Chapter 12

Difference between Probiotics and Pre-biotics and its Best Time of use

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ABSTRACT

Probiotics and prebiotics are essential for enhancing gut health and overall wellness. Prebiotics are indigestible fibers that feed good bacteria on the gastrointestinal tract, whereas probiotics are live microorganisms that, when taken in adequate proportions, have been shown to have positive health effects. Prebiotics are plant-based foods that provide food for beneficial microbes in the gut. Examples of these foods include onions, garlic, bananas, and whole grain products. They improve mineral absorption, promote overall gut health, and aid in digestion by promoting the proliferation and activity of these microorganisms. Prebiotics can be ingested at any time of day as long as they are part of a balanced diet; however, they are best taken throughout the day. Probiotics, on the other hand, are live microorganisms that can be found in supplements and dairy products like yogurt, and cabbage. These good bacteria and yeasts colonize the gut, supporting a variety of biological processes, such as immunological response and digestion, and fostering a healthy microbial habitat. While the best time to take probiotics is dependent on the person and stress, some people find that taking them with meals helps them survive the acidic environment of the stomach, while others find that taking them on an empty stomach is beneficial. Maintaining a healthy gut microbiota and general well-being can be greatly improved by knowing the differences between these two entities and how best to use them.

KEYWORDS
Prebiotics, probiotics, gut health, digestion, beneficial bacteria, fermented foods, microbial environment, dietary fibers, live microorganisms.

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INTRODUCTION

In the past ten years, probiotic and prebiotic demand has increased globally. The ignorance of patients and medical professionals on the use of probiotics and prebiotics is a significant problem (Sanders et al., 2019). According to statistics examining hospitalized patients' perspectives, understanding, and usage of probiotics and prebiotics, patients take probiotics (56%) and prebiotics (33%) for health purposes. However, few know the item's proper usage (Betz 2011). The phrase "gut microbiota" describes the community of bacteria that may amount to 100 trillion in the gastrointestinal tract. Studies on the impact of chemicals that may positively modify gut microbiota, such as probiotics and prebiotics, are being carried out due to the possible benefits of the microbiota to host wellbeing. Probiotics and prebiotics may influence immunological response, gastrointestinal absorption and metabolic processes, and cholesterol metabolism, among other gut microbial activities (Gareau et al., 2010). The World Health Organization (WHO) states that probiotics are live bacteria that, when consumed in the right amounts, can help the host. Probiotic efficacy and usefulness are dependent on the specific strain utilized and its ability to survive and colonize the gastrointestinal tract (Cani, 2018). Probiotic use may aid in the treatment of several conditions, such as necrotizing enterocolitis, antibiotic-associated diarrhea, ulcerative colitis, and irritable bowel syndrome, according to new research (Shen et al., 2014).

A prebiotic is a material that has undergone specific fermentation, altering the gut microbiota's composition and/or activity to have the intended effects on the host's health. While there isn't as much data to support prebiotics' advantages

for these conditions, those with gastrointestinal disorders may benefit from them the most (Scaldaferri et al., 2013). While some evidence does support the use of probiotics and prebiotics as dietary supplements for specific illnesses, not all studies support their use as supplements (Szajewska et al., 2012). The adaptability and efficiency of the gut microbiota are important characteristics. A healthy gut community assists in immunological control, homeostasis maintenance, and defense of the host against invasive microbes (Coyte et al., 2015). Atopy, metabolic syndrome, colon cancer, and inflammatory intestinal disorders are just a few of the inflammatory, pathogenic, and metabolic illnesses that can be supported by a gut microbiota that is disturbed by dietary changes, antibiotic use, aging, or infection (Walker and Lawley, 2013). The makeup and/or function of the gut microbiota can be altered by several techniques, including intestinal microbiota transplants, the use of probiotics and other live microorganisms, and the administration of non-digestible dietary supplements like prebiotics (Deehan et al., 2017).

Probiotics

Live bacteria known as probiotics enhance the health of the host when given in the right amounts. (Hill et al., 2014). Probiotics contain a wide variety of microorganisms. Therefore, it's critical to keep in mind that they are classified according to their genus, species, and strain names. Using *Lactobacillus rhamnosus,* a well-researched probiotic, as an example. The strain identifier is GG, the genus is *Lactobacillus,* and the species is *Rhamnosus*. It takes all three elements to recognize a probiotic. The reader can connect a particular strain to papers outlining safety evaluations and health advantages by using the complete name. Furthermore, even within the same species, the health benefits of one strain may not translate to another, even while shared processes between strains occasionally lead to comparable clinical results (Ritchie and Romanu, 2012).

Most species of Lactobacillus and Bifidobacterium can produce organic acids, such as lactate and acetate. The digestive system and other organs may gain from the organic acids that colon microorganisms create in several ways. By preventing the growth of dangerous bacteria and promoting the growth of advantageous gut microbes, they significantly contribute to the improvement of the gut environment. Butyrate is produced as a result, and intestinal epithelial cells are powered by it (Sanders et al., 2018).

Depending on the product category and region, probiotic product quality might vary greatly, including dependability and accuracy of the label. The regulatory frameworks controlling the manufacture of probiotics and the conditions for claim substantiation are not yet harmonized globally (O'Toole et al., 2017). A panel of probiotic specialists has been assembled by the US Pharmacopeia (Rockville, Maryland, US) to provide advice and guidelines on quality-related matters, including the recognition, counting, and standards for contaminating bacteria about probiotic dietary supplements (Flach et al., 2018). Probiotics have the potential to significantly impact the gut ecosystem's functioning to enhance health and nutritional condition (Versalovic, 2013).

Source of Probiotics

The principal sources may originate from human sources, including human breast milk or the large or small intestine. It could also come from animal sources or other dietary biotopes, such as fermented foods or raw milk. High levels of adherence to the human intestinal epithelial barrier set apart probiotic strains isolated from human microflora from other strains, perhaps increasing their safety. It has not been demonstrated that certain bacteria and germs found in probiotic-containing dietary goods and supplements are safe for ingestion by humans or other animals (Zommiti et al., 2020). Probiotic dietary supplements and foods contain bacterial strains that may be important participants in the following processes: cholesterol levels and metabolism; colonization in the gastrointestinal, respiratory, and urogenital tracts; lactose metabolism; calcium absorption and vitamin synthesis potential; the reductive potential of yeast and vaginal infection; alleviation of constipation and diarrheal disorders; reduction of gastritis and ulcers; alleviation of acne, rash faces, and skin issues; and the production of natural antimicrobials (Ricci et al., 2017).

Probiotics Action Mechanism

For the past 20 years, probiotic microbe research has progressed substantially, mostly in areas related to probiotic cultures' properties and selection criteria, potential uses, and direct and/or indirect benefits on human health (Carter et al., 2017). Probiotics are vital to the growth of the microflora that lives in the human gastrointestinal tract (GIT) because they maintain homeostasis or the optimum microbial equilibrium surrounded by pathogens and beneficial bacteria. These beneficial bacteria may aid in the native microbiota's recovery from antibiotic therapy by maintaining this equilibrium (Oelschlaeger, 2010). Probiotics also possess the extraordinary capacity to prevent harmful gut bacteria from doing their activities. Probiotics therefore have a great deal of potential to prevent food poisoning because they inhibit the growth of resistant pathogens such as *C. perfringens, Campylobacter jejuni, Salmonella enteritidis, Escherichia coli, multiple species of Shigella, Staphylococcus, Yersinia, Campylobacter coli, and Listeria* sp. (Saint-Cyr et al., 2017).

The research found that the synthesis of antimicrobial compounds, phagocytosis stimulation, resistance to colonization, anti-mutagenic effects, chemokine production, and impacts on enzyme activity and transport are some of the factors that influence the mechanism of action of probiotic bacteria (Zommiti et al., 2017). The basic theory underlying the health benefits of good bacteria, or "probiotics," has also been unraveled through extensive molecular, bioengineered, and genetic studies. These four mechanisms are closely linked to competition with pathogenic bacteria for nutrition and

adherence to the epithelium; host immunomodulation; and inhibition of bacterial toxin synthesis. Microbial antagonism is achieved through the use of antimicrobial agents (Zommiti et al., 2018).

Probiotic Role in Gut Barrier Function

The mucus layer, the epithelium lining the mucosal tissues, and the immune cells at the sub-epithelial level make up the mucosal barrier. Therefore, by positively impacting barrier robustness, alteration at any of these levels can alter disease states. At the molecular level, epithelial cells play a major role in mediating the barrier effect (Hyland et al., 2014). They communicate with immune cells underneath and with the body as a whole using signaling chemicals. The gut lumen sends chemical signals to them as well. Many gastrointestinal disorders, including irritable bowel syndrome, viral enterocolitis, celiac disease, and inflammatory bowel disease (IBD), are significantly impacted by the gut barrier (Blaut and Klaus 2012). Therefore, choosing probiotic strains that can fortify the gut barrier seems like a pertinent approach with a wide range of effects on many illnesses. *L. rhamnosus* GG or the probiotic blend may interact directly with intestinal epithelial cells and preserve the integrity of the epithelial barrier, according to several experiments conducted on Caco-2 intestinal cells and animals. The ability of LGG to stay in the GIT has been associated with the in vivo creation of pili with a mucus-binding domain (van Hemert et al., 2013).

If these outcomes are repeatable in vivo, they might aid in maintaining homeostasis and excluding pathogens. Additionally, it shows the different ways that different probiotic strains affect the same tissue, in this case, the epithelium all of which help to maintain the barrier effect. In a therapeutic environment, lactobacillus plantarum is administered to the small intestines of healthy persons. (Lebeer et al., 2012. As a result, there are structural alterations in epithelial tight junctions as well as an increase in the tight junction-specific proteins occludin and zonula occludens-1. The *L. plantarum* strain yielded results that are pertinent to an intervention in the corresponding subjects because several diseases, including IBD, IBS, and celiac disease, are linked to increased intestinal permeability to macromolecules and a loss of tight junction integrity (Liu et al., 2011).

Treatments with different strains and species of *Lactobacillus,* such as *L. plantarum, L. acidophilus, L. casei*, and *L. rhamnosus*, result in different gene-regulatory networks and pathways in the human mucosa. One of these pathways is the up-regulation of IL-1b, an activator of the NF-kB signaling cascade, which may stimulate the transcription of genes linked to B-cell maturation and lymphogenesis, ultimately improving the function of the barrier (Van Baarlen et al., 2011). Differential expression of genes involved in wound healing and repair, angiogenesis, the IFN response, calcium signaling, and ion homeostasis affect the vascularization and feeding of epithelial cells. Furthermore, the changes in transcriptional networks that have been discovered bear resemblance to the responses that bioactive substances and drugs evoke, indicating a novel use of probiotics in conjunction with therapeutic and/or preventive nutritional regimes (Wang et al., 2014).

Security of Probiotics

Probiotic bacteria are generally recognized for their safety, having been granted the World Health Organization's GRAS (Generally Regarded as Safe) designation (WHO). The primary factor in the choosing of probiotics is safety for human health. According to Snydman, probiotic strains should be identified by their low level of antibiotic resistance and absence of virulent character (Hanchi et al., 2018). An update on safety concerns and the probiotic potential of the genus *Enterococcus.* The usage of Lactobacilli and Bifidobacteria strains has historically resulted in an excellent safety record for these helpful germs. There is little field research and experience with other bacteria species that are utilized as probiotics. From a conventional frame of view, host susceptibility is never completely safe. While looking for new potential probiotic microorganisms, it might be challenging to identify novel bacterial strains and even new genera with more specialized traits and/or greater potential for good health. A thorough examination, risk-benefit analysis, and safety assessment are required when introducing novel bacteria. In general, probiotics are safe (Landete, 2017). Care should be taken to prevent any potentially harmful effects, while there have been sporadic instances of bad outcomes. Probiotics may theoretically result in four different kinds of side effects, according to a 2002 report jointly released by the Food and Agriculture Organization (FAO) and the World Health Organization (WHO): (i) systemic infections; (ii) detrimental metabolic activities; (iii) excessive immune stimulation in susceptible individuals; and (vi) potential gene transfer (Bull et al., 2013).

Probiotics are becoming more and more popular, and this growth is due to both the diversity of probiotic products available and the introduction of new strains of probiotics. Future studies and research should give a more thorough description of the probiotic microbe under investigation, including its genus, species, and strain level, as well as the daily dosage and duration of treatment (Zoumpopoulou et al., 2018). The three key stakeholders that need to get over the challenges surrounding probiotics are the general public, healthcare professionals, and probiotic manufacturers. They should focus on worldwide regulations and standards and provide recommendations for strain-specific evidence-based therapy (de Melo Pereira et al., 2018).

Pre-biotics

The prebiotics theory was first put forth by Glenn Gibson and Marcel Roberfroid in 1995. "A non-digestible food ingredient that selectively stimulates the growth and/or activity of one or a limited number of bacteria in the colon, thereby improving host health," according to the definition of prebiotics. For more than fifteen years, this definition stayed mostly unchanged (Trompette et al., 2014). A restricted set of carbohydrate group molecules, including lactulose, GOS, and

short- and long-chain β-fructans [FOS and inulin], can be categorized as prebiotics according to this criterion. "A selectively fermented ingredient that results in specific changes in the composition and/or activity of the gastrointestinal microbiota, thus conferring benefit(s) upon host health" is the definition given to "dietary prebiotics" at the 2008 International Scientific Association of Probiotics and Prebiotics (ISAPP) 6th Meeting (Gibson et al., 2010).

While not all prebiotics originate from carbs, the two following characteristics can be used to differentiate between prebiotics that do and those that don't: Fibers are defined as carbohydrates that have three or more degrees of polymerization (DP), and they can't be hydrolyzed by the small intestine's natural enzymes. Remember that it's not required for the fiber to be soluble or fermentable (Slavin, 2013). Cross-feeding, or when one species eats the products of another, was found to enhance the prebiotic effect in 2013. This suggests that the term "selectivity" used in the definition of prebiotics may not be entirely accurate. Although there is ongoing debate on the precise definition of prebiotics (Hutkins et al., 2016).

Sources of Pre-biotics

Prebiotics are vital for human health. Some dietary food products in which they naturally occur are asparagus, sugar beet, garlic, chicory, onion, Jerusalem artichokes, wheat, honey, bananas, barley, tomatoes, rye, soybeans, human and cow's milk, peas, beans, and, more recently, seaweeds and microalgae (Al-Sheraji et al., 2013). Because of their poor food content, they are made industrially. The main components utilized to create prebiotics include lactose, sucrose, and starch. The industrial synthesis of prebiotics has been the subject of numerous pertinent studies, the majority of which fall into the GOS and FOS categories (Varzakas et al., 2018).

Mechanism of Pre-biotics:

Prebiotics alter the makeup and activity of the gut microbiota by giving these microbes sources of energy. Phylogeny indicates that distant bacterial species can frequently ingest a certain prebiotic. Additionally, a functional metagenomics technique was recently published on it. This technique identifies genes from a human microbiota metagenomic collection that break down various forms of prebiotics using a heterologous host, such as *Escherichia coli* (Cecchini et al., 2013). Several species' clones are capable of fermenting FOS, GOS, and xylooligosaccharides (XOS). Among these organisms are Firmicutes, Bacteroidetes, and Actinobacteria. However, some research indicates that a certain prebiotic might be broken down by a particular species.

Two examples of this include the fermentation of fructans and starch by *Bifidobacterium* spp. (Ze et al., 2012). Chain length is another key characteristic that helps toidentify species that can ferment a certain prebiotic. Cross-feeding occurs when complex prebiotic ferments and produces a byproduct that serves as a substrate for another microbe. Resistance starches can be broken down by *Ruminococcus bromii*, and the fermentation products that are produced can be utilized by several species (Scott et al., 2013). Conversely, certain items might negatively impact other species. Prebiotics also can change the environment in the stomach. As mentioned previously, the main products of prebiotic fermentation are acids, which cause the stomach's pH to decrease. Research has demonstrated that a single unit shift in the gut pH from 6.5 to 5.5 can alter the quantity and makeup of the gut microbiota. Changes in pH can affect the populations of species that are sensitive to acid, like Bacteroids, and can also encourage Firmicutes to produce butyrate. The "butyrogenic effect" is the name given to this mechanism (Scott et al., 2014).

Safety of Pre-biotics

Prebiotics are thought to have no negative or potentially lethal side effects. Both polysaccharides and oligosaccharides are indigestible to intestinal enzymes. The gut bacteria carry them to the colon, where fermentation takes place. Thus, the primary reason why prebiotics have adverse consequences is because of their osmotic actions. In this instance, prebiotic users may experience bloating, cramps, gas, and osmotic diarrhea as adverse effects (Svensson and Håkansson 2014). One factor that affects how their detrimental effects appear is how long the prebiotic chain is. It's noteworthy to notice that shorter chain-length prebiotics can be more detrimental. One reason for this phenomenon could be that longer-chain inulin molecules ferment later and more slowly in the distal colon, while shorter-chain inulin molecules are mainly digested and ferment more quickly in the proximal colon (Davani-Davari et al., 2019).

Its safety profile can be influenced by the prebiotic dose in addition to chain length. For instance, osmotic diarrhea and flatulence may result from large dosages of prebiotics (40–50 g/day) and low dosages (2.5–10 g/day), respectively. Note that for prebiotics to be helpful to human health, a daily consumption of 2.5–10 g is necessary. This implies that prebiotics may have mild to moderate adverse effects if used as directed. The majority of prebiotic products on the market contain 1.5–5 g of probiotics per serving (Garg et al., 2018). As potential replacements or additional therapies (synbiotics), prebiotics may provide similar safety concerns as probiotics. Particularly in those with severe malnutrition, a compromised intestinal epithelial barrier (such as severe diarrhea or NEC), or a marked immunodeficiency (e.g., HIV, cancer, transplant). Prebiotics provides a high safety risk of bacteremia, sepsis, or endocarditis. Surprisingly, relevant clinical trials that have solely examined prebiotics have not considered or at least not recorded these potential adverse effects (Tsai et al., 2019).

Difference between Prebiotics and Probiotics

Probiotics are live bacteria or yeast that are consumed in large enough amounts to provide health benefits. These microorganisms naturally resemble the beneficial bacteria present in the human stomach. Probiotics boost immunity, facilitate better digestion, enhance nutritional absorption, colonize the stomach maintain a balance of healthy bacteria, and even promote mental health. Probiotics are frequently found in foods including several yogurt varieties, kefir, sauerkraut, kimchi, miso, tempeh, and other dietary supplements (Quigley, 2019).

Prebiotics are indigestible fibers or substances that provide nourishment for probiotics and other advantageous microorganisms in the gastrointestinal tract. Unlike probiotics, which are real living organisms, prebiotics are substances that promote the growth and activity of helpful bacteria in the stomach. Prebiotics are transported undigested down the digestive tract to the colon, where the local bacteria ferment them. During this fermentation process, short-chain fatty acids are created, including butyrate, acetate, and propionate, which provide energy to the lining cells of the colon and maintain the health of the gut environment. Along with other fruits and vegetables, whole grains, legumes, apples, bananas, onions, garlic, and various nutritional supplements are common sources of prebiotics. Galacto-oligosaccharides (GOS), fructo-oligosaccharides (FOS), inulin, and other prebiotic fibers (Brüssow, 2019).

Best Time of use:

By protecting the bacteria from stomach acid and bile salts, probiotics eaten with food increase the likelihood that the bacteria will enter the intestines alive and begin to function. Oftentimes, timing consistency matters more than the precise time of day. Choose a time that works for your schedule and stick to it each time if you want to get the most out of it (Gu and Roberts, 2019).

By taking prebiotics before meals, you can encourage the growth of beneficial bacteria in your stomach and enhance their fermentation process during digestion. Many different foods, such as whole grains, fruits, and vegetables, contain prebiotics (Cunningham et al., 2021).

Conclusion

In conclusion, probiotics and prebiotics are equally important for maintaining gut health, yet they function differently and offer distinct advantages. Live bacteria known as probiotics can improve gut microbiota balance and replenishment when taken in sufficient quantities. They can strengthen the immune system, promote better digestion, increase nutritional absorption, and enhance general well-being. Probiotics work best when taken with meals, right before bed, or right after taking antibiotics. Indigestible fibers or compounds known as prebiotics nourish the beneficial bacteria in the stomach. By promoting the development and activity of probiotics and other beneficial bacteria, they maintain a healthy gut environment. Prebiotics can be consumed throughout the day by eating foods high in prebiotics, or they can be taken before meals. Probiotics and prebiotics can both offer complete support for gut health and general well-being when added to your routine. Timing and consumption must be consistent, but the ideal strategy may vary depending on personal tastes and lifestyle choices. Speaking with a healthcare provider can provide tailored advice on the best ways to use probiotics and prebiotics, especially for those with certain health issues or illnesses.

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