Probiotics

Live microorganisms, which when administered in adequate amounts confer a health benefit on the host


Health and Nutritional Properties of Probiotics in Food including Powder Milk with Live Lactic Acid Bacteria

In the USA, no legal definition of term “probiotic”
Misuse of the term “Probiotic”

“The most commonly known foods containing probiotics is (sic) yogurt and fermented foods such as Kombucha tea, buttermilk, tempeh, miso, sauerkraut, Kim Chi, and brewer’s yeast.”

health.blogs.foxnews.com/2010/05/04/green-your-tummy-with-probiotics

“Probiotics are live organisms that colonize our gut microbiome.”

health.blogs.foxnews.com/2010/05/04/green-your-tummy-with-probiotics

Probiotic ≠ Live Active Cultures

Probiotic ≠ Normal, commensal bacteria
“FAO definition of probiotic has outlived its usefulness”

Probiotic vs. Pharmabiotic

- Fergus Shanahan, MD
  - Department of Medicine and Alimentary Pharmabiotic Centre, University College Cork
- Lecture: “Clinical Endpoints Using Probiotics & Prebiotics for IBD, IBS, & Infectious Diarrhea”
  - Archived at American Gastroenterological Association GI Learn (http://www.gastro.org/probiotics-and-prebiotics-webinars)
- Proposed use of the term “pharmabiotic” instead
<table>
<thead>
<tr>
<th>Pharmabiotic</th>
<th>Probiotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Broadly defined: live, dead, all microbial cell</td>
<td>More specific term: refers only to microbes</td>
</tr>
</tbody>
</table>

We should insist that the term “probiotic” be used in scientific, marketing and popular press communications only when meeting the scientific definition. “Products Marketed as Probiotics” can be used when we are unsure of the status of scientific validation of health benefits.

Probiotic

Pharmabiotic

Bacteria/yeasts
Let’s take a look back in history
Fermented foods have been part of traditional diets for 1000’s of years
<table>
<thead>
<tr>
<th>Country</th>
<th>Fermented Milk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finland</td>
<td>Piimä and viili</td>
</tr>
<tr>
<td>Causas region</td>
<td>Kefir</td>
</tr>
<tr>
<td>Russia</td>
<td>Koumiss (mare's milk)</td>
</tr>
<tr>
<td>Iceland</td>
<td>Skyr and súrmjólk</td>
</tr>
<tr>
<td>India</td>
<td>Dahi</td>
</tr>
<tr>
<td>South Africa</td>
<td>Amasi</td>
</tr>
<tr>
<td>Iran</td>
<td>Doogh</td>
</tr>
<tr>
<td>Egypt</td>
<td>Zabadi</td>
</tr>
<tr>
<td>West Sumatra</td>
<td>Dadiah (water buffalo milk)</td>
</tr>
</tbody>
</table>
Microbes as therapeutics have been used in traditional healing practices
“Once upon a time, camel poo was eaten supposedly to cure dysentery”

http://dsc.discovery.com/videos(dirty-jobs-camel-poo-cure-all.html
Early probiotic science

- 1899: Tissier identifies bifidobacteria and promoted their therapeutic use for treating infant diarrhea
- 1906: Elie Metchnikoff at Institut Pasteur Paris proposed concept of probiotic: “Bulgarian bacillus”
- 1930’s: Minoru Shirota isolated *Lactobacillus casei* Shirota and developed beverage to promote health in Japan
Probiotic Science

- 1989: first modern usage of term “probiotic” proposed by Roy Fuller (~15 published definitions)
- Probiotics regarded as “peripheral and largely based on uncontrolled experiments and apocryphal stories”
- Very few controlled, human studies on health effects
  - Products/strains poorly defined

Doctors recommend yogurt for patients taking antibiotics or for women with vaginal infections
Probiotic Science

- 1990’s-2000’s: Numerous EU projects on efficacy, safety, mechanisms, technological properties of probiotics
  - PROSAFE, PROTECH, PROEUHEALTH, SYNCAN, etc.
- 1990’s-2000’s: ↑ human studies, many on treatment of gut illnesses
  - Antibiotic associated diarrhea, acute diarrhea
- 2000: GMO probiotic engineered
Clinical studies on probiotic PubMed
Probiotic Science

- ↑ human studies focusing on non-gut endpoints
- ↑ studies on mechanisms
- ↑ studies in US, some publicly funded
- Improved stabilization technologies
Targets for probiotics

Oral microbiology
- Dental caries

Allergy
- Atopic dermatitis
- Asthma

Vaginal infections

Gut function
- Acute diarrhea
- AAD, travelers diarrhea
- *C. difficile*
- Lactose digestion
- IBS symptoms
- Colic
- Inflammatory bowel conditions
- Gut pain sensation

Brain function

Skin microbiology, inflammation

Colds, respiratory infections

Encompassing effects
- Growth parameters of undernourished children
- Reduced absences from work, daycare
- QOL

Metabolic syndrome
- Obesity
- Diabetes
Probiotic Science

- ↑ human studies focusing on non-gut endpoints
- ↑ studies on mechanisms
- ↑ studies in US, some publicly funded
- Improved stabilization technologies
Mechanisms of Action of Probiotics: Recent Advances

S.C. Ng, MRCP,* A.L. Hart, PhD,* M.A. Kamm, MD,† A.J. Stagg, PhD,‡ and S.C. Knight, PhD*

Inflamm Bowel Dis. 2009 Feb;15(2):300-10
Probiotic Science: current status

- ↑ human studies focusing on non-gut endpoints
- ↑ studies on mechanisms
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Probiotic Science: current status

- ↑ human studies
- ↑ human studies focusing on non-gut endpoints
- ↑ studies on mechanisms
- ↑ studies in US, some publicly funded
- Improved stabilization technologies
$L. \text{ acidophilus}$ NCFM in maltodextrin
Probiotic science

- 2001: FAO/WHO probiotic definition
- 2007: Human microbiome project
# Probiotics as Therapy in Gastroenterology

A Study of Physician Opinions and Recommendations

Michael D. Williams, MD,* Christina Y. Ha, MD,† and Matthew A. Ciorba, MD‡

## TABLE 4. Most Commonly Recommended Probiotics by Condition

<table>
<thead>
<tr>
<th>Condition #</th>
<th>All/Private/Academic</th>
<th>IBS 45/25/20</th>
<th>C. difficile 35/24/11</th>
<th>AAD 29/19/10</th>
<th>Pouchitis 22/12/10</th>
<th>Crohn’s 13/12/1</th>
<th>Ulcerative Colitis 13/9/4</th>
</tr>
</thead>
<tbody>
<tr>
<td>All physicians (%)</td>
<td>Align (91)</td>
<td>Align (51)</td>
<td>Align (59)</td>
<td>VSL#3 (59)</td>
<td>Align (54)</td>
<td>Align (54)</td>
<td></td>
</tr>
<tr>
<td>Yogurt (44)</td>
<td>Florastor (49)</td>
<td>Yogurt (45)</td>
<td>Align (50)</td>
<td>Flora-Q (46)</td>
<td>VSL#3 (30)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flora-Q (38)</td>
<td>Florastor (29)</td>
<td>Florastor (48)</td>
<td>Flora-Q (18)</td>
<td>Yogurt (31)</td>
<td>Yogurt (23)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yogurt (26)</td>
<td>Florastor (28)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Private practice (%)</td>
<td>Align (96)</td>
<td>Align (58)</td>
<td>Align (79)</td>
<td>VSL#3 (67)</td>
<td>Align (58)</td>
<td>Align (78)</td>
<td></td>
</tr>
<tr>
<td>Florastor (56)</td>
<td>Florastor (50)</td>
<td>Yogurt (47)</td>
<td>Align (58)</td>
<td>Flora-Q (50)</td>
<td>Flora-Q (22)</td>
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<td></td>
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<tr>
<td>Yogurt (52)</td>
<td>Florastor (33)</td>
<td>Florastor (47)</td>
<td>Flora-Q (25)</td>
<td>Yogurt (33)</td>
<td>Yogurt (22)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yogurt (25)</td>
<td>Florastor (32)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Academic (%)</td>
<td>Align (85)</td>
<td>Florastor (45)</td>
<td>Florastor (50)</td>
<td>VSL#3 (50)</td>
<td>VSL#3 (100)</td>
<td>VSL#3 (75)</td>
<td></td>
</tr>
<tr>
<td>Yogurt (35)</td>
<td>Align (36)</td>
<td>Yogurt (40)</td>
<td>Align (40)</td>
<td>Yogurt (25)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Florastor (20)</td>
<td>Yogurt (27)</td>
<td>Align (20)</td>
<td>Flora-Q (10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

What science will satisfy regulators?

- Developing scientific dossiers:
  - Convincing to regulators that a causal relationship exists between the probiotic and the health benefit
  - Health benefit fits under current regulatory framework

Guidance Document – The Use of Probiotic Microorganisms in Food

Food Directorate
Health Products and Food Branch
Health Canada
April 2009
Probiotic marketing

- 1919: Isaac Carasso begins commercial production of yogurt in Spain
- 1935: Yakult Honsha Japan begins selling Yakult (derived from the word “yogurt” in Esperanto)
- 1970’s: Sweet Acidophilus milk developed at North Carolina State University and sold throughout US
- 1994: DSHEA
  - Flood of dietary supplement “probiotics” onto US market
- 1990: NLEA – allows reduction of risk of disease “Health Claims” on foods
- 2006: Dannon puts “probiotic” on the US map with successful Activia yogurt
- 2006-2010: Activia is followed by plethora of other “probiotic” foods
Consumer awareness of “Probiotics” and probiotic benefits
Greg Stephens, Strategic Consulting, Natural Marketing Institute, November 14, 2009
A look at some current Probiotic products and PMPs (products marketed as probiotics)
Probiotic dietary supplements

- **L. rhamnosus GG**
- **B. longum infantis 35264**
- **Saccharomyces boulardii**
- **L. rhamnosus GR-1**
- **L. reuteri RC-14**
- **8 strain blend, S. thermophilus, 4 Lactobacillus and 3 Bifidobacterium strains**
- **L. reuteri ATCC 55730**
Yogurt/fermented milks

- *L. rhamnosus* GG
- *L. casei* shirotaka
- *L. casei* DN-114 001
- *B. animalis* DN-173 010
- *L. acidophilus NCFM*
- *B. lactis* Bi-07
- *L. casei* DN-114 001
- Strains?
Milk
Juice and drinks with probiotics

*B. lactis* HN019  
*L. acidophilus* CL1285  
*L. casei* Lbc80r  
*L. plantarum* 299v
Nutrition bars

*B. lactis* HN019  
*L. acidophilus* NCFM  
*Bacillus coagulans* BC$^{30}$
Infant formula

*B. lactis* Bb12
Relishes/condiments

Zukay Live Foods(TM) Introduces The World's First Line Of Probiotic Condiments 4-07-2008

Innovative New Company Ventures Into Lacto-Fermented Foods In Pursuit Of Great Taste And Optimal Digestive Health

Zukay Live Foods

mild salsa viva  hot salsa viva  garlic dill relish  horseradish dill relish
Sweetener

*Bacillus coagulans* BC30
Probiotic water
Pizza crust

**World's Healthiest Pizza Launches First Probiotic Pizza in U.S.**

“New Orleans-based World’s Healthiest Pizza introduces the first delivery pizza in the U.S. fortified with the high-survivability probiotics and prebiotics.”
Probiotic lozenges
Probiotic odor eliminator

“Harnessing nature’s ability to restore personal health and the environment”
“Probiotic” toothpaste

Bacteriocins only – no live bacteria
Probiotic gum
Probiotic tampons
For animals

Probiotic Miracle
Probiotics for Dogs

Is your dog's breathe knocking you over? Kissable Probiotic Pet Oral Hygiene Spray can help!

Nutri-Vet Probiotics with Wild Alaskan Salmon Oil for Dogs
Farm animals

Horse treats

PROBIMAX PROBIOTIC HORSE PASTE (probiotic gel) is a microbial probiotic designed to establish and maintain a preponderance of beneficial microorganisms for the intestinal well-being of horses.

Contains beneficial Lactobacillus acidophilus and four other probiotics, to establish a population of good bacteria in horse's gut.
Muranda (the cow) was on Fastrack when she set 2 milking records.
“Probiotic” yogurt for dogs

Yoghund: Frozen Yogurt For Dogs
by J. Foster

I've seen dogs dig up months-old bones... and start chewing on them. And... I've unfortunately witnessed dogs attempt to eat their own... well... let's not get into that.

If you want your dog to eat better than you - check out this frozen organic yogurt.

According to the site:

Our Organic Banana & Peanut Butter recipe features potassium rich bananas, which are also a great source of the probiotic inulin, along with peanuts for flavor and antioxidants. And of course, its primary ingredient is organic, low fat yogurt with live and active cultures, complete with all the benefits of probiotics.
Current marketplace reality:

Products not always what they say they are
Inaccurate content claims

- **Numerous** published assessments of commercial probiotic products
- Key conclusions:
  - Failure of some companies to meet label claim for content
  - Failure to accurately label microbiological genera/species of microbes contained in product
Package labeling

Daily PROBIOTIC

DIETARY SUPPLEMENT

BIFIDOBACTERIUM INFANTIS

Helps your intestinal tract maintain a natural balance that combats occasional...
- Diarrhea
- Constipation
- Irregularity
- Gas & bloating

30 CAPSULES

NEW!

What is a probiotic?
The human digestive tract is colonized by trillions of healthy-promoting “good bacteria” that live in balance with human cells. Unfortunately, our lifestyles often disrupt this healthy balance, creating digestive and other health problems. Probiotics are “good bacteria” that help restore this delicate balance and support digestive and immune health. 1

How does CVS pharmacy Daily Probiotic dietary supplement work?
When taken every day, CVS pharmacy Daily Probiotic dietary supplement helps restore and maintain an optimal bacterial balance, promoting a healthy digestive and immune system. 1

Why take CVS pharmacy Daily Probiotic daily supplement?
By supporting a healthy bacterial balance, CVS pharmacy Daily Probiotic dietary supplement promotes regularity and strengthens your natural defenses against occasional intestinal upsets. 1

What is Bifidobacterium infantis?
Although a different bacterial strain, the Bifidobacterium infantis found in CVS pharmacy Daily Probiotic dietary supplement is the same probiotic species as that in Align®. The B. infantis strain in CVS pharmacy Daily Probiotic dietary supplement is made of naturally derived isolates, not genetically engineered (non-GMO), chosen as safe and effective for human use. 1

CVS pharmacy

Compare to Align®
Conclusions

- The science
  - Exciting
  - Developing
- The global regulatory framework
  - Confusing
  - Limiting
- The market
  - Imaginative
  - Not discouraged by the limitations of the science