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Arabian Medicinal Plants Possessed Gastro protective Effects-Plant Based Review (Part 1)

Prof Dr Ali Esmail Al-Snafi
Department of Pharmacology, College of Medicine, University of Thi qar, Iraq.
Corresponding Author:Prof Dr Ali Esmail Al-Snafi

Abstract: Peptic ulcer disease is one of the main sources of morbidity and mortality worldwide. Many medicinal plants showed gastroprotective activity by many mechanisms, in addition some medicinal plants possessed anti Helicobacter pylori activity. This review will discussed the medicinal plants showed gastroprotective activity.

Keywords: Medicinal plants, Peptic ulcer, Gastroprotective**,** Helicobacter pylori

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I. INTRODUCTION

Peptic ulcer disease is one of the main sources of morbidity and mortality worldwide. It is characterized by erosions in mucosal linings of stomach and duodenum.It is the most common gastrointestinal disorder caused by the alteration in balance between offensive (pepsin, gastric acid and *Helicobacter pylori*) and defensive factors (prostaglandins, bicarbonate ions, mucin, growth factors and nitric oxide)[1].

Plants based remedies have been used widely for gastroprotection all over the world. The gastroprotective activity of plant extracts are evaluated by ulcer area, pH of gastric mucosa, ulcerative index and curative ratio. Inhibition of acidity, elevation in mucus content, inhibition of histamine release, anticholinergic effect, anti *H. pylori* activity and antioxidant potential are prescribed as gastroprotective mechanisms[2-4]. This review will discussed the medicinal plants possessed gastroprotective activity.

Plant with gastroprotective activity

Agrimonia eupatoria

A compound herb preparation containing agrimony has been used to treat 35 patients suffering from chronic gastroduodenitis. After 25 days of therapy, 75% of patients claimed to be free from pain, 95% from dyspeptic symptoms and 76% from palpitation pains. Gastroscopy indicated that previous erosion and haemorrhagic mucous changes had healed [5].

Alhagi maurorum

Ethanolic extract of *Alhagi maurorum* exerted gastroprotective effects against ulcers induced by phenylbutazone, indomethacin and ethanol, increase locomotor activity , and induced sexual stimulation [7].
The anti-ulcerogenic effects of an aqueous extract of *Alhagi maurorum* (AME) (150, 300 and 450mg/kg, PO) was evaluated *in* two models of gastric ulcers induced by alcohol and water immersion restraint-stress in rats. The AME protected rats against water immersion restraint-stress and ethanol-induced ulcers in a dose-dependent manner. In water immersion restraint induced ulcerated rat, the AME increased pH and reduced gastric acid content [9].

Alhagi maurorum ethanolic extract (oral daily 100mg/kg bw) and ranitidine (oral daily 100mg/kg bw) were used in rats to protect against administration of aspirin ASP (oral 200mg/kg body weight) for two times through the 10 days. Some rats were sacrificed after first and second aspirin administrations and the rest were sacrificed in the end of the experiment. Gastro fluid volume has been decreased in ASP group, and acid output was decreased for plant extract followed by ranitidine. No ulcer patterns have been shown in the histopathological study, but some inflammation in the gastric wall and vascular change dilatation of blood vessels were detected [10].

Chrysoeriol 7-O-xylosoid and kaempferol-3- galactorhamnoside showed a promising antiulcerogenic activity with curative ratios 66.31%, 69.57%, 75.49%, and 77.93%, respectively in ethanol 50% (v-v) induced gastric ulcer in rats when used in a dose of 100 mg/kg [11].

Aloe vera

Aloe-emodin inhibited growth of *Helicobacter pylori* in a dose-dependent fashion. *Aleo vera* inhibited gastric acid secretion in mice and rats and has protective effects against gastric mucosal damage in rats. Pretreatment with *Aloe vera* extract reduced aspirin-induced gastric mucosal injury by 70% in experimental rats. *Aloe vera* extracts also suppressed the ulcerogenic effects of stress in experimental rats. Intraperitoneal injection of ethanol extract exerted a gastroprotective effect in acute gastric mucosal lesions induced by 0.6 M HCl in rats. A clinical study showed that *Aloe vera* gel might be helpful in treating patients with duodenal ulcers [12-19].

Alpinia galanga

The constituents of *Alpinia galanga* exerted antiulcer and antisecretory effects. 1'S-1'- Acetoxychavicol acetate and 1'S-1'-acetoxyeugenol acetate, isolated from seeds have markedly inhibited the ethanol-induced gastric mucosal lesions in rats. Ethanolic extract at a dose of 500mg/kg, was significantly reduce gastric secretion in pyrolic ligation and hypothermic restraint stress models in rats, a significant cytoprotective effect has been reported against 80% ethanol, 0.6M HCl, 0.2M NaOH, and 25% NaCl induced gastric cytodestruction [20-23].

Ammannia baccifera

The whole *Ammannia baccifera* was extracted with ethanol and the ethanolicextract was fractionated with petroleum ether, methanol, chloroform and water. All the fractions were tested for their antiulcer property at a dose of 400mg/kg bw po against pyloric ligation and indomethacin induced gastric ulcer model in albino rats. All the fractions of *Ammannia baccifera* significantly inhibited ulcer index. The fractions reduced gastric volume, total acidity, free acidity and increased pH of gastric juice. The methanolic fraction produced more significant ($p<0.001$) antiulcer activity followed by aqueous, petroleum ether and chloroform fractions in pylorus ligation model. The antiulcer activity was almost comparable to that of reference standard ranitidine (20mg/kg bw po). All fractions shown similar results (reduction in ulcer index and increased percent inhibition) in indomethacin induced ulcer model [24].

The chloroform and ethanol extracts of *Ammannia baccifera* were evaluated for antioxidant, gastric antisecretory, and gastroprotective properties. Ethanol extract of *Ammannia baccifera* (EAB) at a dose of 200 mg/kg reduced the free acidity to 142.66 mEq/L and total acidity to 451.22 mEq/L. It reduced the gastric secretion with increase in pH from 2.2 to 3.15. Possessing good antisecretory activity, it also reduced the ulcer by 92.2% in aspirin and pylorus ligation induced gastric ulcer models. EAB increased the mucus secretion and adherent mucus in the tissues with a 71.43% reduction of ulcerin HCl-ethanol induced ulcer models, at a dose of 200 mg/kg [25-26].

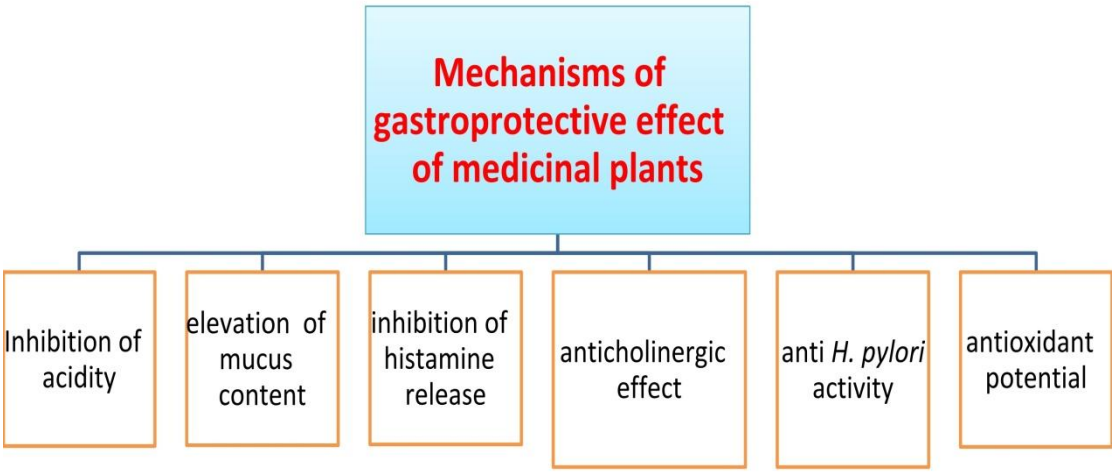

Fig 1: The mechanism of gastroprotective effects of medicinal plants

Anchusa italica

The antiulcer activity of different extracts from the aerial parts and the roots of *Anchusaitalica*was investigated. No antigastric ulcer activity was recorded in indomethacin-induced gastric damage in rats [27-28].

Anchusa strigosa

Anti- ulcer activity of different root extracts of *Anchusa strigosa* was studied in ethanol-induced ulcer model in rats. Petroleum ether-soluble fraction was the most effective in reducing ulcer index and gave 91% protection. Chloroform soluble fraction gave 86% protection while butanol-soluble fraction was less effective (65% protection). On the other hand, water-soluble fraction was not effective in protecting the stomach from the ulcerative agent [29].

The ulcer index values expressed as a percentage of total stomach surface area affected by the ulcer was lowered when *Anchusa strigosa* root extracts was administration at a dose of 0.080 g prior to ethanol induction of stomach ulcer in rats. Treatment of the induced ulcer in guinea pigs was achieved by oral administration of *Anchusa strigosa* root extracts at the therapeutic dose of extract of 0.286 g/kg body weight/day for 24 days [30]. A pepsin inhibitor of undetermined chemical composition was isolated from the aqueous extracts of the roots of *Anchusa strigosa*. The extract of 1 g dry roots inhibited 9380±390 µg of pepsin [31].

Anethum graveolens

Anethum graveolens seed extracts possessed significant mucosal protective and antisecretory effects in the gastric mucosa lesions induced in mice by oral administration of HCl (1 N) and absolute ethanol . The acidity and total acid content were reduced by the orally or intraperitoneally administration of the extracts[32]. *Anethum graveolens* seed extracts exerted moderate activity against *Helicobacter pylori*[33-34].

Apium graveolens

The antiulcerogenic activity of *Apium graveolens* extracts was evaluated in rats by the HCl/EtOH method. Inhibition of gastric lesions by *A. graveolens* extracts was dose-dependent for both aerial part (53–76%) and seeds (51–95%) extracts. The methanolic and aqueous extracts in a dose of 300 mg/ kg exhibited highly significant inhibition of gastric lesions (91% and 95%, respectively) which was similar to that induced by omeprazole (94%). *Apium graveolens* boiling water extract (5%) inhibited the mean height of rabbit jejunum smooth muscle contractions to 35% in comparison with normal contractions[35-36].

Asphodelus fistulosus

Asphodelusfistulosus possessed stomach protective and antiulcerogenic effects against ethanol induced gastric lesions [37]. *Asphodelusfistulosus* also induced relaxation of rabbit gastric smooth muscles [38-39].

Bacopa monnieri

Fresh *Bacopa monniera* juice exerted significant antiulcerogenic activity[40]. Bacopa have a protective and curative effect for gastric ulcers. In rats, the Bacopa extract standardized for bacoside-A was evaluated for its prophylactic and healing effects in five models of gastric ulcers. At a dose of 20 mg/kg for 10 days, Bacopa extract significantly healed penetrating ulcers induced by acetic acid, significantly strengthened the mucosal barrier, and decreased mucosal exfoliation. The extract also alleviated stress-induced ulcers as observed by significant reduction in lipid peroxidation in rat gastric mucosa. It was also exerted anti *H. pylori* effect[41-42].

Bauhinia variegata

In gastric ulcer induced by pyloric ligation and in aspirin induced ulcer model in rats, the ethanolic extract of *B. variegata* decrease the volume of gastric secretion, total free acidity and ulcer index[43-44].

Bellis perennis

The methanolic-eluted fraction of the methanolic extract from the flowers of *Bellis perennis* was found to inhibit gastric emptying in olive oil-loaded mice at a dose of 200 mg/kg, orally [45-46].

Benincasa hispida

The free radical scavenging and antiulcer potential of the methanol extract of *Benincasa hispida* seeds was evaluated by DPPH method for antioxidant effect and by using pyloric ligation, water immersion stress and indomethacin induced gastric ulcer model for antiulcer effects in rats. The methanolic extract showed concentration dependent DPPH radical scavenging activity. It was also inhibited gastric ulceration by decreasing the gastric volume and free and total acidity. The high dose (300 mg/kg bw) showed significant reduction in the above parameters which was comparable to the standard drug ranitidine ($p<0.05$). The methanol extract of *Benincasa hispida* seeds caused 52.7, 67.4 and 61.2% inhibition of ulcers in pyloric ligation, water immersion stress and indomethacin induced ulcer models, respectively at a dose of 300 mg/kg[47-48].

Antiulcer activity of petroleum ether and methanol extracts of *Benincasa hispida*were also investigated in rats. Petroleum ether and methanol extracts were administrated orally at a dose of 300 mg/kg bw, and omeprazole (reference standard) at the dose of 20 mg/kg bw. Both extracts produced significant reduction in

ulcer index ($P < 0.05$) in all the models (ethanol-induced gastric mucosal damage, pylorus ligated ulcer model, cold and restraint stress-induced gastric ulcer model), and the results were comparable with that of omeprazole-treated group. Furthermore, a significant reduction in vascular permeability ($P < 0.05$) was also observed. However, in cold and restraint stress-induced gastric ulcer model, MDA content was significantly reduced along with increase in CAT levels as compared to control group[49].

Various doses of the methanol extract of *Benincasa hispida* (MEBH) (0.2-1 g/kg, ip) were administered to Swiss albino mice to investigate the anorectic effect. (MEBH) significantly reduced the cumulative food intake over a 7 hours period in a dose-dependent manner. The percentage reduction of cumulative food intake at 7th hour for MEBH treated mice with 0.2, 0.6 and 1 g/kg was 27%, 38% and 54% respectively. The 4 hours gastric emptying was not significantly influenced by MEBH when compared to control. It was postulated that the anorectic activity of *Benincasa hispida* was mediated through the central nervous system without affecting the gastric emptying[50].

Bidens tripartita

Intragastric administration of methanolic and aqueous extracts of the aerial parts of *Bidens tripartite* (500 mg/kg bw) to rats showed antiulcer activity against aspirin-induced, but not indomethacin-induced ulcers[51-52].

Brassica nigra

Internally, mustard is a stimulating condiment and appetizer, and excites gastric activity and promotes digestion. If the amount be large, however, it is intense irritation and promptly causes vomiting[53-54].

Bryophyllum calycinum

The methanol-soluble fraction of the leaf extract inhibited the development of a variety of acute ulcers induced in the stomach and duodenum of rats and guinea pigs. Premedication tests in rats revealed that the extract possessed significant protective action against the gastric lesions induced by aspirin, indomethacin, serotonin, reserpine, stress and ethanol. A significant protection with extract was occurred for aspirin-induced ulcer in pylorus-ligated rats and for histamine-induced duodenal lesions in guinea pigs. A significant enhancement of the healing process was also occurred in acetic acid-induced chronic gastric lesions in rats[55-56].

Calendula officinalis

Calendulozide B-trioside, isolated from rhizomes of *Calendula officinalis*, in doses of 5, 10, 20 and 50 mg/kg exerted an antiulcerous action in 3 experimental ulcer models of different genesis (caffein-arsenic, butadion and ligation of pylorus) and also displayed a certain antiphlogistic and sedative action (87). The influence of *Calendula officinalis* on heparin-binding epidermal growth factor (HB-EGF)-like growth factor gene expression in KATO-III cells under the stimulation of *H. pylori* strain N6 using real-time PCR was investigated with and without addition of and *Calendula officinalis*. Addition of *Calendula officinalis* led to a significant reduction of *H. pylori* induced increase in gene expression of HB-EGF (reduced to 75.32±1.16% vs. control; $p<0.05$) [57-58].

170 patients with duodenal ulcers and/or gastroduodenitis, treated with a herbal combination containing calendula showed improvement of symptoms in 90% [59]. 24 adults with non-specific colitis treated with herbal tea included calendula, showed improved symptoms in 96% of the patients within two weeks [60].

Calotropis procera

The protective effect of methanolic extract of *Calotropis procera* latex was investigated on experimentally induced gastric ulcers in rats. The methanolic extract was found to inhibit mucosal damage in both ethanol (85-95%) and aspirin (70- 80%) model, with maintaining the tissue integrity and significant reduction in gastric hemorrhage. Oxidative stress markers (glutathione, thiobarbituric acid reactive substance and superoxide dismutase) were found to be regulated[61-62].

The gastromucosal protective effect of chloroform extract (CH) and hydroalcoholic extract (HE) of the stem bark of *Calotropis procera* was investigated in rats. CH extract at 400 mg/kg was found to have a significant gastromucosal protective effect. As part of investigations to obtain compounds with gastromucosal protective effects, a bioassay was carried out with fractions obtained from the CH extract with n-hexane (NF1), 1-butanol (BF1), ethyl acetate (EF1) and chloroform (CF1). The HE extract of the stem bark was fractionated with n-hexane (NF2), 1-butanol (BF2), ethyl acetate (EF2), chloroform (CF2) and water (WF2).The fractions were evaluated for their gastromucosal protective effects. Fractions NF1 and BF2 (20 mg/kg) showed gastromucosal protective effects which further supported by histopathological examination of the open excised rat stomach [63].

The chloroform fraction of *Calotropis procera* root extract demonstrated significant anti-ulcer activity against aspirin, indomethacin, ethanol, indomethacin + ethanol, or stress-induced ulcerations. Significant inhibition of gastric secretory volume and total acidity in pylorus ligated rats were observed to occur with the extract. It was also observed that the root extract significantly inhibited arachidonic acid metabolism induced by soyabeian lipoxygenase. The anti-ulcer activity of the extract might be attributable to the inhibition of 5-lipoxygenase [64].

The methanol and acetone extracts from *Calotropis procera* exhibited strong anti-H. pylori activity, almost comparable activity with tetracycline, but were found to be less potent thanamoxicillin and clarithromycin [65].

Capsicum annuum* and *Capsicum frutescens

The effect of aqueous extracts of *Capsicum frutescens* on the healing acute gastric ulcer induced by aspirin was investigated in rats (at doses of 300 and 600 mg/kg bw for seven days). The results revealed that oral administration of the aqueous extract at a dose of 600mg/kg bw, reduced the length of gastric ulcer, volume of gastric juice, and improved histopathological changes [66-67].

Capsaicin protected the gastric mucous against ulceration by ethanol when used at low concentrations (0.13–160 μM) in rats. Capsaicin exerted protective effects against ethanol- and indomethacine-associated gastropathy in 84 healthy human subjects, with a dose dependent decrease in base gastric acid output (ED50 for 400 μg capsaicin) and increased gastric emptying [68-69]. Gastrointestinal system also contained capsaicin-sensitive sensory nerves which plays a crucial role in maintenance of gastrointestinal mucosa integrity against injurious interventions. A low dose of capsaicinoids could increase the basal gastric mucosal blood flow and gastric mucus secretion, and facilitate gastric epithelial restitution, which were beneficial to gastrointestinal defense [70].

Carthamus tinctorius

Inhibition zone of the methanol extract of *Carthamus tinctorius* at concentration of 2 mg/disc against *H. pylori* clinical isolates was 18.77±0.56mm, while, MIC and MBC for the same extract were 691.25 and 691.25 μg/ml, respectively [71]. 200 and 400mg/kg of *Carthamus tinctorius* extract with carbachol protected rat from gastric ulceration after pylorus ligation. The doses were significantly decreased volume of gastric secretion, free acidity, mEq/dl of gastric secretion, total acidity, mEq/dl of gastric secretion and ulcer index . They significantly increased the PH of gastric juice and gave 78 and 83% gastric protection respectiviley[72-73].

Carum carvi

Pretreatment with oral doses of 250 and 500 mg/kg was found to provide a dose dependent protection against ulcerogenic effect of different necrotizing agents in rats, ethanol induced histopathological lesions, depletion of stomach wall mucus and nonprotein sulfhydryl groups (NP-SH) and pylorous ligated accumulation of gastric acid secretion. The mechanism of action might be due to flavonoids related suppression of cytochrome P450 IAI (CYPIAI) which known to convert xenobiotics and endogenous compounds to toxic metabolites [74-75].

The antiulcerogenic activity was also evaluated by the HCl/ethanol method, which causes injury to the gastric mucosa. The results showed that *C. carvi* essential oil enhanced a significant inhibition of 47%, 81% and 88%, respectively,for three doses (100,200 and 300 mg/kg) of essential oil used, which was similar to that induced by omeprazole (95%) ($p < 0.005$) [76].

Extracts from the *Carum carvi* was investigated for a potential anti-ulcerogenic activity against indometacin induced gastric ulcers in rat as well as for their antisecretory and cytoprotective activities. The extracts produced a dose dependent anti-ulcerogenic activity associated with a reduced acid output and an increased mucin secretion, an increase in prostaglandin E2 and a decrease in leukotrienes release [77]. In addition, methanol extracts of *Carum carvi* showed anti *H. pylori* effect with MIC of 100 microg/ml [78].

Casuarina equisetifolia

The anti-ulcer effect of the Ethanol extract of *Casuarina equisetifolia (L.)* extract was studied in albino rats. Ethanolic extract at the doses of 200 and 400 mg/kg was administered orally to evaluate anti-ulcer activity in ethanol, indomethacin, and cold-restraint stress induced gastric ulcer models in Albino rats. Ethanol extract caused dose dependent inhibition in ethanol induced gastric lesions, ethanol extract showed 70.37 % protection at 400 mg/kg, and 52.7% protection at 200 mg/kg, In indomethacin induced gastric lesions, ethanol extract showed 68.3% protection at 400 mg/kg and 51.7% protection at 200 mg/kg, it also showed dose dependent inhibition in cold-restraint stress induced gastric lesions. Ethanol extract showed 75.02% protection at 400 mg/kg, and 45.86% protection at 200 mg/kg. All the results were found statistically significant ($p \leq 0.05$) [79-80].

The anti-*Helicobacter pylori* and urease inhibition activities of extracts of *Casuarina equisetifolia* were investigated. The extracts exhibited lower activity than the standard antibiotics used in this study [81].

Centaurea cyanus

Pharmacological studies carried out on Wistarrats with stress-induced ulcer shown a very gastro-protective activity (protection percents over 80%) of the *Centaurea cyanus* extract [82]. Moschamine a safflomide-type phenylpropenoic acid amide found in *Centaurea cyanus* was a very potent COX-II inhibitor, it inhibited COX-II by 54% ($p < 0.014$), at the concentration of 0.1 μ mol/ l [83-84].

Chenopodium album

The effect of alcoholic extract of *Chenopodium album* was investigated in rats to evaluate the antiulcer activity by using three models, pyloric ligation, ethanol and cold restraint stress induced ulcers. Alcoholic extract significantly decreases the volume of gastric acid secretion, free acidity, total acidity and ulcer index with respect to control. Sections of ulcerated area revealed that there was a significant increase in regenerated glandular epithelium width after treatment with the alcohol extract. The collagen content in the ulcerated tissue was significantly increased by alcohol extract and ranitidine as positive control. No significant difference on capillary density in scar tissue was observed after treatment with alcohol extract or ranitidine [85-86].

Citrullus colocynthis

The *Citrullus colocynthis* seed methanolic extract was evaluated for anti-ulcerogenic activity by pyloric ligation induced ulcers model in Wistar albino rats. *Citrullus colocynthis* (200 mg/kg) showed maximum inhibition of gastric volume 1.68±0.18, free acid 39.86±3.86 and total acidity 61.23±1.87 at dose of 200 mg/kg. The maximum percentage inhibition of ulcerogenicity by the extract in pyloric ligation model was 71.57% at a dose of 200 mg/kg [87-88].

Citrus species

The antiulcer activity of aqueous extract of the fruits of *Citrus medica* was evaluated against ethanol-induced ulcers in rats. The rats were pretreated with the extract at two doses (250 and 500 mg/kg po) and the antiulcer effect was compared with that of ranitidine (20 mg/kg po). The extract of both doses showed a significant reduction in ulcer formation. Histopathological sections showed significant decrease in mucosal ulceration, inflammatory mucosal changes and submucosal edema compared to ethanol treated group and the ranitidine group. It was concluded that, the fruits of *Citrus medica* possesses significant antiulcer activity against ethanol-induced ulcers in rats and the antiulcer activity could be due to the presence of flavonoids as these compounds have well documented antiulcer activity [89-90].

Clitoria ternatea

The antiulcer potential of aqueous and ethanolic extracts of *Clitoria ternatea* was evaluated in different experimentally induced ulcer models in rats. Ethanolic extract (200 and 400 mg/kg) and aqueous extract (200 and 400 mg/kg) of whole plant were examined in pylorus ligation and indomethacin induced gastric ulcer in rats. Various parameters like volume of gastric acid secretion, pH, total acidity, ulcer index and antioxidant parameters were determined and compared between extracts, standard and vehicle control group following ulcer induction. Among different dose of alcoholic extract, high dose showed significant antiulcer activity in pylorus ligation and indomethacin induced ulceration [91-92].

Cordia myxa

The protective effects of *Cordia myxa* fruit extract (CME) was investigated against indomethacin-induced gastric ulcer in rats. Gastric ulceration was induced by a single intraperitoneal injection of indomethacin (30 mg/kg bw). CME was administered orally at a dose of 125 mg/kg bw, while ranitidine (RAN), which used as a reference drug, was given at a dose of 50 mg/kg bw, two weeks prior to indomethacin injection. Pretreatment with CME produced significant reduction in gastric mucosal lesions, malondialdehyde (MDA), and serum tumor necrosis factor (TNFα) associated with significant increase in gastric juice mucin content and gastric mucosal catalase (CAT), nitric oxide (NO), and prostaglandin E2 (PGE2) levels. A similar increase in mucin content, NO and PGE2 was not observed with RAN although it generated a preventive index of 75.9%. RAN significantly increased pH value and decreased pepcin activity, and gastric juice free and total acidity. Histological studies of stomach mucosa confirmed these results. Stomach of rats administrated with RAN showed leukocytic infiltration in submucosal layer. Meanwhile, stomach of rats administrated CME either alone or with RAN showed no histopathological changes. CME can protect indometacin-induced gastric ulceration due to its antioxidative and mucin enhancing properties. The protection afforded by co-administration of CME and RAN was found to be better than that of RAN alone [93-94].

Coriandrum sativum

The effect of coriander pretreatment on gastric mucosal injuries caused by NaCl, NaOH, ethanol, indomethacin and pylorus ligation accumulated gastric acid secretions was investigated in rats. Pretreatment at oral doses of 250 and 500mg/kg, was found to provide a dose-dependent protection against the (i) ulcerogenic effects of different necrotizing agents; (ii) ethanol-induced histopathological lesions; (iii) pylorus ligated accumulation of gastric acid secretions and ethanol related decrease of nonprotein sulfhydryl groups (NP-SH). Results of gastric mucus and indomethacin-induced ulcers demonstrated that the gastro protective activity of Coriander might not be mediated by gastric mucus and/or endogenous stimulation of prostaglandins. The authors suggested that the protective effect against ethanol-induced damage of the gastric tissue might be related to the free-radical scavenging property of different antioxidant constituents (linanool, flavonoids, coumarins, catechins, terpenes and polyphenolic compounds) present in coriander. The inhibition of ulcers might be due to formation of a protective layer of either one or more of these compounds by hydrophobic interactions [95].

The effect of selected indigenous medicinal plants of Pakistan was evaluated on the secretion of interleukin-8 (IL-8) and generation of reactive oxygen species (ROS) to rationalize their medicinal use and to examine the anti-inflammatory and cytoprotective effects in gastric epithelial cells. AGS cells and clinically isolated *Helicobacter pylori* strain (193C) were employed for co-culture experiments. *Coriandrum sativum*, demonstrated significant suppression of ROS from *Helicobacter pylori*-infected cells ($p<0.01$) [96].

Crocus sativus

An aqueous suspension of saffron was subjected to evaluate its gastric antiulcer activity induced by pylorus ligation (Shay rats), indomethacin and various necrotizing agents including (80% ethanol, 0.2 M NaOH and 25% NaCl) in rats. Gastric wall mucus and non-protein sulfhydryl contents were estimated in rats. Histopathological assessment of rat stomach was also carried out. The saffron aqueous suspension at doses (250 and 500 mg/kg) decreased gastric secretion and ulcer index in Shay rats and indomethacin treated groups. Gastric wall mucus was enhanced. A large margin of safety was observed in animals after acute and chronic treatment [97-98].

The effects of an ethanol and aqueous extract of saffron *Crocus sativus* and its constituents safranal and crocin was investigated on stress-induced reduction in food intake, weight gain and anorexic time in mice. Male albino mice were irregularly exposed to a trial of electroshock stress for 7 days. Then, the anorexic time as well as the animal's food intake and weight were recorded. Intraperitoneal administration of the aqueous but not the ethanol extract (10, 50 and 100 mg/kg) significantly reduced the anorexic time. The results were similar for crocin (1, 5 and 10 mg/kg; ip). In addition, a reduction in weight gain was observed in the controls as well as in the groups that received alcohol extract or safranal. The plasma corticosterone level did not increase in the aqueous extract and crocin treated animals. The authors concluded that the saffron aqueous extract and its constituent crocin reduce side effects of electroshock stress in mice [99].

The beneficial effect of saffron (*Crocus sativus*) aqueous extract (SAE) on the 1-Methyl -3- nitro -1-nitrosoguanidine (MNNG)-induced gastric cancer was investigated in rats. Different concentrations of SAE were administered to rats. After sacrificing, the stomach tissue was investigated by both pathologist and flow cytometry, and several biochemical parameters were determined in the plasma (or serum) and stomach of rats. Pathologic data indicated the induction of cancer at different stages from hyperplasia to adenoma in rats was inhibited by SAE administration; 20% of cancerous rats treated with higher doses of SAE was completely became normal at the end of experiment and there was no rat with adenoma in the SAE treated groups [100].

Cuminum cyminum

The stomach of pentobarbitone-anesthetized rats was perfused at 0.15 ml/min with aqueous extracts of cumin or acetylcholine (1 microgram/ml or 10 micrograms/ml solutions, in 40 min blocks, twice in each experiment bracketed by saline perfusions. The acid content in the samples was estimated by titration with 0.1N NaOH with phenolphthalein as indicator. Cumin increased stomach acid secretion from 0.08 to 0.02. ($p < 0.05$) [101-103].

The antiulcer activity of the aqueous extracts of leaves of dried fruits of *cumin* against the diclofenac sodium induced stomach ulceration has been studied in rats in comparison with omeprazole. Cumin extract accelerated the healing process to different extents. Healing activity of the aqueous extracts of combination of *piper betel* and *cumin* was found to be beter than healing activity of aqueous extracts of cumin and piper betel alone. Aqueous extract also enhance gastric mucin protection and regeneration [102,, 104].

Cynodon dactylon

The effect of 50% ethanolic extract of *Cynodon dactylon* Pers was evaluated in gastro-ulcerogenic potential of indomethacin. 50% ethanolic extract of *Cynodon dactylon* was administered in the dose of 300 and 600 mg/ kg orally 30 minutes prior to ulcer induction in male Sprague-Dawley rats by oral

administration of indomethacin. Famotidine was used as a reference standard drug. The antiulcer activity was assessed by determining and comparing the ulcer index in the test drug group with that of the vehicle and standard groups. Both the doses, 300 and 600 mg/ kg of test drug showed a protective effect on indomethacin-induced ulcers with 56.74% and 79.61% ulcer inhibition rate, respectively [105-106].

The gastro-protective effect of *Cynodon dactylon* was studied in alcohol and indomethacin induced gastric mucosal damage. The control group received only ulcerogen, whereas the standard control group and test compound groups were pretreated with ranitidine (25mg/kg) and *Cynodon dactylon* (300 and 450mg/kg of the plant juice powder, intragastrically) respectively, before exposure to ulcerogen. 4 hours after exposure to ulcerogen the rats were sacrificed, stomachs were dissected out and opened. The total number of ulcers, size of each ulcer was noted and ulcer index was calculated.. In alcohol model the rats pretreated with *Cynodon dactylon* showed significant protection as compared to control and ranitidine pretreated groups. However in indomethacin model the rats pretreated with ranitidine gave better protection [107].

The extract of *Cynodon dactylon* was investigated for its anti- ulcer activity against pylorus ligation, aspirin induced and ethanol induced gastric ulcer in rats at 100, 200, 300 mg/kg bw. A significant reduction ($p<0.01$) in ulcer index was seen in *Cynodon dactylon* extract treated rats of pylorus ligation, aspirin induced and ethanol induced gastric ulcer models. The gastroprotective effect was further confirmed by histopathological examination of rat stomach [108].

Alcoholic extract of *Cynodon dactylon* was evaluated at 200, 400, and 600 mg/kg bw, orally for pylorus ligated and indomethacin induced gastric ulcer models in albino rats. Alcoholic extracts at 400 and 600 mg/kg showed significant ($p>0.001$) antiulcer activity, comparable to the standard drug ranitidine [109].

Cyperus rotundus

The antiulcer activity of crude extract of *Cyperus rotundus* was studied in rats at a dose of (300mg/kg and 500mg/kg). Ulcer was induced in rats by aspirin 300 mg/kg. Crude extract induced significant antiulcer effect [110-111].

The protective effects of *Cyperus rotundus* on gastric mucosal damage induced by ischemia and reperfusion was studied in rats. Ischemia/reperfusion model was designed as 30 min ischemia followed by 60 min reperfusion by clamping the celiac artery. The *Cyperus rotundus* extracts were given at the doses of 100 or 200 mg/kg to prevent postischemic gastric mucosal injury. Antioxidant enzymes activity such as malondialdehyde and glutathione-peroxidase were measured in the gastric tissue. Histopathological sections were examined for ischemic injury. The mean ulcer index of rats treated with 200 and 100 mg/ kg *Cyperus rotundus* were significantly lower ($p<0.05$) than that of control rats. The activities of antioxidant enzymes were significantly enhanced ($p<0.05$) by treatment with *Cyperus rotundus* extracts [112].

Decoctions of *Cyperus rotundus* rhizome were given orally (1.25, 2.5, 4.0 g crude drug/kg) to rats 30 min before ethanol showed gastric ulcer inhibitory effect in a dose dependent manner [113].

The ulcer-preventive role of *Cyperus rotundus* was studied in rats treated with non-steroidal anti-inflammatory drugs. Oral administration of different doses of *Cyperus rotundus* rhizome methanolic extract (250 and 500 mg/kg) significantly inhibited aspirin-induced gastric ulceration in animals in a dose-dependent manner (49.32% and 53.15%, respectively), which was also comparable with the standard gastric ulcer drug ranitidine. Administration of *Cyperus rotundus* rhizome methanolic extract also significantly increased the activity of superoxide dismutase, cellular glutathione and glutathione peroxidase, and inhibited the lipid peroxidation in the gastric mucosa of ulcerated animals in a dose-dependent manner [114].

Dactyloctenium aegyptium

The ethanolic extract of *Dactyloctenium aegyptium* was investigated for its anti-ulcer activity against aspirin plus pylorus ligation induced gastric ulcer in rats, HCl -Ethanol induced ulcer in mice and water immersion stress induced ulcer in rats at 300 mg/kg body weight orally. A significant ($P<0.01$, $P<0.001$) anti-ulcer activity was recorded in all the models. Pylorus ligation showed significant ($P<0.01$) reduction in gastric volume, free acidity and ulcer index in animals treated by *Dactyloctenium aegyptium* extract compared to control. *Dactyloctenium aegyptium* extract also caused 89.71% ulcer inhibition in HCl- Ethanol induced ulcer and 95.3% ulcer protection index in stress induced ulcer[115-116].

Dalbergia sissoo

The antiulcer effects of *Dalbergia sissoo* stem bark methanol extract (DSME) was studied against the diclofenac sodium-induced ulceration in rat. The DSME (200 mg/kg and 400 mg/kg body weight) was orally administered to rats once a day for 10 days in diclofenac-treated rats. The gastroprotective effects of DSME were determined by assessing gastric-secretory parameters such as volume of gastric juice, pH, free acidity, and total acidity. Biochemical studies of gastric mucosa were conducted to estimate the levels of nonprotein sulfhydryls (NP-SHs), lipid peroxidation [thiobarbituric acid reactive substances (TBARSs)], reduced glutathione (GSH),

hydrogen peroxide (H_2O_2), levels of scavenging antioxidants, catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), glutathione-S-transferase (GST), and myeloperoxidase (MPO). Moreover, adherent mucus content and histological studies were performed on stomach tissues. Administration of DSME significantly decreased the ulcer index, TBARSs, H_2O_2, and MPO activity in gastric mucosa of the ulcerated rats. Activities of enzymic antioxidants, CAT, SOD, GSH-Px, GST and GSH, and NP-SH contents were significantly increased with DSME administration in the gastric mucosa of diclofenac-treated rats. Volume of gastric juice, total and free acidity were decreased, whereas pH of the gastric juice was increased with the administration of DSME + diclofenac[117].

The antiulcer activity of crude ethanolic bark extract of *Dalbergia sissoo*(EBED) was evaluated using pylorus ligation and Indomethacin induced ulcer model in Wistar albino rats. The study revealed the significant decrease ($p<0.01$) in mean ulcer index in EBED treated group in both models compared to control. Furthermore, there were significant decrease ($p<0.01$ and $p<0.001$) in the offensive factors like free and total acidity, pepsin content and protein content whereas significant increase in the defensive factors like total carbohydrate content ($p<0.01$) and ratio of total carbohydrates and proteins as compared to control in dose dependent manner[118-119].

Daucus carota

The therapeutic potential of 50% ethanol extract from *Daucus carota* roots (EDC) was studied as antisecretory, gastroprotective, and in vitro antacid capacity using experimental rats. Assessment of EDC antisecretory and in vivo antacid capacities was carried out using a pyloric ligation induced ulcer model. The gastroprotective effect was assessed with an absolute ethanol induced ulcer model. The integrity of gastric mucosa was evaluated using the estimation of glutathione and gastric mucus level and with histopathological examination of gastric mucosal cells. The in-vitro antacid capacity was evaluated using a titration method. The effect of the extract on the liver was assessed by measuring serum biochemical parameters. The EDC significantly ($p < 0.01$-0.001) reduced gastric lesions in both models. It also significantly ($p < 0.05$-0.001) reduced the volume of gastric content, the total acidity was significantly ($p < 0.05$-0.001) reduced with the doses of 100 mg/kg and 200 mg/ kg EDC. The mucus content and glutathione level increased significantly ($p < 0.05$) in the absolute alcohol-induced ulcer. The EDC also showed in-vitro antacid capacity. Histopathological studies further confirmed the effects of EDC by inhibiting congestion, edema, hemorrhage, and necrosis in gastric mucosa[120].

The anti peptic ulcer effects of the aqueous and methanolic extracts of Daucus carota umbels was investigated against ethanol induced gastric ulcer in rats. A significant protection against ethanol induced ulcer was observed with both aqueous and methanolic extracts. Methanolic extract of Daucus carota was more potent, it showed significant protection against ethanol induced gastric ulcer with a curative ratio of 46.8 and 68.7%, at a dose of 250 mg/kg body weight, respectively[121].

The gastroprotective potential of the fresh juice extract of the roots of *Daucus carota* (200 and 400 mg/kg bw, orally) was studied in gastric ulcerations experimentally induced by pylorus ligation, aspirin and ethanol induced. The *Daucus carota* extracts were significantly decreased gastric volume, free acidity, total acidity and ulcer index, while it increased the pH and the mucus content as compared with control. The *Daucus carota* extract at a dose of 400 mg/kg produced 60.45, 56.80 and 43.51 % significant inhibition when gastric ulceration were induced by pylorus ligation, aspirin and ethanol, respectively[122].

The gastroprotective effect of 4.08 g carrot juice administered by feeding tube was studied on the hydrochloric acid concentration in the stomach in aspirin-induced Wistar-strain rats. The result of carrot juice consumption together with aspirin shows a statistically significant reduction in HCL concentration in the stomach ($p<0.05$). The result was also significant when compared with Misoprostol[123-124].

Desmostachia bipinnata

The anti-ulcerogenic activity of *Desmostachia bipinnata* was studied in ethanol induced gastric damage in rats. Three treatment groups received the ethanol extract of *Desmostachia bipinnata* (L.) Stapf in doses of 150, 250 and 300 mg/kg and another two treatment groups were administered compounds and trycin and trycin-7-glucoside isolated from the ethanol extract of *Desmostachia bipinnata*, respectively in a dose of 100 mg/kg. The total extract (200 and 300 mg/kg) and two of the isolated compounds (trycin and trycin-7-glucoside.100 mg/kg each) showed a very promising antiulcerogenic activity with curative ratios; 68.31, 70.54, 77.39 and 78.93%, respectively[125]. In studying the potential in vitro antihelicobacter activity of selected Egyptian plants,

The methanolic extract of Desmostachya bipinnata (DEM) proved to be the most active one, where its MIC was 40 µg/ml. After fractionation of the DEM extract, ethyl acetate fraction exhibited excellent antihelicobacter activity. By further fractionation and purification, using TLC and column chromatography, a

flavonoid compound was isolated, with MIC value of 62 µg/ml. The isolated compound was spectroscopically identified as 4'-methoxy quercetin-7-O-glucoside[126-127].

Dianthus caryophyllus

Eugenol in doses (10-100 mg/kg) also possessed anti-ulcerogenic effects in gastric ulcers induced by different ulcerogenic agents. The gastroprotective effectcould be attributed to the opening of ATP-sensitive potassium (KATP) channels, free radical scavenging, decreased acid-pepsin secretion, increased mucin production and prevention of the deleterious rise in nitric oxide level[128].
Eugenol also possessed antidiarrhoeal effects in diarrhoea induced by castor oil , It also induced relaxant effects on isolated gut muscle [129-131].

Dodonaea viscose

The gastroprotective effect of Dodonaea viscosa was studied in two different models (ethanol and indomethacin induced gastric ulcer) in wistar rats. Gastric protection was evaluated by measuring the ulcer index, gastric glutathione assay, alkaline phosphate assay and histopathological studies. Gastric secretion studies were done by pyloric ligation experiment. Water and ethanol extract (500 mg/kg body weight) showed moderate activity compared to hexane extract. Hexane extract of Dodonaea viscosa dose dependently inhibited ethanol induced gastric lesions, causing 90% protection at 500 mg/kg, 81% protection at 250 mg/kg, and 70% protection at 125 mg/kg and it also dose dependently inhibited indomethacin induced gastric lesions, causing 92% protection at 500 mg/kg, 77% protection at 250 mg/kg, and 52% protection at 125 mg/kg. The various degrees of inhibition were statistically significant ($p \leq 0.05$). Hexane extract of *Dodonaea viscosa* (500 mg/kg) also decreased the amount of total acid in gastric juice[132-133].

Erigeron Canadensis

The 70% ethanolic extract of the aerial parts of E. canadensis was found to protect the gastric ulcer induced by HCl/ethanol in mice. The administration of HCl/ethanol produced lesions on the gastric mucosa which were significantly and dose-dependently reduced from 74.4%, ulceration percentage to 14.4%, in the animals pretreated with % ethanolic extract of the aerial parts of E. Canadensis orally at the doses of 1 (54.6-10.2mm^2), 10 (21.6-6.4mm^2) and 100 mg/kg (10.6-4.5mm^2). In the group pretreated with extract at the dose of 100 mg/kg, the protective effect was higher than that of sucralfate used as a reference drug. Under histological evaluation, pre-treatment with extract reversed the alterations such as inflammation, edema, moderate hemorrhage and a great loss of epithelium cells presented by HCl/ethanol treated stomachs, and the histological aspect was similar to those observed in normal stomach and the pretreated group with the reference drug[134-135].

***Eucalyptus* species**

The ulcer-healing promoting effect of the methanol extracts of *Eucalyptus camaldulensis* leaves was investigated in acetic acid induced-ulcer in rat. The results showed that methanol extracts of *Eucalyptus camaldulensis* leaves reduced the size of the ulcer from day 5 in animals treated with 500mg/kg body weight of reconstituted extracts at 24 hours interval . At the end of the experiment (i.e. day 14) most of the ulcers has reduced by half the original size with 46.67 ±3.33 % decrease in diameter compared to the controls (distilled water and ranitidine) which afforded 21.67 ±1.05% and 59.17 ± 1.54% decrease in diameter respectively[136].
The in vitro anti- *Helicobacter pylori* of *Eucalyptus camaldulensis* was investigated in six strains of H. pylori (ATCC 4504, ATCC 47619, A2, TI8984, 019A, and A6). The minimum inhibitory concentrations of the crude extracts against all the tested strains ranged from 12.5 to 400 mug/ml[137-138].

Euphorbia hirta

The antiulcer effect of *Euphorbia hirta* (200 & 400mg/kg orally), were studied in many ulcer inducing models in rats. The *Euphorbia hirta* showed significant protective effect at both doses on all ulcer models. In pyloric ligation model, *Euphorbia hirta* at doses of 200 and 400 mg /kg inhibited ulcer formation significantly (50.46% and 87.43% respectively) and reduced gastric secretion. In HCl/Ethanol induced ulcerated rats, gastric wall mucus was significantly preserved by the *Euphorbia hirta* pretreatment at doses of 200 and 400 mg/kg. The *Euphorbia hirta* gastroprotective potential was attributed to preservation of gastric mucus secretion and anti secretary action[139-140].

Foeniculum vulgare

Both *F. vulgare* essential oil and anethole (100 mg/kg, oral administration) provided significant protection toward ethanol induced gastric lesions in rats[141].

The gastric ulcer protective potential of an aqueous suspension of *Foeniculum vulgare* was evaluated against different acute gastric ulcer models , pyloric ligation (Shay), hypothermic restraint stress, indomethacin and by necrotizing agents (80% ethanol, 0.2 M NaOH and 25% NaCl). Pretreatment with *Foeniculum vulgare* suspension, 250 and 500 mg/ kg bw orally (intraperitoneally in Shay rat model) showed a dose-dependent ulcer protective effects in all the models. Furthermore, it offered protection against ethanol-induced depletion of gastric wall mucus, replenished the reduced nonprotein sulfhydryls concentration and modulated malondialdehyde contents in the gastric tissue. Ethanol induced histopathological lesions was reversed by *Foeniculum vulgare*[142].

The anti-ulcerogenic and antioxidant effects of aqueous extracts of *Foeniculum vulgare* (FVE) (75, 150 and 300 mg/kg) was evaluated in ethanol-induced gastric lesions in rats. Pretreatment with FVE significantly reduced ethanol-induced gastric damage. The anti-ulcerogenic effect of FVE was highest and in 300 mg/kg group ($P < 0.001$). Pretreatment with FVE also significantly reduced the MDA levels, and significantly increased GSH, nitrite, nitrate, ascorbic acid, retinol and β-carotene levels[143].

The antiulcerogenic property of *Foeniculum vulgare* was evaluated in Wistar albino rats. The aqueous suspension of fennel was given in two doses (250 and 500 mg/kg body weight, orally). Gastric acid secretion studies were undertaken using pylorus ligated (Shay) rats. Gastric lesions in the rats were induced by noxious chemicals including ethanol, strong alkalis and indomethacin. The levels of gastric wall mucus (GWM), nonprotein sulfhydryls (NP-SH) and malondialdehyde (MDA) were also measured in the glandular stomach of rats following ethanol administration. The gastric tissue was also examined histologically. In pylorus-ligated Shay rats, the suspension of fennel significantly reduced the basal gastric acid secretion, titratable

acid and stomach ulceration (64 %, 39 % and 100 %), respectively. The suspension significantly ($P < 0.001$, $P < 0.01$ and $P < 0.01$) attenuated gastric ulceration induced

by necrotizing agents (80 % ethanol, 0.2 mol/l NaOH, 25 % NaCl) respectively and indomethacin was found to be ($P < 0.01$). The cytoprotective and antiulcer effect was further confirmed histologically. Furthermore, the suspension significantly replenished the ethanol-induced depleted levels of GWM ($P < 0.001$), NP-SH ($P < 0.05$) and diminished ($P < 0.01$) (MDA) concentration of the stomach[144].

Glycyrrhiza glabra

Carbenoxolone a glycyrrhizate analog was effective in clinical trials in the treatment of gastric and duodenal ulcer at the medium dose of 100 mg three times a day. Liquorice can raise the concentration of prostaglandins in the digestive system that promote mucus secretion from the stomach, it was also prolonged the life span of surface cells in the stomach and has an anti-pepsin effects[145-149].

The anti-H pylori activity of glycyrrhizic acid, glycyrrhetinic acid and a novel lipophilic derivative of glycyrrhetinic acid monoglucuronide acetylated GAMG was tested against 29 Helicobacter pylori strains. Glycyrrhetinic acid was the most potent compound ($MIC_{50/90}$, 50/100 mg/l), inhibiting 79.3% of the strains at MIC <50 mg/l[150].

In a trial of 40 patients receiving either 3.0 or 4.5 g Deglycyrrhizinated licorice (DGL) daily for eight weeks. Patients were assessed for relief from epigastric pain, nausea, vomiting, x-ray of ulcer craters to determine changes in size, and frequency of relapse. All patients showed significant improvement after 5-7 days[151].

In more larger trial carried out on 874 patients with chronic duodenal ulcers. Patients were received DGL, cimetidine, or antacids. No differences were recorded among groups in the rate of ulcer healing, but patients in the DGL group showed less occurance of relapses[152].

***Gossypium* species**

The aqueous and ethanolic extracts of flowers of *Gossypium herbaceum* L. increases healing of gastric ulcer and possess potential antiulcer activity[153].

Hedera helix

The ulcer preventive efficacy of water extracts of H. helix was investigated in ethanol-induced ulcer model in rats. Water extracts of H. helix (300 mg/kg, ip) significantly ($p<0.01$) decrease the ulcer index (1.38 vs 3.17 in control) and rise macroscopic curative ratio (56.6%)[154].

Helianthus annuus

The anti-ulcer activity of hydroalcoholic extracts of *A. indicum*, *H. annuus* and combination of both was evaluated against ethanol induced gastric ulcer and pyloric ligation induced gastric ulcer in Albino Wistar Rats. All extracts showed significant anti-ulcer activity. The protective effect was found to be in the following order: combined hydro alcoholic extract of *A. indicum* and *H. annuus* > hydro alcoholic extract of *H. Annuus* > hydro alcoholic extract of *A. Indicum*[155-156].

Hibiscus cannabinus

The antiulcer properties and percentage protection of *Hibiscus cannabinus* seed oil were evaluated towards many ulcer-inducing models in rats. *Hibiscus cannabinus* seed oil showed an ulcer protective effect towards ethanol, non-steroidal anti-inflammatory drugs (NSAIDs) and cold restrain stress induced ulcers. *H. cannabinus* seed extract (HSSE) exhibited an exceptionally high ulcer protection of 74.98 ± 0.78% against NSAIDs induced ulcer. The gastric lesions were controlled primarily by both mucosal protection and acid inhibition[157-158].

Hibiscus sabdariffa

The gastro-protective potential of *Hibiscus sabdariffa* against indomethacin-induced gastric ulcer was evaluated in the rat. 70% alcoholic extracts of *Hibiscus sabdariffa* (100,400, 800 mg/kg) were gavaged to rats for 4 consecutive days. Gastric ulcers were induced by the one time gavage of indomethacin (30mg/kg). The animals were killed 6 h after the indomethacin administration. Ulcer index was significantly and dose-dependently decreased in rat treated with *Hibiscus sabdariffa*[159].

The anti-ulcerogenic property of ethanolic extract of dried calyces of *Hibiscus sabdariffa* in different ulcer models was studied in Wistar albino rats. The extract at 250 and 500 mg/kg body weight, orally showed a significant effect in cold restraint stress, pylorus ligation, necrotizing agents (80% ethanol, 0.2 M NaOH and 25% NaCl) and indomethacin-induced gastric ulcer models. The extract was also significantly decreased the basal gastric acid secretion, significantly increased gastric wall mucus secretion and non-protein sulfhydryl concentrations in gastric tissue and significantly reduced the ethanol-induced elevated levels of malondialdehyde in the rat stomach[160].

Jasminum sambac

The gastroprotective effects of ethanolic extracts of J. sambac leaves (62.5, 125, 250, and 500 mg/kg) was studied against acidified ethanol-induced gastric ulcers in rats. Ulcer group exhibited significantly severe mucosal injury as compared with omeprazole or extract which shows significant protection towards gastric mucosal injury, the plant promoted ulcer protection as it showed significant reduction of ulcer area (grossly), marked reduction of edema and leucocytes infiltration of submucosal layer (histologically) compared with ulcer group. Immunohistochemistry showed overexpression of Hsp70 protein and downexpression of Bax protein in rats pretreated with extract[161].

The antiulcer activity of flower extract of *J. sambac* was studied in gastric ulcers induced by oral administration of ethanol or by pyloric ligation in rat. The ulcer index in the test extract treated animals was found to be significantly less in all the models compared to vehicle control animals[162].

The methanolic extract of Jasminum sambac (MEJS) leaves was studied against swimming stress induced gastric ulceration in rats. The extract reduced the incidence of gastric ulceration in stressed rats at dose of 100 mg/kg and 200 mg/kg po[163-164].

Juglans regia

The gastro protective effect of aqueous extract of *Juglans regia* leaves was studied in albino rats. The aqueous leaf extract of *Juglans regia* was investigated for its anti- ulcer activity against pylorus ligation, aspirin induced and ethanol induced gastric ulcer in rats at 500mg/kg body weight po. A significant reduction ($p<0.01$) in ulcer index was seen in leaf extracts of *Juglans regia* treated rats of pylorus ligation, aspirin induced and ethanol induced gastric ulcer models. The gastro protective effect was further confirmed by histopathological examination of rat stomach[165].

Juniperus communis

The anti-ulcer property of *Juniperus communis* was studied in acetyl salicylic acid, serotonin, indomethacin, alcohol and stress-induced gastric ulcerations in rats and histamine-induced duodenal lesions in guinea pigs. The crude leaf extract at doses of 50 mg and 100 mg/kg, ip, significantly inhibited aspirin, serotonin, indomethacin, alcohol and stress-induced gastric ulcerations in rats and histamine-induced duodenal lesions in guinea pigs. The healing rate of acetic acid induced ulcer in rats was also enhanced significantly by the leaf extract. Biochemical analysis of gastric juice revealed that the extract significantly decreased its volume and total acidity, but did not alter its pH and peptic activity[166-167].

II. CONCLUSION

Many medicinal plants showed gastroprotective activity by many mechanisms. This review discussed the gastroprotective activity of medicinal plants.

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