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Alpha-lactalbumin: what it is, use and benefits

Index

Introduction

A-lactalbumin (α-LA) is a small **protein** found in **human whey** and of many animal species to which multiple biological actions are attributed such as stress reduction [1], antibacterial activity [2], antihypertensive action [3], regulation of cell growth, anti-ulcer activity [4], immunomodulating, but above all specific intestinal actions.

"All diseases originate in the intestine" reads one of the most famous aphorisms of Hippocrates, father of medicine, who after more than 2000 years, retains his unchanged truth and which is confirmed in his renewed interest by academics belonging to specific branches of medicine, such as gynecology and endocrinology.

In recent years, in fact, the scientific literature has highlighted the **correlation between intestinal alterations and different metabolic pathological** conditions such as, for example, insulin resistance [5], PCOS [6], diabetes [7] and obesity. In the same way it was possible to see how **taking care of the intestine is central to different diseases and, therefore, for health.**

The objective of this page is precisely to investigate the activities of α-LA in the intestine, analyzing all the possible benefits on the metabolism in certain clinical contexts such as PCOS, diabetes and obesity.

What is alpha-lactalbumin and why it is important

A-LA is the **main serum protein of human milk** (it makes up 40% of proteins in breast colostrum), but it is also present in cow's milk and in that of other mammals. From a physiological point of view, it is a protein synthesized in the epithelial cells, at the level of the Golgi apparatus, of the mammary gland in which **it plays a fundamental role in the synthesis of lactose [8].**

A-LA is indispensable for the production of breast milk.

This small protein is also present in cow's milk and consists of 123 amino acids, which, in their native state, form a compact globular structure, stabilized by four disulfide bridges (Cys6-Cys120, Cys61-Cys77, Cys73-Cys91 and Cys28-Cys^{111}).

Bovine α-LA has a high sequence homology with the human one (76% overlap) [9] and therefore could be a perfect substitute.

A-LA also shows a **close structural analogy with lysozyme**, often used as a "**natural antibiotic**", and both proteins are synthesized under the control of genes that come from a common ancestral gene.

A-LA, thanks to its amino acid composition, **has a high nutritional value.** In fact, it is rich in essential amino acids such as tryptophan (a precursor of serotonin, also known as a "good mood hormone"), cysteine (a precursor of glutathione, a known antioxidant reserve in our body), which are fundamental especially for the feeding of infants.

A-LA is rich in essential amino acids such as tryptophan and cysteine, fundamental above all for the feeding of newborns. These characteristics make it perfect for the fortification of food products and food for medical purposes, even in lactose-free foods [10]

How is alpha-lactalbumin absorbed?

One of the most interesting characteristics of α-LA, on which many of its biological activities depend, **is its ability to bind metal cations: it is therefore a metalloprotein.** Indeed, α-LA has two binding sites for calcium, one stronger (called primary) and another weaker and less stable (called secondary) [11] both in bovine and human proteins.

In addition to calcium, α-LA binds other mono-di-tri-valent cations [12] such as Na +, Mg ++, Zn ++, Fe ++, Al +++, which compete for the same binding site for calcium.

Orally administered A-LA passes intact through the stomach unlike all the other proteins that precipitate in the gastric environment , and reaches the duodenal level, where it is attacked by pancreatic enzymes. From the proteolytic digestion of α-LA, by pepsin, trypsin and chymotrypsin, different fragments or "Biopeptides" are obtained, responsible for multiple biological actions: antibacterial [2], anti-inflammatory [13], analgesic [14], antihypertensive [15], immunomodulatory, pro-apoptotic [16], trophic and antiperistaltic.

A-LA, administered orally, passes undisturbed through the stomach, unlike all the other proteins that precipitate in the gastric environment

Alpha-lactalbumin: difference between probiotics and prebiotics

Over the years, the attention of researchers has focused **on the specific intestinal actions of probiotics** – which is now very popular – defined as <<**microorganisms capable, once ingested in adequate quantities, of exercising beneficial functions for the organism>> [17].**

To fulfill their function, however, they must arrive in a condition of "vitality" in the intestine and **survive the acidic environment of the stomach** and then multiply. A recent study has evaluated the qualitative-quantitative aspects, as well as the vitality and therefore the resistance to gastric and intestinal juices, of 10 oral formulations of probiotics, currently on the market in Italy.

The results showed that 7 out of 10 products show a significant reduction in the bacterial strains that make them up after only 30 minutes of incubation in a "gastric-like" environment and **that products containing Bifidobacterium lactis and/or Lactobacillus rhamnosus do not exceed the gastric wall and intestinal [18].**

For this reason, the focus of research has shifted rather to prebiotic actions in the context of which those of a protein, alpha-lactalbumin, emerge which are essential for recovering and maintaining intestinal eubiosis and therefore the balance of the whole organism.

What is the role of alpha-lactalbumin

In the presence of an altered metabolic picture, the use of α-LA finds its rationale in the specific intestinal actions with which the protein is equipped.

1. First, **α-LA, through its prebiotic and antibacterial action, controls the establishment of a correct intestinal flora,** preventing the dysbiotic flora from proliferating. In a recent meta-analysis that evaluated 12 randomized controlled studies (total population: 684 diabetic patients) it emerged that the use of some bacterial strains, including those stimulated by α-LA such as L. acidophilus, B. short, B. longum and B. infantis, is associated with a significant improvement in the glycated hemoglobin and HOMA-IR in patients with type 2 diabetes [8].

2. In addition, by reducing cytokines and phlogistic mediators, **α-LA helps to counteract the inflammation that accompanies dysbiosis** in obese and non-obese subjects, an effective or predisposing cause to insulin resistance.

3. A recent study has shown that hydrolyzed **α-LA exerts a protective effect against inflammation and insulin resistance in adipose tissue** in mice fed a high-fat diet. The results of the study showed that α-LA significantly reduces body weight, blood sugar, insulin level and HOMA-IR, decreasing the expression of genes by pro-inflammatory factors such as IL-6, TNF-α, MCP-1 in the adipose tissue of mice [19].

4. In addition, α-LA, through the trophic and mucoprotective function, **supports the barrier function of the intestine,** reconstituting and preserving its integrity.

A-LA prevents the "bad" bacterial flora from taking root and its metabolites from crossing the intestinal wall, triggering the inflammatory response.

Alpha-lactalbumin and intestinal actions

What most aroused the interest of many academics towards this milk protein are the **direct actions exerted on the intestine, the indirect effects of the prebiotic action and therefore its role in the prevention and treatment of metabolic disorders "microbiota-dependent. "**

Research in the field of **neonatal nutrition** has been aimed at at least 100 years for the emulation of **breast milk**, considered a **"superfood" thanks to which the infant can develop its own intestinal microbiota**, and therefore also an **immune system**. In addition, infants exclusively breastfed for the first 6 months of life are better protected from allergies, asthma, dermatitis, diabetes mellitus, obesity and hypertension [17].

But what makes this food so special? Why is it so precious and difficult to replace?

Scientific evidence has led us to speculate that many of the health actions reported for whey are attributable to α-LA. From various studies conducted even *in vivo* on infants fed with α-LA formula, it appears to be able to reduce intestinal permeability and activate defensive/absorbent processes [5].

Properties and benefits

The action of α-LA on gastrointestinal symptoms emerged for the first time in Lien's study [20] and confirmed by Davis in a subsequent

study [21].

Scientific evidence shows that **α-LA performs specific intestinal actions**: intestinal prebiotic/antibacterial, anti-inflammatory, mucoprotective, trophic and absorbent.

- **Intestinal Prebiotic/Antibacterial**
  A-LA selectively promotes the growth of commensal bacteria"good", so-called probiotics, or microorganisms capable of bringing beneficial effects on the health of the host.

- **Anti-inflammatory**
  Indeed, **α-LA reduces the levels of proinflammatory cytokines** and inflammatory mediators such as PGE_2, IL-6, TNF-α [11], implicated in gastrointestinal disorders.

- **Mucoprotective**
  A-LA stimulates the secretion of mucins, increasing the protective mucus layer in the body and in the antrum of the stomach. It therefore exerts an **"anti-ulcer"** action by protecting the gastric mucosa from stress-induced ulcers, alcohol [12] or NSAIDs. The α-LA, through the production of mucins, strengthens the intestinal barrier by counteracting the trans-mucosal passage of potentially pathogenic bacteria [22].

- **Trophism**
  A-LA stimulates the secretion of Glucagon-like peptide-2 (GLP-2), a 33 amino acid peptide produced mainly by intestinal cells. To date, it is known that this hormone plays a critical role for the trophism of intestinal crypts, stimulating the proliferation and regeneration of the intestinal mucosa and inhibiting its apoptosis. The correlation between GLP-2 and trophic action has also been highlighted in pathological conditions such as celiac disease, inflammatory bowel disease and obesity [23]. **In summary, α-LA, through the stimulation of GLP-2, performs the most important intestinal functions.**

- **Absorptive**
  A-LA is able to improve the intestinal absorption of some micronutrients. Its "carrier" function of minerals is widely documented, the absorption of which increases: the α-LA has, in fact, 2 binding sites for calcium, one of which can be occupied by other cations such as zinc or iron. Recently, a binding site for Vitamin D has also been observed [24]. In addition, some peptides released during protein digestion have a high affinity for iron. In addition, α-LA stimulates the intestinal absorption of micronutrients through the aforementioned actions:

1. by promoting the growth of lactobacilli and bifidobacteria, α-LA, on the one hand acidifies the pH of the intestinal tract which increases iron solubilization, on the other leads to the formation of short chain fatty acids (SCFA) such as acetate, butyrate and propionate. The latter promote the proliferation of epithelial cells and increase the expression of the genes that regulate iron transport (DMT);
2. through the stimulation of GLP-2, the α-LA "activates" the enzymes present on the brush edge of the enterocytes responsible for the absorption of micronutrients such as myo-inositol [25].

In addition, α-LA is capable of improving the bioavailability of myo-inositol, in vitro and in vivo, also through the modulation of the tight junctions that regulate the paracellular diffusion of enterocytes.

The administration of α-LA is therefore able to maximize the absorption of micronutrients, such as iron and myo-inositol, both taken with food and with a supplementation [25].

Myo-inositol and alpha-lactalbumin

The use of α-LA together with **myo-inositol** arises from the desire to research to overcome the problem of **inositol-resistance**. We now

know that myo-inositol has several beneficial effects for the body, as in the case of PCOS.

For further information read: **The benefits of myo-inositol for the polycystic ovary**

However, in about 30% of cases there would be a phenomenon of inositol-resistance, or a lack of absorption capacity of inositols.

A study conducted on 18 healthy volunteers [25] evaluated the previously exposed positive absorbent action of α-LA, focusing attention on the absorption of myo-inositol (MI). In fasting subjects, the endogenous plasma concentration of MI is approximately 30 μmol/l with a half-life of 22 minutes.

MI seems acts synergistically with α-LA in promoting its passage. This can be correlated with a direct effect of MI on the permeability of tight junctions, as can be assumed by recalling the effects obtained with phytates.

A subsequent clinical study of PCOS women with anovulation [26] evaluated the therapeutic advantage of MI plus α-LA administration. The new therapy allowed to bring clinical success (ovulation) from 62% to 95% of women.

The evidence deriving from these studies therefore convincingly demonstrates the effectiveness of the combination of MI and α-LA to overcome the problem of inositol-resistance.

Conclusions

Given the centrality of the intestine in influencing the metabolic structure and therefore the state of health/disease of the whole organism, the interest of numerous scholars has focused on

understanding the underlying mechanisms but above all on the search for interventions aimed at restoring the intestinal eubiosis. Due to the low resistance to the GI barrier, the initial attention to probiotics has gradually shifted towards the actions of prebiotics, among which emerge those of α-LA, a protein that is naturally found in breast milk.

Unlike a probiotic, α-LA does not just simply "repopulate" the intestinal microbiota, but it "remodels" it in order to activate the endogenous mechanisms of defense and repair in the intestine, altered by incorrect eating habits, from drugs and especially from stress.

Hence the fundamental importance that α-LA plays both in the feeding of infants and in adults to promote the maturation of the GI tract, as well as to restore and maintain the integrity of the intestine as a central metabolic control organ.

Thanks to its specific intestinal actions, it can play a key role in certain clinical contexts such as:

- **PCOS**;
- diabetes;
- obesity.

Today we know that alpha-lactalbumin supplementation represents an effective, valid and safe strategy.

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Altri argomenti che potrebbero interessarti

Myo-inositol

D-chiro-inositol

40:1

PCOS

Overweight