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Review Article

Functional Foods and the Gut Microbiome

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ABSTRACT

The diversity of microorganisms that inhabits the gut play vital roles as determinants of human health. Among other factors, diet has a significant impact on gut microbial composition and function. This is as a result of the biotransformation of food components and the production of metabolites by the microorganisms. Examples of gut microbiota include *Bifidobacterium, Lactobacillus, Streptococcus, Saccharomyces cerevisiae*. The interplay between the diet, gut microbiota, and the host occurs as the diet changes the gut microbiota composition and function, which in turn affects the host biochemical processes. Thus, diet is currently considered one of the most critical factors that control microbiota structure and metabolism. Functional foods such as probiotic products, prebiotics, symbiotic and dietary polyphenols can modulate the microbiota. This is a result of the health benefits associated with these foods. More knowledge of the interactions between functional foods and specific intestinal bacteria could contribute to a better understanding of both positive and negative interactions in vivo and the identification of new microorganisms inhabiting the gut.

Keywords: Probiotics, Prebiotics, Synbiotics, Gut microbiota.

Introduction

Functional foods are foods that have functional (naturally occurring, biologically active) components, which tend to confer health benefits far more than ordinary nutrition. It was reported that the components are crucial in the prevention of disease.[1] Functional foods, as defined by Health Canada, are products that look like traditional foods but are proven to offer some physiological benefits. The combination of foods with some herbal medicines forms the basis for most outstanding traditional functional foods.

Functional foods include the following:

- Foods enhanced with biologically active substances (for example, probiotics) and
- Derived food compounds added to conventional foods (for example, prebiotics).
- Normal foods containing inherent biologically active substances (for example, dietary fibre, dietary polyphenol, phytochemical).

Functional foods show some similarities in appearance with conventional foods. Still, functional foods exhibit physiological advantages with the ability to diminish the danger of constant sickness past essential dietary capacities, including support of gut well-being, unlike conventional foods.[2]

Probiotics as functional food

Probiotics, as defined by FAO/WHO in 2001, are live microorganisms that on ingestion in the right proportion confers a health benefit on the host. The probiotics concept was hypothesised by Elie Metchnikoff 1900 years ago after he observed that the Bulgarian peasants live longer and healthier, which was traceable to the intake of products associated with fermented milk. He noted that organisms that shield the gut from the destroying impact of other harmful bacteria are present in yoghurt. Due to their preventive and curative properties, a series of beneficial microbes have gained usage over the years as probiotics both in human and animal feeds formulation.[3]

Criteria for selecting probiotics

The primary criteria in selecting suitable bacteria species include adequate dose, ability to remain viable with processing and during storage, ability to survive intestinal transit, and aspiring health impacts on consumers.[4]

Locally fermented foods as potential probiotics vehicles

Fermented foods form part of the foremost African food. The fermentation process describes the anaerobic breakdown of organic substrates into acids or alcohol through the action of enzymes produced by microorganisms, majorly bacteria, and yeasts.[5] Fermentation helps in nutritional enhancement, health stimulating, flavour addition, and food preservation.[6] Fermentation contributes to the development of the nation's economy by creating diverse food for constant availability, increases farmers' income, and causes a reduction in harvest losses.[7] Some of the locally fermented foods in Nigeria include; Iru from locust bean (*Parkia biglobosa*), Ugba from oil bean seed (*Pentaclethra macrophylla*),[8] Garri from cassava (*Manihot esculenta*), Lafun from cassava (*Manihot esculenta*), Ogiri from melon seed (*Colocynthis citrullus, Coloncythis vulgaris*),[8] Amasi, Banu, Ogi, Injera, Mahewu and Kunu. Lactic Acid Bacteria (LAB) have been shown by several studies to be present during the fermentation of many African indigenous foods.[9] Aside from the regular role they play during fermentation, lactic acid bacteria have also been shown to have a series of applications in food fermentation products that have health benefit when consumed by individuals across the globe.[9] A specific strain of LAB often play the role of probiotics when present adequately in a diet, and this has given them relevance in the industries and in some optimised local fermentation processes where they are being used as starter cultures.[10]

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Prebiotics as functional food

Prebiotics are short-chain carbohydrates (SCCs) that cannot be digested by human digestive enzymes.[11] They are a non-metabolisable food component that transits to the colon, where it undergoes fermentation by selected microorganisms.[11] The host gain from this when it selectively permits the growth of one or more useful microbes. Prebiotics definition somehow resembles dietary fibre definition, but it differs because of its preference for large groups of resident microbes. Presently, only non-digestible carbohydrate (CHO) molecules (disaccharides, oligosaccharides, polysaccharides), resistant starches, and sugar polyols have been shown to exhibit prebiotic properties. Commonly used prebiotics in human diets includes; Lactulose, Galactooligosaccharides(GOS), Fructooligosaccharides (FOS), inulin and inulin hydrolysates, Maltooligosaccharides, and Resistant starch.

Synbiotics as functional foods

Prebiotics has limited capacity in the sense that it can influence the growth of only available bacteria in the large intestine. In contrast, probiotics are the species introduced that have to compete for nutrition and conditions available for growth with the resident commensal organisms. Resident microbes already inhabit most of the ecological niches present, thereby making it hard for newly introduced probiotics to thrive and be established. Based on this simple fact, synbiotics was developed, which is the mixture of both probiotics and prebiotics. The rationale behind this being that when the right proportion of probiotics and prebiotics are present, prebiotic should help probiotics to thrive well in the gut until they are established.[12] Synbiotics are being used in food product formulation to maximise their synergic effects.

Dietary polyphenols as functional foods

Dietary polyphenols are naturally occurring compounds in plants like fruits, vegetables, cereals, wine and coffee. Based on their structure and chemical compositions, they are classified into flavonoids and non-flavonoids.[13] Flavonoids are divided into flavones, dihydroflavonols, flavonols, flavonols, anthocyanidins, isoflavones and proanthocyanidins. It is widely known for its antioxidant, anti-inflammatory, anticancer and neurone protection properties. Fruits such as apple, pineapple, avocado, grapes, guava, pomegranates to mention but few are good sources of polyphenols.

Microbiota and microbiome

Humans have been tagged one of the most complex living unit owing to evolution. Microbiotic cells form the more significant part of the total human cells with up to 10 to 100 trillion residing within a single individual, thereby forming up to fifty per cent of the total cell count.[14] The microbiome is referred to as the microbial occupant of a population.[15] Microbiome connotes the community of commensal, symbiotic and pathogenic microorganisms competing with our body space and has a great impact on the determination of well-being and disease.[16] Microbiota means a microbial community; commonly described based on the habitat that it occupies while microbiome is the total genomes and genes found among the members of microbiota.[17]

Gut microbiota

Numerous populace of microorganisms colonised the human gut, predominantly bacteria as evaluated, a grown-up adult is made up of 100 trillion cells in their microbiota, which makes it exceed the whole of human cells by 101.[19] It was reported that the ability of the intestinal microbiome to carry out the function of metabolism is roughly 10^2-times more prominent than that of the human liver and is traceable to the consequence of the incredible assorted variety of microorganisms framing the populace and thus the number of genes present in them.[20]

Functions of the gut microbiota

Mutualistic relationship exists among the gut microbiota and the human host, and the bacteria assist in the homeostatic regulation of the host body while the host intestine creates a suitable environment that supports the growth of the bacteria.[21]

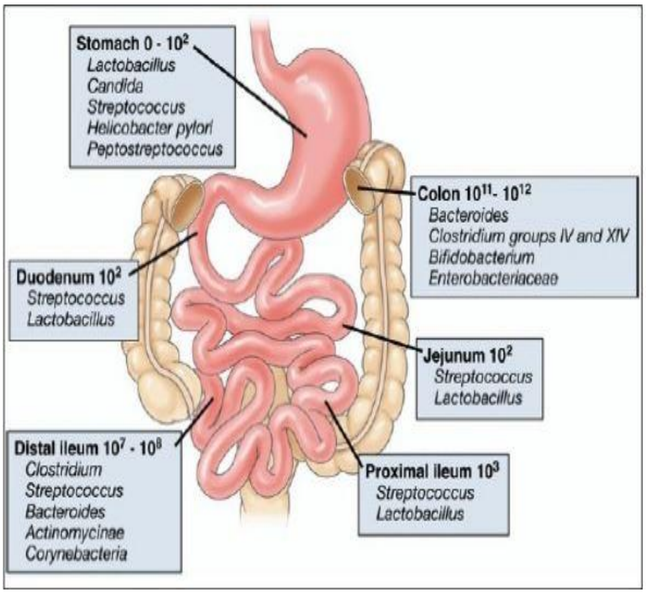

Figure 1: Microorganisms occupying different parts of the gut and their abundance.[18]

It was reported that the gut microbiota play a crucial role in digestion, absorption and energy production as well as the production of vitamins K2, folate and short-chain fatty acids (SCFAs) for the host.[22-24]

Other functions of the gut microbiota include building and boosting of the intestinal immune system, secretion of antimicrobial products which act against pathogenic bacteria, maintaining gut integrity, utilises non-digestible ingredients from food, producing nutritional factors such as Vitamins, detoxifying the malicious xenobiotics and influencing the host health.[25] These functions are indispensable, because without gut microbiota or with its removal with wide range anti-infection agents, the noticeable problem can occur, for example, inappropriate build-up of the intestinal immunity and the development of gut pathogenic organisms.[25]

The gut microbiota is crucial in digestion, and it shows some variation at each anatomic site of the gut which is as a result of change in some factors such as temperature, pH, redox potential, oxygen tension, water activity and light.[26] The gut microbiota plays its role mostly in the colon where there is no secretion of digestive enzymes to carryout metabolism of indigestible macronutrients in the ileum.[26,27] Polysaccharides and oligosaccharides form the primary indigestible macronutrients which are later fermented by the commensal bacteria of the colon thereby leading to the production of short chain fatty acids (SCFAs) and phenolic compounds which are further metabolised to produce or synthesise bioactive compounds.[27] Bacterial proteinase and peptidase produced by some species like *Propionibacterium spp.*, *Clostridia spp.*, *Prevotella spp.*, *Bifidobacterium spp.* and *Bacteroides spp.* aid the fermentation of protein in the colon.[26,27]

Gut microbiota also helps in determining brain health. It was reported that mood, memory and also cognition could be affected by gut microbiota and it has been clinically and therapeutically associated to some disorders such as alcoholism, restless leg syndrome, fibromyalgia and chronic fatigue syndrome.[28-30] Alteration in the gut microbiome composition are communicated to the central nervous system through the vagus nerve, and this have a direct effect on cognition, behaviour and stress reactivity.[31] Neurotransmitters like noradrenaline, serotonin, acetylcholine and gamma-aminobutyric acid (GABA) can be synthesised by gut microbiota and this may increase the neurotransmitter levels in the CNS which affect the performance of the CNS.[32-34]

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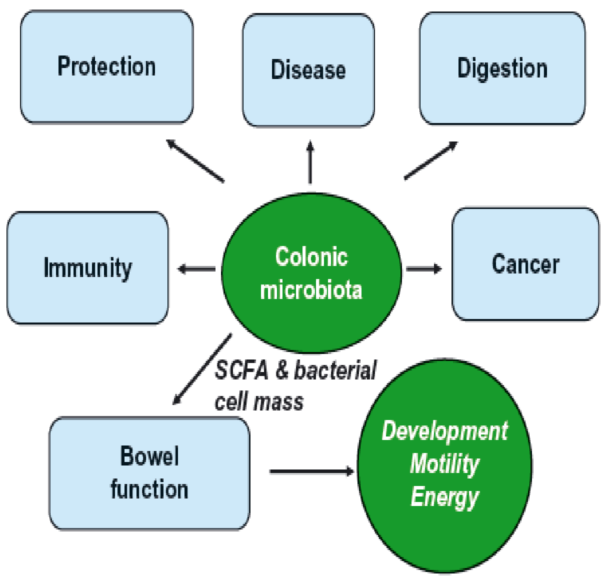

Figure 2: Impact of colonic microbiota in health and disease.[35]

Dietary polyphenols and the gut microbiome

Polyphenols exhibit the prebiotic-like effect. Corroborating this effect, increased abundance of *Bifidobacterium spp.*, *Lactobacillus spp.* and increased production of short chain fatty acid (SCFA) with decreased abundance of *Bacteroides*, *Prevotella* and *Clostridium* groups was observed in the in-vitro evaluation of the modulatory polyphenols from the effect of green tea, Oolong tea and black tea on the gut microbiome[36]. Also, Resveratrol increased the abundance of *Bifidobacteria spp.* and *Lactobacilli spp*. It simultaneously decreased *Escherichia coli* and *Enterobacteria* in the colon microbiome of a Dextran Sulphate Sodium-induced colitis rat model[37].

Probiotics and the gut microbiome

Probiotics tend to modulate the gut microbiota based on three significant mechanisms which include: Trophic Interactions, Direct Stimulatory or Inhibitory Impact, Indirect Stimulatory or Inhibitory Impact which can be as a result of the change in the production of host-derived molecules.

Trophic interactions

Many probiotics are capable of rapidly metabolising of simple carbohydrates to produce metabolites like lactic acid, acetic acid or propionic acid. Metabolic outputs can be altered as a result of the integration of probiotics into the trophic networks of carbohydrate breakdown. The setup of in-vitro models of gut fermentation that resembles the colonic ecosystem unveiled the interaction between probiotics and networks of microbes. Some of these models are beads coated with mucins,[20] mucosal biofilms,[38] or the introduction of polymer beads[39] to stimulate the gut and overcome rapid washout. A sampling at a different region of the colon that is not easily reached is favoured.[40] Different studies have reported increased production of SCFA in response to probiotics which can be as a result of augmented LAB and *Bifidobacteria*. For example, in an invitro GI model simulator of human intestinal microbial ecosystem, there was an observed increased *Bifidobacteria* and SCFA levels in response to the administered *Enterococcus faecium* CRL 183 and increased number of *Bifidobacterium* and *Lactobacillus* as well as acetate in response to administered *Lactobacillus acidophilus* CRL 1014.[41] Also, butyrate-producing bacteria that can make use of acetate or lactate is produced in response to *Bifidobacterium* supplementation. Beyond dietary carbohydrate metabolism, the trophic impact may be as a result of Exopolysaccharide (EPS) produced by probiotics which tend to support the growth of gut flora. For instance, Murine pathogen *Citrobacter rodentum* was suppressed in response to a cell-surface associated exopolysaccharide from *Bifidobacterium breve* UCC2003.[42]

Direct stimulatory impact

In this second mechanism, the presence of some residing members of the gut communities is altered or inhibited as a result of the inhibitory effects exhibited by the probiotics. Probiotics tend to compete for the nutrients, which may eventually lead to the decreased levels of other residing bacteria. For instance, *Clostridium difficile*, *Salmonella* enteric serovar *Typhimurium* tends to be inhibited in the presence of *Bifidobacterium breve* UC2003, which is capable of competing successfully for sialic acids. Resident commensals or pathogens can also be competitively displaced from their adherence sites, just as it occurs in mannose adhesion. Likewise, *Bacteroides thetanotaomicron* is inhibited by a growth-limiting factor such as vitamins12 produced by some probiotics.[43]

Indirect stimulatory impact

This third mechanism involves the host's response to probiotics supplementation, which result in the modulation of the gut microbiota. Different components produced by the host such as secretory IgA(sIgA), mucus and antimicrobial peptides helps to protect the intestinal epithelium from invasion by pathogenic microorganisms. The gut microbiota can be coated by sIgA, which is produced by the B cells.[44] In a study carried out with fluorescent probes in healthy individuals, it was observed that sIgA coats 24-74% of faecal bacteria. To complement this result, increased faecal sIgA has been linked to the consumption of some probiotics.[45]

Prebiotics and the gut microbiome

Prebiotics is defined as "selectively fermented ingredients which permit specific changes, both in the composition and activity in the gastrointestinal microflora that confers health benefits on the host"[11]. Different studies have shown increased abundance of Bifidobacteria in response to GOS and fructans supplementation. Prebiotics play its functional role in reducing constipation, aiding digestion, and in controlling inflammatory bowel disease due to increased *Bifidobacterium* and *Lactobacillus spp*.[46] *Bifidobacteria* have been shown by various studies to have a direct link in conferring health benefit in babies.[47] Apart from the response of *Bifidobacterium* and *Lactobacillus spp* to prebiotic supplements, some studies have shown that other groups of gut bacteria are also stimulated. In a survey, FOS supplementation led to an increased abundance of *Bifidobacteria* and *Collinsella aerofaciens*.
Supplementation of infant formulas with galacto-oligosaccharides (GOS) has been on the increase recently as a result of GOS being a significant component of the breast-milk[48]. In a GOS supplementation trial carried out on 18 adults, the stimulation of` *bifidobacteria* numbers (majorly *Bifidobacterium adolescentis* and *Bifidobacterium catenulatum*) in half of the adults' population with an increased population of *F. prausnitzii* was observed.[48] The individual differences in response to GOS supplementation were also observed in the study conducted on older people that showed variation in the abundance of *Bifidobacterium* present.[49] Arabinoxylan supplements have been displayed in an animal study to increase the abundance of *Bifidobacterium spp*. alongside *Bacteroides spp*, *Prevotella spp.* and *Roseburia spp*. The result suggests the beneficial effects on lipid and cholesterol accumulation.

Synbiotics and the gut microbiome

Synbiotics combines the impact of both probiotics and prebiotics. This synergistic effect helps to impact gut microbiota, maintain intestinal balance, and the effect help in the prevention and treatment of gut-related diseases such as Inflammatory Bowel Disease (IBD), among others.

Future perspective

More understanding of the relationship between human microbiota, functional foods, and the host can help in the amelioration of diseases and also help to shapen the future of medicine. There is a need for

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research to be carried out on the impact of some of our indigenous foods and locally fermented products which have in one way or the other fulfilled the criteria of functional foods. More insight is needed into what makes some of these locally fermented foods functional as this can help to optimise their production line and improve on their quality and quantity, thereby helping to solve the problem of food scarcity and diet-associated diseases in Nigeria and Africa as a whole.

Conclusion

Dietary interventions and targeted nutritional therapies, like medical foods and nutritional supplements, hold great promise for preventing and treating microbiota-associated diseases.

The present rise in the consumption of functional foods shows our capacity to alter the human microbiota owing to changes in our diet, which tend to have a direct impact on the physiology of the host, thereby extending their life span. This will help in the formulation of new drugs that can solve the problem and complications associated with gut imbalance leaving little or no side effects. However, much research needs to be done before these can be fully achieved.

Conflict of interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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