



Role of Phytochemical-Rich Foods in Mitigating Diarrhea among Diabetic Patients

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ABSTRACT

Diabetic patients often experience chronic diarrhea due to complications such as autonomic neuropathy, altered gut microbiota, and the effects of diabetes medications. Phytochemical-rich foods, abundant in fruits, vegetables, and whole grains, have shown promise in mitigating these gastrointestinal issues. These natural compounds, including flavonoids, phenolic acids, and terpenoids, possess anti-inflammatory, antioxidant, and antimicrobial properties that may help regulate gut motility, reduce inflammation, and improve gut barrier function. This review explores the potential of phytochemical-rich foods to alleviate diabetic-induced diarrhea, highlighting their mechanisms of action and the need for further research to optimize their use in dietary interventions for diabetic patients.

Keywords: Phytochemicals, Diabetes Mellitus, Chronic Diarrhea, Gut Microbiota, Anti-inflammatory and Antioxidant

INTRODUCTION

Phytochemicals from medications and herbal remedies used in managing diabetes mellitus have some advantages in long-term diarrhea in diabetic patients. They add value to the dietary meals, slow gut motility, limit the induction of inflammation in the gut, or block chemical-inspired germ permeability [1]. A community of naturally occurring compounds that include flavonoids and phenolic compounds - numerous of which exist in plant by-products - and provide for the contribution of color, flavor, and antioxidant protection to meals, are called phytochemicals [2-4]. Also, they exert anti-inflammatory, anti-glycative, and antimicrobial effects. Fruit and juice by-products are concentrated resources of polyphenols, and employing juice processing consequences in the production of quantity of easily discarded food by-products [2]. The most studied and popular polyphenol is anthocyanin, a group of pigments that exist in the cell vacuoles of red, purple, and blue fruit by-products. These compounds are typically extracted from grapes and red cabbage [5].

People with diabetes mellitus are predisposed to bouts of diarrhea [1-3]. This occurs often as a result of the numerous diabetes-related complications, diabetes drugs, and altered gut microbiota. At diabetes diagnosis, the illness normally presents future consequences, yet the incidence of long-term diarrhea is usually overlooked [2]. The treatment of diabetes will help mitigate long-term diarrhea [4]. The management of diabetes involves the use of a balanced diet, use of non-insulin medications when necessary, and daily exercise [6-8]. The presence of diarrhea presents a challenge to the diabetic patient in controlling the blood glucose. The management of hyperglycemia will usually correct the diarrhea, though in some patients, the long-term diarrhea continues, even after the normalization of blood sugar has occurred. In addition, diarrhea seen in diabetes linked to other health conditions will not be corrected by the sole adjustment of blood sugar control. The treatment of this diarrhea presents a conundrum; the advantages and demerits of diabetes treatment must be weighed and analyzed particularly if the patient is on medications (insulin and non-insulin drugs) [9].

Background and Rationale

As a result, the World Health Organization (WHO) has recommended the use of medicinal plants to mitigate diarrhea conditions [10]. Medicinal plants are rich sources of traditional medicine products, which are free from toxic chemicals, easier for preparation, and freely available in different ecological habitats. The diabetic conditions are always linked to oxidative stress, and these toxicants are the source of autoantigens, which can damage the productive cells of the gut and hence promote diarrhea among the diabetic conditions [11-13]. Therefore, the utilization of phytomedicinal remedies containing phytochemicals which possess both antidiabetic and antioxidant activities will be an additional advantage, and hence this chapter briefly reviews the role of phytochemicals-prepared foods in alleviating diabetic-induced diarrheal complications [8]. The chapter is commenced with novel therapeutic aspects, pharmacokinetics, and mechanisms of diabetes-induced diarrhea, followed by a description of several common medicinal plants that mitigate diabetes-induced diarrhea. Finally, the chapter ends and discusses the terms and prospects of future research [9]. Globally, the public health risks associated with diabetes account for a third of all global disease burden. According to the International Diabetes Federation (IDF), 1 in 11 adults is suffering from diabetes worldwide, and it was estimated that about 642 million people would be living with diabetes by 2040 [14]. Among the diabetes complications, diarrheal diseases remain a major cause of morbidity and mortality among diabetic patients, especially in children. The diabetic diarrheal complications are much annoying and linked to various factors such as autonomic neuropathy, excessive fat intake, diabetes, and certain antibiotics [15-18]. The majority of the public health risk populations present in some of the Southeast Asian countries, where the prevalence of diabetes is quite high. Regarding anti-diarrheal drugs, they may exacerbate the disease condition or even pose a risk to patients with heart diseases as well. Hence, it is essential to have a safe preventive strategy with no further side effects from medicinal plants [19].

Scope and Objectives

Annual benefits that phytochemical-rich foods confer on the world's human population are supported by reliable, qualitative, and reproducible epidemiologic, bioactivity characterization, and clinical definition of their roles in cell modulation and health promotion [20]. Qualifiers such as fiber of cell contents (i.e., both soluble and insoluble forms) of fruit, vegetable, and grain sources serving as key macronutrient ingredients that human ancestors consumed from the beginning of the evolutionary past appear associated with natural picking and long-term colonization of place [21]. This has been determined as a gene and environmentally driven selection served to meet human metabolic needs; particularly when considering dietary fiber's effects on protective health behaviors, quality-of-life metrics, and phytochemical regulation of energy intake; reduction in body mass index (weight loss) and prevention of colon cancer; concluding with positive implications for human heart health, the common cold, and common health complaints from university students on foods and dietary phenomenon [22]. Conversely, communication of the positive health benefits afforded by the ingestion of such foods actually appear to be needed outside of designed studies investigating the unhealthy or toxic impacts of non-fermented, pectin-rich [23]. Alleviation is scarce, hence the need to fill previously unmet knowledge gaps about the relationship that exists between, and among plant-based foods rich in non-nutritive secondary metabolites (NNSMs), diabetic secretory diarrhea, and pharmacologic behavior [18-21]. Efforts demonstrating a broad and easily approachable view for the development, progression, and measured therapies in relation to uncontrolled diabetes-induced secondary health complications has never been more meaningful. In view of this avocation, this discourse discusses the scientific foundation and levels of evidence linking causation to symptom relief among phytochemical-rich foods and related metabolic diseases; involving the development of diarrhea in the setting of diabetes, and counteractive bioactivities of foods and NNSMs on intestinal nutrient malabsorption and secretion [24].

Diarrhea in Diabetic Patients

Gastrointestinal disorders are common among diabetic patients and include upper gut symptoms such as gastroparesis, dyspepsia, heartburn, and gastroesophageal reflux, as well as lower gut symptoms, namely diarrhea and/or fecal incontinence [25]. The presence of such ailments is accompanied by delay in the mixing and transport process of ingested food or beverage within the gut. As a result, several factors are altered, including the hormone secretions, diet composition, and nutrient timing, which affects patients' dietary intake and nutritional status [26-30]. Regarding diabetic diarrhea, as described above, numerous factors influence its occurrence, although dietary intake has an important role in preventing and managing this situation. Unfortunately, managing diabetic diarrhea from a nutritional point of view is complex, since carbohydrate malabsorption, in particular that of sorbitol and fructose, can occur at the same time. Nonetheless, recommendations for the optimal diet of diabetic patients with diarrhea include

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the consumption of low-fat, low-fiber, lactose-free, and fructose-free meals; avoidance of commercial drinks containing sorbitol, mannitol, or xylitol; and the maintenance of frequent snacks throughout the day [31].

Factoring nutritional concerns

Diabetes represents a group of metabolic disorders characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both [26]. If poorly managed, glycemic fluctuations can have deleterious effects on the functioning of major organs such as the eyes, kidneys, teeth, and cardiovascular system. For example, prolonged hyperglycemia has several microvascular sequels that manifest as nephropathy, neuropathy, and retinopathy. In the absence of these microvascular complications, however, the increased transport of substrates occurs in the gut [32]. The resulting osmotic effect causes diabetic diarrhea and typically occurs when the blood glucose level exceeds the renal threshold, and the urinary glucose concentration is higher than the glucose reabsorptive capacity. Other causes of diarrhea in diabetic patients include hepatic cholestasis, colonic hypomotility, and small-intestinal dysmotility. Collectively, about 30% of cases of severe diarrhea have a reversal of their structural changes and consequent improvement of their symptoms when good glycemic control is restored [33-35].

Pathophysiology of Diabetic Diarrhea

Diabetic diarrhea is classified as ulcerative or non-ulcerative. Non-ulcerative diarrhea patients present with abnormal bowel mobility, and symptom presentation such as anal incontinence, fecal leakage, fecal seepage, and foul flatulence; however, hemorrhoids and fissures are rare [32]. Diabetic diarrhea patients have a smaller rectal reservoir and a faster filling rate. The mean residual rectal pressure is significantly lower in patients with severe fecal incontinence compared with that in patients with mild rectal incontinence [30]. The mean rectoanal inhibitory reflex is impaired in diabetic patients with severe fecal incontinence compared with normal and mild incontinence patients. Such abnormalities are associated with the neuronal abnormalities that are associated with both the myenteric and submucosal plexuses. Glucose forms advanced glycation end products through nonenzymatic glycation with proteins, forming fluorescent compounds that intensify oxidative stress [36]. High intracellular glucose levels increase the polyol pathway flux by stimulating aldose reductase which ultimately reduces nicotinamide adenine nucleotide phosphate to nicotinamide adenine nucleotide phosphate and simultaneously reduces the ratio of reduced glutathione to oxidized glutathione causing cell damage [37]. This, in turn, reduces the biosynthesis of neuroprotective prostaglandins, leading to loss of sensation and the occurrence of painless trauma [38]. Diabetic patients exhibit a decreased activity of the Na⁺/K⁺-adenosine triphosphatase, a transmembrane cation-exchange pump that takes part in the etiopathogenesis of neuropathy [15]. Diabetes causes axonal atrophy and decreased nerve conduction, manifested as a reduced amplitude of sensory conduction velocity and decreased sensorimotor nerve conduction, usually measured in the sural and fibular nerves. Diabetic diarrhea is a manifestation of autonomic neuropathy and usually coexists with fecal incontinence. This condition is one of the complications of long-standing diabetes mellitus and is seen in 75 to 10% of such patients. Hyperglycemia leads to morphological changes in nerves and triggers pathogenic factors leading to neuropathy and associated diarrhea. Morphological changes include an increase in endoneural arteriole wall thickness and reduction in the number of caveolae, leading to hyperglycemia-induced capillary magnification [37]. Hyperglycemia-induced caveolae reduction in endothelial cells impairs nitric oxide biosynthesis, and in the absence of this vasodilatory factor, contributes to neuropathic vascular damage resulting in vascular insufficiency, hypoxia, and cell death characterizing diabetic neuropathy. Factors contributing to the development of diabetic neuropathy are related to oxidative, inflammatory, and nitrosative factors. Increased glucose metabolism triggers several metabolic pathways, leading to overproduction of superoxide which, in turn, becomes a precursor of reactive oxygen species [39].

Impact and Burden

It's capitalized that since ancient periods, several traditional plant-based foods have been used effectively for the early avoidance, prevention or cure of different diabetes and associated diseases. The current niches on the consumption of specific phytochemical-rich foods by the diabetic patients or by those who have risk of type 2 diabetes for the prevention of or associated disease diminution [40]. The regular consumption of those contemplated diets, based on the conveyed guidelines, might reduce the prevalence or unfavorable impacts of diabetes and associated diseases [28]. From diabetes to associated diseases, the topics covered under these contemplations include the features of the traditional options, their pharmacological actions and active constituents, experimental activities, and the link between plant-based nutraceuticals and diet-controlled treatment. Several phytochemical-rich foods have exhibited anti-diabetic properties which can enhance the quality of life of diabetic patients [30]. Dissimilar to the usual

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drugs, most of the available phytochemicals for diabetes prevent and ease diabetic symptoms and other related complications, ascribe to its multi-potent effects [40]. The currently recommended dietary guidelines for diabetic patients are mainly based on the declared capabilities of the phytochemicals in different foods. Physiologically, diabetic patients are not common organisms; by thinking about the possible health and lifestyle of the diabetic patients, their eating habits, food cravings, special types of diabetes, specific categories of diabetic patients, the recommended dietary options for dietary contemplation will enhance the quality of life of the diagnosed patients [41].

Phytochemical-Rich Foods

Inhibition of pathogenic microorganisms, a reduction in the production of putrefaction compounds (such as ammonia, indole, p-cresol, and hydrogen sulfide), stimulation of bowel movements, discouragement of the sensation of hunger, improvement of mucosal immunity and gut wall integrity, maintenance of the normal structure of the gut microbiota, and modulation of fermentation and the bowel transit rate are all reasons supporting the application of specific dietary phytochemicals [42]. The concept of using phytochemicals to prevent or alleviate diarrhea is recognized in food science. Lactic acid bacteria aid in maintaining health and preventing diseases [43]. These non-toxic and eco-friendly compounds are widely distributed in nature; however, dietary molecules have deactivated lactic acid bacteria due to the limited availability of material. The monitoring and control of dietary gut microflora using specific dietary phytochemicals would be successful. Therefore, we suggest that phytochemical compounds should be investigated in patients who have diarrhea as the symptoms of diabetes. Foods rich in phytochemicals provide numerous health benefits, including preventing chronic diseases such as diabetes, cardiovascular diseases, and obesity [43-48]. Major phytochemicals like terpenoids, flavonoids, coumarins, and carotenoids are present in fruits, vegetables, and whole grains, and they are classified into specific subclasses that are recommended for daily consumption. Phytochemical-rich foods have been recognized as good sources of treatment against various diseases caused by inflammation, oxidative stress, or infection [49]. The health benefits of individual phytochemicals are well-documented. Plant chemicals possess a wide range of pharmacological properties, such as antibacterial, antioxidant, anticancer, anti-inflammatory, antifungal, anti-diabetic, and anti-atherosclerotic properties. The digestive and supportive functions of good bacteria could be influenced and improved by these natural treatments. In persons with type 2 diabetes, treatment seems to be important because they are highly prone to developing adverse complications such as cardiovascular disease, diarrhea, neuropathy, nephropathy, and retinopathy [50-54].

Health Benefits

In addition to providing essential nutrients and reducing the risk of chronic diseases, specific food sources also encourage good health (well-being and physical health) and may help reduce the risk of hypoglycemia and other metabolic effects after a meal or snack. The nutrient composition of plant-rich extracts shows why common beans are considered healthy [51]. When applying these plant-rich extracts, it is necessary to obtain useful effects related to the levels, bioavailability, and activity of anti-nutrients, and accordingly, evidence that these products can be successfully incorporated into the diet. Some studies have shown that the addition of whole beans and other legume seeds to the diet enhances diabetes management [56]. These beneficial effects of beans on blood sugar management are key to diabetes management, offering potential alternatives to existing diets [58, 59]. To address the question of whether indigenous vegetables from rural areas in Zimbabwe and South Africa are potential sources of selected nutrients that have been linked with the reduction of chronic diseases, with particular emphasis on diabetes, analyzed the nutrient composition of 32 indigenous vegetables from South Africa or Zimbabwe. Their findings showed that indigenous vegetables from both countries are good sources of a variety of nutrients, such as soluble fiber and flavonoids, and can be exploited to reduce chronic diseases. Foods rich in phytochemicals have been shown to prevent and treat various non-communicable diseases, including diabetes, cancer, and cardiovascular diseases. Regarding composition, both studies also found flavonoids to be one of the predominant phytochemicals, which are rich in food sources such as legumes, cruciferous vegetables, berries, onions, and citrus fruits [60-62].

Mechanisms of Action

Defects, deficiencies and disturbances in blood glucose homeostasis, regardless of blood glucose levels, as observed in diabetes, are the common causes of diarrhea among diabetics. Both Type 1 and Type 2 diabetes are responsible for diarrhea in diabetics [61]. In Type 1 diabetes, diarrhea is often linked to phenotypes like polyphagia, polydipsia, and unexplained weight loss such as those observed in untreated Type 1 diabetes [62]. For Type 2 diabetes patients, symptoms like polyphagia, hyperglycemia, unexplained weight loss, neuropathy, or accelerated weight loss are the few important things to observe.

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Consequently, intake of phytochemical-rich foods by diabetic patients may exert several health benefits, such as enhancing digestion and relieving diarrhea and, simultaneously, attenuating the hyperglycemic effect by the inhibition of carbohydrate digestion and glucose absorption [63]. There are several mechanisms of action of phytochemical-rich foods in protecting diabetic patients from diarrhea. The mechanisms of action include acting as anti-diarrheal agents, reducing glycosidase activity, decreasing oxidative stress, reducing bowel permeability, providing dietary fiber, inhibiting angiotensin-converting enzyme, and lessening insulin and weight increments [65]. With such wide arrays of mechanisms, the use of either individual phytochemicals or whole-food matrices may interdependently affect the absorption of nutrients and glycemic response. These added motives might be vital in designing approaches to improve nutritional uptake from diabetic diets that is desirable to alleviate diarrhea, while maintaining the glycemic response within normoglycemic range [66].

Antioxidant Properties

Antioxidants include essential nutrients such as vitamin E, beta-carotene, vitamin C, and selenium. Therefore, an increase in antioxidant intake, especially in fruits and vegetables, is highly suggested for prevention and optimal recovery of diseases such as diarrhea, among others. In this study, the antioxidants in twenty Madagascan vegetables commonly consumed were quantified [67]. Ten main antioxidants were identified, including flavonoids, phenols, proanthocyanidins, and hydroxycinnamic acids in the materials. Consequently, among the antioxidants in the plant, Iran is highly adorned with a significant range of cultivated products, such as numerous phytochemical-producing vegetables, which should be considered for the industrial recovery and purification of these important bio-constituents relied on the diversity of the deployed vegetables [63-68]. Diarrheal diseases are still the second leading cause of death in the less-developed world, with children being the most affected group, accounting for around 12% of the estimated 15 million under-5 deaths worldwide. In developing countries especially, diarrhea is the leading killer of children, accounting for roughly 1.5 million deaths each year. Of these daily deaths, about 60% occur in Africa and South Asian children aged less than two years [60]. The presence of antioxidants in a diet can play a significant role in the improvement and prevention of certain pathologies, such as problems with skin, oral infections, heart disease, hypertension, asthma, and digestive diseases [69-71].

Anti-inflammatory Effects

The phytochemicals inside these edibles are observed to increase the detoxification and defense systems, the effectiveness of the central nervous system, or the sustainment/repair of the covalent-binding stages of the cellular cytoskeleton, such that anti-diarrheal mechanisms are preferred strategies [72]. Processes including modifications to the inflammation-associated elements within diarrheal self-produced infections can be resolved to a degree by food administration, thereby preventing diarrhea-linked events [69]. Here we assess what scientific studies suggest that the above-mentioned administrations are able to control chronic colitis both in vitro and in vivo and determine whether some of these drugs embodied advanced radical scavenging movements towards animal-derived fats that potentially form diarrhea causative agents [68-72]. The colon is a site for electrolyte transport and maintenance of water conditions, colon motility along with immune cell detection and resolution of tissue inflammation. During the colonic phase, the causative agents of damage are transformed, resulting in both pro-inflammatory polymorphonuclear influx and hypertrophy [73]. Anti-inflammatory drugs, such as cyclooxygenase repressive agents, have been demonstrated to control diarrhea in chronic colitis sufferers. Nonsteroidal anti-inflammatory drugs have also been reported to increase the risk of developing colitis, mostly because they inhibit the cyclooxygenase-1 pathway and hence decrease prostaglandin formation as such [74]. In general, extracts from natural sources, namely terpin with tyrosine metabolites and/or serine, have been observed to act as ion loss agents both in vitro and in vivo. Among the food crops like berries, elderberry, and single extracts showed anti-inflammatory actions that possibly developed after reducing upstream cytokine levels and modified expression levels of limit inflammation-linked markers within infected colonic tissues [72-76].

CONCLUSION

Phytochemical-rich foods offer significant potential in managing chronic diarrhea among diabetic patients. Their anti-inflammatory, antioxidant, and antimicrobial properties can enhance gut health by modulating gut motility, reducing oxidative stress, and improving the gut barrier function. The integration of these foods into the diet of diabetic patients could provide a natural, complementary approach to traditional therapies, potentially reducing the reliance on medications and their associated side effects. However, further research is needed to fully understand the mechanisms of action and to establish effective dietary guidelines for incorporating these foods into the management plan for diabetic-

induced diarrhea. This could pave the way for more holistic and sustainable healthcare strategies for diabetic patients globally.

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