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Health Connections
LINKING NUTRITION RESEARCH TO PRACTICE

PROBIOTICS, PREBIOTICS AND SYNBIOTICS:

Evolving Science and Emerging Products

Introduction

The buzz surrounding probiotics has become a roar.[1] Probiotics (healthful bacteria), prebiotics (that provide food for probiotics) and synbiotics (the combination of prebiotics and probiotics) are hot areas in research, clinical practice and the commercial global marketplace.

This issue of *Health Connections* reviews evidence of the health benefits of these food components and suggests ways health professionals can craft food-choice recommendations while the science evolves around these emerging food products.

Living in a Microbial World

Human bodies are highly colonized with 10^{14} microbial cells, concentrated throughout the alimentary canal, but also in the vagina and on skin. Intestinal microbes are important in the development of the post-natal immune system and in acquired immune response and inflammation. The human and microbial cells located in the intestine keep in continuous communication with the rest of the body—interchanging information through nervous, metabolic and endocrine signals. The intestine provides a barrier to infection by pathogenic organisms. It digests and absorbs nutrients, ferments fibers and carbohydrates into short-chain fatty acids that inhibit the growth of harmful bacteria. Healthy intestinal flora can contribute to bowel regularity. Hence, the balance of intestinal bacteria can have systemic health benefits.

Probiotics

Probiotics are "live microorganisms, which when administered in adequate amounts, confer a health benefit on the host."[2] The microorganisms must be alive (they are not alive in products that are pasteurized after fermentation), present in high numbers (generally more than one billion per daily ingested dose), with scientifically established human health benefits as confirmed by legitimate research groups and published in peer-reviewed biomedical journals.[3]

Some probiotics belong to the genera *Lactobacillus* and *Bifidobacterium*, isolated from dairy products or from the human or animal intestinal tracts. There are theoretical risks when ingesting live organisms. A review of the risks of using probiotics in clinical practice suggests that, although *Lactobacillus* and *Bifidobacterium* probiotics have an excellent overall safety record, they should be used with caution, particularly in immunocompromised clients.[4] Individuals who are immunocompromised should likewise inform their health care provider if they are using probiotics.

In the U.S., probiotics are available as:

- Conventional foods such as probiotic-cultured yogurt (e.g., ACTIVIA®)[5] (see footnote regarding product examples) and dairy drinks (e.g., DanActive™)
- Dietary supplements, pills or capsules (e.g., CULTURELLE®)
- Medical foods (e.g., VSL#3®) used under the supervision of a physician.

None currently are biological drugs for the treatment, prevention, cure, mitigation or diagnosis of specific human disease conditions.

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SIDE BAR: Indicated Conditions for Probiotic Use

Proven benefits

- Acute rotavirus diarrhea and gastroenteritis
- Antibiotic-associated intestinal side-effects and diarrhea

Substantial evidence but additional proof required

- Food allergy and atopic eczema
- *Clostridium difficile* infections
- Acute respiratory infections among children in day care centers
- Vaginitis due to *Candida* and Bacterial Vaginosis
- Traveler's diarrhea

Promising areas in ongoing research

- Crohn's disease, ulcerative colitis and pouchitis (inflammatory condition in ileal pouch)
- Allergic conditions such as asthma
- Cystic fibrosis intestinal symptoms and respiratory episodes
- Dental caries and other oral health conditions
- Relieve constipation
- Irritable bowel syndrome
- Colonization by potential pathogens in Intensive Care Units
- Immunoadjuvants for potentiating oral vaccines
- Helicobacter *pylori* infections

Adapted from Gorbach SL. 2002.

Probiotic foods worldwide also include cheese, juice, infant formula and cereals.

Credible research on the effectiveness of probiotics should address the potential for a strong placebo effect (particularly in self-care products), include verification of probiotic survival and transit, define clinically meaningful endpoints in a well-defined population and have adequate statistical power.[1] See Side Bar for a list of conditions indicated for probiotic use categorized on the strength of the science ranging from proven to promising.

Probiotic effects are strain-specific. Clinical data must be evaluated as applicable to the strain tested and no one strain should be expected to provide all effects. For example, appropriate strains of lactic acid bacteria such as *Lactobacillus bulgaricus* can alleviate symptoms of lactose intolerance by providing bacterial lactase to the intestine.

Prebiotics

Prebiotics are non-digestible carbohydrates that survive digestion, enter the colon and selectively enhance the growth or activity of the body's own native beneficial bacteria. Prebiotics change the composition of fecal bacteria by 1) increasing beneficial bacteria—such as lactobacilli and bifidobacteria—that help modulate the activity of the immune system, and by 2) decreasing organisms such as clostridia and protein-degrading *Bacteroides*, which can produce tumor-promoters from metabolism of proteins that escaped digestion in the upper gut.[6] Because prebiotics are non-digestible carbohydrates, they help normalize bowel conditions due to an osmotic effect or other effects on indigenous microbes.

Prebiotics are found naturally in some plants or are produced enzymatically from sucrose, and often are used in dietary supplements. Major prebiotics in the U.S. include fructans and galacto-oligosaccharides (GOS). Fructans include inulin derived from chicory, whole grains, fruits (e.g., bananas), vegetables (e.g., onions, artichokes) or fructo-oligosaccharides (FOS) hydrolyzed from chicory or enzymatically from sucrose. GOS are made from lactose as a by-product of dairy-food processing. Unlike probiotics, which need to be in a viable state to maximize biological activity, prebiotics are not alive and can be formulated into a wide range of food formulations and products prior to cooking. In Japan and Europe, prebiotics are used in baked goods, desserts, breakfast cereals and infant formula, in addition to a wide range of dairy products.

There are limited experimental data on prebiotic use in humans, but some of the most extensively researched areas include antipathogen activities, increased uptake of calcium and magnesium from the colon and reduced levels of undesirable metabolites in the colon.[6]

Synbiotics

Synbiotics are probiotics including both probiotics and prebiotics. The commercial application of synbiotic products is in its infancy but offers the potential to develop prebiotics targeted at specific probiotic strains to optimize health benefits.[6]

Current Status

Research on probiotics, prebiotics and synbiotics is promising. However, further research is needed to substantiate preventive and therapeutic health benefits, mechanism of action, optimal intake, duration of treatment, selection of specific probiotic strains for a targeted outcome and mode of delivery. In the meantime, health professionals can tailor nutrition guidance by matching products with a specific strain for a client's specific condition or by offering guidance about these products as components for healthy diets in general.

PRACTICE POINTS FOR THE HEALTH PROFESSIONAL

- Encourage clients to consume dairy-based probiotics to help them maintain a nutrient-rich diet (high in calcium, protein, vitamins and minerals) that contributes to their overall health needs.
- Query clients on current probiotic use to determine if the product used matches the purpose for which they are taking it. Consider a client's condition (e.g., whether they are taking antibiotics, traveling—especially internationally, if they are elderly or immunocompromised) and be prepared to suggest specific probiotic strains, species, levels and frequency of consumption to provide benefits. Contact manufacturers directly for this information if necessary.
- Follow up with clients regarding compliance, symptom relief and other outcomes. Allow at least several weeks to assess a product. Be pragmatic; products may or may not benefit specific clients. If one product isn't working, another product containing different strains or species of probiotics or different doses may be better for that particular individual.
- Stay current with the research through symposia, scientific reviews and websites of professional, health and regulatory organizations.

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Q. Why are probiotic food products primarily and traditionally dairy foods?

A. When consumers think of 'beneficial bacteria' or 'live active cultures,' they think of fermented dairy products such as yogurt or kefir. Bacteria in many other contexts do not have such a positive image for consumers. Fermented dairy products are one of the few foods that are still a source of beneficial live bacteria. Furthermore, dairy products fit consumers' image of generally healthy foods because of their high nutrient profile, especially calcium and protein. This image coincides nicely with the healthy image of probiotics. Dairy products can be good for delivering probiotics, since they help neutralize stomach pH and increase the chance of the probiotic traversing the stomach and small intestine alive. Many dairy products have a short shelf life and require refrigeration—factors that encourage probiotic survival in the product. Dairy products and other healthy foods augmented with probiotics can increase compliance compared to supplements, which may not be as tasty or fit into daily routines.

Q. How can consumers evaluate the effectiveness of probiotic food products?

A. The best way a consumer can evaluate effectiveness of a probiotic food product is by trying it for several weeks and seeing if any benefits result. At present, the quality of probiotic products available to consumers is mixed. Products are required to be labeled in a truthful and not misleading fashion, but unfortunately, the labels on many products are either inaccurate or tell little about the probiotic and its benefits. Products formulated by responsible companies contain strains that have been properly characterized, are identified on the product label or accompanying information to the strain level, have been verified to impart a health benefit and contain the needed level of viable microbes through the end of shelf life. Manufacturers often provide a toll-free number or website with additional information that is not on the label and consumers should be encouraged to seek information from the manufacturer.

Currently in the U.S., there are no authorized health claims for probiotics. Structure/function claims such as "strengthens the body's natural defenses" or "promotes a healthy digestive system" appear on labels and in other forms of marketing and must be truthful and not misleading.

Q. How should health professionals approach the topics of prebiotics and probiotics with consumers?

A. Health professionals should position prebiotics and probiotics as a healthy addition to the diet. As with any hot topic in nutrition, help consumers set realistic expectations. Since probiotics may only temporarily colonize in the GI tract, these products may need to be used consistently for long-term benefits and their effects may not be immediate. The big challenge is to help consumers differentiate between the different prebiotic and probiotic food products. There may be a tendency to lump them all together, yet some are more effective than others depending on the target condition. Health professionals can find information at www.usprobiotics.org on suggested uses of probiotics including condition, strain, example commercial product and dose. (Note: From the home page, click "Products with Probiotics" then "Probiotic Products with Targeted Health Benefits.")

Q. What is the future in the U.S. regarding marketing and consumption of food products containing prebiotics and probiotics?

A. The success realized for these types of products in Europe and Asia will begin to be realized in the U.S. In addition to dairy-based probiotics, the number and types of products will grow with more foods being carriers of probiotics and prebiotics. As competition intensifies in the marketplace, companies providing responsibly formulated and promoted products will prevail: It will become clearer to the consumer what probiotic products contain and what benefits they can be expected to impart. Continued research will further support currently available products and will provide insights into new benefits, optimized probiotic/prebiotic delivery and better understanding of how and to what extent probiotics and prebiotics may benefit consumers. In the meantime, health professionals will need to be proactive in securing information directly from manufacturers in order to guide clients appropriately in their food choices.

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