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Medicinal plants with gastroprotective potential

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Abstract

Peptic ulcer disease (PUD) is a main source of morbidity and mortality worldwide. It is characterized by erosions in mucosal linings of stomach and duodenum. Non-steroidal anti-inflammatory drugs (NSAIDs) and Helicobacter pylori are mainly responsible for peptic ulcer disease. Histamine receptor blockers and proton pump inhibitors are most prominent therapies in the treatment of peptic ulcer. However, severe adverse effects of NSAIDs have been reported. Therefore, focus is now diverted towards herbal formulations of medicinal plants for the treatment of ulcer. Plants contain different phytoconstituents which are responsible for increasing defensive mechanisms of body against peptic ulcer. The current review focuses on the commonly used gastroprotective plants as antiulcer agents.

Introduction

Peptic ulcer is the most common gastrointestinal disorder (Ayantunde, 2014) caused by the alteration in balance between offensive and defensive factors. Offensive factors include pepsin, gastric acid and Helicobacter pylori. However defensive factors include prostaglandins (PGs), bicarbonate ions, mucin, growth factors and nitric oxide (Raju et al., 2009).

Role of histamine in peptic ulcer

Histamine releases from mast cells also contribute in acid secretions from parietal cells of gastric mucosa. As histamine receptors are present on the surface of parietal cells so histamine binds with these cells and causes the activation of adenylate cyclase which converts ATP into c-AMP. This conversion is responsible for enhanced secretion of hydrochloric acid from parietal cells (Sander et al., 2006). Other factors like smoking, excessive alcohol intake, usage of spicy foods and stress may also contribute to severe damage of gastric mucosa. A study has demonstrated that ulcer incidence is different in Eastern and Western countries.

Gastric ulcer is more common in Eastern countries especially in Asia and prevalence of duodenal ulcer is more in Western countries (Sandler, 2002).

Non-steroidal antiinflammatory drugs and peptic ulcer

Non-steroidal anti-inflammatory drugs (NSAIDs) are most commonly used as analgesic, antipyretic and antiinflammatory. The long-term use of NSAIDs may cause gastric ulcerative lesions and gastric bleeding which increases the morbidity and mortality (Kenneth et al., 2013). NSAIDs interrupt the gastrointestinal mucosal lining by increasing the hydrochloric acid (HCl) secretion (Huang et al., 2002: Wilson et al., 2004: Laine and Jensen, 2012).

Aspirin is most commonly used NSAID and is widely used for the treatment of fever, inflammation and pain. Recently it is also used to treat cardiovascular thrombotic diseases (Laine et al., 2008). Aspirin blocks the activity of both cycloxygenase (COX) 1 and 2 enzymes and reduces the gastric prostaglandin's, blood flow towards gastric mucosa, mucus and bicarbonate ions



secretion. In case of cardiovascular thrombotic diseases aspirin is used at low doses (75-100 mg/day) as antiplatelet drug. It inhibits the thromboxane A2 which results in platelet segregation and shows antithrombotic activity. Aspirin also damages the gastric mucosa by enhancing the leukocyte infiltration in gastric microvasculature (Niv et al., 2005).

Helicobacter pylori and peptic ulcer

Helicobacter pylori is a bacterium which is considered to be a major cause of peptic ulcer. It damages the gastric mucosa via excessive acid secretion from parietal cells by increasing the parietal cell mass due to its inflammatory effects on parietal cells of gastric mucosa. It also reduces the mucus and bicarbonate ions secretion from gastric epithelial linings. H. pylorus stimulates the release of inflammatory mediators like cytokines and polysaccharides and also activates the heat shock proteins which cause the inflammation and damage of gastric mucosa. It is also observed that both H. pylori and aspirin synergistically enhance the gastric mucosal damage and gastric lesions (Velmishi et al., 2014: Perez et al., 2005).

Treatment strategies

In earlier ages surgery was the only treatment for gastric and duodenal ulcers. Ranitidine was introduced as first synthetic antiulcer drug in 1980s which inhibits the gastric acid secretions by blocking the histamine receptors. Recently different drug therapies are used for the treatment of peptic ulcer in combination which include proton pump inhibitors (omeprazole, pantoprazole, rabeprazole, etc), histamine receptor blockers (ranitidine, famotidine, etc), and synthetic prostaglandin E₁ (misoprostol). Antacids (aluminium hydroxide and magnesium trisilicate combination) are also used to decrease the gastric acid secretion (Rang et al., 2003). The drugs used for the treatment of *H. pylori* associated gastric and duodenal ulcers- triple therapy regimen, which includes a proton pump inhibitor (omeprazole, lansoprazole), antibiotics (clarithromycin and metronidazole) (Rakesh et al., 2010: Calvet et al., 2000: Enaganti, 2006).

Proton pump inhibitors

Proton pump inhibitors show their antiulcer activity by blocking the hydrogen potassium ATPase pump (a proton pump) and is present on the surface of parietal cells in gastrointestinal tract. It is mainly responsible for acid secretion. Proton pump inhibitors cause irreversible inhibition of acid secretion and thereby reduce the level of hydrochloric acid in stomach. Effect of a single dose of omeprazole lasts for 2 to 3 days due to its irreversible binding and accumulation in parietal cells

(Sachs et al., 2006). Previous research studies have also shown that after endoscopy proton pump inhibitors are drug of choice to minimize the chances of bleeding (Jeng, 2010; Cheng et al., 2009)

The effectiveness of gastroprotective drug therapies has been decreased due to the severe adverse effects caused by these drugs e.g. tolerance, nausea, vomiting, fatigue, drowziness, stomachache and relapse. Prolonged use of proton pump inhibitors may also reduce the absorption of pyridoxine which requires the acids secreted from parietal cells of gastric mucosa for its absorption. In connection with severe adverse effects of antiulcer drugs, focus is now diverted towards the use of herbal medicines against peptic ulcer (Koehn and Carter, 2005; Nurhidayah et al., 2014). Current review summarizes the most commonly employed gastroprotective medicinal herbs. Extracts of medicinal plants ground significant gastroprotective potential against diverse ulcer inducing agents.

Mechanisms involved in gastroprotective activity of medicinal plants

The consequences of gastroprotective activity of plant extracts are evaluated by ulcer score, ulcer area, pH of gastric mucosa, ulcerative index, curative ratio and oxidative biomarkers. These indicators are altered considerably by using plant extracts. Medicinal plant extracts cause significant reduction in ulcer scores and ulcerative index caused by ulcer inducing agents. However antioxidant potential of medicinal plants also participate in their antiulcer activity which is mainly because of the presence of flavonoids, gums, tannins, saponnins and oleoresins in different parts of plants (Aslam et al., 2013; Panda and Sonkamble, 2012; Abdulla et al., 2010).

Medicinal plants with gastroprotective effect

Acanthus ilicifolius

Acanthus ilicifolius is a plant which is used for the treatment of different diseases. Gastroprotective activity of methanolic leaf extract of A. ilicifolius was determined in albino rats. A. ilicifolius was used at two different doses (100 and 200 mg/kg). Ethanol was used to induce gastric ulcerative lesions. Results of the study demonstrated that methanolic leaf extract of A. ilicifolius showed dose-dependent gastroprotective activity. There was a significant decrease in ulcer score, ulcer index, total acidity and gastric secretion in group pretreated with methanolic leaf extract of A. ilicifolius. Histopathological studies were also performed which showed that methanolic leaf extract of A. ilicifolius significantly reduced the gastric lesions and hemorrhagic bands. Gastroprotective activity of A. ilicifolius was due to the presence of phytoconstituents like flavonoids, alkaloids, tannins, terpenoids and vitamin C as active constituents of methanolic leaf extract of plant (Nizamuddin et al., 2011).

Aloe vera

Gastroprotective potential of *Aloe vera* leaf gel extract has been explored against indomethacin-, pylorus ligation-, and stress-induced ulcerative damage in rats. *A. vera* gel extract was used at three different dose levels 50 mg/kg, 100 mg/kg and 150 mg/kg. There was a significant dose dependent reduction in ulcer scores, gastric secretions, free acidity, total acid output and ulcerative index along with significant increase in mucus production. Phytochemical screening of *A. vera* gel extract showed the presence of active constituents including triterpenoids, proteins, reducing sugars, amino acid, flavonoids and gallic acid. From the results it was obvious that antiulcer activity of *A. vera* gel extract is due to its anti-inflammatory, mucus stimulitory and antioxidant potential (Naveen et al., 2013).

Anogeissus latifolia

A study has demonstrated the gastroprotective activity of aqueous and alcoholic extract of Anogeissus latifolia (bakli) bark against indomethacin-, aspirin- and stressinduced gastric damage. A. latifolia was used at two different doses (100 and 200 mg/kg). In case of stressinduced ulcer model the free radical scavenging activity of A. latifolia was also evaluated. Level of different enzymes include superoxide dismutase, catalase and lipid peroxidase were measured. Results of the study revealed that there was a significant decrease in lipid peroxidation and formation of free radicals in group pretreated with aqueous and alcoholic extract of A. latifolia. So, it was concluded that A. latifolia has potent gastroprotective and antioxidant activity. Phytochemical analysis has shown the presence of gallic acid, tannoid and ellagic acid as active constituents in plant extract which may be responsible for antiulcer activity of plant (Govindarajan et al., 2006).

Andrographis paniculata

Antiulcer and antioxidant activity of aqueous and ethanolic leaf extract of Andrographis paniculata has been evaluated against ethanol (95%) induced gastric ulcerative lesions in rats (Wasman et al., 2011). Both aqueous and ethanolic leaf extracts of A. paniculata were used at two different doses (250 and 500 mg/kg). Gastroprotective activity of A. paniculata was evidenced by reduction in ulcer areas along with significant increase in pH of gastric contents and mucus production in group pretreated with aqueous and ethanolic leaf extract of A. paniculata. The ethanolic leaf extract of A. paniculata showed more %inhibition of ulcer areas as compared to aqueous extract. It was also observed that diterpinoide and diterpinoidal glycosides are main active constituents of A. paniculata which are mainly responsible for its antiulcer and antioxidant potential.

Argyreia speciosa

Argyreia speciosa is most commonly used for the

treatment of nervous disorders, diabetes and ulcer. Gastroprotective potential of butanol fraction of A. speciosa leaf against aspirin-, pylorus ligation-, ethanoland stress-induced ulcerative damage has been explored in rats (Jaiswal et al., 2011). Leaf extract was used at three different doses (50, 100 and 200 mg/kg). Results of the study revealed the dose dependent gastroprotective activity of A. speciosa. There was a significant decrease in ulcer area, gastric volume, total acidity, lipid peroxidation along with significant increase in mucus secretion, catalase levels and pH of gastric mucosa. Phytochemical screening revealed the presence of active constituents in leaf extract including flavonoids, kaempferol 3-O-L-rhamnopyranosid, quercetin and kaempferol which might participate in the gastroprotective potential of A. speciosa (Galani et al., 2010).

Benincasa hispida

Benincasa hispida is a plant which belongs to family Cucurbitaceae. It is most commonly used to treat liver disorders, pyrexia, kidney problems and nervous disorders (Grover et al., 2001). Gastroprotective activity of petroleum ether and methanolic fruit extracts of B. hispida was evaluated in albino rats against ethanol induced ulcer. Results of study revealed that plant extracts significantly increased the catalase level and also showed a significant reduction in malondialdehyde level by inhibiting the lipid peroxidation. So, it was concluded that antiulcer activity of B. hispida was due to its free radical scavenging activity (Manish and Sunita, 2008).

Another research study has demonstrated the antioxidant and antiulcer potential of methanolic seed extract of B. hispida at two different doses (150 and 300 mg/kg). Ulcer was induced by pylorus ligation, indomethacin and water immersion stress in albino rats (Gill et al., 2011). The plant extract showed gastroprotective activity in a dose-dependent manner via significant decrease in ulcer score, ulcer index, total acidity and gastric volume in plant treated groups. However, this gastroprotection at a dose of 300 mg/kg was almost similar to synthetic antiulcer drug ranitidine. Phytochemical investigations had revealed the presence of carbohydrates, proteins, tannins, triterpenes and amino acids in plant extract which might be responsible for antioxidant and antiulcer potential of methanolic seed extract of B. hispida.

Berberis vulgaris

Berberis vulgaris is a shrub. The fruit is rich in vitamin C and it is an oblong shaped red berry (Aghbashlo et al., 2008). B. vulgaris and other plants containing berberine have a history of usage in all medicinal systems (Souri et al., 2004). Fruits, seeds and flowers of barberry contain large amounts of phenolic compounds, gum, pectin, oleoresins and have a small amount of berberine and other isoquinoline alkaloids as active constituents (Mohsen et al., 2011). Anthocyanins and carotenoids are

the phenol compounds present in barberry fruit which have anticholinergic and histamine receptor blocking activity. Barberry fruit also has free radical scavenging activity (Tomosaka et al., 2008).

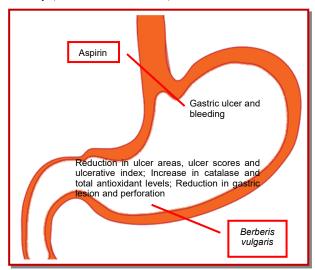


Figure 1: Gastroprtective potential of B. vulgaris

Gastroprotective activity of aqueous seed extract of *B. vulgaris* has been explored against aspirin-induced gastric ulcer in male adult albino mice. *B. vulgaris* was used at three different doses (300, 600 and 900 mg/g) (Figure 1).

Results of the study demonstrated that there was a significant reduction in ulcer area, ulcer score and ulcerative index in *B. vulgaris* seed extract treated group. However this reduction was dose dependent. Oxidative biomarkers were also evaluated which showed that *B. vulgaris* significantly enhanced the catalase and total antioxidant levels (Aslam et al., 2013).

Boswellia serrata

Gastroprotective activity of *Boswellia serrata* has been reported against aspirin- (200 mg/kg) induced toxicity in albino rats. Petroleum ether and aqueous bark extracts of *B. serrata* at a dose of 250 mg/kg were used in the study (Malairajan et al., 2008). Ranitidine was used as reference antiulcer drug at dose of 20 mg/kg. Phytochemical screening of *B. serrata* was also conducted which showed the presence of alkaloids, flavonoids, tannins, oleoresins and carbohydrates as active constituents. As these phytochemicals have antioxidant activity, so it was concluded that gastroprotective activity of *B. serrata* was due to the presence of these phytochemicals in plant extract. *B. serrata* also significantly reduced the gastric acid secretion due to its antisecretory activity (Zeeyauddin et al., 2011).

Calotropis procera

Calotropis procera is a plant which is commonly used in traditional medicine for the treatment of various

diseases. Different parts of C. procera showed purgative and gastroprotective activity. Leaves and bark of C. procera have been found to cure ulcer and stomachache. Gastroprotective activity of methanolic extract of C. procera root was evaluated in albino rats. Ulcer was induced by aspirin, alcohol and stress. Antiulcer activity of C. procera was mainly due to its inhibitory effects on gastric secretion, inflammation and acidity in gastric mucosa. The plant extract significantly reduced the ulcer score, ulcer area and leukocyte infiltration in gastric epithelial lining. Plant extract decreased the formation of free radicals and reduced the level of MDA. Phytochemical analysis was carried out which showed the presence of active constituents including polyphenols, triterpenoids, tannins and steroids in the plant extract. It was concluded that antiulcer activity of plant was mainly because of its active constituents (Prakash et al., 2011).

Careya arborea

Careya arborea is used as therapeutic remedy for the treatment of wounds, bronchiolar constriction and ulcers. However, its antibacterial and free radical scavenging potential is also reported. Gastroprotective potential of ethanolic leaf and stem bark extracts of *C. arborea* has been reported in rats against pylorus ligation- and ethanol-induced ulcerative damage (Kamal et al., 2013; Gupta and Rao, 2014).

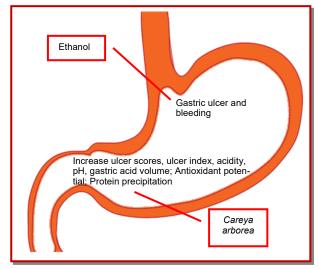


Figure 2: Gastroprtective potential of C. arborea

The ethanolic stem bark extract of *C. arborea* significantly reduced the ulcer score, gastric volume, acidity and ulcerative index at dose of 300 and 600 mg/kg (Kamal et al., 2013). Phytochemical analysis was carried out which showed the presence of flavonoids, tannins and carbohydrates as active constituents. It was concluded that antioxidant potential of *C. arborea* is also responsible for its gastroprotective activity. It was observed that tannins present in the plant extract

precipitate the proteins on ulcer area and suppress the ulcerative damage.

Centella asiatica

Centella asiatica is commonly used for the treatment of psychiatric disorders, melena and kidney infections (Hong et al., 2005; Shetty et al., 2006). C. asiatica also possesses gastroprotective activity as it reduces the formation of free radicals by inhibiting the lipid peroxidation (Cheng et al., 2004; Zaunol et al., 2003). A study showed the gastroprotective activity of methanolic leaf extract of C. asiatica at doses of 100, 200 and 400 mg/kg in albino rats. Ulcerative lesions were induced by the oral administration of ethanol one hour after the pretreatment with methanolic leaf extract of C. asiatica. Results of the study revealed the dosedependent gastroprotective activity of C. asiatica. It was also assumed that antiulcer activity of C. asiatica was due to its free radical scavenging activity which was due to the presence of active constituents like tannins, flavonoids and phenolic contents in leaf extract of plant and also due to its inhibiting effect on white blood cells infiltration in gastric mucosa (Shimizu et al., 2000; Abdulla et al., 2010).

Cenostigma macrophyllum

Gastroprotective activity of hydroalcoholic leaf extract of Cenostigma macrophyllum against indomethacin-, cold stress-, ischemia- and ethanol-induced gastric damage has been evaluated in rats and mice (Viana et al., 2013). The hydroalcoholic leaf extract of *C. macrophyllum* was used at two different doses (100 and 200 mg/kg). There was a significant inhibition of ulcerative lesions along with significant increase in catalase levels in all gastric ulcer models treated with leaf extract of C. macrophyllum. Antiulcer activity of C. macrophyllum is mainly due to release of nitric oxide and free radical scavenging potential. Phytochemical screening of leaf extract have shown the presence active constituents including gallic acid, ellagic acid, quercetin-3-O-β-Dglucopyranoside, methylgallate, tellimoside, quercetin, vitexin, helichrysroside and agathisflavone which may participate in antiulcer and antioxidant potential of C. macrophyllum (Clayton et al., 2012).

Cissus quadrangularis

Mallika et al., (2006) determined the antiulcer potential of methanolic stem extract of *Cissus quadrangularis* (veldt grape) against aspirin-induced ulcerative damage in albino rats. Methanolic stem extract of *C. quadrangularis* was used at a dose of 500 mg/kg. Results of the study demonstrated that *C. quadrangularis* extract showed a significant reduction in ulcerative damage and gastric lesions against aspirin-induced peptic ulcer in rats. Plant extract expressed the anti-secretory potential by reducing the acid and pepsin formation. It also caused a significant increase in the pH of gastric mucosa. Phytochemical screening of *C. quadrangularis*

stem extract has shown the presence of vitamin C, β -carotene and calcium as active constituents which may participate in antiulcer activity of plant.

Curcuma xanthorrhiza

Ethanol extracts of *Curcuma xanthorrhiza* showed gastroprotective activities (Wasman et al., 2012). However, among the different traditional Malaysian plants (*Polygonum minus*, *Andrographis paniculata*, *Curcuma xanthorrhiza*, *Momordica charantia* and *Strobilanthes crispus*), *Polygonum minus* has potentially better inhibition percentage on ulcer area. Another study showed the antiulcer activity of *Curcuma xanthorrhiza* ethanolic leaf extract against ethanol-induced gastric ulcerative lesions in rats (Rahim et al., 2014).

Ulcer area, superoxide dismutase and malondialde-

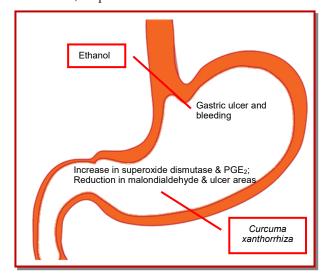


Figure 3: Gastroprtective potential of *C. xanthorrhiza*

hyde were evaluated to assess the effectiveness of plant extract in the treatment of ulcer. It was observed that there was a significant reduction in ulcer area and malondialdehyde levels. It was also noted that *C. xanthorrhiza* is responsible for enhanced production of mucus and PGE₂ in gastric mucosa which protects the gastric mucosal lining from harmful effects of chemicals and drugs. Studies have also shown that the active constituent of *C. xanthorrhiza* is curcumin which is mainly responsible for its antioxidant activity which may participate in antiulcer potential of *C. xanthorrhiza* (Sutha et al., 2014).

Eugenia Jambolana

Eugenia Jambolana is used to treat diabetes mellitus, bacterial infections, nervous disorders and viral infections (Grover et al., 2000). Gastroprotective activity of *E. Jambolana* leaf was evaluated in rats. Results of this study showed that there was a significant decrease in ulcer area and gastric damage in group pretreated with *E. Jambolana* leaves suspension. It was also observed

that E. Jambolana significantly reduced the formation of free radicals and showed potent antioxidant activity. From these results it was concluded that gastroprotective activity of E. Jambolana was due to its free radical scavenging activity (Vidya et al., 2011). Another study has demonstrated the gastroprotective potential of ethanolic seed extract of E. Jambolana against aspirin-, stress- and pylorus ligation-induced gastric ulcerative lesions. Results of the study revealed that seed extract of the plant significantly reduced the ulcer score, ulcerative index and significantly enhanced the gastric mucosal protection. Mechanism involved in antiulcer activity of E. Jambolana was antioxidant potential of plant. Active constituents which are mainly responsible for gastroprotective activity of E. Jambolana include alkaloids, saponins, terpenes, flavonoids and phenolic compounds (Chaturvedi et al., 2007).

Ficus arnottiana

Ficus arnottiana is a plant which contains alkaloids, tannins, flavonoids and carbohydrates (Pushparay et al., 2000). It is most commonly used to reduce blood glucose level, inflammation and stomachache. A study has demonstrated the gastroprotective activity of methanolic leaf extract of *F. arnottiana* against ethanolinduced gastric ulcerative lesions.

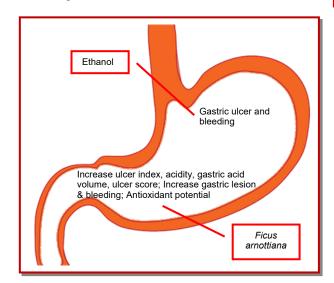


Figure 4: Gastroprtective potential of F. arnottiana

Results of the study concluded that *F. arnottiana* showed dose-dependent gastroprotective activity. Antiulcer activity of *F. arnottiana* was due to the presence of active constituents including flavonoids and tannins in the leaf and root extract. Total gastric acid output, ulcer index and gastric volume were reduced significantly in groups pretreated with methanolic leaf extract of *F. arnottiana* in comparison with control group. Histopathological studies showed that *F. arnottiana* reduced gastric ulcerative lesions and hemorrhagic streaks dose-dependently. It was concluded that

antioxidant activity of *F. arnottiana* may also contribute to its gastroprotective activity (Mazumder et al., 2008).

Guiera senegalensis

Guiera senegalensis is therapeutically a folkloric plant and is used for the treatment of various ailments. Gastroprotective potential of aqueous leaf extract *G. senegalensis* has been explored against aspirin- and ethanol-induced ulcerative damage in rats (Aniagu et

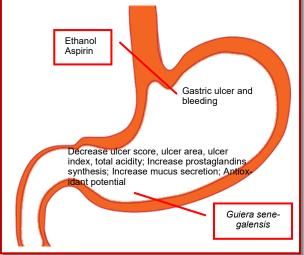


Figure 5: Gastroprtective potential of *G. senegalensis*

al., 2005; Akuodor et al., 2013). Leaf extract of plant was used at three different doses (50, 100 and 200 mg/kg) orally.

There was a significant reduction in ulcer score, ulcer area, ulcerative index and acidity. It was observed that gastroprtective potential of *G. senegalensis* is mainly due to its prostaglandins synthesizing potential. Plant exract also enhanced the mucus secretion in gastrointestinal mucosa. Phytochemical analysis of plant was carried out which showed that plant has potent anti-oxidant potential due to the presence of polyphenolic compounds and flavonoids as active constituents.

Gynura procumbens

Gynura procumbens is an herb which is used for the treatment of different diseases. Studies showed its activity against cancer, inflammation, diabetes and viral infections (Akowuah et al., 2002; Iskander et al., 2002). Antiulcer activity of ethanolic leaf extract of *G. procumbens* was evaluated in rats against ethanol induced gastric ulcerative lesions. *G. procumbens* was used at doses (50, 100, 200 and 400 mg/kg).

Results of the study demonstrated that *G. procumbens* showed dose-dependent gastroprotective activity. Histopathological studies showed significant reduction in hemorrhagic bands and perforations in group pretreated with plant extract. Phytochemicals (phenolic

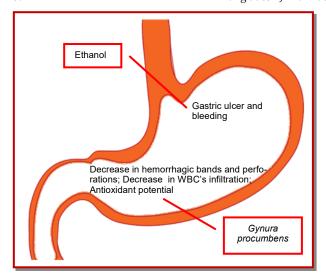


Figure 6: Gastroprtective potential of *G. procumbens*

compounds) are mainly responsible for gastroprotective activity of plant. It was noted that teprenone is the main active constituents of plant which is responsible for significant reduction in white blood cells infiltration in gastric mucosal lining and promotes gastric healing. So, it was concluded that antiulcer activity of *G. procumbens* is mainly due to antioxidant and anti-inflammatory potential of its phytoconstituents (Mahmood et al., 2010).

Gymnosporia emerginata, Solanum pubescence and Anogessius accuminata

Hemamalini et al., (2011) reported the gastroprotective potential of methanolic leaf extracts of three different plants *Gymnosporia emerginata, Solanum pubescence* and *Anogessius accuminata* in albino rats. Ethanol was used to induce gastric ulcerative lesions at a dose rate of 1 mL/kg. All the three plants were used at a dose of 300

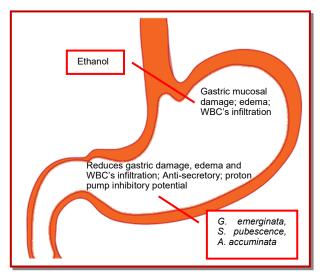


Figure 7: Gastroprtective potential of *Gymnosporia emerginata, Solanum pubescence* and *Anogessius accuminata*

mg/kg orally. At the end of study animals were slaughtered and ulcerative parameters were evaluated.

It was observed from results that all these three plants showed significant gastroprotective activity. Antiulcer activity of all three plants was compared which demonstrated that *S. pubescence* showed maximum gastroprotective activity in comparison with *A. accuminata* and *G. emerginata*. Histopathological studies were performed which showed that there was a significant decrease in gastric ulcerative lesions and hemorrhagic bands in group pretreated with methanolic leaf extracts of *G. emerginata*, *S. pubescence* and *A. accuminata* in comparison with ulcer control group. Phytochemical analysis of all three plants has demonstrated that active constituents (terpeniods and sterols) were mainly responsible for antiulcer potential of these plants.

Hymenaea stigonocarpa

Hymenaea stigonocarpa is a medicinal plant and its stem bark is mainly used to treat ulcer pains, gastric ulcers and inflammation. Gastroprotective potential of methanolic stem bark extract of H. stigonocarpa has been explored against ethanol-, NSAID's-, cysteamine- and ischemia-induced ulcerative damage in experimental rodent models (Patricia et al., 2012). Methanolic stem bark extract of *H. stigonocarpa* was used at four different doses (50, 100, 150 and 200 mg/kg) orally. Results of study demonstrated that plant extract showed inhibition of ulcerative damage in all groups. There was a significant reduction in ulcerative lesions and myeloperoxidase activity along with prevention of glutathione depletion. Phytochemical screening has revealed the presence of active constituents including flavonoids and condensed tannins in the plant extract which are mainly responsible for its gastroprotective activity.

Ipomoea batatas

A study has revealed the gastroprotective activity of methanolic extract of *Ipomoea batatas* tubers (sweet potato) at two different doses (400 and 800 mg/kg). Wistar rats were used in the study and ulcer was induced by aspirin and cold stress. Antiulcer activity of *I. batatas* was evidenced by its significant reduction of ulcerative index, ulcer scores and enhanced levels of superoxide dismutase, catalase and glutathione peroxidase. The results showed that extract of *I. batatas* significantly reduced the lipid peroxidation. It was concluded that gastroprotective activity of *I. batatas* is because of antioxidant potential of phytoconstituents present in sweet potato (Panda and Sonkamble, 2012). The main active constituents of sweet potato were polyphenols and carotenoids (Daniele et al., 2013).

Ixora pavetta

Ixora pavetta is a plant which is used for the treatment of

melena and liver disorders Antiulcer activity of ethanol flower extract of *I. pavetta* was evaluated in rats. Aspirin was used to induce gastric ulcerative lesions at a dose of 200 mg/kg. Results showed that plant extract caused a significant decrease in stomach acidity, gastric acid secretions, ulcer scores and ulcer index but it also significantly enhanced the pH of gastric mucosa at a dose rate of 200 mg/kg. Hsitopathological studies were also performed which showed that plant extract significantly reduced the gastric ulcerative lesions in group pretreated with *I. pavetta* flower extract. Phytochemical investigations have demonstrated the presence of alkaloids, flavonoids and phenolic compounds as active constituents of plant extract (Srinivas et al., 2011).

Jasminum sambac

Jasminum sambac is a plant which is used for the treatment of pyrexia and inflammation. Antiulcer activity of *J. sambac* was investigated against ethanol induced gastric damage in rats.

Ethanolic leaf extract of *J. sambac* was used in four different doses (62, 125, 250 and 500 mg/kg). Results of study showed that there was a significant decrease in total acid output, ulcer score and ulcer index.

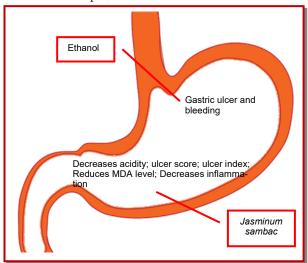


Figure 8: Gastroprtective potential of *J. sambac*

Antioxidant studies were performed which showed significant reduction in MDA levels in group pretreated with leaf extract of *J. sambac*. Histopathological studies showed that inflammation and gastric lesions were also reduced in plant extract treated groups. Phytochemical screening of plant has shown the presence of active constituents including dotriacontanoic acid, hesperidin, dotriacontanol, daucosterol and oleanolic acid (Ahmed et al., 2012).

Jasminum grandiflorum

Some researchers have demonstrated the gastroprotec-

tive activity of ethanolic extract of Jasminum grandi-florum (chameli) leaf against aspirin- and alcohol-induced acute ulcer and acetic acid-induced chronic ulcerative damage in rats. Results of the study showed that plant extract has dose-dependent free radical scavenging activity which was enhanced by increasing the dose of plant extract. Results of study also revealed that plant extract caused a significant decrease in ulcerative lesions, gastric volume and acidity which was comparable to synthetic antiulcer drug. Phytochemical investigations has demonstrated the presence of alkaloids, flavonoids, phenolic compounds, saponins, carbohydrates, carotenoids and glycosides as active constituents (Umamaheswari et al., 2007).

Lafoensia pacari

Lafoensia pacari is a medicinal plant and its bark is mainly used to treat ulcers, inflammation and wounds. Gastroprotective activity of methanolic stem bark extract of L. pacari has been evaluated against ethanol-, indomethacin- and stress-induced acute ulcer and acetic acid-induced chronic ulcerative damage (Tamashiro et 2012). Results demonstrated the potent gastroprotective activity of plant extract. There was a significant decrease in gastric volume, total acidity and proinflammatory cytokines including interleukins and tumor necrosis factor. Phytochemical investigations showed the presence of ellagic acid, saponins, pyrrogalic tannins, steroids, phenols and triterpenoids. Ellagic acid is the most important active constituent in the treatment of ulcers.

Lawsonia inermis

Research studies have demonstrated the antibacterial, antifungal and antitumor activities of Lawsonia inermis. Goswami et al., (2011) evaluated the gastroprotective activity of *L. inermis* in albino rats. Aspirin (200mg/kg) and pylorus ligation were used to induce ulcer in study. Alcoholic, aqueous and chloroform leaf extracts of L. inermis were used in the study. All three extracts were used at two different doses (200 and 400 mg/kg). It was concluded that all extracts of L. inermis reduced the acidity, gastric volume and ulcer index in a dosedependent manner. Chloroform extract showed maximum gastroprotective activity as compared to alcoholic and aqueous leaf extracts. Phytochemical screening showed that alcoholic and aqueous extracts of L. inermis mainly contain active constituents including carbohydrates, tannins, gums, glycosides and phenolic compounds. However, the active constituents of chloroform extract are phenolic compounds and sterols. Active constituents present in plant extract were mainly responsible for gastroprotective potential of *L. inermis*.

Mangifera indica

Mangifera indica is mainly used to treat ulcer, wounds and worm infestation. Antiulcer potential of ethanolic seed extract of *M. indica* has evaluated against alcohol-

induced ulcerative damage in rats (Prabhu and Rajan, 2015). Results of the study demonstrated that there was a significant reduction in ulcer score, ulcer area, ulcerative index and acidity in plant extract treated group. The plant extract significantly reduced the lipid peroxidation via its antioxidant potential. The level of superoxide dismutase and reduced glutathione were significantly increased.

Another study has also demonstrated the antiulcer potential of leaf extract of *M. indica* (Neelapu et al., 2012). Phytochemical screening of plant showed the presence of phytoconstituents which are mainly responsible for the gastroprotective activity of *M. indica*. Active phytoconstituents include tannins, triterpenoids, alkaloids, steroids, coumarins, flavonoids, saponins and phenolic compounds. Results also demonstrated that the leaf extract of *M. indica* possessed antioxidant potential.

Gastroprotective activity of M. indica kernel alone and in combination with vitamin C, vitamin D and zinc sulfate has been evaluated (Nethravathi et al., 2015). Ulcer was induced by ethanol and pylorus ligation. Ethanolic extract of M. indica kernel was used at two different doses (200 and 400 mg/kg) orally. To evaluate the antiulcer potential of M. indica kernel gastric volume, ulcer score, ulcer index, total acid output and curative ratio were measured. Histopathological analysis was also carried out. Results of the study demonstrated that gastroprotection of M. indica kernel alone was almost equivalent to its combination with vitamin C, vitamin D and zinc sulfate. The antiulcer and antioxidant potential of M. indica kernel was mainly due to the presence of active constituents including polyphenols and flavonoids in plant extract.

Mentha longifolia

Gastroprotective efficacy of ethanolic extract of *M. longifolia* has been explored in rats at two different doses (100 and 200 mg/kg) (Gul et al., 2015). Alcohol and aspirin were used as ulcer inducing agents in the study. Histopathological evaluation showed that ethanolic extract of *M. Longifolia* significantly cured the aspirin- and alcohol-induced gastric ulcerative lesions. Active constituents present in *M. Longifolia* include flavonoids and tannins which may participate in its gastroprotective and antioxidant potential. Results of the study revealed that gastroprotective potential of *M. Longifolia* was due to its potentiating effects on defensive factors of gastric mucosa.

Mimosa pudica

Mimosa pudica is a plant which belongs to family Fabaceae and is commonly called as Chue mue. It is mostly used for the treatment of diabetes, convulsions, pyrexia and liver disorders. Antiulcer activity of methanolic and chloroform leaf extracts of M. pudica

was investigated in rats. Aspirin was used to induce gastric ulcerative lesions and ranitidine was used as synthetic antiulcer drug. Methanolic and chloroform extracts of *M. pudica* were used. Both extracts were used at two different doses (100 and 200 mg/kg) for a period of 8 days. Methanolic extract showed maximum gastroprotective activity in comparison with chloroform leaf extract of *M. pudica*. It was also observed that phytoconstituents like flavonoids, alkaloids and tannins are present in *M. pudica* which enhances the gastroprotective activity of *M. pudica* due to their free radical scavenging activity (Vinothapooshan and Sundar, 2010).

Another research study has demonstrated the gastroprotective potential of ethanolic leaf extract of M. pudica in albino rats. Animals were divided into six groups. Ranitidine was used as synthetic antiulcer drug at a dose of 20 mg/kg and ethanolic leaf extract of M. pudica was used at a dose of 100 mg/kg. Aspirin, pylorus ligation and ethanol were used to induce the ulcerative damage. Results of the study revealed that plant extract significantly reduced the ulcerative index, total acidity and gastric volume. Phytochemical screening of plant extract showed the presence of active constituents including quercetin, flavonoids, terpenoids and tannins. Quercetin is responsible for increasing the glycoproteins in gastric mucosa which acts as defensive factor in the protection of gastric mucosa from the harmful effects of offensive factors (Elango et al., 2012).

Momordica charantia

Gastroprotective potential of alcoholic and aqueous fruit extracts of *Momordica charantia* against pylorus ligation, aspirin and stress induced ulcer has been evaluated in rats (Venkat et al., 2011). Both aqueous and alcoholic fruit extracts of *M. charantia* were used at three different doses (100, 200 and 400 mg/kg). Results of the study demonstrated the dose dependent antiulcer activity of *M. charantia*. There was a significant decrease in ulcer score, ulcer area, total acid output and gastric volume in plant extract treated groups. Phytochemical analysis of plant extracts showed the presence of active constituents including glycosides, saponins, alkaloids, sterols, steroidal saponins and mucilages which might participate in gastroprotective potential of *M. charantia*.

Morinda citrifolia

Morinda citrifolia (Noni) is a plant which belongs to family rubiaceae. In traditional medicine it is used to treat diabetes, hypertension, gastrointestinal disorders, nervous disorders and viral infections. Ulcer protective activity of fruit extract of M. citrifolia had been explored against aspirin- and alcohol- induced ulcer in albino rats.

Results of the study demonstrated that fruit extract of *M. citrifolia* caused a significant reduction in ulcer index

and ulcer score in a dose-dependent manner. Aspirin belongs to NSAIDs which induces ulcerative damage by blocking the synthesis of prostaglandins and increasing the activity of 5-lipoxygenase pathway. So, it was concluded that aspirin-induced ulcer was protected by *M. citrifolia* due to its inhibitory effect on 5-lipoxygenase pathway. Phytochemical analysis showed the presence of active constituents including alkaloids, flavonoids, phenolic compounds, carbohydrates, gums and resins in the fruit extract of plant (Muralidharan and Srikanth, 2009).

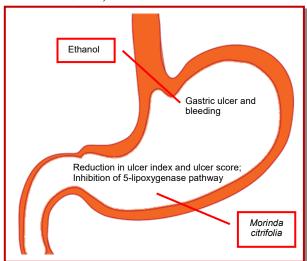


Figure 9: Gastroprtective potential of M. citrifolia

Another study has demonstrated the gastroprotective potential of aqueous fruit extract of *M. citrifolia* at doses (200 and 400 mg/kg) in albino rats. Ulcer was induced by pylorus ligation (Rajeswari et al., 2015). Results of the study revealed that aqueous fruit extract of *M. citrifolia* significantly reduced the ulcerative index, total acid output and gastric volume. It was also observed that plant extract showed 75.3% curative ratio which was approximately equal to synthetic antiulcer drug ranitidine. Phtyochemical screening showed the presence of alkaloids, flavonoids, tannins, triterpenoids, carbohydrates, fats, proteins and steroids as active constituents in the fruit extract of *M. citrifolia*.

Murraya Koenigii

Murraya Koenigii is a plant which is used to treat diarrhea, melena and bacterial infections (Kesari et al., 2005). Gastroprotective activity of aqueous leaf extract of M. Koenigii was determined in rats. Diclofenac sodium was used to induce gastric ulcerative lesions at a dose of 20 mg/kg. The study was conducted by dividing the rats into four groups. 1st group was served as normal control and was on routine feed. Group 2 was treated with synthetic antiulcer drug ranitidine and group 3 and 4 were treated with two different levels of leaf extract of M. Koenigii 200 and 400 mg/kg respectively. Study was carried out for four days and

then at the end of study ulcer index, total acid output and ulcer scores were measured. Results demonstrated that aqueous leaf extract of *M. Koenigii* showed dose dependent gastroprotective activity. Phytochemical screening of the plant has demonstrated the presence of active constituents including alkaloids, sesquiterpione and volatile oils which are mainly responsible for antioxidant and gastroprotective potential of plant extract (Patidar, 2011; Harish et al., 2012).

Ocimum sanctum

Gastroprotective potential of aqueous and ethanolic leaf extract of *Ocimum sanctum* has been investigated against pylorus ligation-, and stress-induced ulcerative damage in rats. Both aqueous and ethanolic leaf extracts were used at three different dose levels 100 mg/kg, 200 mg/kg and 400 mg/kg orally. There was a significant reduction in ulcer index, gastric volume, total acidity, ulcer scores and total acid output along with significant increase in pH of gastric mucosa. Aqueous and ethanolic leaf extract of *O. sanctum* 200 mg/kg showed maximum gastroprotection. Phytochemical screening has revealed the presence of active constituents including flavanoids, fixed oils, saponins and tannins which might be responsible for antiulcer activity of *O. sanctum* (Bharat et al., 2012; Dilpreet et al., 2012).

Phyllanthus niruri

Phyllanthus niruri is a plant which contains large amount of flavonoids, glycosides, tannins and lignans as active constituents and is used for the treatment of bacterial and viral infections like hepatitis B. *P. niruri* is also used for the treatment of high blood glucose level, cancer and kidney stones (Rajeshkumar et al., 2002). A study revealed the gastroprotective activity of *P. niruri* against ethanol-induced ulcer in rats.

Results showed that pretreatment with leaf extract of *P. niruri* significantly reduced gastric ulcerative lesions

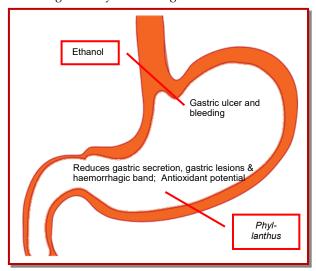


Figure 10: Gastroprtective potential of P. niruri

and acid secretion at doses of 2 g/kg and 5 g/kg respectively. Gastroprotective activity of $P.\ niruri$ was mainly due to its antioxidant potential (Chaudhari and Mengi, 2006).

Picralima nitida

Antisecretory and gastroprotective potential of methanolic extract of Picralima nitida (Stapf) seeds at a dose of 100 mg/kg was evaluated in rats. Cimitidine was used as reference antiulcer drug at a dose of 50 mg/kg in the study. Ulcer was induced by aspirin and pylorus ligation. Results of study demonstrated that stomach emptying time and ulcerative damage were reduced significantly in comparison with ulcer control group. It was observed that plant extract caused a decrease in gastric acidity but the volume of gastric secretions was not affected. Results of the study revealed that the methanolic extract of P. nitida possesses antiulcer activity. Phytochemical screening of the plant extract showed the presence of glycosides, alkaloids, saponins and tannins as active constituents of plant which might be responsible for antiulcer activity of plant extract (Okonta et al., 2011).

Polyalthia longifolia

Polyalthia longifolia is a plant belongs to family Annonaceae. It is most commonly used for the treatment of pyrexia, bacterial, fungal and dermal infections. It is used to reduce high blood glucose level and blood pressure. A study was conducted to evaluate the gastroprotective activity of P. longifolia against aspirin and pylorus ligation induced ulcer in albino rats. Ethanolic leaf extract of P. longifolia at a dose of 300 mg/kg was used. From the results it was obvious that ethanolic leaf extract of P. longifolia showed significant reduction in ulcer index, ulcer score, free acidity and gastric acid secretion in both aspirin- and ethanolinduced gastric ulcerative lesions. So it was concluded that ethanolic leaf extract of P. longifolia has potent gastroprotective activity. Phytochemical screening had showed the presence of terpenoids and alkaloids as active constituents for gastroprotective activity (Malairajan et al., 2008).

Polygala paniculata

Gastroprotective and antisecretory activity of *Polygala paniculata* have been explored in rats against ethanol and indomethacin induced gastric ulcerative lesions. *P. paniculata* was used for the treatment of bronchiolar constriction, inflammation and kidney infections (Kou et al., 2003). Plant extract showed gastroprotective activity in dose-dependent manner. The mechanism involved in the gastroprotecive activity of *P. paniculata* was the enhanced formation of prostaglandins. It was also noted that antiulcer activity of *P. paniculata* was due to the presence of active constituents like flavonoids in hydroalcoholic plant extract which showed potent antioxidant activity and reduced the

formation of reactive oxygen species (Biguetti et al., 2005; Zayachkivska et al., 2005).

Polygonum minus

Gastroprotective potential of aqueous leaf extract of *Polygonum minus* has been explored against ethanolinduced gastric damage in rats (Wasman et al., 2010). Aqueous leaf extract of *P. minus* was used at two different doses (250 and 500 mg/kg). Results of the study revealed that leaf extract of *P. minus* significantly reduced the gastric lesions, ulcer score and significantly enhanced the mucus production and pH of gastric mucosa. Gastroprotection of *P. minus* was also evidenced by reduction in leukocyte infiltration and edema in group pretreated with plant extract. The main active constituents of *P. minus* were gallic acid and phenolic contents which were mainly responsible for its antioxidant activity which might participate in antiulcer potential of *P. minus*.

Pterolobium hexapetalum

Pterolobium hexapetalum is a plant which is used as herbal remedy for the treatment of bacterial and fungal infections. Antioxidant potential of *P. hexapetalum* is also reported. Gastroprotective activity of aqueous and methanolic leaf and fruit extracts of *P. hexapetalum* has explored in Wistar rats against pylorus ligation induced ulcer. Methanolic and aqueous leaf extracts of *P. hexapetalum* were administered at doses of 50 mg/kg and 100 mg/kg respectively. Methanolic and aqueous extracts of *P. hexapetalum* fruit were administered at a dose of 50 mg/kg and 100 mg/kg respectively.

Results of study demonstrated that plant extracts significantly reduced the ulcerative damage. From the results it was observed that there was a significant decrease in acidity, ulcer score and gastric volume in plant treated groups. Phytochemical analysis of plant extract showed the presence of active constituents

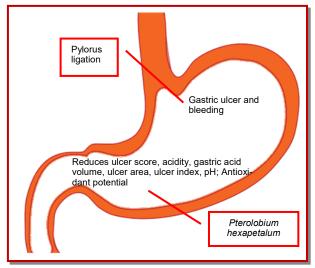


Figure 11: Gastroprtective potential of *P. hexapetalum*

including tannins, flavonoids, polyphenolic compounds and glycosides which were mainly responsible for gastroprotective potential of *P. hexapetalum* (Kavitha et al., 2014).

Solanum nigrum

Solanum nigrum is a plant which is used to treat diabetes, cardiac and liver disorders (Daihan, 2008). Gastroprotective activity of methanolic leaf extract of *S*. nigrum was evaluated in rats. Aspirin was used to induce gastric ulcerative lesions at a dose of 200 mg/kg. Results of study showed that there was a significant decrease in gastric acid secretion, ulcer index, free acidity and ulcer score in group pretreated with methanolic leaf extract of S. nigrum. Curative ratio of methanolic leaf extract of S. nigrum was 77.9%. Histopathological studies were performed which showed that there was a significant decrease in gastric ulcerative lesions and perforations in animals pretreated with methanolic leaf extract of S. nigrum. Hence, gastroprotective activity of S. nigrum was due to the presence of active constituents including flavonoids, alkaloids, tannins and terpenoids which showed potent antioxidant activity (Saravanan et al., 2011).

Swietenia mahagoni

S. mahagoni is a plant which is mainly used to treat hypertension, chest pain and intestinal infections. It also possessed free radical scavenging and antimicrobial potential. Antiulcer activity of ethanolic leaf extract of S. mahagoni at a dose of 200 mg/kg and 500 mg/kg had been explored in rats (Al-Radahe et al., 2013). Ethanol was used to induce gastric ulcerative lesions and omeprzole was used as reference antiulcer drug in the study. There was a significant reduction in gastric ulceration in groups treated with leaf extract of S. mahagoni. There was a significant increase in mucus production in plant extract treated groups. White blood cells infiltration and inflammation was also decreased in plant extract treated group which was also responsible for gastroprotective potential of plant. From the phytochemical analysis it was also observed that teprenone was main active constituent present in plant extract participate in gastroprotective activity of plant.

Terminalia chebula

Terminalia chebula is most commonly used to treat pyrexia, high blood glucose level, GIT disorders, bronchiolar constriction, liver problems, dermal infections, fungal infections and kidney disorders (Chattopadhyay and Bhattacharyya, 2007). Gastroprotective activity of methanolic and chloroform fruit extracts of *T. chebula* was evaluated in albino rats. Gastric ulcer was induced by pylorus ligation and ethanol in rats. Results of study demonstrated that there was a significant decrease in gastric ulcerative lesions, hemorrhagic bands and total acid output in

group pretreated with methanolic fruit extract of *T. chebula* in comparison with ulcer control group. It was also observed that plant extract showed gastro-protective activity in a dose-dependent manner, Phytochemical analysis was also carried out which showed the presence of alkaloids, glycosides, flavonoids, terpenoids, tannins, carbohydrates and phenolic compounds as active constituents in the fruit extract of plant. So it was concluded that the antiulcer potential of *T. chebula* was mainly because of its active constituents (Raju et al., 2009).

Terminalia arjuna

Antiulcer activity of *Terminalia arjuna* (arjun) was evaluated against NSAIDs-induced ulcer in albino rats. Methanol extract of *T. arjuna* bark has been found to cause an increase in non-protein sulfhydryl concentration, pH of gastric mucosa and glutathione level. Results of the study also showed that there was a significant decrease in total acidity, volume of gastric juice, pepsin and acid secretion in group treated with methanolic bark extract of *T. arjuna*. Phytochemical investigations has demonstrated the presence of steroids, phenolic compounds, triterpenoids, flavonoids, tannins and glycosides as active constituents of the plant extract (Rethinam et al., 2007).

Trichosanthes cucumerina

Trichosanthes cucumerina is a plant which belongs to family Cucurbitaceae. Gastroprotective activity of hot water extract of aerial parts of T. cucumerina was evaluated in albino rats. Alcohol was used to induce gastric ulcerative lesions. Results of the study revealed the dose-dependent gastroprotective activity of hot water extract of *T. cucumerina*. There was a significant decrease in ulcer score and ulcer area in group pretreated with hot water extract of T. cucumerina in comparison with ulcer control group. Histopathological studies were also performed which showed that hot water extract of *T. cucumerina* significantly reduced the gastric ulcerative lesions and perforations in groups pretreated with plant extract. Phytochemical screening of plant extract showed the presence of active constituents including alkaloids, saponins polyphenols, tannins and flavonoids which might participate in the antiulcer activity of plant (Arawwawala et al., 2009).

Zanthoxylum rhoifolium

Gastroprotective potential of ethanolic stem bark extract of *Zanthoxylum rhoifolium* against ethanol-, ischemia-, indomethacin- and stress-induced ulcer has been explored in rats and mice. The ethanolic stem bark extract of *Z. rhoifolium* was used at two different dose (250 and 500 mg/kg). Results of the study revealed that plant extract prevented the reduction in non-protein sulfhydril groups along with significant increase in mucus production and catalase levels. Phytochemical screening showed the presence of alkaloids, flavonoids

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and triterpenes in the ethanolic stem bark extract of *Z. rhoifolium* which might participate in gastroprotective activity of plant (Freitas et al., 2011).

Herbal drugs with antiulcer activity

Synthetic antiulcer drugs proclaim severe adverse effects, so the herbal drugs are extensively studied and considered for their antiulcer potential. Clinical research studies have shown that phytochemicals present in different parts of plants have considerable antiulcer potential (Patil et al., 2005; Dilpreet et al., 2012).

Conclusion

From the current review it is concluded that reduction in acid secretions is not only the therapy for peptic ulcer. However, along with reduced acid secretions, enhanced level of defensive mechanisms is also necessary. Plants contain different phytoconstituents which are responsible for increase in defensive mechanisms of body against ulcer. Consequently, efforts should be made for segregation and characterization of the active constituents from herbal sources for their pharmacological activities. The combination of conventional and modern knowledge can generate better gastroprotective drugs with minimum adverse effects.

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Conflict of Interest

Authors declare no conflict of interest

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