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REVIEW ARTICLE

CONSIDERING THE IMPORTANCE OF MEDICINAL PLANTS AND NATURAL PRODUCTS AND THEIR MECHANISMS OF ACTION FOR TREATMENT OF GASTROINTESTINAL DISORDERS

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Summary

Background and Purpose: The application of medicinal plants and herbs to cure diverse animal and human ailments predates recorded history. Gastrointestinal disorders have a high prevalence in human societies.
Methods: This research examined the scientific literature from 1990 to June 2025 by conducting a bibliometric analysis of the literature published on the Web of Science database, including more than one thousand articles. The information provided was obtained from randomized control experiments, analytical observations, review articles, and studies which were gathered from different literature sources such as Google Scholar, Scopus, Science Direct, and PubMed.
Results: The gastrointestinal tract is one of the most important organs in the human body, and it is vulnerable to great diversity of diseases such as infectious and parasitic disorders, constipation, gastroenteritis, reflux, diarrhea, and bloating. Some of the most important medicinal plants which have been used in different traditional medicinal sciences for the treatment of dyspepsia symptoms are chamomile (*Matricaria recutita*), cinnamon (*Cinnamomum verum*), ginger (*Zingiber officinalis*), licorice (*Glycyrrhiza glabra*), peppermint (*Mentha piperita*), and guava (*Psidium guajaba*). The most notable herbs used to treat bloating are aniseed (*Pimpinella anisum*), cassia (*Cinnamomum aromaticum*), celery (*Apium graveolens*), cinnamon (*Cinnamomum verum*), dill (*Anethum graveolens*), fennel (*Foeniculum vulgare*), ginger *(Zingiber officinalis*), parsley (*Petrosilenum crispus*), pennyroyal (*Mentha pulegium*), peppermint (*Mentha spicata*), star anise (*Illicium verum*), and thyme (*Thymus vulgaris*). Phytochemicals such as seaweed-derived polysaccharide, phytohemagglutinin, and allicin have been reported as important components to induce precocious gut maturation. Phytochemicals can also change the composition of gut microbiota, digest normally indigestible molecules into bioavailable molecules, and enhance nutrient availability. *Ganoderma lucidum*, Gegen Qinlian decoction, Huang-qin decoction, and *Glycyrrhiza uralensis* Fisch. are important traditional Chinese medicine with significant effects on intestinal flora and different microbial communities.
Conclusions: The review article aims to study and survey the importance of medicinal plants and herbs while considering their mechanisms of action for treatment of gastrointestinal disorders.

Key words: Celiac disease; Gallstones; Gastritis; Gastrointestinal disorder; Medicinal plant; Peptic ulcer disease

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Highlights:

1. **The gastrointestinal tract is one of the main organs of the human body, which is vulnerable to various diseases.**
2. **Some Chemical drugs have low effectiveness with different negative effects.**
3. **Medicinal plants and herbs are the best alternative options which can influence common gastrointestinal diseases and disorders.**
4. **Medicinal herbs and plants contain high bioactive components with positive influence for the treatment of gastrointestinal disorders.**
5. **Medicinal plants can significantly use for gastrointestinal diseases as these diseases are the complex illnesses of different parts of the gastrointestinal tract, which can influence small intestine, stomach, esophagus, rectum, and large intestine.**
6. **Medicinal plants which can improve gastrointestinal health are *Matricaria chamomilla*, *Mentha spicata*, *Melissa officinalis*, *Artemisia ludoviciana*, *Flourensia cernua*, *Phoradendron californicum*, and *Turnera diffusa*.**
7. **Medicinal plants with natural components can provide effective and safe alternatives to synthetic medications with lower side effects and broader potential for treatment customization.**

Introduction and background

Plant-based treatments and therapies are one of the most important choices for rural societies in different remote regions, especially in developing and under-developed countries (1-5). They can be used in the treatment of different infectious wounds because of their minimal toxic side effects, high effectiveness, renewable nature, and wide availability (6-10). Gastrointestinal disorders can be structural of functional (11,12), and both types may cause severe impairment of psychological wellbeing and negatively influence life quality as well as shortened life expectancy (13-16). Many non-psychoactive cannabinoids, like cannabidiol are appropriate to treat various diseases and disorders of the gastrointestinal tract (17,18). Other signs of gastrointestinal disorders are changed central nervous system processing, visceral hypersensitivity, motility disturbance, changes concerning gut microbiota, and alteration in immune and mucosal functions (19-21).

Celastrol, a triterpene obtained from the root of *Thunder of God Vine* which is very common in traditional Chinese medicine could down-regulate biglycan protein, which is essential for gastric cancer invasion and immigration, activated receptor-interacting protein 1 and 3 (RIP1 and RIP3), and finally promoted the translation of mixed-lineage kinase domain-like (MLKL) from cytoplasm to plasma membrane, inducing to necroptosis of gastric cancer cell (22). List of medicinal plants with anti-ulcer activity are *Terminalia pallida* (Terpenois, tannins, glycosides, flavonoids, alkaloids), *Terminalia chebula* (Carbohydraes, flavonoids, alkaloids, phenols, terpenoids, tannins), *Polyalthia longifolia* (Terpenoids, alkaloids), *Spondias mombin* (Saponins, flavonoids, tannins, phenolics), *Ficus exasperate* (Tannins, flavonoids, saponins, alkaloids), *Toona ciliate* (Sterols, quercetin, terpenoids), *Calligonum cosmosum* (Flavonoids, phenols), *Tephrosia purpurea* (Flavonoids), *Carlina acanthifolia* (Essential oils, flavonoids, inulin), *Ocimum sanctum* (Eugenol, euginal, urosolic acid), *Momordica charantia* (Sterols, steroids, alkaloids, flavonoids), *Ziziphus jujuba* (Tannins, polyphenols, sterols, alkaloids, flavonoids), *Scutia buxifolia* (Tannins, polyphenols, alkaloids, flavonoids), *Madhuca indica* (Flavonoids, triterpenoids), *Maytenus robusta* (Flavonoids, steroids, triterpenes), *Casearia sylvestris* (Triterpenes, tannins), *Ulteria salicifolia* (Tannins, saponins, steroids), *Asparagus racemosus* (Polysaccharides, saponins), *Kaempferia parviflora* (Flavonoids, anthrones, alkaloids), *Passiflora foetida* (Flavonoids, phenolic compounds, alkaloids, proteins, phenols), *Alhagi maurorum* (Sterols, fatty acids, flavonoids), *Bahunia purpurea* (Tannins, sterols, flavonoids), *Cressa cretica* (Proteins, tannins, glycosides, alkaloids), and *Citrullus lanatus* (Antraquinones, saponins, steroids, terpenoids, alkaloids, tannins, flavonoids, phenols) (23-29). Ethnopharmacological researches have indicated that the application of traditional medicine for gastrointestinal disease is commonly practiced in different cultures in various part of the world. Many people in different parts of the world use medicinal plants as their first choice of health care to prevent and cure of different types of gastrointestinal disorders. The main goal of this review article is to study the effects of medicinal plants and herbs by considering different mechanisms for treatment of gastrointestinal disorders.

Gastrointestinal disorders and medicinal plants

The human gastrointestinal microbiota is composed of microbial eukaryotes (protozoan and fungi), archeae, viruses and bacteria (30), although the most diversified and abundant group is bacteria (31). Mechanism of action of plant derived substances against a broad range of gastrointestinal diseases are proanthocyanidin in *Vaccinium macrocaropon* L. which can modify biofilm formation of *Enterococcus faecalis*, and *E. coli* (32-36), zingerone of *Zingiber officinale* Rosc. which can reduce heat-labile enterotoxin (LT)-induced diarrhoea in enterotoxigenic (ETEC) via blocking the binding to GM1 ganglioside receptors of ETEC (37), epigallocatechin of *Camellia sinensis* L. which can inhibit extracellular release of Vero toxin from enterohemorrhagic *Escherichia coli* O157:H7 in enterohaemorrhagic (EHEC) (38), quercetin of *Allium cepa* L. which has role in inhibition of ATPase activity, elevates extracellular phosphatase and galactosidase of *E. coli* (39,40), berberine of *Berberis vulgaris* L. which may target proteins responsible for upholding the structure of cells and for cell division of *E. coli*, *Salmonella* spp., *V. Cholerae* (41,42), eugenol of *Syzygium aromaticum* L. which can inhibit the toxin production of EHEC (43), cinnamaldehyde of *Cinnamomum verum* J. Presl which can inhibit the toxin genes and host receptor expression and reduce toxin-mediated pathology of *C. difficile* and EHEC (43,44), baicalin (5,6,7-trihydroxyflavone) of *Scutellaria baicalensis* Georgi. which can inhibit the toxin production of *H. pylori*, and thymol of *Thymus vulgaris* L. which may disturbance of the cell membrane and cytoplasm of *C. difficile* (45,46). Kemal *et al*. (47) noted that *Artemisia herba-alba* Asso, *Artemisia campestris* L., *Mentha pulegium* L., *Juniperus oxycedrus* L., *Juniperus phoenicea*, and *Lavandula angustifolia* Mill. which have been used widely in Algerian medicinal science, contain high cytotoxic and antioxidant activities as well as caffeic acid, rutin, and catechins that can stimulate gastrointestinal digestion phases.

Herbal-derived products for treating gastrointestinal infections are curry, pomegranate, and turmeric for diarrhoea (48), *Adansonia digitata* fruit for diarrhoea (49), berberine, sulfadimidine and neomycin for acute infective diarrhoea (50), berberine for antibiotic-associated diarrhoea (51), berberine and its combinations with streptomycin, chloramphenicol, sulphaimidine, and iodochlorhydroxyqinoline for acute gastroenteritis and dysentery (52), bismuth and subsalicylate for acute nonspecific diarrhoea (53). *Artemisia maritima* L. can be used for diarrhea, intestinal worms, stomachic and vomiting (54,55), *Tanacetum falconeri* Hook. Can be applied for treatment of diarrhea, vomiting and stomachic (56), *Mentha piperita* L. can be used for treatment of vomiting and diarrhea (57,58), *Hylotelephium telephioides* (Ledeb.) can be consumed for constipation (59), both *Viola serpens* Wall. and *Oxyria digyna* (L.) can be applied for treatment of stomachic, constipation, and diarrhea (60,61), *Persicaria amplexicalus* for stomach disorders (62), *Saussurea gossypiphora* D. for constipation (63), *Aconitum heterophyllum* Wall. for intestinal worms and stomachic (64), *Echinops echinatus* Roxb. For treatment of abdominal pain (65), *Rumex hastatus* D. for stomachic and flatulence (66), *Pistacia khinjuk* stocks for indigestion (67), *Plantago himalaica* Pilg. for diarrhea and stomachic (67), *Vitis vinifera* L. for intestinal worms and constipation (68), *Cicer microphyllum* Benth. for indigestion and vomiting (69), *Capparis spinosa* L. for piles and digestive (70,71), *Artemisia annua* L. for vomiting and diarrhea (72), and *Rheum austral* D. for treatment of constipation and stomachic (73,74). Phromnoi *et al.* (75) reported that *Pisidium guajava* L., and *Punica granatum* L. have high antioxidant and anti-inflammatory activities as well as notable polyphenols with considerable potential for usage in gastric ulcer therapy. Direito *et al*. (76) found that the therapeutic effects of medicinal plants such as *Piper nigrum*, *Artemisia anomala*, *Litsea cubeba*, *Agrimonia Pilosa*, and *Morus macroura* are reductions in tumor necrosis factor-alpha, reductions IL-1β, interferon-gamma, and caspase levels, and increased interleukin (IL)-4, IL10, and expression of antioxidant enzymes, as well as regulation of gut microbiota. *Garcinia cowa* leaf extract contains a new polyprenylated benzophenone, which is called chamuangone, and it possesses significant antibacterial activity against gastrointestinal bacteria (77).

The most common medicinal plants which are common in Persian medicinal sciences to treatment of vomiting and nausea are the roots of *Justicia adhatoda*, bulb of *Allium cepa*, peduncle of *Mangifera indica*, gall of *Pistacia intigeriima*, resin of *Pistacia lentiscus*, kernel and peel of *Pistacia vera*, leaf and seed of *Rhus coriaria*, seed and leaf of *Anethym graveolens*, leaf and root of *Apium graveolens*, seed of *Carum copiticum*, fruit of *Coriandrum sativum*, seed of *Cuminum cyminum*, root and seed of *Foeniculum vulgare*, aerial parts of *Artemisia dracunculus*, root and leaves of *Onopordum acanthium*, leaf of *Cichorium intybus*, fruit of *Berberis asiatica*, fruit of *Berberis vulgaris*, the whole plant of *Parietaria officinalis*, seed of *Descurainia Sophia*, seed of *Cannabis sativa*, the whole plant of *Humulus lupulus*, fruit and latex of *Carica papaya*, oleo-resin of *Cistus ladaniferus*, the whole plant of *Terminalia*

chebula, fruit of *Cycas revoluta*, bark and roots of *Cyperus longus*, fruit of *Elaeagnus angustifolia*, fruit of *Quercus ilex*, flower of *Hypericum perforatum*, seed and aerial part of *Thymus serpyllum*, aerial parts of *Mentha aquatica*, aerial parts of *Ocimum basilicum*, peduncle and leaf of *Mentha piperita*, seed and flower of *Teucrium montanum*, leaves of *Satureja hortensis*, root bark of *Sassafras albidum*, fruits of *Tamarindus indica* and *Trigonella corniculata*, flowers of *Punica granatum*, fruit of *Adansonia digitata*, flower of *Melia azedarach*, fruit of *Morus alba*, the whole plant of *Rheum ribes*, seeds of *Portulaca oleracea*, seed of *Nigella sativa*, root of *Thalictrum foliolosum*, leaf of *Zizyphus sativa*, fruit of *Crataegus azarolus*, fruit of *Cerasus vulgaris*, fruit of *Cydonia vulgaris*, the whole plant of *Pyrus communis*, fruit of *Prunus cerasifera*, petal of *Rosa canina*, fruit of *Citrus limonum*, seed and peel of *Citrus sinensis*, seed and fruit of *Aegle marmelos*, fruits of *Sapindus trifoliatus* and *Solanum melongena*, Rhizome of *Valeriana dioscorides*, roots of *Valeriana jatamansi*, root of *Zingiber zerumbet*, fruit of *Vitis vinifera*, and seeds of *Elettaria cardamomum* (78-83).

In the Eastern region of Saudi arabia, red tea, chamomile, thyme, senna, fenugreek, clove and myrrh used for treatment of diarrhea; fennel, thyme, chamomile, clover and fenugreek to treat constipation; chamomile, anise, mint, myrrh, and marjoram for treatment of irritable bowel syndrome symptoms; ginger, mint, fenugreek, fennel and chamomile to treat dyspepsia and indigestion; and anise, fennel, thyme, black seed, fenugreek and green tea for treatment of gastric acidity and gastric infection (84). Laurindo *et al.* (85) reported that phytochemicals can interfere with different inflammation targets such as NF-κB pathways, and the most important chemical components for treatment of inflammatory bowel diseases are kaempferol, resveratrol, curcumin, astragalin, pinocembrin, sesamol, botulin, berberine, thymol, fisetin, gingerol, lycopene, galangin, euphol, and nobiletin. Medicinal plants which target Nrf2 pathways during treatment of inflammatory bowel diseases and related colorectal cancer are *Cynara cardunculus* L., *Panax ginseng*, *Ficus pandurata*, *Moringa oleifera*, *Ribes nigrum*, *Vaccinium myrtillus*, *Vaccinium myrtillus*, *Vitis vinifera*, *Forsythia suspensa*, and *Artemisia argyi* (85). It is reported that pomegranate has different chemical constituents such as anthocyanins, ellagic acid, punicalagin, citric acid, linolenic acid, and ascorbic acid which has important role in treatment of digestive diseases (86). Heartwing sorrel (*Rumex hastatulus*) contains ethyl acetate, n-Hexane, rutin, and aqueous fractions with anti-inflammatory and antioxidant activity, and anti-ulcer potential which can increases the level of protective glutathione-S-transferase, glutathione, and catalase and down-regulates oxidative stress marker (LPO) (87).

Gallstones

There is a high prevalence of gallstone disease in both developed and developing countries as a consequence of environmental, biochemical, and genetic factors (88-93). Gallstone disease is associated to low serum phytosterol levels, and hypersecretion of cholesterol in bile (94). It can stimulate the gallbladder mucosa and may cause acute/chronic cholecystitis and even gallbladder carcinoma (95,96). The symptoms of gallstone disease are nausea, abdominal pain, and fever, and the main subtypes of gallstones are categorized into three types: phosphate gallstones, pigment gallstones, and cholesterol gallstones (97). As a multifactorial disease which can be affected by both negatively and positively by diet, many samples of the protective impacts of dietary elements can prevent gallstone disease and enhance metabolic pathways (98-100). It is also found that Glutaredoxin-1 (*Glrx1*), and Glrx1-related protein S-glutathionylation can have significant role in gallstone formation via the targeting of cholesterol metabolism (101). Arrout *et al*. (102) discovered that p-cymene of *Syzygium aromaticum* and *Nigella sativa* can be considered as alternative litholytic agent to prevent gallstone formation via their potential anti-inflammatory activity in the gallbladder. Medicinal herbs and plant utilized by patients for the treatment of gallstones in Morocco are onion, celery, parsley, fennel, cumin, caraway, carrot, coriander, date palm, red radish, prickly pear, fenugreek, origanum, saffron, rosemary, lavender, sage, thyme, cinnamon, marjoram, olive, barley, flax, black cumin, apple, pomegranate, green tea, sweet orange, and turmeric (102). Chang *et al*. (103) reported that vegetarian diets may lower symptomatic gallstone disease through cholesterol lowering.

Gastroesophageal Reflux Disease (GERD)

One of the most common diseases of the gastrointestinal system is GERD (104). It is commonly happened with other gastrointestinal motility disorders like functional constipation (105), and it is very common in young infants (106). It is associated a wide range non-esophageal such as angina, chest pain, and respiratory problems, as well as the extensive range of esophageal such as Barrett ,s disease, esophageal cancer, and esophageal ulcer

(107-115). It is discovered that the most important medicinal plants which are useful for treatment of GERD and its symptoms are *Fumaria officinalis*, *Artemisia asiatica*, *Atropa belladonna*, *Ceratonia siliqua*, *Ulmusrubra* bark, *Althaea officinalis* root and leaf, *Aloe vera* leaf gel, *Morus alba* leaf extract, *Curcuma longa*, and *Salvia miltiorrhiza* (116,117). The main mechanisms of medicinal plants and herbs in GERD mitigation are reducing acid production, soothing and protecting the esophagus, increasing digestive function, and alleviating inflammation (118). A famous classic traditional Chinese medicine is Wu Chu Yu Tang derived from the Shanghan Lun which consists of *Ziziphus jujube*, *Zingiber officinale*, *Panax ginseng*, and *Evodia rutaecarpa*, which has been found effective with similar effects to omeprazole for GERD treatment (119). Rose oil is common in Iranian traditional medicine which has high potential to preserve effective components, and it has notable influence as omeprazole in treatment of GERD (120). Zohalinezhad *et al.* (121) found that quince syrup significant enhanced symptomatic status and patient´s condition.

Gastroenteritis

It is a very common paediatric disease and remains a noticeable cause of childhood mortality and morbidity world-wide (122,123). The global burden of gastrointestinal infections combines the effects of severity, incidence, and duration (124-126). *Polygonum Cillinerve* polysaccharide (PCP) is the main active ingredient of *Polygonum Cillinerve*, which can be used to treat transmissible gastroenteritis virus through the Caspase-dependent mitochondrial pathway following miR-181 transfection (127). One of the important traditional Chinese herbal medicines in China is *Cimicifugae* rhizoma, and its polysaccharide component has immune-enhancing activity, significantly transmissible gastroenteritis virus, replication, and inhibited the apoptosis lowering mitochondrial damage (128).

Gastritis

Chronic atrophic gastritis is known by erosion and inflammation of the gastric lining, which is a prevalent digestive disease and known as a precursor to gastric cancer (129,130). The main cause of gastritis is *Helicobacter pylori* infection (131). It is a persistent inflammation of the gastric mucosa which can induce to uncomfortable signs in patients (132,133), and the second cause of death from malignant disease worldwide is gastric cancer (134). Gastritis can cause symptoms such as digestive disturbances, discomfort, and pain affecting many people in both developing and developed countries (135). Hu *et al*. (136) reported that berberine, palmitic acid, co glycosides which are the main ingredient of *Coptis chinensis France* (CCF) is known for its anti-inflammatory activities, and its potent heat-clearing, which can be used in treatment of gastritis. Song *et al*. (137) also found that the effective monomers of Magnolia officinalis var. *biloba*, and *Coptis chinensis* Franch. have special mechanism for treatment of chronic gastritis due to Coptisine, as their main optimal component. Luo *et al.* (138) also concluded that *Seleromitrion diffusa* (Willd). R. J. Wang and *Scutellaria barbata* D. Don have shown therapeutic impacts on chronic atrophic gastritis by acting HIF-1, PI3K-Akt, JNK, and cancer-related and others. Liu *et al*. (139) also recommend *Bryophyllum pinnatum* (Crassulaceae) to treat gastritis because of their main active ingredients such as isorhamnetin, quercetin, beta-sitosterol, eicosapentaenoic acid, kaempferol, cubebininolide, and artemetin as they can target SRC, AKT1, MAPK1, MAPK8, and EGFR.

Ginger also showed anti-gastritis impacts by blocking the activation of MAPK/STAT3 signaling pathway, and it can restore gastrointestinal motility, reduced levels of inflammatory parameters, enhance gastrointestinal hormone levels, and attenuate gastric histopathological damage (140). *Geranii Herba*, is the traditional medicinal plant in northeast China and Korea with gastrointestinal inflammation activity, which can decrease the cell infiltration in gastric mucosa and ulcer ratio (141). Zhang *et al*. (142) found that Huangqi (*Radix Astragali*) can be suggested in treatment of chronic atrophic gastritis, and Boeing *et al*. (143) also showed that the leaves of *Vernonia condensata* Baker demonstrated gastroprotective impacts through gastrinergic pathways, and the inhibition of gastric secretion. Dhondrup *et al.* (144) reported that the Tibetan medicine Liuwei Muxiang Pills (LWMX pills) is a famous traditional Tibetan medicine which can maintain gastric function by suppressing oxidative stress and inflammation. Jinhong Tablet can treat chronic gastritis by decreasing the inflammatory cytokines indirectly or directly to play anti-inflammatory activity due to containing flavonoids contents (145).

Qi-Zhi-Wei-Tong granules can alleviate chronic gastritis, and it can also ameliorate the levels of inflammatory responses, and increased intestinal integrity (146). Qirui Weishu capsule as a famous traditional formula also recommended for treatment of chronic gastritis because of its effectiveness and safe effects (147). Han *et al*. (148)

concluded that Weierning tablet suppressed gastric mucosal cells apoptosis, and reversed intestinal metaplasia, and it inhibited the inflammation of gastric tissue. Zuojin Pill (ZJP) is a classic prescription composed of *Tetradium ruticarpum*, and *Coptis chinensis* which is found as an important therapeutic effect on chronic atrophic gastritis induced by MNNG, which may be closely associated to the inhibition of Akt/PI3K/TGF-β1 signal pathway (149). Chaihu-Shugan-San, which is a famous Chinese prescription composed of *Rhizoma Cyperi*, *Rhizoma Chuanxiong*, *Fructus Aurantii*, *Rhizoma Chuanxiong*, *Fructus Aurantii*, *Radix Glycyrrhizae*, *Radix Paeoniae* Alba, *Pericarpium Citri Reticulatae*, *Radix Paeoniae* Alba, *Pericarpium Citri Reticulatae*, and *Radix Bupleuri* which has been used widely in treatment of different kinds of chronic gastritis due to some important components such as paeonifloring, neohesperidin, naringin, merazin hydrate, liquiritin, isoliquiritigenin, hesperidin, glycyrrhizic acid, glycyrrhetic acid, ferulic acid, and albiflorin (150). The ethanol extract of roots and stem of *Alisma canaliculatum* which can be found in different parts of Taiwan, China, Japan, and Korea has anti-inflammatory potential, and it can suppress inflammatory responses in lipopolysaccharide (LPS)-stimulated macrophages (151).

Silymarin has anti-carcinogenic, antioxidant, and anti-inflammatory activity which can significantly reduce the development of gastric lesions, and inhibits ethanol-induced gastritis in rats (152). Pink knotweed (*Polygonum capitatum*) has both anti-inflammatory and antibacterial effects, and significant advantage in the treatment of *Helicobacter pylori*-associated gastritis (153). An important pungent in *Capsicum annuum* is called Capsaicin which can down-regulate proinflammatory cytokines in gastric mucosa, showed gastric protection against gastric lesion, decreased inflammatory infiltrate in gastric mucosa, and down-regulated cyclooxygenase-2 (COX-2) in gastric mucosa (154). *Taraxacum coreanum* Nakai has been traditionally applied for treating gastrointestinal diseases and gastric ulcer by decreasing inflammation and oxidative stress (155). The dried tuber of *Gastrodia elata* Blume (GEB) is called gastrodiae rhizome, which is called Tianma in Chinese language, could significantly enhance gastric acid secretion, and ameliorate the damages gastric glands via regulating purine metabolisms, and energy (156). Mendivil *et al*. (157) found that Capsaicin decreased inflammatory infiltrate in gastric mucosa, down-regulated proinflammatory cytokines in gastric mucosa, and modulated COX-2 in gastric mucosa.

It is reported that Eupatilin, which is the major ingredient of Artemisiae plants has shown antioxidant and anti-inflammatory activities, which can also increase gastroprotective impacts in gastric ulcer-induced rats (158). The pharmacological activities of traditional Chinese medicine and their major active ingredients on chronic gastritis are (1) repair gastric mucosa such as increase the expression of matrix metalloproteinase-2, reduce the activity of matrix metalloproteinase-9, and regulate TNFR-c-Src-ERK1/2-c-Fod pathway, (2) anti-apoptosis such as increase the ration of Bcl-2/Bax, and inhibit the AKT-Mdm2-p53 signal pathway, (3) anti-oxidation such as increase the content of SOD and GSH, and regulate Nrf2/HO-1 signal pathway, (4) improve gastric function such as inhibit gastric acid secretion, increase PGE2, G-17, PGR and PG I, and improve gastric motility, (5) anti-inflammation such as increase the level of anti-inflammatory cytokine, regulate MAPK, PI3K-Akt, NF-κB signal pathways, and reduce the production of pro-inflammatory cytokines, (6) anti-*Helicobacter pylori*, such as increase the *Helicobater pylori* clearance rate, and inhibit *Helicobacter pylori* infection (159).

Celiac diseases

Celiac disease in the most common intestinal chronic inflammatory disease (160,161), and it is an autoimmune disorder caused by the consumption of gluten which can negatively influence the small intestine (162,163). Gluten-free diet is one of the most important treatment strategies for celiac disease (164). Iacomino *et al*. (164) reported that *Triticum monococcum* amylase trypsin was appropriate for non-celiac wheat sensitivity patient diet, as its amylase-trypsin-inhibitors (ATIs) indicate a higher susceptibility to enzymatic hydrolysis and reduce INF-γ expression and IL-8 on tissue explants, and T-cells from celiac patients. Celiac disease develops in genetically susceptible individuals because of ingestion of gluten forming proteins discovered in cereals such as barley, rye, and wheat (165-167), and one of the notable treatments is a strict gluten-free diet (168,169). It is reported that a combination of a glutamine-specific endoprotease and prolyl endopeptidase from *Sphingomonas capsulata* which is known as latiglutenase showed insufficient advantages in phase II clinical trials, possibly due to its low enzyme activity in the gastric environment (170). The diagnosis of celiac disease is closely associated to the autoimmune response, and usually implies different tests like high serum levels of IgA, excluding selective IgA deficiency, and IgG anti-tTG, serum IgA, and IgG anti-deaminated gliadin peptide, HLA-DQ typing, and serum IgA and endomysial antibodies (171,172). Anemia, osteoporosis, hepatitis, and arthritis are among the extraintestinal manifestation of active celiac disease (173-178).

Diet therapy is an important alternative therapeutic approach which may focus on inhibition of intestinal permeability, enzymatic degradation of gluten, inhibition of the transglutaminase 2 enzyme, modulation of the immune response 1, induction of tolerance, and blocking antigen presentation (179). Wang *et al*. (180) showed that the peanut skin proanthocyanidins (PSPc) can decrease damage by suppressing signaling pathways of inflammation and oxidative stress, and it can also inhibit cell membrane damage and apoptosis in the Caco-2 celiac disease model cells. Lavoignat *et al*. (181) reported that wheat proteins can trigger immunogenic activities, and celiac disease because of their resistance to immunostimulatory and digestion epitopes. Ribeiro *et al*. (182) showed that L-theanine-gluten significantly decrease a T-cell-mediated immune response in celiac disease, and retained the functionality of gluten and the typical viscoelastic behavior. A prolyl endopeptidase was derived from the basidiomycete *Flammulina velutipes*, which could degrade the antigenic epitope of α-gliadin which triggers celiac disease (183). Some of the gluten-free flours are almond flour, coconut flour, rice flour, tapioca flour, chickpea flour, quinoa flour, buckwheat flour, sorghum flour, millet flour, cassava flour, soy flour, potato flour, teff flour, green banana flour, chestnut flour, sesame flour, and chia flour (184).

Peptic ulcer disease

Peptic ulcer is a chronic disease which caused by the infection of *Helicobacter pylori* (185-187), and this recurrent disease, massively influence on the mortality and morbidity of many people (188-189). Peptic ulcer can be treated by various classical clinical experience formulas, Chinese medicine decoctions, and chemical constituents made from plant sources and naturally occurring components (190,191). Peptic ulcer is an acid-induced lesion of the digestive tract which is commonly located in proximal duodenum or stomach, which is characterized by denuded mucosa with the defect extending into the submucosa or muscularis propria (192). The anti-peptic ulcer effects are gastric secretion, cytoprotective activity, angiogenesis promotion, amino acid metabolism, antioxidant activity, anti-inflammatory activity, and gastrointestinal motor activity (193-195). It is because of diminished mucosal defenses, and imbalances in gastric juice pH (196,197). Kuna *et al*. (198) found that alternative therapy for peptic ulcer treatment can be recommended and suggested medicinal plants are Korean red ginseng, *Allium sativum*, *Cistus laurifolius*, *Zingiber zerumbet*, *Zingiber officinalis*, *Camellia sinensis*, *Artemisia asiatica*, and *Curcuma longa*.

The main components of NPK500 capsules which is a *Cassia sieberiana* DC.-based herbal analgesic medicine are betulinic acid, kaempferol, and physcion which possess anti-inflammatory and analgesic activities with significant capability of relief inflammation and acute pain with causing hepatic, renal or gastrointestinal injuries (199). Kumadoh *et al*. (200) observed the positive effects of Brimstone tree (*Morinda lucida* L.), *Cnestis ferruginea* Vahl ex D.C., *Vernonia amygdalina* Del., *Momordica charantia* Linn., *Lantana camara* Linn., *Trema orientalis* Linn., *Psidium guajava* Linn., *Persea americana* Mill., *Spondia mombin* Linn., *Citrus aurantifolia* Linn., *Bidens Pilosa* L., *Maytenus senegalensis* Lam., *Carapa procera* D.C., *Trichilia monadelpha*, and *Cassia siebieriana* D.C. in the management of peptic-ulcer disease. Huang *et al*. (201) reported that two Chinese herbal formula namely Hai-Piao-Xiao and Ban-Xia-Xie-Xin-Tang could be suggested for treatment of peptic ulcer diseases in countries such as China and Taiwan. Photogedunin and gedunin of *Xylocarpus granatum* has shown anti-ulcerogenic activity which may be because of its anti-secretory activity with positive effects against peptic ulcer disease (202). One of the famous Indian traditional medicinal plants is *Anogeissus pendula* Edgew (Combretacae) with high antioxidant activity, and positive effects in treatment of peptic ulcer disease (203). Jesus *et al*. (204) recommended *Hyptis suaveolens* (L.) Poit (Lamiaceae) for application as a gastro protective agent in central region of Brazil. *Piper umbellatum* L. (Piperaceae) is a shrub discovered in Atlantic Forest region, Savannah, and the Amazon of Brazil which is recommended for the treatment of gastric disorders due to its high rutin, quercetin, and flavonoids (205).

Another medicinal plant from Brazil is *Uncaria tomentosa* which can prevent piroxicam- and ethanol-induced ulceration as it has high anti-inflammatory, and antioxidant activities (206). B-Myrcene and some other major components of *Citrus aurantium* could enhance in mucosal malondialdehyde level with significant anti-ulcer activity (207). Memariani *et al*. (208) reported that the beneficial effects of *Pistacia atlantica* oleoresin which contains α-pinene, as complementary medicine and dietary supplement in folk traditional medicine for the treatment of PU. Different components of *Tagetes erecta* L. such as oil, disc florets, and ray can decrease the risk of ulcers, and it has also potential to cure acid pepsin disorders (209). Its extract can also accelerate the gastric healing process, decrease gastric inflammation, and reduce the ulcer recurrence (210). Khan *et al*. (211) showed that the extract of Mangifera indica possess significant impact on amelioration of gastric ulcer by re-inforcing the gastric mucosa,

preventing of indomethacin-induced muco-oxidative stress, and decreasing the secretion of gastric acid. Some of the most important medicinal plants in Nigerian traditional medicines for treatment of peptic ulcer are leaves of *Synclisia scabrida*, the whole plant of *Diodia sarmentosa*, leaves of *Ficus exasperate*, and leaves of *Cassia nigricans*, which reduce both the acidity and volume of gastric secretion, enhanced the pH, and delayed intestinal transit (212).

Bittersweet orange (*Citrus* x *aurantium* var. bigaradia) which is an old hybrid between *Camellia reticulata* and *Citrus maxima* from China with more than 4000 components, especially flavonoids, moreover, it has also contained neohesperidin and hesperidin which can notably aggravate gastric damage by histopathological changes, and enhances ulcer index (213). Stemmoside C of *Solenostemma argel* which is widely distributed in Asia and Africa. It can be used against gastric ulcer progression and tumorigenicity (214). It has been showed that luteolin and kaempferol extract of *Kaempferia galanga* L. galanga have protective impacts against ethanol-induced gastric ulcer (215). Figueiredo *et al*. (216) also reported that the chemical components of *Fridericia chica* L.G. Lohmann (Bignoniaceae) can be used to cure gastrointestinal disorders such as peptic ulcer. Liuwei Anxiao San which is one Mongolian medicinal prescription can be used against gastric mucosal injury in gastrointestinal disorders by suppressing the JAK2/STAT2 pathway (217). In Malay community, *Dicranopteris linearis* (DL) known as resam with high antimicrobial and antioxidant activity, and contains saponins, terpenoids, and flavonoids which is recommended for application for treatment of peptic ulcer disease (185). De Jesus *et al*. (218) tannins are poly-phenols presents in beverages, foods, and plants with potential ability for treatment of peptic ulcers. *Ranunculus millefoliants* extract revealed high gastroprotective impacts that could be because of decrease malondialdehyde quantity, rise superoxide dismutase and catalase, capability upsurge pH then mucus discharge, down-regulating Bcl-2-associated X protein protein, up-regulating heat shock protein 70, and moderate provocative cytokines (219).

Ruscogenin ($C_{27}H_{42}O_4$) is a natural steroid sapogenin product derived from *Tribulus terrestris* with antioxidant and anti-inflammatory activity and suitable for treatment of peptic ulcer (220). Wu *et al*. (221) found that the burdock essence can help abolish *Helicobacter pylori* infection, and increase the therapeutic impacts of conventional medication on gastric mucosal repair in gastrointestinal ulcer patients. *Adinandra nitida*, which is known as Shibi tea, is rich in flavonoid and considered as an important medicinal plant in South China, moreover, Shibi tea water extract (STE), and its major flavonoid camellianin A (CA) can regulate the inflammatory signaling pathways protein levels of NF-κB and IκB-α (222). Mohammad *et al*. (223) noted that henna (*Lawsonia inermis* L.) is effective, low cost, safe and suitable for treatment of gastric ulcer. Orsi *et al*. (224) reported that the methanolic extract obtained from the stem bark of *Hymenaea stigonocarpa* Mart. Ex Hayne (Fabaceae) showed significant gastroprotective, anti-diarrheal, and cicatrizing effects which may be because of the presence of flavonoids and condensed tannins in the fruit and bark of the plants. Propolis is an important natural component which has been used for many years in folk medicine, and it refers to bee glue consists of leaves, plant resins from saps, barks, and buds of plants collected by bees around their vicinity, and its application can enhance the amounts of catalase, superoxide dismutase, glutathione, nitrite, while malondialdehyde contents may decrease which proves their important for management of peptic ulcers diseases (225). *Celosia trigyna* belongs to the plant family Amaranthaceae which is found in Nigeria, Southern Arabia, South Africa, and Congo with anti-ulcerogenic effects, and its hexane extracts, and secondary metabolites such as sterols, pheophytin a, and lutein exhibited high effectiveness in treatment of gastric ulcer (226). Algandaby (227) concluded that *Teucrium polium* extract muco-adhesive formula can be considered as an important therapy for chronic oral ulcers, as its application could significantly decrease TNF-α, MDA, COX-2, and IL-6, and increase catalase and superoxide dismutase activities. The root extracts of *Prangos pabularia* (REPP) application can meaningfully modulated oxidative stress, increase MDA, PGE2, CAT, and SOD, and inflammatory cytokines levels which introduces it as an important remedy for gastric ulcer disorder (228). Hasna *et al*. (229) suggested that fenugreek extract combined with *Bifidobacterium breve* can be an alternative for treatment of diseases caused by *Helicobacter pylori* infection according to Algerian medicinal plant sciences. *Justicia pectoralis* Jacq. which is an important medicinal plant in several Latin American countries such as Brazil has antioxidant and anti-inflammatory activities, and its leaves methanol extract can be used for gastric disorders (230).

In African countries, especially in South Africa, medicinal plants such as *Garcinia kola*, *Sclerocarya birrea*, *Combretum molle*, *Strychnos species*, and *Alepidea amatymbica* have been used for several years for treatment of peptic ulcer and gastritis disease (231). Zhang *et al*. (232) observed that the *Dendrobium officinale* polysaccharide

(DOP) ameliorated gastric ulcer through considerable improve in expression of SOD in tissues, and SOD, GSH, and GSH-PX in serum. In Ethiopia, medicinal plants which have been used for treatment of gastric ulcer are *Urtica simensis*, *Croton macrostachyus*, *Achyranthes aspera*, *Afrocarpus falcatus*, *Aloe gilbertii*, *Aloe macrocarpa*, *Aloe pubescens*, *Asparagus africanus*, *Asystasia gangetica*, *Brassica carinata*, *Brassica oleraceae*, *Calpurnia aurea*, *Carica papaya*, *Carissa edulis*, *Casimiroa edulis*, *Catha edulis*, *Caylusea abyssinica*, *Centaurium pulchellum*, *Cicer arietinum*, *Citrus aurantifolia*, *Citrus sinensis*, *Commiphora hodai*, *Commiphora kua*, *Cordia Africana*, *Croton macrostachyus*, *Cucurbita pepo*, *Dodonaea Angustifolia*, *Enset ventiricosum*, *Erythrina brucei*, *Euphorbia abyssinica*, *Flacourtia indica*, *Galium simense*, *Girardinia bullosa*, *Hibiscus cannabinus*, *Justicia schimperiana*, *Kalanchoe petitiana*, *Leonotis ocymifolia*, *Lepidium sativum*, *Lippia adoensis*, *Momordica foetida*, *Nigella sativa*, *Ocimum lamiifolium*, *Oncoba spinosa*, *Physalis peruviana*, *Plantago lanceolata*, *Psidium guajava*, *Rubus apetalus*, *Rumex nepalensis*, *Rumex nervosis*, *Saliva merjamie*, *Cordia Africana*, *Rumex nepalensis*, *Osyris quadripartite*, and *Plantago lanceolata* (233). Medicinal plants and herbs in Indian traditional medicinal science for treatment of peptic ulcer are *Jasminum grandiflorum*, *Anogeissus latifolia*, *Alchornea castaneaefolia*, *Utleria salicifolia*, *Solanum nigrum*, *Ocimum sanctum*, *Scoparia dulcis*, *Byrsonima crassa*, *Asparagus racemosus*, *Centaurea solstitialis*, *Anacardium occidentale*, *Calophyllum brasiliense*, *Larrea divaricata*, *Hemidesmus indicus*, and *Spartium junceum* (234).

Colorectal polyp

A colorectal polyp is a polyp happening on the lining of the rectum or colon (235), and untreated colorectal polyps can develop into colorectal cancer (236,237). It is usually categorized by its cause and the behavior (238), and they maybe malignant, pre-malignant, or benign (239). Colorectal polyps refer to tissue on the surface of the large intestinal mucosa which is shaped by abnormal hyperplasia of the epithelium (240-242). Polyps are categorized into two major groups, namely adenomatous and hyperplastic polyps (243,244). Various natural components can suppress or induce apoptosis proliferation of tumor cells (245,246). Flavones which have shown anti-colorectal cancer activity are baicalein, apigenin, and digitoflavone (247). Herbal plants and medicinal plant extracts can prevent the growth of colorectal cancer by activating several signaling pathways, cell cycle arrest at different stages, and inducing autophagy or apoptosis (248-250).

Traditional medicinal herbs and plant which have been reported useful for treatment of colorectal polyp are *Curcuma longa*, *Panax quinquefolius*, *Olea europaea* var. *sylvestris*, *Garcinia mangostana*, *Emilia sonchifolia*, *Rabdosia rubescens*, and *Hylomecon vernalis* (251). Flavonoids are considered as the secondary metabolites which have shown high anti-colorectal cancer effects (252-255). Phytochemicals can modulate the production of cytotoxic components such as ROS, and NO by macrophages, moreover, they can polarize macrophages towards the M1 phenotype, inhibit M2 polarization, and increase anti-tumor immune responses (256). High intake of hydroxicinamic acids, total phenolic acids, and flavonols could also decrease the risk of colorectal cancer (257). The main bioactive ingredient of *Cuminum cyminum* is cuminaldehyde which is also known as 4-isoprophylbenzaldehyde which has beneficial effects against human colorectal and cervical carcinoma (258,259). Curcumin has been derived from dried roots of the plant *Curcuma longa* which can be used for the treatment of colorectal cancer (260). It is also proved that apigenin is capable to decrease polyp numbers as well as increasing protein 53 activation via phosphorylation in animal models (261). Cao *et al*. (262) also found the importance of application of berberine in treatment of colorectal disease through multiple targets and channels. Ansari *et al*. (263) reported the inhibitory effects of naringin on colorectal disease via different signaling pathways. Cai *et al*. (264) reported that Xianlian Jiedu Decoction can be suggested for treatment of colorectal disease by reducing metabolic disorders, intestinal microbial flora, and alleviating the level of inflammation. Fernandez *et al*. (265) reported that some important flavonoids such as luteolin and apigenin can be for treatment of colorectal cancer cell lines due to its antitumor activity. Cassotta *et al*. (266) also found that ω-3 polyunsaturated fatty acids, vegetables, and fiber can prevent inflammatory bowel disease related colorectal cancer.

Drimia calcarata bulb extract showed high tannin, total phenolic and flavonoid content as well as significant antioxidant activity, and the methanol extract induced mitochondrial-mediated apoptosis in colorectal HT-29 and Caco-2 cells with beneficial effects for treatment of colorectal cancer (267). Ling *et al*. (268) also showed that berberine can influence macrophages polarization and infiltration, and inhibited tumorigenesis in colorectal cancer. In South America, cocoa powder is found important to prevent colorectal cancer through modulating oxidative

stress (269). It is reported that chemical components of the most important medicinal plants in traditional Chinese medicine like *Smilax china*, *Patrinia scabiosaefolia*, and *Sanguisorba officinalis* can be recommended for treating colorectal cancer as HSD11B2 is the main target protein of them in treating colorectal cancer (270). Nascimento *et al*. (271) also reported that jaboticaba peel is an important source of phenolic acids and cyanidin-3-*O*-glucoside with high antioxidant activity which could mitigate colorectal cancer probably by avoiding triggering inflammation. Khan *et al*. (272) concluded that the alcoholic leaf extract of *Annona reticulata* has anti-proliferative and antioxidant activity, which can improve prevention of colorectal cancer development and dysplasia caused by 1,2-dimethyl-hydrazine. Nomura *et al*. (273) reported that the intake of fruits and vegetables was inversely connected to colorectal cancer risk among men. Nirmala and Ramanathan (274) reported that kaempferol could be notably applied as chemo-preventive agent in colorectal cancer. *Frangula alnus* ethyl-acetate extract (FA), and its dominant component emodin (E) demonstrated high cytotoxic activity against carcinoma cells, modulated cell cycle, and induced cell cycle (275). Polyhydroxybutyrate is a non-toxic polyhydroxyalkanoate polymer produced by different microorganisms which has been reported to increase cardiac performance, enhance cognitive and brain function, and significantly regulate diabetes and appetite suppression for treatment of colorectal cancer (276). Wang *et al*. (277) reported that naringenin is an important component for inhibiting colorectal cancer proliferation, probably via the AMP-activated protein kinase (AMPK) pathway, to induce apoptosis in colorectal cancer and regulate mitochondrial function. Medicinal plants with anti-colorectal cancer bioactive ingredients with high potential in colorectal cancer management are *Musa balbisiana*, *Musa acuminata*, *Punica granatum* L., *Glycine max*, *cruciferous vegetables*, *Hibiscus tosa-sinesis*, and *Hibiscus sabdariffa* L. (278).

Bloating

Among disorders of gut-brain interaction, bloating is a common symptom in the general public (279-281). Abdominal distension and bloating are secondary to an organic disease (282), which can influence social interactions, daily life, and can be triggered by dietary habits (283,284). Bloating is the result of gas release in presence of the notable proper amount of liquid phase with a suitable viscosity (285). Abdominal bloating and distension can develop for different reasons, including a previous infection, food intolerance, delayed intestinal transit, disordered visceral sensation, and an abnormal viscero-somatic reflux (286,287). Application of *Bacillus coagulans* GBI-30, 6086 probiotic can be suggested as it is effective and safe for the relief of bloating and abdominal pain for the patients with symptoms of irritable bowel syndrome (IBS) (288). KAASER is one of the most important Persian herbal formulations comprised of *Piper nigrum* L. berry, *Zingiber officinale* Roscoe. rhizome, and *Trachyspermum ammi* (L.) Sprague seed which is effective to treat patients suffering from bloating and flatulence (289).

It is also reported that usage of vitamin D, psyllium, and probiotic supplementation can be useful in treatment of bowel syndrome (290). It is also discovered that a novel therapeutic of natural origin which contains a mixture of naturally occurring polysaccharides, tannins derived from grape seed extract, pea proteins and β-galactosidase can be used in treatment of distension, bloating, and abdominal pain in patients with lactose intolerance (291). Patch *et al*. (292) reported that application of *Bacillus subtilis* (BG01-4™) can increase specific symptoms of constipation and associated gastrointestinal dysfunction. Bertin *et al*. (293) also emphasized on the beneficial effectiveness of fermented monosaccharide, disaccharide, oligosaccharide, and polyol diet for patients with irritable bowel syndrome. Extracts of *Boswellia serrata* and *Curcuma longa* have antimicrobial and anti-inflammatory effects and their application can significantly reduce irritable bowel syndrome (294).

Pancreatitis

Acute pancreatitis is an inflammatory disease of the exocrine pancreas (295,296) with significant mortality and morbidity (297-299), which is characterized by substantial necrosis, vacuolization, and interstitial edema (300-302). It was a common acute abdominal disease known by inflammation and pancreatic acinar cell death (303,304). Ramakrishnan *et al*. (305) introduced curcumin, rhein, green tea catechin derivatives, resveratrol, emodin, ellagic acid, embelin, eruberin A, and metformin as important anti-fibrotic agents for pancreatic cancer and chronic pancreatitis. Chemical structures of the phytochemicals which show protective effects against acute pancreatitis are withaferin A, Visnagin, Tetramethylpyrazine, Tanshinone IIA, Saikosaponin a, rutin, resveratrol, quercetin, picroside II, oxymatrine, mogroside IIE, luteolin, curcumin, ellagic acid, dihydrokaempferol, emodin, chlorogenic acid, borneol, berberine, carvacrol, calycosin, baicalin, baicalein, artesunate, and acetyl-alpha-boswellic acid (306).

As an important natural flavonoid component which can be found in different vegetables, fruits, and plants, myricetin can alleviate the severity of acute pancreatitis via inhibition of nuclear factor-κB, and cathepsin B activity, and myricetin can be applied as a regulator of Ca^{2+}/CaM-dependent protein kinase kinase 2 (CaMKK2), and calcineurin signaling (307).

It is reported that tectoridin which is an isoflavone, and a type of flavonoid can ameliorate pancreatic injury and inflammation in severe acute pancreatitis mice, as it can target ERK2 to inhibit ERK MAPK signaling pathway (308). Tropolone is an organic component with the chemical formula $C_7H_5(OH)O$, and it is reported that tropolone derivative hinokitiol as an important phytochemical with anti-inflammatory activities can reduce the expression of COX-2, and NF-κB, and reduce the expression of proinflammatory cytokines (309). Chaiqin chengqi decoction can reduce acute pancreatitis by targeting gasdermin D-mediated pyroptosis, and thein is the main active ingredient of it in suppressing pyroptosis (310-312). Wen *et al*. (313) reported that the effectivity of Chaiqin chengqi decoction is mainly because of its ingredients such as chrysin, rhein, baicalin, emodin, and ingredients. Han *et al*. (314) reported that Qing Xia Jie Yi Formula (QXJYF) is an important herbal formula from traditional Chinese medicine which can alleviate acute pancreatitis via inhibition of M1 macrophage polarization by suppression glycolysis. Baicalin is a flavonoid component derived from the root of *Scutellaria baicalensis* Georgi, which is known as *Huangqin*, with anti-inflammatory activity, and it can suppresses oligomerization of phosphorylated mixed lineage kinase domain-like protein (MLKL) by decreasing ROS, and it can also mitigate the severity of caerulein-induced acute pancreatitis in mice (315). Abozaid *et al*. (316) reported that Cinnamic acid nanoparticles (CA-NPs) can be applied as a modulator for the redox signaling pathway of pancreatitis with both anti-inflammatory and antioxidant activity. Nimbolide as the main limonoid of the neem tree, is extensively applied in traditional medicinal treatment in South of Asia with antitumor, anti-inflammatory, and antioxidant activities, and it can protect against cerulein-induced acute pancreatitis, reduce pancreatic inflammation through regulating NF-κB/SIRT1 pathway, and suppress pancreatic apoptosis by modulating cleaved Bcl2, Bax, and caspase 3 expression (317).

Hesperidin is a flavanone glycoside obtained from citrus fruits, and it can provoke deficit in glucose control and insulin secretion, and prevent pancreatic inflammation through increasing antioxidant mechanism (318). Fan *et al*. (319) reported that Wedelolactone can attenuate pancreatitis and some other lung injury in Taurocholate or Caerulein-induced murine models with ability of suppression of ferroptosis and pyroptosis through the up-regulation of glutathione peroxidase-4 (GPX4), as it is a polyphenol obtained from *Eclipta alba*, and *Wedelia chinensis*. Dachengqi decoction (DCQD), is a famous traditional Chinese medicinal formula which consists of *Magnoliae officinalis cortex*, *Aurantii fructus immaturus*, *Natrii sulfas*, and *Rhei radix ex* rhizome, and effective for treating inflammation in different disease conditions, and abdominal pain (320). In another experiment, it is showed that Matrine, which is a natural alkaloid obtained from stems and roots of *Sophora flavescens*, can alleviate ferroptosis and oxidative stress in severe acute pancreatitis (321). One of the most important polyphenols with anti-inflammatory activity is Chlorogenic acid which can significantly influence L-arginine-induced pancreatitis and pancreatitis-associated lung injury (322).

Dihydrokaempferol is one type of flavonoids which can be obtained from *Bauhinia championii* (*Benth*) which can regulate the protein Kelch-like ECH-associated protein (Keap1)/the nuclear factor erythroid 2-related factor 2 (Nrf2) pathway and regulating oxidative stress injury in severe acute pancreatitis (323). Guo Qing Yi Tang is composed of 13 traditional Chinese medicines such as senna leaf, sodium sulfate, raw rhubarb, *Magnolia officinalis*, hawthorn, and *Bupleurum*, which can reduce the level of inflammatory factors, and enhance intestinal mucosal barrier function for treatment of acute pancreatitis (324). Hog plum (*Ximenia americana*) contains heteropolysaccharide with antinociceptive impacts, which can decrease pancreatic enzymes as well as inflammatory parameters of acute pancreatitis (325). *Morus alba* root bark extract has high anti-inflammatory activity due to the presence of Cudraflavone B which can be suggested for treatment of pancreatitis (326). Lima *et al*. (327) reported that 1,8-cineole can attenuate cerulein-induced acute pancreatitis through an anti-inflammatory process, and by combating oxidative stress. Zhang *et al*. (328) in his experiment showed that the extract of *Ligustrum vulgare* L. significantly decreased the fibrotic changes and the inflammatory activity which proves the potent pancreato-protective impacts of it. *Nigella sativa* Linn. is a medicinal plant which is rich in chemical components with anti-inflammatory activity possibly by managing and regulating the expression of ASC protein of the Nod-like Receptor Pyrin domain containing 3 (NLRP3) inflammasome in pancreas that may reduce the activation of caspase-1 (329).

It is also reported that the usage of apigenin to humans could significantly ameliorate the damages to the pancreas (330). Seo *et al*. (331) reported that quercetin 3-*O*-xyloside has significant anti-pancreatitis activity via attenuating intracellular ROS production and ER stress response, and increasing apoptotic cell death. One of the most important phenolic components of long pepper (*Piper longum*), and black pepper (*Piper nigrum*) fruits which can decrease the digestive enzymes and pro-inflammatory cytokines, and it can significantly inhibit the activation of mitogen activated protein kinases that may show its effectiveness as a protective effect against acute pancreatitis (332). Fisetin is a flavonoid contained in different foods such as fruits, teas, wines, and juices which can inhibit the activation of c-Jun NH2-terminale kinase (JNK) and nuclear factor (NF)-κB *in vitro* and *in vivo* with high anti-inflammatory impacts on acute pancreatitis (333).

Chinese herbal ointment Liu-He-Dan which is composed of *Angelica dahurica*, *Phellodendron chinense* Schneid., *Rheum officinale* Baill., *Armeniaca mume* Siebold, flour, honey, and *Mentha haplocalyx* Briq., could be applied to relieve the disease of pancreatitis (334). Anchi *et al*. (335) observed that curcumin which is a polyphenolic derivative from turmeric (*Curcuma longa*) could significantly reduce lipase levels, serum amylase, nitrosative and oxidative stress, and appropriate for treatment of pancreatitis through sustained release microparticle approaches. Choi *et al*. (336) found that berberine inhibited cerulein-induced acute pancreatitis, exerted anti-inflammatory effects, and inhibited inflammatory mediators production in acute pancreatitis. Genistein which is a polyphenolic isoflavone and belongs to the flavonoid in vegetables such as fava beans, and soy beans attenuated cerulein-or taurocholate-induced acute pancreatitis in vivo, and promoted apoptosis of pancreatic acinar cells to protect from acute pancreatitis (337). There is a compound and plant steroid in *Commiphora myrrha*, which is known as Guggulsterone, protected lung injury and the cerulein-induced pancreatic, inhibited the activation of ERK1/2 and JNK in cerulein-induced acute pancreatitis, and inhibited cerulein-induced elevation macrophage and neutrophil infiltration (338). Bansod *et al*. (339) concluded that berberine activated AMPK and downregulated TGF-β/Smad signaling pathway, and attenuated cerulein-induced chronic pancreatitis and associated fibrosis. Kumar and Tamizhselvi (340) also indicated that garlic-derived organosulfur component diallyl disulfide (DADS) alone or combination inhibited NF-κB translocation, and IκB degradation. It is reported that flavonoid C1 from *Coreopsis tinctoria* Nutt. has potential role in treatment of acute pancreatitis through Nrf-2/ARE-mediated antioxidant pathways and due to its antioxidant effects (341).

Moreover, aqueous extract of black tea (*Camellia sinensis*) prevents pancreatitis caused by chronic ethanol (EtOH)+cholecystokinin (CCK) toxicity possibly by increasing antiapoptotic, anti-inflammatory, and antioxidant activity in rats (342). Bashir *et al*. (343) reported that grape seed proanthocyanidins has an effective function as a protector in the oxidative stress-mediated pancreatic dysfunction in rats. One of the most important traditional medicinal plants in Brazil is *Caesalpinia pyramidalis* Tul. from Fabaceae family, and its ethanol inner bark extract could decrease hyperalgesia, lipoperoxidation, and inflammation in common bile duct obstruction (CBDO)-induced acute pancreatitis (344). Visnagin is an antioxidant furanocoumarin component of the plant *Ammi visnaga*, which can decrease inflammatory cytokines in intestine and lungs, and regulated the expression of markers of multiple organ dysfunction syndrome that may prove its effectiveness to prevent cerulein induced acute pancreatitis (345).

Functional dyspepsia

It is commonly known as chronic indigestion which is an upper gastrointestinal disorder (346), and associated complaints may include vomiting, nausea, belching, bloating, etc. (347). Functional dyspepsia is a complicated symptoms referable to the gastroduodenal region of the gastrointestinal tract which consists of burning or pain, early satiety, or postprandial fullness (348-350). Dyspepsia is known as episodic or persistent abdominal pain or discomfort of the upper gastrointestinal tract (351), and it has been linked with a deficiency or dysfunction of digestive enzymes (352). It is an extremely common disorder of gut-brain interaction which can influence the quality of life without an associated increase in mortality (353,354). It most usually presents with bothersome signs after eating (355,356). The positive effects of traditional Chinese medicine and compounds in the treatment of functional dyspepsia have been reported by several researches (357-359).

Mechanisms of traditional Chinese medicine components in treating functional dyspepsia are reduce visceral hypersensitivity for Si-Ni-San, modified Liu-Jun-Zi decoction; relieve anxiety and stress for Zhizhu Kuanzhong capsule, Qi-Zhi-Wei-Tong granules, and Xiangsha Liujunzi granules; regulating brain-gut peptides for Chaihu

Shugan San, Banha-Sasim-Tang, and Xiangsha Liujunzi granules, reduce low-grade duodenal inflammation for Si-Ni-San, promote gastric motility for Pixu I recipe Shugan Hewei decoction, and regulating the gastrointestinal microbiota for Shen-Ling-Bai-Zhu-San, Jiao Sanxian, and Xiaoyaosan (360,361). Saikosaponin D is the basic active monomer of saikosaponin which can improve intestinal cells of Cajal structure and morphology, that may inhibit excessive autophagy, and increased a gastrointestinal motility disorder and functional dyspepsia via regulating substance P and ghrelin levels (362). Liu *et al*. (363) concluded that the application of laminarin in different traditional medicines can regulate somatic and visceral hypersensitivity. Simo Decoction is a famous traditional Chinese medicine which composed of *Radix linderae*, *Semen arecae*, *Radix aucklandiae*, and *Fructus aurantia*, which can improve the production of short-chain fatty acids for alleviation of functional dyspepsia (364). Xiaopi Hewei Capsule which is a classic formula comes from the Chinese Miao minority, which can significantly reduce the symptoms of functional dyspepsia (365). Xiangsha-Liujunzi-Tang is a classical formula for treatment of some digestive disease systems which can reduce the inflammation, and increase the integrity of duodenal mucosa (366). *Cynanchum auriculatum* Royle ex Wight (CA) is a perennial herbaceous plant in Hunan, Sichuan, and Guizhou of China which can be used to treatment of functional dyspepsia with significant effect on ATP-binding cassette transporter inhibitors (367).

Another important traditional Chinese medicine is Wei-Tong-Xin which is the combination of *Aucklandia lappa* Decne, *Rheum palmatum* L., *Pharbitis nil* (L.), *Gleditsia sinensis* Lam. and *Glycyrrhiza uralensis* Fisch., and its application can inactivate the toll-like receptor 4 (TLR4)/MyD88 signaling pathway and inhibit the occurrence of gastric antral inflammation (368). Moghtaderi *et al*. (369) reported a significant connection between functional dyspepsia and stomach dystemperaments after application traditional Persian medicine. Shen-Ling-Bai-Zhu-San which includes *Atractylodes macrocephala*, *Poria cocos*, and *Panax ginseng* could ameliorate dyspepsia, and improve the dysregulated composition and function of the gut microbial community. Ho *et al*. (370) also reported that Modified Ban Xia Xie Xin Decoction, and Xiao Yao Pill can be used instead of chemical drugs with effective impacts, and as alternative medicine for treatment of functional dyspepsia. Gan *et al*. (371) also reported that Ban Xia Xie Xin was more effectual in treatment of functional dyspepsia than Western Medicine. Mohtashami *et al*. (372) also showed that the application of honey-based formulation of black cumin (*Nigella sativa*) seed oil can cause meaningful symptomatic improvement of patients with functional dyspepsia. Pennyroyal (*Mentha pulegium*) extract could eradicate *Helicobacter pylori*, enhance dyspeptic symptoms, and the quality of life in functional dyspepsia patients (373). The extract of *Poria cocos* could increase the effects on functional dyspepsia through multiple pathways (374).

The herbal medicine STW5 which is a composed of drug extracts of milk thistle, Angelica root, chamomile flower, liquorice root, peppermint leaf, lemon balm leaf, and a fresh plant extract of bitter candytuft (*Iberis amara*) and ethanol content of 31% is recommended for treatment of irritable bowel syndrome and functional dyspepsia (375). ZhiShiXiaoPi Tang (ZSXPT) which is a traditional Chinese medicine includes 10 Chinese traditional medicine plants including *Magnolia officinalis*, immature bitter orange, *Pinellia ternate*, *coptis*, *malt*, *Rhizome zingiberis*, *Poria cocos*, *Rhizome atractylodis macrocephalae*, *liquorice*, and *Codonopsis pilosula* can be used against autophagy induced by corticosterone and functional dyspepsia basically by blocking the mTOR pathway in Cort-induced PC12 cells in rats with functional dyspepsia (376). Sufoof-i-Tabkheer is a powder dosage from containing *Elettaria cardamomum*, *Bambusa arundinaceae*, *Coriandrum sativum*, and *Foeniculum vulgare* can be used in treatment of dyspepsia in traditional Iranian medicine (377). Wang *et al*. (378) also reported that Chaihu-Shugan-San as an important and classic traditional Chinese medicine formula is significantly effective in treatment of functional dyspepsia, increases gastric emptying rate, and relieves depression and anxiety in patients. Jin *et al*. (379) reported that silver nanoparticles stabilized by chitosan-polyvinyl alcohol polymers mediated by *Pistacia* extract can be used for treatment of gastric cancer, and functional dyspepsia. Pingwei capsules includes *Rhizoma Atractylodis Lanceae*, *Cortex Magnoliae Officinalis*, *Radix Aucklandiae*, *Fructus Aurantii Submaturus*, *Radix Bupleuri Chinensis*, *Radix Paeoniae Alba*, *Rhizoma Bletillae Striatae*, *Endoconcha Sepiellae*, *Rhizoma Sparganii*, *Bulbus Fritillariae Thunbergii*, *Rhizoma Coptidis*, *Herba Taraxaci Mongolici*, *Rhizoma Corydalis Yanhusuo*, and *Rhizoma Curcumae Phaeocaulis* which can improve gastrointestinal motility in rats with functional dyspepsia (380). Indian Gooseberry and Amal (*Phyllanthus emblica* L.) is a traditional medicine in subtropical and tropical regions like Malaysia, China, India, Pakistan, etc., which is rich in vitamin C, amino acids, flavonoids, fatty acids, sterols, terpenes, tannins, phenolic acids, and alkaloids which can regulate the microbiome structure, and restore homeostasis by stimulating important bacterial abundance, and reduce the negative effects of bacterial abundance (381). Choi *et al*. (382) revealed that *Foeniculi fructus* which is an important traditional medicine in Europe and

China can provide a potential means to treat functional dyspepsia due to its key components such as β-sitosterol, oleic acid, and 12 functional dyspepsia-related genes. Yukgunja-tang (Liujunzi-tang in Chinese, Rikkunshito in Japanese) is an important traditional herbal medicine in East of Asia which includes *Zizyphi Fructus*, *Zingiberis Rhizoma Recens*, *Glycyrrhizae Radix et Rhizoma*, *Poria Sclerotium*, *Atractylodis Rhizoma Alba*, *Ginseng Radix*, *Citri Unshius Pericarpium*, and *Pinelliae Tuber* which also showed high safety, the effectiveness in the treatment of functional dyspepsia (383).

It is reported that Xiang Sha Liu Junzi decoction can promote the gastrointestinal motility disorder in functional dyspepsia with spleen deficiency syndrome which is in connection with reconstruction of the mitochondrial quality control system by restraining PINK1/Parkin-mediated mitophagy and division (384). One of the most important medicinal plants in China is *Amomum tsaoko* Crevost et Lemarie which is a perennial herbaceous plant belonging to the *Zingiberaceae* family which has been used to treat abdominal discomfort, postoperative abdominal distension, and very useful in treatment of functional dyspepsia (385). Therapeutic effects of traditional Chinese medicine on functional dyspepsia include treatment for smoothing liver and regulating stomach, treatment for strengthening spleen and promoting qi stagnation, treatment for acrid dispersing and bitter descending, treatment for eliminating heat and removing dampness, and treatment for warming stomach and invigorating spleen (386). Representative prescriptions in five syndrome types are Chaihu Shugan Powder for liver-stomach disharmony; Simo Decoction, Xiangsha Liujunzi Decoction, and Zhizhu Pills for spleen deficiency with qi stagnation; Banxia Xiexin Decoction for syndrome of intermingled heat and cold; Lianpo Drink and Sanren Decoction for dampness-heat of spleen and stomach; and Huangqi Jianzhong Decoction for deficiency-cold of spleen and stomach (387). It is also reported that application of *Ocimum basilicum* can be appropriate to relieve the symptoms of functional dyspepsia particularly in young and female patients with dysmotility (388).

Malabsorption

Malabsorption can cause a large variety of gastrointestinal signs such as abdominal pain, steatorrhea, constipation, diarrhea, and malnutrition (389,390). As a common clinical condition, it can influence different races around the world because of its structural and functional abnormalities of the intestinal mucosa which make it unable to absorb the nutrients in the diet (391,392). It can be caused by different diseases of the small intestine, biliary tract, diseases of the liver, pancreas, and stomach (393-395).

Bowel obstruction

Bowel obstruction is known as the main common surgical emergency following abdominal procedures (396,397). It is more common in the small bowel than in the large bowel (398,399). Small bowel obstruction in usually caused by adhesions followed by tumors, hernias, foreign bodies, intussusception, gallstones, and inflammatory bowel diseases (400,401). As a rare complication of endometriosis, small bowel obstruction defined as a condition by the presence of endometrial tissue outside of the uterine cavity (402). High fiber diet is appropriate for having the bowels healthy for some people, as fiber, especially insoluble fiber can provide bulk to the stool, which can increase the risk of bowel obstruction. Two doses of modified Dachengqi Decoction herbal formula which was part of traditional Chinese medicine was recommended for patients (403), while Kunitomi *et al*. (404) reported that Daikenchuto did not show significant effectiveness for early bowel obstruction, but it might be suitable for shortening the hospital stay for patients (404). One famous Chinese herbal medicine is Si-Jun-Zi Decoction which composed of four Chinese herbs namely Poria root, licorice root, *Atractylodes macrocephala*, and Ginseng root that can regulate the intestinal immune system, improves the restoration of intestinal function after obstruction by managing intestinal homeostasis which proves its importance for treatment of intestinal obstruction (405).

Anal fistula

The history of anal fistulas goes back to the Ancient Greeks (406,407), which is an epithelized path between anal canal or the rectum and the perianal region (408,409). It is usually challenging to manage the anal fistulas properly (410,411). The anal fistula is the unusual connection between the perianal skin and the anal canal, which can induce to persistent or intermittent purulent drainage (412). It is an internal orifice originating along the anal circumference which is the natural drainage orifice of the infected anal gland (413). Application of a porcine

fistula plug for the treatment of complex anal fistulas is an important and promising technique (414,415). The four types of anal fistula are intersphincteric, transsphincteric, suprasphincteric, and extrasphincter (416-419).

Some of the most important plants for symptomatic treatment of anal fistula are *Zingiber officinale*, *Curcuma longa*, *Commiphora mukul*, *Terminalia chebula*, *Mimosa pudica*, *Emblica officinalis*, *Azadirachta indica*, *Berberis aristate*, *Acacia catechu*, *Cassia tora*, *Leucas cephalotes*, *Rubbia cordifolia*, *Cinnamomum camphora*, *Melia azedarach*, and *Sapindus muskorossi* (420). Santos *et al*. (421) reported that *Baccharis dracunculifolia* extract was able to decrease the lumen of the fistulous tracts and the degree of vascular congestion without totally closing or reducing the local inflammatory process of the fistulous tracts. Comparin *et al*. (422) found that the application of a seton soaked in a glycerin *Aloe barbadensis* Miller extract was important and useful in the treatment of anal fistulas in rats with significantly lower inflammatory process compare to the non-phytotherapeutic seton. The main prescribed herbal components in topical formulation for anal fistula treatment in Persian traditional medicine are gum tragacanth of *Astragalus tragacantha* L., sweat violate oil of *Viola odorata* L., apricot kernel oil of *Prunus armeniaca* L., henna leaf of *Lawsonia alba* Lam., rose oil of *Rosa damascene* Herrm., myrrh (*Commiphora myrrha* (Nees) Engl.), and dry wallflower (*Eryzimum cheiri* (L.) Crantz. (423). Cavasana *et al*. (424) found that the extract of *Aloe vera* was capable to decrease the lumen of the fistulous tract as well as decrease the vascular congestion. Huanglian ointment (HLO) can reduce inflammation and enhance the healing of infected wounds, and its mechanisms are connected to $_{D}$-Glutamine and $_{D}$-glutamate metabolism, linoleic acid metabolism, tyrosine, phenylalanine, tryptophan biosynthesis, alpha-linolenic acid metabolism, ascorbate, and aldarate metabolism (425). Kanazawa Sutra (KanS) is composed of *Capsicum annuum* tincture, *Ficus carica* latex, and *Achyranthes fauriei* Kshara, and powdered *Curcuma longa* rhizome, can be recommended for treatment of anal fistula (426).

Cyclic vomiting syndrome (CVS)

CVS is clinically known by a pattern of stereotypic, recurrent, and usually incapacitating episodes of intense vomiting and nausea which are identified by periods of time free of signs (427-429). It is known as functional and idiopathic gastrointestinal disorder which related to a disorder of brain-gut interaction appearing in pediatric and adult patients around the world (430-432). It is usually categorized as having four phases: prodromal, acute/vomiting/hyperemesis, recovery, and remission/interepisodic, and the common treatment strategies for it is consisting of trigger avoidance, abortive and prophylactic medication therapies, and supportive care (433). As a disorder of gut-brain interaction (DGBI), it represents 3%-14% of cases of unexplained vomiting and chronic nausea (434,435). It was known as a primarily pediatric illness, which is now identified as the disorder which has a similar prevalence in adults (436,437).

Symptoms and signs of this illness mimic other illnesses such as gastroenteritis, food poisoning, and gastroparesis, which make its recognition difficult or with delayed for some years (438-440). Various types of CVS can be categorized according to the differences in clinical features of episodes, specific triggering contexts, and patterns of associated comorbidities (441,442). It is also reported that CVS possibly has a neurological basis with potential links to neuronal excitability and the mechanism of neural circuits is important for vomiting and nausea (443-445). It has been revealed that CVS are characterized by recurrent attacks of vomiting, nausea, and abdominal pain lasting for minutes in both adolescents and children (446-448). Anxiety is prevalent in pediatric CVS warranting screening, and heart rate variability (HRV) may be used as a biomarker for assessing stress as a trigger for CVS episodes (449,450). Some of the most important medicinal plants and herbs which have been used for many years in South part of Asia for treatment and cure of CVS are *Artemisia maritima* L., *Mentha longifolia* (L.), *Tanacetum faconeri* Hook., *Mentha piperita* L., *Allium cepa* L., *Pimpinella diversifolia* DC., *Hylotelephium telephioides* (Ledeb.)H., *Rheum webbianum* Wall., *Oxyria digyna* (L.), *Viola serpens* Wall., *Persicaria amplexicaulis* (D.Don), *Cichorium intybus* L., *Prunus persica* L., *Ficus carica* L., *Prunus armeniaca* L., *Cucumis sativus* L., *Thymus serphyllum* L., *Persicaria vivipara* (L.), *Saussurea gossypiphora* D., *Rhododendron anthopogon* D., *Aconitum heterophyllum* Wall., *Urtica dioica* L., *Cucurbita maxima*, *Ribes alpestre*, *Rheum austral*, *Morus albla*, *Raphanus sativus* L., *Daucus carota* L., *Oxalis corniculata* L., *Berberis lycium*, *Echinops echinatus* Roxb., *Salvia* sp., *Solanum nigrum* L., *Datura stramonium* L., *Cuscuta reflexa* Roxb., *Swertia petiolate*, *Plantago himalaica*, *Juniperus excelsa*, *Aster vinifera* L., *Rosa indica* L., *Chenopodium album* L., *Morus nigra* L., *Xanthium strumarium* L., *Verbascum Thapsus* L., and *Artemisia annua* L. (451,452). Important treatments for cyclic vomiting syndrome are identify and avoid the triggers, fight signs and symptoms during an episode by using natural relief options for migraines, explore

natural nausea remedies such as chamomile tea, ginger tea, and essential oils such as lemon and peppermint, reduce the fever, minimize diarrhea, and ease dizziness (453-456). Treating cyclic vomiting syndrome can be done throw different ways such as medication options such as preventive or prophylactic medications, abortive medications, and lifestyle changes such as avold cannabls use and address stress (457-462).

Conclusion

Plant-derived components can be applied as synergistic agents and biofilm inhibitors with considering innovative findings using different new technologies for development and effective proof-of-concept research of plant-derived options. Nutraceuticals for gastrointestinal disorders are senna, cascara, *Sachharomyces cerevisiae*, *Andrographis paniculata*, boswellic acids, *Curcuma longa*, purple potato extract, *Aloe vera* gel, alginic acid, anthocyanins, curcumin, quercetin, and resveratrol. The most important medicinal plants for treatment of gallstone are saffron, fenugreek, red radish, cumin, fennel, turmeric, pomegranate, sweet orange and green tea, while the most notable medicinal plants for treatment of gastroesophageal reflux disease are *Curcuma longa*, *Aloe vera*, *Althaea officinalis*, *Morus alba*, *Artemisia asiatica*, and *Fumaria officinalis*. For treatment of peptic ulcer, *Zingiber officinalis*, *Zingiber zerumbet*, *Allium sativum*, *Camellia sinensis*, *Curcuma longa*, and *Artemisia asiatica* are common. Chemical components for treatment of pancreatitis are curcumin, luteolin, ellagic acid, borneol, carvacrol, berberine, emodin, oxymatrine, artesunate, baicalein, baicalin, and calycosin. All in all, in conclusion, this review summarizes the importance of different medicinal plants in treatment of various gastrointestinal diseases. In future, more randomized, large, placebo-controlled researches are needed to evaluate the safety and effectiveness of spices and herbs for treatment of gastrointestinal disorders.

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Conflicts of Interest

The authors declare no conflict of interest.

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