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Arabian medicinal plants for the treatment of intestinal disorders- plant based review (part 1)

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Abstract: Intestinal disorders are very common gastrointestinal diseases. Many medicinal plants possessed anti-diarrhoeal, laxative and beneficial effect in colitis, by many mechanisms. The current review was designed to cover the medicinal plants showed beneficial effects in the treatment of intestinal disorders.

Keywords: Medicinal plants, Anti-diarrhoeal, Diarrhoea, Laxative, Constipation Colitis.

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I. INTRODUCTION:

Diarrhoeal diseases are one of the leading causes of morbidity and mortality in developing countries and are responsible for the death of millions of people each year. WHO has initiated a Diarrheal Disease Control Program to study traditional medical practices and other related aspects[1]. Some medicinal plants increase the rate of intestinal absorption, decrease intestinal secretion or reduced intestinal motility. By these mechanisms, they produced constipating effects. However many medicinal plants increase intestinal secretion and increase motility and produced a transient stimulation, therefore they produced laxative effects[2]. This review will highlight the medicinal plants showed beneficial effects in the treatment of intestinal disorders.

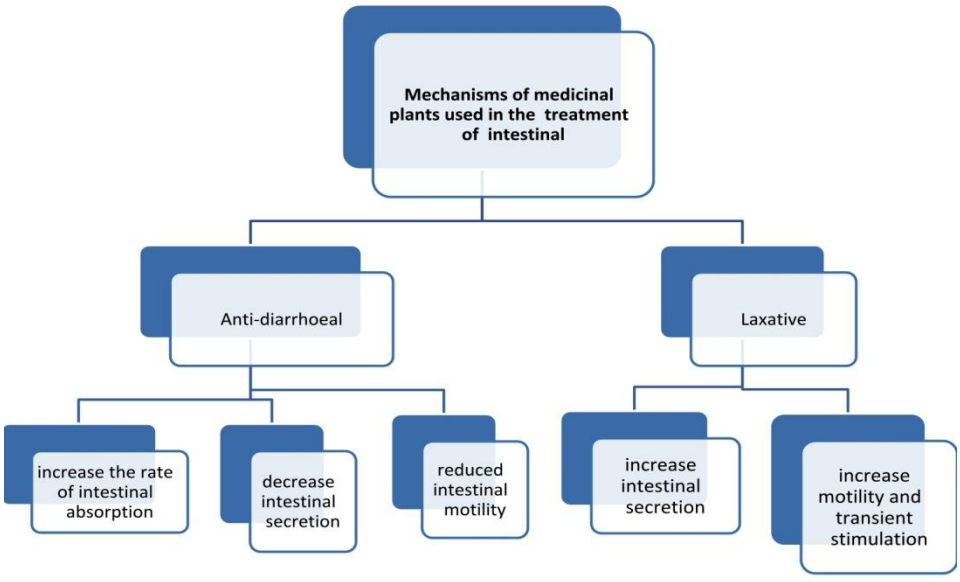

Fig 1: The mechanism of anti-diarrhoeal and laxative effects of medicinal plants

Medicinal plants acting on intestine:

Ailanthus altissima

The methanolic extract of root bark of *Ailanthus altissima* (MEA) was investigated for anti-diarrhoeal activity in castor oil induced diarrhoea and small intestine transit method on mice. The methanolic extract of root bark of *Ailanthus altissima* 200 mg/kg reduced the total weight of the faeces [3-4].

Alhagi maurorum

The antidiarrhoeal activity of *Alhagi maurorum* extract (200 and 400 mg/kg) and its effect on motility of isolated rabbit's duodenum was investigated. *Alhagi maurorum* in a 200 mg/kg dose exhibits a significant anti-diarrhoeal effect against castor oil-induced diarrhea. *Alhagi maurorum* increased the contractile force in concentrations between 0.4 and 1.6 mg/ ml, while higher concentrations (>3.2 mg/ml) caused a rapid depressant effect. The depressant effect appeared to be due to calcium channel blocking effect [5-6].

Aloe vera

The leaf lining (latex, resin or sap) contained anthraquinone glycosides (aloin, aloe-emodin and barbaloin) which are potent stimulant laxatives. These water soluble glycosides are split by intestinal bacteria into aglycones which have laxative action stronger than senna, cascara or rhubarb root. The anthraquinones found in the latex stimulate chloride and water secretion into the large intestine, inhibit their reabsorption and stimulate peristalsis. The onset of action is 6 –12 hours after a single oral dose. On the other hand, it has severe side effects including diarrhea, nausea, and cramping. For medicinal use, the leaf lining is dried and the residue is used as herbal laxative. The products are taken at bedtime which are poorly absorbed after oral administration. These products excreted in urine, bile, feces and breast milk. The products usually avoided during pregnancy due to the risk of stimulating uterine contractions and during lactation due to the risk of excretion in breast milk [7-10].

Anchusa italica

Anchusa italica boiling water extract (5%) inhibited the mean height of rabbit jejunum smooth muscle contractions to 35% in comparison with normal contractions [11-12].

Anethum graveolens

The essential oil of *Anethum graveolens*reduced contractions of rabbit intestine**.** Ethanol extract inhibited acetylcholine and histamine induced contractions of guinea-pig ileum[13-15].

Dill seeds have been used as household remedy to relief digestive problems such as stomachache, indigestion and flatulence. Dill water is believed to have a soothing effect and is given to babies to treat gripe, relieve hiccups and colic[16].The essential oil was a mild carminative and reduced foaming *in vitro*[17].

Asparagus officinalis

The effects of cooked whole asparagus and its purified bioactive, rutin, were studied on colitis symptoms and disease progression in mice. C57BL/6 mice were fed a basal diet supplemented with 2% asparagus or 0.025% rutin for 3 weeks. Colitis was induced by 2% dextran sodium sulfate in drinking water for 7 days. Asparagus diet was determined to contain higher antioxidant capacities than rutin diet through antioxidant assays. During active colitis, consumption of asparagus alleviated some clinical symptoms (stool consistency, stool blood, and spleen hypertrophy) of colitis. In recovery, asparagus-fed mice were improving in terms of regenerating crypts, surface epithelial, and goblet cells, potentially due to its rutin content [18-19].

Asphodelus fistulosus

Asphodelus fistulosus induced relaxation of rabbit intestinal smooth muscles [20].

Avena sativa

Two broiler experiments with almost identical basal diets were conducted to investigate the effect of dietary oat hulls, access to litter and the antimicrobial compound narasin on gizzard erosion and ulceration syndrome (GEU). The effects on particle size of duodenal digesta, ileal starch concentration, caecal *Clostridium perfringens* counts, necrotic enteritis and production performance were also examined. Oat hulls reduced GEU severity and starch levels in the ileum in both experiments. Access to litter reduced GEU scores when oat hulls were included in the feed. Access to litter also improved feed efficiency and reduced *C. perfringens* counts. Oat hulls were associated with improved feed efficiency in Experiment 1 and impaired feed efficiency in Experiment 2. The inconsistent effect of oat hulls on production performance appeared to be related to an association between oat hulls and high *C. perfringens* counts in Experiment 2; an association that was absent in Experiment 1. In general, oat hulls interacted with litter access and narasin in exerting a positive effect on gizzard health. However, the association between oat hulls and necrotic enteritis detected in Experiment 2 suggests that the positive effect of oat hulls on GEU occasionally may be outweighed by a negative effect on gut health [21-22].

Oats have been shown to absorb intestinal toxins and increase excretion of intestinal toxins. The combination of taurine and oat were investigated on endotoxin release in a rat liver ischemia/reperfusion model. The results showed that the combination of taurine (300mg/kg/ day) and oat fiber (15g/kg/ day) significantly reduced endotoxin levels in the portal vein by 36.3% when compared to the control group (0.168±0.035Eu/ml in

the treatment group vs 0.264±0.058Eu/ml in the control group, P<0.01). The treatment by taurine and oat fiber induced 21.5% and 18.4% reduction in endotoxin levels respectively, when compared to the control group (P<0.05) [23].
Oat bran has been proposed as a dietary treatment for ulcerative colitis and has been shown to increase endogenous butyrate production and provide symptomatic relief of abdominal pain [24].

Bacopa monnieri

The ethanol extract of the whole plant of *Bacopa monnieri* was showed antidiarrhoeal effect on castor oil induced diarrhea in mice. It increased mean latent period and decreased frequency of defecation significantly at the oral dose of 500 mg/kg comparable to loperamide 50mg/kg [25-26].

A double-blind, randomized, placebo controlled trial of 169 patients with irritable bowel syndrome , effects of an Ayurvedic preparation containing *Bacopa monniera* and *Aegle marmelos* was compared with standard therapy (clidinium bromide, chlordiazepoxide, and psyllium). Subjects were randomly assigned to standard drug treatment, botanical treatment, or placebo for six weeks. Treatment was administered orally as drug, botanical, or placebo three times daily. Ayurvedic therapy was superior to placebo, however, the two botanicals were not given separately, and the benefit could not link specifically to the Bacopa portion of the Ayurvedic preparation[27].

Benincasa hispida

The methanolic extract of fruit of *Benincasa hispida* (BHFE) was evaluated for its antidiarrheal potential against several experimental models of diarrhea in rats. BHFE treated animals showed significant inhibitory activity against castor oil induced diarrhea and inhibited PGE2 induced enter pooling in rats. It also showed significant reduction in gastrointestinal motility following charcoal meal in rats [28-29].

Bidens tripartita

The crude flavonoids isolated from the aerial parts of the plant (500 mg/kg body weight bw orally) were significantly induced choleretic activity. It also caused an increase of cholic acids and cholesterol in bile[30-31].

500 patients with dysentery, 65 with acute enteritis and 248 with chronic enteritis were used the aerial parts of the plant. Several different dosage forms of the herb were used: 200 g of fresh whole herb and 100 g of dried herb in decoctions (in three divided doses per day); granules containing 5 g of dried aqueous extract, three times daily; 0.5 g tablets of dried aqueous extract, 10 tablets each time three times daily; and injection, 2 ml per injection (dose not stated), 2–3 times daily. The herbal preparations were administered for 3–10 days to patients who already had diarrhoea . 387 of the 500 patients with chronic dysentery were reported to have been cured, 13 had not responded within 3 days. All 313 patients with enteritis were reported to have been cured[32].

Caesalpinia bonducella

Antidiarrhoeal activities of fractions of methanolic leaf extracts of *Caesalpinia crista* were evaluated at two doses (200 and 400 mg/kg) and compared with loperamide in castor oil-induced diarrhoeal model in rat. All fractions exhibited dose-dependent antidiarrhoeal action (P<0.05). Ethyl acetate fraction exerted maximum inhibition (51.11%) against defecation, whereas 57.75% inhibition was obtained for loperamide [33].

Calotropis procera

The dry latex (DL) of *Calotropis procera* was evaluated for its anti-diarrhoeal activity. Like atropine, a single oral dose of DL (500 mg/kg) produced a significant decrease in the frequency of defecation and the severity of diarrhea as well as protecting from diarrhoea in 80 % of rats treated with castor oil. The effects of DL on intestinal transit, castor oil-induced intestinal fluid accumulation (enteropooling) and electrolyte concentration in intestinal fluid were also evaluated . Dry latex produced a decrease in intestinal transit (27%–37%) compared with both normal and castor oil-treated animals. Unlike atropine, dry latex significantly inhibited castor oil induced enteropooling. However, it did not alter the electrolyte concentration in the intestinal fluid compared with castor oil- treated rats [34-35].

Canna indica

The anti diarrheal effect of *Canna indica* methanolic extract was evaluated in castor oil-induced diarrhoea, charcoal meal transit and acetylcholine- induced contractions of the isolated rat ileum models. In the castor oil induced diarrhoea, loperamide (5 mg/kg) 50, 100 and 200 mg/kg of the extract were used and compared with a control (tween 80), while in the gastrointestinal transit, atropine (2.5 mg.kg), 100 and 200 mg/kg were used and also compared with a control (tween 80). A dose of 10 mg/ml of the extract was used against acetylcholine induced contractions in the isolated ileum experiments. The extract of *Canna indica* was

significantly ($p<0.050$) reduced both the castor oil induced diarrhoea and the charcoal plug transit time in a dose dependent manner. In the castor oil induced diarrhoea, the extract decreased the intraluminal fluid content in mice, with the highest reduction recorded at 200 mg/kg dose of the extract, though this was slightly better than that of loperamide. In the charcoal plug transit, both doses of the extract and atropine were significantly ($p<0.05$) decreased the distance travelled by the charcoal plug in the intestine of the mice, with the 200 mg/kg producing an inhibitory effect higher than that of atropine. The effect of *C indica* on the isolated rat ileum showed that the extract produced significant ($p<0.0001$) inhibitory effect on acetylcholine induced contraction [36-37].

Carum carvi

The direct effects of *Carum carvi* ethanol extract was tested in dispersed intestinal smooth muscle cells (SMC) of guinea pigs. Effects of the plant extract on SMC and of acetylcholine (Ach) pretreated SMC were measured by micrometric scanning technique. Ethanol extract of *C. carvi* (2.5 mg/ml, 250 mug/ml, and 25 mug/ml) reduced significantly the response of dispersed SMC to Ach. Pretreatment of SMC with the highest concentration of *C. carvi* ethanol extract (2.5 mg/ml) has significantly inhibited the response of SMC to Ach. The result showed a dose-dependent inhibition of the contraction induced by Ach. This response may explain, in part, the beneficial effect of caraway in relieving gastrointestinal symptoms associated with dyspepsia [38]. It was efficient aromatic carminative and gentle stomachic; both the fruit and the oil are of value in flatulent colic [39-40].

The effect of the *Carum carvi* plant on resumption of bowel motility after Cesarean section was investigated by a randomized controlled pilot study conducted on 20 women undergoing elective Caesarean section under general anesthesia. The patients were randomly divided into two groups. The intervention group drank 10 ml of *Carum carvi* syrup containing 2 g of *Carum carvi* in 20 ml of syrup at 8 to 81/2 hours after surgery. The control group was given 10 ml of the placebo syrup at 8 to 81/2 hours after surgery. Demographic characteristics, time of first peristaltic, first gas passage, first bowel movement, and time until hospital discharge were compared for the two groups. The results showed that compared to the control group, the intervention group had significantly shorter mean interval of the first intestinal sounds (10.0 ± 2.03 h vs. 19.28 ± 3.95 h); mean time to first passage of flatus (15.91 ± 3.73 h vs. 26.82 ± 5.83 h), mean time to first bowel movement (20.31 ± 4.63 h vs. 31.7 ± 10.2 h) and mean length of hospitalization (31.71 ± 7.57 h vs. 50.6 ± 16.49 h) ($p < 0.05$). There were no serious side effects associated with consumption of the syrup. Accordingly, the use of *Carum carvi* after caesarean section can speed the resumption of post-operative bowel motility [41].

The effects of caraway hydroalcoholic extract (CHE) and its essential oil (CEO) were investigated in an immunological model of colitis in rats induced by trinitrobenzene sulfonic acid (TNBS). Different doses of CHE (100, 200, 400 mg/kg) and CEO (100, 200, 400 µl/kg) were administered orally and also doses of CHE (100, 400 mg/kg) and CEO (100, 400 µl/kg) were given intraperitoneally. Administration of the doses started 6 h after induction of colitis and continued daily for 5 consecutive days. CHE and CEO at all tested doses were effective in reducing colon tissue lesions and colitis indices and the efficacy was nearly the same when different doses of plant fractions were administered orally or intraperitoneally [42].

Casuarina equisetifolia

The anti-diarrhoeal effects of ethanolic (90%) extract of *Casuarina equisetifolia* Linn (EECE) was studied in rats. Antidiarrhoeal activity of 90% ethanol extract of *Casuarina equisetifolia* was investigated using castor oil-induced diarrhoea, enteropooling and small intestinal transit models in rats. The weight and volume of intestinal content induced by castor oil were studied by enteropooling method. Standard drug diphenoxylate (5 ml/kg, po) caused significant reductions in fecal output and frequency of droppings whereas EECE at the doses of 200 and 400 mg/kg po significantly ($P<0.001$) reduced the castor-oil induced frequency and consistency of diarrhoea and enteropooling. The gastrointestinal transit rate was expressed as the percentage of the longest distance travelled by the charcoal divided by the total length of the small intestine. EECE at the doses of 200 and 400 mg/kg significantly inhibited ($P<0.001$) the castor oil induced charcoal meal transit. The EECE showed marked reduction in the number of diarrhoea stools and the reduction in the weight and volume of the intestinal contents, as well as a modest reduction in intestinal transit [43-44].

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 % [45-46].

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 [47-48].

However, oral administration of 1/10 LD_{50} of alcoholic extract of *Convolvulus arvensis* blocked diarrhea, enteropooling and intestinal transits induced by castor oil in rats, comparable to that of atropine [48-49].

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 [48, 50].

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 [48, 51].

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^+ (80 mM)-induced contractions as well as shifted the Ca^{2+} concentration-response curves to right, similar to that caused by verapamil. Bioassay-directed fractionation revealed the separation of spasmogenic and spasmolytic components in the aqueous and organic fractions, respectively [52-53].

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 [54-55].

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 [56-57].

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-contracted with K^+ (80 mM), the plant extract (0.003-10 mg/ml) produced relaxation. A rightward shifting of Ca^{++} 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 [58-59].

The effect of quince juice (QJ) and quince hydroalcoholic extract (QHE) on ul\cerative 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 [60].

Cydonia oblonga fruit preparations reduced the gastrointestinal propulsion and inhibited castor oil-induced diarrhoea in mice [61].

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 [62-63].

Cyperus rotuntdus

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 diarrhea 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 92.4 5 % 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 [64-65].

The methanol extract of *Cyperus rotundus* rhizome, given orally at the doses of 250 and 500 mg/kg bw, showed significant antidiarrhoeal activity in 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 [66].

The antidiarrheal activity of the decoction of *Cyperus rotundus* tubers was studied using representative assays of diarrheal pathogenesis. Antibacterial, antigiardial 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 antigiardial 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 [67].

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 [68].

Dactyloctenium aegyptium

Crude extract of *Dactylotenium aegyptium* and its fractions were evaluated to rationalize its use in gastrointestinal ailments. In spontaneous contracting rabbit jejunum preparation, *D. aegyptium* exert concentration dependent spasmogenic effect (0.01-0.1 mg/ml) followed by spasmolytic effect at higher doses (0.3-3.0 mg/ml). Pretreatment of the tissue preparations with atropine resulted in suppression of the spasmogenic response. Furthermore, *D. aegyptium* (1.0 mg/mL) caused relaxation of K^+ (80 mM)-induced spastic contractions in isolated rabbit jejunum preparations and there was non -parallel shift in Ca^{++} dose response curves towards right (0.1-0.3 mg/ml). These effects were comparable with verapamil, a standard Ca^{++} channel blocker. The solvent-solvents fractionation reflected segregations of spasmogenic and spasmolytic effects in respective aqueous and dichloromethane fractions[69-70].

Dalbergia sissoo

The ether, ethanol, and aqueous extracts of *Dalberjia sissoo* bark were studied for anti-diarrhoeal properties in experimental diarrhea, induced by castor oil in rats at te dose of 200 – 400 mg/kg orally, the ether extract showed significant and dose dependent anti-diarrhoeal activity. The extracts also significantly reduced the intestinal transit time in charcoal meal when compared with atropine sulphate (1 mg/kg ip) The ether extract was found to be equipotent to atropine[71].

The ethanol extract of the bark of *D. lanceolaria* showed moderate antidiarrheal activity in castor oil induced diarrhea in mice at the dose of 400 mg/kg at 4 h and in magnesium sulfate-induced diarrhea in mice, activity was good at dose of 100 mg//kg at 6 h but in both model activity was less than diphenoxylate HCl. The extract also reduced intraluminal fluid accumulation in a castor oil-induced, intraluminal fluid accumulation assay, and decreased the intestinal motility in charcoal and barium chloride treated animals at doses of 100, 200 and 400 mg/kg[7[2]].

The protective effect of ethanol extract from D. sissoo Roxb. ex DC. leaves (EDSL) was studied in experimentally induced diarrhoea and peristalsis in mice. Castor oil-induced diarrhoea and magnesium sulphate ($MgSO_4$)-induced diarrhoea tests were used to assess the antidiarrhoeal activity of D. sissoo. Gastrointestinal tract transit of charcoal meal test and barium sulphate milk was used to assess the peristalsis activity of the extract. The EDSL significantly reduced faecal output in castor oil-induced and MgSO4-induced diarrhoea and also significantly reduced the number of diarrhoeal episodes. D. sissoo significantly delayed the onset of diarrhoea induced by both castor oil and $MgSO_4$ and comparable to loperamide, a standard antidiarrhoeal drug. Both D. sissoo and atropine sulphate significantly reduced the peristalsis activity of charcoal meal and barium sulphate milk in mice[73].

The effect of a decoction of dried leaves of *Dalbergia sissoo* was evaluated in diarrhea. Antibacterial, antiprotozoal, and antiviral activities of the plant decoction were checked by agar dilution method, tube dilution method, and neutral red uptake assay, respectively. Cholera toxin (CT) and *Escherichia coli* labile toxin (LT) were assayed by ganglioside monosialic acid receptor . Suckling mouse assay was used to assess *E. coli* stable toxin (ST). As a measure of colonisation, the effect against adherence of *E. coli* and invasion of *E. coli* and *Shigella flexneri* to HEp-2 cells were studied. The decoction had no antibacterial, antiprotozoal, and antiviral activity. It inhibited the production of cholera toxin (CT), and increased the production of labile toxin (LT). Binding of both LT and CT to the GM1 receptor was reduced[74-75].

Desmostachia bipinnata

The antidiarrhoeal effect of both alcoholic and aqueous extracts of the roots of *Desmostachya bipinnata* were studied in rats against castor oil induced diarrhoea and charcoal meal test at the doses of 200 and 400 mg/kg body weight. The alcoholic extract and to a lesser extent aqueous extract significantly reduced the weight of the faces and decreased the propulsion of charcoal meal through the gastrointestinal tract[76].

The crude aqueous-methanolic extract of D. bipinnata produced an atropine-sensitive spasmogenic effect in rabbit jejunum up to 5 mg/ml, followed by a partial relaxation at 10 mg/ml. With atropine preincubation, a verapamil-like inhibitory effect was evident against spontaneous and high K^+ (80 mM)–induced contractions. The maximum stimulant effect was comparable with the acetylcholine-induced maximum contraction and was similarly reproducible in guinea pig ileum. On activity-directed fractionation, inhibitory effect was concentrated on organic and stimulant effect in aqueous fraction[77].

The hydro-alcoholic extract of *D. bipinnata* whole plant showed no laxative activity in rats. The results of laxative activity showed minimal increase of feces output at the dose of 500 mg/kg and the increase was negligible when compared with that of the standard drug sennosides (10mg/kg)[78-79].

Dodonaea viscose

The anti-diarrheal activity of the alcohol and aqueous extracts of the roots of *Dodonaea viscosa* was investigated by castor oil induced diarrhea in mice. The number of diarrheal episodes and mean weight of stool of mice was determined as evaluation parameters. The percentage protection ofextract treated animals was compared with loperamide treated animals. The results revealed that the alcohol and aqueous extracts significantly reduced diarrhea in mice with reduction in weight of stools[80-81].

***Eucalyptus* species**

A new triterpenoid acid, eucalyptanoic acid isolated from the fresh uncrushed leaves of *Eucalyptus camaldulensis* var obtusa along. This compound and its acetyl and acetylmethyl derivatives were tested for spasmolytic activity. Its acetylmethyl derivative was found to be the most active spasmolytic, mediated through blockade of calcium influx at 1 mg/ml[82].

The triterpenoid camaldulin (3β-formyloxyurs-11-en-28,13β-olide), ursolic acid lactone acetate and ursolic acid lactone isolated from Eucalyptus camaldulensis var. obtuse, showed spasmolytic activity and possessed calcium antagonist activity[83-84].

Euphorbia hirta

The lyophilized decoction of *Euphorbia hirta* whole plant showed antidiarrhoeic effects in experimental diarrhoea induced by castor oil, arachidonic acid, and prostaglandin E2. The lyophilized decoction delayed small intestinal transit accelerated by castor oil but not in normal conditions[85].

Euphorbia pilulifera inhibited contractions induced by cholinergic and histaminic drugs, allergic reactions, and direct muscular action on smooth muscle (ileum, uterus)[(47)]. The growth of Entamoeba histolytica was inhibited by polyphenolic extract of the whole plant, the minimum active concentration was less than 10 pg/ml. At a concentration of 80 µg/ml in an organ bath, the extract exhibited more than 70% inhibition of acetylcholine and/or KCI -induced contractions on isolated guinea pig ileum[86-87].

Foeniculum vulgare

The anti-colic effectiveness of fennel seed oil emulsion was studied in infantile colic (125 infants, 2 to 12 weeks of age). The use of fennel oil emulsion eliminated colic, according to the Wessel criteria, in 65% (40/62) of infants in the treatment group, which was significantly better than 23.7% (14/59) of infants in the control group ($P < 0.01$). Side effects were not reported for infants in either group during the trial[88].

Acetylcholine induced spasm followed by treatment of hydro distilled fruit extract of *Foeniculum vulgare Mill* showed prominent antispasmodic activity . Also treatment of hydro distilled extract of *Foeniculum vulgare Mill* showed receptor blocking action (antispasmodic) as that of standard agent (atropine) on isolated guinea pig ileum[89].

The laxative effect of a phytotherapic compound containing (*Pimpinella anisum* L., *Foeniculum vulgare* Miller, *Sambucus nigra* L., and Cassia *augustifolia*) was evaluated by a randomized, crossover, placebo-controlled, single-blinded trial included 20 patients with chronic constipation. Half of the subjects were received the phytotherapic compound for a 5-day period, whereas the other half received placebo for the same period. Both treatment periods were separated by a 9-day washout period followed by the reverse treatment for another 5-day period. Mean colonic transit time assessed by X ray was 15.7 hours (95%CI 11.1-20.2) in the active treatment period and 42.3 hours (95%CI 33.5-51.1) during the placebo treatment ($p < 0.001$). Number of evacuations per day increased during the use of active tea; significant differences were observed as of the second day of treatment ($p < 0.001$). Patient perception of bowel function was improved ($p < 0.01$), but quality of life did not show significant differences among the study periods. The findings of the randomized controlled trial revealed that the phytotherapic compound exerted laxative effects and is a safe alternative option for the treatment of constipation[90].

Foeniculum vulgare ethanolic fruit extract administration (500 mg/kg) to rats caused a 33% increase of the collected bile volume that was statistically significant ($P<0.0l$) compared with control values. The bilirubin content in the collected bile was similar in both treated and control groups[91].

Fumaria parviflora

The effects of *Fumaria parviflora* were evaluated in gut motility disorders in experimental animals. The *in vivo* prokinetic and laxative assays were conducted in mice. The effects on contraction of the smooth muscles were investigated using isolated intestinal preparations (ileum and jejunum) from different animal species [mouse, guinea-pig and rabbit]. The aqueous-methanol extract of *Fumaria parviflora*, showed partially atropine-sensitive prokinetic and laxative activities in the *in vivo* in mice at 30 and 100 mg/kg. In the *in vitro* studies, the aqueous-methanol extract of *Fumaria parviflora* (0.01-1 mg/ml) caused a concentration dependent atropine-sensitive stimulatory effect both in mouse tissues (jejunum and ileum), and rabbit jejunum but had no effect on rabbit ileum. In guinea-pig tissues (ileum and jejunum), the crude extract showed a concentration dependent stimulatory effect with higher efficacy on ileum and the effect was partially blocked by atropine, indicating the involvement of more than one types of gut-stimulant components [atropine-sensitive and insensitive] [92-93].

Hedera helix

The effect of two main active substances extracted from the plant (α-hederin and hederacoside C) and the whole dry extract of Hedera helix on gut motility was evaluated on isolated rat stomach corpus and fundus strips. Results revealed that α-hederin in the concentration ranged from 25 to 320µM significantly changed the spontaneous motoric activity of rat stomach smooth muscle. The observed reaction (the contraction, and its force) was concentration dependent. Hederacoside C, did not alter the motility of rat isolated stomach corpus and fundus strips when administered in the concentration up to 100 µM, however, if applied in the concentration of 350 µM it induced a remarkable contraction of smooth muscle. Eventually, the whole extract of Hedera helix in a dose containing 60 µM of hederacoside C produced a strong contraction which strength was comparable with the reaction induced by acetylcholine[94].

The effect of α-hederin on smooth muscle was studied on rat isolated stomach corpus and fundus strips, under isotonic conditions. The results revealed that the application of verapamil significantly inhibited the contraction evoked by α-hederin. The incubation of stomach strips in calcium-free modified Krebs-Henseleit solution did not change the force of the observed contraction in comparison to the reaction of the preparations incubated in regular incubation solution (M K-HS). The replacement of M K-HS by calcium-free chelator-containing solution inhibited totally the reaction to α-hederin. Accordingly, it appeared that α-hederin-induced contraction results from the influx of calcium which is located in intercellular spaces or bound to the outside of the cell membrane. The Ca2+ influx occurs predominantly through voltage-dependent calcium channels of L-type[95]. in vitro antispasmodic activity on isolated guinea-pig ileum with acetylcholine as spasmogen was carried out to determine the antispasmodic activity of Hedera helix . In order to determine the phytochemical basis for the antispasmodic activity, bioassay guided fractionation and subsequent isolation of phenolic compounds (flavonols, caffeoylquinic acids) and saponins (hederacoside C, alpha-hederin, hederagenin) was also carried out. Significant activity was found for both saponins and phenolic compounds, the PE values being approx. 55 and 49 for alpha-hederin and hederagenin, 54 and 143 for quercetin and kaempferol, and 22 for 3,5-dicaffeoylquinic acid, respectively. In view of their relative high concentration in the plant, the saponins contribute most to the anti-spasmodic activity, followed by dicaffeoylquinic acids and the flavonol derivatives[96].

Helianthus annuus

The antidiarrheal activity of ethanolic extract of the leaves of Helianthus annuus was evaluated using castor oil induced diarrhoea model and gastrointestinal transit model IN mice for antidiarrheal activity. Ethanolic extract of the leaves of Helianthus annuus (at various doses :250 & 500mg/kg bw) significantly decreases the severity of diarrhea[97-98].

Hibiscus rosa-sinensis

The ameliorative effect of hydroalcoholic extract of leaves of Hibiscus rosa sinensis (HRS) in acetic acid induced experimental colitis was investigated in male wistar rats. Intrarectal instillation of acetic acid (2ml, 4%) caused enhanced ulcer area, ulcer index, spleen weight, colon weight to length ratio, colonic MPO, MDA, NO and TNF-α. It caused significant decrease in the level of SOD and GSH. Pretreatment with HRS for 7 days exhibited significant effect in lowering of oxidative stress, colonic NO, TNF-α and elevation of SOD and GSH at a dose of 100 and 200 mg/kg[99].

Hibiscus sabdariffa

The and antidiarrheal effect of the ethanolic calyx extract of Hibiscus sabdariffa was studied using castor oil-induced diarrheal model mice. The extract demonstrated a significant antidiarrheal activity against castor oil-induced diarrheal in mice in which it decreased the frequency of defecation and increased the mean latent period at the doses of 250 and 500 mg/kg bw ($P<0.01$)[100].

The effects of aqueous extracts of the calyces of Hibiscus sabdariffa on intestinal transit were determined was studied in experimental rats. The dried calyces of Hibiscus sabdariffa was pulverized and 10% extracts of powder were administered orally to rats at varying doses(0.5/100g, 1ml/100g, 2ml/100g bw). After 30 minutes, each animal was then given 1.5 ml of a dye solution orally. 1 hour after administering the dye each rat was sacrificed and the intestine carefully dissected out. The length of the intestine and the transit point of the orally administered dye were then measured. The transit point was calculated as a percentage of the total length of the intestine. Hibiscus sabdariffa caused significant reduction in the transit points of the dye[101].

***Hyoscyamus* Species**

The crude extract of H. niger seeds (Hn.Cr) exhibited antidiarrhoeal and antisecretory effects against castor oil-induced diarrhoea and intestinal fluid accumulation in mice. The crude extract of H. niger seeds (Hn.Cr) caused a complete concentration-dependent relaxation of spontaneous contractions of rabbit jejunum, similar to that caused by verapamil, whereas atropine produced partial inhibition. Hn.Cr inhibited contractions induced by carbachol (1 microM) and K^+ (80 mM) in a pattern similar to that of dicyclomine, but different from verapamil and atropine. Hn.Cr shifted the Ca^{2+} concentration-response curves to the right, similar to that caused by verapamil and dicyclomine, suggesting a Ca^{2+} channel-blocking mechanism in addition to an anticholinergic effect. In the guinea-pig ileum, Hn.Cr produced a rightward parallel shift of the acetylcholine curves, followed by a non-parallel shift with suppression of the maximum response at a higher concentration, similar to that caused by dicyclomine, but different from that of verapamil and atropine. In guinea-pig trachea and rabbit urinary bladder tissues, Hn.Cr caused relaxation of carbachol (1 microM) and K^+ (80 mM) induced contractions at around 10 and 25 times lower concentrations than in gut, respectively, and shifted carbachol curves to the right. Only the organic fractions of the extract had a Ca^{2+} antagonist effect, whereas both organic and aqueous

fractions had anticholinergic effect. A constituent, beta-sitosterol exhibited Ca^{2+} channel-blocking action. These results suggest that the antispasmodic effect of H. niger is mediated through a combination of anticholinergic and Ca^{2+} antagonist mechanisms. The relaxant effects of Hn.Cr occur at much lower concentrations in the trachea and bladder than intestinal[102].

Inula graveolens

The Anti-diarrheal effects of the methanolic extract of *Inula graveolense* were examined in rats. At the doses of 200 ($P < 0.05$) and 400 mg/kg body weight ($P < 0.01$), the extract displayed remarkable an- tidiarrheal activity by reducing the rate of defecation and retardation of intestinal transit time of charcoal meal compared to normal saline control group, the effect was dose dependent and similar to loperamide (5 mg/kg)[103-104].

Juglans regia

Juglans regia (walnut) extract was evaluated in acute and chronic murine colitis. In the acute colitis model, mice were given 4% dextran sulfate sodium (DSS) for 5 days. Walnut extract (5 mg/kg/day and 20 mg/kg/day) was dissolved in PBS and administered once daily by oral gavage, beginning 2 days before DSS administration. Severe colitis was induced by DSS administration for 5 days. In contrast, administration of walnut extract significantly reduced the severity of DSS-induced murine colitis, as assessed by the disease activity index and colon length. In the histopathological analysis, histological grading showed that walnut extract significantly reduced overall colitis score in comparison to the scores of the PBS-treated controls. Immunohistochemical analysis showed that the DSS-induced phospho-IKK activation in intestinal epithelial cells was significantly decreased in walnut extract–treated mice. Immunoreactivity for occludin was significantly inhibited by the treatments with walnut extract. Walnut extract was also significantly reduced the severity of chronic colitis in mice[105].

Juniperus communis

The antidiarrheal effects of the aqueous extract of *Juniperus phoenicia* leaves were studied using several experimental models of diarrhea. The results revealed that the aqueous extract caused a dose dependent protection of rats against castor oil induced diarrhea and reduced castor oil induced enteropooling. The extract also caused a dose dependent decrease in intestinal transient and showed a significant dose dependent relaxant effect (EC_{50} 65.1±8.4 mg/ml) on rat ileal smooth muscle. The intraperitoneal LD_{50} value was 1587±143 mg/kg in mice[106-107].

II. CONCLUSION:

Intestinal disorders are very common gastrointestinal diseases. Many medicinal plants possessed anti-diarrhoeal, laxative and beneficial effect in colitis, by many mechanisms. Some medicinal plants increase the rate of intestinal absorption and or reduced intestinal motility. By these mechanisms, they produced constipating effects. However many medicinal plants increase intestinal secretion and increase motility and produced a transient stimulation, therefore they produced laxative effects. The current review discussed the medicinal plants showed beneficial effects in the treatment of intestinal disorders.

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