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The Interplay Between Gut Microbiota, Medicinal Plants, and Diarrheal Diseases

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ABSTRACT

Diarrheal diseases remain a leading cause of morbidity and mortality, particularly among children in developing countries, largely due to poor sanitation, malnutrition, and limited access to clean water. A growing body of evidence highlights the crucial role of gut microbiota in maintaining gastrointestinal health and the onset of diarrheal conditions. At the same time, medicinal plants—long utilized in traditional medicine—offer promising antidiarrheal and antimicrobial properties. This review examines the tripartite relationship between gut microbiota, diarrheal pathogens, and medicinal plants. It discusses how gut dysbiosis exacerbates vulnerability to enteric infections, and how specific phytochemicals in medicinal plants may restore microbial balance, enhance host immunity, and inhibit pathogenic organisms. Emerging research using high-throughput sequencing and metabolomics sheds light on how plant-derived compounds interact with microbial communities to exert therapeutic effects. Understanding these interactions provides a foundation for developing integrative, natural treatments targeting gut health and reducing the global burden of diarrheal diseases.

Keywords: Gut microbiota; Diarrhea; Medicinal plants; Dysbiosis; Phytochemicals; Antimicrobial activity.

INTRODUCTION

Diarrhea is a significant global health issue, particularly affecting children under five, where it ranks second in mortality, following pneumonia, mainly due to a lack of safe drinking water and sanitation. Contaminated food and feces contribute to its spread, caused by excessive fluid secretion or insufficient absorption in the intestines. It is characterized by frequent loose, watery stools alongside symptoms like abdominal pain, bloating, fever, and vomiting. Various microorganisms, including Escherichia coli, Salmonella, Shigella dysenteriae, Vibrio cholerae, Campylobacter jejuni, and protozoa such as Giardia lamblia and Entamoeba histolytica, are known to cause diarrhea and dysentery. Opportunistic pathogens can emerge from normally sterile environments within the human body, like the intestine and vagina, becoming pathogenic under certain conditions. Commensal Escherichia coli may mimic the diseases caused by their pathogenic counterparts. Research has identified specific clones of extra-intestinal and intestinal pathogenic E. coli, linked to disease production in mouse models, revealing genetic connections that enable these microbes to adapt to new environments. In recent years, concerns over synthetic drug toxicity have led to increased interest in medicinal plants with antibacterial and antidiarrheal properties [1, 2].

Overview of Gut Microbiota

The human gastrointestinal tract is densely populated with microbial communities. Although technical variations exist, the gut microbiota is most commonly examined using fecal samples. A recent paradigm shift in microbiome research was prompted by an increased appreciation of the role of microbes in host physiology and pathology, particularly after the advent of high-throughput sequencing technologies. It is now recognized that the gut microbiota performs vital ecological functions, covering energy harvest, biosynthesis of vitamins and amino acids, and epithelial barrier expansion, thus providing evidence that microbial dysbiosis causes diseases, including neurodegenerative diseases and pain syndromes. In keeping with the increasing recognition of the enormous ecological composition and dynamics of the gut microbiota, knowledge of research techniques to elucidate their dynamic interplay with diverse environmental factors is advancing rapidly using high-throughput sequencing, transcriptomics, proteomics, and metabolomics. However, the basic understanding of the interplay between the gut microbiota and the host immune systems is limited. Although gut dysbiosis is associated with aberrant immune systems, evident causative evidence in zebrafish and human studies remains elusive. Many questions remain about how microbes produce immunomodulatory metabolites, detect host-microbe-environmental changes, and direct gut homeostasis in a microbiota-ecosystem context. Considering the enormous technological advancements in metabolomics, single-bacterial-cell analysis, and advanced imaging and modeling techniques, it is increasingly likely that the microbiota-host homeostasis will be elucidated on a multi-system and organism scale. To better understand the pathophysiology of critically ill patients, there is an urgent need to characterize the composition and function of the gut microbiota, using high-throughput sequencing and multi-omics approaches. Knowledge of therapeutic intervention strategies from environmental exposures, including medicinal plant-derived phytochemicals, is also critical. Despite the limitations of current strategies designed to better restore the gut microbiota, it is anticipated that a better understanding of the interplay between the gut microbiota, medicinal plants, and diarrheal diseases will lead to the development of innovative and effective therapeutic strategies against gut dysbiosis-associated diarrheal diseases [3, 4].

Definition and Composition

The gut microbiota consists of a complex ecosystem comprising bacteria, viruses, archaea, eukaryotes, and other microorganisms. Recent sequencing-based culture-free metagenomic studies have shown thousands of species of archaea and viruses, millions of eukaryotes, and hundreds of thousands of fungi in the human gut microbiome. Given the close symbiotic relationship existing between the gut microbiota and the host, it is not surprising to observe a divergence from the normal microbiota composition (generally referred to as dysbiosis) in a plethora of disease states ranging from chronic GI diseases to neurodevelopmental disorders. The gastrointestinal (GI) system has a complex and important role in the body. The gut microbiota is defined as the microorganisms that inhabit the gastrointestinal tracts. In the newborn, the gut is sterile. By the end of the first year of life, its microbiota composition is already similar to that of an adult. Incorporation of gut microbiota begins at birth and undergoes further colonization with the introduction of solid foods. Colonization also occurs via vertical transmission from the mother and horizontal transmission from contacts after birth. Once colonization is established, microbial diversity is high, but community composition remains variable. The microbiota composition becomes more stable in adulthood and remains largely unchanged despite minor fluctuations with lifestyle changes. Changes in composition or abundance, including the loss of beneficial microbes, constitute dysbiosis. These changes are tied to diseases, including type 2 diabetes, metabolic syndrome, obesity, irritable bowel syndrome, inflammatory bowel disease, colorectal cancer, nonalcoholic fatty liver disease, liver cancer, and neurodevelopmental disorders. Alternatively, the microbiota can also change in response to interventions. Depending on the type and stage of disease, these include the development of microbiome modulators mostly aimed at changing the composition of the host microbiota, or of microbial-based solutions to replace some of the defective microbes and their associated benefits. Given the contribution of host genetics in many diseases associated with a dysbiotic microbiota, dual therapeutic strategies may also be required to restore the environment required to re-establish an effective communication between the host and the targeted microbiota [5, 6].

Role In Human Health

Even though it is still unclear whether a healthy gut microbiota is entirely associated with health and absence of disease, it is undoubted that gut microbiota structure and composition play a role in human health and some diseases. Gut microbiota have multiple interrelated protective functions preventing colonization by pathogens; filtering, processing and absorbing nutrients; producing bioactive metabolites, etc. Gut microbiota introduces attractors in the form of an ecological niche or conditions for colonization, and pathogens use these added values to outcompete gut microbiota. However, these protective functions are often impaired and damaged. It is generally believed that breakdown of the balanced microbiota (dysbiosis) can cause several pathogenic transformations in the host body or the environment, which lead to several diseases. These life-threatening diseases caused by pathogen infections include breakdown of gut barrier leading to chronic diarrhea and enteric fever, urinary tract infection, respiratory tract infection, skin infection and wound infection, etc. Gut microbiota modulate gut homeostasis and development, and dysbiosis of microbial communities has been implicated as the cause for several acute and chronic pathological conditions in the gastrointestinal tracts, such as inflammatory bowel disease, irritable bowel syndrome, and gut microbiota related metabolic diseases, such as obesity and diabetes 2. Pathogens can exploit mechanisms analogous to those used by gut microbiota to cause diseases. Medicinal plants are of great importance in the prevention and treatment of diseases, especially in developing countries. They are traditionally utilized for the treatment of the diseases by regulatory authorities. More than 400 medicinal plants are reported to possess both in vitro and in vivo antibacterial activities against enteric pathogens or pathogens causing gastroenteric infectious diseases. Confirmation of antibacterial/antimicrobial activity of these plants by independent laboratories will lead to the identification of bioactive molecules, essential for development of effective and safe drugs against enteric pathogens. Medicinal flowers or flowering tops are also used for the formulations of anti-cough, anti-asthma and anti-allergy drugs by herbal medicine industries. Characterization of gut antimicrobial peptides or other components of gut microbiota having antimicrobial activities will be an important contribution in the field of research. Identification of gut microbiota-based therapeutic strategies against pathogen-induced diseases can lead to new treatment approaches for the diseases. Regulatory authorities should take initiatives to ensure the quality and efficacy of herbal medicines [7, 8].

Factors Influencing Gut Microbiota

Numerous factors significantly influence gut microbiota composition. Some factors establish microbial communities while others affect gut microbiota indirectly through environmental changes. Genetically-determined factors like host genetics, diet, birth mode, and environmental influences such as age, high-fat diet, exercise, and antibiotics provide crucial insights into gut microbiota dynamics. There are notable species-specific differences in gut microbiota. Vaginally-delivered infants have dominant genera in their feces that mirror those in their mother's vagina, remaining present for days or weeks. Gut microbiota typically matures around 1 year of age and varies among different metropolitan environmental contexts. Changes in gut microbiota evolve with age and diet, with adult features detectable for years post-breastfeeding. The gut microbiota exhibits considerable site specificity, remaining stable and consistent within individuals over time. Enterotypes cluster individuals based on dominant taxa in fecal samples, although previous research combined multiple genera. Birth mode and extended breastfeeding are key factors in early life gut microbiota composition, with breastfed infants, irrespective of delivery mode, showing Bifidobacteria-dominant microbiota and greater diversity, especially in healthy growth trajectories observed in RDA analysis post-delivery [9, 10].

Medicinal Plants and Their Properties

Phytomedicines, or medicinal plants (MPs), have a long history of use in curing ailments. However, the rise of synthetic drugs and ignorance about alternative medicines led to a decline in their use. Recently, there has been a resurgence in interest in phytomedicines, particularly in developing countries. Transmission of diseases occurs through water, food, and contact surfaces, with some zoonotic factors involved. Various MPs like Clerodendrum myricoides, Capsicum frutescens, and Tephrosia villosa are recognized for managing diarrhea. Research revealed 18 plants effective in preventing and treating diarrhea, with 15 key plants identified, such as Mentha spicata and Hypericum perforatum, confirming their efficacy. Seven herbs showed significant inhibition of E. coli, S. Flexneri, and vibrio pathogens, affirming the role of these plants in diarrhea treatment. Phytochemical screenings of 14 identified plants demonstrated the presence of flavonoids, tannins, alkaloids, steroids, saponins, and phenolic compounds, suggesting potential therapeutic activities. The percentages of plants containing these compounds varied but indicated a rich diversity and potential for combating diarrheal pathogens [11].

Diarrheal Diseases: An Overview

Diarrheal disease is the second commonest cause of mortality in under-five children worldwide, resulting in 525,000 deaths annually, and the first cause of morbidity and malnutrition in under-five children. Based on a systematic review and meta-analysis study, the Amhara region in Ethiopia was not an exception and different rates of diarrhea prevalence among under-five children were reported: Overall, the pooled prevalence of diarrhea in the Amhara region was 21 with a national prevalence of 22 %. Diarrhea is defined as increased frequency of bowel movements resulting in loose or watery stools. It can be classified as acute or chronic based on duration 1. Diarrheal disease encompasses more than 100 distinct disease entities with diverse etiologies. Some of these entities are nonspecific and tend to improve without treatment. Others, such as those caused by specific infectious organisms, lead to more severe manifestations with greater risk of complications and death. In both parts of this classification system, bacteria, viruses, or parasites may be identified as the causative agent. Diarrhea continues to be a significant cause of morbidity in adults and especially in children, accounting for nearly a million deaths per year. It is one of the most prominent global health problems. In developing countries, diarrheal disease still is a major cause of death. In this regard, it is suspected that GIT microflora imbalance and plus environmental factors played a significant role in the high prevalence of defects. Diarrhea remains a major health problem in developing countries, leading to poor development. In general, infection of the GIT is one of the major concerns in under-fives that leads to various malnutrition metabolic disorders especially undernourished problems and water borne diseases. Once watery stools appear it will lead to a vicious cycle. It has been a problem in rural areas for decades and it is due to environmental factors in case of rich megadiversity of medicinal plants, favorable GIT microflora imbalance, and lack of proper WASH strategy. The high prevalence of infection in under-fives in this region is alarming since it is suspected of derailing the efforts to mitigate malnutrition understanding and resolution of this event is of paramount importance [12, 13].

The Link Between Gut Microbiota and Diarrheal Diseases

The gut microbiota is a complex ecosystem of trillions of microorganisms residing in the gastrointestinal tract, colonizing the gut shortly after birth and influenced by diet, delivery mode, and genetics. It stabilizes in adulthood and maintains homeostasis. Recent interest has grown in how gut microbiota relates to health and disease, especially regarding probiotics, prebiotics, and dietary changes to address dysbiosis. Diarrheal diseases remain a major issue for children under five in developing countries, often resistant to conventional treatments. Plant-derived compounds, widely used in traditional medicine, have shown promise in treating these diseases, although their mechanisms of action are not well understood. Traditional knowledge emphasizes that the effectiveness of these compounds relates to their bioavailability and compatibility, which can be affected by gut microbiota. Consequently, research is increasingly focused on the impact of medicinal and nutraceutical phytocompounds on gut microbiota and their potential in mitigating enteric pathogen-induced diarrhea using advanced rodent models and next-generation sequencing for microbial profiling. Evidence shows that treatment with medicinal plants can enhance beneficial microbiota while reducing harmful types. Despite encouraging results, significant challenges remain in developing plant-derived treatments into effective therapies for diarrheal diseases. A comprehensive approach that considers the relationship between plant drugs and gut microbiota holistically is essential for advancing our understanding of their interactions and improving treatment outcomes [14, 15].

Role Of Medicinal Plants in Managing Diarrheal Diseases

Diarrhea is a serious health problem affecting 3–5 billion cases of world population each year. It occurs as passing loose, watery, and more than three stools per day with a frequency of five or more in neonates and other children. Almost 1.4 million children under the age of five die annually due to diarrheal diseases. Unhygienic conditions and practices are responsible for diarrhea in developing countries. Diarrhea is highly contagious, especially in crowded and low-income societies, affecting areas with poor sanitation and water supply. Oral rehydration therapy (ORT) has been proven as the method of choice in severe acute watery diarrhea as it is the cheapest and best management. ORT is an inexpensive and highly effective means for treating diarrheal dehydration. Antibiotics are indicated for severe cholera to shorten the course of the disease. Anti-secretory drugs reduce the volume and duration of the disease and are more effective in non-cholera diarrhea. Antidiarrheal drugs are widely sought by patients, but there are rare efficacious drugs in this category. Most important is the need to ascertain the exact etiology of diarrhea, whether it is secretory or osmotic, due to a pathogen which is infectious or non-infectious. The use of herbal medicines has been documented from ancient times to cure diseases. Over 70% of the world population uses traditional and indigenous medicine for primary health care, especially in developing countries. In South East Asian countries, the main system of healing is Ayurveda, originating in India. Literature surveyed about antidiarrheal remedies in Ayurveda reveals a wide spectrum of research carried out. The country is bestowed with a wealth of medicinal plants with antidiarrheal actions. This plant has been adopted in Ayurvedic medicine by the indigenous systems and extensively used by tribes to treat diarrhea. This literature is an attempt to collate scientific information about antidiarrheal plant medicines claimed in the Ayurvedic classics and to explore their pharmacological properties, efficacy, and safety in the management of diarrhea. Various studies have demonstrated that certain medicinal plants possess bioactive compounds that can inhibit the pathogens responsible for diarrheal diseases, thereby providing a natural alternative to conventional treatments. Additionally, these plants often contain antimicrobial and anti-inflammatory properties that can aid in restoring gut health and promoting recovery [16, 17].

Synergistic Effects of Gut Microbiota and Medicinal Plants

The intestine's health depends on microbiota composition and metabolic activity, as well as nutrients and medicinal plants. These interactions can enhance intestinal health and disease prevention. Specific diets can alter the gut microbiome during conditions like obesity, colorectal cancer, and inflammatory bowel disease. Chenopodium formosanum's fruit is rich in phenolic compounds and dietary fiber, with its water extract modulating α-glucosidase and α-amylase activities, influencing gut microbiota in mice. Hot water extracts of certain medicinal plants also shift gut microbiota in rats. Serum pre-treatment from diesel-exposed rats with Crataegus pinnatifida var. major extracts improved microbiota composition and liver methylated DNA levels. Phenolic compounds in these plants inhibit CDC degradation by gut microbiota. Combining healthy diets with plant-derived compounds can enrich gut microbiota, yielding health benefits. Studies revealed that υ-3 fatty acids reduce Coprococcus spp. and an unclassified Lachnospiraceae genus, prompting inquiry on dementia treatments involving gut microbiome-enhancing foods. Mice on a fructooligosaccharide diet showed increased Lactobacillus abundance linked to reduced weight gain and rectal temperature, despite promoting some pathogens' growth. Further research is essential to explore the links among healthy dietary components, beneficial gut microbiota, and overall health [18, 19].

Challenges in Research and Application

The use of non-prescription medicine involving medicinal herbal plants is gaining popularity and use worldwide. The herbal medicines are inexpensive and readily available in all localities. Majority of the people in developing countries use herbal preparations for their ailment without the intervention or supervision of trained medical practitioners. Education of the health care practitioners on how to use traditional medicines can help in the integration of the traditional medicines in the medical field. It is worrisome to note that there are no scientific studies to support claims made on the use of these herbs. Oftentimes, the herbs used may be efficacious to the particular ailment but may have potential side effects and consider blood glucose levels. Bacterial diarrhea is a global problem and the second major cause of death in children under five. Diarrhea is the passing of watery stools more than three times a day and is caused by a variety of agents including bacterial pathogens such as Vibrio cholera O1, Vibrio cholera non O1, Escherichia coli -Enteropathogenic, Enterotoxigenic, Enteroinvasive, Shigella dysenteria, Shigella flexneri, Salmonella typhi and Salmonella paratyphi. Antibiotics have been used to treat bacterial diarrhea especially in cases where diagnosis indicates severe or life threatening conditions. However, antibiotic-resistant bacteria such as extended spectrum β-lactamase producing bacteria are an emerging threat, leading to treatment failures. Plant bioactivity can lead to the discovery of new natural antibiotics which could solve the problem. Plant derived medicines have been used to treat various ailments for centuries. The plants have been researched for their anti-diabetic potential and this has been evaluated by monitoring blood glucose levels in rats induced with diabetes. Furthermore, studies have shown the high prevalence of anti-diabetic plants and their use on the different species. Despite this, there is a dearth of literature for those effective in treating diarrhea, due to insufficient screening and research currently on gut microbiota [20, 21].

Future Directions in Research

The interaction between gut microbiota and herbal medicines in relation to diarrheal disease provide further understanding of the functions of plant-derived compounds obtained from probiotics or TCM. Besides its anti-diarrheal function, TCMs can regulate gut microbiota composition and functions and promote gut microbiota restoration. The gut microbiota, as a connection between traditional herbal medicines and the gut-brain axis, attracted extensive interest and relevant studies mushroomed. However, these microbial-related studies mainly focused on diseases, while medicinal plants mostly as one important therapeutic source remain less studied. Medicinal plants may also inhibit or exacerbate diseases in a microbiota-dependent manner, which may provide new insights for the anti-diarrheal mechanisms and biomedical applications of TCM. It is tempting to investigate those but the complexities, including an elaborate metabolic possession in relation to various modulatory gut microbiota followed by gut microbiota-linked biological functions, necessitate the robustness of experimental evidence and carefully designed ecologically relevant scenarios. This chapter in this book focuses on the gut microbiota in the interaction with plant-derived bioactive compounds in relation to diarrheal diseases, highlighting an in-depth understanding of the profound impact of herbal medicines on gut microbiota in the context of physiological and pathological conditions followed by a reconsideration of advancing the TCMs in response to emerging clinical problems [22, 23].

Public Health Implications

Diarrheal diseases are a major public health concern accounting for large morbidity and mortality rates among infants and young children globally. Diarrheal mortality among children aged less than five years has been largely reduced over the past decades due to the implementation of the Global Action Plan for Prevention of Diarrheal Disease and the expansion of Water, Sanitation, and Hygiene (WASH) programs and interventions. However, it remains a major threat to child survival especially in low and middle-income countries. Bacterial pathogens, including Escherichia coli, Salmonella enterica serovar Typhi, Shigella spp, Vibrio cholerae, and Campylobacter jejuni are among the major causes of bacterial diarrhea worldwide. The common management of bacterial diarrhea relies primarily on antibiotics. Although effective in reducing the duration of illness and decreasing complications associated with bacterial diarrhea, the emergence of antibiotic-resistant bacteria limits the application of antibiotics as a treatment for bacterial diarrhea worldwide. In fact, the World Health Organization (WHO) reported that antibiotic misuse and overuse among animal husbandry and agriculture account for more than 60% of total antibiotic consumption in low and middle-income countries. In addition, over-the-counter sales of antibiotics without prescriptions, unregulated practices of clinicians, and contamination of antibiotic compounds into the environment are major contributors to the increasing antimicrobial resistance. Therefore, continued research to discover new natural antibiotics from plants is urgently needed to mitigate the adverse health impacts of antibiotic-resistant bacteria. Plant-based traditional medicinal knowledge can be a valuable source of possible antimicrobials. Diarrhea is a public health problem in developing countries. Traditionally, the people of Debre Markos town have been using different medicinal plants to manage the problem. However, there are limited scientific reports on the antibacterial activities of the traditionally used plants. In the study, the leaf and stem bark of three medicinal plants, Gunnera perpensa, Clausena anisata, and Rhamnus prinoides, were assessed for their effectiveness against selected diarrheagenic pathogens. The overall objective of the study was to evaluate the antimicrobial activity of the leaf and stem bark extracts of Gunnera perpensa, Clausena anisata, and Rhamnus prinoides against selected diarrheagenic pathogens, and to identify the chemical composition of the leaf and stem bark extracts of the selected plants using thin layer chromatography [24, 25].

CONCLUSION

The intricate interplay between gut microbiota, diarrheal pathogens, and medicinal plants represents a promising avenue for improving gastrointestinal health, particularly in vulnerable populations. While gut dysbiosis contributes significantly to the onset and severity of diarrheal diseases, medicinal plants offer a diverse arsenal of bioactive compounds capable of modulating microbial balance and enhancing host defense mechanisms. Integrating traditional plant-based remedies with modern microbiome science could yield innovative, low-cost, and accessible treatments. However, further multidisciplinary research is required to elucidate the mechanisms of interaction, standardize plant-based formulations, and ensure their safety and efficacy. A holistic understanding of these biological interactions holds the key to mitigating diarrheal diseases and fostering sustainable healthcare solutions rooted in both tradition and science.

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