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دانشگاه علوم پزشکی و خدمات بهداشتی درمانی کردستان

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Probiotics

• 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.”**

- **The micro biota of a newborn develops rapidly after the birth .**
- **It is initially dependent mainly on :**
- **the mother's micro biota,**
- **mode of delivery,**
- **birth environment**
- **and rarely genetic factors .**
- **The maternal vaginal and intestinal flora constitutes the source of bacteria, which colonizes the intestine of the newborn.**
- **After infancy probiotics are supplied to us by**
- **raw foods;**
- **lactic acid fermented foods such as yogurt and cheese;**
- **and probiotic supplements.**

Where do Probiotics come from???



The probiotic concept:

- **effects exerted by <u>viable microorganisms</u>**
- **applicable <u>independent</u> of the <u>site of action</u> and <u>route of administration.</u>**
- **include sites such as the oral cavity, the intestine, the vagina, and the skin.**
- **In the case of probiotic foods, the health effect is usually based on <u>alteration of the gastrointestinal micro flora</u> and, therefore, based on survival during gastrointestinal transit.**

Gut Microflora



- **Microbiologically, the gut has <u>three principal regions:</u>**
- **the stomach, small intestine, and colon.**
- **The stomach has very <u>low</u> bacterial numbers**
- **Facultative anaerobes such as lactobacilli, streptococci, and yeast are present at ;100 colony forming units (CFU) per millilitre due to the low environmental pH .**
- **The small intestine has a larger bacterial load that consists of facultative anaerobes such as lactobacilli, streptococci, and enterobacteria as well as anaerobes such as B ifidobacterium spp., Bacteroides spp., and clostridia at levels of ;10^4–10^8 CFU/ml.**
- **However, the 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)**
- **Chronic diarrhea**
- **Stress**



Imbalance of intestinal micro flora results in:

- **Poor nutritional response**
- **Reduced efficacy of medications**
- **Physiological dysfunction**
- **Accelerated aging**
- **Cancer**
- **Deficient immune response**
- **Susceptibility to infection**
- **Physical discomfort**



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.**

The protective and immune barrier of the human gastrointestinal (GI) tract is diverse.It includes :

- **the epithelial layer**
- **the mucous layer**
- **the mechanics of peristalsis**
- **desquamation**
- **actions of secretory IgA**

All of which impact bacterial attachment

- **After attachment, colonic bacteria are prevented from mixing with the host's eukaryotic cells by the epithelial layer, which acts as a vital barrier to invasion.**

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 or by the production of antimicrobial substance in the guts.**

- **It should have a good adhesion/ colonization to human intestinal tract and influence on gut mucosal permeability.**
- **It should be antagonistic against carcinogenic/ pathogenic organism.**
- **It should posses clinically proven health benefit, e.g. gastrointestinal disorders, persistant diarrhoea, clostridium difficle colitis, antibiotics associated diarrhoea, acute infantile gastroenteritis.**
- **It should have technologic properties for commercial viability such as stability of desired characteristics during processing, storage and transportation.**

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



Mechanism for the benefit of Probiotics:

- **Adherence and colonization of the gut**
- **Suppression of growth or epithelial binding/invasion by pathogenic bacteria and production of antimicrobial substances**
- **Improvement of intestinal barrier function**
- **Controlled transfer of dietary antigens**
- **Stimulation of mucosal and systemic host immunity**

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 β- D- galactosidase enzymes that break down lactose .**

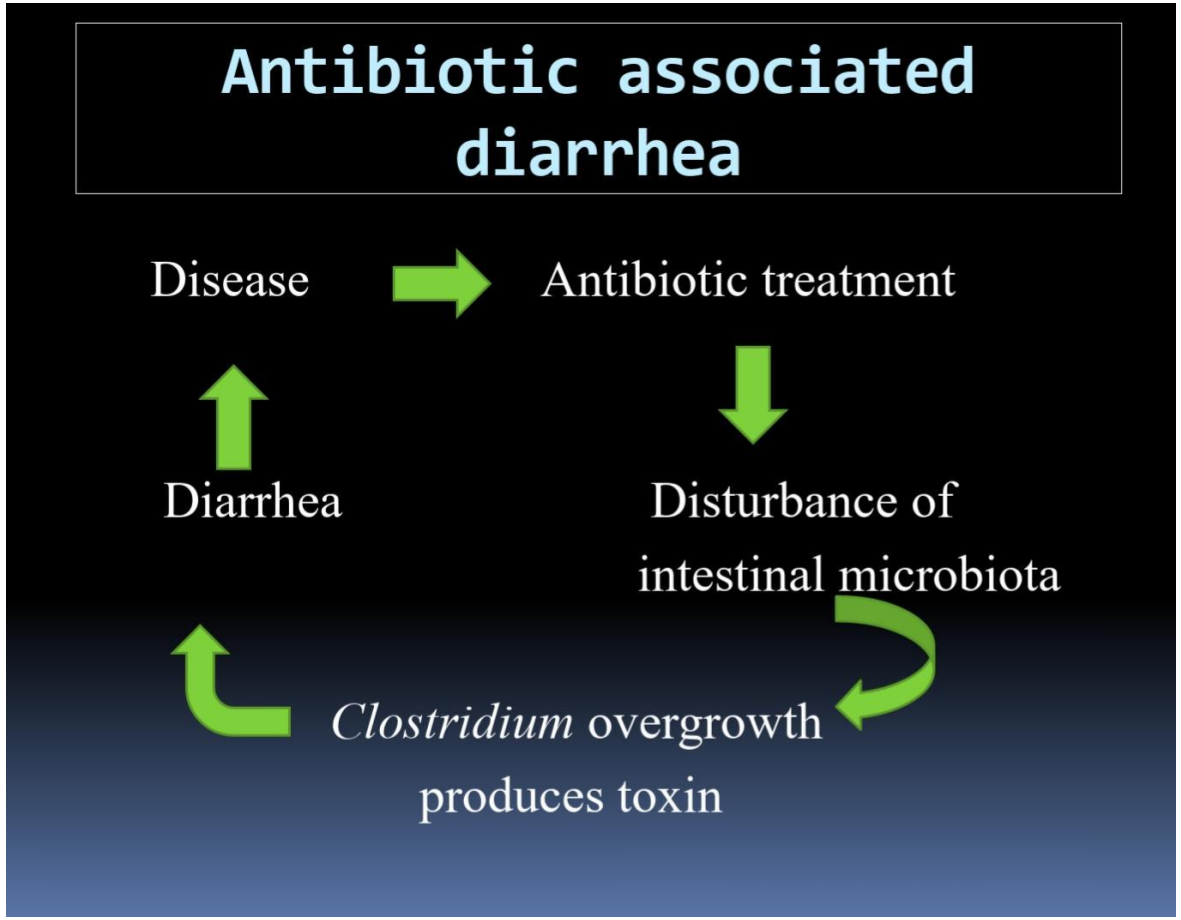
- **Produce a wide range of antimicrobial substances -acidophilin and bacteriocin etc. help to control pathogenic bacteria .**
- **Produce vitamins (especially Vitamin B and vitamin K)**
- **Act as barriers to prevent harmful bacteria from colonizing the intestines**

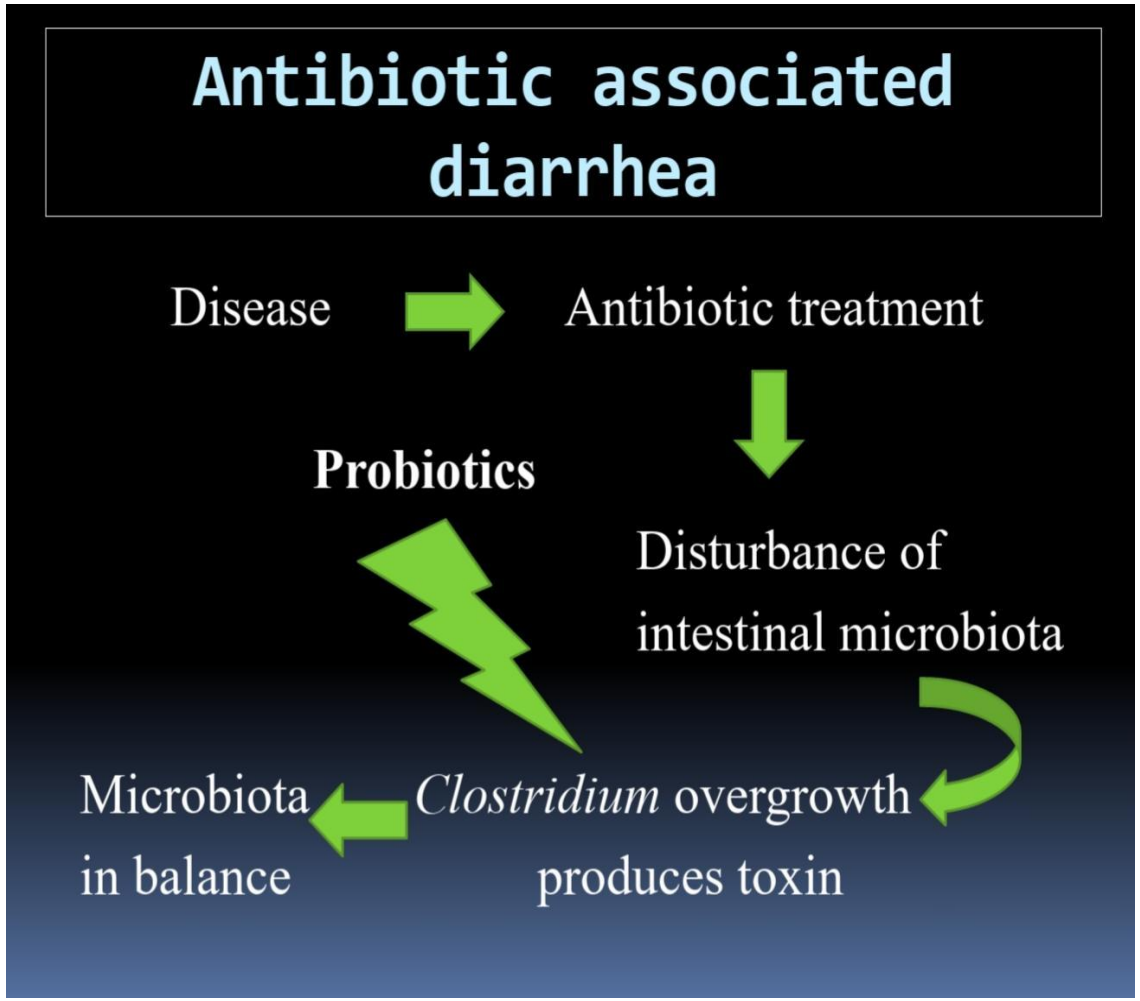
Effects of probiotics on pathogenic bacteria

- **Probiotics reduce plasma levels of bacterial endotoxin concentrations, by inhibiting translocation of bacteria across the GI lumen into the bloodstream.**
- **Decreases in translocation of bacteria may occur as a result of the ability of probiotics to tighten the mucosal barrier.**
- **There are several ways probiotic microflora can prevent pathogenic bacteria from adhering and colonizing gut mucosa.**
- **Probiotics disallow colonization by disease-provoking bacteria through competition for nutrients, immune system up-regulation, production of antitoxins, and up-regulation of intestinal mucin genes.**

- **Probiotics lower colon luminal pH and foster growth of non-pathogenic commensal bacteria by SCFA (Short Chain Fatty Acid) production. One SCFA, acetic acid, has antimicrobial activity against molds, yeasts, and bacteria.**

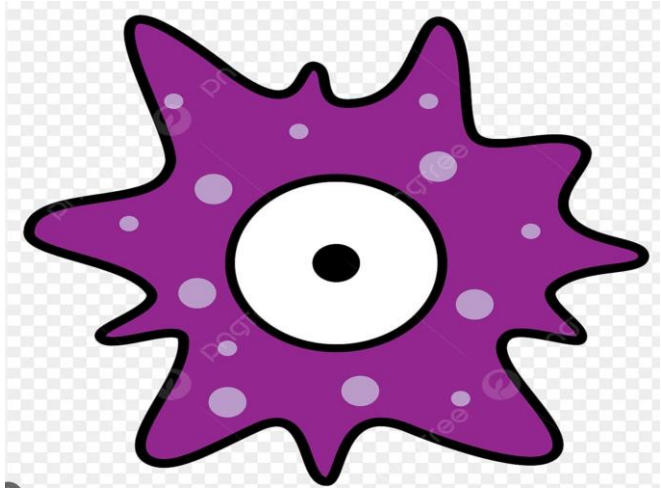
- **Probiotics exert protective effects through production of hydrogen peroxide and benzoic acid, which inhibit many pathogenic, acid-sensitive bacteria .**


Antibiotic associated diarrhea
Disease
Antibiotic treatment
Disturbance of intestinal microbiota
Clostridium overgrowth produces toxin
Diarrhea


Antibiotic associated diarrhea
Disease
Antibiotic treatment
Probiotics
Disturbance of intestinal microbiota
Clostridium overgrowth produces toxin
Microbiota in balance

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**

- **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**

Hepatic Diseases

Mechanisms by which probiotics may treat Hepatic Encephalopathy:

- **Decreased portal blood ammonia by reduced bacterial urease activity**
- **Decreased pH due to less ammonia absorption**
- **Less intestinal permeability and improved gut epithelium**
- **Decreased inflammation and oxidative stress due to reduced ammonia toxins**
- **Reduced uptake of other toxins**



Helicobacter pylori Infections



- **It is the most common chronic bacterial**
- **infection in humans and causes :**
  - **Chronic gastritis**
  - **Peptic ulcers**
  - **Gastric adenocarcinoma**
  - **Lymphoma and a number of non-gastrointestinal disorders.**
- **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.***
- **Possible mechanisms by which *L. salivarius* eradicates *H. pylori* include the ability of the former to bind to gastric epithelial cells, to produce a high quantity of lactic acid, and to proliferate rapidly.**

Use of probiotics beyond GIT



- **Allergy: Probiotics have the potential:**

➢**To modify the structure of antigens**

➢ **Reduce their immunogenicity**

➢**Reduce intestinal permeability**

➢**Generation of proinflammatory cytokines that are elevated in patients with a variety of allergic disorders**

Probiotics in Pregnancy:



- **Bacterial vaginosis , increases the risk of preterm labour and infant mortality .**
- **Probiotics decrease the risk of bacterial vaginosis and maintain normal lactobacilli vaginal flora**
- **Studies using *L. rhamnosus* GG and *B. lactis* BB12 have shown that atopic dermatitis, a condition that causes severe skin rashes in up to 15% of babies, can be prevented in 50% of cases if mothers ingest probiotics during pregnancy and newborns ingest them during the first 6 months of life**

Use of probiotics

- **All probiotics works effectively, if taken after meals, when stomach acid is lowest.**
- **Stomach acid destroys up to 99.9% of probiotics, if taken before a meal but only about 90%, if taken after meal.**
- **Thus, after meal intake ensures maximum delivery to the small intestine, where they reproduce rapidly, populating the colon.**
- **They do most of their good work in the small and large intestines, but they also help the mouth and esophagus to remain uninfected.**

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. brev***

Strains of bacteria one should look for in a probiotic:

- **It is important to choose a high quality formula that contains the right strains of bacteria for optimum results .**
- **It is best to choose a probiotic that contains the entire family of lactobacillus bacteria.**
- **The family members are *: L. acidophilus, L. delbrueckii, L. casei, L. bulgaricus, L. caucasicus, L. fermenti, L. plantarum, L. brevis, L. helveticus, L. leichmannii, L. lactis, L. bifidus, and L.sporogenes.***

- **It is important that the complete family of 13 strains is present. Most people don’t realize this family works in harmony only if the complete family is present.**
- **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.**

- ***Bifidobacterium breve*** **- Helps prevent rotavirus-induced diarrhea and activates your immune system. Also helps IBS.**
- ***Bifidobacteria infantis*** **- Inhibitory effect on some strains of E. coli. Protects against gastroenteritis (inflammation of the stomach and bowels) and is useful in the prevention and therapy of solid tumors (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*** **- Able to eliminate harmful nitrates commonly found in foods. 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*** **- Produces a high amount of lactic acid, thus completely inhibiting the growth of Helicobacter pylori (H. pylori) bacteria, which are now known to be the major cause of peptic ulcers. It is also effective against Salmonella typhimurium**

- ***Lactobacillus casei-*** **Provides protective activity against Listeria bacteria 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 the chlorination process, sometimes found in springs or water wells, infection causing nausea, diarrhea, fever and abdominal cramps. Beneficial in the treatment of diarrhea associated with rotavirus, E. coli and Salmo/nella.**
- ***Lactobacillus sporogenes*** **– Can reduce LDL (harmful) cholesterol levels, while increasing HDL (healthy).**
- ***Streptococcus thermophilus -*** **Its antioxidant activity scavenges the body for free radicals. Effective in maintaining vaginal and intestinal health.**

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**

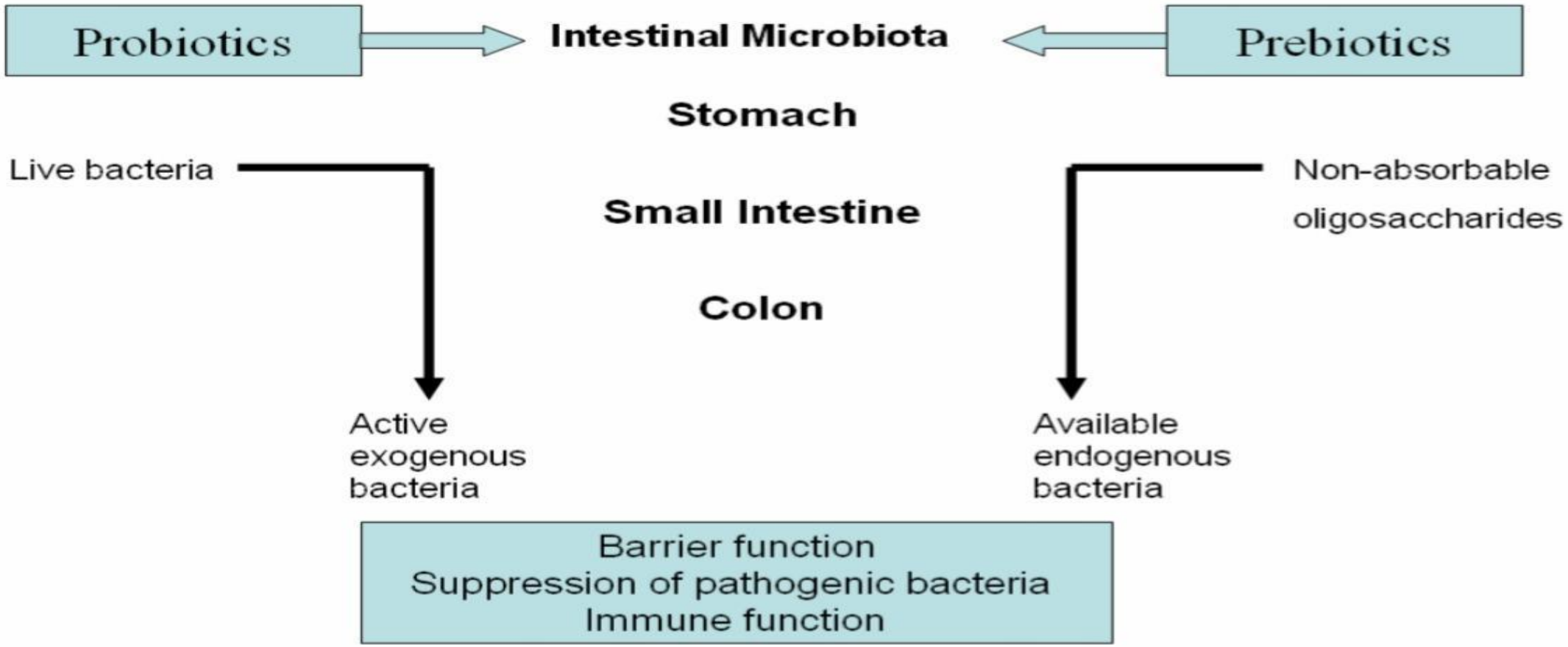
➢ **Beneficial effects**

- **Selective stimulation**
- **Improved host health**



- **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.**

Concept of Probiotics and Prebiotics



Food grade commercial prebiotics

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

Food grade oligosaccharides in commercial production

- **The purely vegetable Fructo-oligosaccharides or Fructofibres® consist of inulin and oligofructose, which are inert polysaccharides.**
- **Inulin and oligo-fructose, cannot be split by the enzymes of the upper digestive tract and pass through the intestine without being digested or absorbed.**
- **They therefore have no significant calorie value (1–2 kcal/g). Components of food that cannot be broken down by digestive enzymes pass through the small intestine, intact, increasing bulk or faecal mass. They may then undergo fermentation by the intestinal flora in the large intestine.**

- **Fructo-oligosaccharides alter the intestinal microflora balance in a positive way.**
- **Fructofibres® stimulate the proliferation of the health-promoting bacteria in the gastro-intestinal tract and encourage their metabolic selectivity.**
- **These effects promote a healthy digestive tract and increased resistance to infection.**

Characteristics of an ideal prebiotics

- **It should not be hydrolyzed or absorbed in the upper part of G.I. tract..**
- **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**

➢**More efficient implantation**

➢**Stimulating effect of Probiotics**

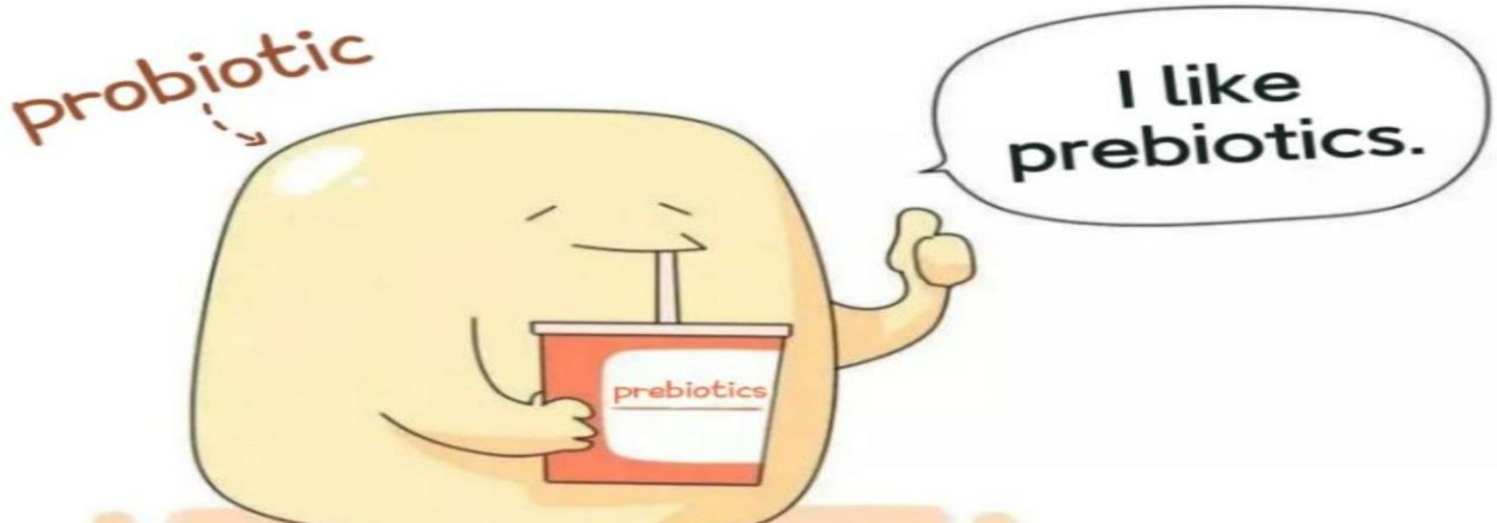


Some of the major health benefits of synbiotics:

- **Improved survival of live bacteria in food products, prolonged shelf life,**
- **Increased number of ingested bacteria reaching the colon in a viable form**
- **Stimulation in the colon of the growth and implantation of both exogenous and endogenous bacteria**
- **Activation of metabolism of beneficial bacteria, 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)**

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**

	Beneficial Bacteria
Yoghurt	***. thermophilus, L. bulgaricus & L. acidophilus***
Cheeses	***L. acidophilus, L. brevis, L. casei, L. caucasicus, L. helveticus, L. lactis, L. plantarum, S. cremoris, S. faecium***
Acidophilus milk	***L. acidophilus***
Bulgaricus milk	***L. bulgaricus***
Yakult	***L. casei,***
Bifidus milk	***B. bifidum, B. longum***
Buttermilk	***L. Lactis, S. cremoris***
Sour cream	***S. cremoris***
Kefir	***L. acidophilus, L. caucasicu***

Postbiotics

- Postbiotics are bioactive compounds produced **during the digestion of prebiotics and probiotics.** They are the "**waste products" of gut microbiota,** including metabolites, short-chain fatty acids, and antimicrobial peptides, which can benefit the host. These
- **What they are:**
- Postbiotics are a relatively new term for the beneficial substances produced by gut bacteria after they are no longer alive or inactivated.
- **How they're formed:**
- They are created as byproducts during the fermentation of food in the gut, especially when consuming prebiotics (food that feeds gut bacteria) and probiotics (live bacteria).

Example of postbiotics

- **Short-chain fatty acids (SCFAs):** Like butyrate, acetate, and propionate, which are important for gut health and help healthy bacteria thrive.
- **Vitamins:** Including **vitamins B and K**, which are produced by gut bacteria.
- **Antimicrobial peptides:** These substances can help control the growth of harmful bacteria.
- **Other metabolites and cell components:** Including cell lysates, functional proteins, and extracellular polysaccharides.

- **Benefits:**
- **Support gut health:** SCFAs, in particular, are important for gut health and can help healthy bacteria flourish.
- **Promote immune health:** Some postbiotics may help regulate the immune system and improve immune responses.
- **Help manage allergies and other conditions:** Postbiotics have shown some promise in managing allergies, eczema, and even diarrhea.
- **How to increase postbiotic production:**
- Eating a diet rich in prebiotics (fiber from fruits, vegetables, grains, and legumes) and probiotics (fermented foods like yogurt, kefir, tempeh, and kimchi) can help increase the production of beneficial postbiotics.

12 Probiotic Foods



1.Yogurt



2. Kefir



3. Sauerkraut



4. Tempeh



5. Kimchi



6. Pickles



7. Buttermilk



8. Miso



9. Kombucha



10. Some Cheeses



11. Natto



12. Fermented Veggies

Prebiotic Foods

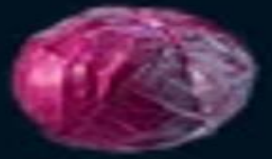
Prebiotics are non-digestible compounds within our food that feed healthy gut bacteria.


Mushrooms


Artichoke


Onions


Asparagus


Cabbage


Apples


Watermelon


White Peaches


Grapefruit


Bananas


Chickpeas


Wheat Pasta


Red Kidney Beans


Oats


Wheat Bread

