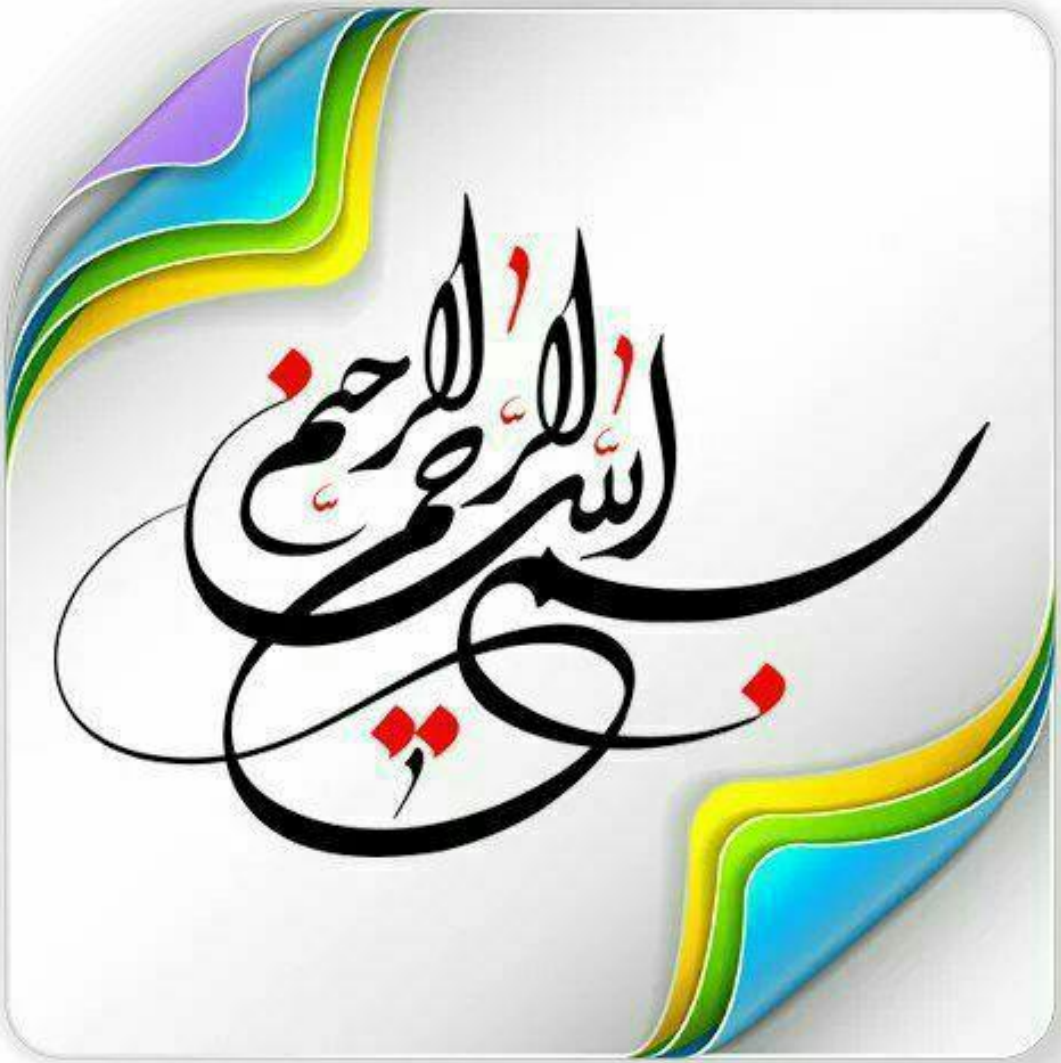
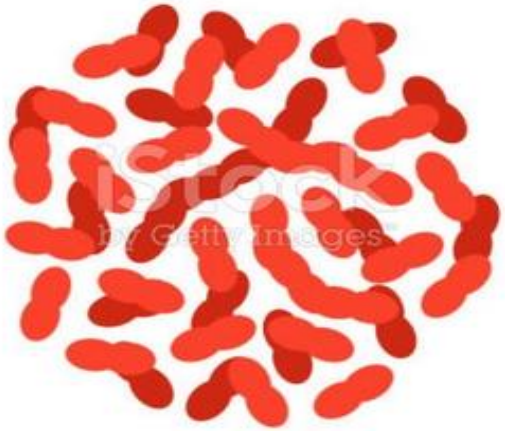

بسم الله الرحمن الرحيم


PROBIOTICS

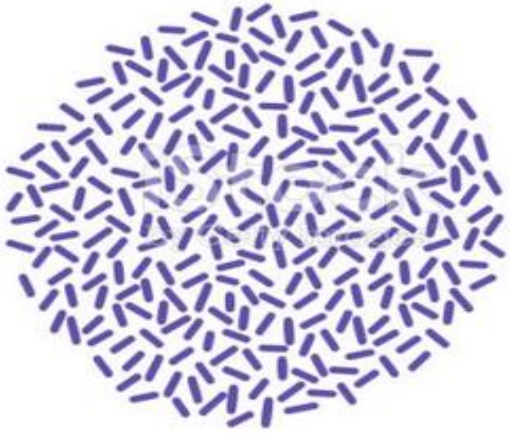
Probiotics are live bacteria and yeasts that have been found to help promote better digestive health and support your immune system. These microorganisms exist in your intestines and help to break down food, absorb nutrients, and minimize harmful bacteria that may otherwise cause disease. You can get more probiotics by incorporating probiotic-rich foods or supplements into your diet. Foods containing probiotics include yogurt, and kefir.

PROBIOTICS

LACTOBACILLUS

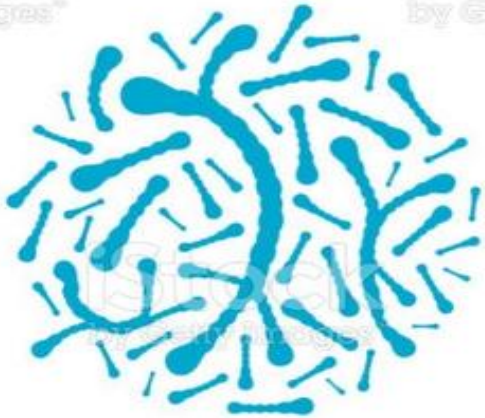


LACTOCOCCUS



PROPIONIBACTERIUM

STREPTOCOCCUS THERMOPHILUS



BIFIDOBACTERIUM

BULGARICUS

ProBioticS

Aids digestion

It improves bowel movement

They reach the Intestine alive.

They can be ingested as food.

They produce beneficial effect on health.

Prevent harmful bacteria from multiplying in the intestine.

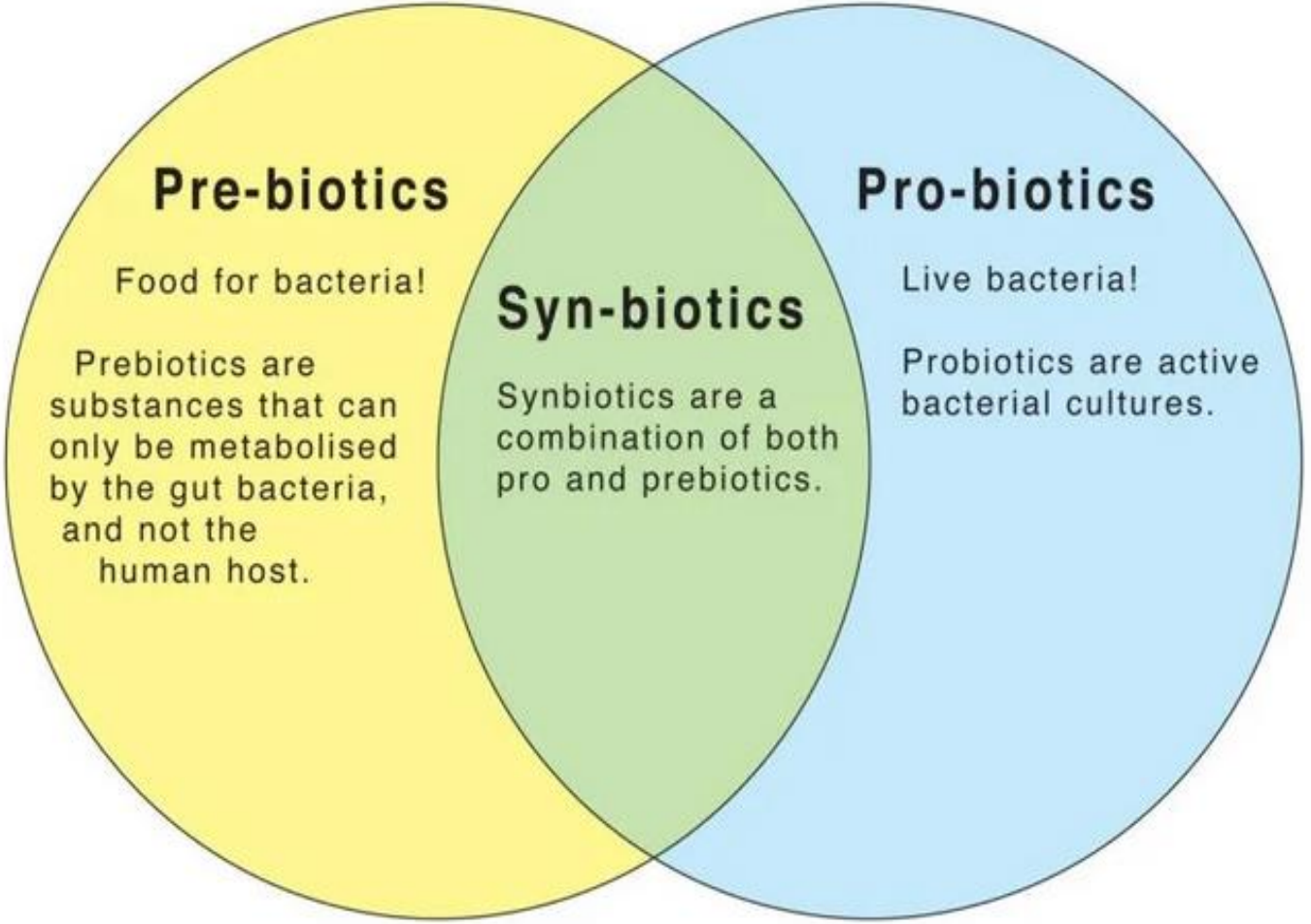
World Health Organization (WHO) defines "probiotics" as "**live microorganisms** that, when administered in **adequate amounts**, confer a perceived **health benefit** on the host". These intentionally ingested microorganisms consist **mainly of bacteria but also include yeasts.** Products containing dead microorganisms and those made by microorganisms are, by definition, not probiotics.

Probiotics (Greek *pro*, for, and *bios*, life) confer various benefits especially to individuals who experience major changes in their normal microflora due to disease, surgery, or other medical treatments, or whose normal microflora changes for other reasons, such as poor diet. Oral administration of probiotic organisms reestablish the natural balance of gastrointestinal flora and return the host to normal health and nutrition.

Probiotic microorganisms are host-specific; thus a strain selected as a probiotic in one animal may not be suitable in another species. Probiotics are subcategorized into probiotic drugs, probiotic foods (e.g., foods, food ingredients, and dietary supplements), direct-fed microbials (probiotics for animal use), and designer probiotics (genetically modified probiotics).

Prebiotics

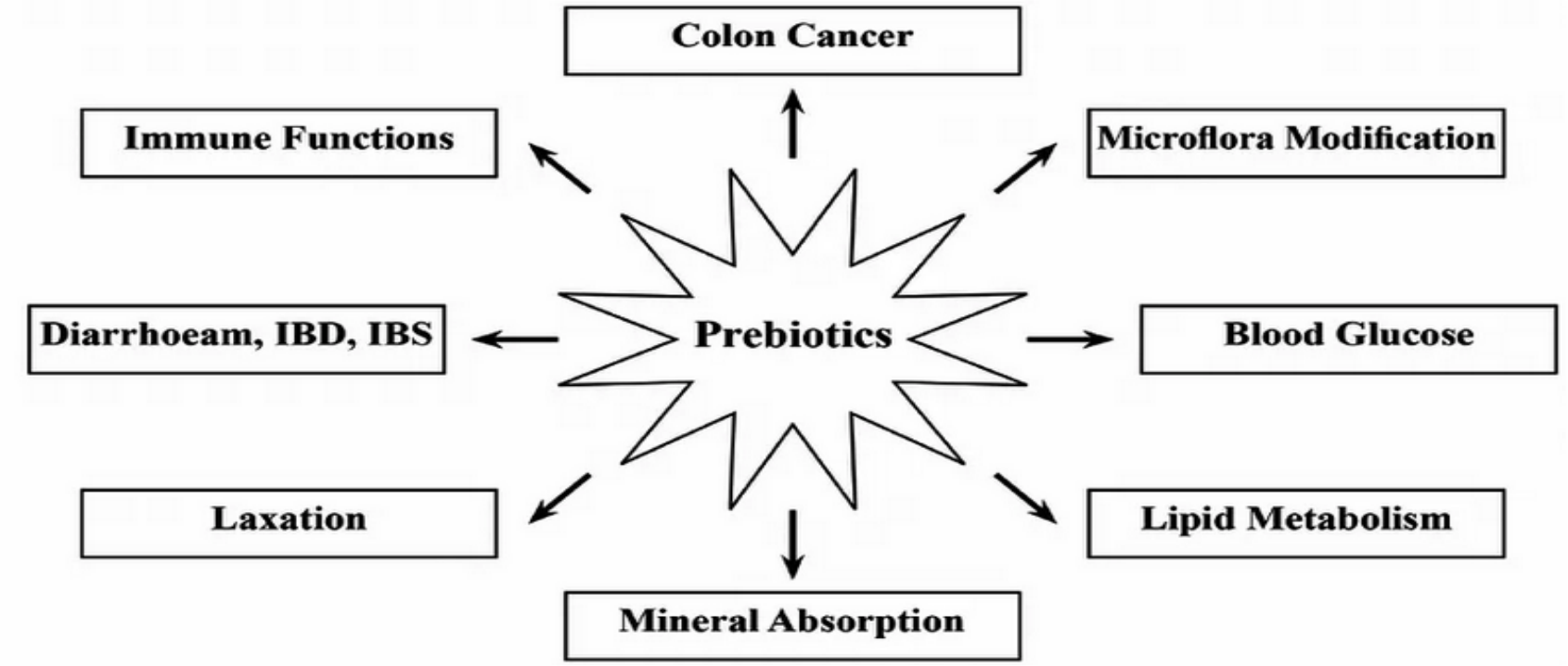
Probiotics should **not be confused with prebiotics** which are food ingredients, typically complex carbohydrates (mostly consisting of nonstarch polysaccharides and oligosaccharides) that escape digestion in the upper gastrointestinal tract and are available for microorganisms living in the colon.



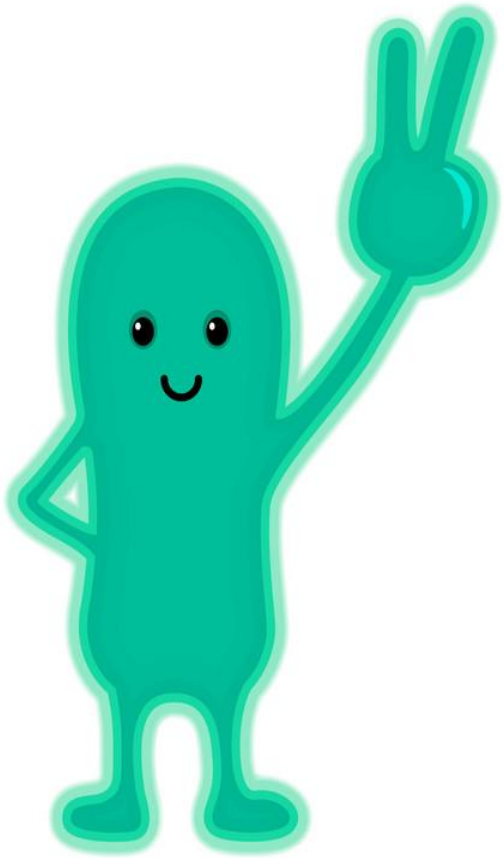
Health Benefits of Prebiotics

The use of both prebiotics and/or probiotics is intended to influence the gut environment for the benefit of human health and their beneficial effects extend beyond the gut. Fermentation of oligofructose in the colon results in a large number of physiologic effects, including:

- Increasing the number of bifidobacteria in the colon
- Increasing calcium absorption
- Increasing fecal weight
- Shortening gastrointestinal transit time
- Possibly lowering blood lipid levels

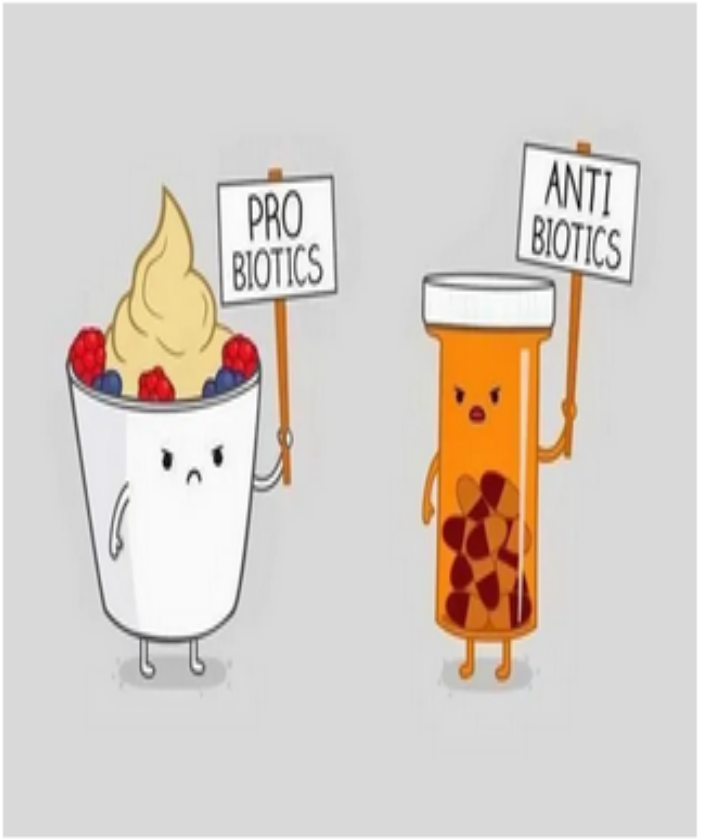


Possible health benefits of prebiotics (image source)



PROBIOTIC

Probiotics vs. Antibiotics

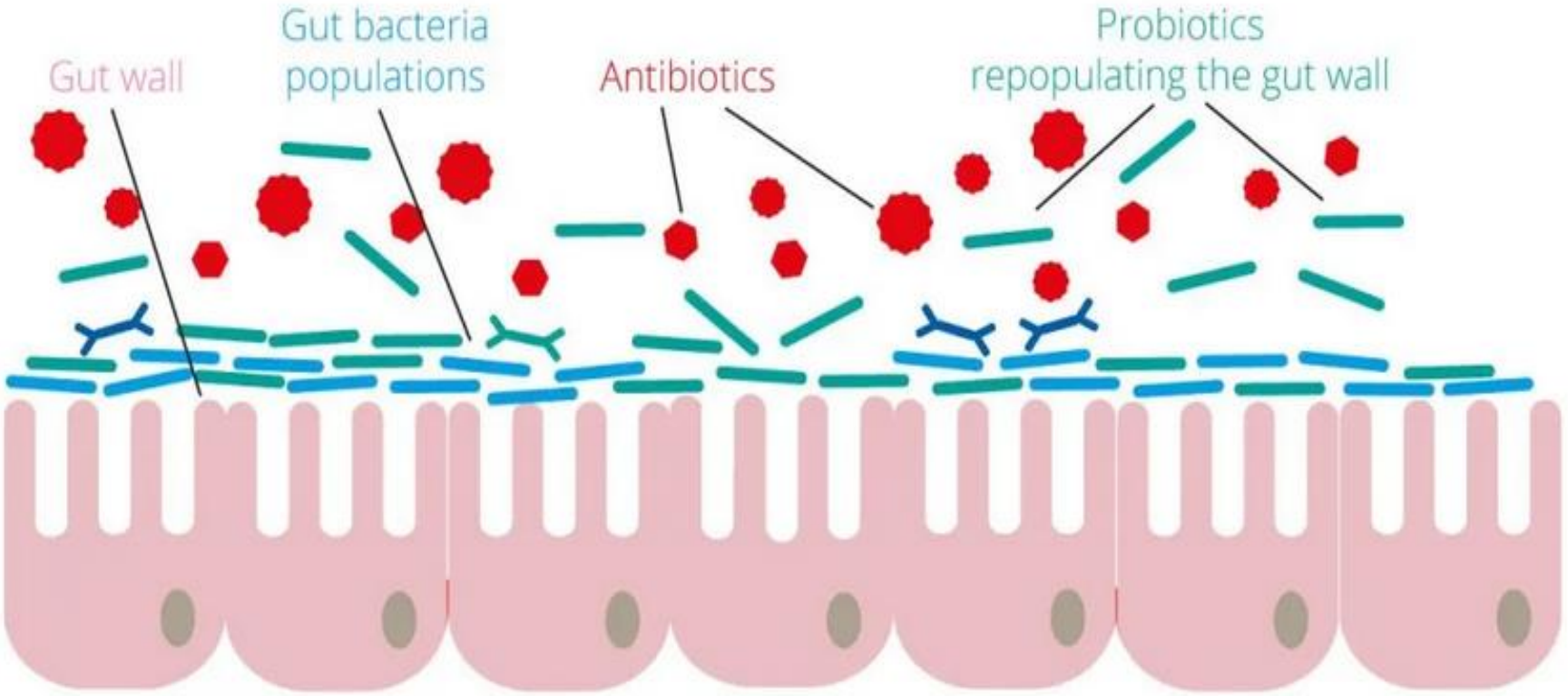


The term "**probiotic**" literally means "**for life**" and "**antibiotic**" literally means "**opposing life**" are two opposing categories of supplements or drugs. **Antibiotics** (Greek *anti*, against, and *bios*, life) are used to prevent and treat infections caused by pathogenic bacteria whereas **probiotics** (Greek pro, for, and bios, life) are used to replenish good bacteria.

For example, during the course of antibiotics treatment, good bacteria of the gut are also wiped out, taking probiotics helps to restore the gut microbiome, thus restoring the healthy state of the gut.

Antibiotics along the gut cell wall

Antibiotics kill both good and bad bacteria. Probiotics help to replenish the good bacteria populations.



Probiotic Microorganisms

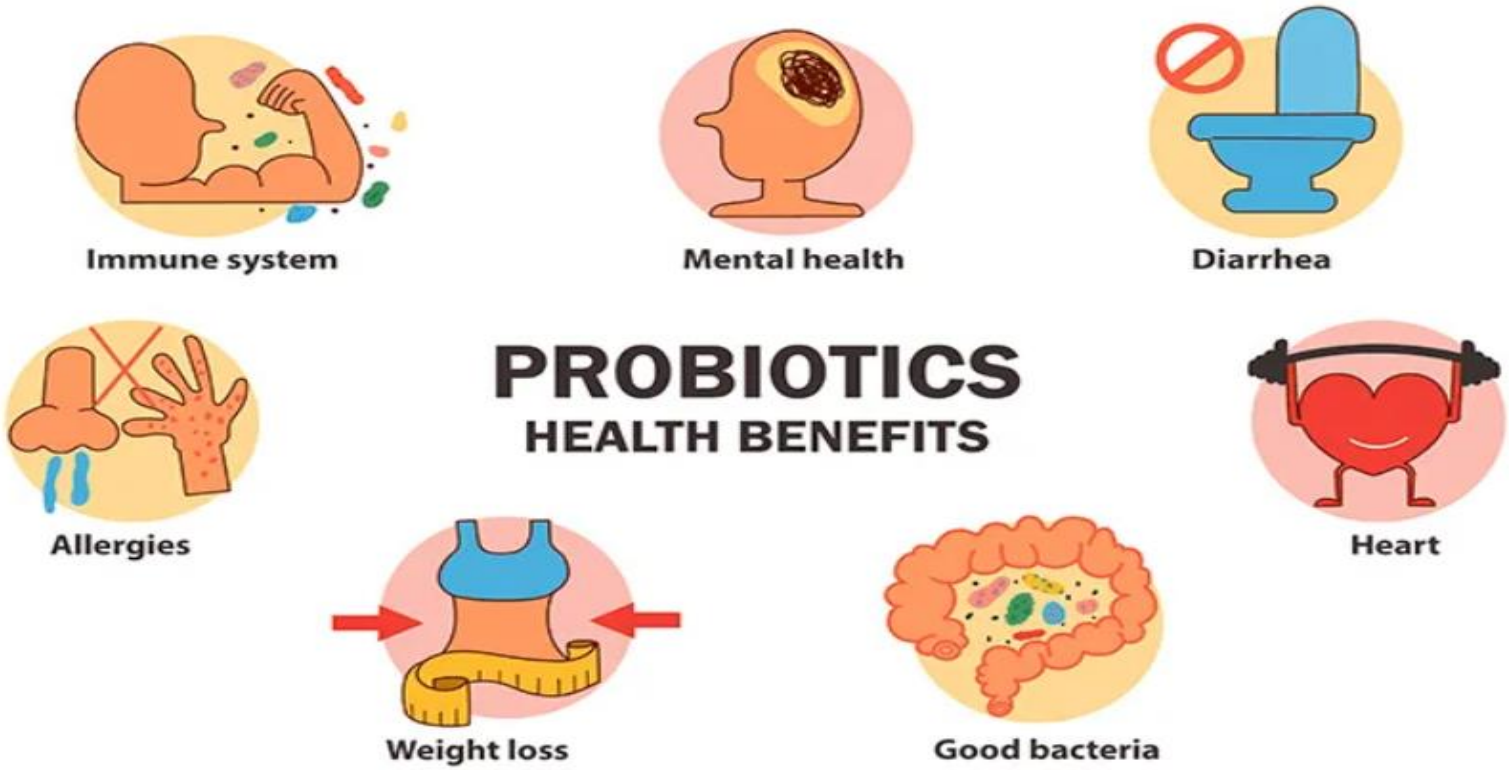
- A probiotic should contain a number of viable cells greater than 10^6 to 10^8 per dose to be efficacious. Seven microorganisms most often used in probiotic products are ***Lactobacillus, Bifidobacterium, Saccharomyces, Streptococcus, Enterococcus, Escherichia,*** and ***Bacillus.***
- These beneficial microorganisms are **naturally present in fermented foods** (such as yogurt, kefir, etc), may be added to other food products, and also available as dietary supplements or as drugs. Probiotic microorganisms from commercial providers come in a variety of forms, including powders, pills, liquid suspensions, and food products.

Microorganisms selected for probiotic use should exhibit the following characteristics:

- Adhere to the intestinal mucosa of the host
- Be easily cultured
- Be nontoxic and nonpathogenic to the host
- Exert a beneficial effect on the host
- Produce useful enzymes or physiological end products that the host can use
- Remain viable for a long time
- Withstand HCl in the host's stomach and bile salts in the small intestine

Health Benefits of Probiotics

Numerous clinical trials have proven the health benefits of probiotics but the exact mechanisms of the health benefits are not fully understood. Gut health is the most important target for probiotics. Prevention and treatment of different forms of diarrhea is one of the most successful and best-documented health benefits of probiotics.

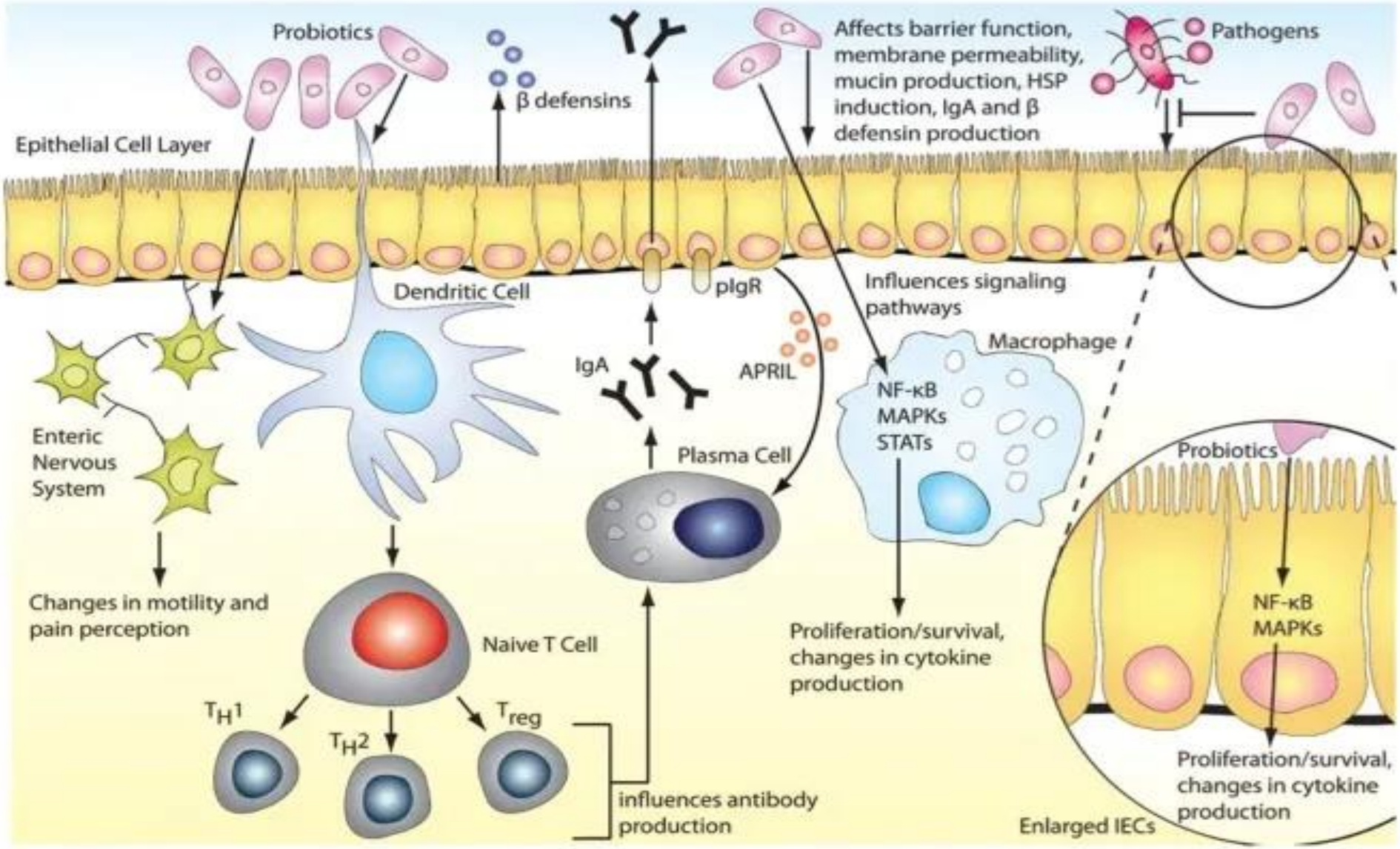


Health benefits of probiotics (Image source)

- *Lactobacillus*, *Bifidobacterium*, *Escherichia*, *Enterococcus*, and *Saccharomyces* are some of the most widely used probiotic microorganisms.

- There are several possible explanations of how probiotic microorganisms displace pathogens and enhance the development and stability of the microbial balance in the large intestine.

Mechanisms


Probiotics
β defensins
Affects barrier function, membrane permeability, mucin production, HSP induction, IgA and β defensin production
Pathogens
Epithelial Cell Layer
Dendritic Cell
pIgR
Influences signaling pathways
Macrophage
IgA
APRIL
NF-κB
MAPKs
STATs
Enteric Nervous System
Plasma Cell
Probiotics
Changes in motility and pain perception
Naive T Cell
Proliferation/survival, changes in cytokine production
NF-κB
MAPKs
T_H1
T_H2
T_{reg}
influences antibody production
Proliferation/survival, changes in cytokine production
Enlarged IECs

Competition with pathogens for nutrients and adhesion sites

The beneficial bacteria prevent the colonization of pathogenic microorganisms by competitive inhibition for microbial adhesion sites. For example, *Lactobacillus casei* and *Lactobacillus plantarum* competitively inhibit the attachment of enteropathogenic *Escherichia coli*.

Inactivation of pathogenic bacterial toxins or metabolites

Some members of the intestinal microbiota influence the onset of carcinogenesis by producing enzymes, such as glycosidase, azoreductase, nitroreductase, and β-glucoronidase, which transform pre-carcinogens into active carcinogens. Human studies have shown that the ingestion of *L. acidophilus* or *Lactobacillus casei* results in reduced levels of the above enzymes in the stools of volunteers. It's not yet confirmed that consumption of these probiotic microorganisms actually reduces the incidence of cancer.

Production of substances that inhibit pathogen growth

Probiotic microorganisms produce organic acids, fatty free acids, ammonia, hydrogen peroxide, and **bacteriocins**, all of which have antimicrobial activity. For example, *L. casei* produces a low-molecular-weight antibacterial substance that is inhibitory to both Gram-positive and Gram-negative enteric bacteria. Probiotics suppress the growth of pathogens also by inducing the host's production of β-defensin and IgA.

Stimulation of nonspecific immunity

Oral administration of different probiotics have shown adjuvant-like effects on intestinal and systemic immunity. Enhanced phagocytic activity against intracellular pathogens and enhanced immunoglobulin A (IgA) responses against pathogenic viruses have been demonstrated in several studies. Probiotics may be able to fortify the intestinal barrier by maintaining tight junctions and inducing mucin production.

In-vitro and in-vivo studies suggest that probiotics may modulate the immune response by promoting endogenous host defense systems. Probiotic bacteria can modify various immune parameters, including humoral, cellular, and nonspecific immunity

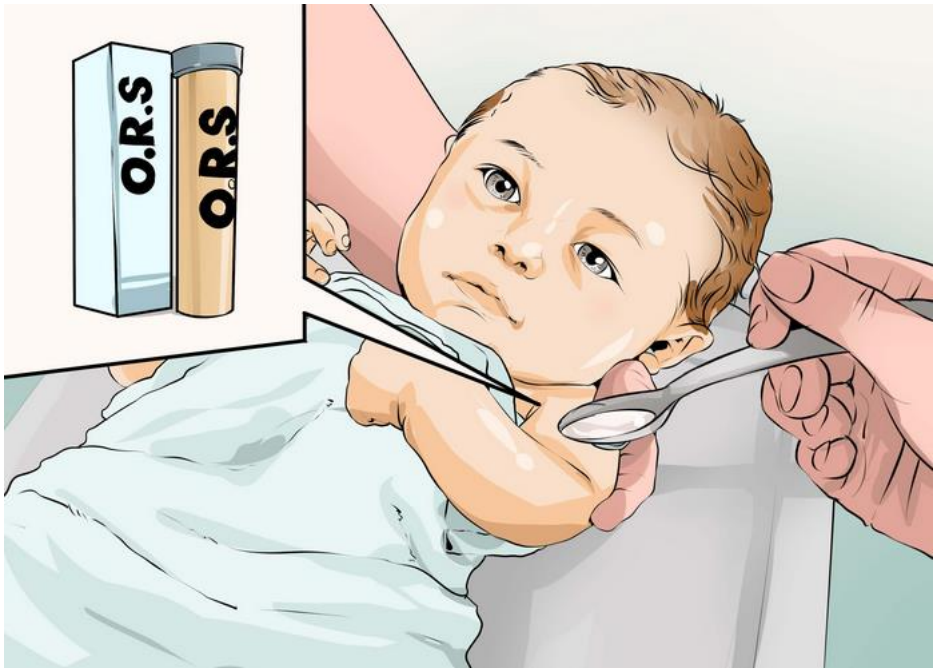
- Enhance the activity of natural killer cells in the elderly
- Induces mucus production
- Activate macrophage by lactobacilli signaling
- Stimulate secretory IgA and neutrophils
- Inhibit release of inflammatory cytokines, etc.

Prevention of Dirrhea

Consumption of probiotics microorganisms such as *Lactobacillus rhamnosus* GG, *Bifidobacterium lactis* BB-12 and *Lactobacillus reuteri* SD2222 has shown a significant reduction in incidence or duration of certain diarrheal illnesses such as rotavirus diarrhea. Prophylactic use in hospitalized children has also resulted in a reduction in the risk of acquiring nosocomial diarrhea.

Mechanisms that have been proposed for this protective effect include competitive blockage of receptor sites (resulting in inhibition of virus adherence and invasion), enhancement of the host immune system, and production of substances that inactivate virus particles.

توجه



در موارد اسهال حاد با دزیدراتاسیون شدید و متوسط به هیچ وجه پروبیوتیک جایگزین مایع درمانی مناسب نخواهد شد

Kids and Diarrhea

- Some of the best proof that probiotics work comes from studies of diarrhea in children, especially when it's caused by rotavirus. Probiotics might cut bouts of infectious diarrhea by half a day to about 2 days.
- Some research shows that the bacteria strains most likely to help are *Lactobacillus reuteri*, *Lactobacillus rhamnosus*, and the probiotic yeast *Saccharomyces boulardii*, although other strains might be useful. A mix of a few different probiotics may also treat this type of diarrhea.

Main results

Cochrane Database Syst Rev. 2010 Nov; 2010(11): CD003048.
Published online 2010 Nov 10. doi: 10.1002/14651858.CD003048.pub3

Probiotics for treating acute infectious diarrhoea

- Sixty-three studies met the inclusion criteria with a total of 8014 participants. Of these, 56 trials recruited infants and young children. The trials varied in the definition used for acute diarrhoea and the end of the diarrhoeal illness, as well as in the risk of bias. The trials were undertaken in a wide range of different settings and also varied greatly in organisms tested, dosage, and participants' characteristics. No adverse events were attributed to the probiotic intervention.
- Probiotics reduced the duration of diarrhoea, although the size of the effect varied considerably between studies.
- The average of the effect was significant for mean duration of diarrhoea (mean difference 24.76 hours; 95% confidence interval 15.9 to 33.6 hours; n=4555, trials=35) diarrhoea lasting ≥4 days (risk ratio 0.41; 0.32 to 0.53; n=2853, trials=29) and stool frequency on day 2 (mean difference 0.80; 0.45 to 1.14; n=2751, trials=20).

- The differences in effect size between studies was not explained by study quality, probiotic strain, the number of different strains, the viability of the organisms, dosage of organisms, the causes of diarrhoea, or the severity of the diarrhoea, or whether the studies were done in developed or developing countries.

Authors' conclusions

- Used alongside rehydration therapy, probiotics appear to be safe and have clear beneficial effects in shortening the duration and reducing stool frequency in acute infectious diarrhoea. However, more research is needed to guide the use of particular probiotic regimens in specific patient groups.

BMJ

- To compare the efficacy of five probiotic preparations recommended to parents in the treatment of acute diarrhoea in children. Design Randomised controlled clinical trial in collaboration with family paediatricians over 12 months. Primary care. Children aged 3-36 months visiting a family paediatrician for acute diarrhoea. Children's parents were randomly assigned to receive written instructions to purchase a specific probiotic product: oral rehydration solution (control group); Lactobacillus rhamnosus strain GG; Saccharomyces boulardii; Bacillus clausii; mix of L delbrueckii var bulgaricus, Streptococcus thermophilus, L acidophilus, and Bifidobacterium bifidum; or Enterococcus faecium SF68.

- Primary outcomes were duration of diarrhoea and daily number and consistency of stools. Secondary outcomes were duration of vomiting and fever and rate of admission to hospital. Safety and tolerance were also recorded. 571 children were allocated to intervention. Median duration of diarrhoea was significantly shorter ($P<0.001$) in children who received L rhamnosus strain GG (78.5 hours) and the mix of four bacterial strains (70.0 hours) than in children who received oral rehydration solution alone (115.0 hours). One day after the first probiotic administration, the daily number of stools was significantly lower ($P<0.001$) in children who received L rhamnosus strain GG and in those who received the probiotic mix than in the other groups. The remaining preparations did not affect primary outcomes. Secondary outcomes were similar in all groups

- . Not all commercially available probiotic preparations are effective in children with acute diarrhoea.
- Paediatricians should choose bacterial preparations based on effectiveness data.

Cochrane Database of Systematic Reviews | Review - Intervention

New search Conclusions changed

Probiotics for the prevention of Clostridium difficile-associated diarrhea in adults and children

Joshua Z Goldenberg, Christina Yap, Lyubov Lytvyn, Calvin Ka-Fung Lo, Jennifer Beardsley, Dominik Mertz, Bradley C Johnston Authors' declarations of interest

Version published: 19 December 2017 Version history

https://doi.org/10.1002/14651858.CD006095.pub4

Main results

Thirty-nine studies (9955 participants) met the eligibility requirements for our review. Overall, 27 studies were rated as either high or unclear risk of bias. A complete case analysis (i.e. participants who completed the study) among trials investigating CDAD (31 trials, 8672 participants) suggests that probiotics reduce the risk of CDAD by 60%. The incidence of CDAD was 1.5% (70/4525) in the probiotic group compared to 4.0% (164/4147) in the placebo or no treatment control group (RR 0.40, 95% CI 0.30 to 0.52; GRADE = moderate). Twenty-two of 31 trials had missing CDAD data ranging from 2% to 45%. Our complete case CDAD results proved robust to sensitivity analyses of plausible and worst-plausible assumptions regarding missing outcome data and results were similar whether considering subgroups of trials in adults versus children, inpatients versus outpatients, different probiotic species, lower versus higher doses of probiotics, or studies at high versus low risk of bias. However, in a post hoc analysis, we did observe a subgroup effect with respect to baseline risk of developing CDAD. Trials with a baseline CDAD risk of 0% to 2% and 3% to 5% did not show any difference in risk but trials enrolling participants with a baseline risk of > 5% for developing CDAD demonstrated a large 70% risk reduction (interaction P value = 0.01)

Among studies with a baseline risk > 5%, the incidence of CDAD in the probiotic group was 3.1% (43/1370) compared to 11.6% (126/1084) in the control group (13 trials, 2454 participants; RR 0.30, 95% CI 0.21 to 0.42; GRADE = moderate). With respect to detection of *C. difficile* in the stool pooled complete case results from 15 trials (1214 participants) did not show a reduction in infection rates. *C. difficile* infection was 15.5% (98/633) in the probiotics group compared to 17.0% (99/581) in the placebo or no treatment control group (RR 0.86, 95% CI 0.67 to 1.10; GRADE = moderate). Adverse events were assessed in 32 studies (8305 participants) and our pooled complete case analysis indicates probiotics reduce the risk of adverse events by 17% (RR 0.83, 95% CI 0.71 to 0.97; GRADE = very low). In both treatment and control groups the most common adverse events included abdominal cramping, nausea, fever, soft stools, flatulence, and taste disturbance.

Authors' conclusions

Based on this systematic review and meta-analysis of 31 randomized controlled trials including 8672 patients, moderate certainty evidence suggests that probiotics are effective for preventing CDAD (NNTB = 42 patients, 95% CI 32 to 58). Our post hoc subgroup analyses to explore heterogeneity indicated that probiotics are effective among trials with a CDAD baseline risk >5% (NNTB = 12; moderate certainty evidence), but not among trials with a baseline risk ≤5% (low to moderate certainty evidence). Although adverse effects were reported among 32 included trials, there were more adverse events among patients in the control groups. The short-term use of probiotics appears to be safe and effective when used along with antibiotics in patients who are not immunocompromised or severely debilitated. Despite the need for further research, hospitalized patients, particularly those at high risk of CDAD, should be informed of the potential benefits and harms of probiotics.


Thank you