almond | Amygdalin | Protection against gastric ulcer | *in vivo* | 71 |
| *Anethum* | Dill | Seed ethanolic extract | Inhibiting acid secretion and the | *in vivo* | 72 |
| botanical | extract | activity | mode of study | reference |
|-----------|---------|----------|--------------|-----------|
| *Apium graveolens* L. | Seeds powder, Aqueous and ethanolic extracts of seeds | Protection against gastric ulcer, attenuation in the changes in gastric juice volume, pH, acid-output and ulcer index, acid buffering activities, peptic binding activity | *in vitro* | (74) |
|  | Hydroalcoholic extract | Potent spasmylocytic activity in ileum | *ex vivo* | (75) |
|  | Hot water and acetone extracts of seeds, Methanolic and aqueous extracts of leaves | Inhibition of gastric ulcers | *in vivo* | (76) |
|  | Ethanol and aqueous extracts of leaves | Antimicrobial activity against enteric pathogens, Inhibition of spontaneous rat ileum contractions | *ex vivo* | (77) |
| *Aquilaria agallocha* Roxb. | Ethanol extract | Analgesic, anti-inflammatory | *in vivo* | (80) |
| *Artemisia absinthium* L. | Essential oil containing trans-sabinyl acetate, myrcene, β-thujone | Anti-fungal, antibacterial activity | *in vitro* | (81) |
|  | Ethanol extract of aerial parts | Anti-gastric ulcer effects, decrease in volume of gastric juice and acid output | *in vivo* | (38) |
|  | Powder, Methanol extract, Methanol extracts, Essential oil, aqueous extract, Aqueous extracts ethanolic extract, A multiherbal preparation containing ethanolic-aqueous extracts | TNF-α suppression, remission of symptoms of CD, Anti-inflammatory, Antibacterial (GI pathogens), Anti-inflammatory, anti-nociceptive, Antihelmintic | RCT | (39) |
|  | *Boswellia* spp. | Cure upper abdominal complaints | RCT | (83) |
|  | *B. serrata* oleo-gum-resin | Complete resolution of ulcers in chronic colitis, loss of friability of mucosa, and granulation, loss of hypercellularity of lamina propria without distorted crypt architecture in rectal mucosa, healing of ulcers and loss of fibrous tissue and chronic inflammatory cells | clinical trial | (84) |
|  | *B. serrata* gum-resin hydroalcoholic extract | Antidiarrheal activity, inhibition of acetylcholine- and electrical field stimulation-induced contractions in the isolated guinea-pig ileum, Gastric ulcer protective effect | *in vivo, ex vivo* | (85) |
|  | Boswellic acids, *B. serrata* gum-resin extract, acetyl-11-keto-β-boswellic acid | Attenuating leukocyte-endothelial cell adhesive interactions, ameliorating inflammation-associated tissue injury in a rat model of experimental IBD, Gastric ulcer protective effect | *in vivo* | (86) |
|  | Boswellic acids | Attenuating the recruitment of both leukocytes and platelets, blunting P-selectin expression, protecting the colonic mucosa against tissue injury, and reducing colitis activity | *in vivo* | (88) |
|  | β-boswellic acid derivatives | *H. pylori* urease inhibitory activities | *in vitro* | (89) |
| *Brassica oleracea* | Hydroalcoholic extract of leaves | Protection against gastric ulcer | *in vivo* | (90) |
| Plant Name                      | Part Used                  | Extract Type               | Activity                                                                 | In Vitro | Reference |
|-------------------------------|----------------------------|----------------------------|--------------------------------------------------------------------------|----------|-----------|
| *L. Carum carvi*              | Essential oil              | Methanol extract of seeds  | Anti-H. pylori, in vitro                                                | in vitro | (91)      |
|                               |                            | Ethanol extract of seeds   | Treatment of intestinal dysbiosis                                         | in vitro | (92)      |
|                               |                            | Powdered seeds             | Inhibiting the response of intestinal smooth muscle cells to acetylcholine | ex vivo   | (93)      |
|                               |                            | Alcoholic extract          | Modulatory role on tissue lipid peroxidation, antioxidant profile and preventing 1,2-dimethyhydrazine-induced histopathological lesions in colon cancer rats | in vivo   | (94)      |
|                               |                            |                            | Anti-ulcerogenic activity; reducing acid output, increasing mucin secretion, increasing prostaglandin E2 release, decrease in leukotrienes, protection against gastric ulceration | in vivo   | (95)      |
| *L. Carum copticum*           | Ethanol and aqueous extract of fruits | Ethanol and aqueous extract of fruits | Antidiarrhoeal activity                                                  | in vivo   | (96)      |
| Benth. & Hook.f.              | Aqueous extract of fruits  |                            | Inhibitory effect on ACh-induced contraction in rat’s ileum              | ex vivo   | (97)      |
|                               | Aqueous extract            | An equal mixture of methanol, diethyl ether and petroleum benzene extract | Treatment of peptic ulcer, Anti-H. pylori                                 | in vivo   | (98)      |
|                               |                            |                            |                                                                          |          | (99)      |
| *Cissus quadrangularis*       | Methanol extract of stem   | Methanol extract of stem   | Attenuation in levels of TNF-α, IL-1β, microvascular permeability, activity of nitric oxide synthase-2, mitochondrial antioxidants, lipid peroxidation, DNA damage, Decrease in tissue damage glutathione, superoxide dismutase and catalase, reducing size of NSAID induced ulcer crater, restoration of mucosal epithelium | in vivo   | (100, 101) |
| Labdanum                      | Stem extract               |                            | Attenuation in aspirin-induced gastric lesions, an increase in uric acid, antioxidant enzymes, SH groups, decrease in lipid peroxidase, TNF-α, xanthine oxidase, myeloperoxidase activities | in vivo   | (102)     |
|                               | Methanol extract           |                            | Increase in the mucosal defensive factors like mucin secretion, mucosal cell proliferation, glycoproteins, and life span of cells in experimentally induced gastric ulcer | in vivo   | (103)     |
| *Cistus ladaniferus*          | Chloroform extract         | Chloroform extract         | Potent anti-H.Pylori, in vitro                                           | in vitro | (104)     |
| Curtis Labdanum               | Aqueous extract of aerial parts | Aqueous extract of aerial parts | Effective against reserpine- and serotonin-induced mucosal congestion and haemorrhagic ulcers | in vivo   | (105)     |
|                               | Aqueous extract of leaves and stems | Aqueous extract of leaves and stems | Antispasmodic action in the rabbit jejunum through calcium channel blockade | ex vivo   | (106)     |
|                               | Aerial parts aqueous extract | Aerial parts aqueous extract | Anti-diarrhoeal activity in castor oil-induced diarrhoea                 | in vivo   | (107)     |
| *Commiphora mukul* Engl.      | Guggulsterone              | Guggulsterone              | Anti-inflammatory activities in mouse models of colitis by targeting lamina propria T cells | in vivo   | (48)      |
|                               |                            |                            | Activation of the mitochondria-dependent pathway and the extrinsic pathway of apoptosis in colon cancer cells, inhibition of the growth of HT-29 xenografts | in vitro | (49)      |
|                               |                            |                            | Inducing apoptosis, inhibition of angiogenesis and metastasis in colon cancer cells through | in vitro | (108)     |
| Plant Name                        | Part Used                          | Activity                                                                 | Study Type | References |
|----------------------------------|------------------------------------|--------------------------------------------------------------------------|------------|------------|
| *Commiphora opobalsamum* Engl.   | Arabian balsam tree                | Protecting against gastric ulcers, analgesic and anti-inflammatory activity | *in vivo*  | (109)      |
| *Costus speciosus* (L.Koenig) Sm. | Crêpe ginger                       | Inhibiting the growth of colorectal cancer cells                         | *in vitro* | (112)      |
| *Crocus sativus* L.              | Saffron                             | Anti-H. pylori effects                                                  | *in vitro* | (113)      |
| *Cupressus sempervirens* L.      | Mediterranean cypress              | Inhibition of the growth of *H. pylori*                                  | *in vitro* | (118)      |
| *Cydonia oblonga* Mill.          | Quince                              | Diminishing inflammation and ulcer indices in TNBS-induced ulcerative colitis | *in vitro* | (120)      |
| *Cymbopogon schoenanthus* (L.) Spreng. |   | Anti- *E. coli*, anti-*Enterobacter aerogenes*                              | *in vitro, in vivo* | (122) |
| *Cyperus rotundus* L.            | Java grass                          | Gastric ulcer inhibitory effect                                          | *in vivo*  | (125)      |
| *Dorema ammoniacum* D. Don       | Gum ammoniac tree                  | Anti-*H. pylori*                                                         | *in vitro* | (127)      |
| *Eugenia Caryophyllata* Thunb.   | Clove                               | Protection against gastric ulcer                                         | *in vivo*  | (128)      |
| *Foeniculum vulgare* L.          | Fennel                              | Suppressing ROS generation in *H. pylori*-infected gastric epithelial cells | *in vitro* | (116)      |
| *Glossostemon bruguieri* Desf.   | Dombeya arabica                     | Anti-ulcerogenic and antioxidant effects                                 | *in vivo*  | (77)       |
| *Hordeum vulgare* L.             | Barley                              | Anti-inflammatory                                                        | *in vitro*, *in vivo* | (130, 131) |
| *Hyoscyamus niger* L.            | Henbane                             | GI antispasmodic effect through a combination of anticholinergic and Ca²⁺-antagonist mechanisms. | *in vivo* | (132)      |
| *Iris florentina* L.             | Iris                                | Decrease in the volume of gastric                                        | *in vivo*  | (133)      |
| *Lawsonia inermis*               | Henna                               |                                                                           |            |            |

*Oleo-gum-resin powder* blocking STAT3 and VEGF expression. *Reduction in symptoms of uncomplicated hemorrhoids grade 1 and 2.* *Hyoscyamus niger* L. *Hordeum vulgare* L. *Hyoscyamus niger* L. *Iris florentina* L. *Lawsonia inermis* *Cupressus sempervirens* L. *Cupressus sempervirens* L. *Cyperus rotundus* L. *Crocus sativus* L. *Commiphora opobalsamum* Engl. *Costus speciosus* (L.Koenig) Sm. *Dorema ammoniacum* D. Don *Eugenia Caryophyllata* Thunb. *Foeniculum vulgare* L. *Glossostemon bruguieri* Desf. *Hordeum vulgare* L. *Hyoscyamus niger* L. *Iris florentina* L. *Lawsonia inermis*
| Plant Name                     | Extract/Component                              | Activity                                                                 | Study Type | Reference |
|-------------------------------|-----------------------------------------------|--------------------------------------------------------------------------|------------|-----------|
| *Linum usitatissimum* L.      | Aqueous extract of leaves                     | Antibacterial activity                                                   | in vitro   | (134)     |
|                               | Crude extract of lignans of seeds             | Protection and recovery against gastric ulcers                           | in vivo    | (135)     |
|                               | Seeds oil and mucilage                        | Protection against gastric ulcers                                        | in vivo    | (136)     |
|                               | Aqueous-methanol extract of seeds             | Antidiarrheal and antispasmodic activities through inhibition of Ca²⁺ channels | in vivo, Ex vivo | (137)     |
| *Malus domestica* Baug.       | Methanol extract of fruit flesh containing polyphenols | Preventing aspirin-induced gastric injury, countering aspirin-induced up-regulation of HB-EGF and COX-2 expression | in vivo    | (138)     |
|                               | Fruit juice                                   | Antiulcerative activity                                                 | in vivo    | (139)     |
|                               | Fruit sauce                                   | Anti-diarrheal activity                                                 | in vivo    | (140)     |
|                               | Hydroalcoholic extract of aerial parts        | Protective effect against ethanol-induced gastric mucosal lesions by reducing gastric lesions and malondialdehyde and increasing glutathione levels in gastric tissue or whole blood | in vivo    | (141)     |
|                               | aqueous-methanolic extract of aerial parts    | Antidiarrheal, antisecretory and antispasmodic activities through K⁺-channels activation and weak Ca²⁺ antagonist effect | in vivo    | (142)     |
|                               | aqueous extract of aerial parts               | Spasmolytic activity by cAMP-cGMP-phosphodiesterases inhibition         | in vitro   | (143)     |
|                               | decoction of aerial parts                     | Potent anti-diarrheal and antioxidant: protection against castor oil-induced diarrhea and intestinal fluid accumulation | in vivo    | (144)     |
| *Matricaria chamomilla* L.    | Chamomile gel and aqueous extract containing catechin and cinnaamic acid | Attenuating acetic acid induced UC antioxidant and anti-inflammatory effects | in vivo    | (145)     |
| *Myristica fragrans* Houtt.   | Nutmeg crude suspension and petroleum ether extract of seeds | Anti-diarrheal effect                                                  | in vivo    | (146)     |
| *Nardostachys jatamansi* DC.  | Spikenard hydro-ethanolic extract             | Anti-H. pylori activity                                                 | in vitro   | (147)     |
| *Nymphaea lotus* L.           | White lotus Aqueous extract                   | Protection against gastric ulcer                                          | in vivo    | (148)     |
| *Nymphaea alba* L.            | White water rose Ethanol extract of rhizome   | Antioxidant and analgesic                                               | in vivo, in vitro | (149)     |
| *Olea europaea* L.            | Olive Olive oil                               | Preventing the indomethacin-induced gastric damages in rats, enhancing efficacy of indomethacin for reducing carrageenan-induced paw edema, anti-inflammatory effect against paw edema | in vivo    | (43)      |
|                               | A 30-day period of diets containing olive oil | Attenuating gastric secretory function, suppression of serum gastrin and higher levels of peptide YY. | Patients with gallstones | (44)      |
|                               | Polar fraction of extra-virgin olive oil      | Inhibition of NF-κB driven transcription and nuclear translation in AGS cells (a model for gastric inflammation) | in vitro   | (46)      |
|                               | Virgin olive oil extracts rich in phenolic compounds especially dialdehydic form of decarboxymethyl ligstroside (Ty-EDA) | Strong anti-H. pylori activity, decrease acid secretion in the GI tract, reduction in the size of peptic ulcers | in vitro   | (45)      |
|                               | Leaves extract                                | Attenuation of the ethanol-induced gastric lesions, prevention of an increase in gastric lipid peroxidation, prevention of a decrease in antioxidative enzyme activity | in vivo    | (150)     |
| *Opopanax chironium* W.D.J.Koch | Sweet myrrh                                  |                                                                        | -          | -         |

**Note:** The table above provides a summary of the activities of different extracts from various plants. The activities include antibacterial, anti-diarrheal, anti-inflammatory, antioxidative, analgesic, anti-ulcerative, and anti-secretory effects, among others. The study types vary from in vitro to in vivo and in vivo, Ex vivo. The references are cited in parentheses next to the corresponding activities.
| Phoenix dactylifera L. | Date | Aqueous and ethanolic extracts of fruits | Ameliorative effect on ethanol-induced gastric ulcer | in vivo (151) |
|-----------------------|------|-----------------------------------------|---------------------------------------------------|---------------|
|                      |      | Ethanol and water extracts of the flesh and pits | Enhancing the GI transit | in vivo (152) |
| Pimpinella anisum L. | Anise | Aqueous suspension of fruits | Cytoprotective and anti-ulcer activities against experimentally-induced gastric lesions | in vivo (153) |
| Pistacia atlantica Desf. | Persian turpentine tree | Aqueous and ethanolic extracts of fruits | Antioxidant and antimicrobial activities | in vitro (154) |
| Pistacia atlantica subsp. kurdica | Baneh tree | Essential oil of oleo-gum-resin | Antimicrobial activity | in vitro (155) |
| Pistacia lentiscus var. Chia | Mastic | Oleo-gum-resin, essential oil | Anti-colitis activity | in vivo (156) |
| Portulaca oleracea L. | Purslane | Aqueous and ethanolic extracts | Gastric anti-ulcerogenic effects | in vivo (158) |
| Punica granatum L. | Pomegranate | Methanol extract of peel | Potent anti-\(H.\) \(pylori\) | in vitro (159) |
|                      |      | Aqueous-methanolic extract of flowers | Gastric anti-ulcerogenic effects | in vivo (160) |
|                      |      | Ethanolic extract of pericarp ethyl acetate and n-butanol fractions | Anti-enterohemorrhagic \(E.\) \(coli\) | in vitro (161) |
|                      |      | Aqueous extract of peels | Antidiarrheal effects | in vivo (162) |
|                      |      | Methanol-water extract of flowers and its ellagic acid rich fraction | Attenuation of colonic inflammation in UC, attenuation of histamine, myeloperoxidase and oxidative stress | in vivo (163) |
| Rosa × damascena Mill. | Damask rose | Hydroalcoholic extract of flowers | Inhibition of ileum contraction at mg concentrations, stimulatory effect on ileum at µg concentrations | ex vivo (164) |
|                      |      | Flowers essential oil containing geraniol and citronellol | Inhibitory effect on ileum contraction | ex vivo (165) |
|                      |      | Hydroalcoholic extract of flowers | Improving macroscopic and histopathological parameters of acetic acid-induced colitis | in vivo (166) |
| Rhus coriaria L. | Sumac | Crude methanolic extract | Anti-secretory, antidiarrheal and antispasmodic properties through \(Ca^{2+}\) blockade | in vivo, in vitro (167) |
| Santalum album L. | Indian sandalwood | Ethanol extract | Anti-\(H.\) \(pylori\) activity | in vitro (168) |
|                      |      | Hydroalcoholic extract of leaves | Analgesic effect | in vivo (169) |
|                      |      | Methanol extract of wood | Anti-diarrheal activity | in vivo (170) |
|                      |      | Hydro-alcoholic extract | Protection against gastric ulcer | in vivo (171) |
|                      |      | Methanolic extract of wood | Analgesic and anti-inflammatory activities | in vivo (172) |
| Tanacetum balsamita L. subsp. Balsamitades (Schultz Bip.) Grierson | Meadow salsify | Ethanol extract of aerial part | Antibacterial properties | in vitro (174) |
| Tragopogon pratensis L. | Goatsbeard | Ethanol extract of aerial part | Alleviating colitis via anti-inflammatory effects | in vivo (175) |
| Tragopogon graminifolius | | Hydroalcoholic extract of aerial part | Protection against gastric ulcer | in vivo (176) |
Trigonella foenum-graecum L. 
Fenugreek Aqueous extract and a gel fraction of seeds Gastric ulcer protective effects in vivo (177)

Valeriana celtica L. 
Alpine valerian - - -

Viola odorata L. 
Sweet violet Aqueous extract of aerial parts Cyclotides Hydro-ethanol extract Antibacterial effects in vitro (178) Anti-gastrointestinal nematodes in vitro (179) Strong inhibitor of IL-8 secretion from H. pylori-infected epithelial cells in vitro (116)

Ziziphus spina-christi (L.) Wild. 
Christ’s Thorn jujube Methanol extract of stem bark Anti-diarrhoeal effects in vivo (180)

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