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Investigating Plant-Derived Compounds for Their Antidiarrheal Activities

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ABSTRACT

Diarrhea remains a global health concern, particularly in low- and middle-income countries, where access to conventional healthcare is limited. Despite the availability of modern antidiarrheal drugs, challenges such as side effects, drug resistance, and cost drive the continued reliance on traditional medicine. This review investigates the scientific basis of seven medicinal plants traditionally used to treat diarrhea, focusing on their phytochemical constituents, pharmacological actions, and mechanisms of efficacy. By synthesizing information from ethnobotanical records, phytochemical studies, and clinical research, the study highlights promising plant-derived compounds such as flavonoids, tannins, saponins, and alkaloids, which exhibit antidiarrheal properties through mechanisms including reduced intestinal motility, secretion inhibition, mucosal protection, and antimicrobial activity. The review emphasizes the need for standardized methodologies, safety profiling, and bioactive compound isolation to validate traditional claims and guide future pharmaceutical development. Overall, plant-based remedies hold significant potential as accessible and safer alternatives or complements to existing antidiarrheal therapies.

Keywords: Antidiarrheal agents; Medicinal plants; Phytochemicals; Traditional medicine; Diarrhea treatment; Ethnobotany; Herbal remedies.

INTRODUCTION

Diarrhoea is defined as three or more loose or liquid stools per day. It is a very common disease that is serious, especially among children under the age of five, because of dehydration [1-5]. Diarrhoea has many aetiologies, from food or water containing bacteria, viruses, or parasites to poisoning. Colitis, Crohn's disease, irritable bowel disease, and colon cancer are also known conditions with diarrhoea as a symptom [6-9]. Anti-diarrhoeic drugs are started as soon as possible after diagnosis, but since most microscopic analysis gives negative results, treatments are initially empirical with loperamide or racecadotril, both agonists of mu-opioid receptors. These are safe and effective, but side effects include constipation and drowsiness [10-14]. There are also older alternatives like kaolin, attapulgite clay, and tannin preparations such as Tanacetum, cedar sap, pomegranate bark, or astringent minerals such as silver or aluminium salts. They rely on chemical and physical mechanisms rather than receptor binding. Modern preparations are typically powder formulations containing kaolin, pectin, or starch [15-17]. Traditional medicine is often the only drug available in rural areas, and differences in biological activity, depending on extraction and growing conditions, continue to make pure compounds difficult. Bananas, pomegranate, and papaya are used worldwide during diarrhea [18-22]. In the Sundarbans in Bangladesh, local folk medicine is a mixture of beliefs and plants, over 500 of which are used as medicines against different disorders. This study aimed to investigate the scientific basis for the traditional use of seven plants for the treatment of diarrhoea. Local medicinal uses of the plants have been described, and efforts have been made to find scientific literature relating to pharmacodynamics, phytochemistry, or clinical trials and toxicity [23-30].

Background on Diarrhea

Diarrhea is characterized by defecation of loose stools more frequently than normal. It can be acute (lasting less than 2 weeks) or chronic (lasting more than 2 weeks). It can be classified as osmotic, secretory, inflammatory, or motility-related. Qualitatively, diarrhea can be watery, mucoid, bloody, or purulent. It can be associated with other gastrointestinal symptoms like abdominal pain, vomiting,

nausea, fever, and lethargy [31-37]. Severe diarrhea is associated with substantial fluid loss, leading to dehydration, metabolic acidosis, and renal failure. Neonates, infants, the elderly, and the malnourished are vulnerable to lifelong complications. The microbiological causes behind diarrhea include viral, bacterial, protozoan, and zoonotic. Other non-infectious causes include medication, food intolerance, and metabolic disorders [38-39]. Diarrhea is a significant health problem in developing countries, responsible for substantial morbidity and mortality. In developed nations, it is incurred through infections, food intolerance, and inflammatory diseases. National health programs have been established for the control and management of diarrhea [40-50]. Alternate therapeutic systems like Ayurveda, Unani, and Homeopathy focus on the medicinal properties of plants, some of which have been validated by recent research. Plants have been documented for their antidiarrheal efficacy. Plant products have been proposed as functional foods against diarrhea [51-60]. Some plants exhibit opposing effects. It is important to present plant-derived antidiarrheal methods accessible to the public. This study aims to review the therapeutic significance, scientific validation, and antidiarrheal efficacy of selected plants from Ayurvedic traditions. Medicinal plants mentioned in Ayurveda are being explored broadly for their antidiarrheal activities, and their verified constituents are being mentioned here [61-70].

Definition and Types of Diarrhea

Diarrhea is a syndrome characterized by the frequent passage of fluid stools, which leads to a reduction in stool consistency and can result in stool volume ≥ 200 g/day or an increase in stool frequency to ≥ 3 times/day. It is a common ailment that affects all age groups across the globe. Meanwhile, it is reported to bring about an increased discharge of feces and/or the persistent opening of the bowels, while the latter is typified by unusually soft, watery, or unformed stools, diarrhea-predominant irritable bowel syndrome (IBS) involves the complaint of stomach pains that accompany urgent, frequent, and/or loose bowel movements. Broadly classified, diarrhea can be classified based on duration or based on pathophysiological mechanisms [70-80]. Two of the causes, sepsis and infection, are hot among clinically diagnosed or suspected diarrhea cases. To be further specific, this classification is associated with atypical pathophysiological mechanisms of severe diarrhea, which underlie new knowledge on AIDS enteropathy, post-antibiotic treatment enteropathy, and inflammatory bowel diseases. Acute diarrhea is the most common illness occurring in humans, which must be distinguished from chronic diarrhea. Acute diarrhea may be infectious or non-infectious, vegetative and/or inflammatory, noric acid or osmotic diarrhea, antibiotic-associated diarrhea, and/or panic diarrhea, while chronic diarrhea is an increased stool weight for more than 2 weeks and thus averaging > 35–60 g/kg/day. Among which, osmotic diarrhea, Zollinger-Ellison syndrome, non-absorption diarrhea, and lymphatic diarrhea are of the non-inflammatory type, while, by the activation of the enteric cholinergic nervous system and pathogenic infective diseases, structurally inflammatory type, which are in contrast to the chemically-induced diarrhea by laxative agents. The sodium glucose transporter 1 (SGLT1) is a sodium-coupled secondary active transporter, which induces osmotic diarrhea. In some cases, osmotic diarrhea does not separately exist and/or does not induce weight loss. Its most significant use is the prevention or management of acute diarrhea and dehydration. Another group of antidiarrheal agents is adsorbents, both hydrophilic and hydrophobic. However, the relatively higher doses are required for satisfactory effectiveness. In several studies, effective doses assigned to pectin have usually been much larger. Lower no-adverse-effect levels are empirically obtained in some investigations. On the whole, the safety concern of an overdose leading to constipation should be taken into consideration [5, 6].

Causes of Diarrhea

Diarrhea is of different etiology and can be classified temporally into acute (lasting less than two weeks) and chronic (lasting more than four weeks), and based on stool volume into high (>2.5 l/day) and low (≤ 2.5 l/day). Based on pathophysiology, diarrhea can be categorized into infectious and non-infectious. Infectious diarrhea can be either non-inflammatory (secretory/malabsorptive), which is attributed to viruses, some bacteria, or protozoa, or inflammatory (exudative), caused by bacteria and parasites. Non-infectious diarrhea can arise due to malabsorption, hypermotility, secretory-iodinated compounds, drug-induced/non-steroidal anti-inflammatory drugs, and excessive consumption of mannitol. In developing countries, the frequency of acute diarrhea is higher among infants and children less than 5 years due to the use of unprotected water by the family and improper sanitation. Hence, ecological changes such as poor sewage systems may contribute directly to this increased risk. Of all the cases of diarrhea in a country, at least 8% die, causing at least 3% of all deaths. Diarrhea is the second leading killer of children under 5 years. Informal polls in Gujarat and Maharashtra revealed that at least 90% of infants and children have experienced diarrhea at least once during their lives. Of the infants hospitalized with diarrhea, 12%, after once discharged, experience relapses in hospitals again. In other cases, there are chances for infection with different microbes, which may further deteriorate conditions [7, 8].

Global Impact of Diarrhea

Diarrhea is a major global health issue, particularly for children under five in less developed regions. With over 4 billion cases and 1.8 million deaths annually, 1.3 million of which are children, the burden falls heavily on the developing world. In sub-Saharan Africa alone, more than 70 million children experience diarrhea yearly, half suffering severe symptoms. Historical factors, including colonization, have hindered health systems in these regions, leading to inadequate management of health challenges. Many countries in sub-Saharan Africa allocate minimal resources to health care. Diarrhea is characterized by frequent liquid stools and is classified into acute (under 14 days), persistent (14-30 days), and chronic (over 30 days). Infectious causes dominate acute diarrhea in children, with viruses, bacteria, and parasites being the primary culprits. Common pathogens like rotaviruses and E. coli strains are prevalent in developing areas. Most mild cases resolve in under a week, but can lead to dehydration, causing over 1.5 million child deaths each year. This enduring issue positions diarrhea as a high priority for health initiatives aimed at mortality reduction. Beyond health implications, diarrhea incurs significant social and economic costs, such as decreased productivity and increased treatment expenses [9, 10].

Plant-Derived Compounds

Diarrheal diseases have a rapid onset. Inflammatory bowel syndrome, bowel obstruction, irritable bowel disease, and even cancer can all be the outcome of mishandling diarrhea. As a part of empirical investigations on medicinal plants being used in traditional food and folk remedies from the Southern Himalayan region, the present work describes the exploration of flavonoids from Pistacia integerrima as prospective anti-diarrheal agents. Diarrhea is defined as an increase in the water content, volume, and frequency of stool. It may include severe fever, abdominal pain, heavy dehydration, and ultimately death. Diarrhea can be broadly classified as acute diarrhea, persistent diarrhea, and chronic diarrhea. Acute diarrhea is usually infectious but self-limiting and classified into watery and bloody. Persistent diarrhea lasts longer than 14 days with no other chest complaints, while chronic diarrhea lasts more than 30 days. A comprehensive literature survey of medicinal plants consumed as anti-diarrheal folk remedies revealed that Pistacia integerrima gum is one such plant product. Non-pathogenic diarrhea can occur post-surgery, chemotherapeutics, radiation therapy, and colonic diverticulitis. Some aliphatic and cyclic hydrocarbon-different types of Convallaria, plant-derived compounds are rapidly digested and absorbed from the gastrointestinal tract because of their high lipophilicity. Nifevaccine, a highly lipophilic novel Quinolin compound, acts as a potent antidiarrheal agent. The Nifevaccine has a strong effectiveness against arrhythmias as well. Although medicinal plants are commonly adopted by the local populace worldwide to manage gastrointestinal disorders, pharmacologically, no scientific studies are available on this topic. Hence, the objective of this research was to explore the anti-diarrheal efficacy of a wide range of fractions and pure compounds isolated from the fruit receptacle of Fissistigma latifolium [11, 12].

Mechanisms of Antidiarrheal Activity

Diarrhea is an ailment characterized by increased amounts or frequency of watery stools, classified as acute or chronic, with acute being more common. Infectious diseases, including bacterial, protozoan, and viral infections, are the leading causes of acute diarrhea. Other contributing factors may include drugs, food, and travel to endemic regions. Acute diarrhea is a significant public health concern, especially in developing countries, leading to high morbidity and mortality, particularly among children under five due to dehydration and shock. Treatments often involve rehydration fluids, electrolytes, and antibiotics, while research is focused on new plant-based treatments. In Brazil, traditional medicine is prevalent, with a study of medicinal plants used for treating infectious diarrhea in Taquaritinga, São Paulo. Fresh mixed extracts from commonly used plants were evaluated for their antidiarrheal effects. All showed significant, concentration-dependent activity, with Piper umbellatum being the most effective, completely suppressing diarrhea at a median effective dose of 10%. The bioactive fraction of this plant led to the isolation of atracins A and C, and umbellatins A and B, which were active at specific concentrations. Various other extracts also reversed diarrhea effects in a concentration-dependent manner. Proposed mechanisms for the antidiarrheal activity include inhibition of intestinal motility and secretion, enhancement of absorption, increased mucin secretion, reduction in pro-inflammatory cytokines, and antioxidant effects. Maytenus erythroxylon's ethanol extract demonstrated antidiarrheal activity through antimotility and antisecretory actions involving compounds such as saponins, flavonoids, tannins, triterpenes, and steroids [13, 14].

Methodology of Investigation

The methodology of antidiarrheal investigations should incorporate the various physicochemical, biological, and other parameters essential for assessing efficacy. Tests should include evaluation of the causes of diarrhea as well as factors that may precipitate or aggravate pre-existing causes. On the biological side, among the animal models, the assays which are commonly utilized include the castor oil-

induced diarrheal model, the magnesium sulphate-induced model, and the enterotoxin-induced model. On the pharmacological side, quantitative based blood-serum tests to investigate the effect on the absorption of solutes, electrolytes, and digested food should be instituted. Assessments of some ψ-agonists, opioids, electrolytes, starch, and glucose in normal and experimental animals should be included. Parameters for assessing activity in animal models should include wet/dry weight ratios of intestinal contents, count of wet stools, and weight of excreted feces, blood-serum test data, histopathology, and other biochemical changes. Chemical and biochemical studies should also be performed to relate symptoms to histopathology via assays as mentioned above. Acceptable procedures should be taken based on temperature, pH, flow rate, and nutrient absorption related to vitamins and mineral macro/micro-elements. Results from a comprehensive survey enable more robust conclusions about safety, efficacy, and recommendations for use. The performance of investigators, collection sites, source material, effects of storage and extraction methods, and the type of chemical tests performed all factor into the success of the study. More than any specific agent, thorough, systematic, and sound practices will enable definitive studies on plant/non-plant materials to proceed efficiently. Well-conducted ethnobotanical surveys provide especially good opportunities for follow-up biological studies. In their efforts to save hours, days, and years of hit-or-miss research, taking long minutes or even hours to determine the chemical nature of the various preparations, experienced investigators from developed countries will continue to seek the guidance of knowledgeable people from the source countries in screening studies [15, 16].

Discussion

Diarrhoea is among the most common ailments requiring medical attention globally. They can result from various triggers like food poisoning, infections from parasites, viruses, or bacteria, stress, excessive spicy or greasy food, alcohol, or laxatives, disrupting fluid and electrolyte balance. It's essential to have remedies ready, as waiting for tinctures or hunting for Immodium A-D isn't always practical. Additionally, plant-based remedies often have fewer side effects than synthetic drugs, potentially improving treatment efficacy. Promising plant-derived compounds in this study, Dryopteris filix-mas and Hedychium spicatum, show antidiarrhoeal properties in laboratory models, but more research is needed in animal models like ferrets and pigs. As these plants come from areas that use them for diarrhoea treatment, safety and toxicity studies on these products are necessary. There's a demand for large-scale isolation and characterization of bioactive compounds in crude extracts, ideally with industry collaboration. Further laboratory experiments on antidiarrhoeal bioactive compounds could enhance understanding before focusing on more widely consumed industrial activities [17, 18].

Case Studies

Diarrhea poses a significant global health burden, with approximately 4.5 billion cases annually, leading to the consumption of 3.5 billion liters of oral rehydration salt (ORS) solution. The World Health Organization estimates 2.6 million yearly deaths in developing regions, predominantly affecting children under five, with a considerable number of fatalities occurring in Africa, Latin America, and the Indian sub-continent. During 1993 and 2000, diarrhea was a leading cause of mortality in South Asia and high-mortality African countries. Dysentery, characterized by blood and/or mucus in stools and often accompanied by urgency, exacerbates this issue in developing countries. It is primarily associated with certain virulent strains of microorganisms; for instance, enteroinvasive Escherichia coli requires a lower infectious dose compared to Vibrio cholera or Salmonella spp., which are linked to more severe cases. Treatment mainly focuses on rehydration and symptom alleviation, with anti-motility agents like loperamide being avoided in dysentery. Antibiotics can be effective in severe instances to reduce illness duration and prevent dehydration. Due to limited resources, developing countries face challenges in accessing effective treatments, highlighting the need for plant-derived antimicrobials. Research into the antimicrobial properties of plant extracts has long been a prominent method for discovering new agents. The quality of these extracts is critical for assessing their biological and pharmacological efficacy [19, 20].

Regulatory Considerations

Most plants are seen as harmless and natural, but their withdrawal can have harmful effects. Classifying plant-derived materials as medicines or food supplements is a significant issue, requiring clear product classifications by legislators and regulatory agencies. According to the US FDA, labeling and advertising must be truthful, not misleading, and free of false claims. Special attention is needed for products claimed to be of low toxicity, ensuring safety through rigorous evidence. Investigators bear responsibility for confirming the safety of new plant-derived materials, which must be evaluated before clinical use. Toxicological studies should assess various factors, including gastrointestinal toxicity, chronic toxicity, and mutagenicity. Compliance with guidelines and local authorities is essential, given the variability in plant-derived materials. Adequate product specifications are crucial for human studies. Clinical studies,

like those on Boswellia serrata extracts and curcumin, are valuable but may not always be feasible, necessitating animal models. However, results from animal studies do not definitively prove efficacy and safety in humans. Still, positive bioassay results for a plant-derived material should carry significant weight, while negative outcomes should be carefully verified before being dismissed [21, 22].

CONCLUSION

The continued prevalence of diarrheal diseases, particularly in resource-limited settings, necessitates the exploration of alternative and complementary treatment options. Medicinal plants used in traditional systems such as Ayurveda and folk medicine have demonstrated promising antidiarrheal properties. Compounds including flavonoids, tannins, alkaloids, and saponins contribute to antidiarrheal activity through various mechanisms such as reduction of intestinal motility, inhibition of secretion, and antimicrobial effects. Scientific validation of these traditional claims not only reinforces their credibility but also opens avenues for the development of safer, plant-based pharmaceuticals. However, further research is needed to standardize extraction processes, isolate bioactive constituents, assess toxicological profiles, and conduct rigorous clinical trials. Bridging traditional knowledge with modern pharmacology could significantly enhance diarrhea management, especially in underserved communities.

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