

## Prebiotics, Probiotics, and Synbiotics: Their Therapeutic Role

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Dr. Cortney Mospan has no relevant financial relationships to disclose.

**Goal.** The goal of this lesson is to provide an overview of prebiotics, probiotics, and synbiotics, including definitions, mechanisms of action, and potential therapeutic benefits.

**Objectives.** At the completion of this activity, the participant will be able to:

1. define the terms *prebiotic*, *probiotic*, and *synbiotic* and the differences between these supplements;
2. recognize the mechanism of action of prebiotics, probiotics, and synbiotics in conferring benefit to patients;
3. demonstrate an understanding of conditions in which prebiotics, probiotics, and synbiotics have demonstrated therapeutic benefit;
4. identify patient populations that may benefit from prebiotic, probiotic, or synbiotic use; and
5. list key information to convey to patients, such as storage, appropriate administration, and contraindications for use.

### Background

Substantial interest has developed in health benefits that may be offered by probiotics. In recent years, this has expanded to prebiotics and synbiotics. As a result, these natural products have been introduced to the market both as dietary supplements and as functional foods.

These products are “between” foods and drugs, not truly qualifying as either. FDA does not regulate these products, and maintains a neutral position on them; however, they do periodically review food and supplement packages to ensure that disease-curing claims are not being made.

Since patients may learn about these products from TV advertisements, friends, family, or other providers, pharmacists must be prepared to counsel patients on these products. Patients will likely be unaware of the various prebiotic, probiotic, and synbiotic formulations available as dietary supplements or functional foods, and may not understand the differences in these products and their effects. Pharmacists can play a critical role in advising patients of potential therapeutic benefits, and should stress the importance of selecting a product that delivers the correct type of bacteria and appropriate dose; and stress proper storage. These products should also be of consideration when completing medication therapy management and medication reconciliation services for patients who may consume “functional foods,” such as yogurt and ice cream that have been fortified with one of these supplements.

Within the human gastrointestinal tract, there is a complex microbiota community composed of a plethora of bacterial species. These occur in a natural balance

with self-regulation; when disrupted, significant consequences and illnesses can result. Bacterial colonization progresses throughout life. Humans are practically germ-free at birth, but become colonized with *Escherichia coli* and *Enterococcus* just after birth, from the birth canal. As an infant is nursed, *Bifidobacterium* and *Lactobacillus* become dominant. After weaning, microbiota diversity expands. In adulthood, more than 2,000 species of commensal bacteria exist in the human body with the majority located in the GI tract. GI microbiota has been referred to as an *organ*. Colonization of the intestine is central to the homeostasis of the patient for proper health and development. This is a very complex network of microbiota that does not go unchecked, regulating itself into a proper balance preventing infection and disease.

As diets have changed significantly with the wide utilization of processed foods, there has also been an increase in chronic metabolic and autoimmune conditions. Within the intestinal microbiota, dysbiosis (microbial imbalance inside the body) can easily occur based on dietary intake. Bacterial composition within the body is associated with long-term dietary patterns with protein and animal fat, favoring different bacterial composition from carbohydrate intake. Commensal bacteria confer several benefits to their host, including metabolic, protective,

and nutritional. These benefits are provided through vitamin production, bile acid biotransformation, fermentation of non-digestible carbohydrates, barrier properties against opportunistic infections, maturation and stimulation of local and systemic immune functions, and control against epithelial cell proliferation. Dysbiosis can result in increasing gut permeability, resulting in disruption of both innate and adaptive immunity, moving the host toward a chronic pro-inflammatory response in the gut and elsewhere in the body. The GI tract is the largest immune organ in the body. Proper balance and location of the microbiota is critical. *Klebsiella* within the small intestine produces vitamins B12 and K; whereas in the lungs this microbiota causes pneumonia. Preliminary research has established an association between GI microbiota diversity, inflammatory markers, and health status of elderly patients. With increasing knowledge of the roles of microbiota within the body along with increasing patient interest, the use of prebiotics, probiotics, and synbiotics will likely continue to be studied as potential therapeutic treatments.

Research surrounding these supplements has been rapidly expanding within recent years; however, these studies are challenging to compare and use for broad evidence-based medical practice due to differences in probiotic species studied, clinical outcomes, and study populations. Further, many if not all, of the studies are plagued by small patient populations, shortcomings in study design and interpretation, and lower impact designs such as observational and retrospective designs.

## Prebiotics

These supplements were initially defined as “a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thus improves host health.” In 2008, the definition

was updated by the *International Scientific Association of Probiotics and Prebiotics* to “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.” Classification as a prebiotic requires demonstration that the food component/ingredient is resistant to host digestion, absorption, and adsorption processes. It must then be fermented by microflora that colonize the GI tract, and selectively stimulate the replication and activity of a specific bacterial species.

Initially thought to be confined to the GI tract, prebiotics provide microbiota support in the oral cavity, urogenital tract, and on the skin as well. Well accepted examples of prebiotics include inulin, pectin, fructo-oligosaccharide (FOS), galacto-oligosaccharides (GOS), and resistant starches. Inulin is a natural component of many fruits and vegetables, and is considered a soluble fiber that is almost completely digested in the colon. Inulin has been particularly associated with increased colonization by *Bifidobacterium* spp.

Prebiotic supplements are selectively fermented to result in microbiota composition and activity that confers benefit to the host; they act to restore balance and activity of microbiota within the host and may also provide immunomodulatory effects. Typical doses are 5 to 20 g; the larger the dose, the more diverse bacterial groups that are affected. Stimulation and growth of bacteria commonly surround *Lactobacilli* and *Bifidobacterium* strains (i.e., *L. plantarum*, *L. paracasei*, *B. bifidum*). Prebiotics are also thought to suppress the growth of pathogenic bacteria (*Clostridium perfringens*, *Escherichia coli*, *Campylobacter jejuni*, *Enterobacter* spec., *Salmonella enteritidis*, and *Salmonella typhimurium*). This benefit is thought to be conferred through lowering GI tract pH and creating an unfavorable growth medium.

Prebiotics also offer quality

**Table 1**  
**Mechanisms of Benefit for Probiotics**

- Competition with pathogenic bacteria for binding sites
- Inhibition of bacteria translocation
- Enhancement of mucosal barrier function
- Metabolic effects
- Immune system modulation
- Downregulation of inflammatory responses
- Modulation of gut motor and sensory responses

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improvement for food products, due to textural and gelling properties. A human diet rich in fruits, vegetables, and whole grains provides adequate prebiotic amounts to confer benefits that will be discussed in this lesson; however, with “nutrition transition” from rich in fruits and vegetables to high in fats and sweeteners, prebiotic supplementation may be needed. This transition has been associated with overweight/obesity, and chronic diseases (i.e., heart disease, diabetes, cancers). Interest in decreasing incidence in these conditions has sparked greater interest in the role of prebiotics in health. Dietary sources of prebiotics include artichoke, asparagus, bananas, barley, chicory, flour, garlic, leeks, onions, and wheat bran. Therapeutic benefits of prebiotics will be discussed in the synbiotics section to follow.

## Probiotics

As defined by the World Health Organization (WHO), probiotics are “live micro-organisms which, when administered in adequate amounts, confer a health benefit on the host.” This term is derived from the Greek language and means *for life*. Different strains of probiotic bacteria exert differing therapeutic effects based on their enzymatic activities and specific capabilities. Thus, when recommending a probiotic for use in a specific condition, pharmacists must recommend

strains with evidence for that condition. Within the same species of organism, different strains can have differing therapeutic effects (i.e., *Lactobacillus acidophilus* does not confer the same benefits as *Lactobacillus rhamnosus* strain GG [LGG]). Mechanisms of therapeutic action are described in Table 1.

Providers must follow the FAO (Food and Agriculture Organization)/WHO guidelines when recommending probiotics and in evaluating clinical trial data for these products. Probiotic strains are at least identified by their genus (i.e., *Bifidobacterium*) and species (i.e., *infantis*) and sometimes a more delineated strain (i.e., 35624). The only time in which individual strain identification is not necessary for application is when there is robust clinical evidence that the health benefits desired are induced by multiple strains (i.e., increase in lactose digestion is induced by multiple microbiota).

**Allergies.** Consumption of probiotics by women during pregnancy has growing evidence supporting reduced incidence of allergic conditions of their children during infancy. Like many trials, these are generally small studies; however, a robust study of 41,000 mothers in Norway found that children of mothers who consumed milk or yogurt fortified with *Lactobacilli* probiotics during pregnancy had a 7 percent reduced risk for eczema at six months of age, and a 12 percent reduced risk for hay fever at 18 months to three years. No difference in asthma incidence was found. A potential confounding variable in this study was that breastfeeding may have offered reduced allergy incidence from immunologic benefits. It is thought that probiotics consumed by mothers increase interleukin-10 levels, weakening allergic reactions in infants. Administration of LGG during pregnancy has demonstrated reduced eczema incidence as far as four years into childhood. Additional studies have found that infant formula fortified with LGG or *Bifidobacterium lactis* Bb-12

significantly reduced extent and severity of eczema in infants after two months of administration.

**Acute Diarrhea.** Use of probiotics in acute diarrhea has strong evidence from many clinical trials supporting their therapeutic benefit. Acute diarrhea is defined as more frequent bowel movements than usual for 10 to 14 days, and is frequently caused by viral infections, bacteria (i.e., *Escherichia coli*, *Clostridium difficile*), and parasites (*Giardia lamblia*). Evidence of benefit of probiotics is especially strong in rotavirus-associated diarrhea. A meta-analysis found a mean reduction in duration of 0.7 days, and decrease in stool frequency by 1.6 stools per day. *Lactobacillus reuteri* and LGG have the strongest evidence for benefit, whereas *Saccharomyces boulardii*, *Bacillus clausii*, and *Enterococcus faecium* SF68 have not shown significant benefit on duration or severity of diarrhea. While there is not support for symptom improvement, *Saccharomyces boulardii* has shown benefit in helping children regain weight faster following an acute diarrhea episode.

**Antibiotic-Associated Diarrhea (AAD).** Approximately 11 to 40 percent of children and 5 to 39 percent of adults treated with antibiotics (i.e., amoxicillin, cephalosporins, clindamycin) experience diarrhea. There is evidence that probiotics can prevent AAD; however, evidence is conflicting when specifically looking at *Clostridium difficile* infection (CDI). Two meta-analyses support the use of probiotics (*Lactobacillus rhamnosus* GG and *Saccharomyces boulardii*) in conjunction with antibiotics in an effort to reduce the frequency of diarrhea. Probiotics should be administered within 72 hours of symptom onset for benefit. When looking at CDI, a meta-analysis of 3000 patients found a reduced risk of CDI recurrence; however, this was only for *Saccharomyces boulardii* in conjunction with vancomycin or metronidazole. In conflict, both a systematic review of eight trials and a Cochrane Library review

conclude evidence does not support the routine use of probiotics for CDI prevention.

**Traveler's Diarrhea.** Traveler's diarrhea occurs in 20 to 40 percent of tourists who visit Africa, Central America, South America, and South Asia. It can also occur in avid hikers who may drink natural water supplies in their travels. Evidence has been mixed, likely due to a wide variety in strains studied. A meta-analysis found that probiotics containing *Saccharomyces boulardii* and *Lactobacilli* mixtures (*L. bulgaricus* and LGG) significantly prevented traveler's diarrhea. Strains that have not been found to be effective include *L. acidophilus* and *L. fermentum*. Probiotics must be taken prophylactically for two to three weeks to see benefit in traveler's diarrhea. Use of probiotics in traveler's diarrhea may allow for decreased need for prophylactic antibiotics.

**Irritable Bowel Syndrome (IBS).** IBS is a bowel disorder characterized by altered bowel habits in conjunction with abdominal pain, bloating, flatulence, or discomfort associated with a bowel movement. Bacterial overgrowth in the small intestine results in malabsorption of bile acids in the colon with increased fluid and mucus secretion as part of the disease pathophysiology. *Lactobacillus* and *Bifidobacterium* are involved in the conjugation of bile acids in the intestine, which allows a smaller amount to reach the colon, reducing diarrhea severity and abdominal discomfort.

Some studies suggest that probiotics offer benefit for bloating and flatulence associated with IBS; however, many of the trials have methodology concerns and more data are needed before probiotics can be recommended with confidence for patients with IBS. A meta-analysis of 20 trials did find that probiotics (*Lactobacilli* and *Bifidobacterium*) improved global IBS symptoms while reducing abdominal pain. Due to insufficient data, the analysis could not review individual symptoms. VSL #3 (*Bifi-*

*dobacterium longum*, *B. infantis*, *B. breve*, *Lactobacillus acidophilus*, *L. paracasei*, *L. bulgaricus*, *L. plantarum*, and *Streptococcus thermophilus*) has shown improved symptoms in IBS compared to placebo.

**Inflammatory Bowel Disease (IBD).** IBD is a collection of diseases causing lesions in differing parts of the GI tract, including ulcerative colitis (UC), Crohn's Disease (CD), and pouchitis. Imbalance in intestinal microflora is associated with these conditions. UC has high levels of enteroadhesive and enterohemorrhagic *Escherichia coli*, while CD has lower levels of *Bifidobacterium*. Overall, evidence supports the use of probiotics in either inducing or maintaining remission for these diseases. Like IBS, VSL #3 appears to be the most effective treatment selection when using probiotics in management of IBD conditions.

**Respiratory Infection.** Most respiratory infections are caused by viral pathogens, making antibiotic administration inappropriate. However, many healthcare providers receive pressure from their patients to provide antibiotics. As a result, there has been great interest in probiotic prophylaxis in place of antibiotic therapy in management of upper respiratory tract infections (URI). There have been several studies and subsequent systematic reviews and meta-analyses regarding this indication, but it is hard to make a conclusion due to great variances in probiotic strain, dose, and duration of therapy. While the literature shows varying symptom relief, pharmacists can feel fairly confident in recommending probiotics composed of either *Lactobacillus* (*L. acidophilus*, *L. gasseri* PA 16/8) or *Bifidobacterium* (*B. animalis subsp lactis* Bi-07, *B. longum* SP 07/3, *B. bifidum* MF 20/5) for prevention of URI. When looking at themes found in trials evaluated in a recent meta-analysis and systematic review, most trials point toward a five to 10 percent reduction in incidence, half a day to a full day of decreased symptom duration, and a significant reduc-

**Table 2**  
**Sample Probiotic Products**

Common Supplement Brand Name(s)	Probiotic Contents
Activia	<i>Lactobacillus</i> , <i>Bifidobacterium animalis</i> , <i>Streptococcus thermophilus</i>
Align	<i>Bifidobacterium infantis</i> 35624
DanActive yogurt	<i>Lactobacillus casei</i>
Culturelle	<i>Lactobacillus</i> GG (specific strain of <i>L. rhamnosus</i> )
Florajen	<i>Lactobacillus acidophilus</i>
Florastor	<i>Saccharomyces boulardii</i>
VSL #3	<i>Lactobacillus acidophilus</i> , <i>L. plantarum</i> , <i>L. paracasei</i> , <i>L. bulgaricus</i> , <i>Bifidobacterium breve</i> , <i>B. infantis</i> , <i>B. longum</i> , <i>Streptococcus thermophilus</i>

tion in symptoms in those who are sick. A trial looking at adults (aged 18 to 67 years) showed even more promising results shortening duration by almost two days along with decreased symptom severity. A similar study in children aged three to five years found decreased antibiotic use, reduction in days absent from childcare, and decreased fever, cough, and rhinorrhea. Evidence has consistently shown probiotics must preemptively be administered for three to six months to provide benefit. Once a patient is sick, household contacts should not be encouraged to use probiotics due to the longevity of administration that is needed for therapeutic benefit in this instance.

**Vaginal Infections.** *Lactobacilli* (primarily *L. crispatus* and *L. iners*) naturally compose the microbiome of the vaginal tract. These bacteria ferment sugar into lactic acid, lowering the pH of the vagina to prevent the growth of potential pathogens. During pregnancy, a hormonal shift occurs causing cells to stockpile glycogen, creating more supply for *Lactobacilli*. However, disruption in the *Lactobacilli* count can cause infections in non-pregnant women as well, resulting in urinary tract infections (UTIs), vulvovaginal candidiasis (VVC), and

pelvic inflammatory disease. Due to several study limitations (i.e., high attrition rate, recent antifungal use, lack of blinding), it is challenging to fully infer if probiotics can prevent recurrent VVC or other vaginal infections. However, varying *Lactobacilli* strains (LGG, *L. rhamnosus* GR-1, *L. fermentum*, *L. acidophilus*) administered in varying dosage forms (yogurt, vaginal suppository, vaginal solution) have shown promising initial results for improvement in vaginal symptoms and redness in patients with VVC, as well as further prevention of infection in patients with recurrent VVC.

**Product Selection.** When selecting a probiotic for a patient, pharmacists must take into account the bacterial strain, dose, and dosage form. Table 2 provides a brief sample of probiotic products available at the time of writing this lesson. Inadequate dosing may not provide the desired therapeutic effect; however, this remains challenging as the ideal dose is unknown. Doses of probiotics are measured in colony-forming units (CFUs), which is the number of living bacteria that form active colonies when cultured. Generally accepted dosages range from 107 to 109 CFUs. Due to the large vari-



ance in bacterial strains and studied dosages, it should be stressed to patients to follow the manufacturer's recommended dosage, even if different from previous probiotic supplements.

Probiotic supplements are available in multiple dosage forms including capsules, tablets, powders, and functional foods. Probiotics can be found in fermented dairy products (ice cream, yogurt), juices, soy products (miso), and plants (sauerkraut) – these may be added to the product or naturally present. When helping patients select a product, the pharmacist must be assured that the probiotic can withstand processing, storage, delivery, and can survive GI processes (gastric acidity, pancreatic enzyme digestion). Pharmacists should also consider patient desire to use fortified foods as a delivery mechanism for probiotics. Frozen yogurt or kefir are likely not good selections, since the probiotic bacteria die once the product is frozen.

## Synbiotics

These products are a combination of probiotic(s) and prebiotic(s) into one product, that must act in a synergistic manner, according to the United Nations Food & Agriculture Organization. Thus, this term should be utilized only when the product contains a prebiotic that selectively favors the probiotic's growth. Such an example would be a product containing oligofructose and a *Bifidobacterium* probiotic.

Synbiotics have arisen out of challenges of probiotic bacteria to colonize certain areas of the body, i.e., the oral cavity. In areas when probiotics have difficulty colonizing, synbiotics may be more effective. Typical doses of synbiotics vary greatly due to varying combinations of pre- and pro-biotics. Synbiotics are also growing in market share as the addition of a prebiotic to probiotic-containing dairy products has been shown to improve the survival of probiotic through their labeled shelf-life.

### Childhood Development.

A major area of research develop-

ment for synbiotics has focused on children's development, especially in children with failure to thrive (FTT). FTT is defined as a decrease in growth rate according to established reference growth charts, and is associated with developmental delay, emotional, and socioeconomic problems. A study conducted in Iran evaluated the impact of synbiotic formula composed of 100 mg FOS and 150 million CFUs of *Lactobacillus sporogenes* (Natures™ Only, Lactol). After six months of administration, increase in weight was significantly higher in the synbiotic group; however, significant growth improvements were not seen in height. Overall, evidence regarding synbiotic administration with various *Lactobacilli* strains is mixed in FTT.

**Constipation.** Inulin has been found to exert a mild laxative effect in elderly patients with constipation; however, benefits of synbiotics in functional constipation have been conflicting. Functional constipation can be caused by many factors, with limited improvement (30 to 40 percent) offered by therapeutic agents.

There is growing thought that intestinal microbiota may play a role in functional constipation, with imbalance having been identified in stools of patients with constipation. A recent clinical trial evaluated use of Psylllogel Megafermenti® (prebiotic psyllium fiber, and five probiotic *Lactobacillus* and *Bifidobacterium* strains) compared to maltodextrin for an eight-week intervention, evaluating increase in the number of bowel movements with normal consistency and volume and reduction in intestinal transit time (ITT).

The synbiotic group had statistically significant reduction in ITT and increase in normal stool consistency. While this shows promising results, caution for vast extrapolation to patients should be taken as there were only 39 patients in this study. A systematic review and meta-analysis evaluated the benefit of synbiotics in Irritable Bowel Syndrome (IBS) and Chronic

Idiopathic Constipation (CIC). No statistical significance was found in IBS symptom improvement, although only two trials were available for analysis. Synbiotics were found to provide significant benefit in CIC, with a number needed to treat (NNT) of five. This analysis was also limited to two trials.

**Infantile Colic (IC).** IC occurs in 10 to 30 percent of healthy infants during the first three months of life, and has remained a challenging condition to treat due to multifactorial causation (psychosocial, neuro-developmental, and other physiologic factors). The disease pathophysiology is poorly understood and remains a frustrating condition with maternal, family, and child adverse effects. Proposed mechanisms involve excessive crying due to painful intestinal contractions from excessive gas/swallowed air. IC may be a result of dysbiosis from disruption or immaturity of the immune system and epithelial barrier function, leading to colonic inflammation and motor activity dysfunction. The probiotic *L. reuteri* was found effective in reduction of crying in exclusively breast-fed infants, but these results cannot be generalized to all infants. Recent literature has expanded this preliminary evidence to evaluate a synbiotic milk (*Lactobacillus casei*, *L. rhamnosus*, *Streptococcus thermophilus*, *Bifidobacterium breve*, *L. acidophilus*, *B. infantis*, *L. bulgaricus*, and FOS) compared to placebo for 30 days. Treatment success (reduction in daily crying time >50 percent) was significantly higher in the synbiotic group. Symptom resolution (reduction in daily crying time >90 percent) was also higher in the synbiotic group, although this was not statistically significant. Like other trials, the promising results are limited by small study size (45 infants), but do show opportunity for relief in a difficult to manage condition.

Utility of synbiotics is challenging to demonstrate in healthy infants and toddlers, but improvements in health and wellbeing can

be associated with growth. A study was conducted in healthy infants and toddlers, administering milk enriched with *Bifidobacterium longum* (BL999), *Lactobacillus rhamnosus* (LPR), inulin, FOS, and long-chain polyunsaturated fatty acids (LCPUFA), comparing this to control milk. Investigators evaluated several health outcomes, including response to measles and Hepatitis A vaccines; motor, cognitive, and behavioral functions; weight gain between 12 and 16 months; bacterial stool counts; and other developmental markers. There was no difference in adverse effects between the treatment and control group. While most secondary outcomes did not find statistically different outcomes, weight gain/day was higher and statistically significant in the synbiotics group. The difference was approximately 1 g/day, which may limit clinical significance. However, this demonstrates safety and increased probiotic bacterial colonization through synbiotic use in children.

#### Metabolic Function in

**Adults.** A growing area of interest for synbiotic-enriched foods is in regulation of dietary intake and improved metabolic health. Within a clinical trial, patients were administered a control or synbiotic yogurt (containing *Bifidobacterium lactis* Bb12, *Lactobacillus acidophilus* La5, *Lactobacillus casei* CRL 431, and inulin). There was no change in GI transit time; however energy, fat, and protein intakes decreased with similar rates of GI side effects (i.e., abdominal discomfort, bloating, flatulence, etc.). This study provides support for a small body of evidence supporting inulin and oligosaccharides as satiety-promoting (increased sense of fullness) functional foods that may beneficially impact body weight.

#### Patient Counseling

While prebiotics, probiotics, and synbiotics generally have a favorable side effect profile, certain patient populations should avoid these products or should verify safety with their primary care pro-

vider before initiating use. According to the National Institutes of Health, patients with compromised immune systems (i.e., HIV/AIDS, cancer, chemotherapy, chronic steroid use, methotrexate) should not use these products due to risk for systemic infection. Safety is also unknown in elderly and pregnant patients, although these are growing areas of interest for these supplements. These patient populations should be carefully evaluated for safe use. All patients should check with their pharmacist or primary care provider before starting one of these products to ensure they do not interact with any of their medications.

Patients who are taking antifungals should not use *Saccharomyces* containing probiotics as *Saccharomyces* is a yeast, and antifungals will inactivate this product. Many products have special storage requirements. Florastor® should not be refrigerated, but a similarly-named probiotic, Florajen® must be refrigerated. VSL #3 also needs to be refrigerated, but is stable at room temperature for one week, allowing some patient flexibility for traveling. Both Align® and Florastor® can be sprinkled on cold food or drink. Align® should be avoided in patients allergic to soy and milk.

When co-administered with antibiotic or antifungal therapy, administration of these agents must be separated by at least two hours. Prebiotic products may be especially likely to cause mild GI upset, as these are types of fibers. Patients should be made aware of this potential side effect and counseled that gastrointestinal adverse effects can be minimized if the dose is slowly titrated up. These supplements should not be used past their expiration date and may have limited utility close to their expiration due to bacterial life only guaranteed until that expiration date. Patients should also be made aware that most benefits require regular ingestion of sufficient quantity; patients must be prepared to take these daily or may need to plan ahead by several

weeks or months when attempting to prevent infectious diseases. Travel and diet are natural disruptors of microbiota balance, and patients should be instructed on this as well.

#### Summary

The field of prebiotics, probiotics, and synbiotics is rapidly evolving and increasing in popularity. Overall, these supplements appear to cause few potential adverse effects, and have preliminary evidence of benefit in a multitude of conditions. However, most evidence is limited in application due to small study size, design flaws, or lack of homogeneity in dose, bacterial strain, formulation, etc., making it challenging to arrive at an evidence-based recommendation for patients. Pharmacists should always remember that evidence is strain-specific. Additional information can be found at the National Institutes of Health National Center for Complementary and Integrative Health (<http://nccih.nih.gov/health/probiotics>) and US Probiotics (<http://cdrf.org/home/checkoff-investments/usprobiotics>).

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## Prebiotics, Probiotics, and Synbiotics: Their Therapeutic Roles

- Inulin is an example of a:  
a. prebiotic.                      c. synbiotic.  
b. probiotic.
- Which of the following probiotics should be avoided in patients allergic to soy and milk?  
a. *Lactobacillus acidophilus* (Florajen®)  
b. *Saccharomyces boulardii* (Florastor®)  
c. *Bifidobacterium infantis* 35624 (Align®)
- All of the following can use probiotics EXCEPT patients with:  
a. type 2 diabetes.              c. cancer.  
b. heart failure.                d. cochlear implant.
- Antifungals can diminish the therapeutic benefit of which of the following probiotic strains?  
a. *Bifidobacterium breve*  
b. *Saccharomyces boulardii*  
c. *Lactobacillus rhamnosus*
- Which probiotic strain prevents bacterial overgrowth in the small intestine?  
a. *Streptococcus*                c. *Saccharomyces*  
b. *Lactobacillus*
- Which of the following probiotics appears to be the most effective treatment in the management of IBD?  
a. Align                              c. Florajen  
b. Culturelle                        d. VSL #3

- Probiotic and synbiotic supplements should be separated from antibiotic administration by:  
a. 1 hour.                              c. 4 hours.  
b. 2 hours.                              d. 8 hours.
- Pregnant females attempting to prevent allergic conditions in their children may consider which probiotic below?  
a. *Saccharomyces boulardii*    c. *Lactobacillus* GG  
b. *Streptococcus thermophilus*
- Within how many hours of antibiotic-associated diarrhea symptom onset should probiotics be started?  
a. 12 hours                              c. 36 hours  
b. 24 hours                              d. 72 hours
- Direct supplementation of a bacterial species that is known to confer therapeutic benefit is called a:  
a. prebiotic.                              c. synbiotic.  
b. probiotic.
- Benefits of synbiotics are only limited to the GI tract.  
a. True                                      b. False
- Therapeutic benefit of prebiotics occurs through:  
a. absorption in the GI tract.  
b. direct stimulation of microbiota.  
c. fermentation enhancing microbiota balance.  
d. adhesion to pathogenic microbiota.
- Which of the following bacteria reduces vaginal pH to prevent infection?  
a. *Lactobacillus*                        c. *Bifidobacterium*  
b. *Escherichia*                        d. *Saccharomyces*
- Which of the following therapies may patients with chronic idiopathic constipation consider?  
a. Prebiotic                                c. Synbiotic  
b. Probiotic
- Synbiotics may offer metabolic benefit through:  
a. decreased appetite due to side effects.  
b. increased sense of fullness.  
c. decreased ability to absorb food.

.....  
Completely fill in the lettered box corresponding to your answer.

- |                    |                    |                     |
|--------------------|--------------------|---------------------|
| 1. [a] [b] [c]     | 6. [a] [b] [c] [d] | 11. [a] [b]         |
| 2. [a] [b] [c]     | 7. [a] [b] [c] [d] | 12. [a] [b] [c] [d] |
| 3. [a] [b] [c] [d] | 8. [a] [b] [c]     | 13. [a] [b] [c] [d] |
| 4. [a] [b] [c]     | 9. [a] [b] [c] [d] | 14. [a] [b] [c]     |
| 5. [a] [b] [c]     | 10. [a] [b] [c]    | 15. [a] [b] [c]     |

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- Rate this lesson: (Excellent) 5 4 3 2 1 (Poor)
- Did it meet each of its objectives?  yes  no  
If no, list any unmet \_\_\_\_\_
- Was the content balanced and without commercial bias?  
 yes  no If no, why? \_\_\_\_\_
- Did the program meet your educational/practice needs?  
 yes  no
- How long did it take you to read this lesson and complete the quiz? \_\_\_\_\_
- Comments/future topics welcome.

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To receive CPE credit, your quiz must be received no later than August 15, 2019. A passing grade of 80% must be attained. CPE credit for successfully completed quizzes will be uploaded to the CPE Monitor. CPE statements of credit can be printed from the CPE Monitor website. Send inquiries to opa@ohiopharmacists.org.