

PROBIOTICS and GI Benefit



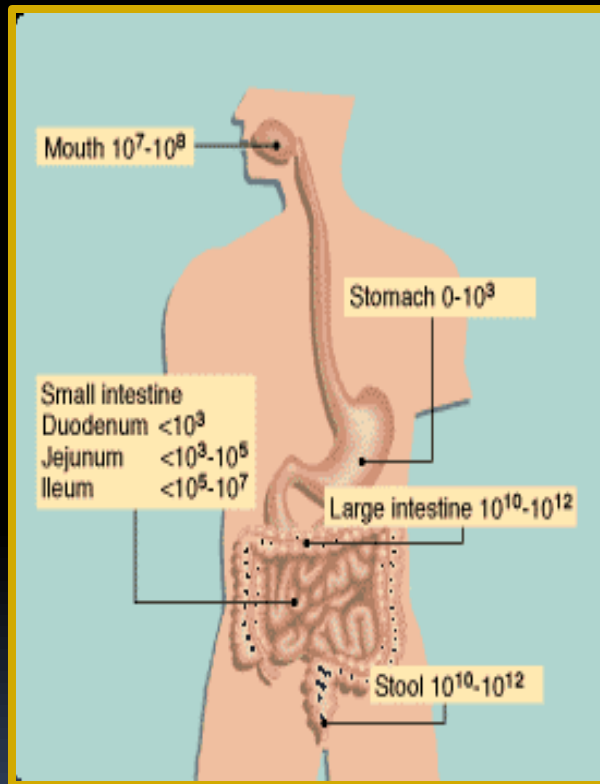
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Azar 91

Gut Micro flora



Intestinal Microflora: Location & Prevalence

- Rare in the esophagus
- Uncommon in the stomach
 - primarily gram (+)
 - $10^2 - 10^4$
- 10^5 in the jejunum – primarily aerobes
- $10^{10} - 10^{12}$ in the colon
 - primarily anerobes
 - 1000x more anerobes than aerobes

Introduction

- Interactions between intestinal microbes and the host may influence a variety of diseases.

Intestinal micro flora can be altered

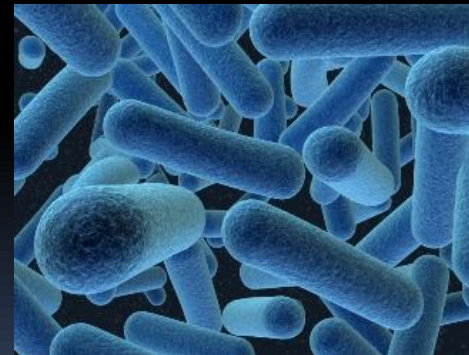
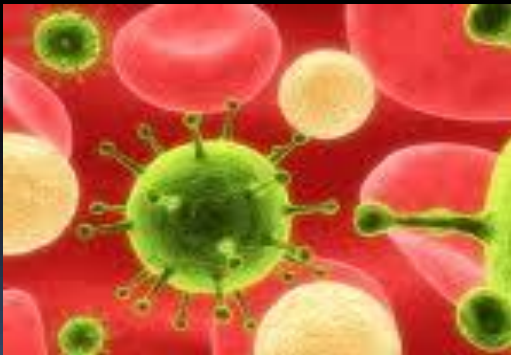
- Administration of antibiotics
- prebiotics (ie, dietary components that promote the growth and metabolic activity of beneficial bacteria),
- probiotics (ie, beneficial bacteria).
- Combination of these methods is also possible (synbiotics)

Probiotics ,prebiotics and synbiotics



DEFINITION

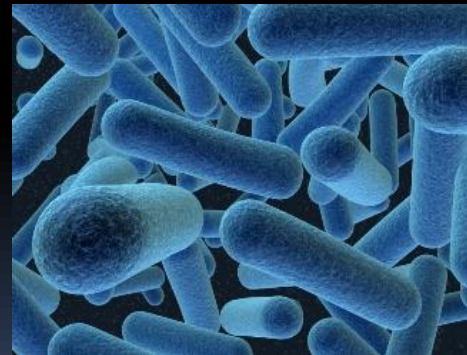
- Probiotic ?



- Probiotics are microorganisms that have beneficial properties for the host.
- Most commercial products have been derived from food sources, especially cultured milk products.

The list of microorganisms

- strains of lactic acid bacilli (eg, Lactobacillus and Bifidobacterium),



The list of microorganisms

- A nonpathogenic strain of Escherichia coli (eg, E. coli Nissle 1917),
- Clostridium butyricum,
- Streptococcus salivarius,
- Saccharomyces boulardii (a nonpathogenic strain of yeast)

- Efficacy in gastrointestinal illnesses



Therapeutic benefit

- Initial studies of selected probiotic species (given alone or in combination) have suggested potential efficacy in several gastrointestinal illnesses (prevention ,adjuvant with medical treatment or prevention of relaps).

Inflammatory disorder

- the best studied of which are the inflammatory bowel diseases (particularly pouchitis) .

Diarrhea illness

- Antibiotic-related diarrhea,
- Clostridium difficile toxin-induced colitis
- Infectious diarrhea

others GI Disorders

- Hepatic encephalopathy
- irritable bowel syndrome
- Food Allergy
- post chemotherapy, post radiation effect



MECHANISMS OF BENEFIT

MECHANISMS OF BENEFIT

- Mechanisms for the benefits of probiotics are incompletely understood.

Four general benefits

- **Suppression of growth or epithelial binding/invasion by pathogenic bacteria**
- Improvement of intestinal barrier function
- **Modulation of the immune system.**

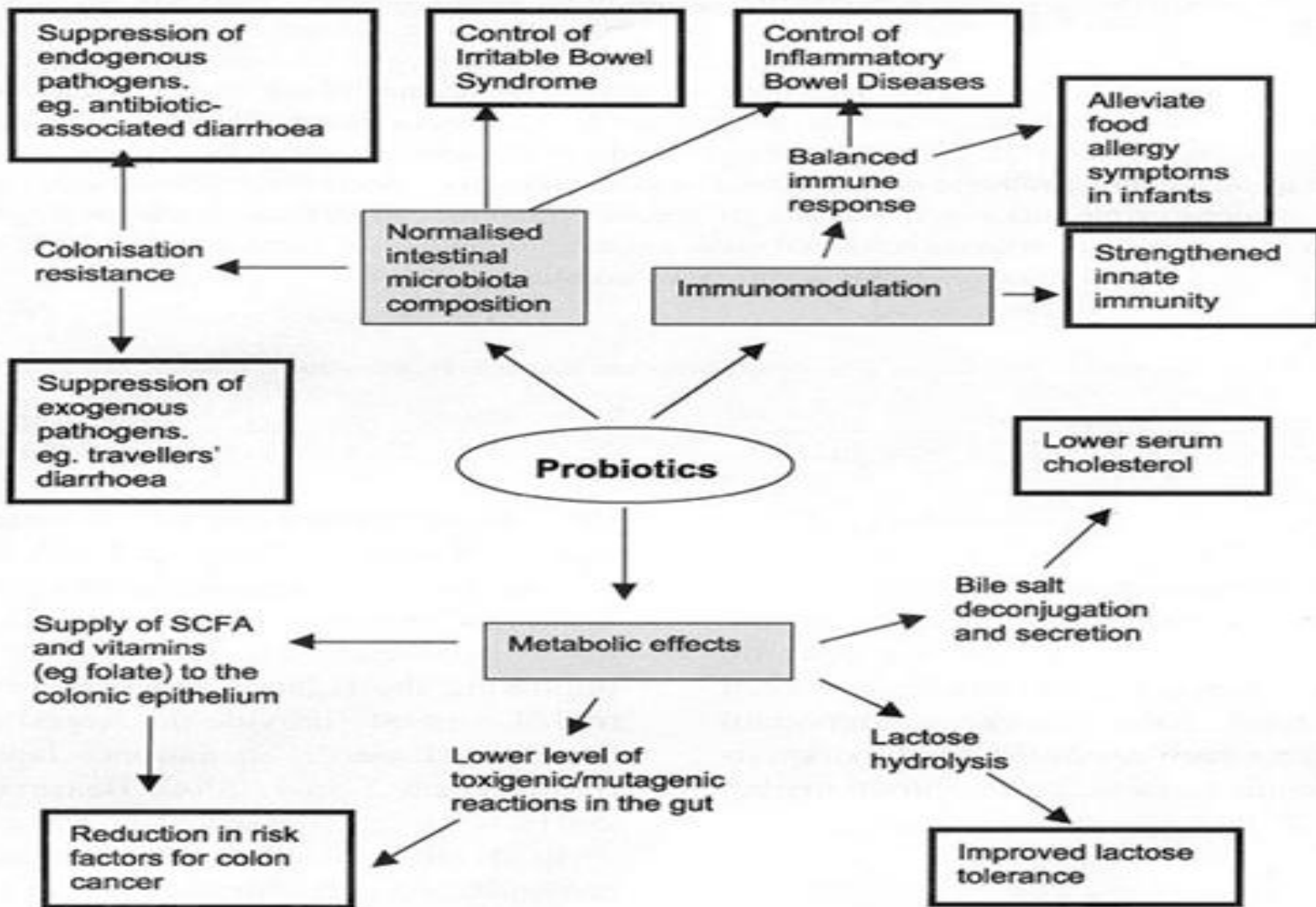
Four general benefits

probiotic induce protective cytokines, including IL-10 and TGF-beta, and suppress proinflammatory cytokines, such as TNF, in the mucosa of patients with pouchitis, ulcerative colitis, and Crohn's disease, in murine experimental colitis, and in isolated splenocytes

Saccharomyces boulardii limited the migration of T-helper 1 cells in inflamed colon tissue in a mouse model of inflammatory bowel disease

Four general benefits

- **Modulation of pain perception.**
 - Some Lactobacillus strains appear to induce expression of micro-opioid and cannabinoid receptors in intestinal epithelial cells and mediate analgesic functions in the gut in a manner similar to the effects of morphine



Proposed health benefits stemming from probiotic consumption.

probiotic preparations have promise in preventing or treating various GI Disorder



Probiotics and GI Disorders benefits

- Several probiotic preparations have promise in preventing or treating various conditions..

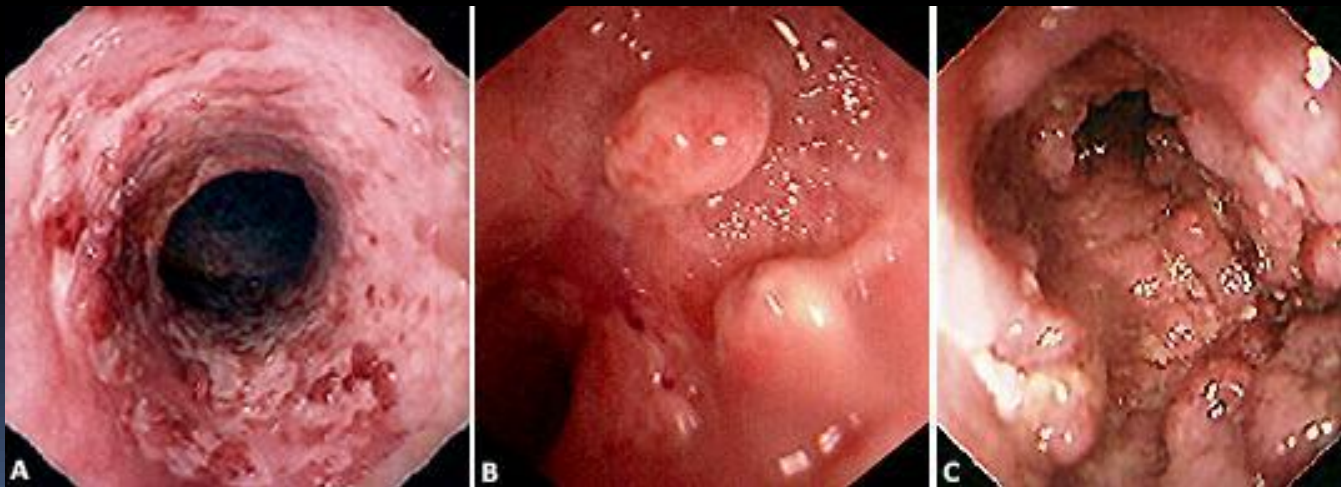
Studies

- Most studies have been small and many have important methodologic limitations

Studies on GASTROINTESTINAL INFLAMMATION



Normal colon



Ulcerative Colitis

Pouchitis

- For the surgical treatment of ulcerative colitis (UC) and familial adenomatous polyposis, proctocolectomy with ileal pouch-anal anastomosis (IPAA)

Pouchitis

- The most frequently observed long-term complication of IPAA is acute and/or chronic inflammation of the ileal reservoir, called pouchitis.
- Symptoms of pouchitis include increased stool frequency, urgency, hematochezia, abdominal pain, fever, and extraintestinal manifestations of inflammatory bowel diseases.

Pouchitis

- Detailed studies of the microflora in patients with pouchitis have demonstrated unique patterns, including the persistence of Fusobacteria and enteric species, increased Clostridium perfringens, and the absence of Streptococcus species in the inflamed pouch .

Pouchitis

- These observations and a high rate of response to various antibiotics support a role for bacteria in the pathogenesis of pouchitis and provide a rationale for clinical trials aimed at altering the microflora with probiotics.

Pouchitis

- Data from small controlled trials suggest a benefit from VSL#3 in the primary and secondary prevention of pouchitis.
- Thus, it is a reasonable option in addition to standard medical therapy, although long-term efficacy is uncertain.

Ulcerative colitis

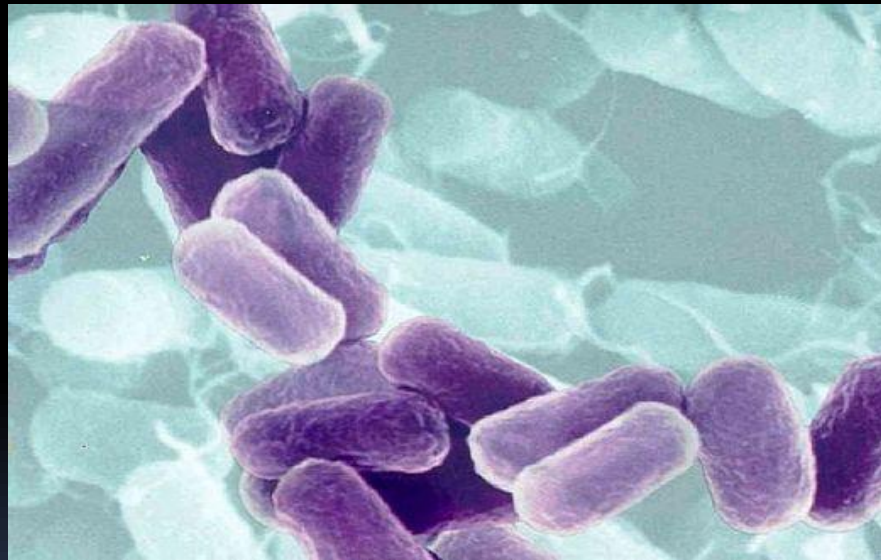
- A benefit of probiotics in ulcerative colitis remains unproven, **but E. coli Nissle 1917** shows promise in maintaining remission and could be considered as an alternative in patients intolerant or resistant to 5-ASA preparations.
- No other probiotic preparation has been validated for this indication.

Crohn's disease

- A benefit of probiotics in Crohn's disease remains unproven.

DIARRRHEAL ILLNESSES

Antibiotic associated diarrhea(AAD)-



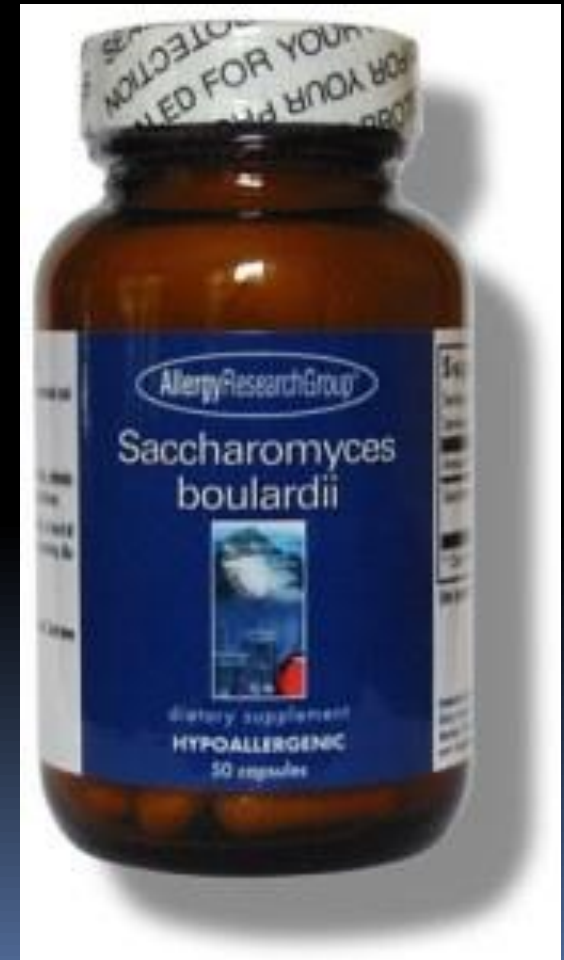
Antibiotic-associated diarrhea

- large, well-conducted studies are needed before probiotics can be recommended for routine prevention of antibiotic-associated diarrhea, although some studies suggest that prophylactic therapy may be beneficial.

Saccharomyces boulardii

- *Saccharomyces boulardii*

- A non-disease causing yeast that survives passage through the intestinal tract, unaffected by antibiotics (although it will be killed by antifungal drugs).
- Based on preliminary data indicating that this yeast could prevent antibiotic-associated diarrhea.
 - Numerous studies, have gone on to prove *Saccharomyces boulardii*, as an effective treatment for active *C.difficile* diarrhea.
 - *Saccharomyces boulardii* disrupts toxins that would normally irritate the intestines,
 - In addition, *Saccharomyces boulardii* stimulates the intestinal immune system to secrete *C.difficile* toxin A-specific antibodies (IgA) in the gut (Qamar et al., 2001).
 - * It is then eliminated after supplementation is stopped.



Infectious diarrhea

- It is reasonable to recommend probiotics to adults and children with presumed infectious diarrheal illness with the hope of reducing the duration of symptoms by 17 to 30 hours.

Infectious diarrhea

- Probiotics that were effective in at least one controlled trial included *Lactobacillus rhamnosus* GG, *Lactobacillus reuteri*, combination *Lactobacillus rhamnosus*, *Lactobacillus reuteri*, and *Bifidobacterium animalis lactis*, and combination *Lactobacillus acidophilus* and *Lactobacillus bifidus*.
- The minimal effective dose appears to be 10 billion colony-forming units given **within the first 48 hours of symptoms.**

CONSTIPATION

- These studies suggest improvement in defecation frequency and stool consistency with *Bifidobacterium lactis* DN-173 010, *Bifidobacterium lactis* BB12, *Lactobacillus casei* Shirota, and *E. coli* Nissle 1917

Constipation

- larger studies are needed before probiotics can be routinely recommended in the management of chronic constipation.

Irritable bowel syndrome

- A definitive therapeutic role remains unproven and needs to be further investigated in defined patient subsets.

Lactose intolerance

- Production of β -D-galactosidase enzymes that break down lactose.

Lactose intolerance

- A benefit of probiotics for lactose intolerance remains unproven.

Hepatic encephalopathy

- Initial studies were associated with an improvement in hepatic encephalopathy.
- However, a large meta-analysis has shown no demonstrable benefit with regard to clinically relevant outcomes (eg, mortality and quality of life).

Others Advantages of probiotics

- **Produce lactic acid-** lowers the pH of intestines and inhibiting bacterial villains such as *Clostridium*, *Salmonella*, *Shigella*, *E. coli*, etc.
- Aid absorption of minerals, especially calcium, due to increased intestinal acidity.

Food allergies

Prevention of Colon Cancer

Heterocyclic amines:

chemical compounds containing at least one heterocyclic ring, which by definition has atoms of at least two different elements, plus the compound has at least one amine group.

The biological function of heterocyclic amines can range from those of **vitamins to carcinogens**.

Carcinogenic heterocyclic amines are created by high temperature cooking of meat (barbeque), for example.



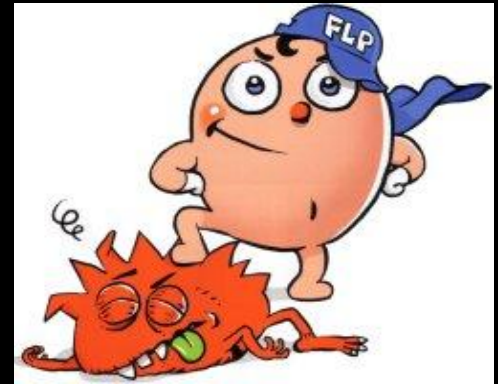
Advantages



- Decreases the production of a variety of toxic or carcinogenic metabolites.
- Produce vitamins (especially Vitamin B and vitamin K)

Advantages

Colon cancer – Certain probiotics (*Lactobacillus bulgaricus*) may help prevent colon cancer by preventing the breakdown of enzymes (β - glucuronidase) that contribute to the growth of cancer causing agents.



- commercially available probiotics



Some of the commercially available probiotics

- VSL#3® (Bifidobacterium breve, B. longum, B. infantis, Lactobacillus acidophilus, L. plantarum, L. paracasei, L. bulgaricus, Streptococcus thermophilus)
- Align® (B. infantis)
- Culturelle® (L. rhamnosus GG)
- DanActive® (L. casei)
- Mutaflor® (E. coli Nissle 1917)
- Florastor® (Saccharomyces boulardii)
- BioGaia : Lactobacillus reuteri protectis

Probiotic Consumption

- Minimum Consumption: 100g of a probiotic food with 10^7 cfu/ g.
- most probiotics do not permanently adhere in the intestine, but exert their effects as they metabolize and grow during their passage through the intestine (colonization). Thus, daily consumption of these bacteria is probably the best way to maintain their effectiveness

Dosage Forms...For the Military

Standard forms:

- Capsules
- Sticks
- Powder blends
- Chewable tablets



Individual customization:

- Capsules
- Sticks
- Chewable tablets
- Sachets
- Tablets



and more upon request...

Food Better Choice

DUE TO-

- synergistic effect between components of foods and probiotic cultures.
- The natural buffering of stomach acid by food also enhances the stability of consumed probiotics.
- Dairy products containing probiotics provide a number of high quality nutrients including calcium, protein, bioactive peptides, sphingolipids, and conjugated linoleic acids.
- incorporating foods containing probiotics into daily food choices can become a lifestyle habit

Side Effects of Probiotics and cautions

- Rare cases cause bloating, diarrhea, abdominal pain.
- If in excess cause infection that require medical attentions.
- People having on underlying disease or compromised immune system cause potential health problems like skin rash, fever, bloody stools etc.
- Sometimes interact with immunosuppressive drugs leading to life threatening conditions. So people taking such drugs should avoid it.

prebiotic ?



Definition



What is a prebiotic?

“Non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thus improve host health”

A prebiotic can typically be CHOs (oligosaccharides); soluble fibre can also be included.

It should increase the number and/or activity of **bifidobacteria and lactic acid bacteria**

Prebiotics

- Examples- insulin, garlic, onions, chicory root, Asparagus, whole wheat, rye, barley

Traditional dietary sources of prebiotics include soybeans, inulin sources (such as Jerusalem artichoke, jicama, and chicory root), raw oats, unrefined wheat, unrefined barley and yacon.

Some of the oligosaccharides that naturally occur in breast milk are believed to play an important role in the development of a healthy immune system in infants, but these are not considered prebiotics, as they do not act through the intestinal microflora.



Characteristics of Prebiotics

- Should not be hydrolysed or absorbed in the upper part of G.I tract.
- Should be a selective substrate for one or a limited number of potentially bacterial commercial to the colon culture protagonist.
- Should be able to alter the colonic microflora towards a healthier composition or selectively stimulates the growth and or activity of intestinal bacteria associated with health and well being.
- Should help increase the absorption of certain minerals such as calcium and magnesium.
- Favourable effect on the immune system and provide improved resistance against infection.

Fructo-oligo-saccharides

- Fructo-Oligo-Saccharides (FOS) is a naturally-occurring water-soluble fiber from fruit and vegetables which feeds the friendly intestinal bacteria.
- FOS generally ensure rapid establishment of the Lactobacilli in the upper small intestine and bifido bacteria in the lower small intestine.
- Some, research suggests that there may be health benefits of supplementing the diet with between 5 and log of FOS,
- It, HMF product, also provides naturally-occurring beta-carotene from the whole freeze-dried apricot. The apricot is used for its soothing effect on the intestinal walls (and great flavor in the powders).
- Townsend letter article
http://www.findarticles.com/p/articles/mi_moISW/is_2003_June/ai_102372155

Inulin

- *Inulin*
 - Inulin is a multi-chain fructooligosaccharide derived from chicory root
 - It is a chain of fructose (a carbohydrate) that is not digestible by your body, therefore, it can pass through the body into the large intestine where it can feed your good bacteria cells
 - Some, research has suggested that Inulin (9 chain links) is more effective than FOS (3 to 4 chain links) at feeding your body's good bacteria. Also, Inulin may be better tolerated by humans and bad bacteria are less likely to feed on it.

Synbiotics

- PROBIOTICS + PREBIOTICS
- Foods containing the combination of probiotics and prebiotics are referred to as sybiotics.
- Improved survival in upper GIT and more efficient implantation.

It is also possible to increase and maintain a healthy bacterial gut flora by increasing the amounts of prebiotics in the diet such as inulin, raw oats, and unrefined wheat.

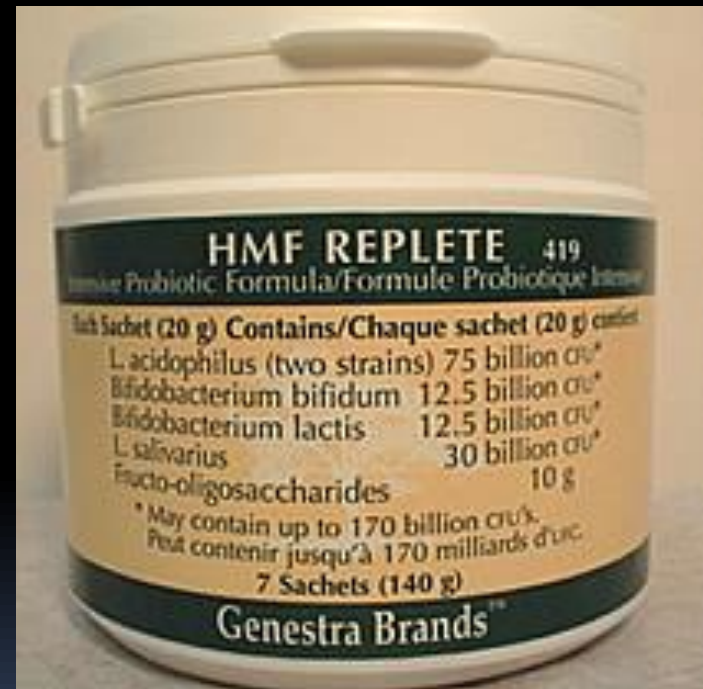
As probiotics are mainly active in the small intestine and prebiotics are only effective in the large intestine, the combination of the two may give a synergistic effect.

Appropriate combinations of pre- and probiotics are synbiotics

Genestra Brands Form Seroyal

New! Oct 2004, all HMF probiotics contain a substantial increase in potency (double) and no price increase.

- HMF Replete contains...
 - *Lactobacillus acidophilus*
 - *Lactobacillus salivarius*
 - *Bifidobacterium bifidum*
 - *Bifidobacterium lactis*
- Fructo-oligosaccharides
 - high concentrations ensure rapid establishment and dominance of probiotic cultures in the GI
- Indicated during and following antibiotic therapy and chemotherapy.





A habit
that can really benefits
our overall health-
"TAKING PRO& preBIOTICS"

