Functional foods and nutraceutical for Gastrointestinal area

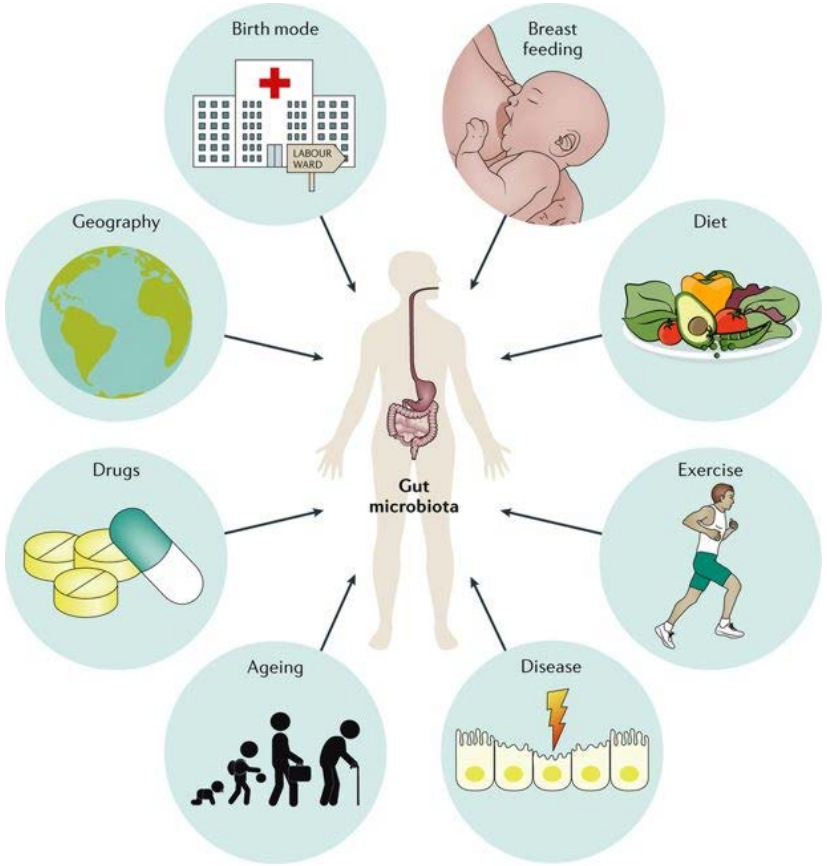
U7

The vitality and functionality of the organism depend on its ability to assimilate, use the nutrients and to eliminate waste substances. Essential processes for life, such as generation of energy, tissue formation and regeneration and detoxification are based on functions coordinated by the digestive system.
Consequently, a diminished activity or a digestive system malfunction leads to a deterioration in health status.

The intestinal mucosa in addition to being equipped for the primary function of the intestine (digestion and absorption) represents one of the main immune defense lines of the body, acting as a barrier and being the seat of the lymphoid tissue associated with the intestine (GALT).

In addition, the intestinal mucosa hosts a resident bacterial flora that is established immediately afterwards birth and remains stable, with some modifications, for the rest of life. This microflora, which represents the intestinal microbiota, plays a fundamental role in maintaining health of the host, contributing to the functionality of the gastro-intestinal system, performing a function of barrier against pathogens and balancing the inflammatory processes taking place in the intestinal mucosa.

Functional foods and food supplements intended for the gastro-intestinal system must comply with the parameters of quality and effectiveness that guarantee and determine the restoration and maintenance of the conditions physiological, supporting the functionality of the digestive system.



Nature Reviews | Gastroenterology & Hepatology

Functional foods and nutraceutical for Gastrointestinal area

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	Prevalenza in Italia (% della popolazione)
Malattie dello stomaco e dell'esofago	
Malattia da reflusso gastroesofageo	44,3%
Infezione da *Helicobacter pylori*	10-20% dei soggetti in età < 50 anni; 40-50% di quelli in età > 50 anni
Ulcera peptica	5-10%
Malattie dell'Intestino	
Malattie Infiammatorie Croniche Intestinali	0,4%
Malattia diverticolare del colon	27-47% Distribuzione per età: 1-2% al di sotto dei 30 anni; raggiunge il 60-70% nelle fasce di età più alte
Malattia celiaca	1%
Disordini gastro-intestinali funzionali	20%
Malattie del Fegato	
Epatopatie virali croniche	4%
Patologie alcol correlate	0,2%
Epatopatie steatosiche non-alcol correlate	NAFLD: circa il 25% della popolazione italiana tra 18-75 anni; NASH: 3-16%*

Changeable common risk factors:
- incorrect feeding
- lack of physical activity
- tobacco consumption
- alcohol abuse
- obesity
- drug abuse

Common non-changeable risk factors:
- sex
- age
- inheritance

Primary prevention

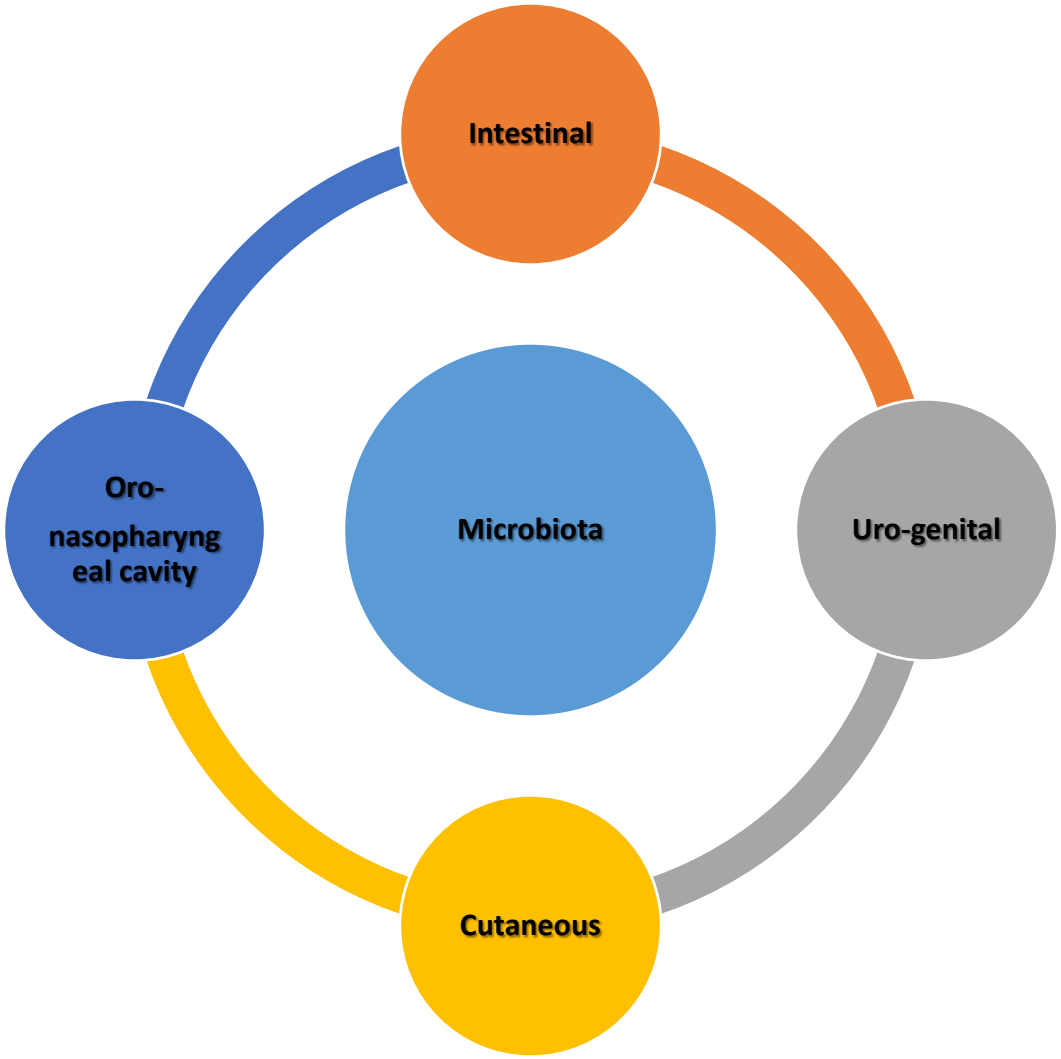
In diseases of the digestive tract primary prevention is aimed at:
- reduce smoking
- reduce alcohol consumption
- control the weight through appropriate lifestyle and nutrition changes
- eliminate / prevent the action of infectious / oncogenic agents
- keep the intestinal microenvironment in a state of balance

*AFLD-NASH aumentano la mortalità globale del 35-85%

Federsalus, 2018

Microbiota

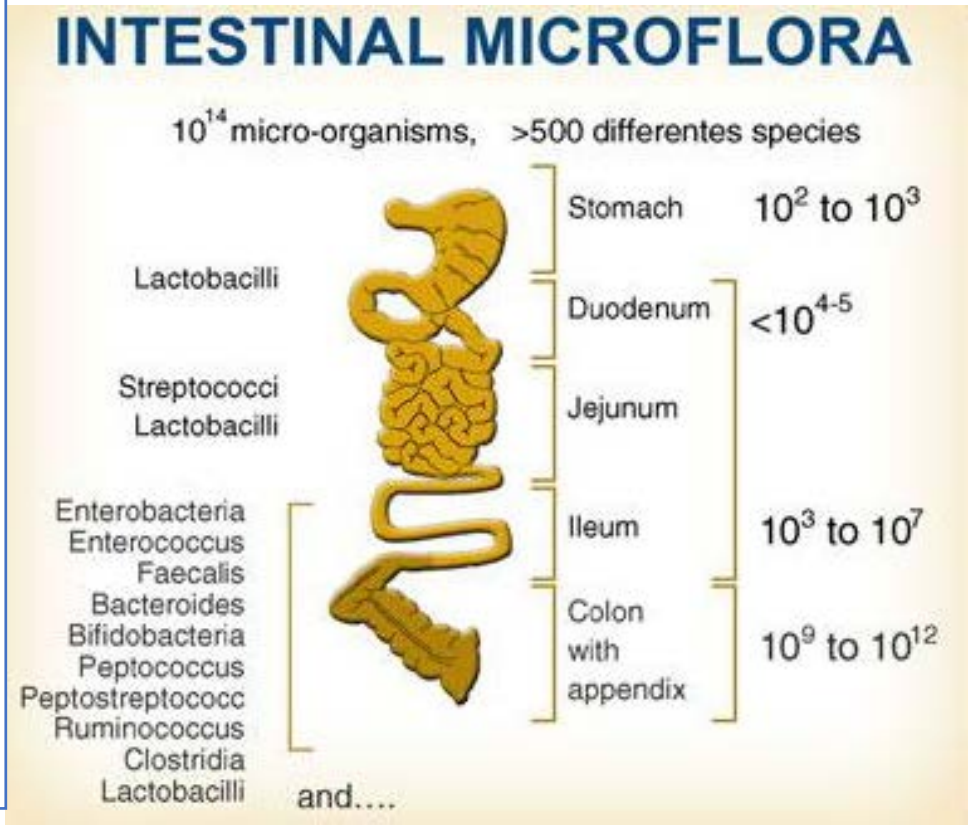
The surface of the human body can be divided into four microbiological compartments, different in their composition but equally important in the life of the individual. They are the skin, the oro-nasopharyngeal cavity, the genital apparatus and the gastrointestinal tract. The set of bacteria "microbiota", present in each of these districts, produces numerous effects on the health of the host, including the protection from the colonization of pathogens through various mechanisms such as the maintenance of specific local metabolic conditions such as to disadvantage their settlement , competing for their adhesion and stimulating immune responses that activate antimicrobial responses. The effects of the microbiota on the immune system are much broader. Furthermore, the microbiota has compartment-specific functions. Among these, one of the most studied is the role on the digestion of food components and the energy conversion exercised by the intestinal microbiota



Each portion of the GI tract is colonized by a specific microflora, whose composition is the result of adaptation to local environmental conditions and commensalistic or parasitic interactions that are established between the components of the microbial community itself, both between and host organization.

Factors that define microbial composition and concentration in specific portions of the GI section are:

-The pH,
-the presence of gastric enzymes,
-sale biliars,
-the speed of peristaltic transit,
-the potential redox,
- the dissolved oxygen tension
-the concentration of nutrients



Functional foods and nutraceutical for Gastrointestinal area

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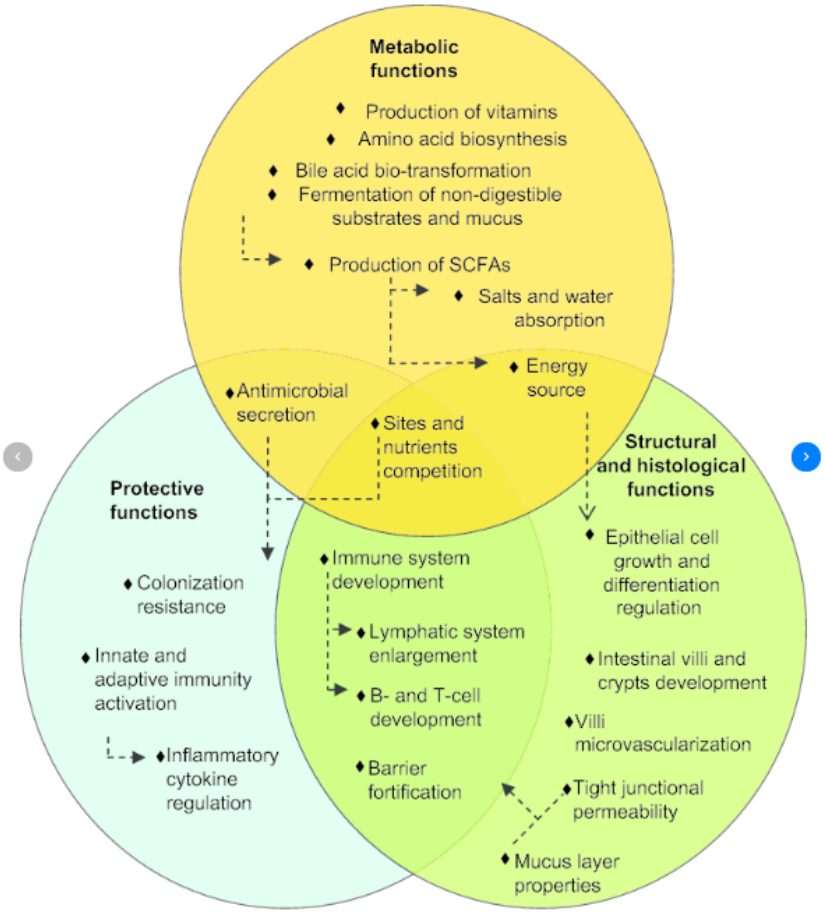

Main beneficial functions of the human gut microbiota. Circles represent the three principal classes of functions performed by the bacteria that inhabit the gut. Arrows represent causal relationships. Abbreviation: SCFA, short chain fatty acid.

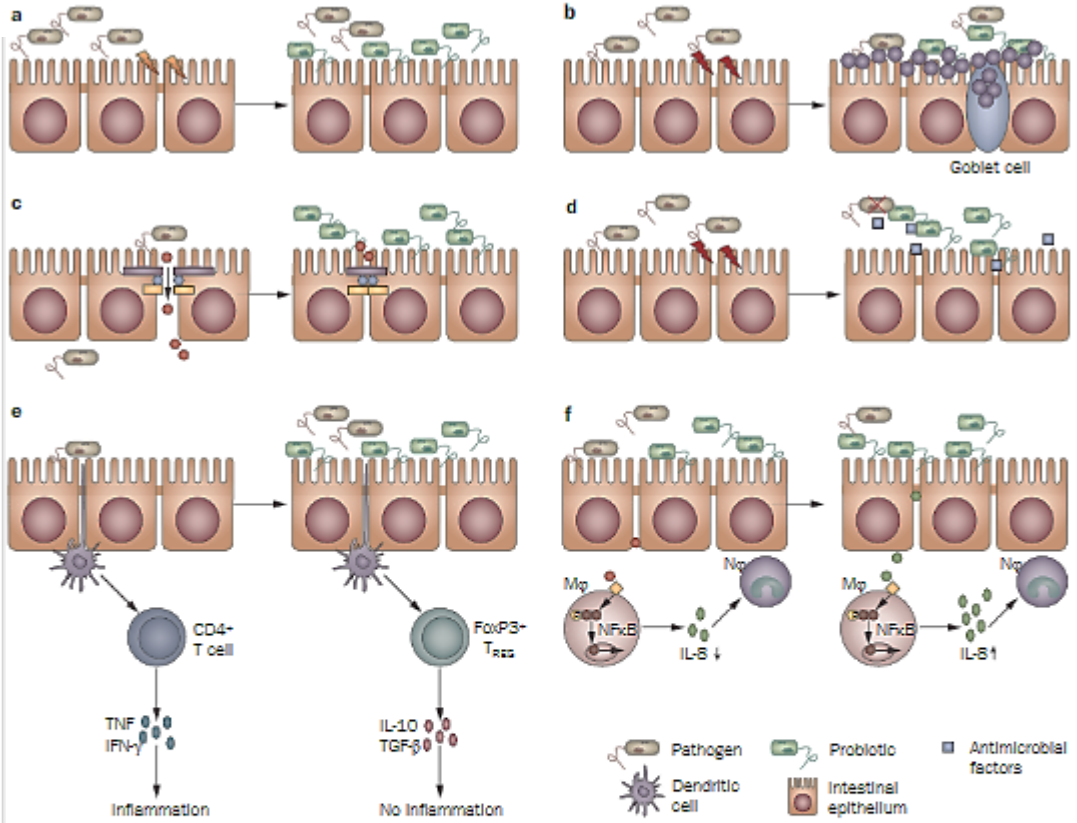

Figure 1 | Potential mechanisms of action of probiotics. Probiotic organisms can provide a beneficial effect on intestinal epithelial cells in numerous ways. **a** | Some strains can block pathogen entry into the epithelial cell by providing a physical barrier, referred to as colonization resistance[55-57] or **b** | create a mucus barrier by causing the release of mucus from goblet cells. **c** | Other probiotics maintain intestinal permeability by increasing the intercellular integrity of apical tight junctions, for example, by upregulating the expression of zona-occludens 1 (a tight junction protein),[59] or by preventing tight junction protein redistribution[60] thereby stopping the passage of molecules into the lamina propria. **d** | Some probiotic strains have been shown to produce antimicrobial factors. **e** | Still other strains stimulate the innate immune system by signaling dendritic cells, which then travel to mesenteric lymph nodes and lead to the induction of T_{REG} cells and the production of anti-inflammatory cytokines, including IL-10 and TGF-β. **f** | Some probiotics (or their products) may also prevent (left-hand side) or trigger (right-hand side) an innate immune response by initiating TNF production by epithelial cells and inhibiting[74] (or activitating) NFκB in Mφ and dampening (or priming) the host immune response by influencing the production of IL-8 and subsequent recruitment of Nφ to sites of intestinal injury. Abbreviations: Mφ, macrophage; Nφ, neutrophil; T_{REG} cell, regulatory T cell.

Prakash S, et al C. Gut microbiota: next frontier in understanding human health and development of biotherapeutics. Biologics 2011; 5: 71-86

Functional foods and nutraceutical for Gastrointestinal area

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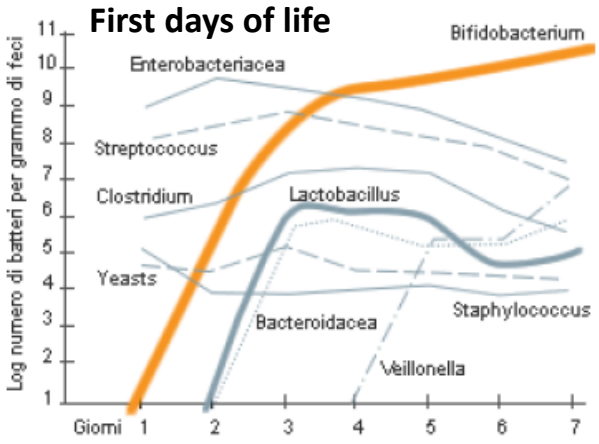
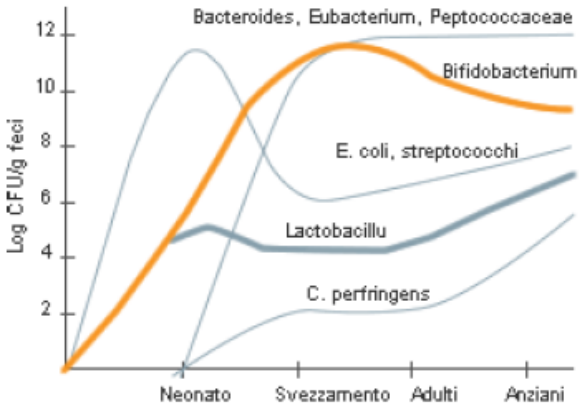


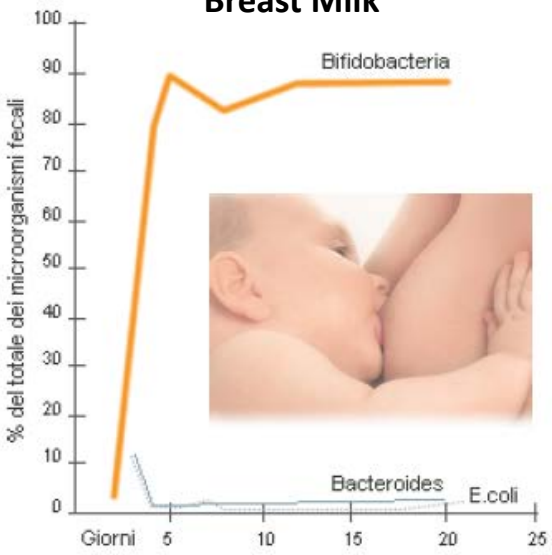


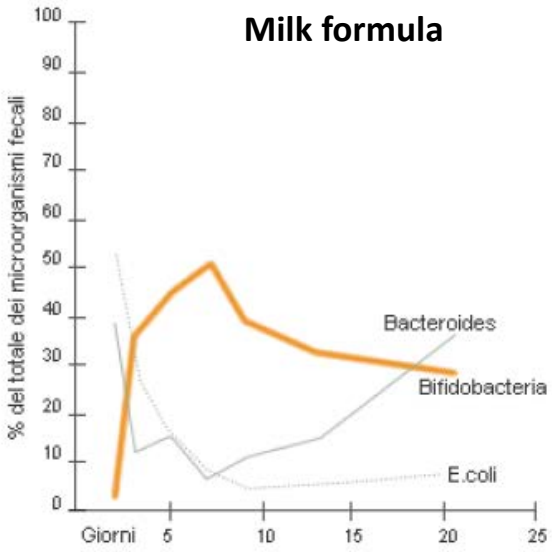
New born microbiota

Mother's microbiota maternal vaginal and intestinal flora constitutes the source of bacteria, which colonizes the intestine of new born.

- Mode of deliver
- Birth environment
- Rarely genetic factors

After infantry probiotics supplied from raw foods; such as lactic acid fermented foods such as yogurt, cheese and probiotic supplements.





Probiotic

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EXPERT CONSENSUS DOCUMENT

The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic

Colin Hill, Francisco Guarner, Gregor Reid, Glenn R. Gibson, Daniel J. Merenstein, Bruno Pot, Lorenzo Morelli, Roberto Berni Canani, Harry J. Flint, Seppo Salminen, Philip C. Calder and Mary Ellen Sanders

www.nature.com/nrgastro

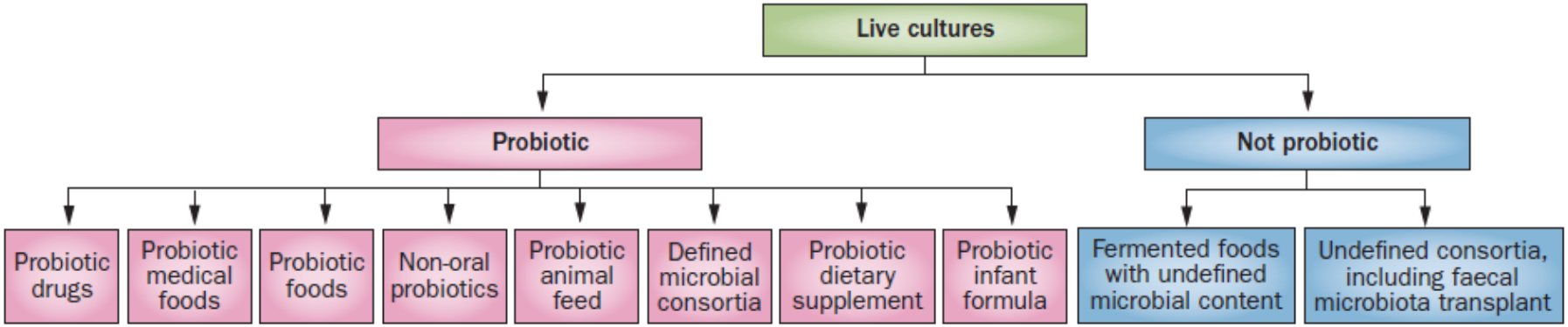

Figure 3 | Overall framework for probiotic products. Evidence of a health benefit is required for a probiotic, at either a strain-specific or group level, depending on the nature of the benefit. Probiotics can have different means of administration, target host species (humans and animals), target populations, target sites (gut and beyond), efficacy end points and regulatory categories. All probiotics must be safe for their intended use. Dead microbes, microbial products, microbial components do not come under the probiotic classification.

Probiotic

Table 1 | Categories of live microorganisms for human use as defined by the expert panel

Description	Claim	Criteria*	Minimum level of evidence required to make claim	Comments
Not probiotic				
Live or active cultures	"Contains live and active cultures"	Any food fermentation microbe(s) Proof of viability at a minimum level reflective of typical levels seen in fermented foods, suggested to be 1×10^9 CFU per serving[73]	No product-specific efficacy studies needed	The terms 'live' or 'active' do not imply probiotic activity Fermented foods containing live cultures might also qualify as a 'probiotic' if they meet the criteria for that category (e.g. evidence that yogurt can improve lactose digestion in lactose maldigesters would qualify it as a 'probiotic'[74,75])
Probiotic				
Probiotic in food or supplement without health claim	"Contains probiotics"	A member(s) of a safe[76,77] species, which is supported by sufficient evidence of a general beneficial effect in humans OR a safe microbe(s) with a property (e.g. a structure, activity or end product) for which there is sufficient evidence for a general beneficial effect in humans Proof of viability at the appropriate level used in supporting human studies[73]	Well-conducted human studies (e.g. these could involve RCT(s), observational studies, systematic reviews or meta-analyses supporting the observed general beneficial effect for the taxonomical category concerned) The evidence does not have to be generated for the specific strain included in the product	Extrapolation of evidence must be based on reasonable expectations that the strain(s) incorporated in the product would have similar general beneficial effects in humans This evidence could be based on taxonomical or functional comparisons
Probiotic in food or supplement with a specific health claim	Specific health claim, such as "helps to reinforce the body's natural defences in children" or "helps reduce the risk of antibiotic-associated diarrhoea"	Defined probiotic strain(s) Proof of delivery of viable strain(s) at efficacious dose at end of shelf-life[73]	Convincing evidence needed for specific strain(s) or strain combination in the specified health indication Such evidence includes well-conducted studies in humans, including: positive meta-analyses on specific strain(s) or strain combinations, as per principles outlined by Cochrane,[78] PASSCLAIM,[79] or GRADE;[80] well-conducted RCT(s) OR strong evidence from large observational studies[81]	Well-designed observational studies are useful to detect the effect of foods on health in 'real life', that is, outside the controlled environment of an RCT (e.g. data on health benefits by dietary fibre are mostly observational) Sample sizes must be large enough to manage confounding factors
Probiotic drug	Specific indication for treatment or prevention of disease, such as "useful for the prevention of relapse of ulcerative colitis"	A defined strain(s) of live microbe Proof of delivery of viable probiotic at efficacious dose at end of shelf-life Risk–benefit assessment justifies use	Appropriate trials to meet regulatory standards for drugs	What constitutes a drug claim varies among countries

*Unless otherwise indicated, all criteria indicated must be met. Abbreviations: CFU, colony forming unit; GRADE, Grades of Recommendation Assessment, Development and Evaluation; PASSCLAIM, Process for the Assessment of Scientific Support for Claims on Food; RCT, randomized controlled trial.

Probiotic

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Factors affecting the intestinal micro ecosystem

- ✓ Antibiotics and other drug intake
- ✓ Microbial infections
- ✓ Diet (highly processed, low fiber foods)
- ✓ Chronic diarrhea
- ✓ Stress
- ✓ Radiation and chemotherapy
- ✓ Colonic therapies for detoxification

Characteristics of Effective Probiotics

Food And Agriculture Organization and World Health Organization defined the following characteristics of probiotic microorganisms:

(1) probiotics should be taxonomically classified and deposited in an internationally recognized culture collection;

(2)they have to remain viable and stable after culture, manipulation, and storage before consumption;

(3) They have to survive to gastric acid and biliary and pancreatic digestion;

(4) they have to induce a host response once ingested by adhering to gut epithelium or by other mechanisms;

(5) they have to yield a functional or clinical benefit to the host when consumed; and

(6) finally they have to be safe, not only regarding the assessment of side effects, but also in relation to antibiotic resistance patterns

Probiotic

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Requirements

General: Safety
Intestinal origin
Resistance to environments and secretions to which it goes (mouth, stomach, intestines ..)

Technological: Food survival in the shelf-life period
Do not reac twith food

Functional: Alive and active in the intestine
Sufficient number (at least 10^9 living cells on the target site)
Ability to adhere to the intestinal epithelium and colonization
Inhibit pathogens
Stimulation of the immune response
Regulation of cell proliferation and intestinal functions
(mucus production, nutrient absorption, mobility, blood flow) through the production of SCFA, enzymes, polyamines, NO etc.

PROCESSO PER LA VALUTAZIONE DEI PROBIOTICI, ALIMENTI CON PROBIOTICI, PREBIOTICI, ALIMENTI CON PREBIOTICI, ALIMENTI CON SIMBIOTICI

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1. **Probiotici**: identificazione tassonomica corretta e condotta con tecniche adeguate della specie e del ceppo
Deposito in una Collezione Internazionale con lo status di IDA
1.**Prebiotici**: identificazione biochimica e del grado di polimerizzazione; se miscele, identificazione dei rapporti fra le miscele

2.Caratterizzazione "funzionale" sia in vitro che nel modello animale

3.Valutazione di sicurezza; determinazione antibiotico-resistenza

4. Dimostrazione di una attività funzionale in umana ottenuta mediante almeno uno studio di efficacia (preferibilmente due, di cui uno condotto da un gruppo indipendente randomizzato, in doppio cieco e controllato) su di un campione adeguato di soggetti

5. Adeguate informazioni in etichetta relative all'ingrediente probiotico/prebiotico/simbiotico

Probiotic

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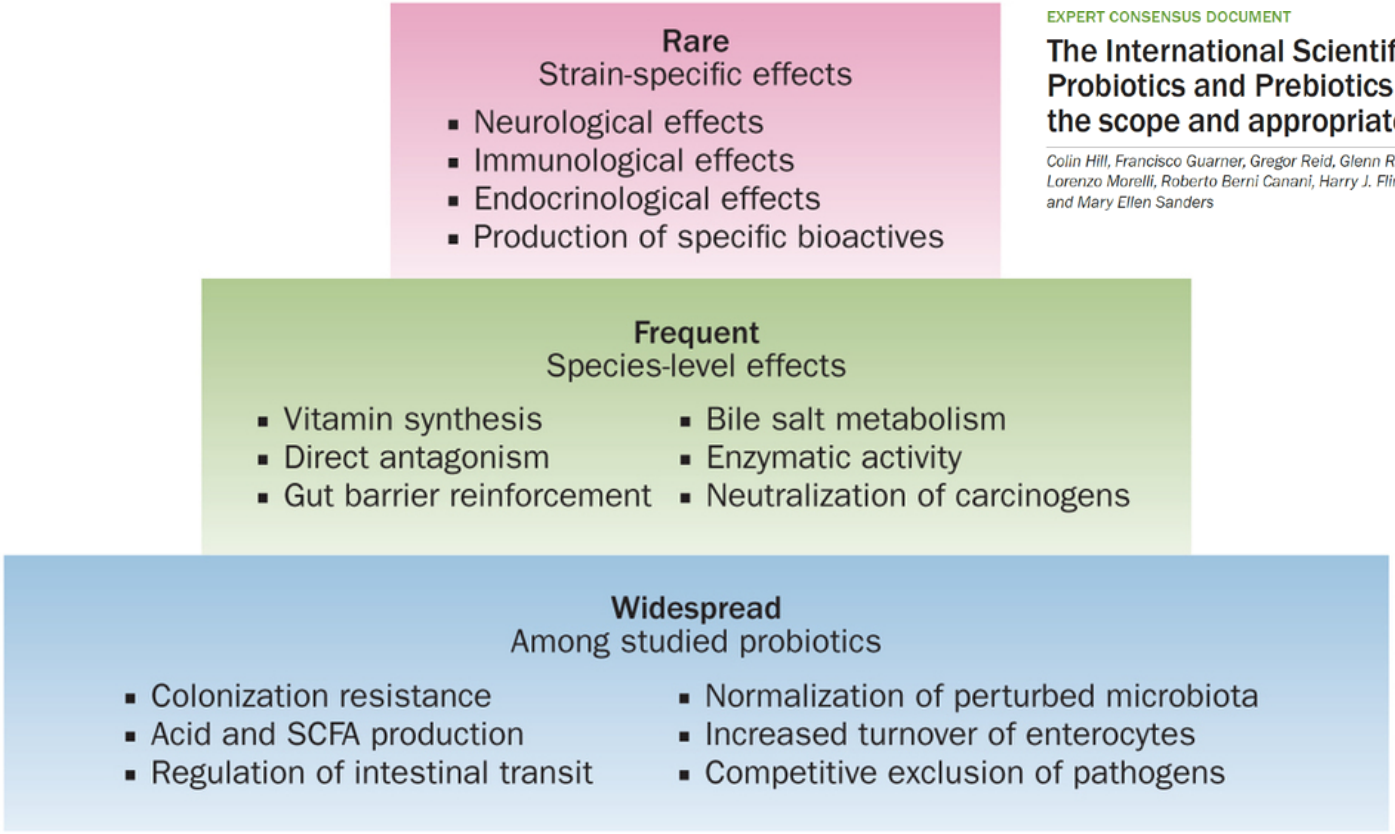

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Figure 2 | Possible distribution of mechanisms among probiotics. Some mechanisms might be widespread among commonly studied probiotic genera; others might be frequently observed among most strains of a probiotic species; others may be rare and present in only a few strains of a given species. Evidence is accumulating on a cross-section of probiotic strains that suggest some generalizations can be made beyond strain-specific effects. Abbreviation: SCFA, short-chain fatty acid.

Probiotic

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Type of Diarrhea	Pathogen	Probiotic used
***Clostridium difficile* diarrhea**	***Clostridium difficile***	*Lactobacillus* GG
Traveler's diarrhea	***Enterotoxigenic Escherichia coli***	*Saccharomyces boulardii*
Pediatric diarrhea	***Campylobacter, Salmonellae, Shigellae***	*Lactobacillus* GG and *Bifidobacterium*

- *Lactobacillus Acidophilus* (is the most important of the first part of the intestine: it prevents bacterial bacteria from climbing from the colon);
-*Lactobacillus Rhamnosus* (colon, inhibits most pathogens (difficult Clostr), and is excellent as antidiarrhoic, reduces intestinal inflammation associated with food allergies, improved atopic dermatitis) (DICOFLOR, LACTOGERMIN)
-*Lactobacillus Casei* (immunostimulant function, IgA increase, rotavirus diarrhea, diverticulitis);
-*Lactobacillus Paracasei* (the most accredited as immunostimulant);
-*Lactobacillus Jonsonii* (bactericide against Helycobacter p., Increases immune defenses, increases tenfold the fecal count of lactobacilli)
-*Lactobacillus Salivarius* (excellent modulator of intestinal inflammation, useful in all gastro-enteric diseases characterized by a significant inflammatory component).
-*Lactobacillus Reuteri* (modulates the immune response particularly through CD4 + T-helper cells in helium, helpful in diarrhea prevention, in inhibition of pathogenic infections modulates Th1 / Th2 balance in human intestinal epithelium, probiotic useful for babies colic) (REUTERS, REUFLOR)
- *Lactobacillus Plantarum & Fermentum* (immune stimulant; it is a fundamental element of vaginal bacterial flora);

Probiotic activities

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Antidiarrheal activity: diarrhea of children
diarrhea from infections
traveler's diarrhea

Anti-inflammatory activity: ulcerative colitis
Chron's disease
urino-genital infections

Antiallergic activity: allergic colitis
lactose maldigestion
food intolerance

Anti-cholesterol activity

Immune disorders

Enteral nutrition

Claim of food properties

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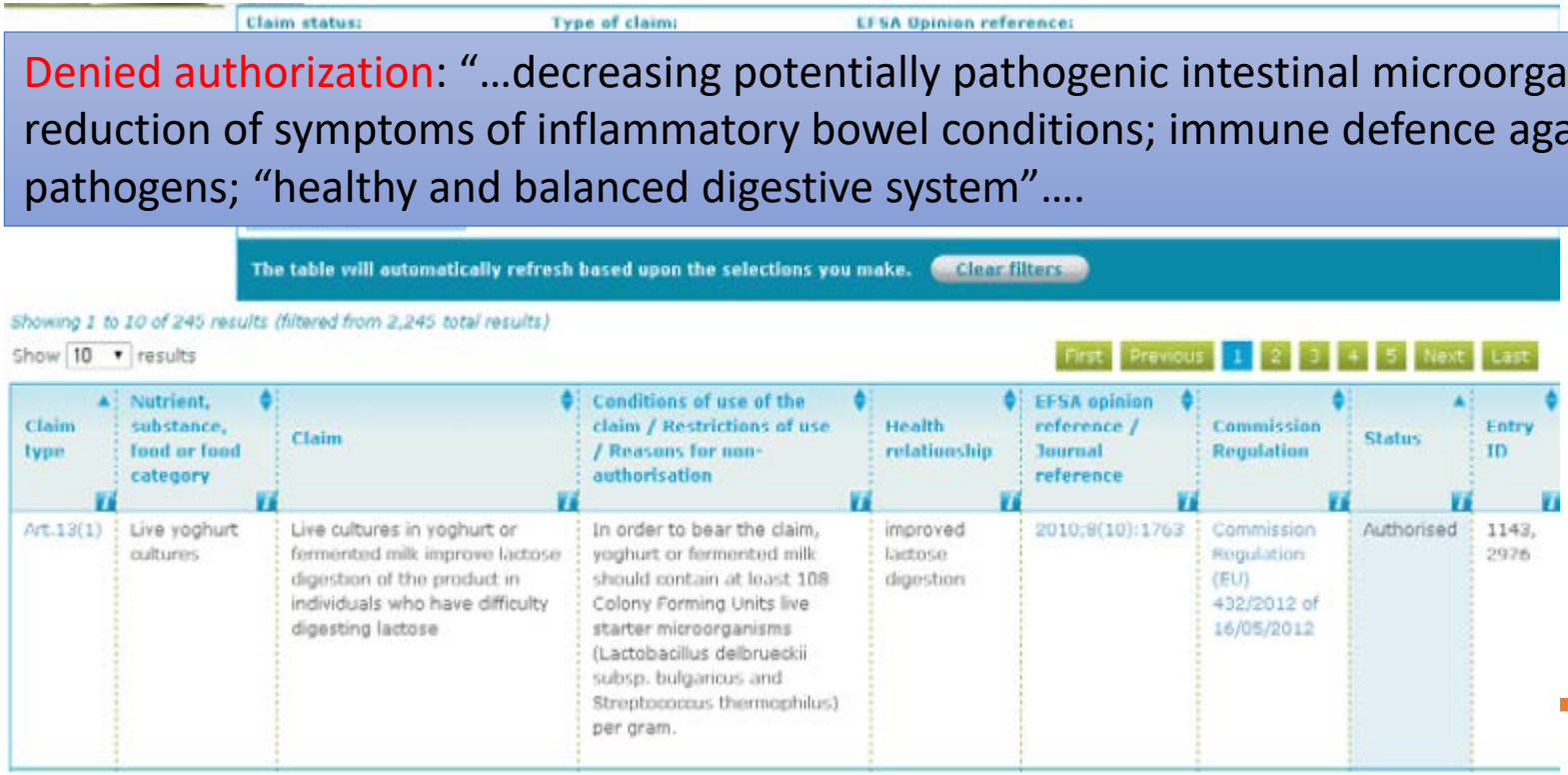
Only one claim authorized in the EU concerning the *Lactobacillus delbruckii* subsp bulgaricus and *Streptococcus thermophylus* for the improving lactose digestion

Indications of use for all other probiotic food products
"Promotes the balance of intestinal flora"

Denied authorization: "…decreasing potentially pathogenic intestinal microorganisms; reduction of symptoms of inflammatory bowel conditions; immune defence against pathogens; "healthy and balanced digestive system"….



Claim status: Type of claim: EFSA Opinion reference:

The table will automatically refresh based upon the selections you make. Clear filters

Showing 1 to 10 of 245 results (filtered from 2,245 total results)

Show 10 results

First Previous 1 2 3 4 5 Next Last

Claim type	Nutrient, substance, food or food category	Claim	Conditions of use of the claim / Restrictions of use / Reasons for non-authorisation	Health relationship	EFSA opinion reference / Journal reference	Commission Regulation	Status	Entry ID
Art.13(1)	Live yoghurt cultures	Live cultures in yoghurt or fermented milk improve lactose digestion of the product in individuals who have difficulty digesting lactose	In order to bear the claim, yoghurt or fermented milk should contain at least 108 Colony Forming Units live starter microorganisms (Lactobacillus delbrueckii subsp. bulgaricus and Streptococcus thermophilus) per gram.	improved lactose digestion	2010;8(10):1763	Commission Regulation (EU) 432/2012 of 16/05/2012	Authorised	1143, 2976

Probiotic

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Probiotic Strain	Commercial Product
L. acidophilus	LA-5; NCDO 1748
Saccharomyces cerevisiae (boulardii)	Florastor Biocodex (Creswell OR)
L. casei Shirota *B. breve* strain Yakult	Yakult
L. johnsonii Lj-1 (same as NCC533 and formerly *L. acidophilus* La-1)	LC-1 Nestlé (Lausanne, Switzerland)
L. reuteri ATCC 55730 ("Protectis")	BioGaia Probiotic chewable tablets or drops
Streptococcus oralis KJ3 *Streptococcus rattus* JH145	ProBiora3 Oragenics Inc. (Alachua FL)
Lactobacilli rhamnosus PBO1 *Lactobacilli gasseri* EB01	EcoVag Bifodan (Denmark)

Probiotic

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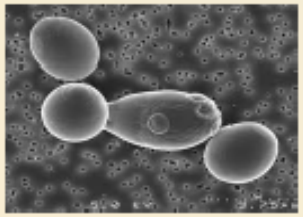
ENTEROLACTIS

Enterolactis è costituito da fermenti lattici vivi di origine umana (Lactobacillus casei, subspeciae casei DG), espressamente selezionati e caratterizzati da forte vitalità e adesività, capaci di riequilibrare rapidamente la composizione della flora intestinale.

Anche tra i **lieviti** vengono annoverati alcuni probiotici: il *Saccharomyces boulardii* è presente in numerosi integratori in quanto in grado di sopravvivere all'acidità gastrica e di resistere alla proteolisi.



Probiotic

DOSAGE FORMS

The dosage forms with which they are presented to the consumer these particular food supplements are from various types to meet the different needs of producers, of retailers and consumers.

There are:

- liquid suspensions
- two-step products
- orosoluble powders
- tablets
- capsules.

Liquid suspensions are the easiest form of handling and recruitment for the patient, but offer scarce guarantees of maintenance of the vitality of microorganisms also with low temperature storage. For this reason, in general, their use is limited to sporogenous lines (eg. Bacillus clausii) which are clearly more resistant.

The two-stage formulation represents a compromise among the advantages of taking a liquid and conservation requirements for probiotics. The solid phase consists of the cap where the probiotic strains are contained in powder form. An advantage of this form is given by the possibility of associating other substances in the liquid phase; a criticality is instead represented by the two primary packaging processes that must be

Orosoluble powders offer the advantage of crossing the stomach faster than the other solid phases by exploiting at most the gastroresistance of the stocks.

Tablets offer the advantage of being able to be coated with substances that increase the gastroresistance, but they pose the problem of the dosage caused from the need to add excipients to get one adequate cohesion; it is also possible that during the process of damage to the population probiotic caused by mechanical and thermal action of compression.

The capsules represent, today, the best protective form for bacteria both during the conservation phase both during the recruitment period, because they offer one gastroresistance linked to intrinsic characteristics of the capsule itself and to the possibility of a further coating with protective substances. Their production does not requires special technological excipients and mechanical forces applied are limited and harmless for probiotics; they also allow accurate dosing.

Prebiotic

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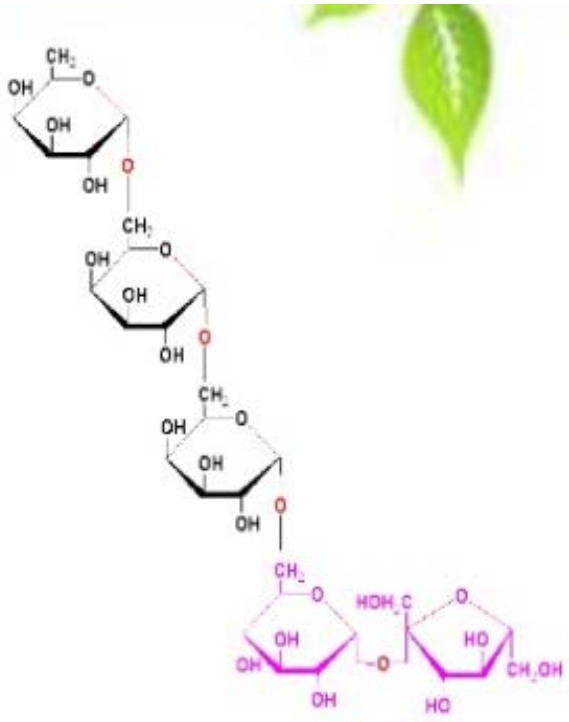
Prebiotics are used selectively only by certain species Of microorganisms, particularly those that contain specific bacterial g lycosidases Which break these substrates into monomers that are easier to use

- Oligosaccharide is the main constituent of prebiotic food products.
- Oligosaccharides stimulate the growth of benefic bacteria and increase the resistance to invading pathogens.
- **The functional oligosaccharides include;**
  - **Fructooligosaccharides (FOS).**
  - Glucooligosaccharides(GOS)
  - **Inulin**
  - Isomaltooligosaccharides (IMO)
  - **Soybeanmeal oligosaccharides (SMO)**
  - Mannan oligosaccharides(MOS)
  - **Galactooligosaccharides**
  - Maltooligosaccharides (MO)
  - **Xylooligosaccharides (XOS)**
  - Pectin-derived acidic oligosaccharides (pAOS).



If ingested in appropriate quantities (5g / day), they are able to selectively favor the growth and / or activity of one or more microorganisms. A prebiotic is considered good if it contains at least 3 grams of prebiotic substance

Prebiotics are soluble oligosaccharides that resist the action of gastric enzymes and Reaching unchanged the colon act as nutrition for some bacterial groups, Stimulating growth and activity, as they are irreparable.

Prebiotic

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Prebiotic factor	Origin	Microbes stimulated	Effects
Oligosaccharides	Onion,garlic, chicory root, burdock, asparagus, Jerusalem artichoke, soybean, wheat bran.	*Bifidobacterium* species	Increase in bifidobacterium, suppression of putrefactive bacteria, prevention of constipation and diarrhea.
Fructooligosaccharides (inulin, oligofructo)	Same as for oligosaccharides	*Bifidobacterium* species *Lactobacillus acidophilus, Lactobacillus casei, Lactobacillus plantarum*	Growth of bifidobacteria and acid promotion.
Fructan	Ash-free white powder from tubers of Jerusalem artichoke.	*Bifidobacterium* species	Growth of bifidobacteria
Human kappa casein and derived glycolmacropeptide	Human milk: chymotrypsin and pepsin hydrolysate.	*Bifidobacterium bifidum*	Growth promotion.
Stachyose and raffinose	Soybean extract	*Bifidobacterium* species	Growth factor.
Casein macropeptide	Bovine milk	*Bifidobacterium* species	Growth promotion.
Lactitol(4-O-β-D-galactopyranosyl)D-glucitol	Synthetic sugar alcohol of lactose	*Bifidobacterium* species	Growth promotion.
Lactutose(4-O-β-D-galactopyranosyl)D-fructose	Synthetic derivative of lactose	*Bifidobacterium* species	Growth promotion.

Symbiotic

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They are those foods or supplements that contain both probiotic microorganisms and substances with prebiotic properties.

The most widespread:

Bifidobacteria + frutto-oligosaccaridi (FOS)
Lactobacilli + Lactitolo
Bifidobacteria + galatto-oligosaccaridi (GOS)

Bifidobacterium Lactis 1 miliardo ufc
fruttoligosaccaridi a catena corta (FOS)

L. Acidophilus DDS-1 5x10 alla nona UFC
L. Bulgaricus DDS-14 1x10 alla nona UFC
L. Rhamnosus 0,5x10 alla nona UFC
Bifidobacterium Bifidum 3,15x10 alla nona UFC
Microalghe Klamath Refractance Window®
Helianthus tuberosus, farina del tubero
(fonte naturale di FOS)
EnzyMax® (maltodestrine fermentate)

Functional gastro-intestinal disorders

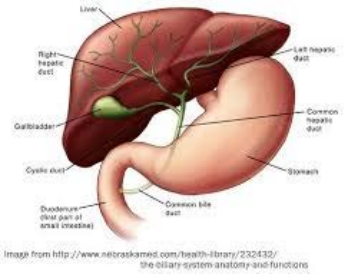
U7

Active ingredients for treating non-alcohol steatotic liver related diseases The corrective treatment of choice to counteract non-alcohol related steatotic liver diseases (NAFLD / NASH) and the associated metabolic comorbidities, consists in the modification of the style of life, with interventions on eating habits aimed at achieving a weight loss of the patient. Oxidative stress represents, according to numerous studies, a key mechanism in producing the liver damage and the consequent progression of this spectrum of diseases.

Vitamin E, as a powerful antioxidant, received a positive opinion from EFSA on the claim "Helps protect cells from oxidative stress" and has been shown to be effective in counteracting the oxidative stress associated with NASH and NAFLD.
Vitamin E, administered to one 800 IU / day dose improves liver histology in non-diabetic patients with NASH.

Tabella 2: Ingredienti che presentano il *claim* ammesso nell'elenco del Regolamento Europeo 432/2012

AREA GASTRO-INTESTINALE	
INGREDIENTI	CLAIM Reg. 432/2012
Vitamina E	Contribuisce a proteggere le cellule dallo stress ossidativo
Lattulosio 10 g/die	Contribuisce ad accelerare il transito intestinale



Nota: Con riferimento alla Vitamina E l'indicazione riportata in tabella può essere impiegata solo per un alimento che è almeno una fonte di Vitamina E come specificato nell'indicazione «FONTE DI [NOME DELLA O DELLE VITAMINE] E/O [NOME DEL O DEI MINERALI]» di cui all'allegato del Regolamento Europeo n. 1924/2006.

Functional gastro-intestinal disorders

U7

adjust liver and digestive function (Angelica*§, Carciofo, Rosmarino).
Plants contribute to:
- regulate the digestive and hepatic function, antispasmodic and cholagogue and choleretic (Angelica, Carciofo, Rosmarino);
- regulate intestinal motility and the elimination of gas (Angelica and Rosmarino);
- help drainage of body fluids and stomach swelling (Black Horseradish)

extracts of picrorhiza,
Schisandra chinensis (Turcz.) Baill.,
milk thistle (cardo mariano),
fumaria
Boldo* (*Peumus boldus* Molina)
Tarassaco§ (*Taraxacum campylodes* G.E.Haglund) } cholagogue and choleretic
choline, inositol, pyridoxine, cyanocobalamin
that can have beneficial effects in maintaining proper liver function

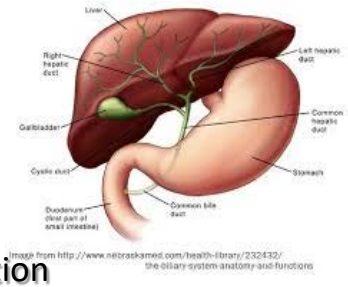


Image from http://www.nebraskamed.com/health-library/232432/the-biliary-system-anatomy-and-functions

Ananas sativum gambi extracts*,
Desmodium adscendens,
Pimpinella anisum,
Citrus oils
Cuminum cymimum§,
Lemongrass
Charcoal } Digestion and aerophagia, colitis, meterosimo, fermentation
Sodium bicarbonate and citric acid (Citrosodina)
Bromelin, Papain, amilasi, lactase, lipase, cellulase

* Interaction with anticoagulant drugs, § interaction with hypoglicaemic drugs and antiarrhythmics

Functional gastro-intestinal disorders

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(Colic gases, carminatives)

- Fennel, fruits^
- Green anise, fruits
- Chamomile, flower heads
- Melissa, e.s. (rosmarinic acid 2%)

(Vomit)

Ginger, root e.s. (gingerol 4%)*(interaction with FANS and anticoagulants)

Licorice, root* (interaction with antipertensive drugs)

^Si definisce telarca prematuro uno sviluppo isolato del seno senza altri segni clinici di pubertà nelle ragazze prima degli 8 anni d'età che esordisce comunemente con uno sviluppo unilaterale del seno. Il foeniculum vulgare è conosciuto sin dai tempi degli antichi Egizi per le sue proprietà calmanti (lenitive) ed è universalmente usato come infuso (tè) per il suo effetto lenitivo nelle coliche gassose e per regolare il movimento intestinale nei bambini. Il foeniculum vulgare contiene concentrazioni significative di anetolo, un composto ad attività estrogenica, tuttavia la possibilità che il consumo di finocchio possa causare importanti effetti estrogeno-simili viene in genere trascurata. La presunta innocuità ha favorito l'uso nella medicina popolare delle preparazioni a base di finocchio da parte delle donne che, dopo il parto, lo consumano per aumentare la montata lattea (effetto galattogeno)

L'uso tradizionale dei medicinali a base di finocchio è indicato, a partire dai 4 anni di età, nelle seguenti condizioni:

- per il trattamento sintomatico di disturbi gastrointestinali riferibili a spasmi di lieve intensità, tra cui meteorismo e flatulenza,
- per il trattamento sintomatico di spasmi (crampi) di lieve intensità associati al ciclo mestruale,
- come espettorante (per favorire l'espulsione di muco) in caso di tosse associata al raffreddore.

Sempre secondo la monografia dell'EMA, di norma la durata del trattamento non deve essere superiore a 1-2 settimane.

Functional gastro-intestinal disorders

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AREA GASTRO-INTESTINALE	
INGREDIENTI	EFFETTO FISIOLOGICO DI CUI ALL'ALLEGATO 1 DM 9 LUGLIO 2012 aggiornato il 27 marzo 2014 "Sostanze e preparati vegetali ammessi"
Aloe	Succo: Regolarità del transito intestinale. Funzione digestiva. Funzione epatica Gel sine cute: Azione emolliente e lenitiva (sistema digerente)
Cassia Angustifolia VAHL.	Foglie, Frutto: Regolarità del transito intestinale
Frangula dodonei Ard.	Corteccia: Regolarità del transito intestinale. Funzione digestiva
Frangula Purshiana Cooper.	Corteccia: Regolarità del transito intestinale. Funzione digestiva

Nota: la tabella sopra non è esaustiva delle sostanze a cui è associato un effetto fisiologico ammesso dalla lista ministeriale per la specifica area di riferimento.

Aqueous extract of biological plants [obtained starting from 315 mg of artichoke leaf (*Cynara scolymus* L.), 315 mg of rosemary leaf (*Rosmarinus offi cinalis* L.), and 315 mg of Angelica root (*Angelica archangelica* L.), put in place for a 15 ml wing] - Black horseradish juice (*Raphanus sativus*) - Concentrated apple juice

Bulking agent (isomalt), sweetener (xylitol), L. reuteri DSM 17938, palm oil, strawberry flavoring and flavor enhancer (citric acid). One tablet consists of a minimum of 100 million live *L. reuteri*Protectis. Net weight per tablet, 450 mg. Excessive consumption may have a laxative effect due to the content of sweeteners in the product.

Sciroppo di fruttosio; acqua; succo di mela concentrato; miele d'acacia; stabilizzante: glicerolo; acqua termale; colina bitartrato; correttore di acidità: sodio lattato; schisandra estratto secco titolato 5% in schizandrina *(schisandra chinensis* frutti, maltodestrina); fumaria estratto secco titolato 0,04% in protopina (*fumaria officinalis* sommità fiorite, maltodestrina); inositolo; conservante: potassio sorbato; picrorhiza estratto secco titolato 4% in glucosidi iridonici (*picrorhiza kurroa* radice, maltodestrina); cardo mariano estratto secco titolato 20% in silimarina (*silybum marianum* frutto, maltodestrina); carciofo estratto secco titolato 7% in acido clorogenico (*cynara scolymus* foglie); aroma naturale di arancio; piridossina cloridrato; vitamina B12 titolato 0,1% (maltodestrina, correttori di acidità: acido citrico, citrato trisodico, cianocobalamina).

Edulcoranti:xilitolo, mannitolo; sodio bicarbonato, acido citrico, aroma: limone; antiagglomerante:magnesio stearato