Better Living Through Bacteria: Probiotics for the Gut and Beyond

Event Type
Live Online

ACPE Expiration Date
6/11/2016

Credits
1 Contact Hour

Target Audience
Nurses, Pharmacists, Pharmacy Technicians

Program Overview
The role of ingesting living microorganisms, or "good" bacteria, found in foods, medical foods, and dietary supplements in the treatment and prevention of various disease states has been theorized for years. In recent years, there have been an increasing number of studies evaluating the beneficial effects of probiotics in numerous health conditions. There are also increasing numbers of and promotion to consumers of probiotic products. Americans' spending on probiotic supplements tripled from the mid 1990s to today. The use of probiotics, whether from food sources, medical foods, or supplements, for management of various conditions will be discussed. The program will cover how these agents are thought to work, conditions for which they are effective, potential risks, and available products.

Nurse Educational Objectives
• List various sources of beneficial bacteria and their advantages and disadvantages
• Identify those conditions in which based on scientific evidence would likely be improved by the use of probiotics
• Apply knowledge of probiotics to a patient case to recommend a supplement, if appropriate

Pharmacist Educational Objectives
• List various sources of beneficial bacteria and their advantages and disadvantages
• Identify those conditions in which based on scientific evidence would likely be improved by the use of probiotics
• Apply knowledge of probiotics to a patient case to recommend a supplement, if appropriate
Pharmacy Technician Educational Objectives
• List products that contain probiotics
• List benefits of probiotics for digestion

Activity Type
Knowledge

Accreditation
Nurse N-836
Pharmacist 0798-0000-13-176-L01-P
Pharmacy Technician 0798-0000-13-176-L01-T

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PharmCon, Inc. has been approved as a provider of continuing education for nurses by the Maryland Nurses Association which is accredited as an approver of continuing education in nursing by the American Nurses Credentialing Center’s Commission on Accreditation.

Faculty
Geneva Briggs, PharmD, BCPS
Owner, Briggs and Associates

Financial Support Received From
Pharmaceutical Education Consultants, Inc.

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Overview

- Probiotic, prebiotics, & synbiotics
- Postulated effects
- Conditions likely to be improved by use of probiotics
- Food sources and supplement products
- Case Study

What are probiotics?

- Live microorganisms, which when given in adequate amounts alter the microflora by implantation or colonization in a compartment of the host and confer a health benefit on the host.
- “For Life”
What are prebiotics?

- A nutrient or non-digestible food ingredient that beneficially promotes the proliferation of probiotics
- Oligosaccharides - inulin, lactulose, lactosucrose and fructo-oligosaccharides
- Health benefits not extensively studied
- Synbiotics - products that combine probiotics and prebiotics

Use of Probiotics

- Awareness of the term “probiotics” has grown from 9% (2002) to 60% of American adults (2009, Natural Marketing Institute’s Health and Wellness Trends Survey)
- 45% (2011) consider themselves very or somewhat knowledgeable on the subject, compared to 36% in 2009 (Dannon survey)
- Supplements: $144.6 million in sales in 2011

Normal Gut Flora

Intestinal Microflora Functions
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Concept of Probiotics

- Elie Metchnikoff
  - “Father of Probiotics”
  - The Prolongation of Life: Optimistic Studies
- Gut dysbiosis

Potential Uses

<table>
<thead>
<tr>
<th>Strong evidence</th>
<th>Less Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Acute diarrhea</td>
<td>• Preventing vaginal and urinary tract infections</td>
</tr>
<tr>
<td>• Antibiotic associated diarrhea</td>
<td>• Treating bacteria vaginosis</td>
</tr>
<tr>
<td>• Irritable bowel syndrome</td>
<td>• C diff related diarrhea</td>
</tr>
<tr>
<td>• Functional constipation</td>
<td>• Eczema</td>
</tr>
<tr>
<td>• Lactose intolerance</td>
<td>• Necrotizing enterocolitis in premature infants</td>
</tr>
<tr>
<td>• Inflammatory bowel disease (Crohn’s disease, ulcerative colitis)</td>
<td>• Prevention of upper respiratory tract infections</td>
</tr>
<tr>
<td>• C diff related diarrhea</td>
<td>• Pouchitis</td>
</tr>
</tbody>
</table>

Most Common Probiotics

- **Bifidobacteria (Actinomycetaceae)**
  - B. Bifidum, B. Breve, B. Infantis, B. Lactis, B. Longum, Bifido, Bifido Bacterium Longum, Bifidobacteria Bifidus, Bifidobacterium, Bifidobacterium Animals, Bifidobacterium Regularis, Bifidum, Bifidus, L. Bifidus, Lactobacillus Bifidus

- **Lactobacillus (Lactobacillaceae)**

- **Saccharomyces boulardii**
  - Brewer’s Yeast, Hansen CBS 5926, Saccharomyces Cerevisiae, S. Boulardi

- **Bacillus coagulans**
  - Bacillus Bacteria, Bacillus Probiotics, Gram Positive Spore-Forming Rod, L. Spp. Bifidus, Lactobacillus Spp., Saccaromyces

*Streptococcus and Enterococcus species are lesser used (family name), underlined items are commonly mislabeled names*
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Most Common Probiotics

- **Bifidobacteria**
  - Normal flora, produce lactic acid, most important for providing barrier to infection
- **Lactobacillus**
  - Normal flora, produce lactic acid, L. rhamnosus GG attaches to intestinal epithelial cells better than L. acidophilus
- **Saccharomyces**
  - Usually non-pathogenic yeast
  - Lyophilized products (lyo)

Use in Specific Situations

**Antibiotic Associated Diarrhea**

- 25 randomized trials have shown reduction in duration and reduced risk of occurrence
  - Both adults and kids
    - S. boulardii, Lactobacillus GG, L. bulgaricus, L. acidophilus, B. longum, L. casei
    - Lactobacillus rhamnosus GG >10⁹ colony-forming units (CFUs)/day colonizes the intestine and reduces diarrhea
- Prevention: Start first day of antibiotics and continue for 2 weeks after end
- Treatment: As soon as symptoms appear
- Supplements with ≥ 5 billion CFU/day appears more effective than less
- Separate probiotic and antibiotic by 2 hours
- Severe diarrhea, bloody stool, or fever – see a doctor

**Other Forms of Diarrhea**

- **Clostridium difficile**
  - Saccharomyces boulardii 250 mg qid x 4 weeks
  - Lactobacillus rhamnosus GG 1.2 billion CFU x 2 weeks
  - Meta analysis of prevention trials – 50-70% reduced risk, multiple bacteria best
- **Rotavirus**
  - Lactobacillus rhamnosus GG 5-10 billion CFU
Other Forms of Diarrhea

• Traveler’s
  – L. rhamnosus GG, S. boulardii and L. acidophilus + B. bifidum
• H. pylori treatment
  – Improves tolerance of antibiotic regimens
  – Eradication rates not affected

Irritable Bowel Syndrome (IBS)

• Typical symptoms: abdominal pain, bloating, and changes in bowel habit
• Predominately affects women
• B. infantis, S. boulardii, L. plantarum and combination probiotics may help symptoms and regularity.

Inflammatory Bowel Disease (IBD)

• Crohn’s disease and ulcerative colitis
• Symptoms: abdominal cramps, pain, diarrhea, weight loss and blood in stool
• UC responds better
  – 75% relapsed in 1 yr on probiotics compared with 92% on placebo
  – 40% versus 34.1% on mesalamine
• Not enough data to identify best probiotic

Functional Constipation

• Trials in adults and kids
• Improvements in defeaction frequency and stool consistency
• B. lactis DN-173 010, L. casei shirota, E. coli Nissle 1917, & L. casei rhamnosus Lcr35 have specifically been studied
Lactose Intolerance

- Inability to digest lactose – gas, diarrhea, bloating
- L. bulgaricus, S. thermophilus, L. acidophilus, Bifidobacteria in yogurt have all been shown to increase tolerance

Vaginal Flora

- Candida
  - Yogurt daily reduces incidence
- Bacterial Vaginosis
  - Prevention: Small decrease in incidence of recurrence
  - Treatment: Combo of metronidazole + probiotics (oral Lactobacillus rhamnosus GR-1 and Lactobacillus reuteri RC-14) better than metronidazole alone
- Products-RepHresh ProB, FloraFemme, Purfem

Food Sources

- Some bacteria won’t survive the gut
- Fermented milk products
  - Yogurt (L. bulgaricus and S. thermophilus + others)
  - Kefir (bacteria & yeast)
  - Acidophilus milk (L. acidophilus)
  - Buttermilk (L. lactis)
  - Sour cream (Lactis)
- Others - unpasturized
  - Soy based products
    - Miso
    - Tempeh
  - Soy yogurt
  - Sauerkraut & Kim Chee

Specific Products

- Lactose Intolerance
- Vaginal Flora
- Food Sources
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Example Yogurts

• All will have *S. thermophilus* & *L. bulgaricus*
  – Improve lactose intolerance
• Dannon
  – Activia – *Bifidus Regularis (Bifidobacterium animalis lactis DN-173 010)*, 3 x/day x 2 weeks improves intestinal transit time and digestive symptoms
  – Danactive – *L. Immunitas (L. casei)*
  – Danimals - *Lactobacillus GG*

Example Yogurts

• Stonyfield - *L. acidophilus, Bifidus, L. casei and L. rhamnosus*
  • Yoplait Yo-Plus: *B. lactis Bb-12*, inulin fiber
    – 1 billion CFUs/container
    – Improves transit time, reduces diarrhea

Quality Considerations in Probiotic Supplements

• The viability of organisms in the product
• Lack of contaminating organisms
• Protection of organisms in the product
• Requirement for refrigeration

Consumer Lab Testing

• Lots of products are labeled with amount of viable cells at time of manufacture and may not contain this at time of consumption

**Supplier Facts**

<table>
<thead>
<tr>
<th>Serving Size: 1 Capsule</th>
<th>Serving Per Container 60</th>
<th>Amount Per Serving</th>
<th>% Daily Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td><em>Probiotic Blend</em></td>
<td>12 Billion CFUs</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Streptococcus thermophilus</em>, <em>Lactobacillus acidophilus</em>, <em>Bifidobacterium animalis lactis DN-173 010</em>, <em>Lactococcus lactis</em>, <em>Lactobacillus rhamnosus</em>, <em>Bifidobacterium breve</em>, <em>Bifidobacterium lactis</em>, <em>Bifidobacterium longum</em>, <em>Lactobacillus paracasei</em>, <em>Lactobacillus plantarum</em>, <em>Lactobacillus casei</em>, <em>Lactobacillus reuteri</em>, <em>Lactobacillus delbrueckii</em>, <em>Lactobacillus helveticus</em>, <em>Bifidobacterium adolescentis</em>, <em>Bifidobacterium longum</em></td>
<td><em>Daily Value not established</em></td>
</tr>
</tbody>
</table>

The numbers of viable bacterial cells (CFUs/dose) found in the supplement listed above are at time of manufacture.

Other Ingredients: Corn maltodextrin, hydroxypropyl methylcellulose, purified water.

Suggested Use: For adults, take one (1) capsule prior to a meal or as directed by your physician. Although not required, refrigeration is recommended.

www.consumerlab.com
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#### Product Labeled Dose Organism Listed amount at manufacturer Allergens

<table>
<thead>
<tr>
<th>Product</th>
<th>Labeled Dose</th>
<th>Organism</th>
<th>Listed amount at manufacturer</th>
<th>Allergens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Align</td>
<td>1 cap/day</td>
<td>Bifidobacterium infantis 35624</td>
<td>1 billion</td>
<td>Milk</td>
</tr>
<tr>
<td>Culturelle</td>
<td>1 cap/day</td>
<td>Lactobacillus GG Inulin 200 mg</td>
<td>10 billion for adults and children</td>
<td>Soy*</td>
</tr>
<tr>
<td>Digestive Health</td>
<td>1 cap/day</td>
<td>Bifidobacterium bifidum and longum</td>
<td>1.5 billion</td>
<td>Soy*</td>
</tr>
<tr>
<td>FloraStor</td>
<td>2 caps QD or BID</td>
<td>Saccharomyces boulardii Iyo</td>
<td>Not listed (250 mg per website, 61.6 billion)</td>
<td>Soy*</td>
</tr>
<tr>
<td>Phillips Colony Health</td>
<td>1 cap/day adults &amp; children</td>
<td>Lactobacillus casei, Bifidobacterium bifidum and longum</td>
<td>1.5 billion for adults ~0.4 billion for children</td>
<td>Soy*</td>
</tr>
<tr>
<td>Digestive Advantage (formerly Sustenex)</td>
<td>1 cap/day adults &amp; children</td>
<td>GrevinHBC30 (Bacillus coagulans) Calcium carbonate 140 mg</td>
<td>2 billion</td>
<td>Soy</td>
</tr>
<tr>
<td>Pronutrients Probiotic</td>
<td>1 powder packet qd</td>
<td>Bifidobacterium animalis subsp. lactis BB12 Lactobacillus rhamnosus GG</td>
<td>2 billion</td>
<td>Milk, wheat</td>
</tr>
<tr>
<td>Trubiotics</td>
<td>1 cap/day</td>
<td>Lactobacillus acidophilus Bifidobacterium animalis</td>
<td>1.5 billion</td>
<td>Milk</td>
</tr>
<tr>
<td>Rephrresh Pro B</td>
<td>1 cap/day</td>
<td>Lactobacillus Rhamnosus GR-1 Lactobacillus Reuteri RC-14</td>
<td>2.5 billion of each</td>
<td>None*</td>
</tr>
</tbody>
</table>

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#### Not Tested by Consumer Lab

<table>
<thead>
<tr>
<th>Product</th>
<th>Labeled Dose</th>
<th>Organism</th>
<th>Listed amount</th>
<th>Allergens</th>
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<td>None*</td>
</tr>
</tbody>
</table>

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#### Marketed as Medical Food

- **VSL#3 & VSL#3 DS**
  - Numerous published trials
  - DS requires a prescription
  - Indicated for dietary management of medically diagnosed ulcerative colitis, ileal pouchitis, or irritable bowel syndrome
  - Contains:
    - *Bifidobacterium breve, longum, infantis; Lactobacillus acidophilus, plantarum, paracasei, bulgaricus; Streptococcus thermophilus*
    - Allergen – milk protein

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#### VSL#3 Dosing

<table>
<thead>
<tr>
<th>Indication</th>
<th>VSL#3 Capsules per day</th>
<th>VSL#3 packets per day</th>
<th>VSL#3 DS packets per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gas and bloating in IBS</td>
<td>2-4 capsules</td>
<td>1 packet</td>
<td>N/A</td>
</tr>
<tr>
<td>Ulcerative colitis (UC)</td>
<td>4-8 capsules</td>
<td>1-2 packets</td>
<td>1 DS packet</td>
</tr>
<tr>
<td>Active UC</td>
<td>N/A</td>
<td>2-4 packets</td>
<td>1-2 DS packets</td>
</tr>
<tr>
<td>Ileal pouch (pouchitis)</td>
<td>N/A</td>
<td>2-4 packets</td>
<td>1-2 DS packets</td>
</tr>
</tbody>
</table>

Dosing for kids available on website www.vsl3.com

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Tips for Patients

- Single microorganism versus combinations of organisms or strains
- Look for products with labeled amount of viable organisms expected to be present through an expiration or "Best By" date
- For yogurts and other dairy products, look for "contains live cultures" or "active cultures"
- Follow directions for storage & preparation
- Watch for allergens (casein, soy, or fish peptide residue)

Recommended Intake

- Best doses are not well established
  - Varies by strain and use
  - Patient need to titrate dose
- Tends to be 1 billion to 10 billion cells (or CFUs) per day.
  - "1 x 10^9" or "10^9" = 1 billion units
  - "1 x 10^{10w}" or "10^{10w}" = 10 billion units
- *Saccharomyces* – 500 mg qd - qid

Adverse Effects/Safety

- Very safe in general (GRAS)
- Diarrhea, gas
- Yeast allergy
- Rare case reports of bacteremia, fungemia, endocarditis
  - Severely ill, immunocompromised, enterically fed and/or with central venous lines
  - Short gut syndrome
  - Fungemia: *Saccharomyces cerevisiae & boulardii*

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Drug Interactions

• Recommended to separate antibiotics from bacteria based probiotics by 2 hours
• Not recommended to take Saccharomyces with antifungals

Case Study

• Mr Jones is a 49 year old who requests your help.
• He has had diarrhea for several years (as long as he can remember)
  – 4-5 very loose BMs/day
  – Some cramping but no bloating or excessive gas
• Has eliminated lactose, fatty foods, and carbonated sodas from diet
  – Improved symptoms but still 2-3 BMs/day

Probiotic Conclusions

• Dysbiosis can be due to antibiotics, immunosuppression, dietary changes and physical stress.
• Probiotics may exert beneficial health effects on the host by altering flora within the body

Probiotic Conclusions

• Potential mechanism of action of probiotics include antiinflammatory effects, preventing pathogenic adhesion, improving immune response, and restoring balance of good bacteria
• Evidence based use of probiotics includes treatment of diarrhea, constipation, IBS, IBD, and lactose intolerance
• Effects may be species specific
• Dosing is not well defined