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Prebiotics from Dioscorea Spp. as an Anti-Inflammatory Source

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Abstract

Gastrointestinal tract is the main hub for microbial communities called gut microbiome that plays a vital role in biosorption of nutrients, synthesis of micronutrients and vitamins, interactions with drugs, etc. To maintain these health benefits by gut microbiome richness in the microbial diversity has to be accomplished. This type of microbial diversity is seen in tribal people which rely on dietary fibers for energy consumption. However, due to urbanization and change in the dietary pattern, microbial diversity is depleted that results in a condition called dysbiosis. This dysbiosis results in the loss of beneficial microorganisms known as probiotics. To revert the depletion of microbial diversity prebiotics can be used as an alternative approach as they selectively stimulate the growth of probiotic microorganisms. Apart from enhancing the growth of probiotics, they must be resistant to the harsh effect of digestive enzymes. The fate of prebiotics is diverse as they have many reported activities such as immunomodulatory, anti-inflammatory, etc. Generally, prebiotics is extracted from plant sources such as chicory and Jerusalem artichoke, etc. However, less literature is available on wild edible plants such as *Dioscorea bulbifera* and *Dioscorea alata* for their prebiotic assessment.

Introduction

Gastrointestinal tract of humans is colonized by trillions of microbial cells forming a complex microbial community that is responsible for the assimilation of nutrients, synthesis of micronutrients, bile salt metabolism, interactions with drugs, and reducing the toxicity of xenobiotic compounds [1,2] . Despite, these functions, gut microbiota plays a vital role in the synthesis of neurotransmitters and other metabolites that is responsible to modulate host immunity, cytokine production, etc However, some studies show the impact of diet on gut microbiome structure and function. Apart from diet modern lifestyle, the overuse of drugs and antibiotics has led to a condition called dysbiosis. Dysbiosis is an imbalance in the composition of gut microbiota which increases the risk of chronic diseases. A western diet rich in fats was found to increase pathogenic microorganisms such as *Escherichia coli*, *Helicobacter pylori,* etc which in turn alleviate intestinal permeability by increasing pro-inflammatory cytokines. Western diet not only increases pathogen abundance but also decreased microbial diversity such as phylum Firmicutes in the gastrointestinal tract that creates a deleterious consequence on hosts. A study by Sonnenburg, 2014, stated gut microbial diversity of tribal population were rich in diversity as they consumed diet based on dietary fibers.

Tribal populations are rich in their traditional knowledge regarding the diversity among plants available around their environment along with their medicinal advantages. In similar terms, genus *Dioscorea* is a wild edible plant of Maharashtra with medicinal properties such as anti-inflammatory, used as a preventive and therapeutic medicine for arthritis, gastrointestinal disorders, high cholesterol, etc. *Dioscorea bulbifera* and *Dioscorea alata* belongs to the family of *Dioscoreaceae* which is culinary named as air potato, potato yam, or air yam and is characterized by an aggressive annual climber with large heart-shaped leaves and prominent veins and potato-like tubers located in leaf axil position along with underground tubers. *Dioscorea* is an important economic plant that is a staple food for tribal which are used for stomach and abdominal pain problems by these peoples. To assess whether these activities are imparted by prebiotics or due to the secondary metabolite content of *Diosocorea*, we purified prebiotics and assessed the prebiotic potential using in-vitro methods. The concept of prebiotics was originated by Gibson and Roberfroid in 1995 that defined them as "a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon and thus improve host health". Prebiotics target human-associated microbiota to improve the health status of the host. There were reports of prebiotics that enhanced the growth of *Lactobacillus* and *Bifidobacterium* genera specifically; these genera are commonly used as probiotics. WHO, FAO in 2002 defined probiotics as "live microorganisms which when administered in adequate amounts confer a health benefit on the host". Beneficial effects of prebiotics are imparted majorly through stimulation of probiotics microorganisms which produces short-chain fatty acids that have a wide diverse role While on the other hand, probiotics play a vital role in the production of antimicrobial compounds, modulate the immune response, lower cholesterol levels, and aid in nutrient absorption, enhance digestion, etc. Not all compounds are prebiotic in nature, to characterize it as prebiotic it must be resistant to pH changes of the gastrointestinal tract, resistant to human digestive enzymes, should be selectively fermented by intestinal microbiota, should impart health benefit of the host by enhancing the growth or activity of probiotics. Apart from stimulating the growth of probiotics; prebiotics also possesses wide diverse roles. They have been reported in increasing absorption, and bioavailability of minerals thereby decreasing the risk of osteoporosis, lowering the synthesis of triglycerides and plasma cholesterol levels thereby preventing a chronic condition of atherosclerosis. To relish the beneficial effects of prebiotics in humans a dose of 2.5-10 g/day must be ingested in the daily diet. However, the therapeutic dose can increase in disease conditions such as treating Crohn's disease by fructooligosaccharides (FOS) with a concentration of 15.

The naturally occurring source of prebiotics is from vegetables and

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fruits such as Jerusalem artichoke, chicory roots, etc. or enzymatically synthesized using substrates such as lactose, sucrose, starch, etc. Majority of the studies are based on plants such as chicory, Jerusalem artichoke, leeks, garlic, and onions but very few works of literature are available on prebiotic assessment from wild edible plants such as *Dioscorea bulbifera* and *Dioscorea alata*.

Prebiotics and Inflammation

The balance of gut microbiome is very crucial as this organ is very sensitive and does often change into several extrinsic and intrinsic factors such as genetics, dietary habits, age, geographic location, and ethnicity [47,48,49]. Amongst above-mentioned factors, dietary habit seems to affect gut microbiome with huge impact that is substantially observed from the research studies focusing on research studies on the effects of dietary interventions on the gut microbiome. These studies also imparted light on the changes seen in different parts of the organs such as skin, lungs, urogenital tract, oral cavity, etc. that is also occupied by a peculiar microbial community. Indian sub-continent harbours the second-highest human population on the planet that houses tremendous genetic and cultural diversity. The typical Indian diet varies from the cultural group and geographical location. Moreover, the sub-continent has a moreover equal population of vegetarians and animal-based diets. In the modern concept of human health, deciphering the composition and functional characteristics of the indigenous microbiome is crucial. A study from Tandon reported from a cohort of 80 Indians residing in an urban area that the gut microbiome of these individuals was rich in Bacteroidetes (71.5%) followed by Firmicutes (18.7%), Proteobacteria (3.8%) and Actinobacteria (0.6%) at a phylum level study. The typical diet reported in the above-mentioned study was simple and complex carbohydrates such as rice, wheat, sorghum, and fiber-rich components such as fruits vegetables, sprouts, etc. The study also reported the dominance of 5 genera viz., *Prevotella, Faecalibacterium, Alloprevotella, Roseburia,* and *Bacteroides* with more than 80% of abundance. Contradictory to urban diet, tribal diet and rural diet show a much more balanced microbiome with the dominance of Firmicutes, followed by Proteobacteria, Bacteroidetes and Actinobacteria studied in south India. Tribal community with this type of microbiome possessed a mixed diet rich in cereal millets such as pearl and finger millets along with moderate consumption of meat but did not consume milk or milk products [3]. While rural diet was rich in rice and lentils along with milk and curd every day and ate meat once a week. At genus level, bacteria such as *Clostridium* (32.7% in tribal; 4.7% in rural) and *Bacteroidetes* (2.6% in tribal; 0.4% in rural) were abundant in tribal population than rural counterparts. While *Streptococcus* (0.4% in tribal; 2.7% in rural) and *Enterobacteriaceae* (0.4% in tribal; 1.2% in rural) were shown to be prevalent in rural groups than in a tribal group. The study also stated the abundance of Firmicutes to an extent of 85.9% in tribal while 63.5% in the rural group. The high prevalence of Firmicutes contains bacteria that are responsible for fermentation and produces short-chain fatty acids (SCFA's). These fatty acids fuel colonic epithelium thereby maintaining the integrity of epithelial cells, influencing metabolism, and aid in epithelial restitution.

The change in dietary pattern and lifestyle among tribal, rural, and urban has a direct correlation on gut microbiota, out of which tribal gut microbiome seems to be healthy and balanced gut microbiota. The rise in such diseases has been attributed to a variety of causes including increased hygiene and changes in gut microbiota occasioned by changes in diet and lifestyle. Inflammation is the local response to cellular injury that is marked by increased blood flow, leucocyte infiltration, and localized production of inflammatory cytokines by immune cells that serves as an initiator for the elimination of toxic agents. Inflammatory regulation is interplay between pro inflammatory and anti-inflammatory cytokines. The human mucus layer of the small and large intestine is being continuously exposed to inflammatory agents most likely through great antigenic load from commensal micro-organisms present in the gut and due to the presence of cell signalling molecules such as Toll-like receptors (TLR). Hence, as reported in many papers, the gut microbiome also plays a role in shaping innate as well as adaptive immunity [4-5]. The microbiota does have the potential to exert both pro- and anti-inflammatory responses that can be linked with the proper functioning of the immune response. Studies have revealed that when mice were fed with dextran sulphate sodium (DSS), they possessed high levels of pro-inflammatory cytokines and resulted in an increased abundance of mucolytic microbes than the group fed with DSS alone. While on the other hand, prolonged inflammation in the gut can lead to ulcer formation, which leads to the development of the lifelong incurable disease such as inflammatory bowel disease and cancer.

However, various non-specific steroidal and non-steroidal anti-inflammatory drugs, and specific biologics are available in the commercial market to tackle the problem imposed by inflammation. These drugs impose side effects on the hosts such as gastrointestinal disturbances, liver toxicity, suppression of the immune system, etc. Hence, to fulfil the need for safe alternative prebiotics can be used for an anti-inflammatory purpose. Prebiotics will not only resolve the problem of inflammation but also improve the gut microbiome towards a healthy profile resulting in maintaining the proper health of an individual. Similar studies were reported by Ferencz and Maria-Ferreira that reported prebiotics such as lipomannan and rhamnogalacturonan possessed the functions of anti-inflammatory, also improving the behavior of mice when fed with DSS. Therefore, prebiotics remains a promising field in science to explore the benefits imparted on hosts.

Conclusion

Prebiotics has been discussed with respect to the systemic effects they exert on the host's health, metabolism, and immune system. The ability to regulate the composition of the microbiota by prebiotic dietary substances and probiotic microorganisms is an interesting approach in the control and treatment of some major diseases. Prebiotics are emerging as promising nutraceuticals in various medical conditions, including IBD. Since prebiotics is easy to administer, inexpensive, and lack significant toxic side effects they may become an attractive alternative or adjunct to standard therapeutics in inflammation conditions.

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