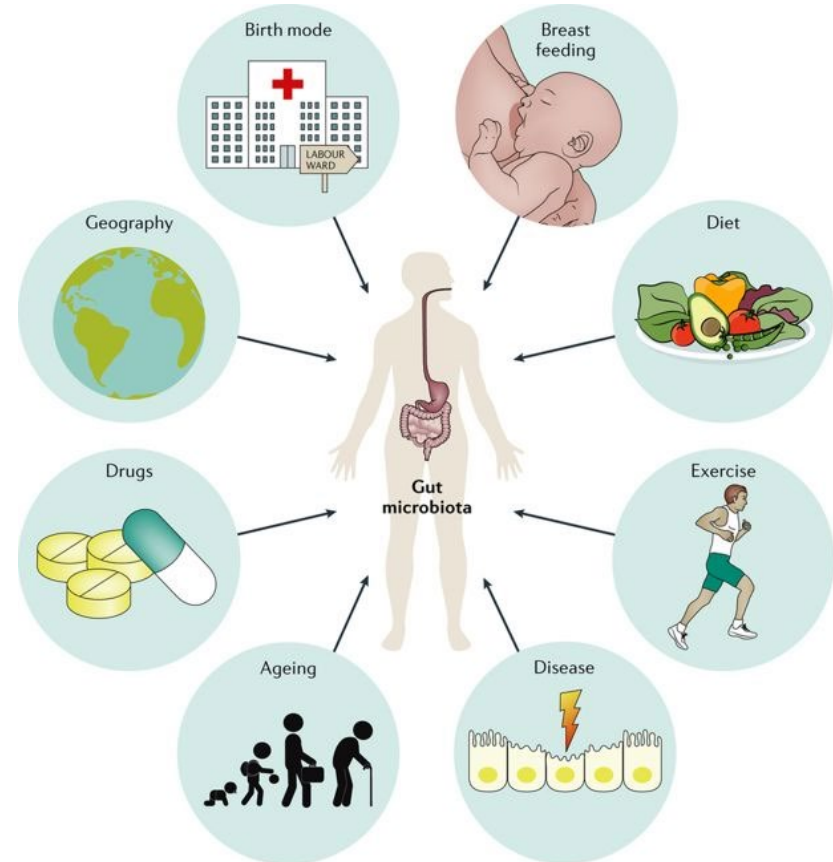


The **vitality and functionality** of the organism depend on its **ability to assimilate, use the nutrients and to eliminate waste substances**. **Essential processes** for life, such as **generation of energy, tissue formation and regeneration and detoxification** are based on functions coordinated by the digestive system.

Consequently, a diminished activity or a digestive system malfunction leads, alteration of the integrity of the gut epithelium 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.



Nature Reviews | Gastroenterology & Hepatology

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.

Prevalenza in Italia (% della popolazione)	
<b>Malattie dello stomaco e dell'esofago</b>	
Malattia da reflusso gastroesofageo	44,3%
Infezione da <i>Helicobacter pylori</i>	10-20% dei soggetti in età < 50 anni; 40-50% di quelli in età > 50 anni
Ulcera peptica	5-10%
<b>Malattie dell'Intestino</b>	
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%
<b>Malattie del Fegato</b>	
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:

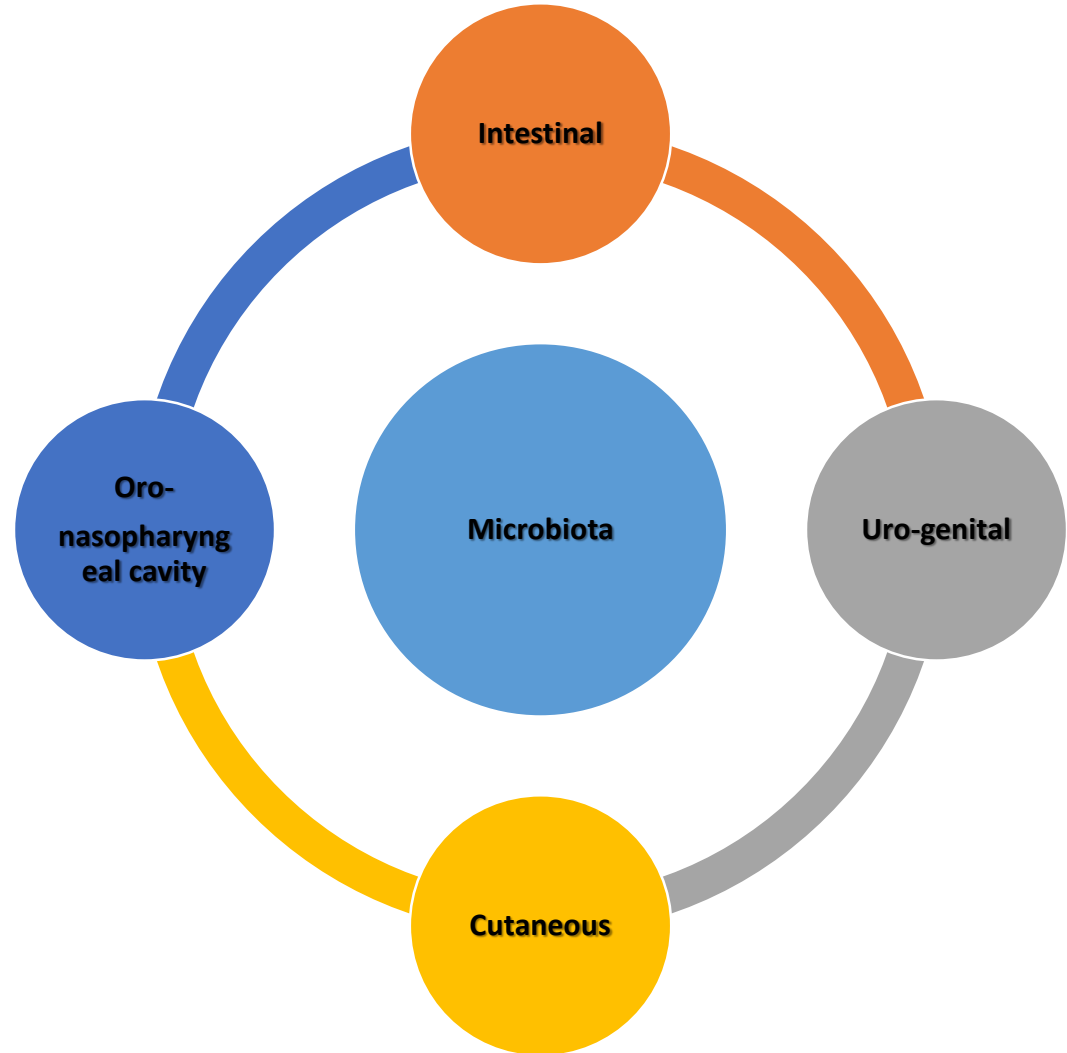
- reduce smoking
- reduce alcohol consumption
- control the weight through appropriate lifestyle and nutrition changes
- eliminate / prevent the action of infectious / oncogenic agents
- keep the intestinal microenvironment in a state of balance

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



## 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

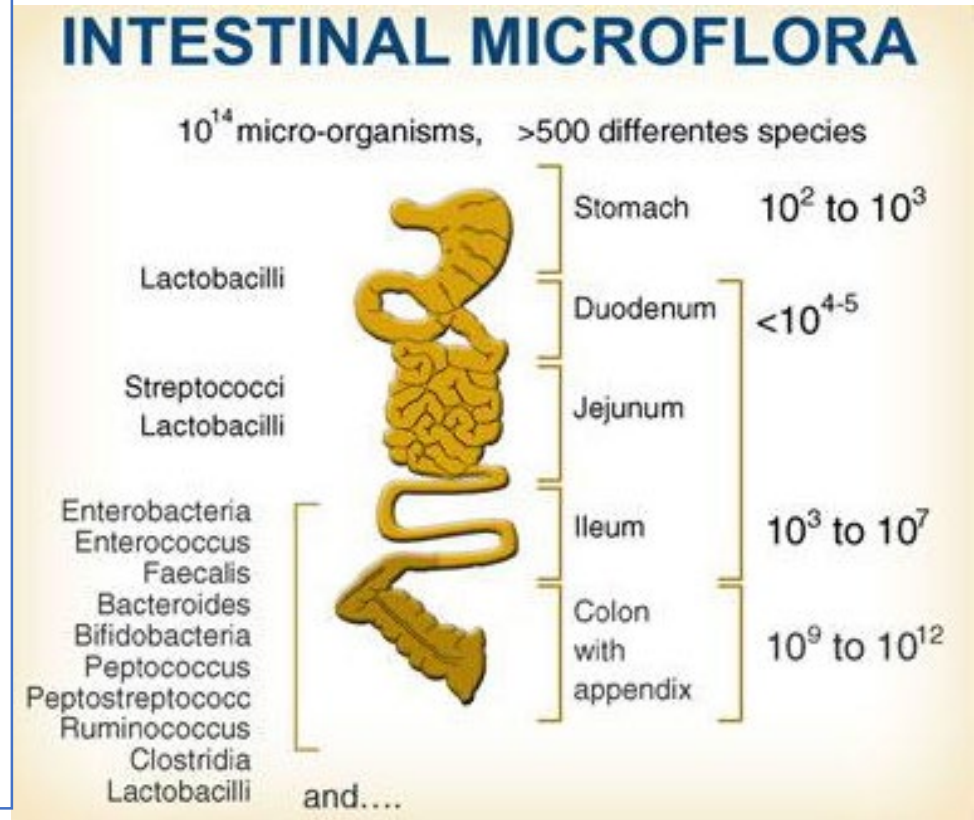




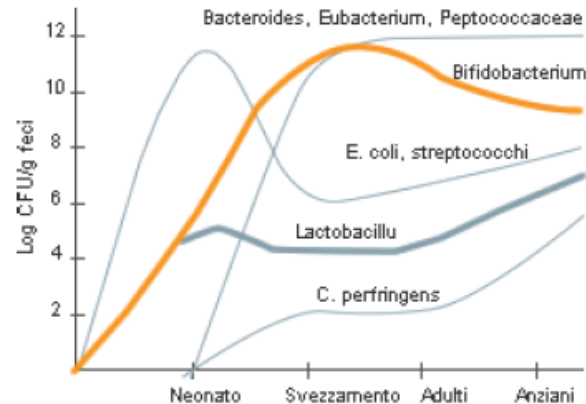
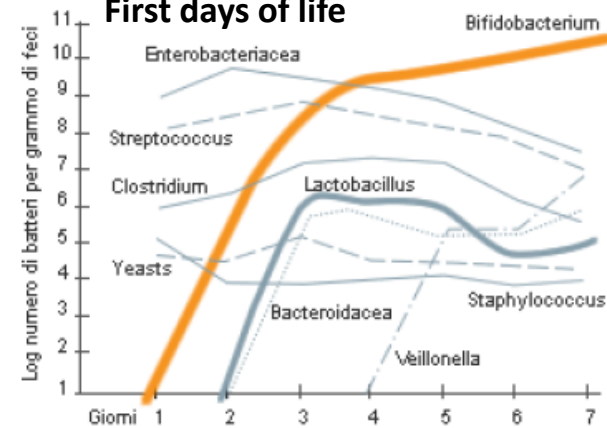
Each portion of the GI tract is colonized by a specific microflora, whose composition is the result of adaptation to local environmental conditions and commensalistic or parasitic interactions that are established between the components of the microbial community itself, both between and host organization.

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

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



## First days of life



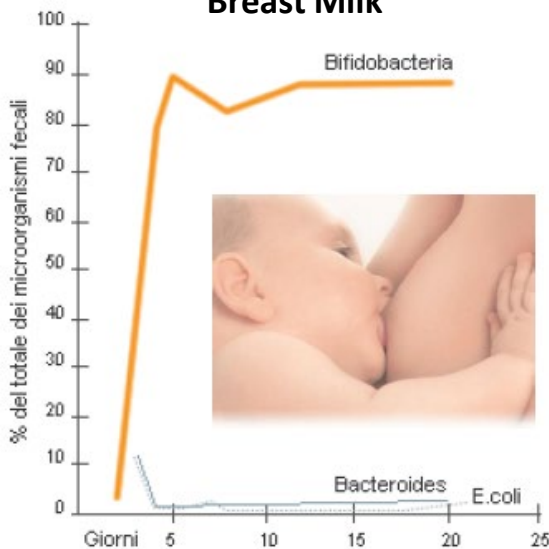
## New born microbiota

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

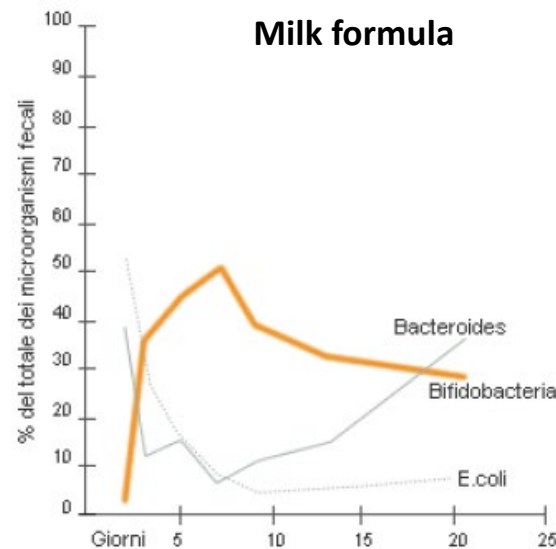
- Mode of deliver
- Birth environment
- Rarely genetic factors

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

## Breast Milk



## Milk formula



## EUBIOSIS

It is a **condition of balance of the intestinal system** (microbiota + intestinal epithelium + GALT).

In particular, the state of eubiosis concerns the microbiota and also **includes the balance between probiotic species** (the microbiota has beneficial species: probiotics which never exceed 15%), **pathogenic species** (there must be few, but in fact they have their own functionality maintain a noise activity of the GALT) **and symbiotic species** (saprophytes which with their presence prevent further rooting of pathogens).

This is an essential condition for maintaining the general health of the intestine and the entire organism.

Eubiosis ensures that **everything works well** all the bio-functional activities of the organism depend on the balanced condition of the intestinal system: **digestion and absorption processes, immune processes, cognitive functions ("intestine-brain axis"), health of the mouth and skin, functioning of the cardiovascular system, functioning of the respiratory system, functioning of the urogenital system.**

## DISBIOSIS

it is defined as the state of alteration of the balance of the gastrointestinal tract and has a primary microbial origin so we could also speak of **dismicrobism**, i.e. the microbiota that alters and brings with it a whole other series of alterations.

### Main causes of dysbiosis:

**diet** (48 hours of altered nutrition are enough to begin to cause damage to the microbiota), **pathologies and drugs** (alteration of drug effect), **cigarette smoke, environmental pollutants and pesticides.**

### What to recommend?

**adequate nutrition, no smoking**, carry out an **intestinal cleansing protocol** at least a couple of times a year (especially in subjects at risk), **detoxify the liver** in spring and autumn (especially for those who take drugs, young women who take contraceptive), **antioxidants.**

**Disbiosis Fermentative** CHO excess abdominal swelling  
**Disbiosis Putrefactive** Protein excess constipation and meteorism



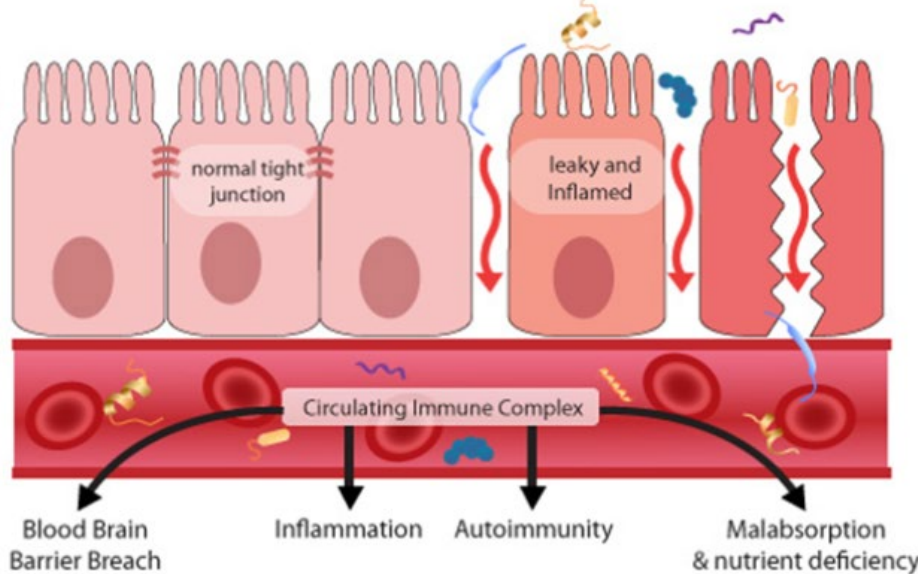
## Leaky Gut Syndrome

Triggers Causing  
Intestinal Damage



Intestinal  
Mucosal Cells

Blood Stream



When **disbiosis** is not controlled a **serious damage to the anatomical component** occurs, the **barrier** becomes abnormally **permeable** and **loses its filter function**, residues not recognized by the **GALT system** which therefore gives a response, they **enter the entero-portal circulation** **overloading the liver** that became unable to carry out its tasks.

Restore eubiosis when?

- After antibiotic therapy
- When the subject reports symptoms directly related to the intestine (alternative bowel movements / constipation / colitis / bloating etc...)
- In case of recurring urogenital pathologies/allergies/atopy/intolerances/dermatitis
- In case of deficiency syndromes (anaemia/ hypovitaminosis)
- In subjects on polytherapy

## 3 phases for recovery in case of acute-severe disbiosis:

1. **Wash out** – a gut cleanse
  2. **Repopulation** – replanting probiotics
  3. **Repair** – recovery of the structural mucosa damage
-



# Restore Eubiosis : wash out

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WASH OUT:

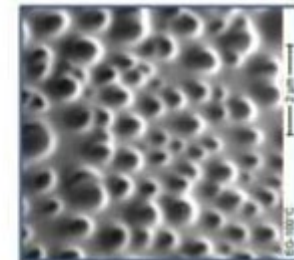
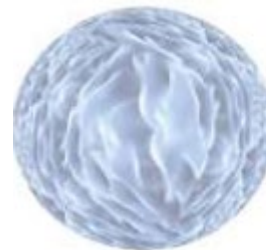
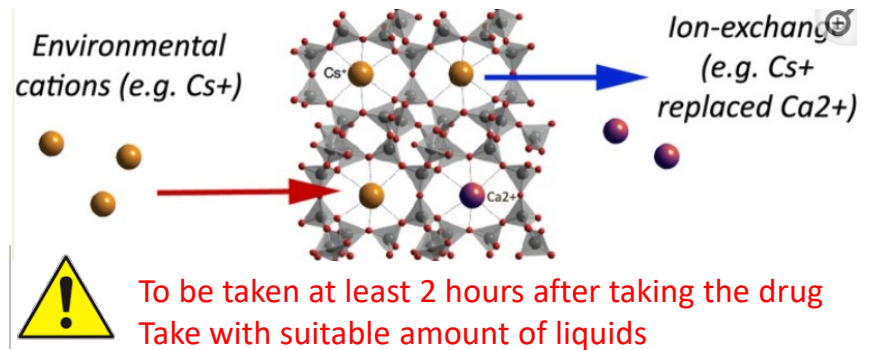


Take care of disturb, person, remedy

**Zeolite:** (silicate) of volcanic origin, which has an enormous surface in nature. Due to its porous properties, the crystalline substance is able to absorb certain substances in its cavities from hollows and channels.

In particular, the clinoptilolite zeolite is valued for its superior properties as a filter and adsorbent for the removal of pollutants (like a sponge). Zeolite is used to strengthen the intestinal wall barrier and support detoxification by binding ammonium and heavy metals in the gastrointestinal tract.

**Silica gel:** (silicate) no odour, no taste, no colour  
1 spoon twice/day far from drugs and food



**No for people in polytherapy**

# Restore Eubiosis : wash out

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WASH OUT:

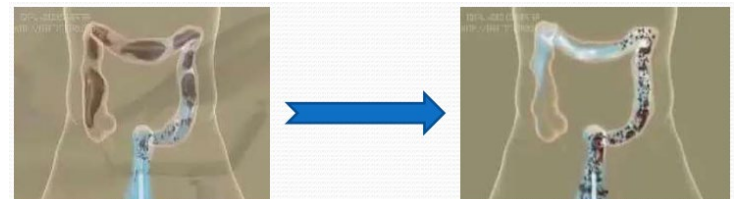


Take care of disturb, person, remedy

**MgO<sub>2</sub>:** develops oxygen in the gastrointestinal lumen which, in turn, leads to the reduction of intestinal germs; acts as laxative.

**Biological control:** It is based on a "competition" mechanism between microorganisms. It also allows cleansing in individuals who use drugs or whose intestines are particularly sensitive for which they cannot use Magnesium. *Saccharomyces Boulardii* species and *Enterococcus faecium* which are MCIs that are transient (they do not stop in the intestine). They are taken at full stomach because they need nourishment, morning and evening for seven/ten days.

**Colon hydrotherapy:** Painless, odorless and natural, this medical treatment completely cleans the intestine, eliminating waste, but also dead cells, mucus and bacteria that prevent the growth of intestinal flora. This restores its correct functioning, detoxifying it, improving digestion and eliminating abdominal swelling.

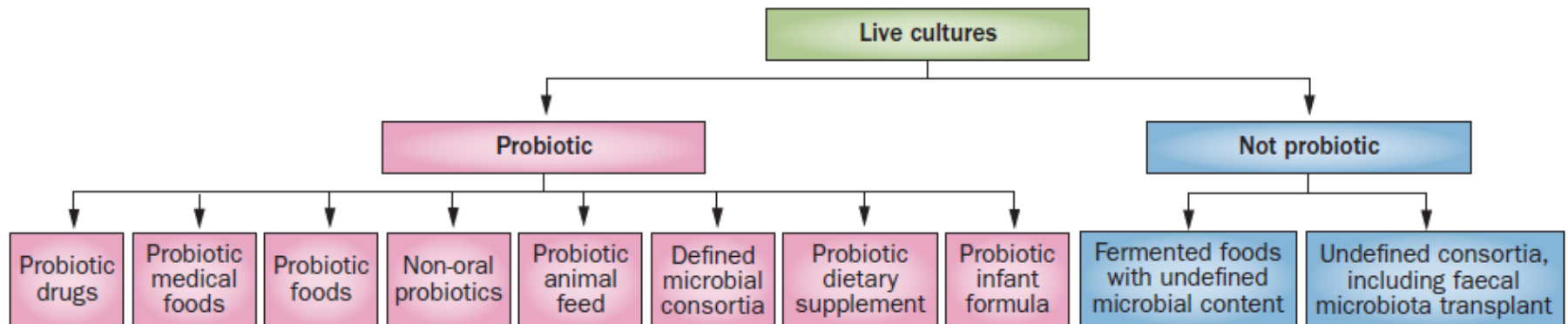


EXPERT CONSENSUS DOCUMENT

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

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**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
<i>Not probiotic</i>				
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 $1 \times 10^9$ CFU per serving <sup>73</sup>	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' <sup>74,75</sup> )
<i>Probiotic</i>				
Probiotic in food or supplement without health claim	"Contains probiotics"	A member(s) of a safe <sup>76,77</sup> 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 <sup>73</sup>	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 <sup>73</sup>	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, <sup>78</sup> PASSCLAIM, <sup>79</sup> or GRADE; <sup>80</sup> well-conducted RCT(s) OR strong evidence from large observational studies <sup>81</sup>	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.



## 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



## 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 react with 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.

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# Probiotic Requirements



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

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

## Identification

Probiotics are identified by their specific strain, which includes the genus, the species, the subspecies (if applicable), and an alphanumeric strain designation. The seven core genera of microbial organisms most often used in probiotic products are *Lactobacillus*, *Bifidobacterium*, *Saccharomyces*, *Streptococcus*, *Enterococcus*, *Escherichia*, and *Bacillus*. Table 1 shows examples of the nomenclature used for several commercial strains of probiotic organisms.

Table 1: Nomenclature for sample commercial strains of probiotics [3]

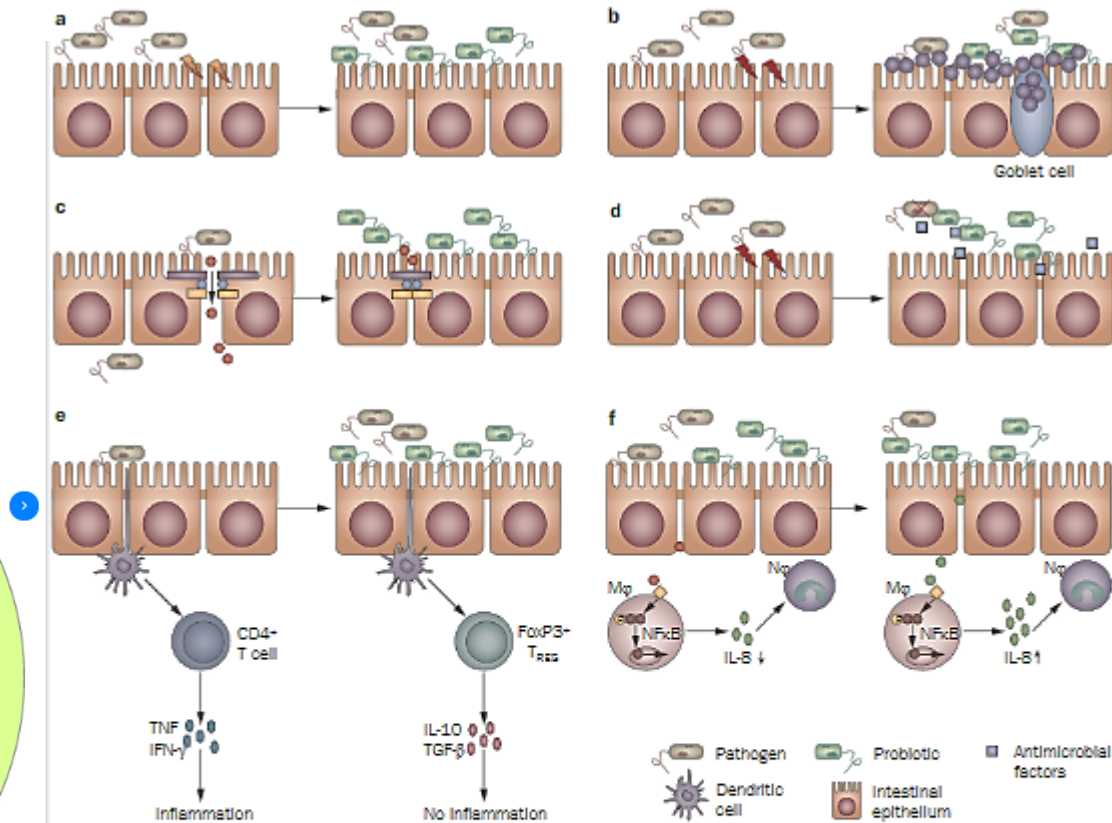
Genus	Species	Subspecies	Strain Designation	Strain Nickname
<i>Lactobacillus</i>	<i>rhamnosus</i>	none	GG	LGG
<i>Bifidobacterium</i>	<i>animalis</i>	<i>lactis</i>	DN-173 010	<i>Bifidus regularis</i>
<i>Bifidobacterium</i>	<i>longum</i>	<i>longum</i>	35624	Bifantis

# Probiotic functions and mechanisms

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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<sup>55-57</sup> 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),<sup>58</sup> or by preventing tight junction protein redistribution<sup>59</sup> 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- $\beta$ . **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<sup>74</sup> (or activating) NF- $\kappa$ B in  $M\phi$  and dampening (or priming) the host immune response by influencing the production of IL-8 and subsequent recruitment of  $N\phi$  to sites of intestinal injury. Abbreviations:  $M\phi$ , macrophage;  $N\phi$ , neutrophil;  $T_{reg}$ , regulatory T cell.

**Rare**  
Strain-specific effects

- Neurological effects
- Immunological effects
- Endocrinological effects
- Production of specific bioactives

**Frequent**  
Species-level effects

- Vitamin synthesis
- Direct antagonism
- Gut barrier reinforcement
- Bile salt metabolism
- Enzymatic activity
- Neutralization of carcinogens

**Widespread**  
Among studied probiotics

- Colonization resistance
- Acid and SCFA production
- Regulation of intestinal transit
- Normalization of perturbed microbiota
- Increased turnover of enterocytes
- Competitive exclusion of pathogens

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**Probiotics exert health effects by nonspecific, species-specific, and strain-specific mechanisms.**

**Non specific mechanisms** include inhibition of the growth of pathogenic microorganisms in the gastrointestinal tract (by fostering colonization resistance, improving intestinal transit, or helping normalize a perturbed microbiota), production of bioactive metabolites (e.g., short-chain fatty acids), and reduction of luminal pH in the colon.

**Species-specific mechanisms** can include vitamin synthesis, gut barrier reinforcement, bile salt metabolism, enzymatic activity, and toxin neutralization.

**Strain-specific mechanisms**, which are rare and are used by only a few strains of a given species, include cytokine production, immunomodulation, and effects on the endocrine and nervous systems. Through all of these mechanisms, probiotics might have wide-ranging impacts on human health and disease.





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

- *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 *Helicobacter 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, REUFLORE)
- *Lactobacillus Plantarum & Fermentum* (immune stimulant; it is a fundamental element of vaginal bacterial flora);

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

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Only one claim authorized in the EU concerning the *Lactobacillus delbrueckii* subsp *bulgaricus* and *Streptococcus thermophilus* 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"....

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 + 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 ( <i>Lactobacillus delbrueckii</i> subsp. <i>bulgaricus</i> and <i>Streptococcus thermophilus</i> ) per gram.	improved lactose digestion	2010;8(10):1763	Commission Regulation (EU) 432/2012 of 16/05/2012	Authorised	1143, 2976

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

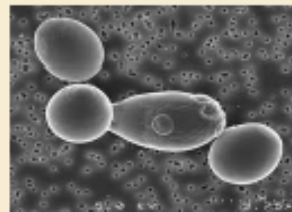


## ENTEROLACTIS



Enterolactis è costituito da fermenti lattici vivi di origine umana (*Lactobacillus casei*, subspecie *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.





## 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.

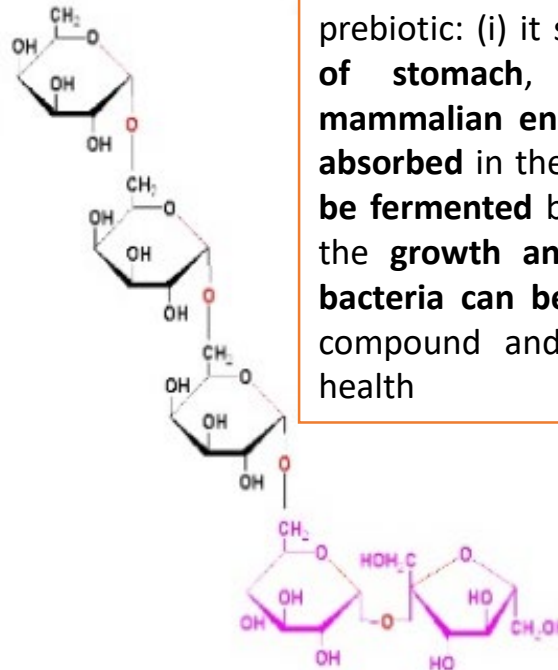
The **capsules** represent, today, the best protective form for bacteria both during the conservation phase both during the recruitment period, because they offer one gastroresistance linked to intrinsic characteristics of the capsule itself and to the possibility of a further coating with protective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

# Restore eubiosis: repopulation Prebiotic

U7

“a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thus improves host health”

- 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).



criteria used to classify a compound as a prebiotic: (i) it should be **resistant to acidic pH of stomach, cannot be hydrolyzed by mammalian enzymes**, and also should **not be absorbed** in the gastrointestinal tract, (ii) it **can be fermented** by intestinal microbiota, and (iii) the **growth and/or activity of the intestinal bacteria can be selectively stimulated** by this compound and this process improves host's health

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



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)

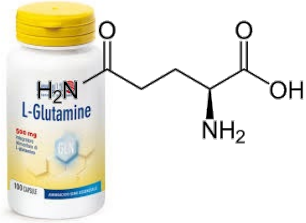


Bifidobacterium Lactis 1 miliardo ufc  
fruttoligosaccaridi a catena corta (FOS)



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)

Severe disbiosis with tissues damage needs repair interventions.



### L-Glutamine

It is a non-essential amino acid that promotes repair because it represents the main source of energy for the cells of the intestinal mucosa and some of the cells of the immune system. It makes the enterocytes stronger, they manage to restore their condition, they manage to tighten the junctions. The SI resumes its structure. The growth of the villi is also stimulated and the absorption capacity of the intestine increases. The health of the microbiota is promoted. Take 2 capsules of 500 mg in the evening (during the nocturnal period no digestion mechanisms occur and the repair action is carried out more easily)



### ALGA KLAMATH

The set of algae are blue-green lake microalgae. It provides significant quantities of minerals, antioxidants and vitamins, important macronutrients, such as essential amino acids and omega 3, this ensures that the enterocyte regains shape and vigor, restoring normal barrier function and permeability.

The recommended intake is 2 to 5 grams per day. It is recommended to take it in a single dose in the morning, i.e. when transit occurs the most



**No in people  
with cancer**

### COLOSTRO BOVINO e MORINDA CITRIFOLIA

bovine colostrum is a stimulator of growth and restoration of the health conditions of the enterocyte. Morinda citrifolia juice has anti-inflammatory, antibacterial, tonic and immune defense-stimulating properties. They favor the balance of the bacterial flora by selecting the microbiota towards the bacterial strains most useful to the intestine bifidogenic shift.

## Symptoms:

### Irritable Bowel Syndrome (IBS):

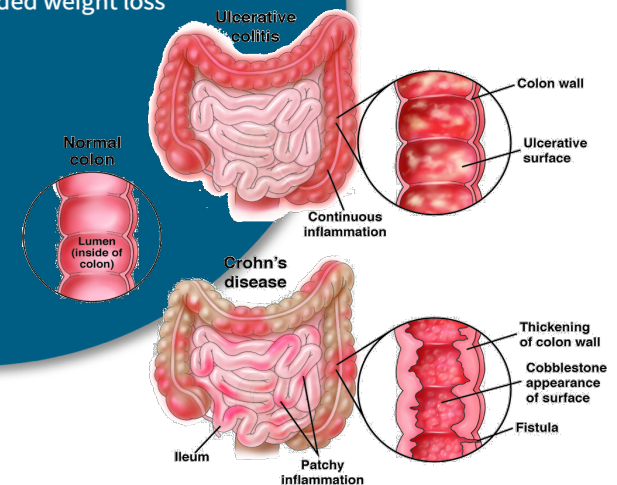
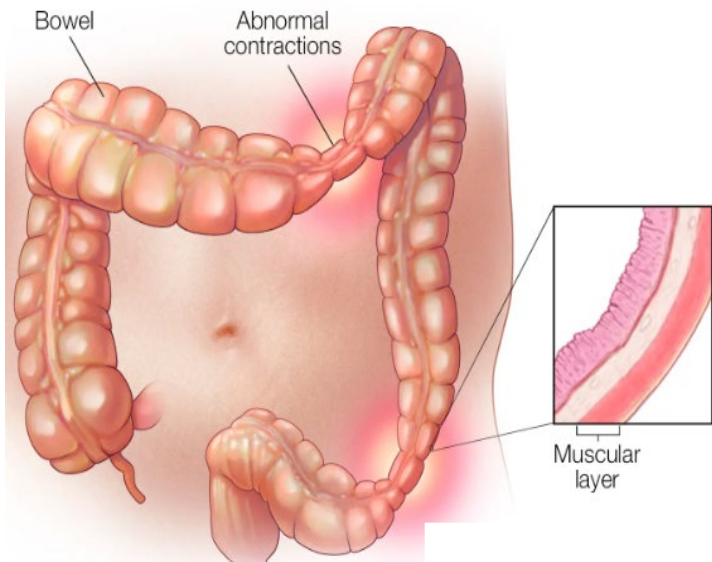
- Bloating
- Gas

### Both

- Abdominal pain
- Cramping
- Changes in bowel movements (diarrhea, constipation or both)

### Inflammatory Bowel Disease (IBD):

- Bloody stool
- Fatigue
- Reduced appetite
- Unintended weight loss

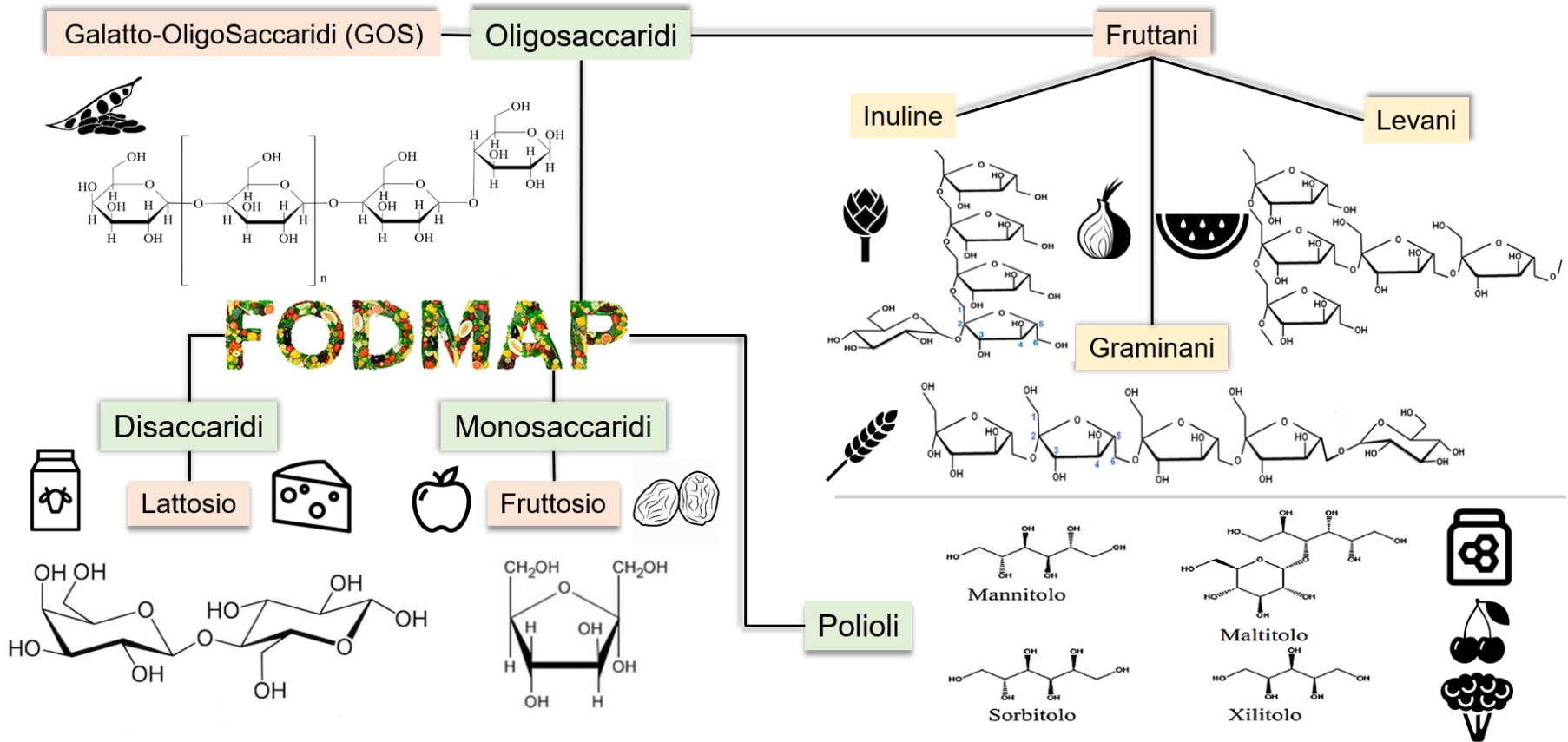


People who have IBD or IBS often **try to treat it by changing what they eat**. There's no specific diet that works for everyone.

**Get more fiber** (from food or supplements). **Avoid lactose**, which is in dairy products. **Cut down on foods** that make you gassy or bloated. **Get more water**. (You can drink it or eat water-rich foods.) **Avoid caffeine and legumes** (beans). **Limit or avoid FODMAPs**, a type of sugar found in some fruits, vegetables, breads, and dairy products.

## LOW FODMAP's DIET

### Tipologie di FODMAP





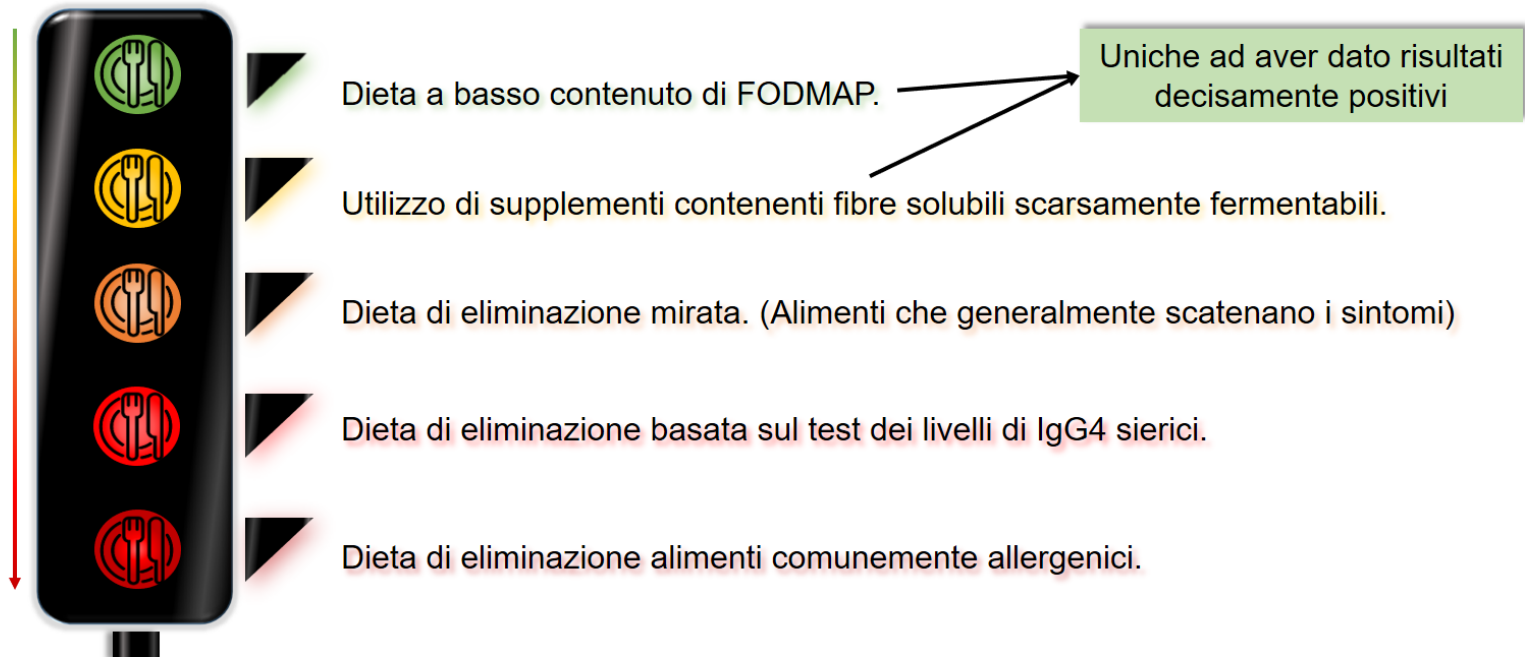
## Comparazione tra i vari approcci dietetici proposti

Nel tempo proposti e testati numerosi approcci dietetici per la riduzione della sintomatologia, ordinati nell'immagine in funzione di:

efficacia dimostrata

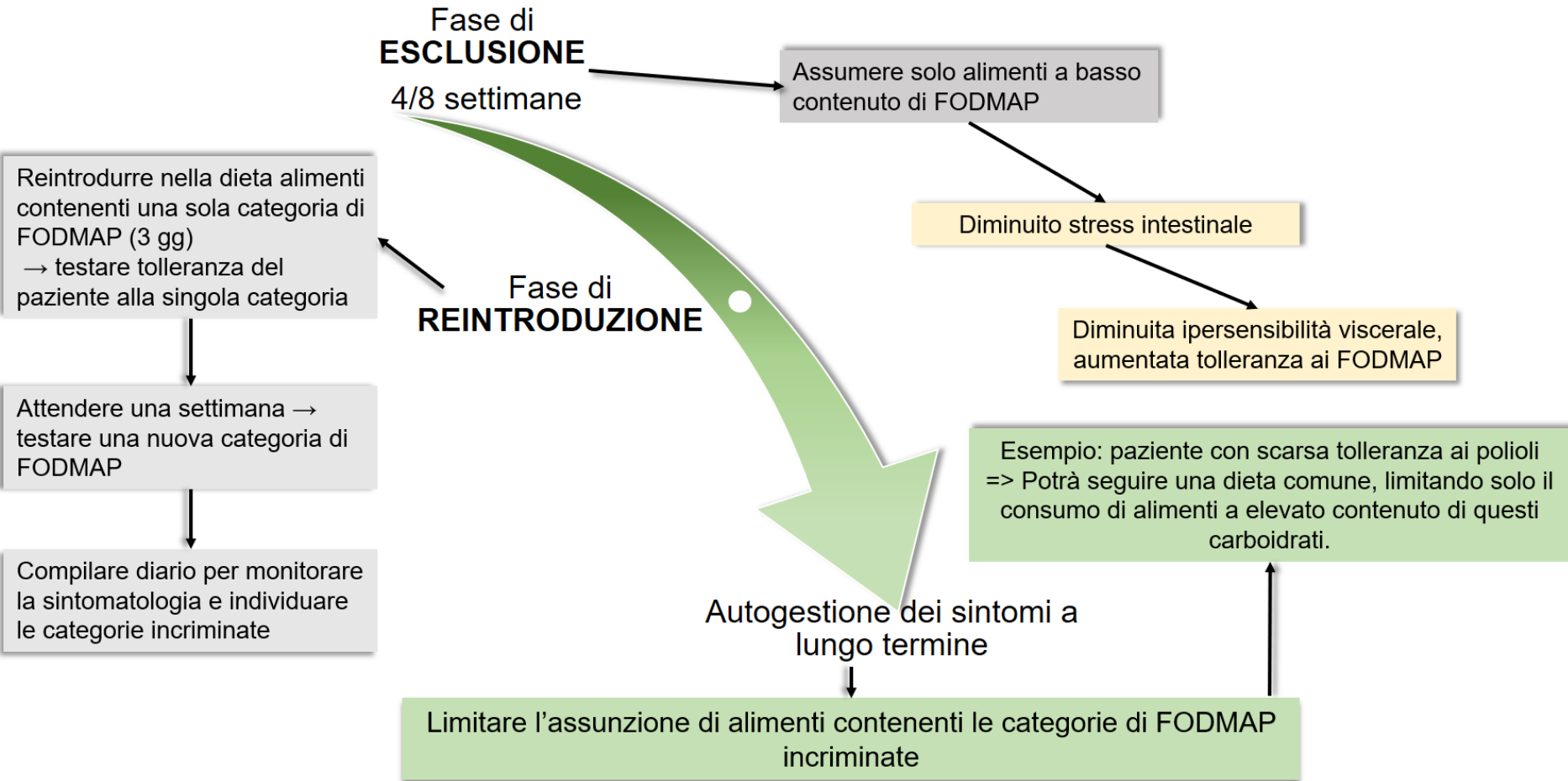
qualità delle prove

forza delle raccomandazioni





## Com'è strutturata la Low FODMAP Diet

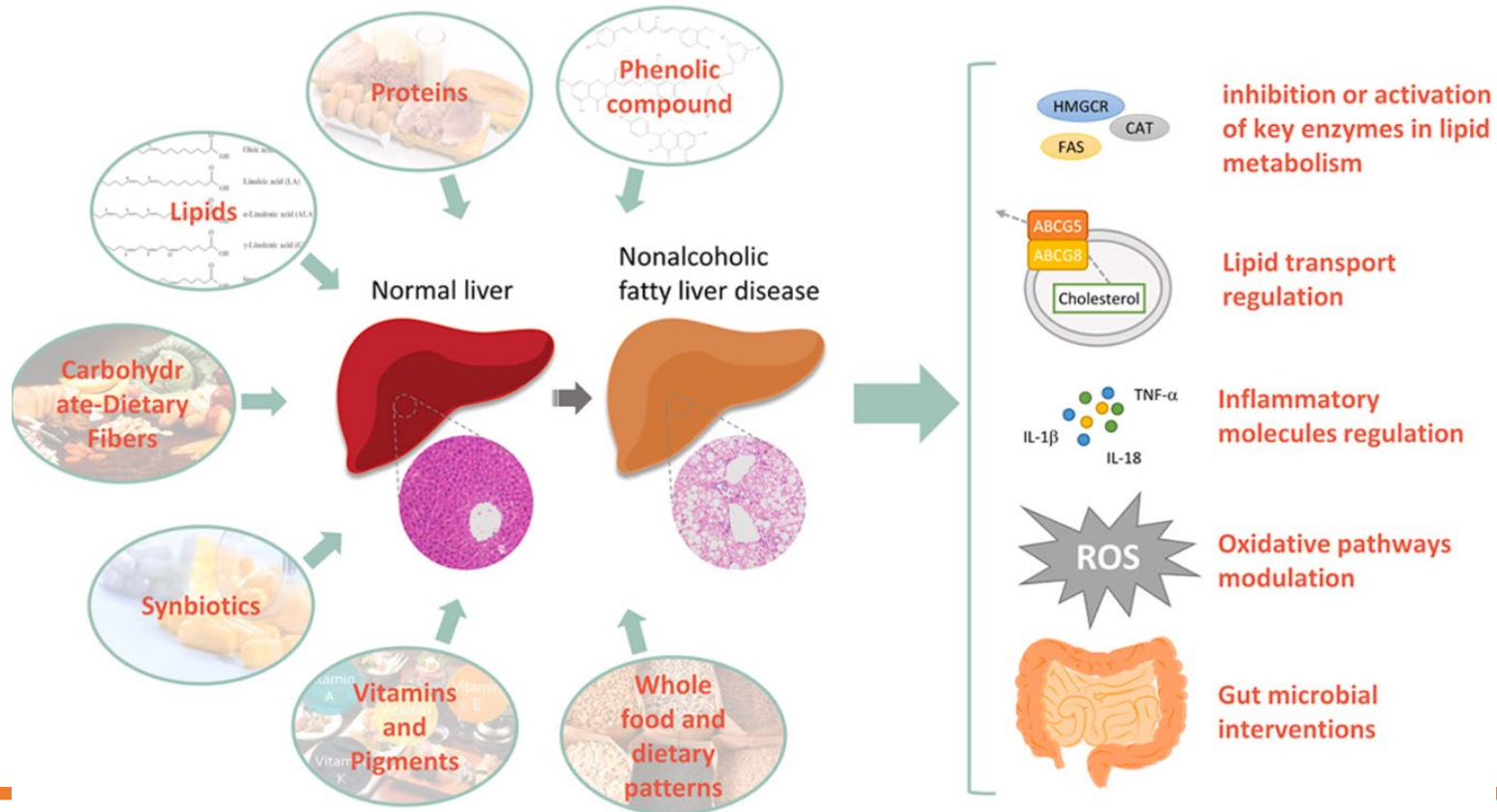




# Functional gastro-intestinal disorders

U7

The problem of **non-alcoholic fatty liver disease (NAFLD)** is widespread, affecting 20% of Western population. NAFLD spans a range of liver disorders from steatosis to non-alcoholic steatohepatitis (NASH), leading to more severe complications including fibrosis, cirrhosis, and hepatocellular carcinoma. Standard recommendations for NAFLD patients include **changes in diet and exercise regimens** with the **goal of weight reduction**. However, with the exception of hypolipidemic treatment, the **pharmaceutical therapies available for clinical treatment are limited** due to the **complex and diverse etiologies driving NAFLD pathogenesis**, the **long period of disease development**, and the **wide genetic and physiological variations** among the disease population.



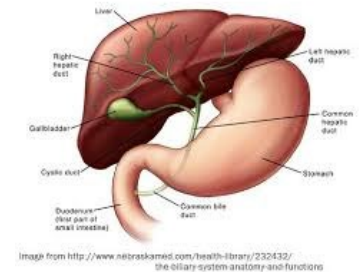
There are a number of strategies for approaching the prevention and treatment of NAFLD, which broadly include the development of new drugs, nutraceuticals, dietary supplements, and nutritional formulas, as well as in vitro and in vivo examination of the underlying mechanisms of pathogenesis.

Active ingredients for treating non-alcohol steatotic liver related diseases. **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, 1 year administration ameliorated hepatic fibrosis and reduced AST, ALT, g-GTP. Vitamin E, administered to one 800 IU / day dose improves liver histology in non-diabetic patients with NASH. **Astaxantine and vit C**

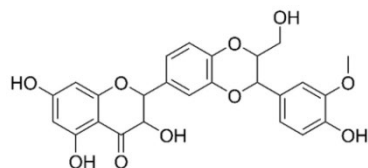
**Tabella 2: Ingredienti che presentano il *claim* ammesso nell'elenco del Regolamento Europeo 432/2012**

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.*

## Silymarin



*Silybum marianum*, (*Carduus marianus* L.)

Family: Asteraceae (Compositae),

Origin: Mediterranean region

Other information: herbaceous annual or biennial plant

### SILYMARIN

standardized **extract** obtained from the **fruits** of *Silybum marianum*,  
Complex mixture of active natural product compounds: the four most abundant components are:

- silybin,
- isosilybin,
- silydianin,
- silychristin.

Strongest **anti-inflammatory** and **anti-oxidant** effects

**traditional phytotherapeutic product** widely used for the treatment of **liver diseases**  
Including hepatitis , cirrhosis and bile secretion dysfunction

Daily dosage:  
210-800 mg

### MECCANISMO D'AZIONE:

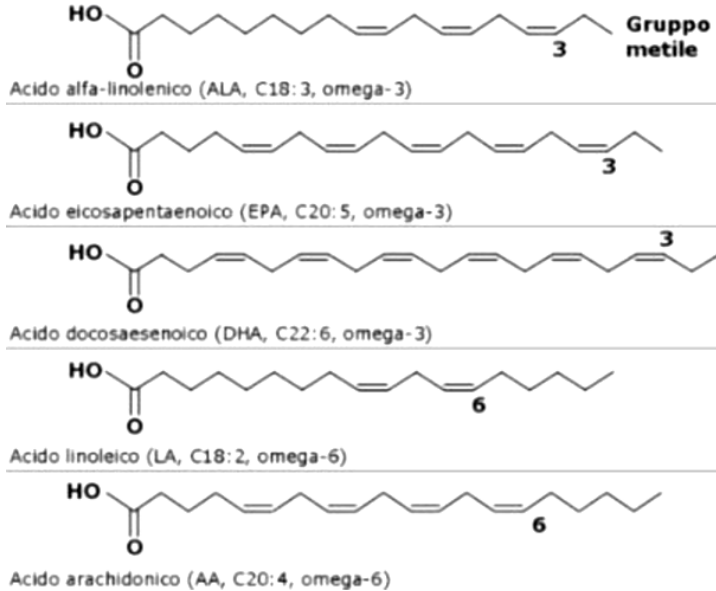
- Radical scavenger:  $\text{ArOH} + \text{R}^{\bullet} \rightarrow \text{ArO}^{\bullet} + \text{RH}$
- ↑ SOD e CAT activity
- ↓ release citochine
- active a pathway that promote FA oxidation:
- ↓ reduced abdominal fat



### ALLEGATO 1 - BOTANICALS

NOME BOTANICO	FAMIGLIA	SINONIMO	PARTE TRADIZIONALMENTE IMPIEGATA	PRESCRIZIONI ETICHETTA	ALTRE PRESCRIZIONI	LG MINISTERIALI DI RIFERIMENTO PER GLI EFFETTI FISIologici
<i>Silybum marianum</i> (L.) Gaertn.	Compositae		herba cum floribus, fructus, tegumen seminis, herba			fructus, tegumen seminis: Funzione digestiva. Funzione epatica. Funzioni depurative dell'organismo. Antiossidante. Metabolismo dei carboidrati. herba: Funzione digestiva. Funzione epatica.

## Omega 3 fatty acids



Fish oil



Perilla oil

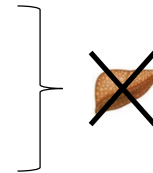


Linseed oil

- Polyunsaturated fatty acids (PUFAs) are critical **nutrients necessary** for many **metabolic and regulatory processes** that govern human health and development.
- **Omega-3** and **omega-6** fatty acids are the most common PUFAs in human metabolism.

### MECCANISMO D'AZIONE:

- ↓ espressione di geni correlati alla lipogenesi
- ↑ espressione di geni correlati alla beta-ossidazione degli acidi grassi
- ↓ accumulo di trigliceridi
- ↓ l'infiammazione e lo stress ossidativo: down-regulation di citochine infiammatorie



Daily dosage:  
ADI of EPA and DHA  $\leq 2$  g

A typical fish oil supplement provides about 1,000 mg fish oil, containing 180 mg EPA and 120 mg DHA, but doses vary widely

# 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 campyloides* G.E.Haglund )

choline, inositol, pyridoxine, cyanocobalamin

that can have beneficial effects in maintaining proper liver function

cholagogue and choleretic

Ananas sativum gambi extracts\*,

Desmodium adscendens,

Pimpinella anisum,

Citrus oils

Cuminum cymimum§,

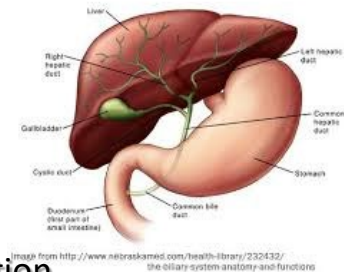
Lemongrass

Charcoal

Sodium bicarbonate and citric acid (Citrosodina)

Bromelin, Papain, amilasi, lactase, lipase, cellulase

Digestion and aerophagia, colitis, meterosimo, fermentation



\* Interaction with anticoagulant drugs, § interaction with hypoglycaemic drugs and antiarrhythmics





(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 estragole, 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.





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