

PREBIOTICS AND PROBIOTICS



Course Name: Clinical Nutrition

Course Code: 0521422

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INTRODUCTION

- ✓ Multiple studies have confirmed their beneficial effects on various aspects of gastrointestinal (GI) tract function, as well as in **treatment and prevention** of certain disorders, although much remains to be elucidated.
 - ✓ A basic understanding of GI microflora characteristics, is recommended for health care providers to assist patients in the selection or use of appropriate prebiotic and probiotic products.
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- **Prebiotics**

- **Substrates selectively utilized** by host microorganisms—the enteric microflora—to support gut health,
- Food components (such as fibers) that are not digested by the human body but are used as food by the GI bacteria to promote their growth and activity.

- **Probiotics**

- **Nonharmful living microorganisms** also recognized to have beneficial health effects when ingested in sufficient amounts.
- Living microorganisms found in foods and dietary supplements that, when consumed in sufficient quantities, are beneficial to health.

The Gut Microbiota

- The microflora of the GI tract is known as the enteric microbiota or flora.
- The GI tract hosts approximately 300–500 species of commensal bacteria, with concentrations of up to 10^9 colony-forming units (CFU)/mL in the terminal ileum and 10^{12} CFU/mL in the colon.
- The enteric microbiota may be far more diverse than has been recognized to date. Only within the past 20 years or so have the GI microbiota and its role in human health and disease been explored in earnest. The extent of microbiota influence on health maintenance and disease development appears to be significant.
- Although understanding of the complex interactions between the GI tract and enteric microbiota remains incomplete, the paradigm of human biology is shifting to embrace the ecology of the individual, including processes of transgenomic and epigenomic co-metabolism with that person's unique GI microbiome.
- More recently, a view of the microbiome as a “superorganism” in a symbiotic relationship with the gut mucosa has been advanced.

Some of the most frequently studied and recommended probiotics include:

The *Lactobacillus* genus, including:

- ✓ *L. acidophilus*
- ✓ *L. rhamnosus*
- ✓ *L. casei*
- ✓ *L. plantarum*

The *Bifidobacterium* genus, including:

- ✓ *Bifidobacterium longum*
- ✓ *Bifidobacterium breve*

PREBIOTICS

- Prebiotics support the enteric microbiota and typically are substances fermented in the colon.
- As noted, they are substrates that are selectively utilized by host microorganisms, conferring a health benefit.
- Some types of fiber act as prebiotics. The undigested fiber enters the colon and is fermented by bacteria, primarily bifidobacteria and lactobacilli.
- Fermentation products, including short-chain fatty acids (acetate, butyrate, and propionate) and lactate, produce an environment favorable to growth of these beneficial bacteria.
- **To be considered a prebiotic**, fiber must **selectively** stimulate the growth and/or activity of one or a limited number of health-promoting bacterial species residing in the colon and benefit the host

Sources and Intake of PREBIOTICS

- Inulin-type fructans (fermentable saccharides), including their **partial hydrolysis** product fructooligosaccharides (FOS), are the most common prebiotics.
- These substances are found in small amounts in asparagus, bananas, chicory (هندباء برية), Jerusalem artichoke, leek (بصل أخضر), onion, soy, and wheat.
- Inulin-type fructans are isolated from such sources and **added to foods** to attain concentrations contributing to prebiotic effects.
- **Other sources of prebiotics are** conjugated linoleic acid, polyunsaturated fatty acid, and human milk oligosaccharides.

Health Effects of PREBIOTICS

- Both inulin-type fructans and FOS significantly **increase bifidobacteria** in the human gut.
- **Doses vary greatly in studies.** The use of prebiotics generally **should not result in adverse effects such as abdominal distention and discomfort.**
- **Beneficial effects of prebiotics supported by some human data include** stool bulking and decreased constipation, better absorption of calcium and magnesium, reduced triglycerides in mildly hypercholesterolemic persons, and stimulation of bifidobacteria growth.
- **Studies using prebiotics for treatment or prevention of diarrhea** have yielded **conflicting** results, which may depend on the underlying disorder.
- Improved vaccine response, decreased GI infections, stimulation of intestinal hormonal peptides, clinical improvement in inflammatory bowel disease (IBD), and reduced tumor growth are other **possible benefits of prebiotics.**
- Some beneficial effects may be enhanced with **SYNBIOTICS**, a mixture of **both prebiotics and probiotics that together appear to improve health and well-being.**

PROBIOTICS

- **Probiotics** are nonpathogenic, living microorganisms that have a beneficial effect on the host when consumed in adequate amounts.
- These products **must withstand** the stresses inherent in processing, storage, and delivery without degradation, and the **probiotic microorganisms must survive** gastric acidity, bile acid lysis, and pancreatic enzyme digestion.
- **Lactic acid–producing bacteria**, especially those of the genera Lactobacillus, Bifidobacterium, and Streptococcus, are most often used in commercially available foods and for studies.
- Beyond early infancy, these microorganisms **do not permanently** colonize the GI tract and **must be ingested regularly in sufficient quantity to maintain their presence**.
- When such bacteria are present in adequate or optimal numbers, **colonization by pathogenic organisms is reduced and mucosal defenses in the GI tract are enhanced**.

PROBIOTICS - continued

Table 20–1 lists possible protective effects of probiotics and postulated mechanisms of action.

For health care providers attempting to interpret data in the clinical setting, caution is warranted:

- **Multiple species** and strains of common probiotic bacteria exist, and effects cannot be extrapolated across species or even across different strains.
- **Dosing** may explain variance in treatment response in published studies. **The optimal dose for a given probiotic is not known**; however, studies showing efficacy typically use a minimum of 10^7 – 10^{10} CFU per dose or 10^8 – 10^{10} CFU daily.
- ❖ In a dose-ranging study, the probiotic capsule dosage form used exhibited poor dissolution characteristics, leading to reduced probiotic efficacy at higher doses relative to that at lower doses. This finding demonstrates the **need to be vigilant** in choosing an appropriate probiotic formulation that has been studied in patients.

Table 20–1 Possible Protective Effects of Probiotics

Effect of Probiotic	Possible Mechanism(s)
GI Barrier Function	
Induce production of protective cytokines mediating EC regeneration and inhibiting Apoptosis	Action through TLRs; intestinal homeostasis and EC protection requires recognition of commensal bacteria by TLRs
	Induction of IL-6
Redistribute and increase expression of factors involved in maintaining EC tight junctions	Altered protein kinase C signalling
Counteract effects or inhibit production of inflammatory cytokines associated with increased EC permeability	IL-10 upregulation (regulatory cytokine)
	Reduced effect of TNF-alpha and INF-gamma
	Reduce TNF-alpha production
	Stimulation of IgA secretion

Table 20–1 Possible Protective Effects of Probiotics – continued 1

Effect of Probiotic	Possible Mechanism(s)
Antimicrobial Activity	
Inhibit growth of potential pathogens	Decreased luminal pH
	Production of bactericidal proteins (bacteriocins)
Inhibit adhesion of pathogenic bacteria to EC	Increased mucin production
	Reduced transepithelial resistance associated with binding of some pathogens
	Competitive exclusion of pathogens from EC surface binding sites due to nonspecific binding associated with the hydrophobic cell surface properties; mucus-binding pili enhance binding to mucosal surface
	Binding to pathogenic microorganisms, thereby preventing interaction between the microorganism and EC surface
Influence production of cryptdins by Paneth cells	Antibacterial action of cryptdins
Alter virulence	Altered secretion of molecules influencing expression of genes controlling virulence

Table 20–1 Possible Protective Effects of Probiotics - continued 2

Effect of Probiotic	Possible Mechanism(s)
EC Inflammatory Responses	
Alter EC cytokine production	Downregulation of bacteria-induced protein kinase C and IL-6
	Inhibition of TNF-alpha-induced IL-8 production
	Downmodulation of genes associated with proinflammatory signal induction
	Attenuation of nuclear factor-kappa B activation

Table 20–1 Possible Protective Effects of Probiotics - continued 3

Effect of Probiotic	Possible Mechanism(s)
Lymphoid Cell	
Enhance antiviral activity	Inhibition of T-cell proliferation
	Induction of macrophages to express increased amounts of inflammatory cytokines and nitric oxide
	Stimulation of granulocyte colony-stimulating factor release by macrophages
	Increased natural killer T-cell activity
Activate macrophages	Increased antigen presentation to B lymphocytes
Regulatory T-Cell Induction	
Increase CD4+ (regulatory) T cells with cell-surface TGF-beta (regulatory cytokine)	Monocyte-derived dendritic cells inducing IL-10 production by T cells

Key: **EC** = Epithelial cell; **GI** = gastrointestinal; **IgA** = immunoglobulin A; **IL** = interleukin; **INF** = interferon; **TGF** = transforming growth factor; **TLR** = Toll-like receptor; **TNF** = tumor necrosis factor.

Sources of Probiotics

- Many traditional foods are **fermented** by bacteria and contain high concentrations of lactobacilli.
- Corn, cassava, millet, leafy vegetables (cabbage), and beans commonly serve as basic foodstuffs for fermentation.
- A few fermented foods are occasionally eaten in the United States, such as brined olives, kimchi (Korean fermented cabbage), miso, sauerkraut, and tempeh, **however, the major food source of probiotic bacteria is “cultured” dairy foods.**
- Many major brands of yogurt contain probiotic bacteria, although viable cultures are not required for yogurt in the United States, and labels do not list the number of viable probiotic organisms.
- **Liquid yogurt drinks (kefir) and cultured fluid milk**, such as sweet acidophilus milk and buttermilk, can contain variable amounts of viable organisms; however, most provide adequate amounts (10^8 viable organisms per g of product).
- With the expanding interest in probiotics, new products with added probiotic organisms are appearing regularly, sometimes with limited or no data on the organisms contained or on the efficacy of the combinations used.

Health Effects of Probiotics

- Interest in probiotics has increased dramatically in the past decade.
- Research covers a wide range of disease states and subjects of all ages (premature neonates to the older adult).
- Clinical data, for the most part, are preliminary; however, moderate-quality evidence supports the use of probiotics to prevent or treat certain gastrointestinal disease states, as well as metabolic and respiratory syndromes, and to modify cardiovascular risk factors.
- **Results may be influenced by the dose, frequency of dosing, and/or organisms in any specific probiotic product.**
- Most studies have been small and have used isolated bacteria (classified as nutritional supplements) or foods with added probiotics, rather than foods that naturally contain the beneficial bacteria.