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IMMUNE BOOSTING MECHANISMS AND FUNCTIONAL FOODS: A CRITICAL EVALUATION OF PREBIOTICS AND PROBIOTICS

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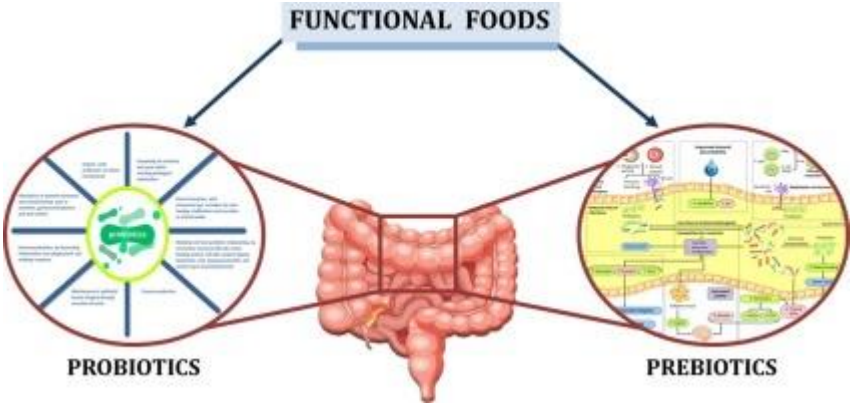
Abstract:

Probiotics and prebiotics play crucial roles in managing the intestinal microbiota in order to improve host health, even though their influence on other body sites are being investigated. Comprehensive studies conducted on the link between the gut immunity and microbiome in recent decades have correspondingly led to ever increasing interests in functional foods, especially probiotics and prebiotics. While positively affecting overall host physiology, different colonic bacteria metabolize dietary prebiotics to produce beneficial metabolites, especially short chain fatty acids (SCFAs) that improve luminal contents and intestinal performance. Thus, this review provides a general perspective of the gut immune system, the immune system and its microbiota. The review also evaluates functional foods with critical but comprehensive perspectives into probiotics and prebiotics, their immune boosting and mechanisms of action. It is recommended that further translational and mechanistic studies are conducted to promote empower poverty-stricken and also communities social life, health.

Graphical abstract:



Keywords:

Microbiota, Prebiotics , Short chain fatty acids, Probiotics, Functional foods.

Introduction:

To release beneficial metabolites, Prebiotics were known to be selectively degraded by host microorganisms. It is suggested that they be incorporated into health management as alternative therapy or complements to pharmaceutical agents, lifestyle and foods, because several investigations and in-depth studies have established probiotics with both clear and unclear mechanisms. Prebiotics are not just enhancers of lactobacilli and bifidobacteria anymore, they have gained recognition regarding their physiological and systemic functions.

The definitions and trending knowledge of both prebiotic and probiotic action mechanisms with regards to immunity were critically evaluated, while capping it all with prospective outlook, concerns, challenges, and

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conclusive remarks. Usually, the gut has been implicated in immune cells activity and overall immunity based on probiotics and prebiotics interventions, even though it is not their only pharmacologically important zone of the body. This review provides an overview of the gut immune system and their microbiota.

Functional foods can regulate the immune system through immune response enhancement or inhibition, which provide host defenses against infection, and suppress allergies and inflammation. There is a trendy demand for various food components that can improve immune response. The production of these food components such as probiotics and prebiotics, is ever increasing with the intention of fighting chronic health problems like diabetes, cancer, non-alcoholic fatty liver disease (NAFLD), cardiovascular diseases and obesity. Presently, the most known functional foods are the probiotics and prebiotics based on their health promoting properties.

An Overview of the Immune System:

The immune system is an interactive network of lymphoid organs, cells, humoral factors, and cytokines. The essential function of the immune system in host defence is best illustrated when it goes wrong; underactivity resulting in the severe infections and tumours of immunodeficiency, overactivity in allergic and autoimmune disease. In this review we have covered the normal function of the immune system in recognising, repelling, and eradicating pathogens and other foreign molecules. The specific immunity is linked to the immunoglobulins (Ig), produced by B cells in response to antigenic attacks, such as pathogens and allergens. The Igs are further divided into IgA, IgG and IgE classes - all produced *via* isotype switching upon activation. Of them all, the IgAs are more relevant to the present review, as they can be found in saliva, tears, sweat, breast milk and mucosal secretions. The IgAs also help in controlling commensal bacteria at mucosal sites as well as protecting the body from infection. T-cells are another group of adaptive / specific immune cells found in the small and large intestines.

Role of Gut Microbiota in Immunity:

The collection of microbial populations that reside on and in the host is commonly referred to as the microbiota. A principal function of the microbiota is to protect the intestine against colonization by exogenous pathogens and potentially harmful indigenous microorganisms via several mechanisms, which include direct competition for limited nutrients and the modulation of host immune responses. This immune system is composed of gut-associated lymphoid tissue and other cells, meant to protect the gut from several types of antigens readily supplied from foods, commensal and pathogenic bacteria. Also, many and diverse intestinal cells are responsible for stimulating IgA isotypes production, which further buffer up the gut immunity.Bacteria like Bifidobacteria possess special transport mechanisms, cellular and extracellular glycosidases, while Bacteroides break down high molecular weight prebiotic carbohydrates which actively digest low molecular weight prebiotic carbohydrates.

Functional Foods:

Functional foods are conventional foods to which specific essential nutrients and food components are added for a targeted physiological function. Because of this, these foods have the potential to provide a health benefit beyond basic nutrition. Functional foods can help fulfill nutrient deficiencies and may provide essential nutrients beyond quantities necessary for normal maintenance, growth, and development. They can also provide other bioactive components that impart health benefits or desirable physiological effects. Some functional foods are regarded as microbial medicines, *i.e.* prebiotics and probiotics meant to target obesity and metabolic syndrome, as

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well as high blood pressure, oxidation, cellular damage and other diseases from raw materials like vegetables, cereals, diary and meat products. among the most prominent and well researched functional foods are the prebiotics and probiotics, which have the capacity of boosting consumers immune status.

Probiotics and Prebiotics

Bacteria in the large intestine ferment prebiotics. This releases byproducts called short-chain fatty acids. These byproducts act as energy sources for the cells lining the colon, called colonocytes, and benefit health in many other ways. Probiotics are thought to help restore the natural balance of bacteria in your gut (including your stomach and intestines) when it's been disrupted by an illness or treatment.

The commonest probiotics used in functional foods and other fermented products include *Bifidobacteria*, Lactobacilli, Enterococci and Leuconostoc spp. Other than these yeasts such as *Saccharomyces* spp., lactic acid bacteria group, are also used as probiotics. In fact, the market for probiotics is ever increasing in size, and consumers demands have risen spontaneously based on the immune-enhancing benefits of probiotics. They are already being sold as conventional foods, dietary supplements, medical foods and drugs in the United States, and are often administrated in capsules, liquid or powder forms. The immune boosting effects and mechanisms of some probiotics are listed in Table 1.

Table 1. The immune boosting effects and mechanisms of selected probiotics.

Probiotic organism	**Immune boosting functions**	**Mechanisms**	**Citation**
Lactobacillus plantarum MON03	Detoxify toxins	Binding *via* surface structures	Jebali et al.
***Lactobacillus kefiri* KFLM3 Saccharomyces cerevisiae KFGY7 *Acetobacter syzygii* KFGM1**	Detoxify toxins	Adsorption and biotransformation	Taheur et al.
***Lactobacillus helveticus* ATCC 12046**	Detoxify toxins	Binding *via* surface structures	Ismail et al.
***Bacillus licheniformis* CFR1**	Detoxify toxins	Enzymic degradation	Rao et al.
Saccharomyces cerevisiae HR 125a	Detoxify toxins	Binding *via* surface structures	Ismail et al.
***Lactococcus lactis* JF 3102, *Lactobacillus plantarum* NRRL B-4496**	Detoxify toxins	Binding *via* surface structures	Ismail et al.
***Streptomyces cacaoi* subsp. Asoensis K234, *Streptomyces luteogriseus* K144, *Streptomyces rimosus* K145**	Detoxify toxins	Enzymic degradation	Harkai et al.
Several other *Lactobacillus* strains	**Secrete IgA**	Stimulate dendritic cells to produce IL-6	Kikuchi et al.

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Probiotic organism	Immune boosting functions	Mechanisms	Citation
	Produce IgA	Stimulate dendritic cells to produce TGF-β	Sakai et al.
	Improve natural killer (NK) cell activity	Stimulate secretion of IL-12	Takeda et al.
	Inhibit Th2 activity	Stimulate secretion of IL-12	Fujiwara et al.
	Inhibit Th2 activity	Stimulate activated T cells death	Kanzato et al.
	Improve oral tolerance	Induce Tregs	Aoki-Yoshida et al.
	Reduce inflammation	Weaken pro-inflammatory cytokines and chemokines by down-regulation of TLR-signals	Shimazu et al.
	Detoxify toxins	Binding *via* surface structures	Chlebicz and Śliżewska
Several other *Bifidobacterium* strains	**Reduce inflammation**	Induce of IFN-β	Kawashima et al.
	Produce IgA	Up-regulate expression of pIgR	Nakamura et al.
	Modulate anti-viral activity	Reduce A20 and improve IRF-3, IFN-b, MxA, RNasel	Ishizuka et al.
	Protect from enteropathogenic infection	Produce acetate and improve intestinal defence with epithelial cells	Fukuda et al.
	Inhibit allergy	Suppress Th2 chemokines	Iwabuchi et al.
	Reduce inflammation	Inhibit IL-17	Miyauchi et al.

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Prebiotics also influence the makeup and function of gut bacteria, promoting the growth of beneficial microbes. According to the International Scientific Association of Probiotics and Prebiotics, in order for a compound to be classified as a prebiotic, it should:

- resist stomach acid and digestive enzymes, plus should not be absorbed in the GI tract
- be able to be fermented by intestinal microbes
- stimulate the growth or activity of intestinal bacteria to improve health

There are many different types of prebiotics, including:

- fructans
- galacto-oligosaccharides
- starch- and glucose-derived oligosaccharides
- pectic oligosaccharide
- non-carbohydrate oligosaccharides

Most prebiotics are considered carbohydrates. However, some prebiotics are not classified as carbohydrates. Cocoa flavonols are an example of non-carbohydrate oligosaccharides.Although prebiotics are often confused with probiotics, they are not the same. Probiotics are live microorganisms found in your gut, certain foods, and supplements that benefit health when taken in certain amounts.On the other hand, prebiotics are nutrients that are dietary compounds that stimulate the growth and activity of certain microorganisms.

Mechanism of Actions:

The validated and proposed action mechanisms of probiotics are represented in Fig. 1. Probiotics are well known to boost the immunity of humans by protecting against gastrointestinal pathogens, thus the mechanisms of action by which they exert their beneficial effects on the host include secretion of antimicrobial substances, competitive exclusion for adhesion sites and nutritional sources, enhancement of intestinal barrier function, and immunomodulation.

Various nutrients can change cell structure, cellular metabolism, and cell function which is particularly important for cells of the immune system as nutrient availability is associated with the activation and function of diverse immune subsets. The most important nutrients for immune cell function and fate appear to be glucose, amino acids, fatty acids, and vitamin D. This perspective will describe recently published information describing the mechanism of action of prominent nutritional intervention agents where evidence exists as to their action and potency.

The action mechanisms of probiotics interfere with the gut epithelial and immune cells composition and functions.Moreover, on the basis of mineral nutrients route, absorption occur in the small intestine *via* active transport mechanisms. The drop in luminal pH due to the production of SCFAs among other acidic metabolites can lead to increased calcium solubility, readily available for passive uptake and consequent immune boosting *via* immune cells activation or bone strength enhancement among other benefits.

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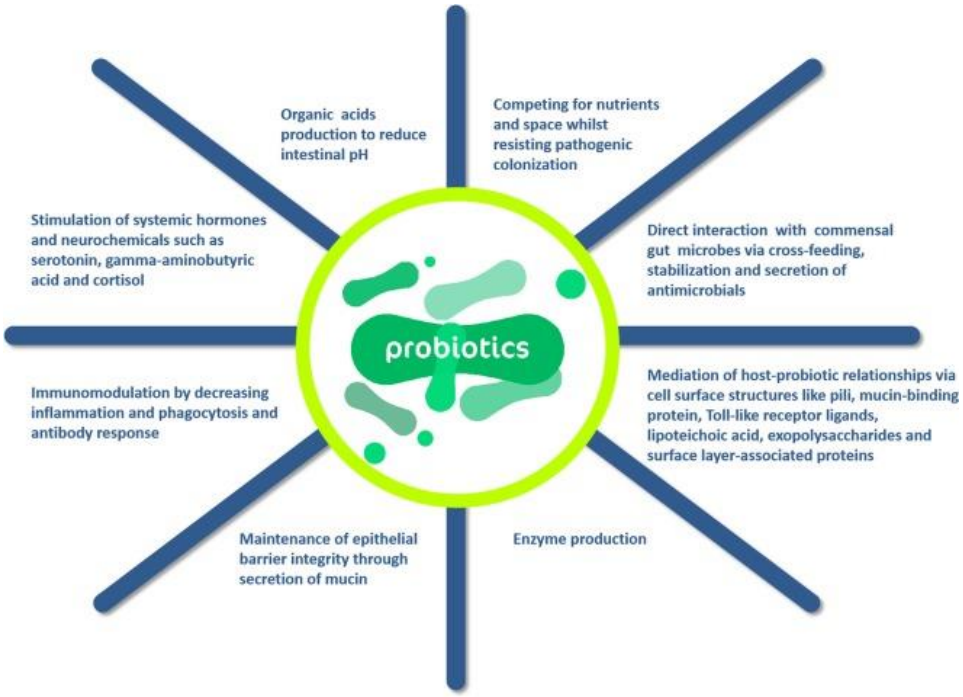

Fig. 1. Action mechanisms of probiotics.

Another mechanism under this category of antimicrobial substances secretion involves the production of acetic and lactic acids for acidification in order to inhibit the growth of pathogens such as *Salmonella* spp. Competitive exclusion mechanism involves adhesion sites and nutrients competition between a probiotic organism and a pathogenic organism. This enables the probiotic to inhibit the pathogen's growth. Intestinal epithelial barriers are well maintained by probiotic organisms to protect against certain intestinal hyper-acidity and diseases like obesity, inflammatory bowel diseases, and irritable bowel syndrome. Probiotics do not only maintain the intestinal barriers, they also potentiate their reparative process after damage. Probiotics are living organisms with immunomodulatory benefits, and some of these immunomodulatory effects are produced when attenuated or dead, implying that probiotic effects are not necessarily obtained from live organisms.

Conclusions:

The consumption of probiotics such as lactobacilli and bidobacteria may proffer an option to antibiotics for prevention and treatment of microbial infections based on certain mechanisms including maintenance of intestinal barrier integrity, antimicrobial toxins production, competing for nutrients and adhesion, as well as modulation of the immune system. Functional foods such as probiotics and prebiotics are the future of health-promoting foods. This is not dissimilar to effects and mechanisms of prebiotics, which are entangled in synergistic processes with the beneficial probiotic organisms. Thus, better comprehension of the mechanisms involved are required, as well as extensive human studies to validate excellent potent probiotic species/strains and effective amount of doses meant for particular diseases. Moreover, more investigations and translational research on probiotics and prebiotics meant to help developing countries' consumers are recommended.Generally, the results of these interventions may be valuable for target populations. Researchers are bestowed with the responsibility of considering the importance of their findings to consumers, as well as their fundamentality to overall conclusions on products' efficacy.

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