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ORIGINAL ARTICLE

Natural products in treatment of ulcerative colitis and peptic ulcer

Amani S. Awaad [a], Reham M. El-Meligy [a,*], Gamal A. Soliman [b]

[a] *Chemistry Department, Faculty of Science, King Saud University, Riyadh, Saudi Arabia*
[b] *Pharmacology Department, Faculty of Pharmacy, Salman Ibn Abd Al Aziz University, Al-Kharj, Saudi Arabia*

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Abstract Ulcerative colitis is an inflammatory chronic disease that affects the mucosa and submucosa of the colon and rectum. Several types of drugs are available such as aminosalicylates. Peptic ulcer disease (PUD) is a common disorder that affects millions of individuals worldwide and it can be considered one of the most important common diseases in the world. Treatment of peptic ulcers depends on using a number of synthetic drugs that reduce the rate of stomach acid secretion (Antiacids), protect the mucous tissues that line the stomach and upper portion of the small intestine (Demulcents) or to eliminate *Helicobacter pylori* (*H. pylori*). In most cases, incidence of relapses and adverse reactions is seen in the following synthetic antiulcer therapy. Accordingly, the main concern of the current article is to introduce a safe drug (or more) of natural origin, to be used for the management of gastric ulcers without side effects.

A widespread search has been launched to identify new anti-ulcer therapies from natural sources. Herbs, medicinal plants, spices, vegetables and crude drug substances are considered to be a potential source to control various diseases including gastric ulcer and ulcerative colitis. In the scientific literature, a large number of medicinal plants and their secondary metabolites with potential anti-ulcer (anti-peptic ulcer and antiulcerative colitis) activities have been reported. Treatment with natural products produces promising results and fewer side effects. Our goal is to collect the published

* Corresponding author. Address: Chemistry Department, Faculty of Sciences, King Saud University, Al-steen Street, Almalaz, P.O. Box 22452, Riyadh 11495, Saudi Arabia. Tel.: +966 14785447x1412; fax: +966 14772245.
E-mail addresses: r_meligy@yahoo.com, relmeligy@ksu.edu.sa (R.M. El-Meligy).

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data in the last 24 years and reviews the natural products reported in the treatment of these diseases and their mechanism of action.

1. Introduction

Ulcers in the gastrointestinal tract could be divided into two common types according to location; ulcerative colitis (lower) and peptic ulcer (upper). Ulcerative colitis (UC) is an inflammatory bowel disease that primarily affects the colonic mucosa. In its most limited form it may be restricted to the distal rectum, while in its most extended form, the entire colon is involved (DiPiro et al., 2002). UC can occur in both sexes and in any age group but most often begins in people between 15 and 30 years of age. The exact causes of UC are still not clear but different factors have been postulated as possible etiologic agents. They are genetic factors, infective agents, immunological basis, smoking, medications and pathological factors (Berardi, 2000).

Peptic ulcer disease (PUD) is an illness that affects a considerable number of people worldwide. It develops when there is an imbalance between the ''aggressive'' and ''protective'' factors at the luminal surface of the epithelial cells. Aggressive factors include *Helicobacter pylori*, HCl, pepsins, nonsteroidal anti-inflammatory drugs (NSAIDs), bile acids, ischemia, hypoxia, smoking and alcohol. While defensive factors include bicarbonate, mucus layer, mucosal blood flow, PGs and growth factors (Harold et al., 2007).

2. Ulcerative colitis

2.1. Symptoms

In patients with UC, ulcers and inflammation of the inner lining of the colon lead to symptoms of bloody diarrhea, passage of pus, mucus, and abdominal cramping during bowel movements (Baumgart and Sandborn, 2007). Most patients with UC experience intermittent bouts of illness after varying intervals with no symptoms (DiPiro et al., 2002). Clinical signs of the disease may be mild, moderate or severe:

- *Mild*: Less than four stools per day, with or without blood, with no systemic disturbance and a normal erythrocyte sedimentation rate (ESR).
- *Moderate*: More than four stools per day with minimal systemic disturbance.
- *Severe*: More than six bloody stools per day, with the evidence of systemic disturbance as fever, tachycardia, anemia, or ESR of more than 30.

2.2. Diagnosis

The diagnosis of UC is made on clinical suspicion and confirmed by biopsy, stool examinations, sigmoidoscopy or colonoscopy, or barium radiographic examination. The presence of extracolonic manifestations such as arthritis, and uveitis may also aid in establishing the diagnosis (DiPiro et al., 2002).

2.3. Treatment with synthetic drugs

Currently, there is no an effective therapy to cure the disease but the mainstream treatment depends on reduction of the abnormal inflammation in the colon lining and thereby relieves the symptoms of diarrhea, rectal bleeding, and abdominal pain. The treatment depends on the severity of the disease; therefore treatment is adjusted for each individual (Botoman et al., 1998). Most people with mild or moderate ulcerative colitis are treated with corticosteroids (dexamethasone) to reduce inflammation and relieve symptoms (Hanauer et al., 2004). Nearly 25% of patients with UC requiring steroids therapy become steroid-dependent after one year, and virtually all develop steroid-related adverse events (Faubion et al., 2001).

Other drugs as **immunomodulators** (azathioprine and 6-mercapto-purine) that reduce inflammation by affecting the immune system (Bresci et al., 1997) and **aminosalicylates** (Rachmilewitz, 1989) are available.

3. Peptic ulcer

3.1. Symptoms

Small ulcers may not cause any symptoms however some big ulcers can cause serious bleeding. Although there are common shared symptoms (Malagelada et al., 2007) which include:

- Feeling of fullness, unable to drink as much fluid.
- Hunger and an empty feeling in the stomach, often 1–3 h after a meal.
- Mild nausea (vomiting may relieve symptom).
- Pain or discomfort in the upper abdomen.
- Upper abdominal pain that wakes you up at night.

In addition to some symptoms in some cases:

- Bloody or dark stools
- Chest pain
- Fatigue
- Vomiting
- Weight loss

3.2. Diagnosis

The following tests could be done to diagnose peptic ulcer:

1. Esophagogastroduodenoscopy (EGD): in which a thin tube with a camera on the end is inserted through the mouth into the GI tract to see the stomach and small intestine. During an EGD, a biopsy may be taken from the wall of the stomach to test for *H. pylori*.
2. X-ray for the upper gastrointestinal tract (GIT) which taken after drink a thick substance called barium.
3. Hemoglobin blood test to check if there is anemia.
4. Stool guaiac to test if there is blood in the stool.

3.3. Treatment with synthetic drugs

Several classes of pharmacological agents have proved to be effective in the management of the acid peptic disorders. These groups include: **antacids** (aluminum hydroxide, magnesium trisilicate), **acid suppressive agents** (Antisecretory drugs) which include proton pump H^+/K^+ ATPase inhibitors (omeprazole, lanzoprazole), histamine H_2 receptor antagonist (cimetidine, ranitidine) and **anticholinergic** (M_1) (pirenzepine), **cytoprotective agents** (sucralfate and prostaglandin analogs (misoprostol), **antimicrobial**s for eradication of *H. pylori* (amoxicillin, clarithromycin) and **Triple therapy** (one week triple therapy consisting of a proton pump inhibitor such as Omeprazole and the antibiotics Clarithromycin and Amoxicillin) (Waller et al., 2005; Katzung, 2004).

A widespread search has been launched to identify new anti-ulcer therapies from natural sources to replace currently used drugs of doubtful efficacy and safety. Herbs, medicinal plants, spices, vegetables and crude drug substances are considered to be a potential source to control various diseases including gastric ulcer and ulcerative colitis. In the scientific literature, a large number of medicinal plants and their secondary metabolites with anti-ulcer potential have been reported.

4. Methodology

4.1. MEDLINE search

To collect the data which support this idea we performed a systematic review using PubMed, Google and MEDLINE databases. All English-language articles published between 1987 and 2011 were searched using the terms 'antiulcerogenic', 'anti-ulcer', 'gastroprotective', 'gastric antiulcerogenic', 'cytoprotective, 'antisecretory', 'peptic ulcer', 'ulcerative colitis', 'antiulcerative colitis', 'natural products', '*Helicobacter pylori*', 'plant extracts' or 'protective'. Plants names, families and authorities were confirmed using http://www.tropicos.org/ and http://www.theplantlist.org/ sites.

4.2. Capturing study design and effects

Details regarding the study design (dose, model [and strain], population, duration and phytochemical group) and effects on UC and PUD were captured in a database.

4.3. Assessing the scientific support for an extract

Evidence for the support of an extract was assessed from multiple studies (i.e., >1 article). The spelling of all extracts and family names was checked at http://www.ipni.org. Botanical descriptions were checked using MEDLINE and by referring to http://www.wikipedia.org and http://www.nybg.org.

5. Results

5.1. Treatment of ulcerative colitis with natural products

The therapeutic effect and mechanism of proanthocyanidins isolated from grape seed (GSPE) were investigated for their activity in the treatment of recurrent ulcerative colitis (UC) in rats. GSPE treatment facilitated recovery of pathologic changes in the colon after induction of recurrent colitis, as demonstrated by reduced colonic weight/length ratio and macroscopic and microscopic damage scores (Wang et al., 2010). Another study (Li et al., 2008) confirmed this fact as, GSPE exerts a beneficial anti-inflammatory effect in the acute phase of TNBS-induced colitis in rats by down regulating some of the mediators involved in the intestinal inflammatory response, inhibiting inflammatory cell infiltration and antioxidation damage, promoting damaged tissue repair to improve colonic oxidative stress, decreasing production of proinflammatory cytokines interleukin IL-1beta, and increasing production of anti-inflammatory cytokines IL-2 and IL-4.

Garcinia cambogia Desr. (Clusiaceae) extract has attracted interest due to its pharmacological properties, including gastroprotective effects. The anti-inflammatory activity of the alcohol extract in TNBS-induced colitis rats was investigated. The results obtained revealed that garcinia administration to colitic rats significantly improved the macroscopic damage and caused substantial reductions in increases in MPO activity, COX-2 and iNOS expression. In addition, garcinia extract treatment was able to reduce PGE (2) and IL-1beta colonic levels. These anti-inflammatory actions could be related to a reduction in DNA damage in isolated colonocytes, observed with the comet assay (dos Reis et al., 2009).

Ginkgo biloba L. (Ginkgoaceae) is a putative antioxidant and has been used for thousands of years to treat a variety of ailments. Some workers in 2008 tested whether the standardized *G. biloba* extract (EGb 761) is an antioxidant that can be used to prevent and treat colitis in mice. They found that, EGb 761 suppresses the activation of macrophages and can be used to both prevent and treat mouse colitis (Kotakadi et al., 2008). Others revealed the probable mechanisms of EGB ameliorated inflammatory injury in TNBS-induced colitis in rats by its modulation of inflammatory mediators and antioxidation (Zhou et al., 2006).

The potential role of *Zingiber Officinale* Roscoe (Zingiberaceae) extract was evaluated in modulating the extent and severity of ulcerative colitis. Results showed a valuable effect of ginger extract against acetic acid-induced ulcerative colitis possibly by its antioxidant and anti-inflammatory properties (El-Abhar et al., 2008).

The protective effects of *Angelica sinensis* (Oliv.) Diels (Apiaceae) polysaccharides could be explained partially by that oxidative stress and GSH (glutathione) depletion which are highly associated with the pathological mechanism of UC, and the protective effects of AS polysaccharides are closely related to the prevention of oxidative stress, which may occur during neutrophil infiltration in the pathological process of UC (Wong et al., 2008).

The effect of *Rheum tanguticum* Maxim. ex Balf. (Polygonaceae) polysaccharide (RTP) on hydrogen peroxide-induced human intestinal epithelial cell injury and they found that, Pretreatment of the cells with RTP could significantly elevate cell survival, SOD activity and decrease the level of MDA, LDH activity and cell apoptosis. RTP may have cytoprotective and anti-oxidant effects against H_2O_2-induced intestinal epithelial cell injury by inhibiting cell apoptosis and necrosis. This might be one of the possible mechanisms of RTP for the treatment of ulcerative colitis in rats (Liu et al., 2005).

Green tea (*Camellia sinensis* (L.) Kuntze, Theaceae) was found to be effective in the treatment of ulcerative colitis. Both diarrhea and loss of body weight can be significantly

attenuated by the treatment with green tea extract. The mechanism of action was associated to remarkable amelioration of the disruption of the colonic architecture, significant reduction of colonic myeloperoxidase (MPO) and tumor necrosis factor-alpha (TNF-alpha) production. Green tea extract also reduced the appearance of nitrotyrosine immunoreactivity in the colon and reduced the up-regulation of intercellular adhesion molecule 1 (ICAM-1) (Mazzon et al., 2005).

A randomized, double-blind, placebo-controlled trial was performed to study the efficacy and safety of aloe vera (*Aloe vera* (L.) Burm.f., Xanthorrhoeaceae) leaves gel for the treatment of mildly to moderately active ulcerative colitis. The results offer that, oral aloe vera taken for 4 weeks produced a clinical, response more often than placebo; it also reduced the histological disease activity and appeared to be safe (Langmead et al., 2004). In similar study, other workers concluded that, wheat grass (*Triticum aestivum* L., Poaceae) juice appeared effective and safe as a single or adjuvant treatment of active distal UC (Ben-Arye et al., 2002). In addition, seeds of *Plantago ovata* Forssk., Plantaginaceae (dietary fiber) might be as effective as mesalamine to maintain remission in ulcerative colitis (Fernández et al., 1999).

D-002 obtained from beeswax and composed of mixture of higher aliphatic primary alcohols. D-002 was found to possess mild anti-inflammatory and effective antiulcerogenic activity. Moreover, it has a protective effect on the pre-ulcerative phase of carrageenan-induced colonic ulceration in the guinea pig through the reduction of leukotriene (LTB 4) in the exudate. In addition D-002 was effective to protect or prevent the damage associated to acetic acid-induced colitis. Upon oral administration of D-002 at doses 25 and 50 mg/kg in both single and repeated experiments, it significantly reduced the wet weight, macroscopic injury; polymorphonuclear infiltration and wall thickness in colonic mucosa of treated animals compared with the controls in both protective and therapeutic alternatives (Noa et al., 2000).

5.2. Treatment of peptic ulcer with natural products

Plants with antiulcerogenic activity were used either as raw materials which obtained by extraction with solvents or as individual isolated compounds.

5.2.1. Total extracts

Many solvents have been used to extract active materials from plants such as; alcohol (ethanol or methanol), ether, chloroform, ethyl acetate, n-butanol and water (Awaad et al., 2011).

The root of *Saussurea lappa* C.B. Clarke (Asteraceae) when extracted using ethyl acetate and tested for its antiulcerogenic properties at two doses 200 and 400 mg/kg orally found to have protective activity against peptic ulcer through its cytoprotective effect (Sutar et al., 2011). The ethanol extract of *Zizyphus oenoplia* (L.) Mill. (Rhamnaceae) root possesses antiulcerogenic activity at a dose of 300 mg/kg with mechanism includes increase in prostaglandin synthesis, the antiulcer activity of this extract is probably due to the presence of flavonoids (Jadhav and Prasanna, 2011). On the other hand, it was reported that *Zizyphus lotus* (L.) Lam. extracts act essentially as cytoprotective agents, as the oral administration of aqueous extracts of its root barks (50–200 mg/kg), leaves (50–200 mg/kg) and fruits (200–400 mg/kg) produced a significant and dose dependent inhibition to the acute ulcer induced by HCl/ethanol. While the methanol, ethyl acetate and chloroform leaves and root barks extracts at the dose of 200 mg/kg exhibited a significant inhibition of gastric lesions (Wahida et al., 2007).

The standardized extracts of *Quassia amara* L. (Simaroubaceae) bark named; Lipro® (4.9 to 48.9 mg/kg) and Ligas® (4.0 to 39.7 mg/kg) showed an important anti-ulcerogenic effect in acute ulcer induction models. Their effect was related to an increase in gastric barrier mucus and non-protein sulfhydril groups (Garcia-Barrantes and Badilla, 2011). Another solvents were used for the extraction, these were; 70% ethanol, 100% ethanol, 100% dichloromethane and 100% HEX. All extracts were given orally at dose of 100 mg/kg. The mechanism of their activities was related to cytoprotective factors, such as mucus and prostaglandins (Toma et al., 2002).

The oral administration of ethanol extract of coconut seed (*Cocus nucifera* L., Arecaceae) at doses of 100 and 200 mg/kg was proved to have an ulcer inhibition of 65.4% and 67.9%, respectively, while the use of another dose (400 mg/kg) of the same extract increased the evince of ulceration when compared with control (Anosike and Obidoa 2010).

The ethanol extract of *Encholirium spectabile* Mart. (Bromeliaceae) aerial parts was evaluated after oral administration for its antiulcerogenic effect at a dose of 100 mg/kg. The extract showed protection to gastric mucosa by 53%, 75%, 52%, and (43%) against ulceration that was induced by four models; absolute ethanol, ethanol/HCl, ibuprofen and ischemia/reperfusion respectively. This protection seems to occur due to the activation of antioxidant systems and the involvement of prostaglandins and the NO synthase pathway (Carvalho et al., 2010).

The methanol extract of *Cissus quadrangularis* L., Vitaceae (CQE) was administrated orally to rats at a dose of 1000 mg/kg, the results revealed protective effects against gastric ulceration better than ranitidine at a dose of 30 mg/kg using aspirin induced gastric ulcer model (Shanthi et al., 2010). Alcohol extract of *Gynura procumbens* (Merr.), Asteraceae, leaves was administrated orally to rats at doses of 50, 100, 200 and 400 mg/kg. It exhibited significant protection against ethanol-induced injury. Such protection was dose dependent and was most prominent at a dose of 400 mg/kg (Mahmood et al., 2010).

Gastroprotective effect of *Zingiber Officinale* Roscoe (Zingiberaceae) rhizome was tested by the extraction of rhizome using 50% ethanol and administrated orally at doses of 50, 100 and 200 mg/kg. It was assessed in different gastric ulcer models in rats; ethanol and acetic acid induced ulcers. The results proved that the extract showed a dose dependent inhibition of ulcer index and it also prevented the oxidative damage of gastric mucosa by blocking lipid peroxidation, decrease in superoxide dismutase and increase in catalase activity (Arun et al., 2010). Other workers proved that, the ethanol extract showed good protective effect against indomethacin-induced gastric ulcer model in the rats at doses of 100, 200 and 400 mg/kg (Anosike et al., 2009). Furthermore, Agrawal et al. (2000) and Moshen et al. (2006) suggested that ginger extract possesses its anti-ulcer properties through augmentation of mucin secretion and decreased cell shedding rather than offensive acid and pepsin secretion.

The leaves of *Butea frondosa* (Roxb.), Fabaceae were extracted using different solvents; petroleum ether, chloroform, ethanol and water, these extracts were given orally at doses of 250 and 500 mg/kg to mice, the extracts showed protection

against chronic gastric ulcers induced by 0.6 M HCl, where the chloroform extract (250 mg/kg) showed a highest activity (Londonkar and Ranirukmini, 2010).

The leaves of *Parkia platycephala* Benth. (Leguminosae) ethanol extract at three doses (62.5, 125 or 250 mg/kg) showed gastroprotective activity against gastric damage induced by ethanol and ethanol-HCl, which are possibly mediated, in part, by the nitric oxide release. In addition, it also exhibits protection against lesions induced by ischemia–reperfusion and it has an antioxidant effect through increase in catalase activity (Fernandes et al., 2010).

The leaves of *Anacardium humile* St. Hil. (Anacardiaceae) when extracted with ethyl acetate extract and administrated orally to rats at a dose of 50 mg/kg can significantly protect gastric mucosa against absolute alcohol-induced ulcer, and this protection might be due to increased PGE2 and mucous production (Ferreira et al., 2010).

Oral treatment with red mangrove *Rhizophora mangle* L. (Rhizophoraceae) bark extract at a dose of 500 mg/kg produced a high level of gastric protection. Mucus content was accompanied by a proportional increase in proteins (Sánchez et al., 2001). It possesses its activity through several mechanisms due to a verity in its active principles. It showed gastroprotective and antisecretory effects, in addition to increase in PGE2 levels in a doses-dependent manner (Sánchez et al., 2010).

Thirunavukkarasu and coworkers studied the bark of *Excoecaria agallocha* L. (Euphorbiaceae) to determine its gastro protective effect, they used the lyophilized cold & hot water extracts at doses of 62.5 & 125 mg/kg in a model of NSAID induced ulcer rat. The results reveled that, the extract decreases the acidity and increases the mucosal defense in the gastric areas (Thirunavukkarasu et al., 2009).

The *Erythrina indica* L. (Febaceae) leaves were found to possess significant antiulcer properties when extracted by methanol and administrated orally to rats at doses of 125, 250 and 500 mg/kg. The investigation was carried out using pylorus ligated and indomethacin induced ulceration models. The obtained effect may be attributed to the presence of polyphenolic compounds (Sachin and Archana, 2009).

Liquorice or *Glycyrrhiza glabra* L. (Fabaceae) leaves, roots and seeds were reported in folk medicine to possess antiulceogenic activity. The total alcohol extract of the seed given orally to rats at a dose of 200 mg/kg showed protection against alcohol mucosa damage appeared as a significant reduction in the ulcer index. In addition, ALP and TBARS were significantly reduced. Liquorice seed extracts have significant mucosal protective and antioxidant effects on the gastric mucosa in rats (Ligha and Fawehinmi, 2009).

Some workers tested the resin obtained from the bark of *Virola surinamensis* (Rol. ex Rottb.) Kuntze (Myristicaceae) for its antiulcerogenic activity after pretreatment of mice with the ethanol extract at a dose of 500 mg/kg orally. The extract inhibited mucosal injury, reduced the formation of gastric lesions induced by indomethacin, stress and pylorus ligature (by 39%, 45% and 31%, respectively) when compared to the animals treated with vehicle (Hiruma-Lima et al., 2009).

The stem bark of *Combretum leprosum* Mart. & Eiche (Combretaceae) was extracted using ethanol and administrated orally, it possessed gastroprotective and anti-ulcerogenic effects, which are related to the inhibition of the gastric acid secretion and an increase of mucosal defensive factors (Nunes et al., 2009).

Gymnosporia rothiana (Walp.) Wight & Arn. ex M.A.Lawson (Celastraceae) leaves extracts were evaluated after oral administration of different doses using ethanol and indomethacin induced gastric ulcer models. All extracts showed significant reduction in ulcer lesion index as well as increase in volume and pH of gastric content in both experimental models. Petroleum ether extract at a dose of 250 mg/kg and methanol extract at a dose of 500 mg/kg were the most effective extracts. The petroleum ether extract exerts its action by increasing gastric mucosal defense (prostaglandin and free radical scavenging) which is attributed to its high levels of terpenoids such as β amyrin, lupeol and friedelin (Jain and Surana, 2009a). Similarly, petroleum ether, chloroform and methanol extracts of *Spathodea falcate* (Bignoniaceae) bark at doses 250, 500 mg/kg possess cytoprotective effect against the same models and possessed the same mechanism of action (Jain and Surana, 2009b).

UlGen (a polyherbal formulation mainly composed of *Glycyrrhiza glabra* L. (Fabaceae; Root), *Saussurea lappa* C.B. Clarke (Asteraceae; Root), *Aegle marmelos* (L.) Corr.-Serr. (Rutaceae; Fruit) and *Santalum album* L. (Santalaceae; Stem) upon oral administration to rats at a dose of 800 mg/kg significantly protected the onset of cold resistance stress induced ulcerations. Also it significantly inhibited gastric ulceration induced by alcohol and aspirin. The cytoprotective effect of this product may be explained by the enhancement of defensive mechanism through an improvement of gastric cytoprotection as well as acid inhibition (Muralidhar et al., 2009).

The fruits of *Terminalia chebula* Retz. (Combretaceae) extract at doses of 250, 500 mg/kg were administrated orally and produced significant inhibition of the gastric lesions induced by pylorus ligation & ethanol induced gastric ulcers, which might be due to its antisecretory activity (Raju et al., 2009).

Oral administration of the aqueous extract of *Matricaria chamomilla* L. (Asteraceae) flowers at a dose of 400 mg/kg prevented gastric ulceration in mice (Karbalay-Doust and Noorafshan, 2009). Others mentioned that, the leaves of *Lasianthera Africana* P. Beauv. (Icacinaceae) ethanol extract which given orally to rats at doses of 1000 and 3000 mg/kg inhibited ethanol-induced, indomethacin-induced and reserpine-induced ulcer models in a dose dependent fashion (Okokon et al., 2009).

Leaves ethanol extract of *Morus alba* L. (mulberry), Moraceae, was found to exhibit significant anti-ulcerogenic activity in rats. Using absolute ethanol induced ulcer model, animals pretreated with plant extracts, orally at 250 mg/kg and 500 mg/kg doses, showed marked reduction of gastric mucosal damage, reduction of edema and leucocytes infiltration of the submucosal layer. A direct protective effect of *M. alba* extracts on gastric mucosal damage and that the gastroprotective action of this plant may be due to its anti-inflammatory and antioxidant properties (Abdulla et al., 2009).

Using a model of alcohol-induced gastric ulcers in mice, the ethanol extracts of five plants named; *Croton zehntneri* Pax & K. Hoffm. (Euphorbiaceae; essential oils from leaves), *Vanillosmopsis arborea* (Gardner) Baker (Asteraceae; essential oils from bark), *Caryocar coriaceum* Wittm. (Caryocaracea; oil from fruit pulp), *Himatanthus drasticus* Mart. Plumel (Apocynaceae; latex), and *Stryphnodendron rotundifolium* Mart.

(Fabaceae; leaves) at doses of 200 and 400 mg/kg for each were tested. The results revealed that, the extracts possessed anti-ulcer activity which may be related to an antacid effect or cytoprotective properties of the plants. Furthermore, the inhibitory effect of these plants may be due to the presence of tannins, terpenes, and fatty acids (Oliveira et al., 2009). The antiulcerogenic effects of the leaves of *Mentha arvensis* L. (Lamiaceae) were studied using different models. The plant was extracted using different solvents (petroleum ether, chloroform and water) and given orally to rats at a dose of 375 mg/kg, the results showed a protective effect against acid secretion and gastric ulcers in ibuprofen plus pyloric ligation, 0.6 M HCl induced and 90% ethanol-induced ulcer models (Londonkar and Poddar, 2009).

The fruit of *Carica papaya* L. (Caricaceae) was reported to have potential activity in the treatment of gastric diseases. The aqueous extract at a dose of 400 mg /kg administrated orally to rats that reduced the ulcer index. *Carica papaya* may exert its gastroprotective effect by a free radical scavenging action (Ologundudu et al., 2008).

The methanol and aqueous extracts of *Coccinia grandis* Linn. (Cucurbitaceae) leaves were administrated orally to rats at doses of 0.5, 1, 2 g/kg, aspirin induced gastric ulcer model was used to test their antiulcerogenic potentials. The extracts produced a significant dose related antiulcer activity which may be related to increase mucus secretion in addition to their antioxidant property (Mazumder et al., 2008). On the other hand, a significant anti ulcer activity was reported for the leaves of *Polyalthia longifolia* (Sonn.) Thwaites (PL) (Annonaceae) when extracted using ethanol and administrated at a dose of 300 mg/kg to animals, using different models (aspirin plus pylorous ligation induced gastric ulcer in rats, HCl–ethanol induced ulcer in mice and water immersion stress induced ulcer in rats) (Malairajan et al., 2008).

Both oil and mucilage of *Linum usitatissimum* Linnaeus. (flaxseed), Linaceae, can provide a cytoprotective effect against ethanol-induced gastric ulcers in rats. Pretreatment of rats with oral flaxseed oil at a dose of 5.0 ml/kg and flaxseed mucilage at a dose of 10.0 ml/kg significantly reduced the number and length of gastric ulcers. The oil was more effective than the mucilage in reducing the number of ulcers (Dugani et al., 2008). The seeds aqueous extract of *Strychnos potatorum* Linn (Loganiaceae) was given orally to rats at doses of 100 and 200 mg/kg exhibited antiulcerogenic activity. This activity was studied using aspirin plus pyloric ligation-induced gastric ulcer model. The results proved that, the extract prevented ulcer formation by decreasing acid secretory activity and increasing the mucin activity, this activity may be attributed to the presence of mucilaginous polysaccharides; mannogalactans (Sanmugapriya and Venkataraman, 2007).

Two plants *Ceiba pentandra* G. (Bombacaceae) bark and *Helicrysum mechowianum* Klatt (Asteraceae) leaves were extracted using water and administrated orally to rats at a dose of 400 mg/kg to study their antiulcerogenic activities. Both extracts significantly reduced the pH and the formation of lesions induced by indomethacin (Ibara et al., 2007).

Clove (the dried flower buds of *Syzygium aromaticum* L. (Myrtaceae)) was extracted with ethanol and the ethanol extract was further extracted by *n*-butanol. The *n*-butanol portion possessed anti-ulcerogenic and antisecretory effects in rats at doses of 50, 100, and 200 mg/kg when given subcutaneously and using indomethacin-induced gastric ulcer model. The extract contains flavonoids, tannins which contributed to the activity (Magaji et al., 2007).

Aloe vera (L.) Burm.f. (Xanthorrhoeaceae) leaf gel ethanol extract was found to be effective in both acute and chronic gastric ulcers. Pretreatment with *Aloe vera* leaf gel extract (150 mg/kg) prevent the formation of lesions induced by two models (indomethacin and ethanol-induced gastric lesions). In addition, treatment with the extract for 15 days significantly reduce the ulcer index, ulcerated surface and significantly elevated the level of glycoprotein content in gastric juice, in the treatment of chronic ulcer. This gastroprotective effect may be mediated by defensive mucosal factors. Furthermore, the ulcer curative properties of *Aloe vera* leaf gel extract have been established by histological studies (Subramanian et al., 2007).

The flavonoid-rich fraction obtained from the methanol extract of *Orostachys japonicus* A. Berger (Crassulaceae) was studied for its anti-ulcerogenic activites using HCl/ethanol-induced and indomethacin/bethanechol-induced ulcer models in mice, at 100 mg/kg dose, the fraction highly reduced the diameter of gastric lesion (Jung et al., 2007).

Shrivastava and coworkers evaluated the antiulcer activity of *Adhatoda vasica* Nees (Acantheceae) leaves using two ulcer models (ethanol-induced and pylorus ligation plus aspirin-induced), they suggested that, the plant has immense potential as an antiulcer agent of great therapeutic relevance (Shrivastava et al., 2006). Other workers studied the hydroalcoholic extract of *Tripleurospermum disciforme* Shultz Bip (Asteraceae) flowers. When administrated orally to rats at 500 and 2000 mg/kg doses, the extract showed a protective effect against ulcer formation in pyloric ligation with significant reduction in ulcer area and ulcer index and the action is not appeared to be mediated through acid reduction (Minaiyan et al., 2006).

Extracts from the plants *Iberis amara* L. (Brassicaceae), *Melissa officinalis* Linnaeus. (Lamiaceae), *Matricaria recutita* L. (Asteraceae), *Carum carvi* L. (Apiaceae), *Mentha piperita* (Lamiaceae), *Glycyrrhiza glabra* L. (Fabaceae), *Angelica archangelica* L. (Apiaceae), *Silybum marianum* (L.) Gaertn. (Asteraceae) and *Chelidonium majus* L. (Papaveraceae) are combined in the form of a commercial preparation known as STW 5 and its modified formulation STW 5-II which lacking the last three plants, were tested for their potential anti-ulcerogenic, antisecretory and cytoprotective activities using indomethacin induced gastric ulcers in rat. All extracts produced a dose dependent activity associated with a reduced acid output and an increased mucin secretion, increase in prostaglandin E2 release and a decrease in leukotrienes. The cytoprotective effect of the extracts could be partly due to their flavonoid content and to their free radical scavenging properties (Khayyal et al., 2001). Further study on the same product was done and the results obtained demonstrated that STW 5 did not only lower the gastric acidity as effectively as the commercial antacid, but it was more effective in inhibiting the secondary hyperacidity. Moreover, STW 5 was capable of inhibiting the serum gastrin level in rats, an effect which ran parallel to its lowering effect on gastric acid production (Khayyal et al., 2006).

Jainu and Shyamala (2006) investigated the antiulcer effect of *Solanum nigrum* L, (Solanaceae) fruits extract (SNE) using cold restraint stress, indomethacin, pyloric ligation and ethanol induced gastric ulcer models while using acetic acid induced ulcer model in rats for evaluating the ulcer healing

activity. They found that, SNE possess antiulcerogenic as well as ulcer healing properties, which might be due to its antisecretory activity. Oral treatment with the methanol extract at doses of 200 and 400 mg/kg significantly inhibited the gastric lesions induced in several models. The extract offers antiulcer activity by blocking acid secretion through the inhibition of H(+)K(+)ATPase and decrease of gastrin secretion.

Leaves and bark of *Alchornea castaneaefolia* (Bonpl. ex Willd.) A. Juss. (Euphorbiaceae) were extracted using hydroethanol, both extracts were studied for their antiulcerogenic properties at doses 500 and 1000 mg/kg for leaves and 1000 mg/kg for bark. Results showed that, both extracts significantly reduced the gastric injuries induced by the combination of HCl/ethanol and lowered the severity of gastric damage formation induced by indomethacin/bethanechol in mice. Leaves extract was also effective in promoting the healing process in chronic gastric ulcer induced by acetic acid in rats. In addition, an enriched flavonoid fraction obtained from leaves extract reduced gastric lesions induced by HCl/ethanol and indomethacin/bethanechol in mice at a dose of 100 mg/kg. It increased prostaglandin production and increased the somatostatin serum levels. Phytochemical investigation led to the isolation of flavonoid glycosides as the main compounds involved in the antiulcer activity (Hiruma-Lima et al., 2006).

The antiulcerogenic activity of *Indigofera truxillensis* Kunth (Fabaceae) was tested in mice and rats using several models; ethanol, piroxicam, hypothermic restraint stress and pylorus ligature. The methanol extract of the aerial parts at doses of 250, 500 and 1000 mg/kg inhibited the gastric lesions in all experiments. The results suggested that, the antisecretory and cytoprotective effects of the methanol extract may be related to the presence of flavonoids detected by phytochemical analysis (Cola-Miranda et al., 2006).

Using ethanol and aspirin-induced gastric ulcerations in rats, some plant extracts were tested to prove their antiulcerogenic activities. Oral administration of the methanol extracts of *Bidens bipinnata* L. (Asteraceae), *Zygophyllum album* L. (Zygophyllaceae), *Plantago major* L. (Plantaginaceae; leaves) and *Schouwia thebaica* Webb (Brassicaceae) at dose of 400 mg/kg significantly decreased the average ulcer index. In addition, *Mentha microphylla* C. Koch (Labiatae), *Conyza linifolia* (Willd.) Täckh. (Asteraceae), *Conyza dioscoridis* (Linn) Desf. (Asteraceae), *Cynanchum acutum* Linn. (Asclepiadoideae) and *Plantago major* L. (Plantaginaceae; seeds) decreased the ulcer index but they were less potent (Atta et al., 2005).

The hydroalcohol extract of the aerial parts of *Trixis divaricata* Spreng. (Asteraceae) given orally to rats at a dose of 1000 mg/kg showed significant anti-ulcerogenic activity. This activity was proved by using two models of ulcer induction; indomethacin and absolute alcohol. Flavonoids and tannins were identified during the phytochemical screening of the hydroalcohol extract and they could be responsible for the effect (Pereira et al., 2005).

The antiulcerogenic effect of *Byrsonima crassa* Niedenzu (IK) (Malpighiaceae) leaves was evaluated using three different extracts; hydromethanol (80% MeOH), methanol (MeOH) and chloroform ($CHCl_3$) extracts. The oral administration of these extracts at doses of 250, 500 and 1000 mg/kg reduced the formation of lesions associated with HCl/ethanol administration in mice (Sannomiya et al., 2005).

The aerial parts of *Zataria multiflora* Boiss. (Lamiaceae) hydroalcohol extract were found to be potent antiulcerogenic agent, it significantly reduced ulcerated area and index in a dose dependent manner in a cysteamine HCl induced duodenum ulcers model when given orally at doses of 200, 400, 800 and 1200 mg/kg (Minaiyan et al., 2005). The methanol extract of *Pausinystalia macroceras* (K. Schum.) Pierre ex Beille (Rubiaceae; stem-bark) was dose dependently (17.5–350 mg/kg) reduced the ulcer indices induced by indomethacin, ethanol and reserpine. The antiulcerogenic effect might be due to its blocking effect on H_2 receptor; protection from oxygen derived free radicals damage on rat gastric mucosa (Nwafor et al., 2005).

Pretreatment with the aqueous extract of *Ageratum conyzoides* L. (Asteraceae) leaves at doses 250 and 500 mg/kg significantly reduced the formation of gastric lesion and marked reduction in submucosal edema in absolute ethanol induced ulcer model (Mahmood et al., 2005).

D-002 or (Abexol) (which is a mixture of higher aliphatic primary alcohols isolated from beeswax) when administered at doses 50, 100, and 200 mg/kg after ulcer induction induced effective healing of acute and chronic gastric ulcers (Molina et al., 2005).

Fixed oil of *Ocimum sanctum* Linn. (Labiatae) had potent antiulcer effect, the mechanism of action was studied using aspirin, indomethacin and alcohol induced ulcer models and it was possibly due to the inhibition of 5-lipooxygenase. On the other hand, upon using histamine, reserpine, and stress induced ulcer models the antiulcer effect was due to its antihistaminic, anticholinergic, and antisecretory properties, respectively (Singh and Majumdar, 1999). In addition, the ethanol

Table 1 Reported alkaloids with antiulcerogenic activity.

Source	Isolated compound	Dose mg/kg	Model used	Reference
Simaba ferruginea A. St.-Hil., Simaroubaceae (rhizome)	Canthin-6-one	NR	EtOH, mice	Almeida et al. (2011)
Voacanga Africana Stapf., Apocynaceae	Alkaoloid (coded as TN)	50–100	HCl-EtOH, EtOH, HCl-EtOH/Indo, PL, CRS and H	Tan and Nyasse (2000)
Enantia chlorantha Oliv. (bark), Annonaceae	7,8-Dihydro-8-hydroxypalmatine	40–80	HCl-EtOH, Ac.a, EtOH and PL	Tan et al. (2000)
Croton lechleri Müll. Arg., Euphorbiaceae	Taspine		Ac.a in rats	Miller et al. (2000)
Capsicum annuum L., Solanaceae	Capsaicin	0.1–2.5	EtOH, Asp (rats).	Kang et al. (1995)
Vinca minor L., Apocynaceae (leaf)	Vinpocetine, vincamine	*p.o.*, or *i.p*	EtOH, Ac.a, Ph-but, H, PL (rats).	Nosalova et al. (1993)
Berberis alkaloids	Matrine and oximatrine	NR	Asp and taurocholic acid in PL rats	Lewis and Hanson (1991)
Papaver somniferum L., Papaveraceae	Morphine		Indo, Asp.	Tazi-Saad et al. (1991)

PL; pyloric ligation, EtOH; ethanol, Indo; indomethacin, CRS; cold resistant stress, C-48/80; mast cell degranulator, Ac.a; acetic acid, Ph-but.; phenylbutazone, Asp; aspirin, NR; Not reported, NR; not reported.

Table 2 Collected Terpenoids with antiulcerogenic activity.

Source	Isolated compound	Dose mg/kg	Model used	Reference
1-Sesquiterpenoids				
Baccharis dracunculifolia DC., Asteraceae (essential oil)	Nerolidol	NR	EtOH (rats)	Klopell et al. (2007)
Centaurea helenioides Boiss., Asteraceae, (flowers)	Grosheimin and cynaropicrin	NR	CRS and EtOH (rats)	Yayli et al. (2006)
Many plants	Xanthatin	NR	NR	Favier et al. (2005) and Maria et al. (1998b)
Fabiana imbricate Ruiz & Pav., Solanaceae (aerial parts)	11-hydroxy-4-amorphen-15-oic acid	100	HCl-EtOH (mice)	Reyes et al. (2005)
Croton sublyratus Kurz., Euphorbiaceae (leaves)	Plaunotol	10, 25, 50	C-48/80, Indo (rats)	Ohta et al. (2005b) and Murakami et al. (1999)
Tasmannia lanceolata (Poir.) A.C. Sm., Winteraceae (leaves)	Drimane-type sesquiterpene dialdehyde, polygodial, its 12a/b acetals, and methyl isodrimeninol	NR	EtOH (rats)	Matsuda et al. (2002)
Xanthium cavanillesii Schouw. & *Artemisia douglusiana* Schouw., Asteraceae	Dehydroleucodine (guaianolide type lactone)	NR	EtOH (rats)	Maria et al. (1998a)
Zingiber officinale Roscoe, Zingiberaceae (rhizome)	b-sesquiphellandrene, b-bisabolene, and zingiberene, and ar-curcumene	NR	HCl-EtOH (rats)	Yamahara et al. (1998)
2-Diterpenoids				
Prumnopitys andina (Poepp. & Endl.) de Laub., Podocarpaceae (Wood and bark)	The abietane diterpene, ferruginol	25, 50	HCl-EtOH (mice)	Rodríguez et al. (2006)
Araucaria araucana (Molina) C. Koch., Araucariaceae (resin)	Labdane derivatives; imbricatolic acid, 15-hydroxyimbricatolal and 15-acetoxyimbricatolic acid	100	HCl-EtOH (mice)	Schmeda-Hirschmann et al. (2005)
Many plants	Dehydroabietanol, *N*-(*m*-nitrophenyl)-, *N*-(*o*-chlorophenyl)- and *N*-(*p*-iodophenyl)abieta-8,11,13-trien-18-amides, *N*-2-aminothiazolyl- and *N*-benzylabieta-8,11,13-trien-18-amides	100	HCl/EtOH (mice)	Sepulveda et al. (2005)
Many plants	Labdane diterpene, solidagenone	100–200	PL, Asp, EtOH (rats)	Rodríguez et al. (2002)
Aparisthmium cordatum Baill., Euphorbiaceae	Cordatin and furano-diterpene, aparisthman	100	HCl-EtOH, Indo/beth, EtOH, CRS, PL (mice, rats)	Hiruma-Lima et al. (2000, 2001)
Croton cajucara Benth., Euphorbiaceae	*Trans*-dehydrocrotonin	NR	HCl-EtOH, CRS (mice, rats)	Brito et al. (1998)
3-Triterpenoids				
Many plants	Boswellic acids	NR	PL, HCl-EtOH, Asp, Indo, CRS (rats)	Singh et al. (2008)
Maytenus robusta Reissek., Celastraceae (leaves)	3,15-Dioxo-21-a- hydroxyfriedelane	NR	EtOH (rats)	Andrade et al. (2008)
Many plants	Oleanolic acid	25–100	EtOH, Asp and PL (rats) & HCl-EtOH (mice)	Rodríguez et al. (2003)
Amphipterygium adstringens (Schltdl.) Standl., Anacardiaceae	3α-hydroxymasticadienonic acid and 3-*epi*-oleanolic acid as well as b-sitosterol	NR	EtOH (rats)	Arrieta et al. (2003)
4-Carotenoids				
Xanthophyllomyces dendrorhous (*Phaffia rhodozyma*)	Astaxanthin		Napr (rats)	Kim et al. (2005)
Many plants	Gefarnate	50, 100, 200	C48/80 (rats)	Ohta et al. (2005a)
Many plants	Teprenone, (tetraprenylacetone)	200	Ac.a (rats)	Kobayashi et al. (2001)
Many plants	Vitamins A and b-carotene	NR	Indo (rats)	Mozsik et al. (1999)

PL; pyloric ligation, EtOH;ethanol, Indo;indomethacin, CRS; cold resistant stress, C-48/80; mast cell degranulator, Ac.a; acetic acid, Beth; bethanechol, Asp; aspirin, Napr; naproxen, C-48/80; mast cell degranulator, NR; not reported.

Table 3 Isolated Saponins with antiulcerogenic activity.

Source	Isolated compound	Dose mg/kg	Model used	Reference
Aralia elata (Miq.) Seem., Araliaceae (root bark)	Araloside	100	HCl-EtOH, Asp, PL (rats)	Lee et al. (2005)
Aesculus hippocastanum L., Sapindaceae (seeds)	Aescin	NR	CRS, PL (rats)	Marhuenda et al. (1993, 1994)
Glycyrrhiza glabra L., Glycyrrhiza radix Br. and *Glycyrrhiza uralensis* Fisch., Fabaceae	Glycyrrhizic acid	NR	Indo (rats)	Aly et al. (2005) and Baker (1994)
Panax ginseng C.A. Mey. (Araliaceae) leaves and roots	Ginsenoside Rb1	NR	HCl-EtOH (mice). Indo, PL (rats)	Jeong et al. (2003) and Sun et al. (1992)

PL; pyloric ligation, EtOH; ethanol, CRS; cold resistant stress, Asp; aspirin, Indo;indomethacin.

Table 4 Collected phenolics with antiulcerogenic properties.

Source	Isolated compound	Dose mg/kg	Model used	Reference
Phenolics and quinones				
Leaves of *Ligularia stenocephala* (Maxim.) Matsum. & Koidz., *L. fischeri* (Ledeb.) Turcz., and *L. fischeri* var. *spiciformis* (Asteraceae)	Caffeoylquinic acids (5-*O*-caffeoylquinic acid, 3,5-di-*O*caffeoyl-*muco*-quinic acid, and 3,5-di-*O*-caffeoylquinic acid)	NR	HCl/EtOH, Indo/beth (rats)	Lee et al. (2010)
Acer tegmentosum Maxim. (Sapindaceae)	Salidroside	10, 20	HCl/EtOH, Indo/beth (rats)	Yoo et al. (2009)
Polygala cyparissias A. St.-Hil. & Moq. (Polygalaceae)	Three xanthones, a-spinasterol (1); 1,3-dihydroxy-7-methoxyxanthone (2); and 1,7-dihydroxy-2,3-methylenedioxyxanthone (3)	50	NR	Klein et al. (2010)
Mangifera indica L. (Anacardiaceae) leaves	Mangiferin (C-glucopyranoside of 1,3,6,7-tetrahydroxyxanthone) and C-glucosylbenzophenone(3-C-b-D-glucopyranosyl-4',2,4,6-tetrahydroxybenzophenone)	10, 30	EtOH and Indo (mice)	Severi et al. (2009) and Carvalho et al. (2007)
Myristica malabarica Lam. (Myristicaceae)	Diarylnonanoids, malabaricones		Indo (rats)	Banerjee et al. (2008b,c)
Piper betle L. (Piperaceae) leaves	Allylpyrocatechol	2 (rats), 5 (mice)	Indo (rats)	Banerjee et al. (2008a) and Bhattacharya et al. (2007a)
Terminalia belerica Roxb. (Combretaceae) fruits	Gallic acid		Indo (rats)	Bhattacharya et al. (2007b)
Many plants	Dialpha-tocopherol acetate	25, 50, 100	Indo (rats)	Valcheva-Kuzmanova et al. (2007)
Sargassum micracanthum (Kützing) Endlicher (Sargassaceae) from marine resources	Plastoquinones and a new chromene	NR	HCl-EtOH (rats)	Mori et al. (2006)
Nigella sativa L. (Ranunculaceae)	Thymoquinone	5, 10, 20, 50, 100	EtOH (rats), ischemia/reperfusion	Kanter et al. (2006), Arslan et al. (2005) and El-Abhar et al. (2003)
Turmeric *Curcuma longa* Linnaeus (Zingiberaceae)	Curcumin	NR	Indo (rats)	Swarnakar et al. (2005)
Many plants	Menadione,	5–45	PL (rats)	Tariq and Moutaer (2005)
Zingiber officinale Roscoe (Zingiberaceae) rhizomes	Ginger-derived phenolics, 6-shogaol, 6-gingerol and 6-gingesulfonic acids	0.1–2.5	HCl-EtOH (rats)	Horie et al. (2004) and Yoshikawa et al. (1994)
Many plants	Eugenol	10–100	EtOH (rats)	Capasso et al. (2000)
Garcinia indica Choisy (Clusiaceae) fruit	Garcinol	NR	Indo, water immersion stress (rats)	Yamaguchi et al. (2000)
Aegle marmelos (L.) Corrêa (Rutaceae) seeds	Pyranocoumarin, luvangetin	NR	NR	Goel et al. (1997)
Rhamnus triquerta Wall. (Rhamnaceae)	Emodin	15	PL, Asp, immobilization stress (rats)	Goel and Das Gupta (1991)
Flavonoids				
Desmostachia bipinnata (L.) Stapf (Gramineae)	Trycin and trycin-7-glucoside	100	EtOH (rats)	Awaad et al. (2008)
Many plants	Cynidin, another anthocynin, DA-6034		HCl-EtOH, Asp, Indo, Ac.a (rats)	Choi et al. (2007)
Alhagi maurorum Boiss. (Leguminosae)	Chrysoeriol 7-O-xylosoid and kaempferol-3-galactorhamnoside	100	EtOH (rats)	Awaad et al. (2006)
Syngonanthus bisulcatus (Koern) Ruhland (Eriocaulaceae)	Isovitexin, luteolin, lutonarin and 5,6,3′,4′-tetrahydroxy-7-O-D-glucopyrade	NR	NR	Coelho et al. (2006)
Garcinia kola Heckel (Clusiaceae)	Kolaviron	100	HCl-EtOH, Indo (rats)	Olaleye and Farombi (2006)
Leaves of *Mikania laevigata* Sch. Bip. ex Baker (Asteraceae)	7-hydroxy-coumarin	100	Indo, EtOH, CRS and Resp (rats)	Bighettia et al. (2005)
Many plants	Apigenin, its 7-*O*-*β*-D-glucuronopyranoside		Indo (rats)	Min et al. (2005)
Scutellaria baicalensis Georgi (Lamiaceae) (root)	Wogonin	30	EtOH (rats)	Park et al. (2004)
Musa balbisiana Colla (Musaceae)	Leucocyanidin, and synthetic analogs hydroxyethylated and tetrallyl derivatives	NR	Asp (rats)	Lewis and Shaw (2001)
Many plants	Rutin (glycoside of quercetin)	200	EtOH (rats)	La Casa et al. (2000)
Many plants	Quercetin	NR	EtOH and Indo (rats)	Di Carlo et al. (1999), Martin et al. (1998), and Lastra et al. (1994)
Many plants	SU-840 (derivative of Sophoradin)	NR	EtOH, Asp, water immersion, CRS	Brzozowski et al. (1998)
Grape-seed	Procyanidin	200	HCl-EtOH	Saito et al. (1998)
Many plants	Kaempferol	50–200 *i.p.*	EtOH, CRS (rats)	Goel et al. (1996)
Many plants	Naringin	NR	CRS, PL, EtOH (rats)	Martin et al. (1994) and Motilva et al. (1993)
Silybum marianum (L.) Gaertn. (Asteraceae)	Silymarin	NR	CRS, PL (rats)	Alarcon de la Lastra et al. (1992)
Many plants	Hydroxychalcones, 2′,4′-dihydroxychalcone	1–10	Indo, water immersion, ac.a (rats)	Yamamoto et al. (1992)

PL; pyloric ligation, EtOH; ethanol, Indo; indomethacin, CRS; cold resistant stress, Ac.a; acetic acid, Beth; bethanechol, Asp; aspirin, Napr; naproxen, Resp; respirine, NR; not reported.

leave extract of the same plant at a dose of 100 mg/kg reduced acid secretion and also potentially elevated the mucoprotective effect (Dharmani et al., 2004).

An oral dose of 500 mg/kg of the ethanol extract of turmeric (*Curcuma longa* Linnaeus, Zingiberaceae) produced significant anti-ulcerogenic activity in rats with gastroduodenal mucosa injuries caused by pyloric ligation, hypothermic-restraint stress, indomethacin, reserpine and cysteamine. It increased the gastric wall mucus significantly and restored the non-protein sulfhydryl (NP-SH) content in the glandular stomachs of the rats (Rafatullah et al., 1990).

5.2.2. Isolated compounds

5.2.2.1. Alkaloids. Table 1.

5.2.2.2. Terpenoids. Table 2.

5.2.2.3. Saponins. Table 3.

5.2.2.4. Phenolic compounds. Table 4.

5.2.2.5. Polysaccharides. Table 5.

5.2.3. Anti H. pylori natural products

Using synthetic antimicrobials such as currently approved antibiotics (amoxicillin and clarimycin) for eradication of *H. pylori* has limitations due to potential development of resistance and low compliance (Debets-Ossenkopp et al., 1999). So new research has been developed in natural products with anti *H. pylori* activity.

Compounds (2-methoxy-1, 4-naphthoquinone (1) and stigmasta-7,22-diene-3β-ol (2)) isolated from *Impatiens balsamina* L. (Balsaminaceae) were evaluated for their anti-*H. pylori* activity. The minimum inhibitory concentrations (MICs) and minimum bactericidal concentrations (MBCs) for (1) were 0.156–0.625 and 0.313–0.625 $\mu g\ ml^{-1}$, respectively, and they were 20–80 $\mu g\ ml^{-1}$ for both of MICs and MBCs for (2) against *H. pylori* resistant to antibiotics (clarithromycin, metronidazole and levofloxacin). The activity of compound (1) was equivalent to that of amoxicillin (Yuan-Chuen et al., 2011).

The ethanol extracts of *Bixa orellana* L. (Bixaceae) Seed, *Chamomilla recutita* L. (Asteraceae) inflorescence, *Ilex paraguariensis* A. (Aquifoliaceae) leaves, *Malva sylvestris* L. (Malvaceae) inflorescence & leaves, *Plantago major* L. (Plantaginaceae) aerial parts and *Rheum rhaponticum* L. (Polygonaceae; Root) were capable of inhibiting the *in vitro* growth of *H. pylori* (Cogo et al., 2010).

Seven carotenoids were isolated from *Malus domestica* Borkh., Rosaceae (Golden delicious apple) peel extract named as (all-*E*)-luteoxanthin, (all-*E*)-neoxanthin, (9′*Z*)-neoxanthin, (all-*E*)-antheraxanthin, (all-*E*)-violaxanthin, (9*Z*)-violaxanthin and (all-*E*)-lutein. Where only three; (all-*E*)-luteoxanthin, (all-*E*)-neoxanthin and (9′*Z*)-neoxanthin exhibited potent anti-*H. pylori* activity with MIC_{50} values of 7.9, 11 and 27 $\mu g/mL$, respectively (Molnár et al., 2010).

The aqueous extract of *Enantia chlorantha* Oliv. (Annonaceae) stem bark possesses both *in vitro* and *in vivo* activities against *H. pylori*. The *in vitro* activity was dose-dependent. The *in vivo H. pylori* eradication potency of the extract was assessed using mice infected with *H. pylori*. Antral mucus sample cultures from mice treated with *E. chlorantha* extract at doses of 500 and 1000 mg/kg for 3 days did not yield any growth (Tan et al., 2010).

When *Nigella sativa* L. (Ranunculaceae) seeds were given to patients with dyspeptic symptoms and found positive for *H. pylori* infection in a dose of 2 g/d along with 40 mg/d omeprazole, it possessed clinically useful anti-*H. pylori* activity. The doses of 1 g/d and 3 g/d of *N. sativa* were less effective, but the *H. pylori* eradication rate achieved with these doses was similar to that obtained with a single antibiotic (Salem et al., 2010). In addition, in an *in vitro* study, *N. sativa* extract produced within 60 min, a 100% inhibition of the growth of all the strains of *H. pylori* that were tested (O'Mahony et al., 2005).

The effects of *Solanum lyratum* Thunb. (SLE), *Solanum erianthum* D. Don and *Solanum torvum* Sw. (Solanaceae) extracts against *H. pylori* were investigated. SLE showed a moderate ability in inhibiting growth of *H. pylori* and also in interrupting the association of bacteria with host cells. Thus, SLE may offer a new approach for the treatment of *H. pylori* by down-regulation of it in the infected gastric epithelium. As it does not directly target bacteria, SLE treatment might not cause development of resistant strains (Hsu et al., 2010a,b). On the other hand, a preventive effect of Japanese apricot (*Prunus mume* Siebold & Zucc., Rosaceae) intake on chronic atrophic gastritis was reported by inhibiting *H. pylori* infection and reducing active mucosal inflammation (Enomoto et al., 2010).

A crude methanol extract prepared from *Brassica oleracea* L., Brassicaceae (fresh broccoli sprout) was extracted with hexane, chloroform, ethyl acetate, and butanol sequentially. Residual water fraction was obtained from the residual aqueous layer. The greatest inhibition zones (>5 cm) were noted for the chloroform extract followed by the hexane, ethyl acetate, butanol and the crude methanol extracts by (5.03 cm, 4.90 cm, 3.10 cm and 2.80 cm, respectively), whereas the residual water fraction did not show any inhibition zone. From the chloroform extract 18 sulforaphane, five sulforaphane-related compounds were positively identified (six amines, six isothiocyanates, and six nitriles), two amines, six isothiocyanates, and one nitrile exhibited >5 cm inhibitory zones for *H. pylori* strain (Moon et al., 2010).

Table 5 Polysaccharides with antiulcerogenic activities.

Source	Isolated compound	Dose mg/kg	Model used	Reference
Fungi of *Ganoderma lucidum* (Curtis) P. Karst (Ganodermataceae)	Polysaccharide fractions	250,500, 1000	Indo, Ac.a (rats)	Gao et al. (2004)
Cladosiphon okamuranus Chordariaceae	Fucoidan	NR	Ac.a (rats)	Shibata et al. (2001)
Beeswax	D-002	100,200	Indo, Ac.a (rats)	Molina et al. (2005)

PL; pyloric ligation, EtOH; ethanol, Indo; indomethacin, Ac.a; acetic acid, NR; not reported.

Essential oil obtained from *Apium nodiflorum* L. (Apiaceae) was assayed *in vitro* against *H. pylori*, resulting in a MIC value of 12.5 μg/ml (Menghini et al., 2010). The fruit of *Feijoa sellowiana* O. Berg (Myrtaceae) aceton extract exerts a potent antibacterial activity against *H. pylori*. Flavone was the active compound of *F. sellowiana* fruits; it showed a high antibacterial activity against *H. pylori* which is significantly more than metronidazole (Basile et al., 2010).

In a randomized pilot study, the effect of pure mastic gum (*Pistacia lentiscus* L., Anacardiaceae) on *H. pylori* eradication in patients suffering from an *H. pylori* infection was studied. Fifty-two patients were randomized to receive either 350 mg three times a day (tid) of pure mastic gum for 14 days (Group A), or 1.05 g tid of pure mastic gum (Group B) for 14 days, or pantoprazole 20 mg twice a day (bd) plus pure mastic gum 350 mg tid for 14 days (Group C) or pantoprazole 20 mg bid plus amoxicillin 1 g bid plus clarithromycin 500 mg bid for 10 days (Group D). *H. pylori* eradication was tested 5 weeks after completion of the eradication regime. Eradication of *H. pylori* was confirmed in 4/13 patients in Group A and in 5/13 in Group B. No patient in Group C achieved eradication whereas 10/13 patients in Group D had a negative result. There were no statistically significant differences between Groups A, B, C although there was a trend in Group A ($p = 0.08$) and in Group B ($p = 0.064$). The difference was significant in Group D ($p = 0.01$). All patients tolerated mastic gum well and no serious adverse events were reported. Mastic gum has bactericidal activity on *H. pylori in vivo* (Dabos et al., 2010).

The purified component, termed (CAH), isolated from the crude alcohol extract of celery (*Apium graveolens* L., Apiaceae) seeds, had potent bactericidal effects against *H. pylori*; the MIC and MBC were 3.15 μg/ml and 6.25–12.5 μg/ml, respectively. CAH formula is $C_{24}H_{32}O_4$ with a dimeric phthalide structure (Zhou et al., 2009).

All part (root, stem, leaf, seed, and pod) extracts of *Impatiens balsamina* L., Balsaminaceae exhibited bactericidal activity against *H. pylori*. The pod extract had significantly lower MIC and MBC (1.25–2.5 and 1.25–5.0 μg/ml, respectively). The acetone and ethyl acetate pod extracts exhibited very strong anti-*H. pylori* activity. This activity exceeded that of metronidazole and approximated to that of amoxicillin (Wang et al., 2009).

Aqueous extract of *Glycyrrhiza glabra* L. (Fabaceae) (1 mg/ml) significantly inhibited the adhesion of *H. pylori* to human stomach tissue. This effect was related to the polysaccharides isolated from the extract, with one purified acidic fraction as a main active polymer. Purified polysaccharides did not exhibit direct cytotoxic effects against *H. pylori* and did not influence hemagglutination (Wittschier et al., 2009). Earlier study concluded that, Licorice extract inhibited the *H. pylori* strains with a MIC range of 50–400 mg/ml *in vitro* (Jafarian and Ghazvini, 2007). In addition, from the methanol extract, three new isoflavonoids (3-arylcoumarin, pterocarpan, and isoflavan) with a pyran ring, gancaonols A–C, were isolated together with 15 known flavonoids. Among these compounds, vestitol, licoricone, 1-methoxyphaseollidin and gancaonol C exhibited anti-*H. pylori* activity against resistant strains (Fukai et al., 2002).

The methanol extract of *Tephrosia purpurea* (Linn.) Pers. (Fabaceae) showed promising activity against clinical isolates and standard strains of *H. pylori*, including metronidazole-resistant strains. The *n*-hexane and chloroform extracts possessed marked activity (Chinniah et al., 2009).

The methanol extracts of *Desmostachia bipinnata* (L.) Stapf (Gramineae) (known as Al-Hagnah) were found to be effective against *H. pylori* with MIC of 40 μg/ml. After fractionation (using diethylether, chloroform, ethyl acetate and butanol sequentially) of the methanol extract, the ethyl acetate fraction exhibited excellent anti *H. pylori* activity from which a flavonoid compound (4′-methoxy quercetin-7-O-glucoside) was isolated and tested against *H. pylori*, the MIC value was 62 μg/ml (Ramadan and Safwat, 2009).

Byrsonima crassa Nied. (Malpighiaceae) contains many compounds with anti-*H. pylori* activity. Both methanol and chloroform extracts inhibit the growth of *H. pylori in vitro* with MIC of 1024 μg/ml (Bonacorsi et al., 2009). The hydroalcohol extracts from grape (*Vitis rotundifolia* Michx. and *Vitis vinifera* L.) Vitaceae (commonly knowen as *Colorino Sangiovese* and *Cabernet Sauvignon*) were tested against *H. pylori*. The *Colorino* extract showed the highest activity with MBC of 1.35 mg/ml, while *Sangiovese* and *Carbernet* MBCs were 4.0 mg/ml. The isolated compound Resveratrol exhibited the highest antibacterial activity (Martini et al., 2009).

Curcumin, diferuloylmethane from turmeric (*Curcuma longa* Linnaeus, Zingiberaceae), has recently been shown to arrest *H. pylori* growth. The antibacterial activity of curcumin *in vitro* was evaluated, the MIC ranged from 5 to 50 μg/ml. In addition, curcumin exhibited *in vivo* anti *H. pylori* effect. Curcumin showed immense therapeutic potential against *H. pylori* infection as it was highly effective in eradication of *H. pylori* from infected mice as well as in restoration of *H. pylori*-induced gastric damage (Chowdhury et al., 2009).

Lycopodium cernuum (Linn) Pic. Serm. (Lycopodiaceae) was reported to have potent anti- *H. pylori* activity. The methanol extract and fractions (hexane, chloroform and ethyl acetate) contain compounds with anti-*H. pylori* activity, The MIC and MBC values ranged from 0.016–1.000 and 0.125–1.000 mg/mL, respectively (Ndip et al., 2008; Ndip et al., 2007).

The essential oil obtained from the dried aerial parts of *Thymus caramanicus* Jalas (Lamiaceae) was tested *in vitro* against *H. pylori*. MIC values range were 14.5–58.0 μg/mL for the clinical isolates (Fereshteh et al., 2009). Other workers studied the crude essential oil of *Dittrichia viscosa* L. (Asteraceae) and its oxygenated fractions for their anti-*H. pylori* activity. They found that, the crude essential oil at a concentration of 0.33 μl/ml was effective against several *H. pylori* strains. In addition, the susceptibility of several *H. pylori* strains to the oxygenated fraction of *Dittrichia viscosa* essential oil suggests the possible use of these natural products in combating this widespread infection (Miguel et al., 2008).

The anti-*H.pylori* activities of the methanol extracts of some plants; *Ageratum conyzoides* L. (Asteraceae), *Scleria striatinux* De Wild. (Cyperaceae), *Lycopodium cernua* (Linn) Pic. Serm. (Lycopodiaceae), *Acanthus montanus* (Nees) T. Anderson (Acanthaceae), *Eryngium foetidium* L. (Apiaceae), *Tapeinachilus ananassae* (Hassk.) K.Schum (Costaceae), *Euphorbia hirta* L. (Euphorbiaceae), *Emilia coccinea* (Sims) G. Don (Asteraceae) and *Scleria verrucosa* Willd. (Cyperaceae) were carried out. All the tested plants demonstrated antimicrobial activity. *A. conyzoides*, *S. striatinux* and *L. cernua* showed very potent antibacterial activity on the isolates. The MIC of the extracts ranged from 0.032–1.0 mg/mL for *S. striatinux*; 0.063–0.5 mg/mL for L. *cernua* and 0.063–1.0 mg/mL for *A. conyzoides*. The MBC of the extracts ranged from

0.098–15.0 mg/mL for *S. striatinux*; 0.098–12.5 mg/mL for *A. conyzoides*, and 0.195–12.5 mg/mL for *L. cernua*. The extracts had a wide spectrum of activity. The three most potent extracts possessed significant ($P < 0.05$) inhibitory activities (Ndip et al., 2007).

The dried inner bark of *Tabebuia impetiginosa* Martius ex DC. (Bignoniaceae) was examined against *H. pylori*. Three compounds were isolated and identified as; 2-(hydroxymethyl) anthraquinone, anthraquinone-2-carboxylic acid, and 2-hydroxy-3-(3-methyl-2-butenyl)-1,4-naphthoquinone (lapachol). One of them, 2-(hydroxymethyl) anthraquinone, exhibited strong activity against *H. pylori*, where as the other two compounds were less effective and exhibiting moderate anti-*H. pylori* activity (Park et al., 2006).

Three lignan compounds (3'-demethyl arctigenin (1), arctigenin (2) and arctigenin glucoside (3) were isolated from dried seeds of *Arctium lappa* L. (Asteraceae). Crude extracts and isolated compounds showed a strong antibacterial activity against a clarithromycin-resistant *H. pylori* strain. Specifically, at a concentration of 50 mg/mL, compounds 1 and 2 each exerted a 100% inhibition against *H. pylori* compared to a standard amoxicillin (5 mg/mL) and clarithromycin (1 mg/mL), while compound 3 and crude extract showed a 95% and 86% inhibition respectively (Kamkaen et al., 2006). Furthermore, six new and five known sesquiterpenes were isolated from *Santalum album* L. (Santalaceae). The crude extracts as well as the isolated compounds showed antibacterial activity against *H. pylori*. Especially, compounds (*Z*)-α-santalol and (*Z*)-β-santalol have strong anti-*H. pylori* activities against a clarithromycin-resistant strain as well as other strains (Ochi et al., 2005).

A total of 32 endophytic fungi isolated from the medicinal herb *Cynodon dactylon* (L.) Pers. (Poaceae) was grown in *in vitro* culture, and the ethyl acetate extracts of the cultures were examined *in vitro* for the anti-*H. pylori* activity. As a result, a total of 16 endophyte culture extracts were potent as anti-*H. pylori* activities (Li et al., 2005). In addition, the effect of cranberry, blueberry and grape seed extracts on inhibiting *H. pylori* has been investigated. The anti-*H. pylori* activity of cranberry juice extract was significantly improved by its synergistic blending with blueberry, grape seed and oregano extract (Vattem et al., 2005).

Good anti-*H. pylori* activity was observed with the alcohol extracts of *Alpina officinarum* (HANCE.) (Zingiberaceae; rhizome), *Alpina oxyphylla* Miq. (Zingiberaceae; fruit), *Angelica tenuissina* Nakai (Apiaceae; root), *Asiasarum heterotropoides* (F. Schmidt) F. Maek (Aristolochiaceae; root), *Lindera strychnifolia* (Siebold & Zucc.) Fern.-Vill. (Lauraceae; root), and *Polygonum cuspidatum* Willd. ex Spreng. (Polygonaceae; rhizome) (Lee et al., 2003). The extracts of *Anthemis melanolepis* Boiss. (Asteraceae), *Cerastium candidissimum* (caryophyllaceae), *Chamomilla recutita* (Asteraceae), *Conyza albida* (Asteraceae), *Dittrichia viscose* (L.) W.Greuter (Asteraceae), *Origanum vulgare* L. (Lamiaceae) and *Stachys alopecuros* (L.) Benth. (Lamiaceae) have been proved active against one standard strain and 15 clinical isolates of *H. pylori* (Stamatis et al., 2003).

Methanol extracts of both *Sanguinaria canadensis* L. (Papaveraceae; rhizomes) and *Hydrastis canadensis* L. (Ranunculaceae; roots and rhizomes) were found to be effective in inhibiting the growth of *H. pylori in vitro*, with a MIC_{50} range of 12.5–50.0 μg/ml. Furthermore, three isoquinoline alkaloids and two benzophenanthridine alkaloids (identified in the active fraction) inhibited the growth of the bacterium with an MIC_{50} of 50.0 and 100.0 μg/ml, respectively. Protopine (a protopine alkaloid) also inhibited the growth of the bacterium, with a MIC_{50} of 100 μg/ml. The crude methanol extract of *H. canadensis* rhizomes was very active, with an MIC_{50} of 12.5 μg/ml. Two isoquinoline alkaloids, berberine and *β*-hydrastine, were identified as the active constituents, and having an MIC_{50} of 12.5 and 100.0 μg/ml, respectively (Mahady et al., 2003).

From *Anthemis altissima* L. (Asteraceae) seven sesquiterpene lactones (sivasinolide (**1**), a new naturally occurring eudesmanolide (altissin, **2**), desacetyl-β-cyclopyrethrosin (**3**), tatridin-A (**4**), 1-*epi*-tatridin B (**5**), 1α,10β-epoxy-6-hydroxy-1,10*H*-inunolide (**6**) and spiciformin (**7**), in addition to 10 known flavonoids (apigenin (**8**), kaempferol 4'-methyl ether (**9**), quercetin (**10**), quercetin 3-methyl ether (**11**), isorhamnetin (**12**), rhamnetin (**13**), 6-hydroxyquercetin 3,6,4'-trimethyl ether (**14**), isoquercetrin (**15**), taxifolin (**16**), and eriodictyol (**17**), and one phenolic acid, chlorogenic acid (**18**) were isolated and tested against *H. pylori*, *in vitro*. Compounds (**1**), (**4**) and (**18**) were active against *H. pylori*. While (**8**) and (**12**) were totally inactive (Konstantinopoulou et al., 2003).

A new rotenoid (derrisin (**1**)), together with 10 known rotenoids (**2**–**11**) were isolated from the roots of *Derris malaccensis* Prain (Fabaceae). Nine of the isolated rotenoids (**3**–**11**) showed antibacterial activity against *H. pylori* (Takashima et al., 2002).

The effect of tryptanthrin and kaempferol, both isolated from *Polygonum tinctorium* Lour., (Cruciferae) against *H. pylori* was evaluated *in vivo* and *in vitro*. Both of the isolated compounds significantly decreased the numbers of *H. pylori* colonies a dose-dependent manner *in vitro*. An additive effect on colony formation was observed with the combined use. In the *in vivo* experiment, oral administration of tryptanthrin and/or kaempferol significantly decreased the numbers of colonies in the gerbils' stomachs (Kataoka et al., 2001).

The anti-*H. pylori* effect of extracts and fractions obtained from *Aristolochia paucinervis* Pomel, Aristolochiaceae (rhizome and leaves) were studied against a reference strain of *H. pylori*. Only the methanol extracts and the hexane fractions of either the rhizome or the leaves exhibited an inhibitory activity at a concentration of $\leqslant$128 μg/ml. The leaf hexane fraction demonstrated a higher inhibitory activity (MIC: 4 μg/ml) than the rhizome hexane fraction (MIC: 16 μg/ml), the leaf methanol extract (MIC: 32 μg/ml) and the rhizome methanol extract (MIC: 128 μg/ml) (Gadhi et al., 2001).

Honey from New Zealand and Saudi Arabia at concentrations approximating 20% (v/v) inhibit the growth of *H. pylori in vitro*. Regional differences in honey activity against *H. pylori* were not detected, nor was the effect of killing related to the presence of hydrogen peroxide in the honey samples. Osmotic effects were shown to be the most important parameter for killing *H. pylori* as all carbohydrate solutions 15% (v/v) inhibited 100% of the *H. pylori* (Osato et al., 1999).

6. Discussion

Peptic ulcer and ulcerative colitis can be considered as the most wide distributed diseases. The symptoms which are people (worldwide) suffering from are mainly; abdominal pain with diarrhea in case of ulcerative colitis and with vomiting and nausea in case of peptic ulcer (Malagelada et al., 2007; Kornbluth and Sachar, 2004).

Folk medicine in different areas all over the world includes many plants with antiulcerogenic activities (Table 6) however

Table 6 An overview of plants with antiulcerogenic effect.

Name	Family	Common name	Traditional antiulcerogenic use	Part used	References
Acer tegmentosum Maxim.	Sapindaceae	Manchu striped maple	N	Leaves and heartwood	Yoo et al. (2009)
Adhatoda vasica Nees	Acantheceae	Vasaka	N	Leaves	Shrivastava et al. (2006)
Aegle marmelos (L.) Corrêa	Rutaceae	Bael fruit, stone apple, bengal quince	Y	Leaves, fruit, seeds	Goel et al. (1997)
Aesculus hippocastanum L.	Sapindaceae	Hippocastanum, bongay, horse-chestnut, conker tree	Y	Seeds	Marhuenda et al. (1993, 1994)
Ageratum conyzoides L.	Asteraceae	Catinga de Bode	Y	Leaves	Mahmood et al. (2005)
Alchornea castaneaefolia (Bonpl. ex Willd.) A.Juss.	Euphorbiaceae	sar-a, sar-ao or gurupía	Y	Leaves and bark	Hiruma-Lima et al. (2006)
Alhagi maurorum Boiss.	Leguminosae	Camelthorn	Y	Aerial parts	Awaad et al. (2006)
Allophylus serratus (Hiern) Kurz	Sapindaceae	Tippani	Y	Leaves	Dharmani and Palit (2006)
Aloe vera (L.) Burm.f.	Xanthorrhoeaceae	Aloe	Y	Leaves gel	Langmead et al. (2004) and Subramanian et al. (2007)
Amphipterygium adstringens (Schltdl.) Standl.	Anacardiaceae	Cuachalalate	Y	Bark	Arrieta et al. (2003)
Anacardium humile St. Hil.	Anacardiaceae	Cajuzinho do cerrado	Y	Leaves	Ferreira et al. (2010)
Angelica sinensis (Oliv.) Diels	Apiaceae	Hasheshat almalak	Y	Ariel parts	Wong et al. (2008)
Anthemis altissima L.	Asteraceae	Tall Chamomile	Y	Aerial parts	Konstantinopoulou et al. (2003)
Aparisthmium cordatum Baill.	Euphorbiaceae	Ariquena queimosa	N	Aerial parts	Hiruma-Lima et al. (2000, 2001)
Apium graveolens L.	Apiaceae	Celery	N	Seeds	Zhou et al. (2009)
Apium nodiflorum L.	Apiaceae	European marshwort	N	Essential oil	Menghini et al. (2010)
Aralia elata (Miq.) Seem.	Araliaceae	Angelica tree	N	Root bark	Lee et al. (2005)
Araucaria araucana (Molina) C. Koch.	Araucariaceae	Monkey-puzzle	Y	Resin	Schmeda-Hirschmann et al. (2005)
Arctium lappa L.	Asteraceae	Bardana, beggar's buttons, burr seed	N	Seeds, root	Kamkaen et al. (2006)
Aristolochia paucinervis Pomel	Aristolochiaceae	Virginia snakeroot, texas snakeroot	N	Rhizome and leaves	Gadhi et al. (2001)
Artemisia douglusiana Schouw.	Asteraceae	Mugwort or common wormwood	N	Aerial parts	Maria et al. (1998a)
Baccharis dracunculifolia DC.	Asteraceae	Alecrim do campo	Y	Essential oil	Klopell et al. (2007)
Bidens bipinnata L.	Asteraceae	Al-shabtah	Y	Ariel parts	Atta et al. (2005)
Brassica oleracea L.	Brassicaceae	Fresh broccoli sprout	Y		Moon et al. (2010)
Butea frondosa (Roxb.)	Fabaceae	Flame of the forest	Y	Leaves	Londonkar and Ranirukmini (2010)
Byrsonima crassa Niedenzu (IK)	Malpighiaceae	Murici-cascudo or murici-vermelho	Y	Leaves	Sannomiya et al. (2005) and Bonacorsi et al. (2009)
Camellia sinensis (L.) Kuntze	Theaceae	Green tea	Y	Leaves	Mazzon et al. (2005)
Capsicum annuum L.	Solanaceae	Chilli	Y	Fruits	Kang et al. (1995)
Carica papaya L.	Caricaceae	Papaya	Y	Fruit	Ologundudu et al. (2008)
Caryocar coriaceum Wittm.	Caryocaracea	Piqui, pequi	Y	Oil from fruit pulp	Oliveira et al. (2009)
Ceiba pentandra G.	Bombacaceae	Kapok	Y	Bark	Ibara et al. (2007)
Centaurea helenioides Boiss.	Asteraceae	Knapweeds	Y	Flowers	Yayli et al. (2006)
Cissus quadrangularis L.	Vitaceae	Sugpon-sugpon (Bis.)	Y	Stem	Shanthi et al. (2010)
Cladosiphon okamuranus	Chordariaceae	Seaweeds	N	Aerial parts	Shibata et al. (2001)
Coccinia grandis Linn.	Cucurbitaceae	Ivy gourd	Y	Leaves	Mazumder et al. (2008)
Cocus nucifera L.,	Arecaceae	Coconut	Y	Seed	Anosike and Obidoa (2010)
Combretum leprosum Mart. & Eiche	Combretaceae	Mofumbo	N	Stem bark	Nunes et al. (2009)
Conyza dioscoridis (Linn) Desf.	Asteraceae	Phonrab	Y	Ariel parts	Atta et al. (2005)
Conyza linifolia (Willd.) Täckh.	Asteraceae	Ayin al katkoot	Y	Ariel parts	Atta et al. (2005)
Croton cajucara Benth.	Euphorbiaceae	Sacaca	Y	Aerial parts	Brito et al. (1998)
Croton lechleri Müll. Arg.	Euphorbiaceae	Dragon's blood, sangre de grado	Y	Aerial parts	Miller et al. (2000)
Croton sublyratus Kurz.	Euphorbiaceae	Codiaeum, variegatum	Y	Leaves	Ohta et al. (2005b) and Murakami et al. (1999)
Croton zehntneri Pax & K. Hoffm.	Euphorbiaceae	Cunha	Y	Essential oils from leaves	Oliveira et al. (2009)
Curcuma longa Linnaeus	Zingiberaceae	Turmeric	Y	Rhizome	Rafatullah et al. (1990)
Cynanchum acutum Linn.	Asclepiadoideae	Moddeid	N	Ariel parts	Atta et al. (2005)
Cynodon dactylon (L.) Pers.	Poaceae	Dog's tooth grass, bahama grass, Indian doab	N	Aerial parts	Li et al. (2005)
Derris malaccensis Prain	Fabaceae	New guinea creeper	N	Roots	Takashima et al. (2002)
Desmostachia bipinnata (L.) Stapf	Gramineae	Al-Hagnah, kussa grass	N	Aerial parts	Awaad et al. (2008)
Dittrichia viscosa L.	Asteraceae	False yellowhead, strong-smelling inula	Y	Crude essential oil	Miguel et al. (2008)
Enantia chlorantha Oliv.	Annonaceae	Banuke	Y	Bark	Tan et al. (2010, 2000)

Table 6 (*Continued*)

Name	Family	Common name	Traditional antiulcerogenic use	Part used	References
Encholirium spectabile Mart.	Bromeliaceae	Macambira de fleche	N	Aerial parts	Carvalho et al. (2010)
Erythrina indica L.	Febaceae	Tiger's claw	Y	Leaves	Sachin and Archana (2009)
Excoecaria agallocha L.	Euphorbiaceae	Milky mangrove	Y	Bark	Thirunavukkarasu et al. (2009)
Fabiana imbricate Ruiz & Pav.	Solanaceae	Pichi	N	Aerial parts	Reyes et al. (2005)
Feijoa sellowiana O. Berg	Myrtaceae	Pineapple guava	N	Fruit	Basile et al. (2010)
Ganoderma lucidum (Curtis) P. Karst (Fungi)	Ganodermataceae	Reishi, or Mannentake, or Ling zhi	N	Aerial parts	Gao et al. (2004)
Garcinia cambogia Desr.	Clusiaceae	Brindleberry	Y	Ariel parts	dos Reis et al. (2009)
Garcinia indica Choisy	Clusiaceae	Kokum	N	Fruit	Yamaguchi et al. (2000)
Garcinia kola Heckel	Clusiaceae	Bitter kola	N	Aerial parts	Olaleye and Farombi (2006)
Ginkgo biloba L.	Ginkgoaceae	Ginkgo	Y	Root	Kotakadi et al. (2008) and Zhou et al. (2006)
Glycyrrhiza glabra L.,	Fabaceae	Liquorice	Y	Roots	Ligha and Fawehinmi (2009)
Glycyrrhiza glabra L., *G. radix* Br., *G. uralensis* Fisch.	Fabaceae	Liquorice	Y	Leaves, roots, seeds	Ligha and Fawehinmi (2009), Aly et al. (2005) and Baker (1994)
Gymnosporia rothiana (Walp.) Wight & Arn. ex M.A.Lawson	Celastraceae	Roth's spike thorn	Y	Leaves	Jain and Surana (2009b)
Gynura procumbens (Merr.)	Asteraceae	Sambung nyawa	Y	Leaves	Mahmood et al. (2010)
Helicrysum mechowianum Klatt	Asteraceae	African beech	Y	Leaves	Ibara et al. (2007)
Himatanthus drasticus Mart. Plumel	Apocynaceae	Sucuba	Y	Latex	Oliveira et al. (2009)
Hydrastis canadensis L.	Ranunculaceae	Goldenseal, orangeroot	Y	Roots and rhizomes	Mahady et al. (2003)
Impatiens balsamina L.	Balsaminaceae		N	All part (root, stem, leaf, seed, and pod)	Yuan-Chuen et al. (2011) and Wang et al. (2009)
Indigofera truxillensis Kunth	Fabaceae	Anileira	Y	Ariel parts	Cola-Miranda et al. (2006)
Lasianthera Africana P. Beauv.	Icacinaceae	Chesters fide JMD	Y	Leaves	Okokon et al. (2009)
Ligularia stenocephala (Maxim.) Matsum. & Koidz., *L. fischeri* (Ledeb.) Turcz., and *L. fischeri* var. *spiciformis*	Asteraceae	Ligularia	Y	Leaves	Lee et al. (2010)
Linum usitatissimum Linnaeus.	Linaceae	Flaxseed or linseed	N	Seeds oil, mucilage	Dugani et al. (2008)
Lycopodium cernuum (Linn) Pic. Serm.	Lycopodiaceae	Club moss	Y	Aerial parts	Ndip et al. (2008) and Ndip et al. (2007)
Malus domestica Borkh.	Rosaceae	Golden delicious apple	N	Peel	Molnár et al. (2010)
Mangifera indica L.	Anacardiaceae	Mango	Y	Leaves	Severi et al. (2009) and Carvalho et al. (2007)
Matricaria chamomilla L.	Asteraceae	Chamomile	Y	Flowers	Karbalay-Doust and Noorafshan (2009)
Maytenus robusta Reissek.	Celastraceae	Spike-thorn	Y	Leaves	Andrade et al. (2008)
Mentha arvensis L.	Lamiaceae	Peppermint	Y	Leaves	Londonkar and Poddar (2009)
Mentha microphylla C. Koch	Labiatae	Alneanaa	N	Ariel parts	Atta et al. (2005)
Mikania laevigata Sch. Bip. Ex. Baker	Asteraceae	Guaco	N	Leaves	Bighettia et al. (2005)
Morus alba L.	Moraaceae	Mulberry	N	Leaves	Abdulla et al. (2009)
Musa balbisiana Colla	Musaceae	Bananna	Y	Fruit	Lewis and Shaw (2001)
Myristica malabarica Lam.	Myristicaceae	Nutmeg	N	Seeds	Banerjee et al. (2008b,c)
Nigella sativa L.	Ranunculaceae	Blackseed	Y	Volatile oil of seeds	Kanter et al. (2006), Arslan et al. (2005), and El-Abhar et al. (2003)
Ocimum sanctum Linn.	Labiatae	Tulsi in Hindi	Y	Fixed oil, leave	Dharmani et al. (2004) and Singh and Majumdar (1999)
Orostachys japonicus A. Berger	Crassulaceae	Tulipa	Y	Ariel parts	Jung et al. (2007)
Panax ginseng C.A. Mey.	Araliaceae	Ginseng	Y	Leaves and roots	Jeong et al. (2003) and Sun et al. (1992)
Papaver somniferum L.	Papaveraceae	Opium poppy	N	Fruits	Tazi-Saad et al. (1991)
Parkia platycephala Benth.	Leguminosae	Visgueira	N	Leaves	Fernandes et al. (2010)
Pausinystalia macroceras (K. Schum.) Pierre ex Beille	Rubiaceae	Abo idágbn, yohimbe bark	N	Stem-bark	Nwafor et al. (2005)
Piper betle L.	Piperaceae	Betel Pepper	Y	Leaves	Banerjee et al. (2008a) and Bhattacharya et al. (2007a)
Pistacia lentiscus L.,	Anacardiaceae	Pure mastic gum	Y		Dabos et al. (2010)
Plantago major L.	Plantaginaceae	Lesan alhamal	Y	Leaves, seeds	Atta et al. (2005)
Plantago ovata Forssk.	Plantaginaceae	Spage seed Isabgol	Y	Seeds	Fernández et al. (1999)

Table 6 (*Continued*)

Name	Family	Common name	Traditional antiulcerogenic use	Part used	References
Polyalthia longifolia (Sonn.) Thwaites (PL)	Annonaceae	False Ashoka, the Buddha tree, Indian mast tree, and Indian Fir tree	N	Leaves	Malairajan et al. (2008)
Polygala cyparissias A. St.-Hil. & Moq.	Polygalaceae	Yuan Zhi	N	Aerial parts	Klein et al. (2010)
Polygonum tinctorium Lour.	Cruciferae	Polygonum	N	Aerial parts	Kataoka et al. (2001)
Prumnopitys andina (Poepp. & Endl.) de Laub.	Podocarpaceae	Lleuque, Mapudungun	N	Wood and bark	Rodríguez et al. (2006)
Prunus mume Siebold & Zucc.,	Rosaceae	Japanese apricot	Y	Fruit	Enomoto et al. (2010)
Quassia amara L.	Simaroubaceae	Bitter ash, suriname wood, quassia	Y	Bark	Garcia-Barrantes and Badilla (2011)
Rhamnus triquerta Wall.	Rhamnaceae	Gaunt	N	Bark	Goel and Das Gupta (1991)
Rheum tanguticum Maxim. ex Balf.	Polygonaceae	Rhubarb	Y	Aerial parts	Liu et al. (2005)
Rhizophora mangle L.	Rhizophoraceae	Red mangrove	N	Bark	Sánchez et al. (2001, 2010)
Sanguinaria canadensis L.	Papaveraceae	Bloodroot	Y	Rhizomes	Mahady et al. (2003)
Santalum album L.	Santalaceae	Sandalwood	N	Aerial parts	Ochi et al. (2005)
Sargassum micracanthum (Kützing) Endlicher	Sargassaceae	Brown alga	Y	Marine resources	Mori et al. (2006)
Saussurea lappa C.B. Clarke	Asteraceae	Costus, kuth, kushta	Y	Root	Sutar et al. (2011)
Schouwia thebaica Webb	Brassicaceae	Al-khosama	Y	Ariel parts	Atta et al. (2005)
Scutellaria baicalensis Georgi	Lamiaceae	Baikal skullcap or huang quin	N	Root	Park et al. (2004)
Silybum marianum (L.) Gaertn.	Asteraceae	Milk thistle	N	Aerial parts	Alarcon de la Lastra et al. (1992)
Simaba ferruginea A. St.-Hil.	Simaroubaceae	Simba	Y	Rhizome	Almeida et al. (2011)
Solanum lyratum Thunb. (SLE), *S. erianthum* D. Don and *S. torvum* Sw.	Solanaceae	Hiyodori-jogo	N	Aerial parts	Hsu et al. (2010a,b)
Solanum nigrum L.	Solanaceae	Enab Althalab	Y	Fruits	Jainu and Shyamala (2006)
Strychnos potatorum Linn	Loganiaceae	Katakam	Y	Seeds	Sanmugapriya and Venkataraman (2007)
Stryphnodendron rotundifolium Mart.	Fabaceae	Canga	Y	Leaves	Oliveira et al. (2009)
Syngonanthus bisulcatus (Koern) Ruhland	Eriocaulaceae	Sempre-vivas	N	Aerial parts	Coelho et al. (2006)
Syzygium aromaticum L.	Myrtaceae	Clove	N	Dried flower buds	Magaji et al. (2007)
Tabebuia impetiginosa Martius ex DC.	Bignoniaceae	Pink Lapacho	N	Dried inner bark	Park et al. (2006)
Tasmannia lanceolata (Poir.) A.C. Sm.	Winteraceae	Mountain pepper (Aus), or cornish pepper leaf	Y	Leaves	Matsuda et al. (2002)
Tephrosia purpurea (Linn.) Pers.	Fabaceae	Fish poison, wild indigo	N	Aerial parts	Chinniah et al. (2009)
Terminalia belerica Roxb.	Combretaceae	Bibhitika	N	Fruits	Bhattacharya et al. (2007b)
Terminalia chebula Retz.	Combretaceae	King of medicine	Y	Fruit	Raju et al. (2009)
Thymus caramanicus Jalas	Lamiaceae			Essential oil from the aerial parts	Fereshteh et al. (2009)
Tripleurospermum disciforme Shultz Bip	Asteraceae	Marigold	Y	Flowers	Minaiyan et al. (2006)
Triticum aestivum L.,	Poaceae	Wheat grass	Y	Leaves juice	Ben-Arye et al. (2002)
Trixis divaricata Spreng.	Asteraceae	Carvalhinha, celidônea, erva-andorinha, erva-de-mulher, erva-lanceta	N	Ariel parts	Pereira et al. (2005)
Vanillosmopsis arborea (Gardner) Baker	Asteraceae	candeia," or can- dle,	Y	Essential oil from bark	Oliveira et al. (2009)
Vinca minor L.	Apocynaceae	Periwinkle; dwarf periwinkle	N	Leaves	Nosalova et al. (1993)
Virola surinamensis (Rol. ex Rottb.) Kuntze	Myristicaceae	Mucuíba	Y	Bark	Hiruma-Lima et al., 2009
Vitis rotundifolia Michx., *Vitis vinifera*	Vitaceae	Grape		Seeds	Saito et al. (1998)
Voacanga Africana Stapf.	Apocynaceae	Voacanga	Y	Aerial parts	Tan and Nyasse (2000)
Xanthium cavanillesii Schouw.	Asteraceae			Aerial parts	Maria et al. (1998a)
Zataria multiflora Boiss.	Lamiaceae	Savory	Y	Aerial parts	Minaiyan et al. (2005)
Zingiber officinale Roscoe	Zingiberaceae	Ginger	Y	Rhizomes	El-Abhar et al. (2008), Arun et al. (2010), and Yamahara et al. (1998)
Zizyphus lotus (L.) Lam.	Rhamnaceae	Jujube (sidr in Arabic, nbeg in Tunisia and annab in Lebanon)	Y	Root barks, leaves, fruits	Wahida et al. (2007)
Zizyphus oenoplia (L.) Mill.	Rhamnaceae	Wild Jujube	Y	Root	Jadhav and Prasanna (2011)
Zygophyllum album L.	Zygophyllaceae	Al-routrat	Y	Ariel parts	Atta et al. (2005)

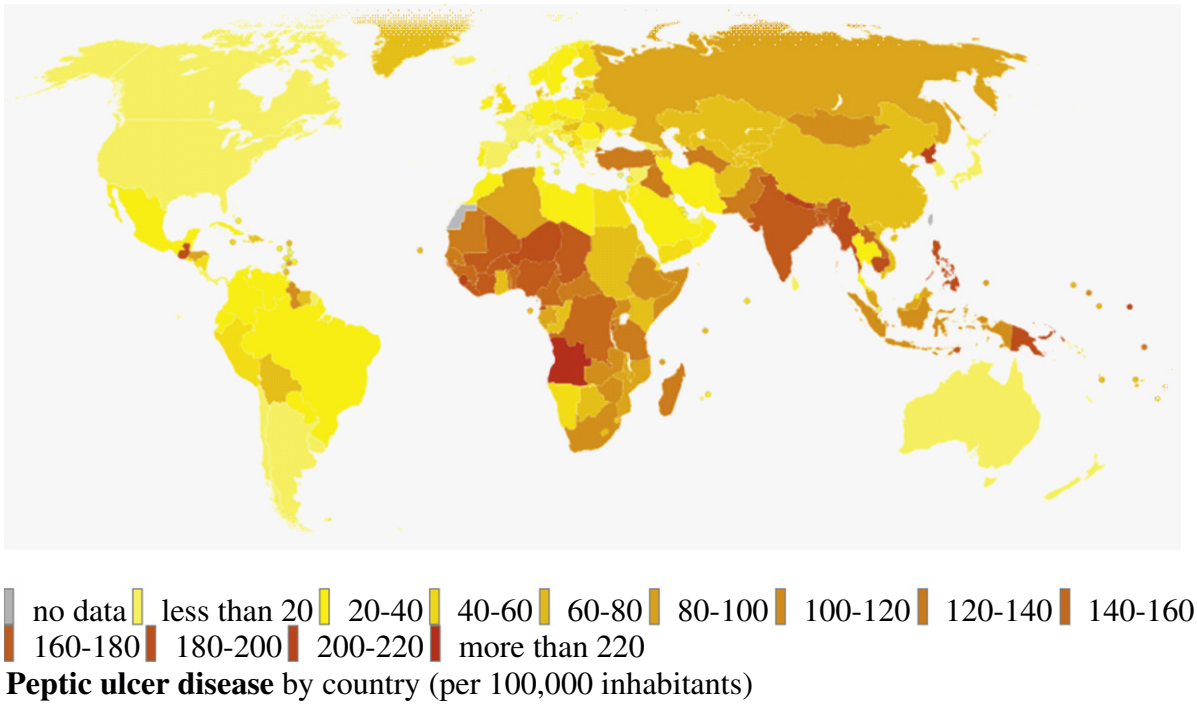

Figure 1 World map of peptic ulcer.

there is no scientific proof for such uses. For the last 24 years many researchers from different countries focused on the scientific proof of these activities. Peptic ulcer as shown in Fig. 1 is more common in Africa and south Asia (Wikipedia, 2011) and this is may be due the excessive use of spices and the stress type of life of the native of this continents. Most of the natural products in these parts are plants belonging to families for African and South Asia, respectively.

Some researcher used the total extract in treatment of both types of ulcers, others studied the effect of the isolated compounds, during their work many phytochemical groups were proofed to have significant activities such as; alkaloids, phenolic compounds, polysaccharides, saponins and terpeins. The most active compounds were phenolic compounds (Lewis et al., 1999; Haslam, 1996).

Natural products exhibit their antiulcerogenic activities through different mechanisms; either prophylactic or therapeutic or both. The prophylactic products possess their effect by their antioxidant potentials or their anti-inflammatory activity while the therapeutic agents either have antisecretory or healing effects. In addition to these the anti-*H.pylori* activity of some plant extracts may explains their antiulcerogenic activity.

The prophylactic (gastroprotective or cytoprotective) mechanism is based on the ability to strengthen defensive factors like prostaglandin synthesis, in addition to other gastroprotective actions, like a stimulant effect on somatostatin synthesis and an inhibitory effect on gastrin secretion (Ferreira et al., 2010; Thirunavukkarasu et al., 2009; Muralidhar et al., 2009). The participation of the antioxidant mechanisms on the gastroprotective effects prevents the oxidative damage of gastric mucosa by blocking lipid peroxidation and by significant decrease in superoxide dismutase, and increase in catalase activity (Carvalho et al., 2010; Almeida et al., 2011). In addition, possible participation of the NO-synthase pathway in the gastroprotection is also suggested (Arun et al., 2010). Furthermore, the anti-inflammatory potentials of an extract may help its gastroprotective activity (Mahmood et al., 2010; Abdulla et al., 2009).

Prophylactic agents with cytoprotective mechanism like extracts of *Saussurea lappa* C.B. Clarke (Sutar et al., 2011), *Zizyphus oenoplia* (L.) Mill. (Jadhav and Prasanna, 2011), *Zingiber Officinale* Roscoe (Arun et al., 2010), *Butea frondosa* (Roxb.) (Londonkar and Ranirukmini, 2010), *Anacardium humile* St. Hil. (Ferreira et al., 2010), *Lasianthera Africana* P. Beauv. (Okokon et al., 2009), *Gymnosporia rothiana* (Walp.) Wight & Arn. ex M.A.Lawson (Jain and Surana, 2009a), *Coccinia grandis* Linn. (Mazumder et al., 2008) and *Zataria multiflora* Boiss. (Minaiyan et al., 2005). Furthermore, prophylactic agents with anti-inflammatory mechanism like extracts of *Gynura procumbens* (Merr.) (Mahmood et al., 2010) and *Morus alba* L. (Abdulla et al., 2009). In addition, there are some extracts possess antioxidant mechanism in the gastroprotection like extracts of *Encholirium spectabile* Mart. (Carvalho et al., 2010), *Parkia platycephala* Benth. (Fernandes et al., 2010), *Glycyrrhiza glabra* L. (Ligha and Fawehinmi, 2009) and *Carica papaya* L. (Ologundudu et al., 2008).

The therapeutic agents may have antisecreatory activity (antagonism of histaminergic and cholinergic effects on gastric secretion or proton pump inhibition mechanism) like extracts of, *Terminalia chebula* Retz. (Raju et al., 2009), *Mikania laevigata* Schultz Bip. (Bighettia et al., 2005) and *Pausinystalia macroceras* (K. Schum.) Pierre ex Beille (Nwafor et al., 2005). While other extracts work by making healing of the ulcer by local mucosal enhancement like *Quassia amara* L. (Garcia-Barrantes and Badilla, 2011), *Matricaria chamomilla* L. (Karbalay-Doust and Noorafshan, 2009) and D-002

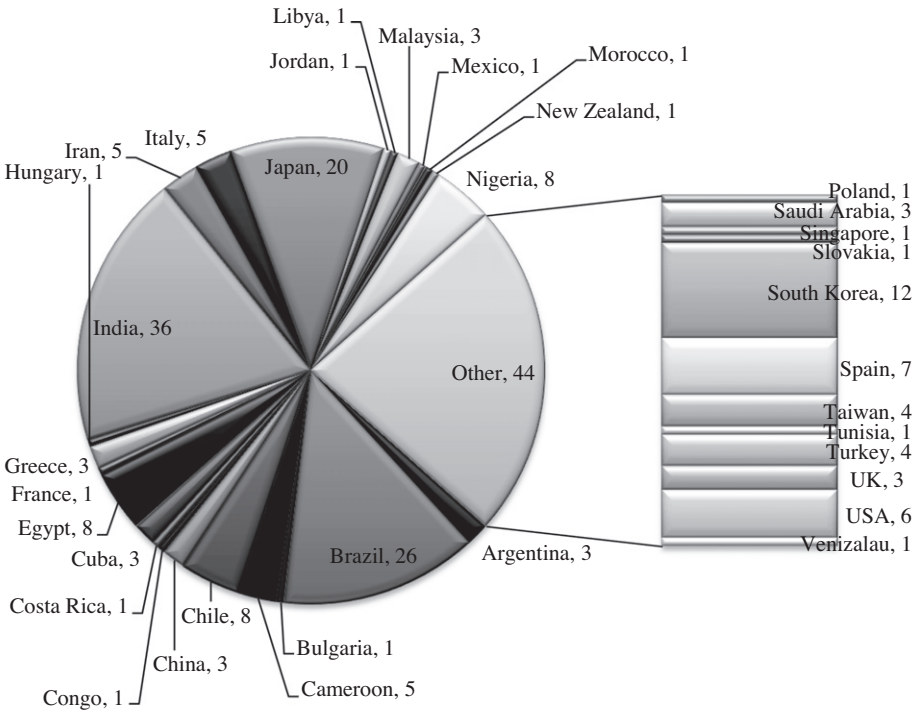

Figure 2 Distribustion of researches in this review.

(mixture of higher aliphatic primary alcohols isolated from beeswax) (Molina et al., 2005).

One of the wound healing mechanisms involves making a thick coating of the extract (like *Rhizophora mangle* L.) which is macroscopically adherent to the gastric mucosa, forming a physical barrier with similar properties as observed in topical wounds (Sánchez et al., 2010).

Some extracts possess both antisecreatory and healing properties like extracts of *Combretum leprosum* Mart. & Eiche (Nunes et al., 2009) and *Excoecaria agallocha* L. (Thirunavukkarasu et al., 2009).

In addition, in this review we found that some plant extracts exihibit their antiulcerogenic activity through both prophylactic and therapeutic mechanisms like *Mentha arvensis* L. (Londonkar and Poddar, 2009), *Polyalthia longifolia* (Sonn.) Thwaites (PL) (Malairajan et al., 2008), *Strychnos potatorum* Linn (Loganiaceae) (Sanmugapriya and Venkataraman, 2007), *Alhagi maurorum* Boiss. (Awaad et al., 2006), *Indigofera truxillensis* Kunth (Cola-Miranda et al., 2006), *Syngonanthus bisulcatus* (Koern) Ruhland (Coelho et al., 2006), *Pausinystalia macroceras* (K. Schum.) Pierre ex Beille (Nwafor et al., 2005).

Most of the reported alkaloids possess prophylactic antiulcerogenic activity through enhancing mucus production in addition to the antioxidant activity (direct as well as indirect antioxidant activities, scavenge the ·OH radicals) (Tan and Nyasse, 2000).

Terpenoids with antiulcerogenic effects are mostly cytoprotective, they increase the mucus production in the stomach through different mechanisms, among these are; it enhanced mucosal PG content, thereby improving gastric mucosal blood flow and secretion of gastric bicarbonate and mucus which accelerates ulcer healing (Ohta et al., 2005b; Murakami et al., 1999) and it acts as antioxidant, reduce lipid peroxide level and increase in the antioxidant enzymes such as superoxide dismutase (SOD) and catalase (CAT) in the gastric mucosa (Rodríguez et al., 2006; Kim et al., 2005). Saponins act mainly through antisecratory mechanism; they inhibit acid secretion, total acid output, and lowered the pH value of gastric juice (Lee et al., 2005).

Phenolic compounds considered being one of the major families of secondary metabolites in plants; they represent a diverse group of compounds such as flavonoids, quinons, tannins and phenolic glycosides. Many phenolics exhibit antiulcerogenic activities, they act through different mechanisms. Antisecratory effect was reported for phenolic glycosides (Severi et al., 2009; Carvalho et al., 2007), while quinons are cytopretective (Lee et al., 2010), they increase PG synthesis.

Flavonoids are important for the normal growth, development and defense of plants. Flavonoids possess both cytoprotective and antisecratory activities. They exerts a gastroprotective action in mammals by increasing endogenous prostaglandin levels, decreasing histamine secreation, inhibiting *Helicobacter pylori* and scavenging oxygen derived free radicals. The antisecratory mechanism includes the antioxidant property (Coelho et al., 2006; Martin et al., 1998; Lastra et al., 1994; Olaleye and Farombi, 2006). Polysaccharides are cytoprotective, they stimulating mucosal regeneration and proliferation and increasing PG synthesis so restoring the gastric mucus levels (Gao et al., 2004).

Aloe vera, ginger and honey showed very significant activities against both peptic ulcer and ulcerative colits, while licorice, turmeric, Al-Hagnah (*Desmostachia bipinnata*), Catinga de Bode (*Ageratum conyzoides*), Chamomile and ginger prooved to treat peptic ulcer through their cytoprotective effect in addition to their anti *H. pylori* effect.

From our review we notice that, most of the researchers were from India, Brazil, Japan and South Korea (Fig. 2).

Declaration of interest

The authors report no declarations of interest. The authors alone are responsible for the content and writing of the paper

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