

# Anti-ulcer Activities of Herbal Remedies as Alternative Therapy

### Dhanya B. Sen<sup>1\*</sup>, Ashim Kumar Sen<sup>1</sup>, Kinjal P. Patel<sup>1</sup>, Ramachandran Balaraman<sup>1</sup>, Umang Shah<sup>2</sup> and Rajesh A. Maheshwari<sup>1</sup>

<sup>1</sup>Department of Pharmacy, Sumandeep Vidyapeeth Deemed to be University, Piparia, Vadodara - 391760, Gujarat, India; dhanyab1983@gmail.com <sup>2</sup>Ramanbhai Patel College of Pharmacy, Charotar University of Science and Technology, CHARUSAT Campus, Changa, Anand - 388421, Gujarat, India

## Abstract

Peptic ulcer is a disorder that commonly has an effect on the digestive system. It is a chronic illness which has impact on approximately, 10% of the mankind. The majority of current therapy regimens are based on western medicine. Proton pump inhibitors (PPIs) and histamine-2 (H2) receptor antagonists, which are commonly used to treat peptic ulcers, have been linked to side effects, relapses, and drug interactions. However, several investigations have shown that herbal medications can efficiently heal stomach ulcers in humans and animals using different processes. As a result, this review will focus on common plants with medicinal value which can be utilized to cure or prevent peptic ulcers.

**Keywords:** Digestive System, Medicinal Herbs, Peptic Ulcer, Proton Pump Inhibitors

# 1. Introduction

For more than a century, peptic ulcer ailment (gastric or duodenal) has been a severe threat to global community. It has resulted in severe morbidity and mortality<sup>1</sup>. Peptic ulcer is an acid-induced digestive tract lesion that generally occurs in the stomach or proximal duodenum and is characterised by uncovered mucosa expanded inside the submucosa or muscularis propria<sup>2</sup>. The occurrence of peptic ulcer ailment in the global inhabitants is believed to be  $5-10\%^3$ . Mucosal distraction in individuals with this ailment has traditionally been thought to be caused by a hypersecretory acidic environment combined with dietary variables or strain. Helicobacter pylori (H. pylori) infection, alcohol and tobacco intake, ingestion of nonsteroidal anti-inflammatory medicines (NSAIDs), and Zollinger-Ellison syndrome are all risk factors

for peptic ulcer development<sup>4</sup>. H. pylori is a primary etiologic element that has a big impact on peptic ulcer disease vulnerability. It is a spiral-shaped, extremely mobile bacteria that causes peptic ulcers by harming the mucosal layer that protects the GI track's lining5. Reduced gastric acidity or increased mucosal protection is both effective treatments and preventions for acidrelated diseases<sup>6-9</sup>. In situations of *H. pylori* infection, the primary treatment for peptic ulcer disease should be the elimination of this infection. Antimicrobial agents such as metronidazole, amoxicillin, tetracycline, clarithromycin and agents which prevent acid secretion or H+, K+ ATPase pump blockers like omeprazole, lansoprazole which inhibit proton pump can be advocated for the treatment. Additionally, medications like cimetidine, ranitidine, and famotidine which belong to the class of histamine receptor antagonists

<sup>\*</sup>Author for correspondence

and bismuth salt which directly interrupt bacterial cell5,<sup>10-14</sup>. A high recurrence percentage (60%) has been observed even the drugs effectively treat the condition. Although traditional regimens are useful, side effects are common and restrict their therapeutic utility<sup>15-18</sup>. Herbal treatments, on the other hand, have been shown in both clinical and experimental research to be effective in treating peptic ulcers while having less negative effects. Furthermore, herbal medication for peptic ulcer costs around one-sixth of what Western medicine costs<sup>19</sup>. The effectiveness, safety, and mode of action of herbal medications in the treatment of peptic ulcers are discussed in this review.

# 2. Pathophysiology of Peptic Ulcer

The pathophysiology of peptic ulcer ailment can be thought of as a mix of defensive (mucus-bicarbonate cover, prostaglandins, cellular renewal, and blood flow in the mucosa) and infuriating mechanisms (hydrochloric acid, pepsin, ethanol, bile salts, drugs). NSAIDs have a significant influence in the aetiology of the disease<sup>20,21</sup>.

The pathology is split into three categories: (a) *H. pylori* positive (b) Non-NSAID associated and *H. pylori* negative (c) NSAID associated.

Infection of *H. pylori* and ulcers of gastroduodenum has a close relationship. Initiation of epithelium-originated cytokines, primarily interleukin IL 8 and IL 1, by *H. pylori* promotes an inflammatory reaction in the stomach mucosa. The discharge of lysosomal enzymes, leukotrienes (LT), and reactive oxygen group by neutrophils and macrophages into the stomach mucosa compromises mucosal resistance and increases the immunopathogenetic procedure of ulcer development<sup>22</sup>.

Ulcers can also occur in some disorders such as high-dose upper abdominal radiotherapy, Zollinger-Ellison syndrome, Cushing's ulcer, idiopathic ulcers even without *H. pylori* infection and NSAID use.

The systemic suppression of constructively articulated cyclooxygenase-1 (COX-1), which is accountable for prostaglandin production, is linked to decrease in blood flow of mucosa, less mucus and bicarbonate discharge, and cell proliferation inhibition in NSAIDs-associated injury of the gastro-duodenal  $mucosa^{23}$ .

# 3. Conventional therapy for Peptic Ulcer

The physician determines the specific treatment for stomach and duodenal ulcers depends on the age of patient, general health, past medical records, pathogenesis, forbearance for medicines and expectations or preferences. Personal factors such as smoking, coffee, alcohol, stress, acid and pepsin secretion, and so on are also thought to take part in the development of stomach or duodenal ulcers. As a result, in many cases, the simplest treatment entails lifestyle modifications such as quitting smoking and drinking alcohol, as well as reducing stress.

Single or combination medications are frequently used to treat peptic ulcers. Blocking receptor sites, such as with an H<sub>2</sub> receptor antagonist (Ranitidine, famotidine etc.), destruction of intracellular mechanism which constitute calcium and/or cAMP, safeguard of gastric mucosa (cytoprotective action; eg. misoprostol, sucralfate etc.) from chemically persuaded injury, H<sup>+</sup>K<sup>+</sup>-ATPase, stoppage of final stage of acid discharge (eg. omeprazole, pantaprazole, rabeprazole etc.), and abolition of *H. pylori* infection (PPI + clarithromycin + metronidazole or amoxicillin etc.) are all examples of medical support. At the moment, traditional open surgery is the only option for those with extremely severe diseases. The most regularly used synthetic antiulcer medicines have a variety of side effects. These medications have reduced morbidity rates, but they have a number of side effects, including illness return, and they are typically prohibitively expensive for lowincome people. As a result, the exploration for non or low-toxic yet similarly effective medications derived from nature is a hot topic.

# 4. Antiulcer Drugs of Herbal Origin

Medicinal plants use in the management of various diseases is as old as humanity, and phytotherapy is well-known. Furthermore, there has been a surge in attention in alternative therapies and the use of herbal commodities, particularly those derived from medicinal herbs, in recent years<sup>24,25</sup>. Medicinal plants are also regarded as a large reservoir of possibly novel medications due to the emergence of diverse adverse effects from the use of conventional drugs for a variety of conditions. Extracts of plant and crude of the same are the most common sources of novel medications, and they have been proved to be effective in the management of gastric ulcers as well<sup>26</sup>.

Some of the herbs reported to be effective in peptic ulcer are:

#### Aegle marmelos

The Bael tree, also known as Aegle marmelos (L.) Correa (Rutaceae), is a deciduous tree with average-size, which is mainly found in subtropical and tropical climes. It is native to India and Southeast Asia, and recently been brought to Florida and Hawaii in the United States. Diarrhoea, indigestion, dysentery, and hyperglycemia have all been treated with portions of the plant. Antiinflammatory, antipyretic, analgesic, antifungal, anti-bacterial, anti-viral, anti-oxidant, anti-ulcer, anti-hyperlipidemic, anti-malarial. antimalignant, and radioprotective actions have been identified in various sections of Aegle marmelos in previous research<sup>27-29</sup>. Further research on the fruits and roots Aegle marmelos revealed that it has gastroprotective and antiulcer qualities via an antioxidant mechanism. In several chronic and acute stomach ulcer models in rats, the 50 percent ethanolic extract of root illustrated dose-reliant ulcer preventive efficacy. The ulcer index was lowered by Aegle marmelos via lowering lipid peroxidation, superoxide dismutase, and enhancing catalase activity<sup>30,31</sup>.

#### Allium sativum

Garlic's health advantages have been widely established throughout history, and *Allium sativum* was primarily used for therapeutic purposes. *Allium sativum's* organosulfur components, such as S-allyl-L-cysteine (SAC) sulfoxides and -glutamyl S-allyl-L-cysteine, are identified to be the principal bioactive chemicals. It is simple to turn raw *Allium sativum* into bioinactive form. As a result, several varieties of its extract have been created, each with a particular composition of bioactive components, and their usefulness has been seen and tested in numerous researches. The antioxidant action of *Allium sativum* extract is established by hunting reactive oxygen species (ROS), preventing oxidation of lipoprotein, and decreasing serum glucose-induced antioxidant enzyme initiation. It also had an anti-tumorigenic impact by boosting apoptosis and inducing cell cycle arrest, as well as suppressing *H. pylori*-generated stomach inflammation in vivo. In vitro studies found that *Allium sativum* extracts containing allicin and allyl-methyl plus methyl-allyl thiosulfinate inhibited *H. pylori* growth<sup>32-35</sup>.

#### Apium graveolens

Celery is a plant species that falls into to the Apiaceae family. In rats, an extract of celery in ethanol is utilised as a treatment for stomach ulcers. Al-Howiriny *et al.* found that extract of celery in ethanol is efficient against gastric ulcer when compared to cytodestructive agents, indomethacin and cold restraint ulcer due to stress in rats. Through its antioxidant properties, *Apium graveolens* extract greatly shields the stomach mucosa and lowers baseline gastric output in rats<sup>36</sup>.

#### Alhagi camelorum

In folklore, Alhagi camelorum Fisch. (Fabaceae) or camel thorn is a therapeutic herb. The whole plant has conventionally been used to cure metabolic, gastrointestinal, and hepatic illnesses, as well as diuretics, wound curing, rheumatic ailments, migraines, fever, warts, and rashes. Other natural actions reported from this plant include antioxidant, anti-dysentry, antinociceptive, ureteral stone ejection, antiulcerogenic, and gastroprotective actions. Aqueous extract of Alhagi camelorum has previously been shown to have considerable protective and antisecretory properties in rat stomach mucosa. Alhagi camelorum is another Alhagi genus species was utilized in traditional medication to cure gastrointestinal inconveniences. In rat stomach mucosa, experimental research on Alhagi camelorum extract revealed considerable mucosal defence and antisecretory activity<sup>37-39</sup>.

#### Asparagus racemosus

Asparagus racemosus Willd. (Family: Liliaceae) is a spiny shrub having a tuberous, undersized rootstock that bears many luscious roots with tubers. It can be found all over Australia's tropical and subtropical regions, and in India, Asia and Africa. In traditional medicine, Asparagus racemosus is used as nerve tonic, aphrodisiac, anodyne, galactagogue, diuretic and antispasmodic. It is also used to treat things like diarrhoea, dysentery, ulcers, neurological illnesses, alcohol peptic withdrawal symptoms, rheumatism, and psychological breakdowns. In the light of past researches on anti ulcer action, root extract of Asparagus racemosus found to increase protective features of mucosa such as cellular mucus, life span of cells, secretion of mucus, and also a noteworthy antioxidant effect with only minor or no action on parameters like pepsin and acid<sup>40-43</sup>.

#### Bupleurum falcatum

*Bupleurum falcatum* is a blossoming plant that belongs to the Apiaceae family. In Chinese and Japanese herbal medication, the roots of *Bupleurum falcatum* have been employed in clinical trials (kampo medicine). A crude saponin portion of *Bupleurum falcatum* demonstrated mild antiulcerogenic efficacy in a pylorus ligated ulcer model, according to Shibata *et al.* It was also previously discovered that the polysaccharide portion of *Bupleurum falcatum* has substantial antiulcer action in mice when exposed to HCl/ethanol<sup>44,45</sup>.

#### Curcuma longa

It is a perennial plant belonging to the Zingiberaceae family commonly found in India and Southeast Asia. Curcumin, one of Curcuma's active ingredients, has anti-inflammatory and antioxidant qualities. It hunts reactive oxygen species and controls MMP action to exhibit antiulcer function due to its antioxidant properties. Curcumin, also known as diferuloylmethane, a yellow colouring agent found in the turmeric plant *Curcuma longa*, is commonly exploited as a spice in Indian and Thai cooking. It has a variety of therapeutic actions, together with anti-inflammatory efficacy caused by PG synthesis repression. During a double-blind investigation, turmeric root extract was found to reduce ache from biliary dyskinesia and to promote

endoscopic curing of peptic ulcers and also symptoms in individuals with non-ulcer dyspepsia<sup>46-49</sup>.

### Carlina acanthifolia

*Carlina acanthifolia* of Asteraceae family is a perennial plant found throughout Eastern Serbia's hills and mountains. The root of *Carlina acanthifolia* is utilised as a diuretic, urinary tract anti-inflammatory therapy, antioxidant, antibacterial, and antiulcer agent. Previous literatures on the effectiveness on the root's essential oil revealed a strong dose-reliant gastro shielding effect in rats that had been subjected to a stress gastric ulcer test induced by ethanol<sup>50-52</sup>.

#### **Camellia sinensis**

It is the most widely consumed non-alcoholic drink on the planet. In rat models, tea seed-derived triterpene saponins have been shown to protect against ethanolinduced stomach mucosal ulcers and black tea extract has been shown to protect against several ulcerogens. Theaflavin (TF) is a powerful antioxidant found in black tea. TF's anti-oxidative activities, PGE2 production, and mucin secretion increase helped to cure an indomethacin-induced stomach ulcer. In the ulcer margin, TF also aids in the suppression of different inflammatory modulators. eNOS regulation could be another mechanism for TF to help repair stomach ulcers<sup>53-57</sup>.

#### **Cichorium intybus**

*Cichorium intybus* L., also known as chicory of Compositae family, is a traditional Uighur medication used widely in China and other Asian nations. Previous pharmacological studies showed that root extract provided considerable GI protection in animal models, which was related to anti-secretory action and promotion of the gastric mucosa's protective barrier<sup>58,59</sup>.

#### **Cistus Laurifolius**

An extract of *Cistus laurifolius* was used in a number of studies on flavonoids. When antibacterial action against *H. pylori* was tested, 3'-demethoxysudachitin and sudachitin were shown to be the majority active molecules. A similar study discovered that *Cistus*  *laurifolius* chloroform extract has potent anti-*H. pylori* action. Seperated flavonoids can be utilised as an added constituent in the usual management of *H. pylori* infection, according to these studies. In the same way, Ustun *et al.* revealed that *Cistus laurifolius* chloroform extract has a substantial anti-*H. pylori* activity<sup>60-62</sup>.

#### Combretum dolichopetalum

Traditional medicine uses *Combretum dolichopetalum* Engl. and Diels of Combretaceae family to cure diarrhoea, stomachache, cramps, blood in the stool, and other GI problems. This plant has been established to have hepatoprotective, anti-inflammatory, antiulcer, and anti-diabetic properties. Root extract demonstrated a substantial protective outcome against duodenal and stomach ulcers in rats caused by indomethacin treatment and cold stress, according to research. Tannins and saponins were formerly thought to be effective in this function<sup>63,64</sup>.

#### Ficus religiosa

*Ficus religiosa* L. (Moraceae), often identified as peepal or sacred (bodhi), is a huge perennial tree native to the sub-Himalayan area, central India, and Bengal. In traditional medicine, it has been used to treat problems with the reproductive organisms, respiratory, gastrointestinal tract, CNS and endocrine systems and contagious disorders. In experiments on rat models, investigations into the gastro-protective properties of several components of *Ficus religiosa* reveal strong antiulcer activity. Its anti-secretary and cytoprotective qualities could be the mechanism for its antiulcer action<sup>65-67</sup>.

#### Glycyrrhiza glabra

Liquorice, often known as licorice, is the root of the plant *Glycyrrhiza glabra* (Fabaceae), which is having a sugary flavour. Liquorice is a legume (similar to beans and peas) originally from southern Europe and Asia. Licorice extracts have been shown to hasten the curing of gastrointestinal ulcers (particularly in the abdomen and oesophagus), probably owing to their antioxidant properties. Cbenoxolone, a succinate derivative of glycerrhetinic acid, was created in London in the early 1960s and has since become the most popular variety of licorice for ulcer healing<sup>68-70</sup>.

#### Gentiana lutea

Gentianae radix is made up of desiccated rhizomes and roots of *Gentiana lutea* L. (Family: Gentianaceae), which appear as sole or branched sub cylindrical sections of various lengths and thicknesses, often 10-40 mm. The gastro-protective activity of Gentian root methanolic extract was investigated, and the results revealed that the healing effect of Gentian roots on gastric wound were linked to increased mucosal protective features via the prostaglandin pathway, with secoiridoid glycosides being accountable for this action<sup>71,72</sup>.

#### Hippocratea excela

It is a climber native to Central America and Mexico. It belongs to the Hipocrateaceae family. In various experimental ulcer models in rats, root and bark isolate of the described herbs were found to have important gastro-defensive capabilities.  $\beta$ -amyrin,  $\alpha$ -amyrin, (–) epicatechin,  $\beta$ -sitosterol and its glycosides were identified as potent gastro-defensive components in H. excels extract. These findings back up the usefulness of this herb as an antiulcer treatment in conventional medicine<sup>73,74</sup>.

#### Kochia scoparia

Gastro-protective properties have been demonstrated for saponins derived from the fruit of *Kochia scoparia*. The activation of mucous membrane protective factors rather than a reduction in acid output is assumed to be responsible for its gastro-protective effects<sup>75,76.</sup>

#### Lagenaria vulgaris

It belongs to the Cucurbitaceae family and is a common vegetable. By modifying glutathione levels, an anti-oxidative pathway, this herb possesses antiulcer capabilities<sup>77</sup>.

#### Moringa olefera

Moringa oleifera Lam. (Moringaceae) is a deciduous tree with soft bark that can be found in a variety of tropical and subtropical climates. Previous research in albino wistar rats found that the ethanolic extract of root bark had antiulcer activity, which could be due to the antisecretory, anti-*H. pylori*, stimulation

of mucous membrane defensive feature, and cytoprotective properties of active constituents such as alkaloids (Moringine and moringinine), antibiotics (Pterygospermin), and triterpen<sup>78</sup>.

#### Myristica malabarica

Rampatri is the common name for this plant, which fall into to the Myristicaceae family. It is a unique spice that's utilised in a variety of Indian dishes. Malabaricone B (MalB) and Malabaricone C are the active ingredients in *M. malabarica* (MalC). The antioxidative characteristics of MalB and MalC, as well as their control of EGFR expression, PGE2 production, and mucin discharge, helped to cure stomach ulcers. Mal B and C also hasten stomach ulcer healing by increasing the levels of VGEF, vWF factorVIII, and endostatin<sup>79,80</sup>.

#### Panax ginseng

*Panax ginseng* c.a. Meyer of Araliaceae family is a perennial natural plant that is mainly cultivated in China and is known around the world. It has also been shown to have a significant gastro-protective action in rats with gastric ulcers induced by ethanol. The ginseng-treated rats revealed a considerable elevation of the cyto-protective heat shock proteins HSP27 and HSP70, which is thought to be a cyto-protective mechanism in ethanol-persuaded stomach injury<sup>81,82</sup>.

#### Picrorhiza kurroa

It is a tiny perennial herb covered with hair belonging to the Scrophulariaceae family that grows in the alpine Himalayan region as well as in some tropical sections of India. The iridoid glycosides, picrosides I, II, III, and kutkoside, are the major active elements of *Picrorhiza kurroa's* roots and rhizomes. Picroside I and kutkoside have been demonstrated to have substantial gastroprotective activities, mostly during their anti-oxidative activity<sup>83</sup>.

#### Polygonum bistorta

*Polygonum bistorta* is a species of Polygonum. Linn, Bistort, or Snakeroot is a tiny perennial plant with a wooden base of the Polygonaceae family. This herb can be found all over the world; however it is most common in northern temperate zones like Europe and North America. *Polygonum bistorta* root (100 g/ml of hydro alcoholic extract) was found to have a powerful inhibitory effect on IL-8 release as an inflammatory moderator in a recent study, which could help to authenticate the conventional use of this plant for GI illnesses caused by *H. pylori* infection<sup>84</sup>.

#### Pistacia lentiscus

Exudates from *Pistacia lentiscus* tree of Anacardiaceae family, found in Mediterranean regions, are known as Mastic which is resinous in nature. The severity of stomach mucosal injury caused by phenylbutazone, aspirin, reserpine, pyloric ligation and restraint cold stress was significantly reduced in this study<sup>85</sup>.

#### Plumbago auriculata

*Plumbago auriculata* Lam. of Plumbaginaceae family is a perennial herb native to Africa and used as an decorative plant in India. It is one of 500 species. Several investigations have found that plumbaginales, such as *Plumbago auriculata*, *Plumbago indica*, and *Plumbago zeylanica* species, have gastro-protective properties, and that lumbagin is a beneficial chemical. According to prior findings, these species roots were cytotoxic and anti-*H. pylori*. They protect the gastrointestinal tract. *Plumbago auriculata* was found to have substantial antioxidant and acid neutralising properties, as well as a gastro-protective ability comparable to Ranitidine<sup>86,87</sup>.

#### Pteleopsis suberosa

*Pteleopsis suberosa* demonstrated protective effect against ethanol and indomethacin-persuaded gastric mucosa damage in clinical studies by stimulating PG production, with a saponin fraction as the most likely active principle<sup>88,89</sup>.

#### **Rumex patientia**

*Rumex patientia* L. (Polygonaceae) is a plant which is having a maximum height of 2 meters and is widely distributed in mid-Anatolia. Previous studies have shown that an extract of *R. patientia* roots in water

reduced the number and extent of ulcerated sites, possibly due to its antioxidant properties<sup>90,91</sup>.

#### Silybum marianum

Silymarin is a flavonolignan compound found in the milk thistle, *Silybum marianum* that has been shown to help with experimentally produced stomach ulcers. Silymarin's antiulcerogenic activity may be due to an inhibitory action on the lipoxygenase pathway, which prevents leukotriene formation<sup>92</sup>.

#### Sophora flavescens

Traditional medicine has historically employed *Sophorae Radix*, or the dehydrated roots of *Sophora flavescens* Aiton (Fabaceae). Vexibinol is a class of flavonoid (flavonol) that is a primary ingredient in the root extract and has been shown to help repair stomach ulcers in rats caused by an HCl/ethanol model, according to the literature. Vexibinol's antiulcer action is due to its stomach mucosal protecting action and inhibitory activity on gastric acid secretion. In an animal model, trifolirhizin, an additional active principle isolated from *Sophora flavescens* root, has exhibited notable benefits on *Helicobacter pylori* infection as well as decreased quantities of stomach secretion and acid yield<sup>93</sup>.

#### Sophora subprostrata

In China, the plant *Sophora subprostrata* is utilized to treat digestive disorders. Sophoradin, a flavonoid produced from the root of *Sophora subprostrata*, has been shown to have gastro-protective and ulcer-curing effects<sup>94</sup>.

#### Spinacia oleracea

Spinach is a blossoming plant belonging to the Amaranthaceae family which is safe to be eaten. It is native to Asia's central and western regions. Spinach is a green leafy vegetable high in nitrates. On rats, Petersson *et al.* discovered that spinach, produces a thicker coating of mucus along the gastric wall, protects against the hydrochloric acid released in gastric fluid and lowers the threat of ulcers<sup>95</sup>.

#### **Tectona grandis**

In Indian medicine, portion of the teak tree, *Tectona grandis*, have been employed in peptic ulcer compositions. Its action appeared to be linked to a change in gastric juice protein content, and it corrected aspirin-persuaded alterations in peptic action, protein, and sialic acid levels<sup>96</sup>.

#### Withania somnifera

*Withania somnifera* is a kind of withania. Dunal, also known as Ashwagandha, is a Solanaceae plant that grows in northern India, Africa and Mediterranean region. Pre-treatment with *Withania somnifera* has been proven to provide significant defence against stomach ulcers activated by stress in studies. A further study found that Withaferin A, a withanolide derived from *Withania somnifera*, inhibited *H. pylori*-persuaded IL-1 generation in dendritic cells, suggesting that it could be used as a potential defensive and therapeutic agent for gastric cancer<sup>97-99</sup>.

### Zingiber officinale

Traditional treatments for GI illnesses have used ground rhizome of *Zingiber officinale*. It's commonly used to treat peptic ulcer disease. Ginger's anti-inflammatory and anti-ulcer qualities may be attributable to its potent thromboxane synthetase activity, as well as its phenolic antioxidants, which inhibit stomach H<sup>+</sup>K<sup>+</sup>-ATPase, and *H. pylori* progression. In animal models, plant extract reduced the incidence of GI ulcers caused by nonsteroidal anti-inflammatory drugs (NSAIDs) and hypothermic restraint stress<sup>100</sup>.

### Zizyphus lotus

*Zizyphus lotus* (Rhamnaceae) is a big shrub found in tropical and subtropical regions around the world, including Asia, South America, North America, Africa, Oceania, and Europe. The antiulcerogenic efficacy of *Zizyphus lotus* extract on gastric ulcer in animal models was investigated, and the results revealed that it may be mediated in part by reduced gastric fluid output, antiacid, demulcent effects, and prevention of *H. pylori* progression. Antisecretory and cytoprotective effect of

root bark aqueous extract can be explained in part by the presence of tannins and flavonoids<sup>101,102</sup>.

# 5. Conclusion

The study of medicinal plants and their qualities has gotten a lot of attention in recent years. These plants have been put to the test to see if they can be used to avoid and treat several ailments. According to the present review, ethnopharmacological and scientific discoveries were usually in agreement, and investigations showed that active constituents in herbal remedies were generally accountable for biological benefits such as antioxidant, anti-inflammatory, and antiulcer capabilities. Therefore, it can be summarized that studying novel gastro-protective herbs and identifying the natural constituents they possess are essential concerns for the development of new medications with fewer unwanted effects, toxicity, price, and effectiveness in the prevention and treatment of various stomach illnesses.

# 6. References

- Malfertheiner P, Chan FK, McColl KE. Peptic ulcer disease. Lancet. 2009; 374(9699):1449-61. https://doi.org/10.1016/ S0140-6736(09)60938-7
- Narayanan M, Reddy KM, Marsicano E. Peptic ulcer disease and *Helicobacter pylori* infection. Mo Med. 2018; 115(3):219-24. PMid: 30228726.
- Lanas A, Chan FKL. Peptic ulcer disease. Lancet. 2017; 390:613-24. https://doi.org/10.1016/S0140-6736(16)32404-7
- Søreide K, Thorsen K, Harrison EM, Bingener J, Møller MH, Ohene-Yeboah M, et al. Perforated peptic ulcer. Lancet. 2015; 386(10000):1288-98. https://doi.org/10.1016/ S0140-6736(15)00276-7
- 5. Prasanthi C, Prasanthi N, Manikiran S, Rao NR. Focus on current trends in the treatment of *Helicobacter pylori* infection: An update. Situations. 2011; 9(1):9.
- Rauws EA. Eradication of *Helicobacter pylori* cures duodenal ulcer disease. In *Helicobacter Pylori* and Gastroduodenal Pathology. Springer, Berlin, Heidelberg; 1993. p. 347-51. https://doi.org/10.1007/978-3-642-77486-7\_63
- Brooks FP. The pathophysiology of peptic ulcer disease. Dig Dis Sci. 1985; 30(11):15S-29S. https://doi.org/10.1007/ BF01309381. PMid:4053922
- 8. Geetha A, Saranya P. A study on the gastroprotective effect of *Andrographis paniculata* and andrographolide in rats

subjected to pylorus ligation. J Pharm Res. 2012; 5(2):787-91.

- Amandeep K, Robin S, Ramica S, Sunil K. Peptic ulcer: A review on etiology and pathogenesis. Int Res J Pharm. 2012; 3(6):34-8.
- Javadzadeh Y, Hamedeyaz S. Floating drug delivery systems for eradication of *Helicobacter pylori* n treatment of peptic ulcer disease. Trends H pylori Inf. 2014; 1:13. https://doi. org/10.5772/57353
- Adibkia K, Hamedeyazdan S, Javadzadeh Y. Drug release kinetics and physicochemical characteristics of floating drug delivery systems. Expert Opin Drug Deli. 2011; 8(7):891-903. https://doi.org/10.1517/17425247.2011.5741 24. PMid:21506906
- Asnaashari S, Khoei NS, Zarrintan MH, Adibkia K, Javadzadeh Y. Preparation and evaluation of novel metronidazole sustained release and floating matrix tablets. Pharm Dev Technol. 2011; 16(4):400-7. https://doi. org/10.3109/10837451003774393. PMid:20429828
- Javadzadeh Y, Hamedeyazdan S. Novel drug delivery systems for modulation of gastrointestinal transit time. In Recent Advances in Novel Drug Carrier Systems, Intech Open Publisher; 2012. https://doi.org/10.5772/50250
- 14. Javadzadeh Y, Hamedeyazdan S, Adibkia K, Kiafar F, Zarrintan MH, Barzegar-Jalali M. Evaluation of drug release kinetics and physico-chemical characteristics of metronidazole floating beads based on calcium silicate and gas-forming agents. Pharm Dev Technol. 2010; 15(4):329-38. https://doi.org/10.3109/10837450903196843. PMid:19694496
- Fujino S, Suzuki Y, Tanaka T. Cost-benefit analysis of medicinal treatment for gastric ulcers. Long-term model including healing and recurrence. Health Policy. 1985; 5:45-72. https://doi.org/10.1016/0168-8510(85)90065-X
- 16. Schunack W. Pharmacology of H2-receptor antagonists: an overview. J Int Med Res. 1989; 17:9A-16A.
- Bright-Asare P, Habte T, Yirgou B, Benjamin J. Prostaglandins, H<sub>2</sub>-receptor antagonists and peptic ulcer disease. Drugs. 1988; 35:1-9. https://doi.org/10.2165/00003495-198800353-00003. PMid:2905237
- Xiao YL, Nie YQ, Hou XH, Xie PY, Fang JY, Yuan YZ, et al. The efficacy, safety and cost-effectiveness of hydrotalcite versus esomeprazole in on-demand therapy of NERD: A multicenter, randomized, open-label study in China. J Dig Dis. 2013; 14: 463-8. https://doi.org/10.1111/1751-2980.12069. PMid:23659834
- 19. The cost for treating gastric ulcer. Available from: URL: http://jibing.qiuyi.cn/wky/2013/0509/132036.html
- Ballinger A, Smith G. COX-2 inhibitors vs. NSAIDs in gastrointestinal damage and prevention. Expert Opin Pharmacother. 2001; 2:31-40. https://doi. org/10.1517/14656566.2.1.31. PMid:11336566

#### **326** Anti-ulcer Activities of Herbal Remedies as Alternative Therapy

- Huang JQ, Sridhar S, Hunt RH. Role of *Helicobacter* pylori infection and non-steroidal anti-inflammatory drugs in peptic-ulcer disease: A meta-analysis. Lancet. 2002; 359:14-22. https://doi.org/10.1016/S0140-6736(02)07273-2
- Noach LA, Bosma NB, Jansen J, Hoek FJ, van Deventer SJ, Tytgat GN. Mucosal tumor necrosis factor-alpha, interleukin-1 beta, and interleukin-8 production in patients with *Helicobacter pylori* infection. Scand J Gastroenterol. 1994; 29:425-9. https://doi.org/10.3109/00365529409096833. PMid:8036458
- 23. Wallace JL, Vong L. NSAID-induced gastrointestinal damage and the design of GI-sparing NSAIDs. Curr Opin Investig Drugs. 2008; 9:1151-6. PMid: 18951293.
- 24. Rates SM. Plants as source of drugs. Toxicon. 2001; 39:603-13. https://doi.org/10.1016/S0041-0101(00)00154-9
- Yesilada E, Gürbüz I, Shibata H. Screening of Turkish antiulcerogenic folk remedies for anti-*Helicobacter pylori* activity. J Ethnopharmacol. 1999; 66:289-93. https://doi. org/10.1016/S0378-8741(98)00219-0
- Falcão HS, Mariath IR, Diniz MF, Batista LM, Barbosa-Filho JM. Plants of the American continent with antiulcer activity. Phytomedicine. 2008; 15:132-46. https://doi.org/10.1016/j. phymed.2007.07.057. PMid:17904832
- Kesari AN, Gupta RK, Singh SK, Diwakar S, Watal G. Hypoglycemic and antihyperglycemic activity of *Aegle marmelos* seed extract in normal and diabetic rats. J Ethnopharmacol. 2006; 107(3):374-9. https://doi. org/10.1016/j.jep.2006.03.042. PMid:16781099
- Rana BK, Singh UP, Taneja V. Antifungal activity and kinetics of inhibition by essential oil isolated from leaves of Aegle marmelos. J Ethnopharmacol. 1997; 57(1):29-34. https:// doi.org/10.1016/S0378-8741(97)00044-5
- 29. Kothari S, Mishra V, Bharat S, Tonpay SD. Antimicrobial activity and phytochemical screening of serial extracts from leaves of *Aegle Marmelos* (Linn.). Acta Poloniae Pharmaceutica. 2011; 68(5):687-92. PMid: 21928713
- 30. Das SK, Roy C. The protective role of Aegle marmelos on aspirin-induced gastro-duodenal ulceration in albino rat model: A possible involvement of antioxidants. Saudi J Gastroenterol. 2012; 18(3):188. https://doi.org/10.4103/1319-3767.96452. PMid:22626798. PMCid:PMC3371421
- 31. Verma M. Investigation on antiulcer activity of *Aegle marmelos* root as experimental, biochemical and histological study. J Pharm Res. 2010; 3:2523-8.
- 32. Park JM, Han YM, Kangwan N, Lee SY, Jung MK, Kim EH, et al. S-allyl cysteine alleviates nonsteroidal anti-inflammatory drug-induced gastric mucosal damages by increasing cyclooxygenase-2 inhibition, heme oxygenase-1 induction, and histone deacetylation inhibition. J Gastroenterol Hepatol. 2014; 29(Suppl S4):80-92. https://doi.org/10.1111/ jgh.12730. PMid:25521739

- 33. Iimuro M, Shibata H, Kawamori T, Matsumoto T, Arakawa T, Sugimura T, et al. Suppressive effects of garlic extract on *Helicobacter pylori*-induced gastritis in Mongolian gerbils. Cancer Lett. 2002; 187(1-2):61-8. https://doi.org/10.1016/S0304-3835(02)00401-9
- 34. Trio PZ, You S, He X, He J, Sakao K, Hou DX. Chemopreventive functions and molecular mechanisms of garlic organosulfur compounds. Food Funct. 2014; 5(5):833-44. https://doi.org/10.1039/c3fo60479a. PMid:24664286
- Cañizares P, Gracia I, Gómez LA, de Argila CM, Boixeda D, García A, et al. Allyl-thiosulfinates, the bacteriostatic compounds of garlic against *Helicobacter pylori*. Biotechnol Prog. 2004; 20(1):397-401. https://doi.org/10.1021/ bp034143b. PMid:14763870
- 36. Al-Howiriny T, Alsheikh A, Alqasoumi S, Al-Yahya M, ElTahir K, Rafatullah S. Gastric antiulcer, antisecretory and cytoprotective properties of celery (*Apium graveolens*) in rats. Pharm Biol. 2010; 48(7):786-93. https://doi. org/10.3109/13880200903280026. PMid:20645778
- Zarei A, Ashtiyani SC, Vaezi GH. A study on the effects of the hydroalcholic extract of the aerial parts of *Alhagi camelorum* on prolactin and pituitary-gonadal activity in rats with hypercholesterolemia. Arch Ital Urol Androl. 2014; 86(3):188-92. https://doi.org/10.4081/aiua.2014.3.188. PMid:25308581
- Gharibn AM, Mard S. Gastroprotective effect of *Alhagi* camelorum on experimental gastric ulcer in rats. Pak J Med Sci. 2007; 32(4):570-3.
- Shaker E, Mahmoud H, Mnaa S. Anti-inflammatory and anti-ulcer activity of the extract from *Alhagi maurorum* (camelthorn). Food Chem Toxicol. 2010; 48(10):2785-90. https://doi.org/10.1016/j.fct.2010.07.007. PMid:20633591
- 40. Hannan JM, Ali L, Khaleque J, Akhter M, Flatt PR, Abdel-Wahab YH. Antihyperglycaemic activity of *Asparagus racemosus* roots is partly mediated by inhibition of carbohydrate digestion and absorption, and enhancement of cellular insulin action. Br J Nutr. 2012; 107(9):1316-23. https://doi. org/10.1017/S0007114511004284. PMid:21899804
- Siram K, Priyambada S, Aryya N, Goel R. Gastroduodenal Ulcer Protective Activity of Asparagus Racemosus: An Experimental, Biochemical and Histological Study. J Ethnopharmacol. 2003; 86:1-10. https://doi.org/10.1016/ S0378-8741(02)00342-2
- Bopana N, Saxena S. Asparagus racemosus-Ethnopharmacological Evaluation and Conservation Needs. J Ethnopharmacol. 2007; 110:1-15. https://doi. org/10.1016/j.jep.2007.01.001. PMid:17240097
- Goel R, Sairam K. Anti-Ulcer Drugs from indigenous sources with emphasis on *Musa sapientum*, *Tamra bhasma*, *Asparagus racemosus* and *Zingiber officinale*. Indian J Pharmacol. 2002; 34:100-10.

- 44. Shibata M, Yoshida R, Motohashi S, Fukushima M. Pharmacological studies on *Bupleurum falcatum* L. IV. Some pharmacological effects of crude saikosides, saikogenin A and syrupy residue. J Pharm Soc Jpn. 1973; 93(12):1660-7. https://doi.org/10.1248/yakushi1947.93.12\_1660. PMid:4798800
- 45. Yamada H, Ra KS, Kiyohara H, Cyong JC, Otsuka Y. Structural characterisation of an anti-complementary pectic polysaccharide from the roots of *Bupleurum falcatum* L. Carbohydrate Res. 1989; 189:209-26. https://doi. org/10.1016/0008-6215(89)84098-4
- 46. Swarnakar S, Ganguly K, Kundu P, Banerjee A, Maity P, Sharma AV. Curcumin regulates expression and activity of matrix metalloproteinases 9 and 2 during prevention and healing of indomethacin-induced gastric ulcer. J Biol Chem. 2005; 280(10):9409-15. https://doi.org/10.1074/jbc. M413398200. PMid:15615723
- 47. Huang MT, Lysz T, Ferraro T, Abidi TF, Laskin JD, Conney AH. Inhibitory effects of curcumin on in vitro lipoxygenase and cyclooxygenase activities in mouse epidermis. Cancer Res. 1991; 51(3):813-9. PMid: 21928713
- Niederau C, Gopfert E. The effect of chelidonium-and turmeric root extract on upper abdominal pain due to functional disorders of the biliary system. Results from a placebo-controlled double-blind study. Medizinische Klinik. 1999; 94(8):425-30. https://doi.org/10.1007/ BF03044726. PMid:10495621
- Prucksunand C, Indrasukhsri B, Leethochawalit M, Hungspreugs K. Phase II clinical trial on effect of the long turmeric (*Curcuma longa* Linn.) on healing of peptic ulcer. Southeast Asian J Trop Med Public Health. 2001; 32(1):208-15. PMid: 11485087.
- 50. Leporatti ML, Ivancheva S. Preliminary comparative analysis of medicinal plants used in the traditional medicine of Bulgaria and Italy. J Ethnopharmacol. 2003; 87(2-3):123-42. https://doi.org/10.1016/S0378-8741(03)00047-3
- 51. Ivancheva S, Nikolova M, Tsvetkova R. Pharmacological activities and biologically active compounds of Bulgarian medicinal plants. Phytochemistry: Adv Res. 2006; 8:87-103.
- 52. Đorđević S, Petrović S, Dobrić S, Milenković M, Vučićević D, Žižić S, et al. Antimicrobial, anti-inflammatory, antiulcer and antioxidant activities of *Carlina acanthifolia* root essential oil. J Ethnopharmacol. 2007; 109(3):458-63. https://doi.org/10.1016/j.jep.2006.08.021. PMid:17011148
- 53. Yoshikawa M, Morikawa T, Li N, Nagatomo A, Li X, Matsuda H. Bioactive saponins and glycosides. XXIII. Triterpene saponins with gastroprotective effect from the seeds of *Camellia sinensis*-Theasaponins E3, E4, E5, E6, and E7. Chem Pharm Bull. 2005; 53(12):1559-64. https://doi. org/10.1248/cpb.53.1559. PMid:16327189
- 54. Morikawa T, Li N, Nagatomo A, Matsuda H, Li X, Yoshikawa M. Triterpene saponins with gastroprotective effects

from tea seed (the seeds of *Camellia sinensis*). J Nat Prod. 2006; 69(2):185-90. https://doi.org/10.1021/np058097w. PMid:16499314

- 55. Maity S, Vedasiromoni JR, Chaudhuri L, Ganguly DK. Role of reduced glutathione and nitric oxide in the black tea extract-mediated protection against ulcerogen-induced changes in motility and gastric emptying in rats. Jpn J Pharmacol. 2001; 85(4):358-64. https://doi.org/10.1254/ jjp.85.358. PMid:11388638
- 56. Maity S, Vedasiromoni JR, Ganguly DK. Anti-ulcer effect of the hot water extract of black tea (*Camellia sinen-sis*). J Ethnopharmacol. 1995; 46(3):167-74. https://doi. org/10.1016/0378-8741(95)01245-9
- 57. Adhikary B, Yadav SK, Roy K, Bandyopadhyay SK, Chattopadhyay S. Black tea and the aflavins assist healing of indomethacin-induced gastric ulceration in mice by antioxidative action. Evid Based Complementary Altern Med. 2011. https://doi.org/10.1155/2011/546560. PMid:20953434. PMCid:PMC2952312
- 58. Krylova S, Vymyatnina Z, Zueva E, Amosova E, Razina T, Litvinenko V. Effects of *Cichorium Intybus* L. Root extract on secretory activity of the stomach in health and ulcer disease. Bull Exp Biol Med. 2015; 159(5):638-41. https://doi. org/10.1007/s10517-015-3035-1. PMid:26468023
- Gürbüz İ, Üstün O, Yeşilada E, Sezik E, Akyürek N. In vivo gastroprotective effects of five Turkish folk remedies against ethanol-induced lesions. J Ethnopharmacol. 2002; 83(3):241-4. https://doi.org/10.1016/S0378-8741(02)00248-9
- Lee SY, Shin YW, Hahm KB. Phytoceuticals: mighty but ignored weapons against *Helicobacter pylori* infection. J Dig Dis. 2008; 9(3):129-39. https://doi.org/10.1111/j.1751-2980.2008.00334.x. PMid:18956590
- 61. Kim DK, Lee JA, Kim YB, Lee KM, Hahm KB. A randomized controlled trial assessing Korea red ginseng treatment of *Helicobacter pylori*-associated chronic gastritis. Korean J Med. 2007; 72:20-8.
- 62. daCosta DiBonaventura M, Yuan Y, Wagner JS, Gilbert JL, Lescrauwaet B, Langley P. The burden of viral hepatitis C in Europe: a propensity analysis of patient outcomes. Eur J Gastroenterol Hepatol. 2012; 24(8):869-77. https://doi. org/10.1097/MEG.0b013e3283551dee. PMid:22617367
- Uzor PF, Ebrahim W, Osadebe PO, Nwodo JN, Okoye FB, Müller WE, et al. Metabolites from *Combretum dolichopetalum* and its associated endophytic fungus *Nigrospora oryzae*—Evidence for a metabolic partnership. Fitoterapia. 2015; 105:147-50. https://doi.org/10.1016/j. fitote.2015.06.018. PMid:26136060
- Asuzu IU, Onu OU. Anti-ulcer activity of the ethanolic extract of *Combretum dolichopetalum* root. Int J Crude Drug Res. 1990; 28(1):27-32. https://doi. org/10.3109/13880209009082770

- Singh D, Singh B, Goel RK. Traditional uses, phytochemistry and pharmacology of *Ficus religiosa*: A review. J Ethnopharmacol. 2011; 134(3):565-83. https://doi. org/10.1016/j.jep.2011.01.046. PMid:21296646
- 66. Saha S, Goswami G. Study of anti-ulcer activity of *Ficus religiosa* L. on experimentally induced gastric ulcers in rats. Asian Pac J Trop Med. 2010; 3(10):791-3. https://doi. org/10.1016/S1995-7645(10)60189-7
- 67. Thorat S, Deshmukh D, Gaikwad D, Grampurohit N. Antiulcer effect on the ethanol extract of the bark & root of *Ficus religoisa* linn. In different experimental ulcer models in rats. Int J Pharm Sci Res. 2013; 4(3):1120-4.
- Turpie AG, Runcie J, Thomson TJ. Clinical trial of deglydyrrhizinized liquorice in gastric ulcer. Gut. 1969; 10(4):299-302. https://doi.org/10.1136/gut.10.4.299. PMid:4889526. PMCid:PMC1552833
- Bafna PA, Balaraman R. Anti-ulcer and anti-oxidant activity of pepticare, a herbomineral formulation. Phytomedicine. 2005; 12(4):264-70. https://doi.org/10.1016/j.phymed.2003.12.009. PMid:15898703
- 70. Dehpour AR, Zolfaghari ME, Samadian T, Vahedi Y. The protective effect of liquorice components and their derivatives against gastric ulcer induced by aspirin in rats. J Pharm and Pharmacol. 1994; 46(2):148-9. https://doi. org/10.1111/j.2042-7158.1994.tb03760.x. PMid:8021806
- Rybczyński JJ, Davey MR, Mikuła A, editors. The Gentianaceae-volume 2: biotechnology and applications. Springer Berlin Heidelberg; 2015. https://doi. org/10.1007/978-3-642-54102-5
- 72. Niiho Y, Yamazaki T, Nakajima Y, Yamamoto T, Ando H, Hirai Y, et al. Gastroprotective effects of bitter principles isolated from Gentian root and Swertia herb on experimentally-induced gastric lesions in rats. J Nat Med. 2006; 60(1):82-8. https://doi.org/10.1007/s11418-005-0014-2
- Navarrete A, Trejo-Miranda JL, Reyes-Trejo L. Principles of root bark of *Hippocratea excelsa* (Hippocrataceae) with gastroprotective activity. J Ethnopharmacol. 2002; 79(3):383-8. https://doi.org/10.1016/S0378-8741(01)00414-7
- 74. Alanis AD, Calzada F, Cervantes JA, Torres J, Ceballos GM. Antibacterial properties of some plants used in Mexican traditional medicine for the treatment of gastrointestinal disorders. J Ethnopharmacol. 2005; 100(1-2):153-7. https:// doi.org/10.1016/j.jep.2005.02.022 PMid:16005589
- 75. Matsuda H, Li Y, Murakami T, Yamahara J, Yoshikawa M. Protective effects of oleanolic acid oligoglycosides on ethanol-or indomethacin-induced gastric mucosal lesions in rats. Life Sci. 1998; 63(17):PL245-50. https://doi.org/10.1016/S0024-3205(98)00426-3
- 76. Saito H, Lee Y, Takagi K, Shibata S, Shoji J, Kondo N. Pharmacological studies of *Panacis japonici* rhizoma. Chem Pharm Bull. 1977; 25(5):1017-25. https://doi.org/10.1248/ cpb.25.1017. PMid:264170

- 77. Mehta VB, Sharma VJ, Shaikh MF, Amin PD, Sathaye S. Evaluation of Antioxidant and immunomodulatory activity of *Lagenaria vul-garis*. Int J Res Pharm Sci. 2011; 2(3):393-8.
- Choudhary MK, Bodakhe SH, Gupta SK. Assessment of the antiulcer potential of *Moringa oleifera* root-bark extract in rats. J Acupunct Meridian Stud. 2013; 6(4):214-20. https:// doi.org/10.1016/j.jams.2013.07.003. PMid:23972244
- 79. Banerjee D, Maity B, Bauri AK, Bandyopadhyay SK, Chattopadhyay S. Gastroprotective properties of *Myristica malabarica* against indometacin-induced stomach ulceration: A mechanistic exploration. J Pharm Pharmacol. 2007; 59(11):1555-65. https://doi.org/10.1211/jpp.59.11.0014. PMid:17976268
- Maity B, Chattopadhyay S. Natural antiulcerogenic agents: An overview. Curr Bioact Compd. 2008; 4(4):225-44. https://doi.org/10.2174/157340708786847889
- Yeo M, Kim DK, Cho SW, Hong HD. Ginseng, the root of Panax ginseng CA Meyer, protects ethanol-induced gastric damages in rat through the induction of cytoprotective heatshock protein 27. Dig Dis Sci. 2008; 53(3):606-13. https:// doi.org/10.1007/s10620-007-9946-6. PMid:17763949
- Sun Y. Structure and Biological Activities of the Polysaccharides from the Leaves, Roots and Fruits of *Panax Ginseng* CA Meyer: An Overview. Carbohydr Polym. 2011; 85:490-9. https://doi.org/10.1016/j.carbpol.2011.03.033
- Debashish B, Sayanti B, Bandyopadhyay SK, Subrata C. Picrorhiza kurroa-phytochemical and pharmacological evaluation. J N Govil Ed. Standardization of herbal/ Ayurvedic formulations. 2009; 24:69-89.
- 84. Ali MZ, Janbaz KH, Mehmood MH, Gilani AH. Antidiarrheal and antispasmodic activities of *Polygonum bistorta* rhizomes are mediated predominantly through K+ channels activation. Bangladesh J Pharmacol. 2015; 10(3):627-34. https://doi.org/10.3329/bjp.v10i3.23714
- Al-Said MS, Ageel AM, Parmar NS, Tariq M. Evaluation of mastic, a crude drug obtained from *Pistacia lentiscus* for gastric and duodenal anti-ulcer activity. J Ethnopharmacol. 1986; 15(3):271-8. https://doi.org/10.1016/0378-8741(86)90165-0
- Paul AS, Islam A, Yuvaraj P. Anti-Helicobacter pylori and cytotoxic activity of detoxified root of *Plumbago auriculata*, *Plumbago indica* and *Plumbago zeylanica*. J Phytopharm. 2013; 2(3):4-8. https://doi.org/10.31254/phyto.2013.21302
- Ittiyavirah SP, Paul AS. Gastroprotective effect of plumbagin and ethanolic extract of *plumbaginales* in experimentallyinduced ulcer. J HerbMed Pharmacol. 2016; 5(3):928.
- De Pasquale R, Germano MP, Keita A, Sanogo R, Iauk L. Antiulcer activity of *Pteleopsis suberosa*. J Ethnopharmacol. 1995; 47(1):55-8. https://doi. org/10.1016/0378-8741(95)01256-D

- 89. Germano MP, Sanogo R, Guglielmo M, De Pasquale R, Crisafi G, Bisignano G. Effects of *Pteleopsis suberosa* extracts on experimental gastric ulcers and *Helicobacter pylori* growth. J Ethnopharmacol. 1998; 59(3):167-72. https://doi. org/10.1016/S0378-8741(97)00109-8
- 90. Süleyman HA, Demirezer LO, Kuruüzüm-Uz A, Akçay FA. Gastroprotective and antiulcerogenic effects of *Rumex patientia* L. extract. Die Pharmazie. 2002; 57(3):204-5. PMid: 11933853
- 91. Süleyman HA, Kuruüzüm-Uz A. Effects of *Rumex patientia* root extract on indomethacine and ethanol induced gastric damage in rats. Die Pharmazie. 2004; 59(2):147-9. PMid: 15025185
- 92. De La Lastra CA, Martin MJ, Marhuenda E. Gastric antiulcer activity of silymarin, a lipoxygenase inhibitor, in rats. J Pharm Pharmacol. 1992; 44(11):929-31. https://doi. org/10.1111/j.2042-7158.1992.tb03239.x. PMid:1361540
- 93. Yamahara J, Mochizuki M, Fujimura H, Takaishi Y, Yoshida M, Tomimatsu T, *et al.* Antiulcer action of *Sophora flavescens* root and an active constituent. I. J Ethnopharmacol. 1990; 29(2):173-7. https://doi.org/10.1016/0378-8741(90)90053-V
- 94. Kyogoku K, Hatayama K, Yokomori S, Saziki R, Nakane S, Sasajima M, et al. I. Anti-ulcer effect of isoprenyl flavonoids. II. Synthesis and anti-ulcer activity of new chalcones related to sophoradin. Chem Pharm Bull. 1979;27(12):2943-53. https://doi.org/10.1248/cpb.27.2943. PMid:540332
- 95. Petersson J, Phillipson M, Jansson EA, Patzak A, Lundberg JO, Holm L. Dietary nitrate increases gastric mucosal blood flow and mucosal defense. Am J Physiol Gastrointest Liver Physiol. 2007; 292(3):G718-24. https://doi.org/10.1152/ ajpgi.00435.2006. PMid:17082222
- 96. Goel RK, Pathak NK, Biswas M, Pandey VB, Sanyal AK. Effect of lapachol, a naphthaquinone isolated from *Tectona grandis*, on experimental peptic ulcer and gastric secre-

tion. J Pharm Pharmacol. 1987; 39(2):138-40. https://doi. org/10.1111/j.2042-7158.1987.tb06962.x. PMid:2882001

- 97. Kim JE, Lee JY, Kang MJ, Jeong YJ, Choi JA, Oh SM, Lee KB, Park JH. Withaferin A inhibits *Helicobacter pylori*induced production of IL-1β in dendritic cells by regulating NF-κB and NLRP3 inflammasome activation. Immune Network. 2015; 15(6):269-77. https://doi.org/10.4110/ in.2015.15.6.269. PMid:26770181. PMCid:PMC4700403
- 98. Umadevi M, Rajeswari R, Rahale CS, Selvavenkadesh S, Pushpa R, Kumar KS, Bhowmik D. Traditional and medicinal uses of *Withania somnifera*. Pharma Innov. 2012; 1(9, Part A):102-10.
- 99. Singh N, Bhalla M, de Jager P, Gilca M. An overview on ashwagandha: a Rasayana (rejuvenator) of Ayurveda. Afr J Tradit Complement Altern Med. 2011; 8(5S):208-13. https://doi.org/10.4314/ajtcam.v8i5S.9. PMid:22754076. PMCid:PMC3252722
- 100. Yamahara J, Hatakeyama S, Taniguchi K, Kawamura M, Yoshikawa M. Stomachic principles in ginger. II. Pungent and anti-ulcer effects of low polar constituents isolated from ginger, the dried rhizoma of *Zingiber officinale* Roscoe cultivated in Taiwan. The absolute stereostructure of a new diarylheptanoid. Yakugaku Zasshi. 1992; 112(9):645-55. https://doi.org/10.1248/yakushi1947.112.9\_645. PMid:1469612
- 101.Wahida B, Abderrahman B, Nabil C. Antiulcerogenic activity of *Zizyphus lotus* (L.) extracts. J Ethnopharmacol. 2007; 112(2):228-31. https://doi.org/10.1016/j.jep.2007.02.024. PMid:17408894
- 102.Bakhtaoui FZ, Lakmichi H, Megraud F, Chait A, Gadhi CE. Gastro-protective, anti-*Helicobacter pylori* and, antioxidant properties of *Moroccan Zizyphus* lotus L. J Appl Pharm Sci. 2014; 4(10):81-7. https://doi.org/10.7324/ JAPS.2014.401015