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Review Article

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Therapeutic significance and pharmacological activities of antidiarrheal medicinal plants mention in Ayurveda: A review

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ABSTRACT

Diarrhea is a serious problem affecting 3-5 billion people per year around the world, especially children of below 5 years. 70% of the world population uses traditional and indigenous medicine for their primary health care. The facts of these indigenous remedies are passed verbally and sometimes as documents. Since ancient time, Ayurveda is the main system of healing in South East Asian countries. Indian literature from ayurvedic texts and other books claim the potency of several plants in the treatment of diarrhea. As the global prospective of ayurvedic medicine is increasing, interest regarding the scientific basis of their action is parallely increasing. Researchers are doing experiments to establish the relation between the claimed action and observed pharmacological activities. In the present article, an attempt was made to compile the scientific basis of medicinal plants used to cure diarrhea in Ayurveda. Literature was collected via electronic search (PubMed, ScienceDirect, Medline, and Google Scholar) from published articles that reports antidiarrheal activity of plants that were mentioned in Ayurveda classics. A total of 109 plant species belonging to 58 families were reported for their antidiarrheal activity. Several Indian medicinal plants have demonstrated promising antidiarrheal effects, but the studies on the antidiarrheal potentials of these plants are not taken beyond proof of concept stage. It is hoped that the article would stimulate future clinical studies because of the paucity of knowledge in this area.

KEY WORDS: Ayurveda, diarrhea, medicinal plant, traditional medicine

INTRODUCTION

Gastroenteritis is a clinico-pathological term that refers to inflammation and oxidative stress of the intestines which leads to disturbance in the balance of secretory and absorptive function of the intestines resulting in diarrhea [1,2]. Hence, diarrhea can be defined as a gastrointestinal disorder in which there is a rapid transit of gastric contents through the intestine, which is characterized by abnormal fluidity and high frequency of fecal evacuation, usually semisolid or watery fecal matter, three or more times/day [1-3]. There is an increase in flow rate of feces with or without the presence of blood and mucus, accompanied by increased secretion and decreased absorption of fluid, leading to loss of water and electrolytes [2,4]. The major causative agents of diarrhea in human beings include a variety of enteric pathogenic bacteria such as *Salmonella typhi*, *Shigella flexneri*, *Escherichia coli*, *Staphylococcus aureus*, *Vibrio cholerae*, and *Candida albicans* [4,5]. Viruses, protozoans, helminths, intestinal disorders, immunological factor, and medications can also cause diarrhea in human being [6-8]. Etiological factors for diarrhea include the food intolerances, contaminated drinking water, undercooked meat and eggs, inadequate kitchen hygiene, poor sanitation [9], bile salts, hormones, irritable bowel syndrome, and intoxication [10]. According to the World Health Organization (WHO), diarrhea affects 3-5 billion people/year worldwide and causes 5 million deaths per annum [11]. Children, however, are more susceptible to the disease, which is the one of the leading causes of death in infants and children below 5 years of age [12].

Due to high mortality and morbidity, especially in children, the WHO together with the United Nations Children's Fund has initiated Diarrhea Disease Control Program to control diarrhea in developing countries. Oral rehydration solution [13], zinc solution [14], probiotics [15], and specific antibiotics have reduced mortality rate in diarrheal disease. However, chronic diarrhea is still a life challenging problem in some regions of the world. Unfortunately, the program does not reach to the needy, and the disease is still a major challenge in front of primary health practitioner as well as researcher. Therefore, the different traditional systems of medicines such as Chinese medicine [16], Japanese medicine [17], acupuncture therapy [18], and ayurvedic medicine [19] are included in this program.

Since ancient time's medicinal plants have been used to treat different ailments due to their accessibility, availability, inherited practice, economic feasibility, and perceived efficacy [20]. Nowadays, use of medicines from plant source increases significantly with conventional therapies. Hence, the plants are gaining more attention by the researchers to find out new and effective agents for different diseases. Several medicinal plants in the different regions of the world have been used to cure diarrhea [19,21].

The knowledge of indigenous medicines is passing from generation to generation orally worldwide [22]. It is, therefore, documentation of such knowledge as well as reported the scientific basis of their pharmacological potential is necessary since they are usually consider as free from adverse effects. A range of medicinal plants were reported for their effectiveness in diarrhea [23-27]. The protective role of these plants is probably due to their anti-inflammatory, antioxidant, and astringent properties [28]. India has a rich plant resources providing valuable medicine, which are conveniently used in Ayurveda, Unani, and other system of medicines for the treatment of various diseases [29]. Keeping this in view, the present article was initiated, with an aim to compile the scientific basis of medicinal plants used to cure diarrhea. A variety of curative agents from these indigenous plants has been isolated. These isolated compounds are belonging to different phytochemical classes such as flavonoids, saponins, terpenoids, steroids, phenolic compounds, and alkaloids [30-32]. Flavonoids and saponins inhibit the release of prostaglandins, autocoids, and contractions caused by spasmogens as well as motility and hydroelectrolytic secretions [33,34] while saponins may prevent release of histamine [35]. Polyphenols and tannins provide strength to intestinal mucosa, decrease intestinal secretion, intestinal transit and promotes balance in water transport across the mucosal cells [36].

Previously, we enumerated a large number of plants, which are used in the ayurvedic system as antidiarrheal [19]. A majority of these plants have been investigated pharmacologically with respect to the potential antidiarrheal activity. In this review, we present ethnopharmacological data of 109 plant species belonging to 58 families mentioned in ayurvedic texts for controlling diarrhea with their possible mechanism of action [Table 1 and Figure 1]. Mostly, leaf (23%), root (14%), barks (11%), fruit (9%), and seed (8%) of the plants are used for antidiarrheal activity [Figure 2].

DISCUSSION

Since ages, human beings have relied on plants as a resource of the therapeutic arsenal in the fight against certain human diseases. Plant-based drugs have formed the basis of traditional medicine systems, i.e., Ayurveda, Siddha, Unani, Homeopathy, and Chinese. Herbal-based therapy is one of the popular and effective practices to overcome the illness. The WHO also promotes utilization of local knowledge of plant-based medicines in health care. It has been reported by the WHO that about 70-80% of the population in developing countries relies on traditional/ethno medicines/for their primary health care. Since ancient time ayurvedic system of medicine is indigenous to and widely practiced in India. Nature has bestowed India with an enormous wealth of medicinal plants. Therefore, their rational uses for combating diseases are described traditionally.

Acharya charaka has mentioned a group of antidiarrheal plants named as *Purish-Samgarahaniya Mahakashaya*, which includes priyangu (*Callicarpa macrophylla*), ananta (*Hemidesmus indicus* R.B.), seed of amra (*Mangifera indica*), katvanga (*Ailanthus excelsa* Roxb.), lodhra (*Symplocos racemosa*), mocharasa (*Salmalia malabarica* Schott and Endl.), samanga – *Rubia cordifolia*, flower of dhataki – *Woodfordia fruticosa*, padma – lotus (*Nelumbo nucifera*), and filaments of padma – lotus (*N. nucifera*). Moreover, he also listed some most useful antidiarrheal plants such as katavanga (*A. excelsa* Roxb.), *mustaka* (*Cyperus rotundus* Linn.), amrita (*Tinospora cordifolia* [Willd.] Miers ex Hook. f. & Thoms.), ativisha (*Aconitum heterophyllum* Wall. ex. Royle.), bilva (*Aegle marmelos* Correa), kumuda (*N.nucifera* Gaertn.), utpala, padma, kutaja bark (*Holarrhena antidysenterica* [Linn.] Wall.), gambhari fruit (*Gmelina arborea* Roxb.), prishniparni (*Uraria picta* [Jacq.] Desv. Ex DC.), and bala (*Sida cordifolia*) [187]. In addition, Acharya Susuruta mentioned that the vacha (*Acorus calamus* Linn.) and haridra (*Curcuma longa* Linn.), etc., are best for *amatisara* (diarrhea where undigested food matter pass in stool) while ambastha (*Cissampelos pareira* Linn.) and priyangu (*C. macrophylla*) are best for pakwatisara (diarrhea where only digested food matter pass in stool) [188].

The ayurvedic Pharmacopoeia mentioned more than 1200 species of plants, nearly 100 minerals and over 100 animal products officially. Although there is no record of pharmacological testing during the period when ayurvedic texts were written. However, nowadays, extensive researches are carried out concerning the phytopharmacological basis of their therapeutic principles. Public, academic as well as government organizations are showing interest in the scientific mechanism of action exerted by these plants. Similar to modern and other traditional medicines, ayurvedic medicines have been also evaluated for their phytopharmacology with the help of advances in science and technology. Scientific screening on laboratory animal and *in vitro* evaluations supports traditional uses of medicinal plants.

In the present scenario, modern pharmaceuticals offer a number of medicines for diarrhea, but diarrhea still remains a major health threat to the people in tropical and subtropical countries. It is one of the leading causes of mortality in children especially under the age of 5 years [12]. Different factors such as infections, malnutrition, food intolerances, intestinal disorders, and some medications may trigger diarrhea [6-8]. Currently, available pharmacological treatments are seem to be insufficient in diarrhea control. It is because of lack of admittance, high cost, and adverse effects of modern pharmaceuticals as well as therapeutic approaches. Therefore, investigations on drugs from different alternative and complementary medicines along with traditional system of medicines were going on.

Table 1: Antidiarrheal medicinal plants

Sanskrit name	Botanical name	Family	Part used	Extract/dose	Standard drug and dose	Model	Mechanism	References
Atibala	*Abutilon indicum* (Linn.) Sweet.	Malvaceae	Leaf	Methanolic and aqueous extract	Loperamide (1 mg/kg)	Gastrointestinal motility test, castor oil-induced diarrhea model, and PGE_2-induced enteropooling model		[37]
Khadir	*Acacia catechu* Willd.	Fabaceae	Heartwood	Ethyl acetate extract (250 mg/kg)	Diphenoxylate (10 mg/kg) and atropine (1 ml/200 g, p.o.)	Castor oil-induced diarrhea model		[38]
Babool	*Acacia nilotica* Delile & Ssp. *indica* (Benth.) Brenan.	Caesalpiniaceae	Bark	Petroleum ether, methanolic and aqueous extract		Castor oil- and magnesium sulfate-induced diarrhea and barium chloride-induced gastrointestinal motility test		[39]
Ativisha	*Aconitum heterophyllum* Wall. ex. Royle.	Ranunculaceae	Root	Ethanolic extract (50, 100, and 200 mg/kg) and isolated aconitine	Loperamide (2 mg/kg, p.o.) and atropine (0.1 mg/kg, s.c.)	Castor oil-induced diarrhea model, Small intestinal transit time, PGE_2-induced enteropooling, and gastric emptying test	Prevented Na^+ and K^+ loss	[40]
Vacha	*Acorus calamus* Linn.	Araceae	Root and essential oil	Methanolic extract and n-hexane fraction		Castor oil-induced diarrhea model, spasmolytic activity	Inhibition of spontaneous and High K^+-induced contractions and antispasmodic action	[41,42]
			Rhizome	Aqueous and methanolic extract (3, 7.5, and 15 mg)		Castor oil-induced diarrhea model		
Bilva	*Aegle marmelos* Correa.	Rutaceae	Unripe fruit pulp	Aqueous extract	-	Antimicrobial activity	Through reduced bacterial adherence to intestinal wall and Invasion of Hep-2 cells	[43-50]
			Leaf	Aqueous extract (50, 100, and 200 mg/kg)	Loperamide (3 mg/kg orally)	Castor oil-induced diarrhea, magnesium sulfate-induced diarrhea, and gastric transit time		
			Fruit	Polyherbal formulation (25, 50, and 100 mg/kg)	Mebarid (10 ml/kg, p.o.)	Castor oil-induced diarrhea model, intestinal secretion model, and antispasmodic effect	Inhibition of intestinal transit of food material and inhibition of intestinal secretion	
			Unripe fruit	Aqueous and methanolic extract		Castor oil-induced diarrhea model		
			Fruit	Aqueous extract	Diphenoxylate and yohimbine	Castor oil-induced diarrhea model		
			Dried fruit pulp	Ethanolic extract	-	*In vitro* antibacterial activity		
			Root	Chloroform extract	-	Castor oil-induced diarrhea model		

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Table 1: *(Contd....)*

Sanskrit name	Botanical name	Family	Part used	Extract/dose	Standard drug and dose	Model	Mechanism	References
			Unripe fruit	(50, 100 mg/kg)	-	Gastrointestinal motility test and castor oil-induced diarrhea model		
Gorakhganja	*Aerva lanata*	Amaranthaceae	Whole plant	Alcoholic and aqueous extract (400 and 800 mg/kg)	Loperamide (3 mg/kg, i.p.)	Castor oil-induced diarrhea		[51]
Aralu	*Ailanthus excelsa* Roxb.	Simaroubaceae	Bark	Chloroform, aqueous and ethanolic extract	Atropine (0.1 mg/kg, i.p.)	Castor oil-induced diarrhea model		[52]
Shirish	*Albizia lebbeck* Benth.	Caesalpiniaceae	Seed	Crude extract	Loperamide (1 mg/kg, i.p.)			[53]
Saptaparna	*Alstonia scholaris* R.Br.	Apocynaceae	Bark	Methanolic extract	Loperamide	Castor oil-induced diarrhea model	Spasmolytic activity mediated possibly through CCB	[54,55]
				Ethanolic extract (250 mg/kg)	Loperamide (50 mg/kg)	Castor oil-induced diarrhea model		
Tanduliya	*Amaranthus spinosus* Linn.	Amaranthaceae	Whole plant	Ethanolic extract (100, 200, and 400 mg/kg)	Yohimbine	Castor oil-induced diarrhea model, charcoal-induced gastrointestinal motility test		[56]
Eshwari	*Aristolochia indica* Linn.	Aristolochiaceae	Root	Aqueous extract and ethanolic extract	Diphenoxylate (5 mg/kg, p.o.)	Castor oil-induced diarrhea model, charcoal-induced gastrointestinal motility test		[57]
Shatavari	*Asparagus racemosus* Willd.	Liliaceae	Root	Ethanolic and aqueous extract	Loperamide (3 mg/kg, p.o.)	Castor oil-induced diarrhea model, gastrointestinal tract motility, PGE_2-induced enteropooling		[58]
Hijjala	*Barringtonia acutangula* (Linn.) Gaertn.	Lecythidaceae	Root	Ethanolic extract (200 and 400 mg/kg)	Diphenoxylate (5 ml/kg, p.o.)	Castor oil-induced diarrhea model		[59,60]
			Leaf and seed	Methanolic extract (200 and 400 mg/kg)	Loperamide (3 mg/kg, p.o.)	Castor oil and magnesium sulfate-induced diarrheal models		
Kovidara	*Bauhinia purpurea* Linn.	Caesalpiniaceae	Leaf	Ethanolic extract		Castor oil and magnesium sulfate-induced diarrheal models		[61]
Kanchnar	*Bauhinia variegata* Linn.	Caesalpiniaceae	Stem bark	(250, 500, and 1000 mg/kg, p.o.)		Castor oil-induced diarrhea, castor oil magnesium sulfate-induced enteropooling, and gastrointestinal motility test using charcoal meal test		[62]
Daruharidra	*Berberis aristata* DC.	Berberaceae	Stem	Aqueous extract	Loperamide (2 mg/kg, po)	Castor oil-induced diarrhea model	Inhibit the intestinal secretary response	[63-65]
			Bark	Ethanolic, aqueous extract and isolated berberine	Loperamide (25 mg/kg)	Castor oil-induced diarrhea model		
			Stem	Ethyl alcohol extract (250, 500 mg/kg)	Loperamide (3 mg/kg orally)	Magnesium sulfate-induced diarrhea, castor oil-induced intestinal secretions		
Sinduri	*Bixa orellana* Linn.	Bixaceae	Leaf	Methanolic extract (125, 250, and 500 mg/kg)	Loperamide (3 mg/kg orally)	Castor oil-induced diarrhea model		[66]

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Table 1: *(Contd....)*

Sanskrit name	Botanical name	Family	Part used	Extract/dose	Standard drug and dose	Model	Mechanism	References
Sallaki	*Boswellia serrata* Roxb. Ex Coleb.	Burseraceae	Gum resin	Hydroalcoholic extract and 3–acetyl–11–keto–b–boswellic acid	Atropine (1 mg/kg)	Upper gastrointestinal transit in croton oil-treated animal, castor oil-induced diarrhea model	Inhibition of acetylcholine-induced contractions by the L-type Ca^{2+} channel blockers	[67]
Parnabija	*Bryophyllum pinnatum* (Lam.) Kurz.	Crassulaceae	Leaf	Aqueous extract (100, 200, and 300 mg/kg)	Loperamide (5 mg/kg)	Castor oil-induced diarrhea model, castor oil-induced enteropooling, small intestinal transit time		[68]
Priyala	*Buchanania lanzan* Spreng.	Fagaceae	Leaf	(200 and 400 mg/kg)	Loperamide (1 mg/kg)	Castor oil-induced diarrhea model, charcoal meal test	Inhibition Na^+-K^+ATPase activity	[69]
Palash	*Butea monosperma* Lam. Kuntze.	Fabaceae	Stem bark	Ethanolic extract	Loperamide (3 mg/kg orally)	Castor oil-induced diarrhea model and PGE_2-induced enteropooling		[70]
Latakaranja	*Caesalpinia bonducella* Flem.	Caesalpiniaceae	Leaf	Methanolic extract and its ethyl acetate, chloroform, and petroleum ether fractions (200 and 400 mg/kg)	Loperamide (5 mg/kg, p.o.)	Castor oil-induced diarrhea model	Antibacterial activity	[71]
Gumohar	*Caesalpinia pulcherrima* L.	Caesalpiniaceae	Bark	Ethanolic extract (500 mg/kg)	Loperamide (50 mg/kg orally)	Castor oil-induced diarrhea model		[72]
Arka	*Calotropis gigantea* R.Br.	Asclepiadaceae	Aerial part	Hydroalcoholic extract (200 and 400 mg/kg)	Atropine (3 mg/kg, i.p.)	Castor oil-induced diarrhea model		[73]
Arka	*Calotropis procera* (Ait.) R.Br.	Asclepiadaceae	Dry latex	(500 mg/kg)	Atropine (0.1 mg/kg, i.p.)	Castor oil-induced enteropooling, electrolyte concentration in the intestinal fluid and intestinal transit		[74-77]
			Latex	Ethanolic extract (250, 500 mg/kg)	Loperamide (4 mg/kg)	Castor oil-induced diarrhea model		
			Leaf	Methanolic extract	Loperamide (3 mg/kg orally)	Castor oil-induced diarrhea model		
				Aqueous and alcoholic extract (100, 200 mg/kg)		Castor oil-induced diarrhea model, charcoal meal test, enteropooling method		
Tea	*Camellia sinensis* (Linn.) O. Kuntze.	Theaceae	Leaf	Aqueous extract		Castor oil-induced diarrhea model and PGE_2-induced enteropooling		[78]
Hinsra	*Capparis zeylanica* Linn.	Capparidaceae	Leaf	Methanolic extract (100, 150, and 200 mg/kg)	Loperamide (3 mg/kg orally)	Castor oil-induced diarrhea model and small intestine transit method		[79]
Erand karkati	*Carica papaya* Linn.	Caricaceae	Fruit	Alcoholic and aqueous extract (100, 200 and 400 mg/kg)	Loperamide (3 mg/kg, p.o.)	Castor oil-induced diarrhea model and magnesium sulfate-induced diarrhea		[80]
Shitiwar	*Celosia argentea* Linn.	Amaranthaceae	Leaf	Alcoholic extract (100, 200 mg/kg)	Atropine (0.1 mg/kg, s c)	Castor oil-induced diarrhea model, charcoal meal test, PGE_2-induced diarrhea		[81]
Patra	*Cinnamomum tamala* Buch.–Ham.	Lauraceae	Bark	Ethanolic extract (25, 50, and 100 mg/kg)		Castor oil-induced diarrhea model		[82]
Twaka	*Cinnamomum zeylanicum* Linn.	Lauraceae	Bark	Aqueous extract (100 and 200 mg/kg)	Loperamide (5 mg/kg)	Castor oil-induced diarrhea model and magnesium sulfate-induced diarrhea		[83]

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Table 1: *(Contd....)*

Sanskrit name	Botanical name	Family	Part used	Extract/dose	Standard drug and dose	Model	Mechanism	References
Patha	*Cissampelos pareira* Linn.	Menispermaceae	Root	Ethanolic extract (25-100 mg/kg)		Castor oil-induced diarrhea model	Inhibitory effect on the concentration of Na^+ and K^+, reduction in the lipid peroxidation and Prevention from oxidative stress	[84]
Hulhul	*Cleome viscosa* L.	Capparidaceae	Whole plant	Methanolic extract	Diphenoxylate (5 mg/kg orally)	Castor oil-induced diarrhea model and PGE_2-induced enteropooling gastrointestinal motility		[85]
Vaamana–haati	*Clerodendrum indicum*	Verbenaceae	Leaf	Methanolic extract and chloroform fraction	-	Castor oil-induced diarrhea model		[86]
Aparajita	*Clitoria ternatea* L.	Fabaceae	Leaf	Methanolic extract (100, 200, and 300 mg/kg)	Loperamide (3 mg/kg)	Castor oil-induced diarrhea model and small intestine transit method		[87,88]
			Root	Alcoholic extract (100, 200, and 400 mg/kg)	Atropine (5 mg/kg, i.p.)	Castor oil-induced diarrhea model, intestinal transit and castor oil-induced enteropooling		
Dhanyaka	*Coriandrum sativum* Linn.	Apiaceae	Leaf	Aqueous extract (150 and 300 mg/kg)	Loperamide (3 mg/kg)	Castor oil-induced diarrhea model		[89]
Varuna	*Crataeva nurvala* Buch.–Ham.	Capparidaceae	Stem bark	Ethanolic extract (500 mg/kg)		Castor oil-induced diarrhea model, castor oil-induced enteropooling, and small intestine transit model		[90]
Jiraka	*Cuminum cyminum* Linn.	Apiaceae	Seed	Aqueous extract	Loperamide (3 mg/kg)	Castor oil induce diarrhea model, PGE2-induced enteropooling model, intestinal transit by charcoal		[91]
Haridra	*Curcuma longa* Linn.	Zingiberaceae	Rhizome	Aqueous extract (200 mg/kg)		Castor oil-induced diarrhea model		[92]
Durva	*Cynodon dactylon* Pers.	Poaceae	Whole plant	Methanolic extract (200 and 300 mg/kg)	Atropine (5 mg/kg orally)	Castor oil-induced diarrhea model, gastrointestinal charcoal meal test, and enteropooling model		[93]
Mustaka	*Cyperus rotundus* Linn.	Cyperaceae	Rhizome	Methanolic extract (250-500 mg/kg)		Castor oil-induced diarrhea model		[94,95]
				Aqueous extract	-	Antibacterial activity against EPEC and EIEC and Shigella flexneri	Antibacterial, antigiardial and antirotaviral activities	
Goraksha	*Dalbergia lanceolaria* Linn.f.	Fabaceae	Bark	Petroleum ether, ethanolic extract	Diphenoxylat (5 mg/kg, p.o.)	Castor oil and magnesium sulfate-induced diarrhea		[96]
Shimsapa	*Dalbergia sissoo* Roxb. ex DC.	Fabaceae	Leaf	Ethanolic extract		Castor oil-induced diarrhea model and magnesium sulfate $MgSO_4$-induced diarrhea		[97]
Kusha	*Desmostachya bipinnata* L.	Poaceae		Alcohól aqueous extract (200, 400 mg/kg)	Loperamide (3 mg/kg, p.o.)	Castor oil-induced diarrhea model, gastrointestinal motility test with charcoal meal test		[98]
Virataru	*Dichrostachys cinerea* W. & A.	Mimosaceae	Leaf bark and root	Ethanolic extract (200 and 400 mg/kg)	Loperamide (5 mg/kg, p.o.)	Castor oil-induced model and small intestinal transit model		[99]
Tinduka	*Diospyros peregrina* Gruke.	Ebenaceae	Bark and seed	(250 and 500 mg/kg)		Castor oil-induced diarrhea model		[100]

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Table 1: *(Contd....)*

Sanskrit name	Botanical name	Family	Part used	Extract/dose	Standard drug and dose	Model	Mechanism	References
Amalaki	*Emblica officinalis* Gaertn.	Euphorbiaceae	Fruit	Ethanolic extract (500 mg/kg)	Loperamide (3 mg/kg)	Castor oil-induced diarrhea model	Inhibition of intestinal motility, antimicrobial action, and antisecretory effects	[101-103]
				Crude extract (500-700 mg/kg)	Loperamide (10 mg/kg)	Castor oil-induced diarrhea model and enteropooling model	Mediated possibly through dual blockade of muscarinic receptors and Ca^{2+} channels	
				Methanolic extract		Diarrhea-induced by castor oil and magnesium sulfate, gastrointestinal motility in charcoal meal tests, and PGE_2-induced enteropooling		
Paribhadra	*Erythrina indica* Lam.	Fabaceae	Leaf	Ethanolic and aqueous extract (500 mg/kg)	Loperamide (5 mg/kg)	Castor oil-induced diarrhea model, PGE_2-induced intestinal fluid enteropooling, and gastro intestinal tract motility model		[104]
Dugdhika Big	*Euphorbia hirta* Linn.	Euphorbiaceae	Whole plant	Ethanolic and water extract (2.0 mg/kg)		Castor oil-induced diarrhea model, PGE_2-induced enteropooling, gastrointestinal motility in both $BaSO_4$ and charcoal meal tests		[105]
Kapittha	*Feronia limonia* Linn. Swingle	Rutaceae	Leaf	Ethanolic extract (250, 500 mg/kg)	Loperamide (50 mg/kg)	Antibacterial activity, castor oil-induced diarrhea model		[106,107]
				Ethanolic extract (500 mg/kg)	Loperamide (25 mg/kg)	Castor oil-induced diarrhea model		
Vata	*Ficus benghalensis*	Moraceae	Leaf	Methanolic (3, 7.5 and 15 mg/kg)		Castor oil-induced diarrhea model	Increasing colonic water and electrolyte re-absorption or by inhibiting intestinal motility	[108,109]
			Root	Ethanolic extract (400 mg/kg)	Diphenoxylate (5 mg/kg, p.o.)	Gastrointestinal motility in charcoal meal test, castor oil-induced diarrhea model, and PGE_2-induced enteropooling		
Kakodumbara	*Ficus hispida* Linn.	Moraceae	Leaf	Methanolic extract	Diphenoxylate (5 mg/kg, p.o.)	Castor oil-induced and PGE_2-induced enteropooling model		[110]
Udumbara	*Ficus racemosa* Linn.	Moraceae	Bark	Ethanolic extract 400 mg/kg	Diphenoxylate (5 mg/kg, p.o.)	Castor oil-induced diarrhea model and PGE_2-induced enteropooling model		[109]
Ashvattha	*Ficus religiosa* Linn.	Moraceae	Stem bark	Hydroalcoholic, acetone extract	Loperamide (3 mg/kg, p.o.)	Castor oil-induced diarrhea model		[111]
Udumber	*Ficus glomerata* L.	Moraceae	Leaf	Methanolic extract (100 and 200 mg/kg)	Atropine (3 mg/kg)	Castor oil-induced diarrhea model, castor oil-induced enteropooling, and intestinal transit		[112]
Parpata	*Fumaria parviflora*	Papeveraceae	Aerial part	Aqueous and methanolic extract	Dicyclomine, (50 and 100 mg/kg) and loperamide (10 mg/kg, p.o.)	Castor oil-induced diarrhea model	CCB blockade of muscarinic receptors	[113]

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Table 1: *(Contd....)*

Sanskrit name	Botanical name	Family	Part used	Extract/dose	Standard drug and dose	Model	Mechanism	References
Kasmari	*Gmelina arborea* Roxb.	Verbenaceae	Root	Ethanolic and N–butanol (200, 400 mg/kg)	Loperamide (3 mg/kg, p.o.)	Castor oil-induced diarrhea model		[114,115]
			Stem bark	Aqueous and methanolic extract (0.5, 1.0 mg/ml)	Loperamide (5 mg/kg)	Castor oil-induced diarrhea model		
Sariva	*Hemidesmus indicus* R.Br.	Apocynaceae	Root	Methanolic extract (500-1500 mg/kg)		Castor oil-induced diarrhea model	Inhibition of intestinal motility and bactericidal activity	[116,117]
				Aqueous and ethanolic extract (100 and 200 mg/kg)	Loperamide (3 mg/kg)	Charcoal meal test and enteropooling model		
Kutaja	*Holarrhena antidysenterica* (Linn.) Wall.	Asclepiadaceae	Seed	Ethanolic extract (200-800 mg/kg), Isolated alkaloid		Castor oil-induced diarrhea model, antibacterial activity against EPEC *in vitro*		[118]
Cirabilva	*Holoptelea integrifolia* Planch.	Urticaceae	Leaf	Ethanolic extract (250 and 500 mg/kg)	Loperamide (3 mg/kg, p.o.)	Castor oil and magnesium sulfate-induced diarrhea model		[119]
Bandhuka	*Ixora coccinea* Linn.	Rubiaceae	Flower	Aqueous extract (400 mg/kg)	Loperamide (5 mg/kg)	Castor oil-induced diarrhea model		[120,121]
			Leaf	Aqueous extract (400 mg/kg)	Loperamide (5 mg/kg)	Castor oil-induced diarrhea model		
Vyaghra errand	*Jatropha curcas* Linn.	Euphorbiaceae	Root	Methanolic extract (50 and 100 mg/kg)	Chlorpromazine (30 mg/kg, i.p.)	Castor oil or magnesium sulfate-induced diarrhea	Inhibition of prostaglandin biosynthesis and reduction of osmotic pressure, decreases in peristaltic activity, Castor oil-induced permeability changes in intestinal mucosal membrane to water and electrolyte	[122,123]
				Petroleum ether and methanolic extract	Chlorpromazine (30 mg/kg, i.p.)	Castor oil-induced diarrhea model, gastrointestinal motility after charcoal meal	Inhibition of prostaglandin biosynthesis and reduction propulsive movement of small intestine	
Madhuca	*Madhuca indica* J. F. Gmel.	Sapotaceae	Dried bark	Ethanolic extract (250 and 500 mg/kg)	Loperamide (50 mg/kg)	Castor oil-induced diarrhea model		[124]
Amra	*Mangifera indica* Linn.	Anacardiaceae	Stem bark and root bark	Methanolic extract (3, 7.5, and 15 mg/kg)		Castor oil-induced diarrhea model	By increasing colonic water and electrolyte reabsorption or by inhibiting intestinal motility	[108,125-127]
			Seed	Alcoholic and aqueous extract	Loperamide	Castor oil-induced diarrhea model		
			Leaf	Aqueous extract (25 and 50 mg/kg)	Loperamide (2 mg/kg)	Castor oil-induced diarrhea model	Enhancement of Na^+-K^+ ATPase activity	
			Seed	Methanolic and aqueous extract (250 mg/kg)	Loperamide (3 mg/kg, p.o.)	Castor oil- and magnesium sulfate-induced diarrhea model		

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Table 1: *(Contd....)*

Sanskrit name	Botanical name	Family	Part used	Extract/dose	Standard drug and dose	Model	Mechanism	References
Pudina	*Mentha longifolia* (Linn.) Huds.	Lamiaceae	Whole plant	Crude extract, petroleum spirit fraction, aqueous fraction (100-1000 mg/kg)	Loperamide	Castor oil-induced diarrhea model	Inhibition of spontaneous and high K^+induced contractions, spasmolytic activity, mediated possibly through CCB	[128,129]
			Essential oil	Essential oil (20-80 mg/kg)	Loperamide (3 mg/kg, p.o.)	Castor oil-induced diarrhea model		
Lajjalu	*Mimosa pudica* Linn.	Mimosaceae	Leaf	Ethanolic extract (200 and 400 mg/kg)		Castor oil-induced diarrhea model and PGE_2-induced enteropooling, gastrointestinal motility in charcoal meal test		[130,131]
			Root	Ethanolic and aqueous extract (150 and 250 mg/kg)		Gastrointestinal motility in charcoal meal test		
Karvellaka	*Momordica charantia* Linn.	Cucurbitaceae	Leaf	Aqueous extract		Castor oil-induced diarrhea model, gastrointestinal transit, intestinal fluid accumulation and gastric emptying		[132]
Shobhanjana	*Moringa oleifera* Lam.	Moringaceae	Leaf	Hydroalcoholic extract (2500 mg/kg)	Loperamide (3 mg/kg)	Castor oil- and magnesium sulfate-induced gastrointestinal motility, castor oil, and PGE_2-induced Enteropooling, charcoal meal test		[133,134]
				Ethanolic extract (150 and 300 mg/kg)	Loperamide (3 mg/kg, p.o.)	Castor oil-induced diarrhea model		
Surabhi–nimba	*Murraya koenigii* (Linn.) Spreng.	Rutaceae	Leaf	Aqueous extract (200 mg/kg) and alcoholic extract (400 mg/kg)	Loperamide (2 mg/kg)	Castor oil-induced diarrhea model, charcoal meal test, and PGE_2-induced diarrhea		[135,136]
			Seed	Hexane extract, carbazole alkaloids kurryam, koenimbine and koenine	Diphenoxylate (5 mg/kg orally) Atropine (0.1 mg/kg, i.p.)	Castor oil-induced diarrhea model and PGE_2-induced enteropooling, gastrointestinal motility in the charcoal meal test		
Kamini	*Murraya paniculata* (L.) Jack.	Rutaceae	Leaf	Ethanolic extract (300 and 600 mg/kg)	Loperamide (50 mg/kg)	Castor oil-induced diarrhea model		[137]
Kadali	*Musa paradisiaca* Linn.	Musaceae	Sap	0.25, 0.50, and 1.00 mL	Loperamide (2.5 mg/kg) Atropine (2.5 mg/kg)	Castor oil-induced diarrhea model, castor oil-induced enteropooling, and gastrointestinal motility	Inhibition Na^+-K^+ atpase activity	[138]
Jatiphala	*Myristica fragrans* Houtt.	Myristicaceae	Flower bud	Aqueous extract and petroleum ether extract	Atropine	Antispasmodic	Inhibited the contraction produced by acetylcholine, Histamine, and prostaglandin	[139]
Kamala	*Nelumbo nucifera* Gaertn.	Nymphaeaceae	Rhizome	(100, 200, 400, and 600 mg/kg)		Castor oil-induced diarrhea model and PGE_2-induced enteropooling and charcoal meal test		[140-142]

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Table 1: *(Contd....)*

Sanskrit name	Botanical name	Family	Part used	Extract/dose	Standard drug and dose	Model	Mechanism	References
			Root bark Rhizome	Methanolic extract (100, 200, 400, and 600 mg/kg)	Atropine (0.1 mg/kg) Diphenoxylate (5 mg/kg)	Castor oil-induced diarrhea and PGE_2-induced enteropooling		
			Seed oil	Crude hexane extract	-	*In vitro* antibacterial activity against *Staphylococcus aureus, Pseudomonas aeruginosa, Salmonella typhimurium, Escherichia coli*, and *Enterobacter aerogenes*		
Trivrita	*Operculina tuperthum*. (Linn.) Silva Manso.	Convolvulaceae	Root	Aqueous, ethanolic extract (300-1000 mg/kg)	Loperamide (10 mg/kg, p.o.)	Castor oil-induced diarrhea model	Possibly through the presence of Ca^{++} antagonist	[143]
Syonaka	*Oroxylum indicum* Vent.	Bignoniaceae	Stem bark	Methanolic extract (400 mg/kg)	Loperamide (66.67 μg/kg, p.o.)	Castor oil-induced diarrhea model		[144,145]
			Bark	Flavonoids rich fraction		Castor oil and magnesium sulfate-induced diarrheal models, barium chloride, and acetylcholine-induced intestinal contraction	Alteration of intestinal motility through modification in L^- type Ca^{2+} channels	
Cangeri	*Oxalis corniculata* Linn.	Gerniaceae	Whole plant	Aqueous and Methanolic extract (160, 320, and 640 mg/kg)	Loperamide (29.6 μg/kg, p.o.)	Castor oil-induced diarrhea model		[146]
Gandhaprasharni	*Paederia foetida* Linn.	Rubiaceae	Root	Ethanolic extract (100, 250, and 500 mg/kg)	Atropine (5 mg/kg)	Castor oil-induced diarrhea model, magnesium sulfate-induced diarrhea, gastrointestinal motility with barium sulfate milk, cisplatin-induced gastrointestinal motility, morphine-induced reduction of motility		[147]
Pind kharjura	*Phoenix dactylifera* Linn.	Palmaceae	Fruit	Aqueous extract (1000 and 1500 mg/kg)	Loperamide (5 mg/kg)	Castor oil-induced diarrhea model, enteropooling model, and gastrointestinal motility test		[148]
Maricha	*Piper nigrum* L.	Piperaceae	Fruit	Piperine			-	[149-153]
			Fruit	Aqueous extract (75, 150, and 300 mg/kg)	Loperamide (2 mg/kg, p.o.) Atropine (5 mg/kg, i.p.) Chlorpromazine (30 mg/kg, i.p.)	Castor oil and magnesium sulfate-induced diarrhea charcoal meal test and castor oil-induced intestinal secretions		
			Fruit	Aqueous extract (300 mg/kg)	Isosorbide dinitrate (150 mg/kg, p.o.) Glibenclmide (1 mg/kg, p.o.) Yohimbine (1 mg/kg, s.c.)	Castor oil-induced diarrhea model	On α_2 adrenergic receptors, potassium channels, and nitric oxide pathway	

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Table 1: *(Contd....)*

Sanskrit name	Botanical name	Family	Part used	Extract/dose	Standard drug and dose	Model	Mechanism	References
				Piperine (8 and 32 mg/kg)		Castor oil, $MgSO_4$ and arachidonic acid-induced diarrhea, castor oil induced enteropooling	Inhibitory effect on prostaglandins	
				Piperine (10 mg/kg)		Castor oil-induced diarrhea model	Concentration-dependent inhibition of spontaneous contractions, CCB effect. Piperine (10-100 μm) caused a rightward shift in the Ca^{++} concentration–response curves in Ca^{++}–free medium	
Karkatasringi	*Pistacia integerrima* (J. L. Stewart ex Brandis)	Anacardiaceae	Gall	Methanolic extract (700 and 900 mg kg)	Loperamide (10 mg/kg)	Castor oil-induced diarrhea model, spontaneous contractions in isolated rabbit jejunum		[154]
Karanja	*Pongamia pinnata* (Linn.) Pierre.	Fabaceae	Leaf	Aqueous extract	-	Antibacterial, antigiardial and antirotaviral activity	Inhibits adherence of EPEC and invasion of EIEC and *Shigella flexneri* to epithelial cells	[155]
Peruka	*Psidium guajava* Linn.	Myrtaceae	Leaf	Aqueous extract	Loperamide (10 mg/kg, p.o.)			[156-158]
			Leaf	Aqueous extract (50-400 mg/kg)		Castor oil-induced diarrhea model		
			Bark	Methanolic and aqueous extract (100 mg/kg)	Loperamide (1 mg/kg, i.p.)	Gastrointestinal Motility, castor oil-induced diarrhea model, and PGE_2-induced enteropooling		
Bijaka	*Pterocarpus marsupium*	Fabaceae	Heartwood	Ethanolic extract (250 and 500 mg/kg,)	Loperamide (5 mg/kg, p.o.)	Castor oil and charcoal-induced gastrointestinal motility test, intestinal transit of charcoal meal		[159]
Dadima	*Punica granatum* Linn.	Punicaceae	Seed	Methanolic extract		Castrol oil-induced diarrhea and PGE_2-induced enteropooling	Antimotility and antisecretory activity	[160-162]
			Peels	Aqueous extract (100, 200, 300, and 400 mg/kg)		Castor oil-induced diarrhea model, spontaneous movement of the isolated rat ileum, acetylcholine-induced contractions test		
			Rinds of fruit	Polyherbal formulation Aqueous extract	Mebarid (10 ml/kg, po)	Castor oil-induced diarrhea model, intestinal secretion, and charcoal meal test		
Mayaphala	*Quercus infectoria*	Fagaceae	Gall	Ethanolic extract (250 and 500 mg/kg)	Loperamide (3 mg/kg, p.o.)	Castor oil and magnesium sulfate-induced diarrhea models		[163]
Sarpagandha	Rauvolfia serpentina Benth. ex Kurz.	Apocynaceae	Root	Methanolic extract (100, 200, and 400 mg/kg)	Diphenoxylate (5 mg/kg, p.o.)	Castor oil-induced diarrhea model		[164]
Manjistha	*Rubia cordifolia* L.	Rubiaceae	Root	Ethanolic extract (50, 100 mg/kg)		Castor oil-induced diarrhea model, gastrointestinal transit time	Decrease in both sodium and potassium excretion in the intestine	[165]

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Table 1: *(Contd....)*

Sanskrit name	Botanical name	Family	Part used	Extract/dose	Standard drug and dose	Model	Mechanism	References
Chandan	*Santalum album* Linn.	Santalaceae	Heartwood	Methanolic extract (200, 400, and 800 mg/kg)		Castor oil-induced diarrhea model	Spasmolytic role relaxed the acetylcholine-induced, 5-HT-induced and K^+-induced contractions	[166]
Asoka	*Saraca asoca* (Roxb.) De Wilde	Caesalpiniaceae	Stem bark	Hydroalcoholic, acetone extract (200 mg/kg)	Loperamide (3 mg/kg, p.o.)	Castor oil-induced diarrhea model		[167]
Kushtha	*Saussurea lappa* Clarke	Asteraceae	Essential oil	100, 300, and 500 mg/kg	Loperamide (5 mg/kg)			[168]
Raj Bala	*Sida rhombifolia*	Malvaceae	Root	Methanolic extract (200 and 400 mg/kg)	Diphenoxylate (5 mg/kg)	Castor oil-induced diarrhea model, intestinal transit, and castor oil-induced intestinal fluid accumulation (enteropooling)		[169]
Kupilu	*Strychnos nux–vomica* Linn. f.	Loganiaceae	Root bark	Aqueous and Methanolic extract (3, 7.5, and 15 mg)		Castor oil-induced diarrhea model		[42]
Kataka	*Strychnos potatorum* Linn.	Loganiaceae	Seed	Methanolic extract	Diphenoxylate (5 mg/kg)	Castor oil-induced diarrhea model, effects on gastrointestinal motility and PGE_2-induced gastric enteropooling		[170]
Lodhra	*Symplocos racemosa* Roxb.	Symplocaceae	Bark	Ethylacetate chloroform, n–butanol and aqueous fraction (300, 500 mg/kg)		Spontaneous movement of the isolated rabbit intestine		[171]
Jambu	*Syzygium cuminii* Linn. Skeels	Myrtaceae	Seed	Aqueous extract (125, 250, and 500 mg/kg)	Loperamide (2 mg/kg, p.o.)	Castor oil-induced diarrhea model, charcoal meal test, castor oil-induced intestinal secretions		[172]
Sharpunkha	*Tephrosia purpurea* (Linn.) Pers.	Fabaceae	Whole plant	Methanolic extract (300 mg/kg)	Verapamil (50 mg/kg)	Castor oil-induced diarrhea model		[173]
Arjuna	*Terminalia arjuna* (Roxb.) W. & A.	Combretaceae	Bark	Methanolic extract (100, 200, and 400 mg/kg)	Loperamide (3 mg/kg)	Castor oil and gastro intestinal motility test		[174]
Bibhitaki	*Terminalia bellirica* Roxb.	Combretaceae	Fruit	Aqueous and ethanolic extract (143, 200, and 334 mg/kg)	Loperamide (3 mg/kg)	Castor oil-induced diarrhea model, PGE_2-induced enteropooling and gastrointestinal motility test		[175]
Parisha	*Thespesia populnea Soland*. Ex. Correa	Malvaceae	Stem bark	Methanolic fraction (100 mg/kg) and residue fraction (10, 25, and 50 mg/kg) of aqueous extract	Loperamide (3 mg/kg) Atropine (3 mg/kg)	Castor oil-induced diarrhea model, PGE_2-induced diarrhea, charcoal meal test	Inhibition of elevated prostaglandin biosynthesis, reduced propulsive movement of the intestine	[176,177]
				Aqueous extract (100, 200, and 400 mg/kg) and alcoholic extract (50, 100, and 200 mg/kg)		Castor oil-induced diarrhea model; PGE_2-induced enteropooling, charcoal meal test		

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Table 1: *(Contd....)*

Sanskrit name	Botanical name	Family	Part used	Extract/dose	Standard drug and dose	Model	Mechanism	References
Guduchi	*Tinospora cordifolia* (Willd.) Miers ex Hook.f. & Thoms.	Menispermaceae	Stem	Ethanolic and aqueous extract	Loperamide (3 mg/kg, p.o.)	Castor oil and magnesium sulfate-induced diarrhea		[178]
Adhapushpi	*Trichodesma indicum* R.Br.	Boraginaceae	Root	Ethanolic extract		Castor oil-induced diarrhea model charcoal meal transit time, castor oil-induced enteropooling		[179]
Methika	*Trigonella foenum-graecum* Linn.	Fabaceae	Whole plant	Aqueous extract (100, 200 mg/kg)	Loperamide (1 mg/kg, i.p.)	Castor oil-induced diarrheal model		[180]
Pind tagar	*Valeriana hardwickii* Wall.	Valerianaceae	Rhizome	Aqueous-Methanolic extract	Loperamide (10 mg/kg)	Castor oil-induced diarrhea model	Inhibited K^+-induced contractions (0.01-0.3 mg/ml), CCB	[181]
Sampushpa	*Vinca major* L.	Apocynaceae	Aerial part	Ethanolic extract (250, 500, and 1000 mg/kg)	Loperamide (3 mg/kg, p.o.) Atropine (5 mg/kg, i.p.)	Castor oil-induced diarrhea model, castor oil and magnesium sulfate-induced enteropooling, gastrointestinal motility test using charcoal meal methods		[182]
Kutaja	*Wrightia tinctoria* Roxb. R.Br.	Apocynaceae	Bark	Ethanolic extract (500 and 1000- 189 mg/kg) and isolated steroidal alkaloid fraction (50 and 100 mg/kg)	Loperamide (0.5 mg/kg), atropine (0.1 mg/kg, i.p)	Castor oil-induced diarrhea model, charcoal meal, PGE_2-induced enteropooling		[183]
Adaraka	*Zingiber officinale* Rosc.	Zingiberaceae	Rhizome	Zingerone	Loperamide (5 mg/kg, i.p.)	Intraluminal pressure changes and expelled fluid volume from the colon	Inhibited spontaneous contractile movements in the isolated colonic segments, Inhibit colonic motility via direct action on smooth muscles	[184]
Badara	*Ziziphus jujuba* Mill.	Rhamnaceae	Leaf	Aqueous extract		Castor oil and magnesium sulfate-induced diarrhea models		[185]
Badara	*Ziziphus mauritiana*	Rhamnaceae	Root	Methanolic extract (25 and 50 mg/kg)	Diphenoxylate (2.5, 5 mg/kg) orally	Castor oil-induced diarrhea model and castor oil-induced fluid accumulation, spontaneous movement of the isolated rabbit jejunum, gastrointestinal transit time	An inhibition of the spontaneous pendular movement of the isolated rabbit jejunum and inhibited acetylcholine-induced contraction of rat ileum	[186]

PGE_2: Prostaglandin E2, CCB: Calcium channel blockade, EPEC: Enteropathogenic *Escherichia coli*, EIEC: Enteroinvasive *Escherichia coli*

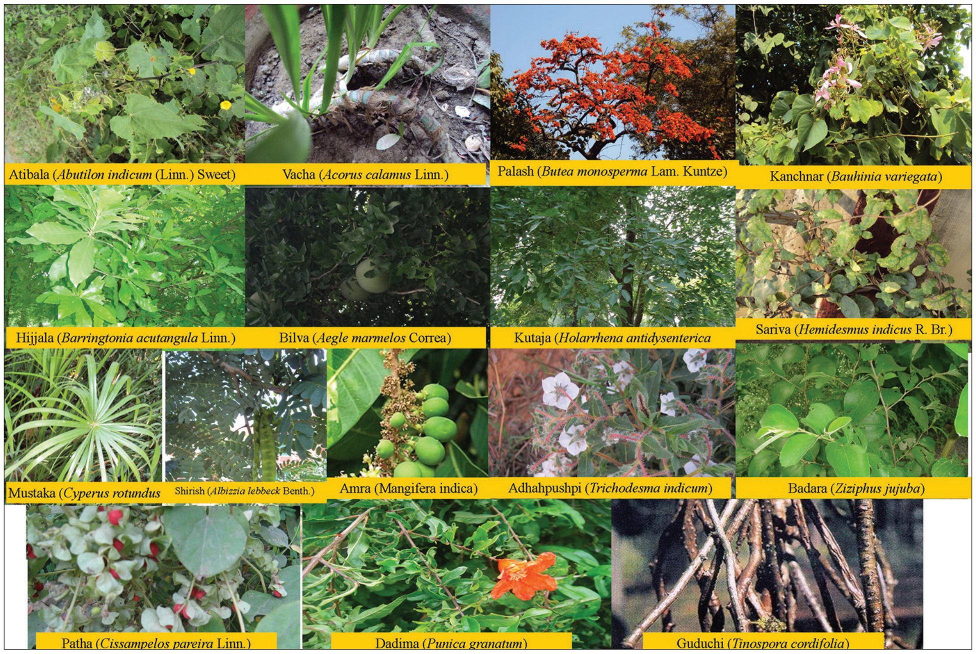

Figure 1: Antidiarrheal medicinal plants

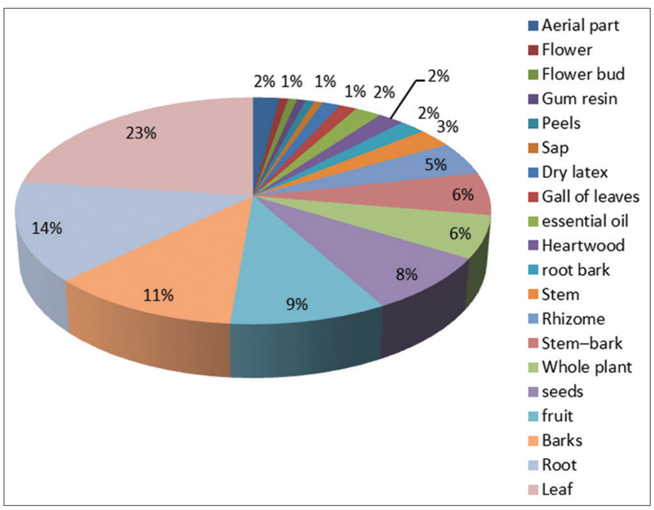

Figure 2: Distribution of plant parts investigated for antidiarrheal activity

Many phytoconstituents such as lupinifolin isolated from *Eriosema chinense*, -omoneukanrin B, dimethoxyflavone isolated from the stem bark of *Stereospermum kunthianum*, 6-(4-hydroxy-3-methoxyphenyl)-hexanonic acid, isovanillin, iso-acetovanillon from *Pycnocycla spinosa* Decne. Ex Boiss., have been evaluated for anti-diarrheal activity. However, in the mentioned list of ayurvedic plants limited isolation of the active constituents have been done which accounts for the numerous scope in this area for analytical, pharmacognostical as well as pharmacological screening of the active principles from these plants. Some of the constituents such as kurryam, koenimbine, koenine, piperine, and berberine are mentioned in the list with reported antidiarrheal activity [189-192].

Newer technologies such as in-silico, docking studies, interaction with enterotoxin from causative oraganism and nanotechnology were also employed in the antidiarrheal agent research works [193,194]. However, unfortunately, such advanced techniques were not used for the above listed ayurvedic plants. However, a few clinical trials reveal that the plants acts via a number of mechanisms, i.e., anti-inflammatory, antisecretory antimicrobial effect against *V. cholerae* and enterotoxigenic *E. coli*, rotavirus, detoxification of toxins and constipate, adsorbent, providing a rich source of calories; antimotility and antispasmodics effects [195].

CONCLUSION

The ethnomedicinal approach for diarrhea is a practical, cost-effective, and a logical for its treatment. Present data show that only a few isolated compounds from plants were investigated for antidiarrheal potential. Therefore, a significant research of chemical and biological properties of such less explored plants is still needed to determine their antidiarrheal efficacy which will possibly define their exact mechanism of actions.

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