Beneficial medicinal plants in digestive system disorders (part 2): plant based review

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Abstract: Many plants possessed beneficial effects in gastric diseases especially peptic ulcer diseases and in intestinal disease especially diarrhea and ulcerative colitis, these plants included: Agrimonia eupatoria, Ailanthus altissima, Alhagi maurorum, Aloe vera, Alpinia galangal, Anchusa italic and Anchusa strigosa, Anethum graveolens, Apium graveolens, Asparagus officinalis, Asphodelus fistulosus, Avena sativa, Bacopa monnieri, Bauhinia variegata, Bellis perennis, Benincasa hispida, Bidens tripartite, Brassica nigra, Bryophyllum calycinum, Caesalpinia bonducella, Calendula officinalis, Calotropis procera, Canna indica, Capsicum annuum and Capsicum frutescens, Carthamus tinctorius, Carum carvi and Casuarina equisetifolia. This review was designed to highlight the pharmacological effects of medicinal plants in gastrointestinal diseases as a second part of our previous review.

Keywords: herbs, plants, gastrointestinal, peptic ulcer, diarrhea, ulcerative colitis

I. INTRODUCTION

In the last few decades there has been an exponential growth in the field of herbal medicine. It is getting popularized in developing and developed countries owing to its natural origin and lesser side effects. Digestive system disorders have a substantial effect on worldwide morbidity and mortality rates. Many plants possessed beneficial effects on gastrointestinal disorders and can be used as alternatives in stomach diseases especially peptic ulcer disease and in intestinal disease especially diarrhea and ulcerative colitis, these plants included: included: Agrimonia eupatoria [1], Ailanthus altissima [2], Alhagi maurorum [3], Aloe vera [4], Alpinia galangal [5], Ammania baccifera [6], Anchusa italic and Anchusa strigosa [7], Anethum graveolens [8], Apium graveolens [9], Asparagus officinalis [10], Asphodelus fistulosus [11], Avena sativa [12], Bacopa monnieri [13], Bauhinia variegata [14], Bellis perennis [15], Benincasa hispida [16], Bidens tripartite [17], Brassica nigra [18], Bryophyllum calycinum [19], Caesalpinia bonducella [11, 20], Calendula officinalis [21], Calotropis procera [22], Canna indica [23], Capsicum annuum and Capsicum frutescens [24], Carthamus tinctorius [25], Carum carvi [26] and Casuarina equisetifolia [27]. This review was designed to highlight the pharmacological effects of medicinal plants in gastrointestinal diseases as a second part of our previous reviews[11,28].

Plants beneficial in gastrointestinal diseases:
I- Effect on stomach:

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 [29-30].

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 [31].
**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 [32-33].

**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 pepsin 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 [34-35].

**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 (linalool, 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 [36].

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) [37].

**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 [38].

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. Intrapерitoneal 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
Crocus sativus - 0 mg/kg bw, orally for ral administration of ns ly before exposure to ulcerogen. 4 hours after exposure to enzymes were significantly enhanced (p<0.05) by t

Cyperus were examined for ischemic injury. The mean ulcer index of rats treated with 200 and 100 mg/kg malondialdehyde and glutathione 200 mg/kg to prevent postischemic gastric mucosal injury. Antioxidant enzymes activity such as min reperfusion by clamping the celiac artery. The reperfusion was studied in rats. Ischemia/reperfusion model was designed as 30 min ischemia followed by 60

Crude extract induced significant antiulcer activity against pylorus ligation, 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 400 mg/kg and 79.61% ulcer inhibition rate, respectively [41-42].

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 posts ischemic 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 [49].
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 [50]. 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 [51].

**II-Effect on intestine:**

*Cicer arietinum*

The antidiarrhoeal activity of the hydroalcoholic extract of *Cicer arietinum* roots and its acetone and methanol fraction was studied based on their effect on Castor oil induced diarrhea in mice. The results showed that the highest reduction in diarrhoea was observed in hydroalcoholic extract (24.63 %), while Loperamide (5 mg/kg) inhibited the castor oil induced diarrhoea by 75.37 % [52].

**Convolvulus arvensis**

The antidiarrhoeal activity of the aerial parts methyl alcohol extracts of *Convolvulus arvensis* (200 and 400 mg/kg) was investigated in castor oil-induced diarrhea in rats, and on the motility of isolated rabbit’s duodenum. Oral administration of methanol extract of *Convolvulus arvensis* in a dose of 400 mg/kg produced no significant effect on the fecal discharge in rats. On the other hand *Convolvulus arvensis* induced a dose-dependent (0.8-3.2 mg/ml) inhibitory effect on the isolated rabbit duodenum. This effect was slow in onset at small doses. Calcium chloride (25 µg/ml) added to the calcium-free solution reversed the contractile response of the rabbit’s duodenum. Acetylcholine and small dose of nicotine reversed the contractile response of the tissues. Moreover, the extract produced its effect after blocking by propranolol or by yohimbine [53-54]. However, oral administration of 1/10 LD<sub>50</sub> of alcoholic extract of *Convolvulus arvensis* blocked diarrhea, enteropooling and intestinal transits induced by castor oil in rats, comparable to that of atropine [54-55].

**Convolvulus scammonia**

Scammony, gum-resin which obtained from the root of *Convolvulus scammonia* was used as a drastic purgative in 1 to 3-grain doses. In large doses it acts as a strong gastro-intestinal irritant, and may cause death, if administered to weak, debilitated persons [54, 56].

The active principle of Scammony (*Convolvulus scammonia*) was inert until it has passed from the stomach into the duodenum, where it meets the bile, a chemical reaction occurring between it and the taurocholate and glycocholate of sodium, whereby it was converted into a powerful purgative [54, 57].

**Coriandrum sativum**

The efficacy of *Coriandrum sativum* on gut modulation was studied, coriander crude extract was evaluated through in vitro and in vivo techniques. Coriander crude extract caused atropine sensitive stimulatory effect in isolated guinea-pig ileum and rabbit jejunum preparations (0.1-10 mg/ml). It exhibited relaxation against both spontaneous and high K<sup>+</sup> (80 mM)-induced contractions as well as shifted the Ca<sup>2+</sup> concentration-response curves to right, similar to that caused by verapamil. Bioassay-directed fractionation revealed the separation of spasmodenic and spasmyloytic components in the aqueous and organic fractions, respectively [58].

**Crotalaria juncea**

The anti-diarrhoeal effects of methanolic extract of leaves of *Crotalaria juncea* (MECJ) was studied against castor oil-induced diarrhoea model and small intestine transit model in rats. The number of droppings and the distance traveled by charcoal in intestine were measured. MECJ at the doses of 200 and 400 mg/kg significantly inhibited (P<0.001) the castor oil induced charcoal meal transit. The MECJ showed marked reduction in the frequency of bowel motion as well as a modest reduction in intestinal transit [59-60].

**Cuminum cyminum**

The effect of aqueous extract of *Cuminum cyminum* seeds (ACCS) was studied against diarrhoea on albino rats. The animals were divided into five groups and the control group was given 2% acacia suspension, the standard group with loperamide (3 mg/kg) or atropine sulphate (5mg/kg) and three test groups administered orally with 100, 250 and 500 mg/kg of ACCS. The antidiarrhoeal effect was investigated by castor oil induce diarrhoea model, prostaglandin E2 (PGE2) induced enteropooling model and intestinal transit by charcoal meal test. The ACCS showed significant (p< 0.001) inhibition in frequency of diarrhoea, defecation time delaying,
secretion of intestinal fluid as well as intestinal propulsion as compared to control. The graded doses of the tested extract showed dose dependent protection against diarrhea [61].

**Cydonia oblonga**

The pharmacological rationalization for the medicinal use of *Cydonia oblonga* in gut and airways diseases was investigated. Results showed that the crude extract of *Cydonia oblonga* seeds (Co.Cr) produced atropine sensitive spasmodic effects in isolated ileum of guinea-pig and rabbit jejunum preparations. In rabbit jejunum, Co.Cr also showed relaxant activity at slightly higher concentrations (0.1-10 mg/ml). When analyzed on rabbit jejunum pre-contrasted with K⁺ (80 mM), the plant extract (0.003-10 mg/ml) produced relaxation. A rightward shifting of Ca²⁺ dose-response curves along with decline in the maximum response was observed after pretreatment with Co.Cr (0.003-0.01 mg/ml), which was similar to the effect of verapamil. The crude extract of *Cydonia oblonga* seeds (Co.Cr) (0.01-10 mg/ml) relaxed CCh (1 μM) and K⁺ (80 mM)-induced contractions of isolated rabbit tracheal preparations, similar to the effect produced by verapamil [62].

The effect of quince juice (QJ) and quince hydroalcoholic extract (QHE) on ulcerative colitis (UC) induced by TNBS (trinitrobenzene sulfonic acid) was studied in rats. Rats were grouped and fasted for 36 hr before colitis induction. TNBS was instilled into the colon with a hydroalcoholic carrier and then treated for 5 days starting 6 h after colitis induction with different doses of QJ (200, 400, 800 mg/kg), QHE (200, 500 & 800 mg/kg) orally, QJ (400 mg/kg) and QHE (200 and 500 mg/kg) intraperitoneally. The colon tissue was removed and tissue damages were scored after macroscopic and histopathologic assessments. The examined doses of QJ and QHE were effective to reduce the extent of UC lesions, only the greatest doses (500 and 800 mg/kg) resulted in significant alleviation. Weight/length ratio as an illustrative of tissue inflammation and extravasation was also diminished with quince treatments [63].

*Cydonia oblonga* fruit preparations reduced the gastrointestinal propulsion and inhibited castor oil-induced diarrhoea in mice [64].

**Cynodon dactylon**

The hexane, dichloromethane, ethyl acetate and methanol extracts of *Cynodon dactylon* whole plant were tested for anti-diarrheal activity on castor oil induced diarrhea, gastro intestinal motility by charcoal meal and entero pooling models in albino rats. Methanol extract exhibited considerable inhibition of castor oil induced diarrhea. Methanol extract also showed a significant decrease in gastrointestinal motility by charcoal meal and decrease in weight of intestinal contents in enteropooling models. The results indicated that the plant possessed good anti-diarrheal activity [65-66].

**Cyperus rotundus**

An aqueous extract of tubers of *Cyperus rotundus* (ACR) was tested for its antidiarrhoeal and antispasmodic activity. Antidiarrhoeal effect of ACR was evaluated in castor oil induced diarrheaa in mice and antispasmodic effect was evaluated by charcoal meal test in mice at a dose of 125, 250, 500 mg/kg. The % inhibition of diarrhoea was 30.36 %, 37.90 %, 45.45 % and 92.45 % for ACR 125, 250, 500 mg/kg orally and loperamide 2 mg/kg dose orally respectively. ACR 125, 250, 500 mg/kg orally and atropine sulphate 2 mg/kg dose orally produced 24.35 %, 31.48 %, 36.75 % and 55.94 % inhibition of intestinal transit respectively [67-68].

The methanol extract of *Cyperus rotundus* rhizome, given orally at the doses of 250 and 500 mg/kg bw, showed significant antidiarrheal activity on castor oil induced diarrhoea in mice. Among the fractions, tested at 250 mg/kg, the petroleum ether fraction and residual methanol fraction showed antidiarrhoeal activity, the latter being more active as compared to the control. The ethyl acetate fraction did not show any antidiarrhoeal activity [69].

The antidiarrheal activity of the decoction of *Cyperus rotundus* tubers was studied using representative assays of diarrheal pathogenesis. Antibacterial, antiangiardial and antirotaviral activities were studied. Effect on adherence of enteropathogenic *Escherichia coli* (EPEC) and invasion of enteroinvasive *E. coli* (EIEC) and *Shigella flexneri* to HEp-2 cells was evaluated as a measure of effect on colonization. Effect on enterotoxins such as enterotoxigenic *E. coli* (ETEC) heat labile toxin (LT), heat stable toxin (ST) and cholera toxin (CT) was also assessed. The decoction showed antiangiardial activity, reduced bacterial adherence to and invasion of HEp-2 cells and affected production of CT and action of LT. The decoction of *Cyperus rotundus* did not exerted marked antimicrobial activity and it is exerted its antidiarrheal action by mechanisms other than direct killing of the pathogen [70].

The effect of *Cyperus rotundus* was investigated on adherence and enterotoxin production of 2 groups of *E.coli* enteropathogenic (EPEC) and enterotoxigenic (ETEC). A decoction of the root bulbs of *Cyperus rotundus* was prepared by boiling 1gm of plant material in 16 ml distilled water till the volume was reduced to 4 ml. The decoction was then centrifuged at 2500 RPM for 10 minutes and filtered through a
membrane of 0.22 μ pore size before use. A significant inhibition in labile toxin production was noted at 24 hours, at a 1:2 dilution and at 72 hours at 1:2 and 1:100 dilution. Stable toxin was inhibited at 1:10, 1:100 and 1:1000 dilutions, maximum inhibition seen at 1:1000. An inverse correlation was observed between the stable toxin production and the concentration of the decoction [71].

II. CONCLUSION

The review was designed to highlight the gastrointestinal effects of the medicinal plants to open the door for their clinical uses as a result of efficacy and safety. Furthermore, it is of the utmost importance to conduct phytochemical investigations and clinical trials on the most promising species.

REFERENCES

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