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PHARMACOLOGICAL ASSESSMENT OF MEDICINAL FLORA WITH ANTIDIARRHEAL PROPERTIES: INTEGRATING TRADITIONAL WISDOM AND CONTEMPORARY THERAPEUTICS

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ABSTRACT

Diarrheal illness continues to be a predominant cause of morbidity and death, especially in children under five years of age in tropical and developing areas. Notwithstanding worldwide initiatives like the WHO Diarrheal Disease Control Program, the prevalence of diarrheal diseases endures due to inadequate sanitation, contaminated drinking water, and restricted access to contemporary healthcare. Traditional medicine remains essential in the management of diarrhea, with herbal medicines serving as the foundation of treatment in several communities. This article examines the pathophysiology of diarrhea and emphasizes the pharmacological potential of medicinal plants utilized as antidiarrheal medicines. The syndrome results from disruptions in the absorption of intestinal water and electrolytes, causing accelerated stool transit and dehydration. While oral rehydration treatments effectively address dehydration, they do not diminish stool volume or frequency, requiring further therapeutic measures. Various plant species, including *Annona muricata, Alchornea cordifolia, Kigelia africana, Punica granatum,* and *Ruta chalepensis*, have exhibited considerable antidiarrheal efficacy in diverse animal models via mechanisms such as antisecretory, antimotility, anti-inflammatory, and antimicrobial actions. Phytochemicals such as apigenin, friedelin, and 1,8-cineole are responsible for these actions. Nonetheless, several conventional therapies remain insufficiently investigated scientifically, exhibiting little clinical validity. This highlights the necessity for comprehensive phytochemical characterization, standardization, and clinical trials to guarantee effectiveness and safety. Utilizing these conventional herbal resources might facilitate the creation of economical, accessible, and safer antidiarrheal treatments, especially in resource-constrained environments.

Introduction:

In tropical regions, diarrhea is typical. In some regions of the world, diarrhea results in higher disease and results in more babies and children. A prominent source of morbidity and mortality, particularly in developing nations, is a diarrheal illness, which has long been acknowledged as such. The Diarrheal Disease Control Program (DDC), established by the World Health Organization (WHO), includes research on traditional medical practices as well as assessments of health promotion and prevention strategies [1]. Although there are many different methods for managing diarrhea, the great majority of individuals in developing nations still rely on herbal medications to treat their diarrhea [2]. Children under the age of five had the highest rate of diarrheal deaths [3]. Despite efforts to reduce it by numerous governments and international organizations, the incidence of diarrheal diseases continues to be high. Determining and assessing natural remedies that can be used as alternatives to those that are currently prescribed is crucial. Utilized anti-diarrheal medications, which are not always easily available or without side effects [4]. Due to factors including inadequate sanitation and pipe-borne water, diarrhea creates major challenges, especially for youngsters [5]. In many nations around the world, it is common to practice utilizing medicinal herbs to cure diarrhea as part of traditional medicine. The majority of the time, however, these customs have been passed down orally, without knowledge of the potential mechanisms, security, or effectiveness of herbal remedies [6]. Diarrhea is a prevalent symptom. Approximately 25% of the US population experiences an episode of acute diarrhea annually, while up to 5% suffer from chronic diarrhea. Most acute diarrheas are self-limiting illnesses of the gastrointestinal system caused by food or waterborne pathogens, lasting up to one week. Many afflicted people refrain from seeking medical care and resort to over-the-counter treatments with inconsistent efficacy. At most, these over-the-counter treatments (or even prescription pharmaceuticals) just reduce the length of symptoms by around one day. The primary danger associated with acute diarrhea is dehydration and the loss of electrolytes. The difficulties of diarrhea can be addressed with oral rehydration solutions; however, these solutions do not diminish the volume or frequency of stools, and patients frequently seek more symptomatic relief. Chronic diarrhea is more likely than acute diarrhea to prompt people to consult their physician. Evaluation may identify a particular etiology for persistent diarrhea in around 50% of patients, while the remainder is ascribed to functional problems, such as diarrhea-predominant irritable bowel syndrome [7].

Pathophysiology of Diarrhea-

In a healthy state, the gut assimilates nearly all water and electrolytes consumed or produced during digestion. It is estimated that 9 to 10 liters of fluid enter the jejunum, including ingested food and beverages, saliva, gastric juice, bile, pancreatic juice, and succus entericus from the duodenum; however, the typical stool water content is only 80 to 100 milliliters, indicating an absorptive efficiency of approximately 99%. A mere 1% decrease in absorptive efficiency may lead to stools that are more liquid, less solid, and more often expelled, culminating in the condition known as "diarrhea." This disruption may result from modified rates of mucosal absorption or secretion due to injury to the absorptive mucosa, bacterial toxins, enteric nervous system function, or hormonal influences. Decreased absorptive efficiency may result from fast intestinal transit, malabsorption, maldigestion, or surgical modifications that lead to short bowel syndrome or the excision of essential bowel segments, such as the terminal ileum. Diarrheal diseases often include disruptions in mucosal function and gastrointestinal transit. Consequently, diarrhea is a prevalent symptom associated with several disorders.

Table 1: A brief discussion of common anti-diarrheal plants

S. No.	Botanical name/ family	Common name/ English name	Part used	Type of extraction	Animal model	Effective dose	Reference standard	References
1	*Annona muricata/ Annonaceae*	Soursop(tropical areas in South and North America)	Fresh fruits	Methanol	Swiss albino mice	0.2 ml of castor oil	loperamide 5mg/kg BW	[8]
2	*Alchornea cordifolia/ (Euphobiaceae)*	Christmas bush / tropical Africa	Fresh leaves	Ethanol	Male mice and Wistar rats	castor oil (0.2 mL)	morphine (25 mg/kg)	[9]
3	*Combretum hypopilinum/(Combretaceae)*	Jar taramniya , jar ganye, buski daneehi, katankara,	leaves	methanol	swiss albino mice	0.5 ml of castor oil	loperamide 5mg/kg	[10]
4	*Kigelia afrikana (Bignoniaceae)*		Fresh leaves	Aqueous	Adult male Wister rats	castor oil (1 mL/rat)	10mg/kg loperamide	[11]
5	*Pentaclethra macrophylla/(Mimosaceae)*	African oil bean tree / Eastern and Western Nigeria	leaves	Aqueous Ethanol	Adult albino mice ,Wistar rats	castor oil (1 mL/rat),	10mg/kg loperamide	[12]
6	*Byrsocarpus coccineus/(Connaraceae*	West Africa	Fresh leaves	Aqueous	Albino rats and mice	castor oil, 0.2 ml/mouse	morphine (10 mg/kg, s.c.)	[13]
7	*Curcuma alismatifolia/(Zingiberaceae)*	Bangladesh.	dried leaves	methanol: water	male Swiss albino mice	castor oil at a dose of 1 ml/animal orally (p.o.).	loperamide (3 mg/kg p.o.).	[4]
8	*Punica granatum/(Pomegranate)*	Anar/ India and Bangladesh	Mature fruits	Methanol extract	Swiss albino mice	0.5 ml of castor oil	Loperamide at a dose of 3 mg/kg orally.	[14]
9	*Bombax buonopozense/ (Bombacacea)*	Vabga (Dagbani) and Kurya (Hausa)/Afrika	leaves	Methanol extract	Adult wistar rats	1 ml of castor oil orally	(Loperamide 3mg/kg).	[15]
10	*Jatropha curcas/ . (Euphorbiaceae)*	Tropical America	Roots	Methanol extract	Swiss albino mice	castor oil 4 ml / kg,8 ml/kg and magnesium sulphate (2g / kg, p. o.)	chlorpromazine 30 mg/ kg I.P	[6]
11	*Ruta chalepensis / (Rutaceae) Vernonia amygdalina*	Rue tropical Africa	Fresh leaves	methanol	Swiss albino mice	0.5 ml of castor oil orally	loperamide (3 mg/kg.bw)	[16]
12	*Neorautenenia mitis/(Fabaceae)*	Central, South, and West Africa	Tubers	Aqueous	Wister albino rats	1 mL of castor oil orally	Loperamide 10 mg/kg	[17]
	Vitellaria paradoxa/(Sapotaceae.)	Africa	Stem bark	Aqueous	Wister albino rats	1 mL of castor oil orally	Loperamide 10 mg/kg	[17]
	Senna surattensis/ (Fabaceae)		leaves	Aqueous	Wister albino rats	1 mL of castor oil orally	loperamide 10 mg/kg	[17]
	Hydnora abyssinica/ (Hydnoraceae)		roots	Aqueous	Wister albino rats	1 mL of castor oil orally	loperamide 10 mg/kg	[17]
13	*Cordia Africana/ (Boraginaceae)*	Ethiopia	root bark	methanol	Swiss albino mice	0.2 mL of castor oil	loperamide, 3 mg/kg body weight	[18]

14	*Mentha microphylla/ (Labiatae)*	Egypt	Aerial parts leaves	methanol	rabbit	1 ml of castor oil orally	diphenoxylate (5 mg kg−1)	[2]
	Conyza dioscoridis/ (Compositae)	Egypt	Aerial parts	methanol	rabbit	1 ml of castor oil orally	diphenoxylate (5 mg kg−1)	[2]
	Alhagi maurorum / (Leguminosae)	Egypt	Aerial parts	methanol	rabbit	1 ml of castor oil orally	diphenoxylate (5 mg kg−1)	[2]
	Convolvulus arvensis (Convolvulaceae)	Egypt	Aerial parts	methanol	rabbit	1 ml of castor oil orally	diphenoxylate (5 mg kg−1)	[2]
	Conyza linifolia (Compositae) *Zygophyllum album(Zygophyllaceae)*	Egypt	Aerial parts	methanol	rabbit	1 ml of castor oil orally	diphenoxylate (5 mg kg−1)	[2]
15	*Euphorbia paralias. family Euphorbiacae,* *Bidens bipinnata family Compositae,* *Cynachum acutum. family Asclepiadaceae* *Plantago major. family Plantaginaceae* *Diplotaxis acris (Forssk.) Boiss.Cruciferae,* *Convolvulus fatmensis Ktze family Convolvulaceae* *Schouwia thebaica family Cruciferae*			methanol methanol methanol methanol methanol methanol methanol	Rat mice	1 ml of castor oil orally and 0.5 ml of a 5% charcoal suspension	diphenoxylate (5 mg/kg) atropine sulphate (1 mg/kg)	[19]
16	*Pyrenacantha staudtii (Icacinaceae)*	tropical Africa and found in secondary jungles of southern Nigeria, Western Cameroon and across central Africa to Uganda and Angola	Fresh leaves	Aqueous	Healthy, male and female Balb C mice	castor oil (3 ml/kg, p.o.) 3 ml/kg of activated charcoal meal	10 mg/kg (p.o.) of loperamide, atropine sulphate (1 mg/kg, p.o.)	[20]
17	*Manihot esculenta (Euphorbiaceae,)*	cassava or tapioca/ tropical and subtropical regions like Africa, Asia, and Latin America	Fresh leaves	ethanol	adult Wistar rats	2 ml of freshly prepared castor oil orally. 1 ml of freshly prepared charcoal meal (10% active charcoal in 100 ml of 5% aqueous gum acacia) orally.	Loperamide (5 mg/kg) Atropine sulfate (5 mg/kg)	[21]
18	*Carum copticum (Umbelliferae)*	Ajowain /east of India, Pakistan, Iran, and Egyp	Seeds	ethanol	Male albino rats	2 mL of castor oil 1 mL of charcoal meal (5 % activated charcoal suspended in CMC)	loperamide (3 mg/ kg P.O) atrophine sulphate at 0.1 mg/ kg BW ip	[22]

19	*Caesalpinia bonducella /(Fabaceae)*	tropical and subtropical regions of Asia and the Caribbean	leaves	methanol.	Young Long-Evans rats	castor oil (1 mL) orally	loperamide (5 mg/kg, p.o.)	[23]
20	*Indigofera spicata(Fabaceae)*	Ethiopia	roots	methanol	Swiss albino mice,	0.5 ml castor oil	3 mg/kg lopiramide atropine sulfate 0.1ug/g IP	[24]
21	*Strychnos potatorum (Loganiaceae)*	'Nirmali' in West Bengal, 'Kotaku' in Orissa, 'Tetankotai' in Tamilnadu; in English it is called 'Clearing Nut /Tree'tropical and subtropical regions.	powdered seeds	methanol	Wistar rats	1 ml of castor oil	diphenoxylate 5 mg /. kg, p.o	[25]
22	*Rhus semialata (Anacardiaceae*	Assam, Khasia, Naga and Sikkim in India upper Burma, China, and Japan	fruits	methanol	Wister albino rats	1 ml of caster oil orally	diphenoxylate 50 mg/kg body weight, orally	[26]
23	*Cyperus tegetum/ (Cyperaceae)*	mat stick, madur kat hi(Bengali)/ Paschim Medinipur district of West Be ngal	powdered rhizome s	methanol	Swiss mice	1 ml castor oil	loperamide 3 mg/kg orally.	[27]
24	*Myracrodruon urundeuva/ . (Anacardiaceae)*	Aroeira Brazil	bark	ethanol	Female Wistar rats	castor oil (2 mL/rat, p.o.)	Chlorpromazin e (30 mg/kg, p.o.)	[28]
25	*Ziziphus mauritiana/ (Rhamnaceae)*	merely jujube, Chinese date, Indian plump	root	methanol	Adult male wistar rats	0.5 ml of castor oil orally	diphenoxylate (5 mg/kg) orally	[29]
26.	*Punica granatum (Punicaceae)*	'Dalim' (Bengali) 'Anar' (Hindi) warm valleys and outer hills of the Himalayas and is cultivated throughout India.	seeds	methanol	Wister albino rats	1 ml of castor oil orally 1 ml of charcoal meal	diphenoxylate (5 mg/kg) orally atropine (0.1 mg/kg, i.p.)	[30]
27.	*Swietenia macrophylla (Meliaceae)*	tropical America, Mexico and South America	Seeds	petroleum ether	Swiss albino rats	Castor oil at a dose of 1 ml/animal orally	diphenoxylate (50 mg/kg body weight)	[31]
28.	*Piliostigma reticulatum (Caesalpiniaceae)*	forests of West African countries such as Côte d'Ivoire, Mali and Burkina Faso	Stem bark	ethanol	Healthy young adult albino Wistar rats	2 ml of castor oil orally	loperamide (5 mg/kg body weight)	[32]

29.	*Boswellia diazielii** *Burseraceae*	Papery bark tree	Bark	Aqueous	Male and female wistar rats	1.0 ml of castor oil orally	5 mg/kg of diphenoxylate	[33]
	Acacia nilotica *Mimosaceae*	Thorn mimosa	Bark	Aqueous	Male and female wistar rats Male and female	1.0 ml of castor oil orally	5 mg/kg of diphenoxylate	[33]
	*Pisidium guajava** *Myrtaceae*	Guava	Leaf	Aqueous	wistar rats	1.0 ml of castor oil orally	5 mg/kg of diphenoxylate	[33]
30.	*Lannea acida* *Anacardiaceae* *Euphorbia hirta*	Atina barteri	Bark	Aqueous	Male and female wistar rats	1.0 ml of castor oil orally	5 mg/kg of diphenoxylate	[33]

The findings indicate that the leaf extract of *Hemigraphis alternata* is nontoxic and may serve as a source of plant compounds exhibiting anti-inflammatory, anti-nociceptive, and anti-diarrheal properties [34]. Another study assessed the antidiarrheal activity of the ethanolic extract from the aerial portions of Vinca major in rats. The impact of the ethanol extract from the aerial components of Vinca major on castor oil-induced diarrhea, castor oil and magnesium sulfate-induced enter pooling, and gastrointestinal motility assessed with charcoal meal techniques was investigated. This extract (250, 500, and 1000 mg/kg, p.o.) was evaluated for its effects on latent durations and fecal frequency in castor oil-induced diarrhea. Gastrointestinal transit experiments with charcoal meal, castor oil, and magnesium sulfate (500 mg/kg, p.o.) were performed to induce enter pooling. The findings indicated a significant ($p<0.05$) reduction in fecal output at a dosage of 500 mg/kg, administered orally, in castor oil-induced diarrhea, peristaltic movements during the charcoal meal test, and intestinal fluid secretions in castor oil and magnesium sulfate-induced enter pooling, demonstrating its antidiarrheal efficacy. The findings indicate that the ethanolic extract of Vinca major aerial parts exhibits antidiarrheal properties [35].

In another study, the ethanolic extract of the whole plant of *Evolvulus alsinoides L*. (Convolvulaceae) was examined for its anti-inflammatory, antipyretic, and anti-diarrheal effects in female albino rats. Initial phytochemical investigations were conducted to verify the existence of active chemical ingredients in the plant extract, yielding favorable results for flavonoids, alkaloids, and cardiac glycosides. The pharmacological findings indicated that the ethanolic extract at doses of 250 mg/kg and 500 mg/kg body weight significantly ($P < 0.05$) inhibited carrageenan-induced rat paw edema and markedly ($P < 0.05$) reduced hyperpyrexia generated by Brewer's yeast in rats. The extract demonstrated significant anti-diarrheal efficacy against castor oil-induced diarrhea at a dosage of 500 mg/kg. This research has scientifically validated the old assertion that the entire plant of *Evolvulus alsinoides* possesses anti-inflammatory, antipyretic, and anti-diarrheal properties [36].

Historically, *Dodonaea viscosa* has been utilized for the treatment of different disorders, including diarrhea. This study aims to assess the antidiarrheal efficacy of the 80% methanolic leaf extract of *D. viscosa* against castor oil-induced diarrhea in murine models. Various dosages of 80% methanolic leaf extract of *D. viscosa* (100, 200, and 400 mg/kg) were assessed for their antidiarrheal efficacy utilizing castor oil-induced diarrhea, gastrointestinal transit, and enter pooling models in Swiss albino mice. All test dosages of the plant extract

demonstrated substantial ($P < .05$) reduction in the frequency of defecation of wet feces and total fecal output compared to the control group. Consistently, across all administered doses, the plant extract exhibited a substantial ($P < .05$) decrease in intraluminal fluid buildup relative to the untreated group. Furthermore, at elevated dosages, the plant extract demonstrated considerable ($P < .05$) antimotility activity relative to the control. In conclusion, these data demonstrated that the 80% methanolic leaf extract of *D. viscosa* corroborated the traditional assertion of the plant's antidiarrheal properties, but more research is necessary [37]. Carpesterol acetate is obtained from the plant of the Solanaceae family, used in the treatment of Diarrhea [38]. Researcher reveals the result indicates that *Pterocarpus erinaceus* extract produced significant antidiarrheal activity, and the action may be attributed to inhibition of gastrointestinal movement and fluid secretion [39]. The root of *Indigofera spicata Forssk.* has demonstrated significant antidiarrheal efficacy, corroborating its traditional use [24]. Capparis decidua has notable ethnomedicinal uses, encompassing antirheumatic, analgesic, anthelmintic, laxative, renal disinfectant, diuretic, and treatments for cough, diarrhea, dysentery, cholera, cardiovascular problems, and digestive tract disorders [40]. Kalanchoe pinnata, a significant medicinal plant belonging to the stonecrop family, is extensively found in India and tropical and subtropical regions globally. It has been documented for its traditional application in numerous ailments, including abdominal discomfort, boils, bruises, cholera, lacerations, diabetes, diarrhea, dysentery, flatulence, headaches, nephrolithiasis, indigestion, insect bites, scabies, lesions, urinary insufficiency, and wounds [41]. This research indicates that the methanol leaf extract of *Hymenocardia acida* is effective against acute diarrhea and may function as an anti-motility agent. This so corroborates the conventional application of the plant in the treatment of diarrhea. The morbidity and death associated with diarrhea have posed a significant global health problem. The scientific community is increasingly favoring herbal ways to treat ailments due to the detrimental effects of modern drugs. Despite the extensive availability of traditional anti-diarrheal plants with demonstrated efficacy, insufficient attention has been given to the utilization of these Phyto preparations for the treatment of diarrhea and related conditions. The innovative drug delivery method, when utilized in herbal medicine, may improve efficacy and diminish the undesirable effects of numerous herbal constituents and plants. This is the fundamental premise governing the integration of novel drug-delivery techniques in herbal treatments [42]. Excessive tumor accelerates suppuration. Toothpaste with anthraquinones may cause gastrointestinal pain, while Aloe gel has been formulated to prevent diarrhea [43]. Numerous scientific studies demonstrate that these herbal extracts exert their anti-diarrheal benefits by functioning as antisecretory agents, possessing anti-peristaltic properties, and exhibiting anti-microbial and anti-spasmodic actions. Although certain plants have been thoroughly examined and active phytoconstituents have been extracted and identified, such research is rather few. Certain antidiarrheal phytoconstituents, such as Apigenin and Friedelin, are recognized for their diverse therapeutic benefits in addition to their anti-secretory and antimotility properties. Apigenin, extracted from the aerial components of *Dracocephalum kotschyi,* is a compound that has various pharmacological properties. This molecule has been extensively studied for its efficiency against many cancers, arthritis, osteoporosis, and inflammation, and it plays a significant role in the nervous system, demonstrating effectiveness against Alzheimer's and other neurological disorders. Specific phytochemicals, like Eriosematin E (a prenylated flavanone), Stachysrosane, and 1,8-cineole (a terpenoid oxide), have received little research attention. The primary plants and phytomolecules may thus be further investigated for their additional pharmacological effects. Several historically recognized medicinal herbs have been shown to exhibit significant anti-diarrheal activity. Several extracts, including Mangifera indica (leaf), the herbal composition of *Vernonia amygdalina* (leaf) and *Cymbopogon citratus* (leaf), *Polygonatum verticillatum* (rhizome), *Mimosa diplotricha* (leaf), *Pelargonium luridum* (root), *Croton macrostachyus* (aerial parts), *Oxalis barrelieri* (whole plant), *Pseudocedrela kotschyi* (leaf), *Maytenus erythroxylon* (leaf), *Khaya senegalensis* (stem bark), *Croton grewioides* (aerial parts), *Amaranthus trocolor* (leaf), *Spondias mombin* (stem bark), *Salvia schemperi* (leaf), *Cistus salviifolius* (aerial parts), and *Salacia lehmbachhi* (leaf), demonstrated significant efficacy against diarrhea, with 80%–100% inhibition recorded

across various tested parameters. These prospective herbal extracts ought to be employed as a foundation for novel herbal medicine discovery, aimed at identifying active plant molecules, subsequently undergoing rigorous pre-clinical and clinical evaluations for effectiveness and safety.

Conclusion-

Diarrheal illnesses persistently exert a considerable health burden globally, particularly in low- and middle-income nations. While contemporary medications offer symptomatic alleviation, issues of accessibility, price, and adverse effects persist as significant problems. Medicinal herbs have historically functioned as efficacious traditional treatments for diarrhea, exhibiting a range of pharmacological properties such as antimotility, antisecretory, anti-inflammatory, and antibacterial effects. A diverse selection of herbs, including *Annona muricata, Punica granatum, Vinca major,* and *Dodonaea viscosa*, has demonstrated encouraging outcomes in animal models, frequently similar to traditional medications such as loperamide and diphenoxylate. Active phytoconstituents like apigenin and friedelin have prospects for the development of innovative medicinal treatments. Nevertheless, most of these plants have not undergone a comprehensive investigation regarding their mechanisms, standardization, or clinical effectiveness. Future investigations should include phytochemical characterization, preclinical and clinical studies, and the formulation of standardized herbal preparations. Enhancing the scientific foundation for these traditional medicines might facilitate the development of cost-effective, culturally endorsed, and efficacious antidiarrheal treatments to tackle a significant global health issue.

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