The microbiota and its role in maintaining the well-being of the organism

The term **microbiota** is used today to identify the complex ecological system composed of billions of microorganisms, not only bacteria, but also fungi, protozoa, viruses, present in our body. Sometimes it is confused, and it is used interchangeably, with **microbiome**, which refers, instead, to the totality of the genetic heritage possessed by the microbiota itself.

This set of microorganisms lives in perfect **symbiosis with the organism**, taking nourishment from the latter, and returning to it substances useful for its proper functioning. These interactions between microbiota and organism are so close that the health of one inevitably depends on that of the other. It is almost possible to say that *"the human gut microbiota has a metabolic activity equal to an organ in the organ*".

Thanks to this activity, the microbiota is able to perform certain beneficial functions for the host, such as:

- to perform a protective function, acting as a "selective barrier" against the proliferation of pathogenic bacteria.
  The microbiota, in fact, prevents harmful microorganisms (or potentially such) from proliferating, thanks to the "competition" of the beneficial intestinal flora ("barrier effect").
- to promote the development and maturation of the immune system by modulating the quantity and quality of our body's immune response.
  This close interaction between microbiota and immune system would serve, in fact, to "teach" first and then to "train" the various functions of the latter.
- to help regulate the intestinal motility.
  The microbiota, in fact, can help stimulate intestinal nerve cells by facilitating the natural mechanism of contraction and relaxation of the colon during the digestion phase.
- to allow the synthesis of some vitamins, such as vitamin K, B9 (folic acid), vitamin B12, essential for our body.
- to ferment the carbohydrates present in the fibers ingested with the diet in energy, through the production of butyric acid (which acts as nourishment for the cells of our colon).
- to contribute to the digestive function, working incessantly to allow the absorption of nutrients introduced with food.

Microbiota and nutrient absorption

It has been extensively studied how the gut microbiota is able to interact with various dietary components and generate metabolites capable of regulating the metabolic functions and activities of the host.

Although the number of metabolites produced by the gut microbiota is rather modest, many studies suggest that the contribution of the latter to the host's "metabolome" may be much larger and even cover hundreds of different chemical species.

Colonization by different microorganisms in each section of the gastrointestinal tract can therefore have a huge impact on the microenvironment and thus positively or negatively affect the bioavailability of micronutrients (minerals and vitamins).

Microbiota and vitamin D metabolism

If we consider vitamin D alone, for example, in the literature we have several lines of evidence that underline how the human intestinal microbiome and the metabolism of vitamin D are integrally related.

Specifically, a 2015 study conducted in a mouse model showed a close relationship between the expression of the vitamin D receptor in the intestine and the microbiota, in particular the bacteria that produce butyrate.

An increase in the expression of this receptor may predispose to an increased bioavailability of the vitamin itself.

In a clinical study conducted on 567 men it was shown that several bacteria belonging to the phylum *Firmicutes* were positively associated with serum levels of vitamin D.

Obviously, a positive relationship between the microorganisms present in the intestine and the metabolism of vitamins, such as vitamin D, can occur as long as the microbiota turns out to be "healthy", that is, until a correct balance is maintained between all the microorganisms, especially between the so-called "good" bacteria and those pathogenic or potentially such. Having a microbiota in balance, in fact, is important for the production and absorption of vitamins.

A proper lifestyle and a balanced diet are the key to promoting the health of the intestinal microbiota. If, however, this is not enough, it is possible to use probiotic products.

Probiotics: they are not all the same

Probiotics are " *live microorganisms that, when administered in adequate amounts, confer a health benefit on the host*". This is the definition still accepted and used today of probiotic, provided by a group of experts from FAO (Food and Agriculture Organization) and WHO (World Health Organization) in 2001 and adopted, then, also by our Ministry of Health.

We talk, therefore, about microorganisms that must be kept alive and vital, not only during the production processes, but for the entire life span of the product itself; these microorganisms must be present in adequate quantities so that, once they reach the intestine, they can multiply and colonize the intestinal environment. Only in this way, it is possible to observe beneficial effects on the body, thanks to their ability to promote the balance of intestinal microbiota.

Several lines of evidence show that the use of specific probiotic strains are even able to increase the absorption and bioavailability of some vitamins, including vitamin D.

Probiotics: L. paracasei DG, a strain widely characterized and studied

In a recent *in vitro* and *in vivo* study on a mouse model, a group of researchers, starting from the assumption that vitamin D is fat-soluble and that lactic acid bacteria may have biosurfactant properties, that is, which contribute to the emulsion, has tested, *in vitro*, six bacterial strains belonging to the Lactobacillaceae family to verify if they could improve the bioavailability of Vitamin D: *L. paracasei* DG, *L. paracasei* LPCS01, *L. paracasei* Shirota, *L. rhamnosus* GG, *L. reuteri* DSM 17938, and *L. acidophilus* LA5.

The obtained results showed a significant increase in cholecalciferol in the aqueous phase only for the strains *L. paracasei* DG and (albeit less markedly) *L. rhamnosus* GG. In particular, *L. paracasei* DG cells showed greater biosurfactant capacity compared to the other tested strains. This effect appears to be strain-specific, since the solubilization capacity of vitamin D3 was negligible for the other two strains of the same species.

The DG strain was then selected for subsequent *in vivo* observations. Administered in combination with Vitamin D3 once daily for one week, it increased serum concentration of 25(OH)D by approximately 50% compared to the control group, by approximately 62% compared to vitamin D3 alone for one week and by approximately 55% compared to administration of *L. paracasei* DG cells alone.

What could be the reasons for this increased activity carried out by the DG strain?

As reported in the article, it can be hypothesized that the exopolysaccharide (EPS) rich in rhamnose, which accumulates on the outer cell surface of *L. paracasei* DG, may play a significant role in this context. In fact, by covering the bacterium it could explain its greater emulsifying capacity compared to the other tested probiotic strains. The presence of this unique EPS, present only on the DG strain, also gives it other important properties: 1) a high ability to resist environmental stresses such as stomach acids and bile salts (a fundamental characteristic for a probiotic strain) and water deficiency, and 2) the ability to modulate the cross-talk with the host's immune system.

Precisely this last characteristic is fundamental to explain the immunomodulating and anti-inflammatory properties of the *L. paracasei* DG strain, also shown against SARS-CoV-2. In a recent *in vitro* study, published on probiotics and COVID-19, the strain not only demonstrated antiviral immune response-boosting activity and significantly inhibited SARS-CoV-2 infection, suppressing virus replication by about 50%, but also significantly reduced the expression levels of certain genes such as IL-6, CXCL8, TSLP (pro-inflammatory markers) and increased the transcription levels of IL-10 (anti-inflammatory marker) compared to those of the control.

All data, that are then confirmed in the published clinical studies on the strain, testify to its high quality.

It is known that in the choice of probiotic, in addition to the appropriate clinical risk/benefit assessments, it is also necessary to consider other aspects, such as the ability to survive gastrointestinal transit and to effectively promote the rebalancing of the intestinal microbiota, thus favoring the production of SCFAs and the modulation of the immune system.

L. casei DG® (*Lactobacillus paracasei* CNCM I1572) has shown, in humans, to survive gastrointestinal transit by arriving alive and vital in the intestine, to modulate the balance of the intestinal microbiota and to induce a statistically significant increase in fecal levels of short-chain fatty acids and, as indicated above, thanks to its peculiar EPS (exopolysaccharide) that covers the bacterium as a sort of natural "microencapsulation", to induce a positive modulation of inflammatory markers in different experimental models.

In choosing a probiotic strain it is, therefore, essential to remember that not all probiotics can boast these characteristics and that the supporting scientific evidence can make the difference.

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