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A PHARMACOLOGICAL REVIEW ON NATURAL ANTIULCER AGENTS

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ABSTRACT

Herbal medicines have great importance in maintaining the health of every person. Demands of Herbal medicines are increasing in both developed and developing countries due to growing recognition of natural plants being lesser no. of side effect, easily available in surrounding place with low coast. A peptic ulcer in the stomach is called a gastric ulcer. One that is in the duodenum is called a duodenal ulcer. Peptic ulcers happen when the acids that help you digest food damage the walls of the stomach or duodenum. The most common cause is infection with a bacterium called *Helicobacter pylori*. Another cause is the long-term use of non-steroidal anti-inflammatory medicines (NSAIDs) such as aspirin and ibuprofen. Stress and spicy foods do not cause ulcers, but can make them worse, as many as 70-90% of ulcers are associated with *Helicobacter pylori*, a spiral-shaped bacterium that lives in the acidic environment of the stomach. Literature suggests that number of synthetic drugs are used in the management of peptic ulcers but elicit several adverse effects. Therefore Indian herbal plants stand out as being exceptional for its ethnic, ethobotanical and ethno-pharmaceutical use. In this review attempts have been made to know about some plants which may be used in treatment or prevention of peptic ulcers. This article reviews the antacid / anti-peptic, gastro protective and/or antiulcer properties of the most commonly employed herbal medicines.

Key words: peptic ulcers, *Helicobacter pylori,* gastric ulcer

INTRODUCTION:

Ulcer is a common disorder of the gastrointestinal system, which causes much discomfort to patients, disrupting their daily routines and causes mental agony[1]. Peptic ulcer is defined as a break off in the continuity of the mucosa of stomach or duodenum as a consequence of some medications like non-steroidal anti-inflammatory drugs (NSAIDS), gastric acids and pepsin finally causes lesions in intestinal mucosa[2]. Basically, word "peptic" is derived from Greek term "peptikos" whose meaning is related to digestion .Various reports indicates that old age group patients are more prone to gastric ulcer. Younger individuals have higher risk of duodenal ulcers [3, 4].

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The pathogenesis of peptic ulcer disease includes a complex imbalance[5] between gastric offensive factors like acid, pepsin secretion, *Helicobacter pylori (H.pylori),* bile salts, ethanol, some medications like NSAIDS, lipid peroxidation, nitric oxide (NO) and defensive mucosal factors like prostaglandins (PG's), gastric mucus, cellular renovation, blood flow, mucosal cell shedding, glycoproteins, mucin secretion, proliferation and antioxidant enzymes like catalase (CAT), superoxide dismutase (SOD) and glutathione level.

Peptic ulcer can be categorized on the basis of location and on the severity of disease. Numerous other factors are also responsible for progression of peptic ulcers like tumor necrosis factor-α (TNF α), reactive oxygen species (ROS), release of histamine, incidence of apoptosis and bile acids secretion[6,7].

Pathophysiology

Peptic ulcer is one of the world's major gastro-intestinal disorders, embracing both gastric and duodenal ulcers, and affecting 10% of the world population[8]. The patho-physiology of peptic disease is attributed to the imbalance between aggressive factors like acid, pepsin, and Helicobacter infection, and the local mucosa defenses like bicarbonate secretion, mucus and prostaglandins[9]. *Helicobacter pylori* infection, use of non-steroidal anti-inflammatory drugs-NSAIDs, emotional stress, alcohol abuse, and smoking are the principal etiological factors associated with peptic ulcer[10].

In *Helicobacter pylori* infections a gram negative bacterium colonizes the human stomach, and is a risk factor for the development of peptic ulcer and gastric adenocarcinoma[11,12].

Tissue damage to the gastrointestinal mucosa (or hemorrhagic injury) is produced by exogenous compounds as well, mainly NSAIDs and ethanol[13]. NSAIDs damage the stomach by suppressing synthesis of gastric prostaglandins. Gastric acid exacerbates NSAID effects by deepening superficial lesions, interfering with platelet aggregation, and impairing the ulcer healing process.

The suppression of stomach acid secretions is a key therapeutic target for ulcers, and includes the use of antacids, specific muscarinic M1 receptor antagonists, targeting gastrin receptors and histamine H2 receptors, and the use of proton pump inhibitors.

The exposure of gastric mucosa to aggressive factors such as absolute ethanol, stress, and ischemia followed by reperfusion, and the use of NSAIDs produce pathological changes and the development of inflammation, hemorrhagic erosions, and ulcers with the acute involvement of free radicals, or Reactive Oxygen Species (ROS)[14-16].

These radicals are normally neutralized by the action of the antioxidant system consisting of organic substances containing thiol groups such as glutathione, vitamins C and E, NADPH, antioxidant enzymes such as peroxidase, superoxide dismutase, glutathione peroxidase, glutathione reductase and others[17].

When there is an imbalance between ROS and the antioxidant defense mechanisms, ROS lead to oxidative modifications in the cellular membrane and intracellular molecules resulting in peroxidation of membrane lipids, accumulation of lipid peroxides, and cellular damage[18].

Mucosal defensives are nitric oxide-NO[19], mucus[20], bicarbonate[21], gastrin[22] and prostaglandins [23], as well mucosal blood flow[24].

3.0 Classification of peptic ulcer[25, 26, 27]:

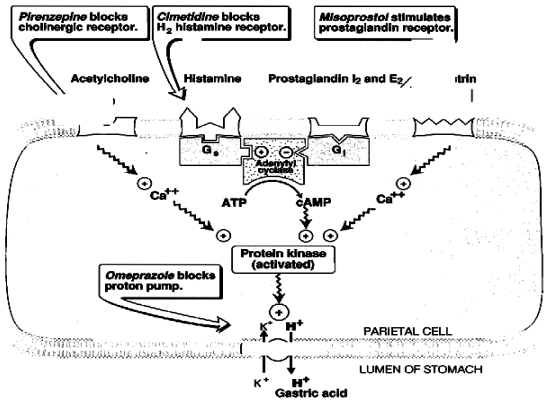
A) Ulcer by Region/Location

a) Duodenum (called duodenal ulcer)
b) Oesophagus (called esophageal ulcer)
c) Stomach (called gastric ulcer)
d) Meckel's diverticulum (called Meckel's diverticulum ulcer; is very tender with palpation)

B) Modified Johnson Classification of peptic ulcers:

a) Type I: Ulcer along the body of the stomach, most often along the lesser curve at incisura angularis along the locus minoris resistentiae.
b) Type II: Ulcer in the body in combination with duodenal ulcers, associated with acid over secretion.
c) Type III: In the pyloric channel within 3 cm of pylorus, associated with acid over secretion.
d) Type IV: Proximal gastro esophageal ulcer
e) Type V: Can occur throughout the stomach, associated with chronic NSAID use (such as aspirin).

Figure 1: Drugs Used To Treat Peptic Ulcer Disease[28]



Plant extracts and phyto constituents in peptic ulcer: in various medicinal plants are used traditionally in the treatment of peptic ulcer. Plants and phytomedicines exhibit their action by various mechanisms like antioxidant, cytoprotective, antisecretory action.

Jasminum grandiflorum

Jasminum grandiflorum L. is a folk medicine. Antiulcer activity of *Jasminum grandiflorum L.* was investigated using 70% ethanolic extract of leaves. It also produces *in vitro* antioxidant activity[29] . Ethanolic extract of leaves produces antisecretory activity which is observed by the significant (P<0.01) reduction of the gastric juice volume, free acidity and total acidity and increase in gastric juice pH when compared to ulcer control in aspirin plus pylorus ligation- induced ulcer model. Extract also produce significant (P<0.01) reduction in ulcer index in ethanol induced ulcer may be due to its antioxidant activity. In acetic acid induced chronic ulcer model gastric lesions occur due to the release of histamine, which increases the capillary permeability and back diffusion of hydrochloric acid (HCl). Pretreatment with the extract showed complete regeneration of mucosal glandular structure. Thus antisecretory and antioxidant activities of the extract may responsible for its antiulcer activity.

Anogeissus latifolia

Bark of *Anogeissus latifolia* (Roxb. ex DC.) Wall. ex Guill. & Perr. important for its ethno botanical uses. Gastroprotective effect of 50% aqueous alcoholic extract of the bark of *Anogeissus latifolia* was studied[30]. The plant has also been reported for its wound healing and radical scavenging activity [31,32]. In aspirin induced ulcer *Anogeissus latifolia* bark extract (200 mg/kg) protects gastric mucosa 66% and the protective action may be due to its 5-lipoxygenase inhibitory effect. Extract produces gastroprotective effect on ethanol induced ulcer as dose dependent manner. *Anogeissus latifolia* extract also active against the cold resistant stress induced ulcers (84.16%) and pylorus ligation (67.64%) at 200 mg/kg may be due to its histamine antagonistic, anticholinergic, antisecretory and antioxidant effect. Extract contain high percentage of the gallic acid and ellagic acid (0.95% w/w and 0.25% w/w respectively). Thus high percentage of the gallic acid and ellagic acid in the extract justifies the potent antioxidant activity of the plant and which may be important for its antiulcer activity.

Alchornea castaneaefolia

The hydroethanolic extract of the leaves and bark obtained from *Alchornea castaneaefolia A.* Juss. showed significant ulcer preventive effect[33] . Leaves and bark extract at dose of 1000 mg/kg orally significantly inhibit ulcer formation 88% and 86% respectively in HCl/ethanol induced ulcer on mice and 62% and 60% respectively in indomethacin/bethanechol induced ulcer models. Pre-treatment with leaf extract protect gastric mucosa 55% in hypothermic restraint stress-induced ulcers in mice and 34% in pylorus ligated mice, but it does not produce any anti secretory effect in shay model. Leaf extract also decreased the mean area of chronic ulcer and proved effective in promoting the healing process in chronic gastric ulcer induced by acetic acid in rats. Enriched flavanoidic fraction was isolated from hydroethanolic extract of leaf and administration separately, it (100 mg/kg) produced 52% and 79% gastroprotection against HCl/ethanol and NSAIDs induced gastric lesions respectively. But it did not show any significant increase in mucoprotective effect in pylorus ligated animals. Pretreatment with enriched flavanoidic fraction shows drastic increase of prostaglandin E2 levels which is markedly reduced on indomethacin treatment. Enriched flavanoidic fraction also produce marked decrease in the serum gastrin level and almost three times increase in serum level of somatostatin hormone when compared to the negative control. Gastrin is a gastrointestinal hormone stimulates of the gastric acid secretion[34] and somatostatin is a regulatory peptide produce potent inhibitory effects on gastric acid, pepsin and gastrin secretion[35] . Phytochemical investigation shows presence of various flavonoids glycosides in extract. So *Alchornea castaneaefolia* produced its action by strengthen defensive factors like prostaglandin synthesis, in addition to other gastroprotective actions, like a stimulant effect

on somatostatin synthesis and an inhibitory effect on gastrin secretion.

Utleria salicifolia

Utleria salicifolia Bedd. Ex. Hook. F. is one of the ethnobotanical plant found in south western ghats of India. The 50% ethanolic extract of*Utleria salicifolia* rhizome posses antiulcer activity in dose dependent manner[36]. It produces 14.48-51.03%, 28.80-56.52%, 13.22-60.74%, 21.22-77.14% and 20.0-84.37% protection in pylorus ligation, aspirin, ethanol, cold-restraint stress and acetic acid induced ulcer respectively. Mucus secretion and bicarbonate secretion are the first line of defense against potential ulcerogens. *Utleria salicifolia* extract significantly (P<0.001) increased gastric wall mucus in ethanol induced ulcer, proved its cytopotective activity. Rhizome extract of *Utleria salicifolia* (100 and 200 mg/kg) also protect ulcer by 68% and 90% against cysteamine induced duodenal ulcer in rats. Lipid peroxidation level is an indicator for the generation of ROS in the tissue [37] . Free radicals induce cell degeneration via peroxidation of membrane lipids, breaking of DNA strands and denaturing cellular proteins result injury in cell[38] . Antioxidant activity of the extract observed against cold-restraint stress induce ulcer with increased superoxide dismutase (SOD) and decreased lipid peroxidation level when compare to ulcer control. It also decreased elevated level of plasma corticosterone. Thus antiulcer effect of extract of *Utleria salicifolia* may be due to its increase in first line of defense system, free radical scavenging activity and provide close relationship between free radical scavenging activity and the involvement of endocrinological (plasma corticosterone) responses.

Solanum nigrum

Solanum nigrum Linn. is a traditional medicine and recommended in ayurveda for the treatment of gastric ulcers. Antiulcer effect of *Solanum nigrum* fruits extracts was investigated in various ulcer induced model in rodents[39] . The aerial parts of *Solanum nigrum* extract show antisecretory action[40]. *Solanum nigrum* fruit also posses antioxidant, hepatoprotective and antitumor activity [41, 42, 43] . Pre-treatment with*Solanum nigrum* fruits extracts at higher dose significantly inhibited the gastric lesions induced by cold restraint stress (76.6%), indomethacin (73.8%), pyloric ligation (80.1%) and ethanol (70.6%). *Solanum nigrum* fruits extracts healed acetic acid induced chronic ulcer also. Extract decrease the volume of gastric acid, acid concentration, acid output, pepsin concentration and pepsin output in pyrolus ligated animals. Significant increase in plasma concentrations of the gastric hormone, gastrin and an increase in the gastric mucosal H^+K^+ATPase activity were observed in ethanol induced ulcerated rats. Increased acid secretion, generation of free radicals and hyperoxidation of lipid causes ulcer in stress and ethanol induced ulcer. Gastrin hormone significantly reduced with pretreatment with extract which regulates gastric acid secretion, releases of histamine and gastric endocrine cell proliferation [44] . Thus anti-secretary activity of *Solanum nigrum*mainly related to the inhibition of H^+K^+ ATPase and suppression of gastrin release, while its ulcer protective and ulcer healing activities may be primarily related to an antisecretory and antioxidant activity.

Ocimum sanctum

Ocimum sanctum Linn. (Tulsi) one of the important medicinal plant in ayurveda reported for anti-carcinogenic, anthelmintic, anti-rheumatic, anti-stress, anti-bacterial, anti-septic, antioxidant, anti-stress and antifertility activity [45-49] . The ethanolic extract of leaves of*Ocimum sanctum* shows antiulcerogenic activity[50] . Extract of *Ocimum sanctum* (100 mg/kg) produced protection index 65.07%, 63.49%, 53.87%, 62.06% and 61.76% in cold restraint, aspirin, alcohol, pyrolus ligation and histamine induced ulcer respectively. Accumulation of gastric acid and pepsin which leads to autodigestion of gastric mucosa and generation of free radicals causes ulcer in pyrolus ligated model[51,52] . *Ocimum sanctum* found to reduce free and total acidity, peptic activity and increased mucus secretion of gastric juice in pylorus ligation induced ulcer model. Incidence of ulcer in different ulcer model due to increased acid secretion, decrease in mucosal defense factor and generation of free radicals.

So antiulcerogenic activity of *Ocimum sanctum* either due to the effect on acid secretion or on cytoprotection or on both. *Ocimum sanctum* also found effective in acetic acid induced chronic ulcer model. Healing of ulcer depends on regeneration of mucosal glandular structure and migration of epithelial cells to cover ulcer crater. So the ulcer healing property of *Ocimum sanctum may* be due to its cytoprotective activity coupled with antisecretory effect. The antiulcer effect of fixed oil of *Ocimum sanctum* was also investigated [53] . Fixed oil of dried seeds produce antiulcer potential on various ulcer models like aspirin, indomethacin, alcohol, histamine, reserpine, serotonin, stress and aspirin plus pylorus ligated induced ulcer models. Significant reduction of ulcer index was observed in dose dependent manner. Results proved that, *Ocimum sanctum* and its active constituents are effective therapeutic agent to treat gastric ulcer.

Scoparia dulcis

Freeze-dried aqueous extract of the aerial parts of *Scoparia dulcis L.* produced reduction gastric hypersecretion and ulcer in rodents[54] . Aqueous freeze-dried extract of *Scoparia dulcis* mixed up with water and extracted with n-butanol. The antiulcerogenic activity of the resulting aqueous phase and butanolic phase which is flavonoid-rich were also investigated. Pre-treatment with the aqueous extract of *Scoparia dulcis*(0.5-1 g/kg, p.o.) produce significant reduction in ulcer in dose dependent manner against indomethacin and ethanol induced ulcer. Aqueous extract and flavonoid-rich fraction produce antiulcer effect by decreasing volume of gastric juice, total acidity and by increases in pH in pyrolus ligated induced ulcer. But the water phase was found inactive. Flavonoid-rich fraction found 4-8 times more active than the aqueous extract in the pylorus ligature model. Both histamine and bethanechol stimulated gastric acid secretion but potently inhibited by aqueous extract of Scoparia *dulcis*. So it may due to blockade or inhibition of a common target in the cascade of events that leads to gastric acid secretion such as the H^+K^+ ATPase. Flavonoid-rich fraction inhibit H^+K^+ ATPase, it (0.01-1 mg/ml) prevented the hydrolysis of Mg^+-ATP by the isolated rabbit gastric H^+K^+ ATPase with IC_{50} = 500 µg/ml. Cirsitakaoside and quercetin active principle of flavonoid-rich fraction produces inhibition of the gastric H^+K^+ ATPase activity *in vitro* [55,56] . Inhibition of gastric secretion by the aqueous extract of *Scoparia dulcis* may be due to the inhibition of the H^+K^+ ATPase enzyme.

Byrsonima crassa

Byrsonima crassa Niedenzu (IK) is a folk medicine, bark and leaves are used in antiemetic, diuretic, febrifuge, ulcer, gastritis and diarrhea [57]. Antiulcerogenic effect of hydromethanolic, methanolic and chloroform extracts of the leaves of *Byrsonima crassa*[58] investigated against HCl/ethanol-induced gastric ulcer. Ethanol treatment causes solubilization of mucus with a concomitant fall in the transmucosa potential difference and increase Na^+ and K^+ flow into the lumen, pepsin secretion, the loss of H^+ ions and the histamine content in the lumen. DNA, RNA and protein level also depressed by ethanol leading to flow stasis and injured areas[59]. Generation of free radicals also play important role in pathogenesis of ethanol induced peptic ulcer. Choloform extract (250, 500 and 1000 mg/kg) inhibited ulcer formation by 59%, 57% and 69% respectively, hydromethanolic extract (250, 500 and 1000 mg/kg) reduced the incidence of gastric lesions by 74%, 78% and 92% respectively and the methanolic extract reduced the ulceration by 93% and 99% at the doses of 500 mg/kg and 1000 mg/kg. Phytochemical investigation methanolic extract shows the presence different flavanoids. Science the catachol and flavonoids possessing antioxidant ant antiulcer activity so extract may be involved in the scavenging of the reactive oxygen species on the surface of gastric mucosa, thus protecting cells from gastric injury.

Asparagus racemosus

Antiulcer effect of methanolic extract of fresh roots of *Asparagus racemosus* Willd was investigated[60]. Extract showed protective effect against gastric ulcers induced by cold restraint stress, pyloric ligation, aspirin plus pyloric ligation, acetic acid and cysteamine induced duodenal ulcers but it was found ineffective

against aspirin and ethanol induced ulcer. In pylorus ligated ulcers extract produce increased individual mucopolysacharide leading to increase in total carbohydrates but did not decrease acid, pepsin secretion and did not produce any effect on cell proliferation. So, protective effect of *Asparagus racemosus* against pylorus ligated ulcers may be due to its cytoprotective nature without influencing acid secretion or neutralising intra-gastric acidity. *Asparagus racemosus* was found ineffective against aspirin induced ulcers because extract may not able to overcome the loss of protective effect caused by decrease in prostaglandins and absence of effect on cell proliferation, as damage caused by aspirin. Activity of *Asparagus racemosus* against aspirin plus pylorus ligated ulcer may due to its cytoprotective activity apart from prostaglandins synthesis. Free radicals are one of the important factors that contributed in stress induced ulcer. Treatment with extract significantly decreases the lipid peroxidation level which can correlate with its antioxidant activity. The polysaccharide fraction of plant has been reported to possess significant antioxidant activity *in vitro*[61]. Thus antiulcer effect of *Asparagus racemosus* against stress induced ulcer may due to its antioxidant activity. *Asparagus racemosus* healed chronic gastric ulcers produced by 50% acetic acid. The increase in defensive mucosal factors may have a beneficial role in protecting ulcers induced by acetic acid. Therefore, ulcer healing and gastroduodenal ulcer protecting effect of *Asparagus racemosus* may be due its mucosal defensive factors rather than offensive factors.

Centaurea solstitialis

Crude extracts from the spiny flowers of *Centaurea solstitialis L.* ssp. showed antiulcer effect against water immersion and immobilization induced ulcers in rats[62]. Sesquiterpene lactones have been isolated and identified as the active constituents of the chloroform extract of the flowering aerial parts of the plant which produce antiulcer activity against ethanol induced ulcer in rats[63]. Three guaianolide type sesquiterpene lactones like chlorojanerin, 13-acetyl solstitialin A and solstitialin A were isolated from the extract found that chlorojanerin and 13-acetyl solstitialin A are the active constituents. Antiulcer effects chlorojanerin and a mixture of 13-acetyl solstitialin A (95%) and solstitialin A (5%) were investigated which significantly produce antiulcer effect on indomethacin, indomethacin plus HCl/ethanol, *N*Gnitro-l-arginine methyl ester plus ethanol, *N*-ethylmaleimide plus ethanol, water immersion restraint stress and serotonin induced ulcer but found ineffective against ulcer induced by pyloric ligation and diethyldithiocarbamate[64]. Mixture found effective against cysteamine induced duodenal and ethanol induced (oral administration) gastric lesions, but was ineffective when ethanol administered subcutaneously. Chlorojanerin found active against ethanol induced ulcer (oral and subcutaneously induced) but inactive against cysteamine induced ulcer. Chlorojanerin and mixture does not produce any effect on gastric secretion and pH but significantly decrease titratable acidity and titratable acid output, so antiulcer effect may due to their neutralizing effect on gastric acid not because of anti secretory effect. Compounds do not produce antioxidant activity as it ineffective against diethyldithiocarbamate induced ulcer. The cytoprotection may be the major reason for their ulcer protective effect.

Anacardium occidentale

Antiulcerogenic effect of a 70% ethanolic extract of cashew *(Anacardium occidentale* L.) leaves was investigated against HCl/ethanol induced ulcer and found that extract inhibit gastric lesions significantly in dose dependent manner[65]. Freeze-dried hydroethanolic extract was washed with petroleum ether first and then extracted with dichloromethane and methanol. The dichloromethane (3.92 mg/kg) and methanol fractions (257.12 mg/kg) considered as 400 mg/kg of hydroethanolic extract and were tested for their anti-ulcer activity. Methanol fractions produce significant ulcer protection but dichloromethane fraction did not produce ulcer protection against HCl/ethanol induced ulcer, Anti *H. pylori* effect of fruits of cashew also investigated[66]. Phytochemical investigation shows the presence of various flavonoids, mainly quercetin glycosides and saponins in

ethanol extract Flavonoids are free radical scavengers, plays important role in gastric ulcer also an increase mucosal prostaglandin content and decrease in histamine secretion from mast cells by the inhibition of histidine descarboxylase[67]. Quercetin was also found to prevent gastric mucosal lesions[68]. Various saponins also found to possess antiulcer activity[69,70]. Since methanol is a bad solvent for tannins so the active component of the methanolic fraction is a substance other than tannin. Therefore, flavonoids and saponin are mainly responsible for antiulcer activity of *Anacardium occidentale.*

Calophyllum brasiliense

Stem bark of *Calophyllum brasiliense* Camb, used in peptic ulcer traditionally. Dichloromethane fraction obtained from the hexane extract of stem bark of *Calophyllum brasiliense* produce significant inhibition of gastric ulcer in dose dependent manner against various ulcer models[71]. Dichloromethane fraction (250 mg/kg) shows 97% and fraction (200 mg/kg) produces 96% and 99% protection against ethanol, indomethacin and hypothermic restraint-stress induced gastric lesions respectively. Ethanol produce ulcer by generating oxygen free radicals, reduce gastric mucosal non-protein sulfhydryl (SH) levels and stimulate the formation of leukotriene. Dichloromethane fraction showed a significant increase in nonprotein sulfhydryls concentration, indicates that the gastroprotective effect of fraction at least partly involves the sulfhydryl mechanism. Hypothermic restraint stress produces hyperacidity and decreases mucosal pH but does not produce any effect on gastric mucosal sulfhydryl levels[72]. Thus protective effect of fraction in this model is independent of sulfhydryl mechanism. Bark fraction produce significant inhibition of gastric fluid volume, total acidity and increase in gastric pH in both pylorus ligated and 2 hrs bethanechol stimulated animals. Therefore increase in gastric mucus and/or an increased prostaglandin generation may be due to the enhanced gastric pH in fraction treated animals. So, gastroprotection effect of bark extract may due to stimulation of gastric mucus, preventing sulfhydryl depletion, by elevation of gastric pH and antisecretory property.

Rhizophora mangle–

Gastroprotective effect of the aqueous bark extract of *Rhizophora mangle L.* investigated against diclofenac induced gastric ulcer in comparison with omeprazole as a standard drug[73]. Pretreatment with extract reduce ulcerated area in dose dependent manner. *Rhizophora mangle* increase prostaglandin production though NSAIDs induced depletion. Polyphenolic compounds found in *Rhizophora mangle may* be stimulate prostaglandin formation and responsible for its effect. Antioxidant property of the extract also evaluated, it increases superoxide dimutase and glutathione peroxidase level which depleted in diclofenac treated group. Extract also prevent lipid peroxidation *in vitro* prove its potential use as a drug for free radical pathologies. Polyphenolic compounds have cytoprotective property and produce antiulcerogenic activity in other plants. Antiulcerogenic activity of tannins may due to their protein precipitating and vasoconstricting effects[74]. Their astringent action also can help to prevent ulcer formation. Microscopically it was found that *Rhizophora mangle* extract form a thick coating adherent to the gastric mucosa which is beneficial to protect gastric mucosa. Results indicate that the ulcer protective effects of *Rhizophora mangle may* 0because of its antioxidant and cytoprotective properties.

Larrea divaricata

Anti-ulcerogenic effect of the methanolic extract of *Larrea divaricata* Cav. leaves was investigated against absolute ethanol and 0.6N HCl induced ulcer in rats[75]. Dose dependent ulcer protection found in case of pretreatment with the extract. Extract inhibit ulcer by 97% and 100% against 0.6N HCl induced ulcer at a dose of 300 mg/kg and 400 mg/kg and produce 96%, 96% ulcer protection in ethanol induced ulcer at a dose of 300 mg/kg and 400 mg/kg. Effect of extract on blocking endogenous sulfhydryl (SH) groups with *N*--ethylmaleimide was also studied in ethanol induced ulcer animals. Because ethanol produce of free radicals and decrease of the levels of nonprotein SH compounds in the gastric

mucosa leads gastric ulcer. But antiulcer effect of extract was not decreased when endogenous SH groups were blocked by *N*-ethylmaleimide. Thus, SH groups are not involved in the anti-ulcerogenic activity of the *Larrea divaricata. In vitro* antioxidant activity of the extract also studied using 1,1diphenyl-2-picrylhydrazyl (DPPH) test method. So, antiulcerogenic activity of methanolic extract of *Larrea divaricata may* due to its antioxidant activity.

Hemidesmus indicus

Hemidesmus indicus var. *indicus is* a traditional medicine for gastric ailments widely distributed in India, consists essential oils and phytosterols like hemidesmol, hemidesterol and saponins. Antiulcerogenic activity of aqueous ethanolic extracts of the roots *Hemidesmus indicus* collected during flowering and vegetative periods were investigated. Extract decreased aggressive factors like pepsin and proteins and increases defensive factor like pH, hexose, hexosamine, fucose and sialic acid. As a result carbohydrate protein ratio is increased, which indicate the increase in mucin activity[76]. This result suggests that increase in glycoprotein content of the gastric mucosa. Increase in potassium and sodium ion concentration in extract treated group also observed indicates increase in bicarbonate ion concentration, which plays an important role in protecting the gastric mucosa against HCl. Flowering period root extract produce better antiulcer effect than the vegetative period root extract. This may be due to the change both in quality and quantity of the chemical composition, Antiulcer activity of the extracts may be due to the presence of saponins, terpenoids and amino acids which shows gastroprotective activity.

Spartium junceum

Flowers of *Spartium junceum L.* traditionally used in the treatment of peptic ulcer. Methanolic and aqueous extracts of the flower shows antiulcer activity. Anti-ulcerogenic activity of various fractions obtained from the methanolic extract of *S. junceum* flowers by successive solvent extraction also investigated[77]. Aqueous fraction possesses very high and ethylacetate extract fraction showed weak antiulcerogenic activity. Significant anti-ulcerogenic activity of both butanol fraction and final-H_2O fraction-2 also investigated. As aqueous fraction shows highest activity, it was again fractionated by ion-exchange chromatography first on Amberlite-2 and then by molecular sieving on Sephadex LH-20. Fraction LH/Fr.2-9 possesses good ulcer inhibitory effect on oral administration, but showed a high toxicity when injected intraperitoneally. Active fractions LH/Fr.2-9 produce 100%, 94.6% and 83.9% ulcer protection against ethanol, stress and pylorus ligation induced ulcer respectively. Fraction inhibits gastric acid secretion, titratable acidity, acid output and possesses anti-peptic activity in pylorus-ligated rats. It increases gastric pH but did not produce any effect on the hexosamine content of the gastric mucosa. Through bioassayguided fractionation process spartitrioside isolated as main active constituent. Antiulcrogenic activity of spartitrioside also investigated against ethanol induced ulcer. Active saponin fractions found ineffective against *Helicobacter pylori*[78]. Result suggested that the inhibitory effect of fraction on stressinduced lesions may due to decreased acid secretion. Antiulcerogenic activity of active fraction and spartitrioside against ethanol induced gastric lesions may because of its cytoprotective activity.

Amomum subulatum

Amomum subulatum Roxb. (large cardamom) commonly used as a spice. Crude methanolic extract of fruits of large cardamom possess antiulcer activity[79]. Ethanol reduces the secretion of bicarbonates and production of mucus results ulcer in gastric mucosa[80]. Total methnolic fraction (860, 1720 mg/kg), petrol soluble fraction (262 mg/kg), ethyl acetate soluble fraction (196 mg/kg), methanol insoluble fraction (790 mg/kg) and essential oil (200 mg/kg) produce significant ulcer protection against ethanol induced ulcer but methanol soluble fraction (465 mg/kg) found ineffective. Petrol soluble, ethyl acetate soluble, methanol insoluble fraction also found to increase gastric wall mucus in ethanol induced ulcer, so antiulcer effect may due to cytoprotective and strengthening effect on gastric mucosa. Ethyl acetate soluble fraction produce highest activity and shows presence of

phenolic compound. Thus phenolic compounds (flavanones, aurones or anthocyanins) present in this fraction, may be responsible for gastroprotection effect. Total methanolic extract of the fruit does not show any significant ulcer protection against aspirin induced ulcer. Aspirin causes ulcer by inhibition of cyclooxygenase pathway of arachidonic acid metabolism results overproduction of leukotriene and other products of 5-lipoxygenase pathway[81]. So ulcer protective effect of fraction is involved in direct protective effect of on gastric mucosa.

Table 1: Medicinal Plant with Gastroprotective Activity and their beneficial properties

Plant Name	Ayurvedic/ Common Name	Gastroprotective and other beneficial effect
Tabernaemontana divaricata	Crape jasmine	Anthelminthic, antiulcer
Phyllanthus niruri	Gulf Leafflower,	Gastroprotective
Stachys lavandulifolia	Chaye-e-Kohi	Anxiolytic, antiulcer
Cissus sicyoides	Possum Grape Vine	Rheumatism, anti ulcer
Cynanchum auriculatum;	Baishouwu	Antidote. Gastroprotective
Terminalia arjuna	Arjun, Arjuna	Heart diseases, Anti uclers,
Salvia officinalis	Garden sage	Antispasmodic, Anti ulcer
Lippia sidoides	Rosemary pepper	Antimicrobials, gastroprotective
Jatropha isabelli	Yagua rova	Gastroprotective
Ficus indica	Bargad	Antidiabetic, anti ulcer
Voacanga Africana	Voacanga	Anxiety, gastroprotective
Enantia chlorantha	Moambe jaune	Malaria, Gastroprotective
Solanum nigrum	Black Nightshade	Antipyretic, antiulcer
Maytenus ilicifolia	Cancerosa	Anticancer, gastroprotective
Abarema cochliacarpos	Barbatimao	Gastroprotective
Rhizophora mangle	Red mangrove	Antioxidants, anti ulcer
Anchusa strigosa	Prickly alkanet	Gastroprotective
Strychnos pseudoquina	Quina do Cerrado	Hypoglycemic effect, anti ulcer
Bauhinia variegate	Orchid tree	Anti asthamatic , antiulcer
Centella asiatica	Gotu Kola	Antibacterial, anti ulcer
Aspilia Africana	Wild sunflower	Anti rheumatic, gastroprotective
Benincasa hispida	Winter melon	Anti-pyretic, gastroprotective
Azadirachta indica	Neem	Antioxidant, analgesic, antiulcer
Kielmeyera coriacea	Páu santo	Gastroprotective
Garcinia cambogia	Brindal Berry	Gastroprotective
Plectranthus amboinicus	Cuban oregano	Cough, gastroprotective
Alstonia scholaris	Indian Devil tree,	Malarial fever, gastroprotective
Morinda citrifolia	Indian mulberry	Antidiabetic, gastroprotective
Ficus arnottiana	Paraspipal	Wound healing, anti ulcer
Asparagus racemosus	Satavari, Safedmusli	Immunostimulants, antiulcer
Carica papaya	Papaya	Aphrodisiac, gastroprotective
Cereus peruvianus	Night Blooming	Insecticide, gastroprotective
Condonopsis pilosula	Codonopsis ,	Antidiabetic, gastroprotective
Calotropis procera	Milkweed	Leprosy, tonic, anti ulcer
Guiera senegalensis	Dry-zone mahogany	Gastroprotective
Atractylodes ovata	Pai shu	Anti diarrheal, gastroprotective
Gentian root and Swertia	Chirayata	Dyspepsia, gastroprotective

CONCLUSION:

From this review on "Medicinal/Herbal plant which may effective in the treatment of ulcer or which show anti ulcer activities" we can say that the medicinal plant have a vital role against many diseases (the medicinal plant that have not available in any synthetic form). There are various medicinal plant and there extracts (contain active chemical constituents eg: tannins flavonoids etc.) have significant antiulcer activity in *invivo* experiment on animal models. It has muco-protective activity and gastric anti-secretary when compared with that of reference drugs. The extracts are non-toxic even at relatively high concentrations. The antiulcer activity is probably due to the presence of flavonoids in all this plants. The above-mentioned medicinal plants could prevent ulcer in rats in a dose-dependent manner. A variety of botanical products have been reported to possess antiulcer activity; finally, it should be noted that substances such as flavonoids and tannins that possess antiulcer activity are of particular therapeutic importance. The antiulcer activity of the drug can be attributed to free-radical scavenging property, inhibition of acid secretory parameters and strengthening of gastric mucosal barrier. The results of this study indicate that extracts of leaves and plants extracts of some medicinal plant have good potentials for use in peptic ulcer disease. It is concluded from this study that the drug may possesses antiulcer activity in different gastric ulcer models if used in the animal model.

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