



# **BASIC CONCEPTS OF PROBIOTICS, PREBIOTICS AND SYNBIOTICS**

# History of Health Claims


- **Persian version of the Old Testament states “ Abraham owed his longevity to the consumption of sour milk.”**
- **Metchnikoff claimed that the intake of yogurt containing lactobacilli results in a reduction of toxin-producing bacteria in the gut and this increases the longevity of the host.**

# Probiotic Concept

- **Probiotic ( Greek Language) “ for life” .**
- **It was first used by Lilly and Stillwell in 1965 to describe “substances secreted by one microorganism which stimulates the growth of another”.**
- **Parker was the first to use the term *probiotic* in the sense that it is used today “organisms and substances which contribute to intestinal microbial balance”.**
- **In 1989, Fuller attempted to improve Parker’s definition of probiotic with the following distinction: “A live microbial feed supplement which beneficially affects the host animal by improving its intestinal microbial balance.”**



## **Probiotic concept:**

- **effects exerted by viable microorganisms**
  - **applicable independent of the site of action and route of administration.**
  - **include sites such as the oral cavity, the intestine, the vagina, and the skin.**
  - **health effect is usually based on alteration of the gastrointestinal micro flora and, therefore, based on survival during gastrointestinal transit.**
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# *Probiotics: An edge over Antibiotics*

## **Antibiotics:**

- **Emergence of antibiotic resistance micro-organisms.**
- **Unpleasant side effects**

## **Probiotics:**

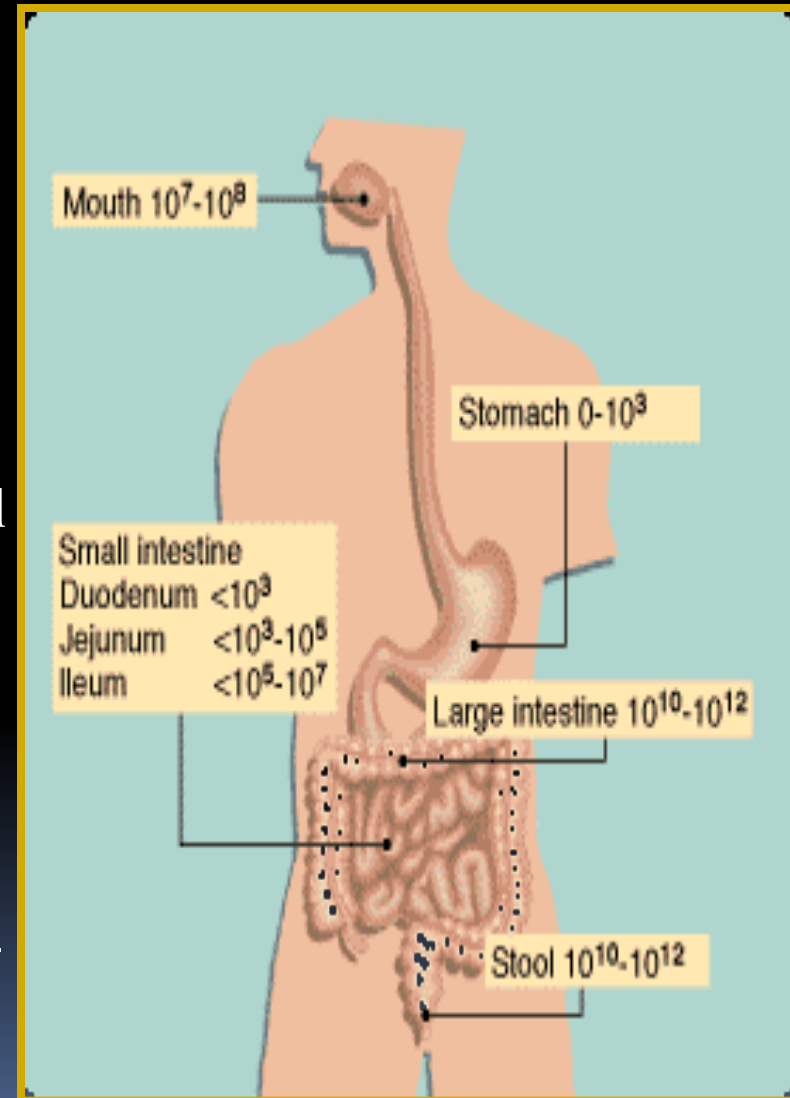
- **Non- invasive**
- **Preventive**
- **Free from undesirable side effects**

# *Where do Probiotics come from???*

- **The micro biota of a newborn develops rapidly after the birth .**
- **It is initially dependent mainly on :**
  - **mother's micro biota,**
  - **mode of delivery,**
  - **birth environment**
- **After infancy probiotics are supplied to us by raw foods; lactic acid fermented foods such as yogurt and cheese; and probiotic supplements.**

# Gut Microflora

- Gut has three principal regions: stomach, small intestine, and colon.
- Stomach has very low bacterial numbers (lactobacilli, streptococci, and yeast are present; 100 colony forming units (CFU) per millilitre due to the low environmental pH .
- Small intestine has a larger bacterial load that consists of facultative anaerobes (lactobacilli, streptococci, and enterobacteria, anaerobes (*Bifidobacterium* spp., *Bacteroides* spp., and clostridia at levels of  $10^4$ – $10^8$  CFU/ml.
- Colon has a total population of  $10^{11}$ – $10^{12}$  CFU/ml of contents




# Factors affecting the intestinal micro ecosystem

- Any action taken to kill ‘bad’ bacteria essentially kills ‘good’ bacteria as well.
  - **Antibiotics and other drugs intake**
  - **Microbial infections**
  - **Diet (highly processed, low-fiber foods)**
  - **Stress**





# **Imbalance of intestinal micro flora results in:**


- **Poor nutritional response**
  - **Accelerated aging**
  - **Cancer**
  - **Deficient immune response**
  - **Susceptibility to infection**
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# Therapeutic Modulation of Gut Microflora

- **The gut microflora is an important constituent in the intestine's defence barrier.**
- **Specific aberrancies in the intestinal microbiota may predispose the host to disease.**
- **The normal gut microbiota can prevent the overgrowth of potential pathogens in the GI tract.**



**It includes :**


- **the epithelial layer**
  - **the mucous layer**
  - **the mechanics of peristalsis**
  - **actions of secretory IgA**
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# Selection of probiotic organism

- **Safety**
- **Origin**
- **Functional aspects**
- **Survival**
- **Adherence, colonisation**
- **Immune stimulation**
- **Genetic stable**
- **Prevention of pathogens**

# Major pre-requisite properties for a microbe to be accepted as a probiotic are:

- It should be non-pathogenic, non-toxic and non-allergic.
- It should be capable of surviving and metabolizing in upper G.I. tract secretion in the gut environment e.g. Resistant to low pH, organic acids, bile juice, saliva and gastric acid.
- It should be human in origin, genetically stable and capable of remaining viable for long periods in field condition.
- It should be able to modulate immune response and provide resistance to disease through improved immunity

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- **It should have a good adhesion/ colonization to human intestinal tract**
  - **It should be antagonistic against carcinogenic/ pathogenic organism.**
  - **It should possess clinically proven health benefit, e.g. gastrointestinal disorders, persistent diarrhoea, clostridium difficile colitis, antibiotics associated diarrhoea, acute infantile gastroenteritis.**




# Established effects of probiotics

- **Aid in lactose digestion**
- **Resistance to enteric pathogens**
- **Anti-colon cancer effect**
- **Anti-hypertensive effect**
- **Small bowel bacterial overgrowth**
- **Immune system modulation**
- **Blood lipids, Heart disease**
- **Urogenital infections**
- **Hepatic encephalopathy**

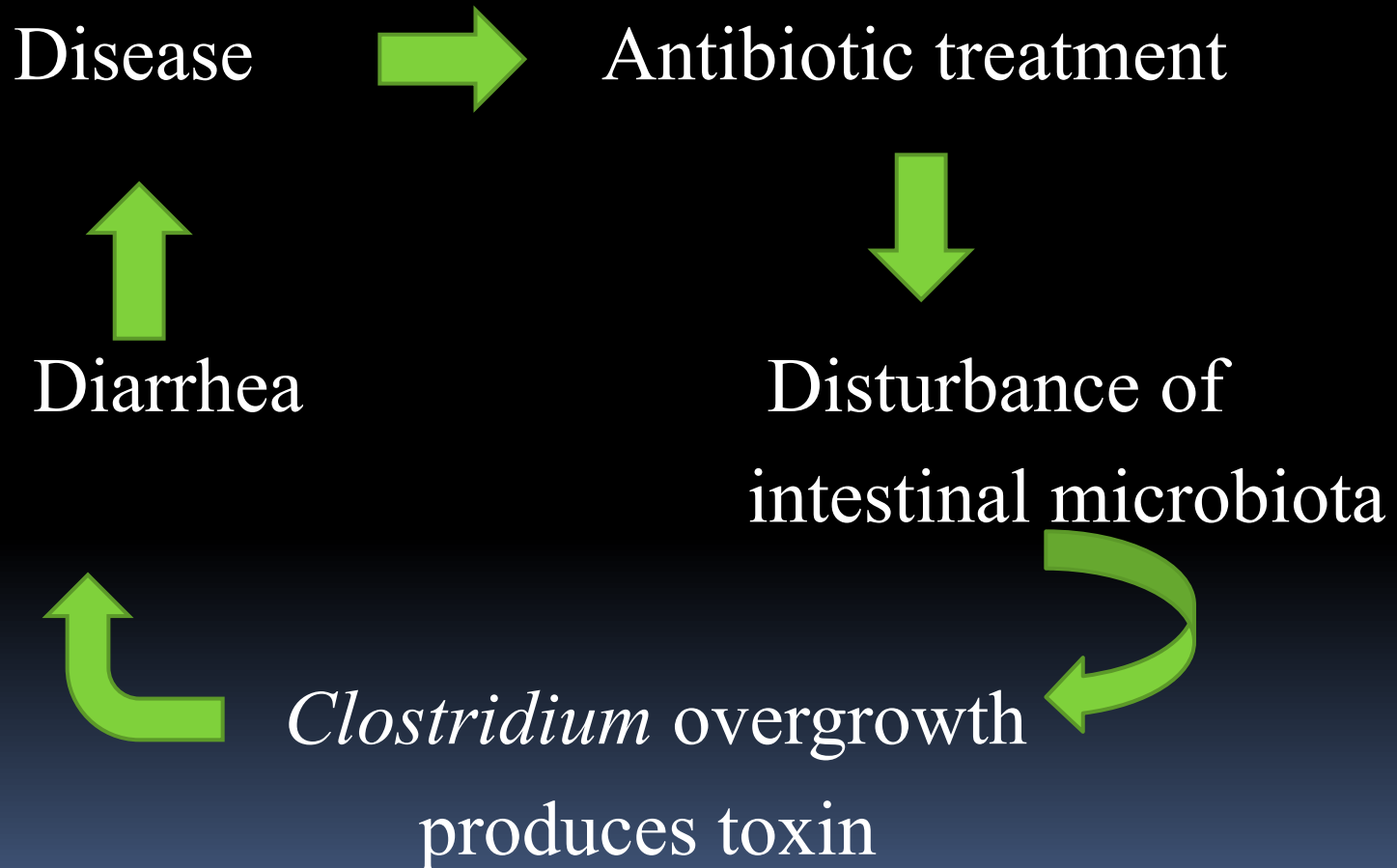
# Advantages of Probiotics

- Produce lactic acid- lowers the pH of intestines and inhibiting bacterial villains such as *Clostridium*, *Salmonella*, *Shigella*, *E. coli*, etc.
- Decreases the production of a variety of toxic or carcinogenic metabolites.
- Aid absorption of minerals, especially calcium, due to increased intestinal acidity.
- Production of  $\beta$ - D- galactosidase enzymes that break down lactose .

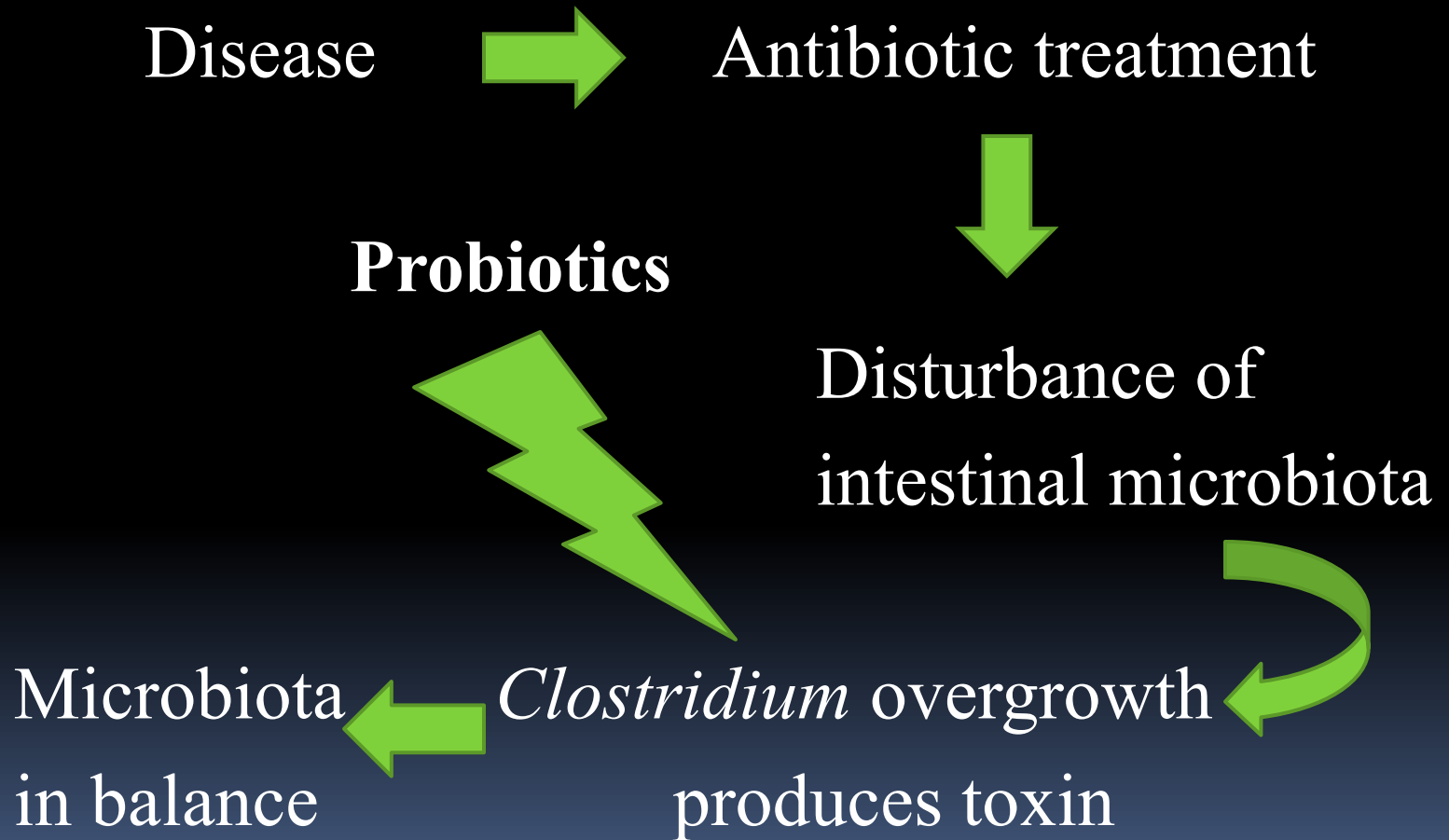


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- **Produce a wide range of antimicrobial substances - acidophilin and bacteriocin etc. help to control pathogenic bacteria .**
  - **Produce vitamins (especially Vitamin B and vitamin K)**
  - **Act as barriers to prevent harmful bacteria from colonizing the intestines**

# Antibiotic associated diarrhea




# Antibiotic associated diarrhea



# Probiotics and Cancer

- **Enzymes (Glycosidase, B- glucuronidase , azoreductase , and nitroreductase ) of the intestinal flora convert the precarcinogens to active carcinogens**
- **Probiotics reduce:**
  - **Faecal concentrations of enzymes**
  - **Secondary bile salts**
  - **Reduce absorption of harmful mutagens that may contribute to colon carcinogenesis.**
- **Activity of *L. acidophilus* and *L. casei* supplementation in humans helped to decrease levels of these enzymes**

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- **Several mechanisms have been proposed as to how lactic acid bacteria may inhibit colon cancer:**
    - **Enhancing the host's immune response**
    - **Altering the metabolic activity of the intestinal microflora**
    - **Binding and degrading carcinogens**
    - **Producing antimutagenic compounds**
    - **Altering the physiochemical conditions in the colon**

# *Helicobacter pylori* Infections

- **It the most common chronic bacterial infection in humans and causes :**
  - **Chronic gastritis**
  - **Peptic ulcers**
- **In vitro studies have suggested that lactic acid bacteria may inhibit or kill *H. pylori* by acting as a bactericide.**
- **Bifidobacteria and *B. subtilis* may inhibit the growth or attachment of *H. pylori*.**

# Probiotic strains currently used

## *Lactobacillus* species

- *L. acidophilus*
- *L. plantarum*
- *L. casei subspecies rhamnosus*
- *L. brevis*
- *L. delbreuckii subspecies bulgaricus*


## *Bifidobacterium* species


- *B. adolescentis*
- *B. bifidum*
- *B. longum*
- *B. infantis*
- *B. breve*

## Others

- *Streptococcus salivarius* ssp. *thermophilus*
- *Lactococcus lactis* ssp. *lactis*
- *Lactococcus lactis* ssp. *cremoris*
- *Enterococcus faecium*
- *Leuconostoc mesenteroides* ssp. *dextranicum*
- *Propionibacterium freudenreichii*
- *Pediococcus acidilactici*
- *Saccharomyces boulardii*



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- **A good probiotic should have most of these strains:**
  - *Bifidobacterium bifidum* - Protects the body against invasive pathogens, salmonella and rotavirus. Helps suppress tumors and reduce inflammation. Helps protect against diarrhea and intestinal infections and strengthens immune system.


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- *Bifidobacterium breve* - Helps prevent rotavirus-induced diarrhea, activates immune system, helps IBS.
  - *Bifidobacteria infantis* - Inhibitory effect on some strains of E. coli. Protects against gastroenteritis and is useful in the prevention and therapy of breast tumors.
  - *Bifidobacteria lactis* - Enhances resistance to oral salmonella typhimurium. Enhances natural immune function. Helps alleviate constipation, prevents diarrhea and decreases chronic inflammation of the colon.

- *Bifidobacterium longum* - Inhibits the development and growth of colon, liver and breast cancers in laboratory animals. Helps prevent diarrhea caused by antibiotic use, helps constipation and reduces fecal odor.
- *Lactococcus lactis* - A natural antibiotic that reduces the ability of pathogenic microbes to grow and cause infection.
- *Lactobacillus salivarius* - Completely inhibit the growth of *Helicobacter pylori* bacteria (major cause of peptic ulcers).

- ***Lactobacillus casei***- Provides protective activity against **Listeria** which have been found to cause the inflammation and infection of the brain and spinal cord (Spinal Meningitis). Inhibits activity in tumor cells and stimulates beneficial activity in normal cells.
- ***Lactobacillus reuteri*** - Controls **Cryptosporidium parvum** (C. Parvum), a parasite that survives chlorination process, infection causing nausea, diarrhea, fever and abdominal cramps.
- ***Lactobacillus sporogenes*** – Can reduce LDL (harmful) cholesterol levels, while increasing HDL (healthy).

# Prebiotics

- **The term prebiotic was introduced by Gibson and Roberfroid who exchanged “pro” for “pre,” which means “before” or “for.”**
  - **A non-digestible food ingredient**
  - **Beneficial effects**
    - **Selective stimulation**
    - **Improved host health**

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- **Prebiotics acts as cofactors for probiotics.**
  - **Complex carbohydrates pass through the small intestine to the lower gut where they become available for some colonic bacteria but are not utilized by the majority of the bacteria present in the colon.**
  - **The main end products of carbohydrate metabolism are short-chained fatty acids, namely acetate, butyrate and propionate, which are further used by the host organism as an energy source.**

# Food grade commercial prebiotics

- **Lactulose**
- **Galactosaccharides**
- **Fructo-oligosaccharides**
- **Isomalto-oligosaccharides**
- **Lacto-sucrose**
- **Gentio-oligosaccharides**
- **Xylooligosaccharides**

# Characteristics of an ideal prebiotics

- It should not be hydrolyzed or absorbed in the upper part of G.I. tract.
- It should be a selective substrate for one or a limited number of potentially bacterial commercial to the colon.
- It should be able to alter the colonic micro flora towards a healthier composition or selectively stimulates the growth and/or activity of intestinal bacteria associated with health and well being.
- It should help in increasing the absorption of certain minerals such as calcium and magnesium.
- It should or may have a favorable effect on the immune system and provide improved resistance against infection.
- Human could consume nearly 10 g of non-digestible fermentable carbohydrates without noticeable side effects and recommended a dose of 5 to 8 g of oligofructose and 10 g of inulin per person.



# Synbiotics

- **Synbiotic = Probiotic + Prebiotic**
- **The concept of synbiotics has been proposed to characterize health-enhancing foods and supplements used as functional food ingredients in humans (Gibson, 2004).**
- **Potential synergy between pro- & prebiotics**
- **Improve survival in upper GIT**
- **Stimulating effect of Probiotics**

# Some of the major health benefits of synbiotics:

- **Increased number of ingested bacteria reaching the colon in a viable form**
- **Antagonistic toward pathogenic bacteria**
- **Production of antimicrobial substances (bacteriocins , hydrogen peroxide, organic acids etc)**
- **Immunostimulation**
- **Anti-inflammatory, Anti-mutagenic, Anti-carcinogenic, and production of bioactive compounds (enzymes, vaccines, peptides etc)**

# Products in the international market using synbiotic health foods concept.

## ▪ Product

- Actifit
- Probioplus
- Symbalance
- Proghurt
- Fysiq
- Vifit
- Fyos
- “On Guard” (Liquid yoghurt)
- Impact
- Orafti’s synergy- 1
- Synbiotic supplement

## ▪ Producer

- Emmi, Switzerland
- Migros, Switzerland
- Tonilait, Switzerland
- Ja naturlich naturprodukte, Austria
- Mona, Netherlands
- Sudmilch / Stassano, Belgium, Germany, UK
- Nutricia, Belgium
- LBL Foods, US
- National Cancer Institute, USA

# Administration of probiotics

- *“The specific microorganisms shall be viable, active & abundant at the level of at least  $10^7$  cfu /g in the product to the date of minimum durability”*
- **Minimum Consumption: 100g of a probiotic food with  $10^7$  cfu/ g.**

# Functional Foods

- **Food is regarded “functional” if consumed as part of a usual diet, providing benefits to one or more target functions in body, beyond basic inherent nutrition.**
- **The first functional food products were launched in Japan where a food category called FOSHU (Foods for Specific Health Use) was established in 1991 to reduce the increasing health-care costs.**

# Probiotic based functional foods

## Cultured Dairy Products

- Yoghurt
- Cheeses
  
- Acidophilus milk
- Bulgaricus milk
  
- Yakult
  
- Bifidus milk
- Buttermilk
- Sour cream
  
- Kefir

## Beneficial Bacteria

- *S. thermophilus, L. bulgaricus & L. acidophilus*
- *L. acidophilus, L. brevis, L. casei, L. caucasicus, L. helveticus, L. lactis, L. plantarum, S. cremoris, S. faecium*
  
- *L. acidophilus*
- *L. bulgaricus*
- *L. casei,*
  
- *B. bifidum, B. longum*
- *L. Lactis, S. cremoris*
- *S. cremoris*
  
- *L. acidophilus, L. caucasicu*