

# A critical review on the plants used for the treatment of ulcer in Kerala

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Article

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## ABSTRACT

Peptic ulcer disease and its complications remain the cause of significant morbidity worldwide, representing a major burden for health care resources. Although potent anti-ulcer drugs are available, most of them produce several toxicities, thus emphasizing the need to search for new alternatives. As high as 80% of the world population depends on plant-derived medicines for the first line of primary health care, reinforcing the theory that plant extracts can be good sources of new drugs. This review focuses to consolidate the evidence-based information on antiulcer plants used in Kerala accumulated in databases (Google Scholar, PubMed, Scopus, Science Direct and Web of Science) upto January 2019. Plants like *Acacia nilotica* L., *Achyranthes aspera* Linn., *Aegle marmelose* L., *Alillum sativum* L., *Aloe barbadensis* Miller, *Annona muricata* L., *Bacopa monnieri* Linn., *Carica papaya* Linn., *Centella asiatica* Linn., *Curcuma longa* Linn., *Elatoria cardamom* L., *Hibiscus rosa-sinensis* L., *Mangifera indica* L., *Mimosa pudica* L., *Moringa oleifera* L., *Ocimum sanctum* Linn., *Piper nigrum* L., *Phyllanthus embilica* L., *Terminalia chebula* Retz., and *Zingibera officinalis* Roscoe. are available in Kerala, reported with antiulcer property. The secondary metabolites present in the plants like alkaloids, flavanoids, terpenoids, tannins, glycosides, terpenes, and resins also have an important role in reliving ulcers due to its antisecretory, antioxidant, and cytoprotective properties. This review summarizes the botany, ethnopharmacology, phytochemistry and mechanism of action of antiulcer plants.

**Key Words:** Alkaloids, antiulcer, flavanoids; terpenoids.

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## INTRODUCTION

Peptic ulcer is a group of ulcerative disorders that occur in the areas of the upper gastrointestinal tract that are exposed to acid-pepsin secretions. The most common causes of peptic ulcer are *H. pylori* infection and NSAID use. It can affect one or all layers of the stomach or duodenum. The two most common types of peptic ulcer are gastric ulcer and duodenal ulcer<sup>[1]</sup>. Duodenal ulcer is 2-4 times more prevalent than gastric ulcer type<sup>[2]</sup>. Gastric ulcers occur in the stomach, characterized by pain and are common in older age group. Nausea, vomiting and weight loss are the other symptoms of gastric ulcers. Although patients with gastric ulcers have normal or diminished acid production, yet ulcers may occur even in complete absence of acid<sup>[3]</sup>. Duodenal ulcers are found at the beginning of small intestine and are characterized by severe pain with burning sensation in upper abdomen that awakens patients from sleep. Generally, pain occurs when the stomach is empty and relieves after eating. Duodenal ulcer is more common in younger individuals and predominantly affects males<sup>[4]</sup>.

## 2. Prevalence of peptic ulcer

Peptic ulcer is one of the world's major gastrointestinal disorders and affecting 10% of the world population<sup>[5]</sup>. About 19 out of 20 peptic ulcers are duodenal. It is estimated that 15000 deaths occur each year as a consequence of peptic ulcer. The annual incidence estimates of peptic ulcer hemorrhage and perforation were 19.4–57 and 3.8–14 per 100,000 individuals, respectively. The average 7-day recurrence of hemorrhage was 13.9% and the average long-term recurrence of perforation was 12.2%<sup>[6]</sup>. According to the latest WHO data published in 2017 peptic ulcer disease deaths in India reached 57,658 or 0.66% of total deaths. The age adjusted death rate is 5.79 per 100,000 of population ranks India 53 in the world<sup>[7]</sup>. In the Indian pharmaceutical industry, antacids and antiulcer drugs share 6.2 billion rupees and occupy 4.3% of the market share<sup>[8]</sup>.

Peptic ulcer occurs in the gastrointestinal tract which is exposed to gastric acid and pepsin i.e. the stomach and duodenum. The etiology of peptic ulcer is not clearly known. It results probably due to the imbalance between aggressive and protective factors in the stomach<sup>[9]</sup>. Aggressive factors

include *Helicobacter pylori*, hydrochloric acid (HCl), pepsins, nonsteroidal anti-inflammatory drugs (NSAIDs), bile acids, ischemia, hypoxia, smoking and alcohol, while defensive factors include bicarbonate, mucus layer, mucosal blood flows, prostaglandins (PGs) and growth factors<sup>[10]</sup>.

In this context, the use of medicinal plants has gained interest of many researchers. Natural products are in continuous expansion all over the world and became the most attractive source of new drug and relatively less expensive, safe to use even at higher doses for the treatment and prevention of many diseases<sup>[11]</sup>. According to World Health Organization, medicinal plants would be the best source to obtain a variety of drugs. Therefore, such plants should be investigated to better understand their properties, safety and efficacy<sup>[12]</sup>. In order to achieve this aim, various sources like ancient traditional books, journals, libraries and internet were explored for each of the medicinal plants for peptic ulcers and all retrieved articles were evaluated to achieve clinical evidence for their efficacy and possible mechanisms. There by this review aims to summarize the antiulcer activity of medicinal plants found in Kerala.

### 3. Antiulcer plants (Table 1)

#### 3.1. *Acacia nilotica* (L.)

*A. nilotica* belongs to the family of Mimosaceae. It is commonly known as “babul tree” and locally called as karuvelam. *A. nilotica* is commonly found all over India in dry and sandy localities, this species occurs only in Travancore district in low altitude dry forests where it attains larger dimensions<sup>[13]</sup>. The bark, leaves pods and flowers have traditionally been proved for various ailments like cancer, cold, congestion, cough, diarrhea, dysentery, fever, hypertension, hemorrhoid, ophthalmic, sclerosis, small pox, tuberculosis, leprosy, bleeding piles, leucoderma and menstrual problems<sup>[14]</sup>. Pharmacologically reported activities include anti-inflammatory<sup>[15]</sup>, antioxidant<sup>[16]</sup>,

antidiarrhoeal<sup>[17]</sup>, antihypertensive and antispasmodic<sup>[18]</sup>, antibacterial<sup>[19]</sup>, anthelmintic<sup>[20]</sup>, antifungal<sup>[21]</sup>, antiplatelet aggregatory<sup>[22]</sup>, analgesic<sup>[15]</sup>, antipyretic<sup>[23]</sup>, antiviral<sup>[24]</sup>, anticancer<sup>[25]</sup> antidiabetic<sup>[26]</sup> and acetyl cholinesterase (AChE) inhibitory<sup>[27]</sup>. Phytochemically tannins 25%-60%, mucilage 20%-30%, flavonoids, resins, saponins & alkaloids have been isolated from different parts of *A. nilotica*<sup>[28]</sup>. The gastroprotective effect of *A. nilotica* young seedless pod extract was evaluated for antiulcer activity. Different extracts like ethanolic, 50% hydroethanolic (50:50), 70% hydroethanolic (70:30) and aqueous of young seedless pods were examined in pylorus ligation, swimming stress and NSAID induced gastric ulcers in wistar rats.

The hydroethanolic extracts 70% and 50% at the dose of 100 and 200 mg/kg significantly ( $P \leq 0.05$ ) reduced gastric volume, free acidity, total acidity, ulcer index and increased the mucin content. Further the 70% hydroethanolic extract also showed better protection as compared to 50% hydroethanolic extract, which was comparable to cimetidine treatment. Whereas, ethanolic and aqueous extracts were not found to be effective in reducing pylorus ligation-induced gastric ulceration. In swimming stress and NSAID induced ulcer models the 70% hydroethanolic extract at 100 and 200 mg/kg significantly ( $P \leq 0.05$ ) decreased the ulcer index and increased the mucin content. Similar protection was also observed after treatment with diazepam<sup>[28]</sup>. From the study they concluded that the hydroethanolic extract of young seedless pods of *A. nilotica* has antiulcer activity in pylorus ligation, swimming stress and indomethacin induced ulcer rat models. Moreover the 70% hydroethanolic extract contains more amounts of phenolic components and it shown high antiulcer activity, which indicates that the phenolic component of the extract was found to be responsible for the activity of the extracts<sup>[28]</sup>.

**Table 1:-** Antiulcer plants in Kerala

S.I. No	Plant	Plant part used	Extract	Dose (mg/kg)	Standard	Mechanism of action
1	<i>Acacia nilotica</i>	Seedless pod	Ethanolic and hydroethanolic extract	100 and 200	Cimetidine 10 mg/kg	Antisecretory, mucosal defense mechanism, reduce gastric motility, antioxidant <sup>[28]</sup>
2	<i>Achyranthes aspera</i>	Leaf	Ethanolic extract	200, 400, and 600	Omeprazole 10 mg/kg	Antisecretory and antioxidant <sup>[29]</sup>
3	<i>Aegle marmelos</i>	Leaf	Ethanolic extract	200 and 400	Omeprazole 20 mg/kg	Cytoprotective <sup>[42]</sup>
4	<i>Allium sativum</i>	Garlic bulb	Aqueous extract	200, 300 and 400	Ranitidine 50 mg/kg	Antioxidant, anti-inflammatory, immune cell modulatory and calcium modulatory actions <sup>[53]</sup>
5	<i>Aloe barbadensis</i>	Aloe vera powder	Powder water	200	Omeprazole 20 mg/kg	Cytoprotective, <sup>[60]</sup> anti-inflammatory, <sup>[211]</sup> gastric mucus production, <sup>[60]</sup> antioxidant, <sup>[60]</sup> anti secretary, <sup>[60]</sup>
6	<i>Annona muricata</i>	Leaf	Hydroalcoholic extract	50, 100, 200 and 400	Omeprazole 30 mg/kg	By mediating the synthesis of prostaglandins, <sup>[73]</sup> decreases the gastric secretion and motility and increases blood flow <sup>[212]</sup>

7	<i>Bacopa monnieri</i>	Whole plant	aqueous, ethanolic and carbon tetrachloride extracts	200 and 400	Omeprazole 20 mg/kg	Cytoprotective, Antioxidant, spasmolytic, increase gastric mucosal production, increases prostaglandin production <sup>[82]</sup>
8	<i>Carica papaya</i>	Unripe fruit, seed	Hydro alcoholic extract	250 and 500	Rabeprazole 20 mg/kg	Antisecretory, <sup>[98]</sup> Cytoprotective, <sup>[96]</sup>
9	<i>Centella asiatica</i>	Leaf	Ethanolic extract	100,200 and 400	Omeprazole 20 mg/kg	Antioxidant, anti-inflammatory, reduction in gastric motility, <sup>[106]</sup>
10	<i>Curcuma longa (curcumin)</i>	Compound	Curcumin	5,10,20,40, 80 and 100	Omeprazole 20 mg/kg	Antisecretory, cytoprotective, antioxidant, and anti-inflammatory <sup>[116]</sup>
11	<i>Elettaria cardamomum</i>	Dried fruits	Methanolic extract	100, 300 and 500	Ranitidine 50 mg/kg	Decrease in gastric motility and inhibition of production of some products of 5-lipoxygenase pathway <sup>[118]</sup>
12	<i>Hibiscus rosa-sinensis</i>	Leaf	Methanolic extract	200 and 400	Omeprazole 50 mg/kg	Antisecretory activity <sup>[124]</sup>
13	<i>Mangifera indica</i>	Seed kernel	Ethanolic extract	100, 200 and 400	Ranitidine 32 mg/kg	Antisecretory activity <sup>[140]</sup> Cytoprotective action by increasing the mucus secretion <sup>[214]</sup> , gastroprotective properties in an experimental rat model by reducing gastric juice volume and acidity. <sup>[215]</sup>
14	<i>Mimosa pudica</i>	Leaf	Ethanolic extract	100	Ranitidine 20 mg/kg	Cytoprotective, Antisecretory, Antiulcer activity is due to the flavonoids and quercetin. Quercetin may increase the amount of natural glycoproteins, the most important proteins in the gastric mucosa, which may in turn facilitate the defense against an aggressive action. Quercetin also stimulates the synthesis of cyclooxygenase and of local prostaglandins. <sup>[142]</sup>
15	<i>Muringa oleifera</i>	Root, bark	Ethanolic extract	150,350 and 500	Omeprazole 30 mg/kg	Cytoprotective, Antisecretory, Increased mucus secretion <sup>[150]</sup>
16	<i>Ocimum sanctum</i>	Leaf	Aqueous and ethanolic extract	100, 200 and 400	Ranitidine 20 mg/kg	Antisecretory, Cytoprotective <sup>[165]</sup>
17	<i>Piper nigrum</i>	Fruit	Aqueous extract	500		Inhibition of gastric motor activity, Stimulation of prostaglandin synthesis, Mucosal defense mechanism <sup>[179]</sup>
18	<i>Embilica officinalis</i>	Dried Fruit	Hot and cold water extract	270	Ranitidine 27mg/kg	It decreased the gastric motility there by decreased the gastric erosions, <sup>[191]</sup> . Decrease in the acid and pepsin secretion (antisecretory activity). Increase in the secretion of mucosal protective factors. Mucus secreted from the mucus neck cells covers the gastric mucosa thereby preventing physical damage and back diffusion of hydrogen ions <sup>[213]</sup> . It acts as antioxidant by decreasing the gastric gastric peroxidase activity and it could be due to the presence of Emblicanin A and B in its extract. <sup>[213]</sup> cytoprotective action
19	<i>Terminalia chebula</i>	Fruit	Methanolic extract	250 and 500	Omeprazole 20 mg/kg	Antisecretory, Cytoprotective <sup>[192]</sup>
20	<i>Zingiber officinale</i>	Root	Aqueous extract	200 and 400	Omeprazole 10 mg/kg	5-lipoxygenase inhibitory effect, <sup>[210]</sup> Antisecretory <sup>[216]</sup> , Increased mucin secretion <sup>[217]</sup>

### 3.2. *Achyranthes aspera L.*

*A. aspera* (Amaranthaceae) is commonly known as kadaladi, vankadaladi, valiyakadaladi. The plant is found in Kottayam, Kazargod, Trivandrum, Malapuram and Alapuzha district in dry deciduous forests and forest plantations, also in the plains<sup>[13]</sup>. Traditionally the plant has been used to treat fever especially for malarial

fever, dysentery, asthma, hypertension, and diabetes<sup>[29]</sup>. Pharmacologically reported activities include diuretic, anti-inflammatory, antifungal, abortifaciant, larvicidel, hypoglycemic, antifertility and anticancer<sup>[30]</sup>. The major phytochemical constituents like carbohydrates, sugars, alkaloids, saponins, flavonoids, tannins are present in

*A. aspera*<sup>[29]</sup>. The gastroprotective effect of *A. aspera* leaves were evaluated on pyloric ligation and ethanol induced ulcer model by Vijay *et al.*<sup>[29]</sup>. *A. aspera* leaves 200, 400 and 600 mg/kg ethanolic extract significantly reduced the ulcer index  $P \leq 0.05$  by 200 mg/kg,  $P \leq 0.01$  by 400 mg/kg, and  $P \leq 0.001$  by 600 mg/kg when compared to the ulcer control. In addition to this it also reduced the total acidity, free acidity, pH and gastric volume. The extent of gastro protection showed by the *A. aspera* extract 600 mg/kg was 59.55% and 35.58% respectively against pyloric ligation and ethanol induced ulceration when compared to the standard drug omeprazole 83.14% and 50.25% respectively. *A. aspera* exerts cytoprotective effect in addition to its gastric antisecretory activity that could be due to the presence of flavonoids and tannins responsible for its protective effect by maintaining an efficient gastric mucosal microvascular supply<sup>[29]</sup>.

### 3.3. *Aegle marmelose* L.

*A. marmelose* (Rutaceae), commonly known as koolakam, koovalam, vilvam, mavilavu. The plant chiefly grows throughout Kerala in dry, open forests on hills and plains at altitudes from sea level to around 1200m<sup>[13]</sup>. Traditionally, the unripe fruits are used as astringent, aid in digestion and stomach irritation. The half-ripe fruits are astringent, digestive and antidiarrheal. The ripe fruits are supposed to be more useful than the raw fruits and are used to prevent subacute and chronic dysentery<sup>[31]</sup>. Their leaves are traditionally used for the treatment of fever, abdominal pain, urinary troubles, heart palpitation, dysentery, dyspepsia, stomach pain, seminal weakness, vomiting and swellings<sup>[32]</sup>. Antioxidant<sup>[33]</sup>, hepatoprotective<sup>[34]</sup>, antidiabetic<sup>[35]</sup>, cardio protective<sup>[36]</sup>, antipyretic, anti-inflammatory, and analgesic<sup>[37]</sup>, antimicrobial<sup>[38]</sup>, antifungal<sup>[39]</sup>, antidyslipidemic<sup>[40]</sup>, anticancer<sup>[41]</sup>, and antiulcer<sup>[42]</sup>, are the pharmacologically reported activities. The antiulcer activity of 200 and 400 mg/kg ethanolic extract of *A. marmelose* leaves on rats were evaluated by Sharmin *et al.*<sup>[42]</sup>.

The ethanolic extract of *A. marmelose* leaves at 400 mg/kg body weight showed significant reduction in ulcer spots in the stomach when compared to the control. Moreover, administration of ethanolic extract of *A. marmelose* and standard drug omeprazole both produced highly significant ( $P \leq 0.001$ ) antiulcer effect compared to control group. Percentage protection of ulcer with 400 mg/kg body weight of ethanolic extract of *A. marmelose* was found to be 56.33% when compared to the standard antiulcer drug omeprazole (50.44%)<sup>[42]</sup>.

### 3.4. *Alillum sativum* L.

*A. sativum* (Liliaceae) is commonly known as garlic and locally known as veluthulli. This plant is a bulbous herb found in Idukki and Palakkad districts of

Kerala<sup>[13]</sup>. Traditionally, it has been used in reducing cholesterol, blood pressure, free radicle scavenger, anti-platelet activity, thromboxane inhibiting activity and cardioprotective<sup>[43]</sup>. Pharmacologically reported activities are antimicrobial, antioxidant<sup>[44]</sup>, antihypertensive<sup>[45]</sup>, cardioprotective<sup>[46]</sup>, anti-atherosclerotic<sup>[47]</sup>, antidiabetic<sup>[48]</sup>, cancer chemopreventive<sup>[49]</sup>, neuroprotective<sup>[50]</sup>, nephroprotective<sup>[51]</sup> and immunomodulatory<sup>[52]</sup>. Potentially active phytochemical constituents in this plant are alliin, allicin, allinase, ajoene, peroxidase, arginine, selenium, germanium and tellurium<sup>[43]</sup>. The antiulcer activity of aqueous extract of *A. sativum* in pyloric ligation induced peptic ulcer in rats was evaluated by Arunachala *et al.*<sup>[53]</sup>. The rats were treated with 200, 300, and 400 mg/kg of aqueous extract of *A. sativum* for 10 days and it reduced the gastric volume, total acidity and free acidity, ulcerative index, total calcium, thiobarbituric acid reactive substances, myeloperoxidase levels and increase in total protein and reduced glutathione level in a dose dependent manner. The 400 mg/kg of aqueous extract of *A. sativum* showed significant ( $P \leq 0.05$ ) ulcer protective effect when compared to the standard ranitidine treated group. It has been concluded that the ulcer protective effect of aqueous extract of *A. sativum* may be due to its antioxidant, anti-inflammatory, immunosuppressive and anti-secretory action. Therefore, the aqueous extract of *A. sativum* may be a potent herbal candidate for the treatment of peptic ulcers<sup>[53]</sup>.

### 3.5. *Aloe barbadensis* Miller

*A. barbadensis* is a perennial drought resisting herb belongs to the family Liliaceae. It is commonly known as *aloe vera* and locally known as kattarvazha, kattalai, Kattuvala, ghritakumari. This plant is found throughout Kerala<sup>[13]</sup>. Traditionally the plant is used to treat burns, allergic reactions, acid indigestions, ulcers, diabetes skin diseases, uterine tonic, blood purifier, dysentery, diarrhea, piles and inflammatory conditions. Pharmacologically reported activities are anti-aging<sup>[54]</sup>, antioxidant and immunomodulatory<sup>[55]</sup>, antibacterial, antifungal<sup>[56]</sup>, antiviral<sup>[57]</sup>, anti-mutagenic<sup>[58]</sup>, anti-diabetic<sup>[59]</sup>, and anti-ulcer<sup>[60]</sup>. The antiulcer effect of *aloe vera* was evaluated in non-steroidal anti-inflammatory drug induced peptic ulcers in albino rats by Sai *et al.*<sup>[60]</sup>. *A. barbadensis* 200 mg/kg showed antiulcer effect with mean ulcer index of  $20 \pm 1.79$  compared to the standard omeprazole treated group with mean ulcer index of  $10 \pm 1.96$ . *A. barbadensis* possessed cytoprotective effects and acid reducing effects like omeprazole<sup>[60]</sup>.

### 3.6. *Annona muricata* L.

*A. muricata* (Annonaceae) is commonly known as guanabana, graviola, prickly custard apple and locally known as cancer chakka, mullanjakka, mulluathi, mullathi. *A. muricata* trees are found throughout Kerala<sup>[13]</sup>.



Traditionally, *A. muricata* it has been used for fever, pain, respiratory and skin illness, internal and external parasites, bacterial infections, hypertension, inflammation, diabetes and cancer<sup>[61]</sup>. The pharmacologically reported activities are antimicrobial<sup>[62]</sup>, anti-inflammatory<sup>[63]</sup>, anti-protozoan<sup>[64]</sup>, antioxidant<sup>[65]</sup>, anxiolytic and anti-stress<sup>[66]</sup>, antitumoral<sup>[67]</sup>, antiulcer<sup>[68]</sup>, wound healing<sup>[69]</sup>, hepato-protective<sup>[70]</sup>, hypoglycemic<sup>[71]</sup>, and hypotensive activities<sup>[72]</sup>. The antiulcerogenic activity of the hydroalcoholic extract of leaves of *A. muricata* was evaluated in mice by Elizangela *et al.*<sup>[73]</sup>. The mice were treated with 50, 100, 200 and 400 mg/kg of hydroalcoholic extract of *A. muricata*. Gastric lesions were induced in mice by absolute ethanol, acidified ethanol and indomethacin. In ethanol induced ulcer model hydroalcoholic extract of *A. muricata* pretreatment at doses of 50, 100, 200 and 400 mg/kg before the administration of absolute ethanol produced a significant reduction in lesion area by 92.89%, 94.13%, 97.79% and 96.55%, respectively. From this detail it has been found that the hydroalcoholic extract of *A. muricata* at a dose of 200 and 400 mg/kg was more effective than the standard drug omeprazole (30 mg/kg p.o.), which showed a significant reduction in gastric lesion areas of 95.79%. Whereas in indomethacin induced ulcer model hydroalcoholic extract of *A. muricata* at 200 mg/kg proved to be the most effective dose, by reducing the incidence of ulcers by 94.13%. Hydroalcoholic extract of *A. muricata* at 400 mg/kg also decreased the incidence of ulcers significantly by 91.67%. Omeprazole (30 mg/kg) reduced lesion rates by 96.82% compared with the ulcer control group. In acute gastric lesions induced study, the mice by acidified ethanol pretreatment with hydroalcoholic extract of *A. muricata* at doses of 50, 100, 200 and 400 mg/kg, showed a reduction in lesions of 47.69%, 76.23%, 80.20% and 93.22%, respectively. At a dose of 400 mg/kg, hydroalcoholic extract *A. muricata* was as effective as the standard drug (omeprazole), which reduced the ulcer area by 93.22%. The study confirmed that the gastroprotective action of *A. muricata* leaves and that this activity is modulated or mediated by the synthesis of prostaglandins, thereby determining the phytotherapeutic potential of this species to treat stomach ulcers and gastritis<sup>[73]</sup>.

### 3.7. *Bacopa monnieri* L.

*B. monnieri* (Scrophulariaceae) is commonly known as bacopa, thyme leaved gratiola and locally known as brahmi, neerbrahmi. This plant is found throughout Kerala<sup>[13]</sup>. Traditionally it has been used to improve memory and intellect, anxiety, poor cognition and lack of concentration, as a diuretic and as an energizer for the nervous system and the heart. Specific uses include treatment of asthma, insanity and epilepsy. The plant has been utilized extensively as a nootropic, digestive aid and to improve learning and respiratory function<sup>[74]</sup>. Pharmacologically reported activities are sedative and tranquillizer<sup>[75]</sup>, cognition<sup>[76]</sup>, antioxidant<sup>[77]</sup>, antidepressant<sup>[78]</sup>, antianxiety<sup>[79]</sup>, adaptogenic<sup>[80]</sup> and

gastrointestinal disorders<sup>[81]</sup>. The antiulcerogenic activity of *B. Monnieri* on ethanol-induced gastric ulcer model was evaluated by comparing the efficacy of 200 and 400 mg/kg of aqueous, ethanolic and carbon tetrachloride extracts<sup>[82]</sup>. The histopathological results and microscopic damage scores of the treated animals with aqueous and carbon tetrachloride extracts of *B. monnieri* exhibited moderate to poor protection against gastric ulcers when compared with treatment with standard drug (Omeprazole). On the other hand, the ethanolic extract of *B. monnieri* (200 and 400 mg/kg b.w.) potentially regulated the inflammatory response that correspond to omeprazole (20 mg/kg b.w.) as evidenced by reduced ulcer index and microscopic score along with the results of histopathological evaluation. It has been reported that flavonoids and phenols are present in the three extracts. The presence of high flavonoid and phenolic contents may favor the ethanolic extract of *B. monnieri* to possess significant protective effect against ulcer when compared with other two extracts. Pretreatment with both doses (200 and 400 mg/kg) of all three extracts (except carbon tetrachloride extract of *B. monnieri* of 200 mg/kg) showed significant result ( $P \leq 0.01$ ) for UI value when compared with ulcer control. Both aqueous and carbon tetrachloride extracts of *B. monnieri* showed significant difference ( $P \leq 0.01$ ) in UI values when compared with the reference drug (omeprazole, 20 mg/kg). The ethanolic extract of *B. monnieri* (400 mg/kg) showed significant protection against gastric ulcer same as omeprazole (20 mg/kg b.w.)<sup>[82]</sup>.

### 3.8. *Carica papaya* L.

*C. papaya* belongs to the family Caricaceae. It is locally known as papaya, kappalanga, karmmoose, kappanga, ampapaya. This herbacious tree is found throughout Kerala<sup>[13]</sup>. Traditionally it has been used as antihypertensive, wound healing, anti-inflammatory, anthelmintic and antiulcer<sup>[83]</sup>. Pharmacologically reported activities are antioxidant<sup>[84]</sup>, antihypertensive<sup>[85]</sup>, anti-inflammatory<sup>[86]</sup>, antimicrobial<sup>[87]</sup>, antifungal<sup>[88]</sup>, histaminergic<sup>[89]</sup>, diuretic<sup>[90]</sup>, anti-amoebic<sup>[91]</sup>, anti-tumour and immunomodulatory<sup>[92]</sup>, anthelmintic<sup>[93]</sup>, antimalarial<sup>[94]</sup>, hypoglycemic<sup>[95]</sup>, antiulcer<sup>[96]</sup> and anti-sickling<sup>[97]</sup>. Papain, chymopapain, pectin, carpain, carposide, carotinoids, vitamin C and antheraxanthin are pharmacologically important compound in this plant<sup>[83]</sup>. Ramandeep *et al.* evaluated the antiulcer activity of hydroalcoholic extract of unripe fruit of *C. papaya* in experimental rats. In this study they were used 250 and 500 mg/kg of hydroalcoholic extract of *C. papaya* in pylorus ligation and forced swimming induced ulcer models<sup>[98]</sup>. In both ulcer models, reduced ulcer index, gastric volume, free acidity and total acidity suggested that hydroalcoholic extract of *C. papaya* fruits have the antisecretory and antiulcerogenic activity. From the study it has been found that the hydroalcoholic extract of *C. papaya* 250 mg/kg showed decreased number of erosions in mucosa but still there is inflammation with

areas of haemorrhage. Further there was a decreased extent of gastric mucosal rupture. Whereas 500 mg/kg effectively decreased the epithelial cell loss, gastric lesions and haemorrhage<sup>[98]</sup>.

### 3.9. *Centella asiatica* L.

*C. asiatica* (Apiaceae) is commonly known as gotu kola, Indian penny – wort, pohekula, sadeleaf and locally known as kodangal, kudakan, mutthil, vellara. *C. asiatica* is a prostrate herb found throughout Kerala in wet places of the plain and deciduous forest<sup>[13]</sup>. Traditionally it has been used as a best herb for improving memory and intellect. It also used in CNS disorders like epilepsy, schizophrenia and cognitive dysfunction, renal stones, leprosy and skin diseases, anorexia and asthma. In other traditional systems, it has been additionally used in the management of diarrhoea, cholera, measles, jaundice, leukorrhoea, haematemesis, hepatitis, urethritis, toothache, syphilis, smallpox, neuralgia, rheumatism, toothache and as an antipyretic, analgesic and anti-inflammatory. Poultices have been used to treat contusions, closed fractures, sprains and furunculosis<sup>[99]</sup>. Pharmacologically reported activities include management of fibroblast proliferation and collagen synthesis<sup>[100]</sup>, antioxidant activity<sup>[101]</sup>, antiulcer<sup>[102]</sup>, anticancer<sup>[103]</sup>, anti-bacterial activity<sup>[104]</sup> and anti-inflammatory activity<sup>[105]</sup>. The roots are rich in amino acids, especially aspartic, glutamic, serine, threonine, alanine, lysine and histidine<sup>[99]</sup>.

The antiulcer activity of *C. asiatica* leaves extract against ethanol induced gastric mucosal injury in rats was evaluated by Abdulla *et al.*<sup>[106]</sup>. Adult Sprague Dawley rats treated orally with carboxymethyl cellulose (CMC) solution (ulcer control group), Omeprazole 20 mg/kg (reference group), and 100, 200 and 400 mg/kg *C. asiatica* leaf extract in CMC solution (experimental groups) for the experiment. *C. asiatica* leaf extract showed a dose dependent reduction in the gastric ulcer, edema and leucocytes infiltration of mucosal layers when compared to the control. The protection was most prominent at a dose 400 mg/kg of leaves extract. From the study it has been found that the mechanism of antiulcer activity may be due to antioxidant, anti-inflammatory and also due to the reduction in the gastric motility<sup>[106]</sup>.

### 3.10. *Curcuma longa* L.

*C. longa* Linn. (Zingiberaceae) is commonly known as turmeric and locally known as manjal. This plant is a rhizomatous herb found throughout Kerala<sup>[13]</sup>. Traditionally it has been used for dressing wounds, treat bites, burns, acne, skin diseases, respiratory ailments, dental diseases, digestive disorders such as dyspepsia and acidity, indigestion, flatulence, ulcers, antioxidant, antifertility as well to alleviate the hallucinatory effects of hashish, and other psychotropic drugs<sup>[107]</sup>. Pharmacologically reported

activities are anti-inflammatory<sup>[108]</sup>, antioxidant<sup>[109]</sup>, chemopreventive and chemotherapeutic activity<sup>[110]</sup>, antiulcer<sup>[107]</sup>, anticoagulant<sup>[111]</sup>, antidiabetic<sup>[112]</sup>, antimicrobial<sup>[113]</sup> antifungal<sup>[114]</sup> and antiviral<sup>[115]</sup>. Phytochemical constituents in this plant are curcumin, demethoxycurcumin, bisdemethoxycurcumin, protein, fat, minerals, carbohydrates, phellandrene, sabinene, cineol, borneol, zingiberene, and sesquiterpenes<sup>[111]</sup>. Karolin conducted a comparative evaluation of the antiulcer activity of curcumin and omeprazole during acute phase of gastric ulcer. Results obtained showed that curcumin and omeprazole significantly decreased gastric lesion formation ( $P < 0.001$ ) in the gastric wall from  $33.15 \pm 3.899$  lesions/animal in control group to  $4.000 \pm 0.6602$  and to  $8.215 \pm 0.8787$  lesions/ animal in treated groups with curcumin and omeprazole, respectively. Therefore, the preventive index was re-corded  $85.75 \pm 2.851$  and  $71.71 \pm 2.697\%$  for curcumin and omeprazole treated group, respectively. It also reduced the plasma peroxide, gastric acidity and IL-6 whereas; gastric mucin content and VEGF level are increased. Curcumin exerts its anti-ulcer activity not only by affecting oxidative stress and total antioxidant capacity but also by inhibiting IL-6 secretion and preventing apoptosis. Furthermore, curcumin promotes gastric ulcer pre-vention/healing by induction of angiogenesis in the granular tissue of ulcers<sup>[116]</sup>.

### 3.11. *Elatoria cardamom* L.

*E. cardamom* belongs to the family of Zingiberaceae. It is commonly known as cardamom and locally known as ealakkaya, eallam, elam, elattari. This plant is found in Palakkad, Idukki, Kollam, Pathanamthitta, Malappuram, Kannur, Thiruvananthapuram, Thrissur and Wayanad districts of Kerala<sup>[13]</sup>. Traditionally it has been used for aromatic, cardiac, carminative, deodorant, digestive, diuretic, expectorant, purgative, stimulant, thirst reliever and tonic. It is also useful in asthma, burning sensation, cold and cough, diseases of bladder and kidney, flatulence, heart weakness, indigestion, scanty urine and piles<sup>[117]</sup>. Pharmacologically reported activities are anti-inflammatory, analgesic, insecticidal, anthelmintic, laxative, antiulcer, diuretic. Terpeneol, terpinene, cineol, limonene, sabinene are the phytochemical constituents in this plant<sup>[117]</sup>. The gastroprotective effect of cardamom was evaluated in the gastric lesions induced by aspirin, ethanol and pylorus by Jamal *et al.*<sup>[118]</sup>. Rats were treated with methanolic extract of cardamom, petroleum ether soluble fractions, petroleum ether insoluble fractions, essential oil and CMC<sup>[118]</sup>.

First, they conducted experiment on ethanol induced ulcer model, in that experiment Wistar rats were treated with methanolic extract (500, 300 and 100 mg/kg), Petroleum ether soluble fraction (50 mg/kg), petroleum ether insoluble fraction (450 mg/kg) and essential oil (50mg/kg) in order to determine the fraction containing most

active principle. The pretreatment with methanolic extract (500, 300 and 100 mg/kg) showed a dose dependent reduction in the severity of the lesions. The petroleum ether soluble and petroleum ether insoluble fractions showed significant inhibition of ulceration by 50% and 54.8%, respectively. Petroleum ether soluble fraction is found to be more active when compared to petroleum ether insoluble fractions and moreover petroleum ether soluble fraction at a dose 100 mg/kg produced sub maximal response. The essential oil was found to be more active than petroleum ether soluble fractions (73.3% and 50.0% inhibition, respectively). They found that the active principles in essential oil are responsible for gastro protective action. In addition to that, essential oil reduced 65% of the ulcer index<sup>[118]</sup>.

For their second experiment, aspirin induced ulcer models were used. In that animals were treated with methanolic extract (500 mg/kg) and its petroleum ether insoluble fraction (450 mg/kg) and petroleum ether soluble fractions (50, 37.5, 25 and 12.5 mg/kg), essential oil (12.5 mg/kg) and ranitidine (50 mg/kg). All the fractions showed significant inhibition of ulceration. Petroleum ether soluble fraction was found to be more active than essential oil and ranitidine. Thus, they concluded that constituents other than essential oil present in petroleum ether soluble fractions are also involved in the gastroprotective action. However, it significantly inhibited the ulcer formation (71.7%) in aspirin induced gastric ulceration in Shay rats. The ulcer index (mm) in the control and PS-treated rats were  $1.06 \pm 0.07$  and  $0.30 \pm 0.04$ , respectively<sup>[118]</sup>.

Finally, they were used pyloric ligation induced ulcer models treated with CMC (10 ml/kg), ranitidine (50 mg/kg), methanolic extract (500 mg/kg) and petroleum ether soluble fractions (50 mg/kg). In that experiment they found that pretreatment with ethanolic extract (500 mg/kg) and petroleum ether soluble fractions (50 mg/kg) did not have any significant effect on the gastric ulcers induced by pylorus ligation. On the basis of these findings, they came to a conclusion that, gastroprotective action of petroleum ether soluble fractions and essential oil are due to the inhibition of the overproduction of some products of the 5-lipoxygenase pathways and also due to the decrease in the gastric motility and further studies were needed to test this hypothesis<sup>[118]</sup>.

### 3.12. *Hibiscus rosa-sinensis*

*H. rosa* (Malvaceae) is commonly known as Shoe flower and locally known as ayamparathi, chembarathi. This plant is an annual or perennial herbaceous bush found throughout Kerala<sup>[13]</sup>. Traditionally the leaves and flowers are observed to be promoters of hair growth and aid in healing of ulcers. Flowers have been found to be effective in the treatment of arterial hypertension and to have significant antifertility effect<sup>[119]</sup>. Pharmacologically reported

activities are anti-spermatogenic and androgenic<sup>[120]</sup> anti-tumor<sup>[121]</sup>, anticonvulsant<sup>[122]</sup>, anti-diabetic<sup>[123]</sup>, antiulcer<sup>[124]</sup> and hair growth promoter<sup>[125]</sup>. Phytochemical constituents in this plant are anthocyanins and flavonoids, cyanidin-3,5-diglucoside, cyanidin-3-sophoroside-5-glucoside, quercetin-3,7-diglucoside, quercetin-3-diglucoside, a cyclopeptide alkaloid, cyanidin chloride, quercetin, hentriacontane and vitamins: riboflavin, ascorbic acid and thiamine have been reported<sup>[119]</sup>.

The antiulcer activity of methanolic extract of *H. rosa* leaves was evaluated by Srivastava *et al.*<sup>[124]</sup> using pylorus ligation induced ulcer model. In their experiment animals were treated with Sodium CMC, 0.3%, standard drug omeprazole (80 mg/kg), methanolic extract of *H. rosa* (200 and 400 mg/kg) respectively and the extracts showed a reduction in the parameters like volume of acid, free acidity, total acidity and ulcer score. The methanolic extract (400 mg/kg) showed highly significant ( $P \leq 0.001$ ) reduction whereas the methanolic extract (200 mg/kg) showed significant ( $P \leq 0.01$ ) reduction in all the parameters when compared with control<sup>[124]</sup>.

### 3.13. *Mangifera indica* L.

*M. indica* (Anacardiaceae) commonly known as mango tree and locally known as amaram, manga, mampazham, mavu and moochi. This tree is found throughout Kerala in evergreen and semi-evergreen forests<sup>[13]</sup>. Traditionally it has been used to treat diabetes, gastric disorders, asthma, mouth sores, bleeding hemorrhoids, lung hemorrhage, anemia, nerve disorders and cough<sup>[126]</sup>. Pharmacologically reported activities include anticancer,<sup>[127]</sup> anti-inflammatory<sup>[128]</sup>, antidiabetic<sup>[129]</sup>, antioxidant<sup>[130]</sup>, antibacterial<sup>[131]</sup>, antifungal<sup>[132]</sup>, anthelmintic<sup>[133]</sup>, gastro protective<sup>[134]</sup>, hepatoprotective<sup>[135]</sup>, immunomodulatory<sup>[136]</sup>, Anthelmintic<sup>[137]</sup>, Antiviral<sup>[138]</sup> and antihyperlipemic effects<sup>[139]</sup>. Pharmacologically important compounds like mangiferin, quercetin, catechin, ellagic acid, shikimic acid, friedeline,  $\alpha$ -amyrin,  $\beta$ - amyrin, gallic acid, ferulic acid, cinnamic acid, and vanilline have been reported<sup>[126]</sup>. The antiulcer activity of ethanolic extract of *M. indica* seed kernel using acid ethanol induced ulcer model was evaluated using acid ethanol induced ulcer model by Prabhu *et al.*<sup>[140]</sup>. In the study female albino rats of Wistar strains were treated with ethanolic extract of *M. indica* (100, 200 and 400 mg/kg b.w.) for 15 days. *M. indica* seed kernel (400 mg/kg) significantly ( $P \leq 0.05$ ) reduced the ulcer index, pH, total acidity, LPO and protein levels. Percentage ulcer protection was found to be 70% and it also acted as a good antioxidant<sup>[140]</sup>.

### 3.14. *Mimosa pudica* L.

*M. pudica* (Fabaceae) commonly known as sensitive plant, humble plant, touch me not and locally known as theendarmani, thottalvadi, thottavadi. This is a stout

stragling prostrate shrubby plant found throughout Kerala as a weed<sup>[13]</sup>. Traditionally it has been used in diseases due to corrupted blood and bile, billious fever, piles, jaundice, leprosy, ulcers, small pox<sup>[141]</sup>. Pharmacologically reported activities are anti-hyperglycemic, antidiarrheal, anti-convulsant and cytotoxic<sup>[141]</sup>. The ethanolic leaf extract of *M. pudica* was evaluated in rats by using ethanol, aspirin and pylorus ligation induced ulcer models by Elango *et al.*<sup>[142]</sup> *M. pudica* ethanolic extract 100 mg/kg body weight and ranitidine 20 mg/kg body weight for 5 days. It showed antiulcer activity in all the three models and significantly ( $P \leq 0.01$ ) reduced the ulcer incidence when compared to the control. It also showed a decrease in gastric volume, free acidity and total acidity in the animal groups treated with ethanolic extract. From the study it has been found that *M. pudica* the protection against ulcerations in aspirin and ethanol induced ulcer models indicate cytoprotective action by extracts of *M. pudica* and anti-secretory activity of the extracts was noticed in pylorus ligation induced ulcer model<sup>[142]</sup>.

Quercetin is pharmacologically important compound present in this plant, which has the power to prevent gastric mucosal lesions induced by various models (pylorus ligation, ethanol induced, cold restraint stress). It may also increase the amount of natural glycoproteins, the most important proteins in the gastric mucosa, which may in turn facilitate the defence against an aggressive action and stimulates the synthesis of cyclooxygenase and local prostaglandins. Other mechanisms proposed include inhibition of the gastric proton pump and lipoxygenase pathway, or inhibition of lipid peroxidation<sup>[142]</sup>.

### 3.15. *Moringa oleifera* L.

*M. oleifera* (Moringaceae) commonly known as drumstick tree and locally known as muringa, moringa and sigru. This tree is found throughout Kerala<sup>[13]</sup>. Traditionally it has been used for treating heart burn, diarrhea, malaria, diabetes, blood pressure, cholesterol, ulcer, inflammation, cold and urinary problems<sup>[143]</sup>. Pharmacologically reported activities are cardiac stimulant, anticancer<sup>[144]</sup>, antiepileptic, antipyretic, wound healing<sup>[145]</sup>, analgesic<sup>[146]</sup>, antispasmodic<sup>[147]</sup>, radioprotective<sup>[148]</sup>, antioxidant and hepatoprotective<sup>[149]</sup>, antihypertensive, diuretic, anti-diabetic, cholesterol lowering, antibacterial, neuroprotective and antifungal<sup>[143]</sup>. Phytochemical constituents in this plant are fatty acid, protein, vitamin C, calcium, terpenoids, flavonoids, lectins, amino acids, minerals, linoleic acid, oleic acid, palmitic acid and linoleic acid<sup>[143]</sup>.

Choudhary *et al.* assessed the antiulcer potential of *M. oleifera* root-bark extract in albino Wistar rats using ethanol-induced and pylorus ligation-induced gastric ulceration by treating with three different doses of the extract (150, 350, and 500 mg/kg) for 15 consecutive days. The

350 and 500 mg/kg of *M. oleifera* significantly ( $P \leq 0.01$ ) decreased the ulcer index as compared to the control group. The percentage protections against gastric ulcers were 82.58%, 85.13%, and 86.15% at the doses of 150, 350, and 500 mg/kg, respectively, in pylorus-ligated ulcer model and 55.75%, 59.33%, and 78.51%, respectively, in ethanol-induced ulcer model. It also reduced the free acidity, total acidity, and ulcer index and increased the pH of gastric content compared with the control group.<sup>[150]</sup>

### 3.16. *Ocimum sanctum* L.

*O. sanctum* (Lamiaceae) commonly known as Basil, Sacred basil, holy basil and locally known as govindapushpam, krishnathulasi, thulasi, thrithavu, karuthathrithavu. This plant is a subshrub found throughout Kerala<sup>[13]</sup>. Traditionally it has been used for common colds, headaches, stomach disorders, inflammation, heart disease, various forms of poisoning and malaria<sup>[151]</sup>. Pharmacologically reported activities are antidiabetic, hypolipdemic and antioxidant<sup>[152]</sup>, cardioprotective activity<sup>[153]</sup>, wound healing<sup>[154]</sup>, radioprotective<sup>[155]</sup>, gastroprotective<sup>[156]</sup>, anti-microbial<sup>[157]</sup>, immunomodulatory<sup>[158]</sup>, analgesic, antipyretic and anti-inflammatory<sup>[159]</sup>, sexually transmitted diseases<sup>[160]</sup>, anti-fertility<sup>[161]</sup>, anthelmintic<sup>[162]</sup>, anticancer<sup>[163]</sup>, thyroid activities<sup>[164]</sup>. Phytochemical constituents in this plant are carvacrol, caryophyllene, eugenol, linalool, urosolic acid<sup>[151]</sup>.

In 2013 Bharat *et al.*, evaluated the antiulcer activity of aqueous and ethanolic leaf extract of tulasi in albino rats. The dose 100, 200 and 400mg/kg of *O. sanctum* has been used for the study. The aqueous and ethanolic extract of *O. sanctum* (200 mg/kg bw) showed significant ( $P \leq 0.05$ ) reduction in gastric volume, free acidity, total acidity, combined acidity and ulcer index as compared to the control group of pyloric ligations, cold restraint stress and forced swim endurance ulcer induced model and it also shown anti- secretory mechanism. This study showed that aqueous and ethanolic leaf extract of *O. santum* is effective as that of the standard synthetic drug Ranitidine<sup>[165]</sup>.

### 3.17. *Piper nigrum* L.

*P. nigrum* (Piperaceae) commonly known as black pepper and locally known as kurumulaku, mulakukodi, nallamulaku. It is a glabrous climber found throughout Kerala in evergreen, semi-evergreen forests and also cultivated<sup>[13]</sup>. Traditionally it is used for carminative, stimulant and stomachic<sup>[166]</sup>. Pharmacologically reported activities are antihypertensive and antiplatelets<sup>[167]</sup>, antioxidant<sup>[168]</sup>, antitumor and immunomodulatory<sup>[169]</sup>, anti- asthmatics<sup>[170]</sup>, analgesic and anticonvulsant<sup>[171]</sup>, anti-inflammatory<sup>[172]</sup>, anti-diarrheal<sup>[173]</sup>, antispasmodic, anxiolytic, antidepressants<sup>[174]</sup>, hepato-protective<sup>[175]</sup>, antibacterial<sup>[176]</sup>, antifungal, anti-thyroids, antiapoptotic,



anti-metastatic, antimutagenic, anti-spermatogenic, anticolon toxin<sup>[177]</sup>, insecticidal and larvicidal activities<sup>[178]</sup>. Phytochemical constituents in this plant are Phenolics, flavonoids, alkaloids, amides and steroids, lignans, neolignans, terpenes, chalcones, piperin<sup>[166]</sup>. AL-Saeed *et al.* studied the effect of aqueous extract of *P. nigrum* on some physiological and histopathological parameters in aspirin induced gastric ulcer model rabbits. In the study, he was reported that the aqueous extract of *P. nigrum* showed a significant ( $P \leq 0.05$ ) increase in RBC, WBC, PCV, Hb and a significant decrease in the glucose, cholesterol and activities of AST and ALT when compared to the respective controls. Whereas aspirin and *P. nigrum* treated group showed significant reductions in RBC, WBC, Hb, PCV and MCHC when compared to the respective controls. Moreover, treatment with aqueous extract of *P. nigrum* (500 mg/kg) for 30 days was found to be inhibiting the ulcers induced by aspirin. It prevented the increase of gastric acid secretions, depletion of stomach wall mucus and prevented the histological changes caused by aspirin. It has been found that it might be due to the stimulation of bioenergetics processes in the gastric epithelium under the influence of *P. nigrum*<sup>[179]</sup>.

### 3.18. *Phyllanthus embilica* L.

*P. embilica* (Phyllanthaceae) commonly known as Indian gooseberry, emblic myrobalan and locally known as nellikka, nelli, amalakam. It is a deciduous tree found in dry and moist deciduous forests, throughout the tropics of Kerala<sup>[13]</sup>. Pharmacologically reported activities are antioxidant<sup>[180]</sup>, anticancer<sup>[181]</sup>, antigenotoxic<sup>[182]</sup>, anti-inflammatory<sup>[183]</sup>, antidiabetic<sup>[184]</sup>, antidepressant<sup>[185]</sup>, antiulcerogenic<sup>[186]</sup>, wound healing activities<sup>[187]</sup>, eye disorders<sup>[188]</sup>, cardiovascular diseases<sup>[189]</sup> and neurodegenerative diseases<sup>[190]</sup>.

Joshi *et al.* evaluated the gastric motility of *P. embilica* and *Asparagus racemosus* in cold stress induced gastric damage. They were compared the effect of four different formulations of *P. embilica*, namely dry powder, hot water extract, cold water extract and incinerated powder and *A. racemosus* were administered orally in the dose of 270 mg/kg for 7 days. In case of no stress induced animals the % GE for drug treated groups was 64.16±17.29, 58.33±5.95, 50.00±7.56 and 64.50±16.15 in rats treated with dry powder, hot water extract, cold water extract and incinerated powder respectively. The percentage gastric emptying of rats administered Ranitidine was 58.00±19.51%, gastric emptying shown by *A. racemosus* was 76.66±5.88, which was significantly greater than the control group. None of the *P. embilica* groups showed significant gastric motility changes as compared to control group and ranitidine ( $P \leq 0.05$ ). Whereas in case of cold stress induced animal models treated with all the formulations of *P. embilica* and *A. racemosus* reversed the stress induced decrease in gastric emptying. All test groups

showed improvement in percentage of gastric emptying time which was found to be statistically significant ( $P \leq 0.01$ ) as compared to control group, hot water extract showed highest improvement in gastric emptying. Thus they came to a conclusion that the mechanism of antiulcer activity of *P. embilica* and *A. racemosus* due to the gastric motility enhancing effect<sup>[191]</sup>.

### 3.19. *Terminalia chebula* Retz.

*T. chebula* (Combretaceae) commonly known as gallnut, black myrobalan, and chebulic myrobalan and locally known as kadukka, pulicakku, putanam. It is a deciduous tree found in dry and moist deciduous forests of Idukki, Thiruvananthapuram, Kozhikkode, Wayanad, and Palakad districts of Kerala<sup>[13]</sup>. Traditionally has been used for treating constipation, diarrhea, ulcers, gastroenteritis, asthma, cough, dyspnea, dyspepsia, hemorrhoids, candidiasis, parasites, malabsorption syndrome, hepatomegaly, vesicular and renal calculi, urinary discharges, tumors, skin diseases, leprosy, intermittent fever, rheumatism, arthritis, gout, neuropathy, paralysis, memory loss, epilepsy, depression, diabetes, cardiovascular diseases, anorexia and wounds<sup>[192]</sup>. Pharmacologically reported activities are antibacterial, antifungal, antiviral, anticarcinogenic, antioxidant, adaptogenic and antianaphylactic, hypolipidemic, hepatoprotective, cardio protective, antidiabetic, wound healing, antiulcer, immunomodulatory and chemo preventive<sup>[193]</sup>. The antiulcer activity of methanolic extract of *T. chebula* fruits was evaluated in wistar rats by using pylorus ligation and ethanol induced ulcer models by Raju *et al.*<sup>[192]</sup> It has been found that in both models the extract (250 mg/kg and 500 mg/kg) shown a significant ( $P \leq 0.01$ ) reduction in gastric volume, free acidity and ulcer index as compared to control. In pyloric ligation induced ulcer model the protection index was found to be 76 % and 82 % at the dose of 250 and 500 mg/kg in comparison to control and the omeprazole reference standard drug shown 84% reduction of ulcer. Where as in ethanol induced ulcer model methanolic extract of *T. chebula* has shown significant protection index of 54% and 66% with the dose of 250 and 500 mg/kg respectively in comparison to control, omeprazole as reference standard drug was reduction of ulcer 72%. Finally, they concluded that *T. chebula* fruit extract have potential antiulcer activity in the both models. These results may further suggest that methanolic extract was found to possess antiulcerogenic as well as ulcer healing properties, which might be due to its antisecretory activity<sup>[192]</sup>.

### 3.20. *Zingibera officinalis* Roscoe.

*Z. officinalis* (Zingiberaceae) commonly known as ginger and locally known as andrakam, chukku, erukizhangu, inchi. It is a rhizomatous herb found throughout Kerala<sup>[13]</sup>. Traditionally it is used for nausea,

vomiting, asthma, cough, palpitation, inflammation, dyspepsia, loss of appetite, constipation, indigestion and pain<sup>[194]</sup>. Pharmacologically reported activities are antioxidant and antimicrobial<sup>[195]</sup>, anticancer<sup>[196]</sup>, antidiabetic<sup>[197]</sup>, anti-inflammatory<sup>[198]</sup>, analgesic<sup>[199]</sup>, antipyretic<sup>[200]</sup>, immunomodulatory<sup>[201]</sup>, anti-platelet aggregation<sup>[202]</sup>, antiangiogenic<sup>[203]</sup>, hepato-protective<sup>[204]</sup>, antiemetic<sup>[205]</sup>, neuroprotective<sup>[206]</sup>, anthelmintic<sup>[207]</sup>, gastro protective<sup>[208]</sup> and cardiovascular<sup>[209]</sup>. Terpenes, alcohols, ketones, flavanoids, carotenoids, gingeroles, phytoestrogens and vitamin C are the phytochemical constituents present in it<sup>[194]</sup>. In 2014, the anti-ulcerogenic effect of *Z. officinale* (Ginger) roots in rats was evaluated by Uz Zaman *et al.* using indomethacin induced gastric damage [210]. The ginger roots extract (200 and 400 mg/kg) significantly ( $P \leq 0.001$ ) inhibited the gastric damage induced by indomethacin. The percentage inhibition of gastric ulcers was 40.91%, 57.58% and 65.91% by 200 and 400 mg/kg of *Z. officinalis* and omeprazole respectively. The 400 mg/kg of aqueous extract of *Z. officinalis* was found to be more effective than 200 mg/kg. The ginger roots extract has the potential to prevent the gastric damage resulting from indomethacin (NSAID) administration<sup>[210]</sup>.

## DISCUSSION AND CONCLUSION

From this study, it is clear that medicinal plants have portentous role in healing ulcers. WHO reported that 75% of the world population in developing world depends on the botanical medicines for their basic healthcare needs. The medical research and commerce exploiting many valuable experiences from the oral health traditions because the plants are easily available at cheap rate and another very important advantage is, it has very lesser side effects when compared to the synthetic drugs. Plants containing secondary metabolites like alkaloids, flavanoids, terpenoids, tannins, phenolic compounds, glycosides, terpenes, and resins have an important role in relieving ulcers. These compounds protect the gastric mucosa from lesions produced by various ulcer models and against different necrotic agents. Studies reported that its activity is due to antisecretory mechanisms by inhibiting H<sup>+</sup>/K<sup>+</sup> proton pump, decreasing histamine levels by preventing its release from gastric mucosa, cytoprotective action by increasing the mucosal blood flow, stimulating the synthesis of mucosubstances, bicarbonate secretion and also by increasing the prostaglandin levels. The antioxidant compounds found in plants like quercetin, gracinol, rutin, gallic acid, ellagic acid,  $\beta$  sitosterol, babaloin, isobarbaloin, etc. also has an important role reducing ulcer. Most of the plant extract contains antioxidant compounds; it acts by scavenging the free radicles and there by protect the gastric muosa from free radicle induced membrane damage. Therefore, the combination of traditional and modern knowledge can produce better drugs for the treatment of peptic ulcer with fewer side effects.

## CONFLICT OF INTEREST

There are no conflicts of interest.

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