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COBIOTICS A NEW CONCEPTION OF PROBIOTICS

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Introduction. A new achievement in the study of probiotics was the formulation of a new concept - cobiotics. Cobiotics are more functional than synbiotics, since they are a combination of probiotics, prebiotics and digestive enzymes. This concept improves the nutritional value of synbiotics by incorporating various types of digestive enzymes and adding enzymes to isolate prebiotics from their natural sources. Cobiotics were first made in Belgium. The ingredients used in cobiotics create synergy that enhances their effectiveness and improves the effect of cofactors.

The term "Cobiotic" was introduced in 2013, which describes products that provide nutritional benefits to the consumer, as well as probiotics. Cobiotics are based on the idea that if you put the right probiotics, the right prebiotics (fuel for the probiotics) and the extra food component in the intestine, this will contribute to good bacterial growth, suppress the growth of "bad" bacteria and improve overall health. Cobiotics encourage the growth of good bacteria, discourage the growth of bad bacteria and help create an overall healthy microbiota environment in the gastrointestinal tract.

The molecules present in food are very large, and they cannot get into the cells of bacteria or into human cells. Therefore, the digestive glands secrete enzymes that break down these macromolecules into small compounds (amino acids, sugar, fatty acids, minerals, etc.) - these small compounds are cobiotics [1, 2].

Cobiotics (lat. "Co-" means "together"; gr. "Bios" - "life") are the factors that improve / strengthen the vital functions of beneficial bacteria and the human body. The main cobiotics are useful compounds from food: amino acids, small carbohydrate molecules, fatty acids, minerals, and other elements that feed on bacteria and cells. The exclusiveness of cobiotics is that they act not only on bacteria (as prebiotics), but also on human cells. Therefore, they systematically improve the condition of the digestive tract and the whole body.

Cobiotics are recommended for the treatment and prevention of various intestinal disorders. As a result of its action, cobiotics create optimal conditions for the development of intestinal microflora and create the necessary conditions for activating the renewal of the epithelium of the small and large intestines.

The presence of amylolytic and lipolytic enzymes in cobiotics significantly reduces the overload of the digestive system, improving the absorption of carbohydrates, lipids and proteins in the small intestine. Cobiotics help control weight and reduce the viscosity of food that is not digested in the large intestine, which makes it possible to more effectively manifest its activity in the intestinal microflora.

Cobiotics contain some types of fibers (prebiotics) necessary for the development, balance and maintenance of the diversity of the intestinal microflora. Cobiotics enhance synergy with the immune system: help reduce the stress of the hepatic, pancreatic and digestive systems; and thus, promote better and easier

digestion. Cobiotics also help to balance triglyceride and cholesterol levels, due to the decomposition and elimination of fats. Cobiotic include substances that are utilized by probiotics, as well as by the host. Unlike prebiotics, which are utilized only by probiotics, but not by the host [3].

Cobiotics are a catalyst that helps the body break down food into small pieces that feed on probiotics and intestinal cells. They also destroy food debris that stimulates the activity and growth of putrefactive bacteria, and also promotes the growth of beneficial bacteria that inhibit the growth of bad bacteria in the intestine. Some enzymes react with food materials and release nutrients that stimulate probiotics. The enzymes of protease and amylase, when included in the form of a cobiotic combination, function as a lactogenic factor (stimulate the growth of lactobacilli). Cellulose and hemicellulose enzymes, on the other hand, function as bifidogenic, that is, stimulate the growth of bifidobacteria.

Mechanism of cobiotics action:

- cobiotics plant powerful probiotic bacteria in your gut;
- cobiotics deliver prebiotic fiber, a probiotic food source, to supercharge probiotic growth;
- cobiotics also directly provide other essential nutritional or therapeutic benefits.

Lactobacillus probiotics respond best to cobiotic nutrients since they reside largely in the ileum section of the small intestine. Bifidobacterium probiotics on the other hand do utilize cobiotics but rarely see them since they reside primarily in the large intestine where it’s unusual to see free cobiotics floating around (most are absorbed by the body or utilized by microbes in the small intestine).

For example, the probiotic Theralac contains three important *Lactobacillus* strains that benefit from cobiotics: *Lactobacillus paracasei* F-19, *Lactobacillus acidophilus* LA-1 and *Lactobacillus rhamnosus* H-1. All three of these strains benefit significantly from the cooperative action of digestive enzymes that release cobiotics. Enzalase® has been formulated to release cobiotics deep within the ileum section of the small intestine where *Lactobacillus* colonization always needs help.

Enzalase® - the food supplements contains 12 plant-source digestive enzymes in a high potency, acid-proof, deep release formulation that is compatible with probiotics, such as: alpha-amylase, alpha-galactosidose, bromelain protease, cellulose, glucoamylase, hemicellulose, invertase, lactase, lipase, neutral protease, papain, protease, pectinase.

Laboratory studies demonstrate that cobiotics, such as amino acids, glucose and acetic acid, stimulate Lactobacilli by 100-800% in flask cultures when controlled against simulated intestinal juice [4].

Probiotics and digestive enzymes are, indeed, synergistic within the intestinal tract. Enzymes process and digest food as it moves through the intestines and in doing so help feed probiotics. Probiotics stimulate digestive enzymes by enhancing the absorption of nutrients released by these enzymes since the end products of enzyme action can inhibit further enzyme activity if not removed by absorption.

Bifidobacteria require special feeding in order to do well in the colon; although our research shows they gain a small advantage from cobiotics (cobiotics are so

bioactive they disappear in the ileum and rarely make it into the colon) they need a more direct source of nutrition in order to effectively colonize the colonic wall. Prebiotics are that source of nutrition. Prebiotics are soluble fiber substances, mostly oligosaccharides or short chain sugar polymers, present in fruits and vegetables and certain grains. Prebiotics are not digested in the human small intestine but pass into the colon where they support Bifidobacteria growth and colonization and can be called bifidogenic. Fructooligosaccharides (FOS) and inulin are two bifidogenic prebiotics that get attention today although there are others such as partially hydrolyzed guar gum (PHGG) and certain marine hydrocolloids like sodium alginate that are equally effective. FOS type prebiotics are now added to a variety of functional foods with a mixed bag of results that range from improved intestinal function to the exact opposite: Pain, bloating and excess gas. Part of the problem stems from the use of synthetic FOS which is never found alone in nature but always in foods that contain other compounds that moderate bloating and gas (probably by controlling the growth of undesireable microbes that also consume FOS).

The answer you may think is to eat more fruits, vegetables and grains that are bifidogenic. But, eating these foods is just half the answer. The problem with bifidogenic foods like those above is prebiotics that don't release and become available to the Bifidobacteria in the colon. The prebiotic soluble fibers are often bound within a matrix of insoluble fibers and lignins that varies in complexity from one food to another. For example, the fiber matrix in rye bread is quite complex and many people don't get the FOS released so it passes out in the stool and is wasted. Enzalase®, in addition to its protein, carbohydrate and fat digesting enzymes, contains a powerful group of fiber digesting enzymes that assist in the release of prebiotics from natural foods. When you take complex of digesting enzymes you stop wasting these precious prebiotics and start utilizing them to feed your Bifidobacteria.

This unique high potency mixture of fiber digesting enzymes goes after the insoluble fibers that bind the soluble prebiotic fibers, releasing the latter into the lower digestive tract. The digestion does not go to completion, this would not be desirable, it proceeds just enough to open up the complex fiber matrix to let the prebiotics out. The secret behind this discovery lies not just with the enzyme blend above but with the deep release technology that gets a portion of the enzyme activity into the lower intestinal tract. This assures that the prebiotics will show up close to where the Bifidobacteria live [4, 5].

Characteristic of some cobiotics.

NM504, which Microbiome Therapeutics (MBT) calls «cobiotic», is a mixture of inulin, beta glucan a proprietary mix of antioxidants, primarily anthocyanis and polyphenols. It works in three ways. It shifts the makeup on of the gut microflora, it addresses part of the physical environment in the gut by altering viscosity and it addresses the chemical component by providing more antioxidants. Admitted that when talking about «shifting» the makeup of the gut microflora, there are little agreements as to what the ideal makeup should be. Research has shown in differs from person to person and from culture to culture. But when it's out of whack, the effects are obvious.

Another group of cobiotics – cobiotics based on antioxidants. Antioxidants get a lot of overhyped claims, especially from people who want to sell them as a way to avoid aging or cancer (but nothing can prevent you from aging, and nothing can completely remove the risk of getting cancer). But that doesn't mean they're useless; it just means you have to look beneath the unsubstantiated hype to find the actual benefits.

One of those benefits is gut health. Antioxidants can work their antioxidant magic on the lining of the gut, protect the cells lining the gut by controlling inflammation, and help support the growth of healthy bacteria. They also seem to magnify the effects of other gut-healing strategies like prebiotics and probiotics, so they're a valuable addition to a gut-healing diet.

One way that antioxidants can be beneficial to the gut is through protecting the lining of the gut. The cells lining the gut, called epithelial cells, have a tough job: they have to let the good stuff (like nutrients) into your bloodstream, but keep out everything that doesn't belong (whether it's actively bad stuff like dangerous bacteria or just food that hasn't been digested yet).

Some evidence suggests that antioxidants can help protect the cells lining the gut in ways that might be particularly important for people with inflammatory gut conditions or serious infections. For example, in humans, Helicobacter pylori infection can cause the cells of the gut lining to die more quickly, but antioxidants help protect against this. This is a huge benefit, because problems with the lining of the gut are involved in the development of autoimmune diseases and other inflammatory conditions.

The gut flora, aka the gut microbiome, gut biome, or gut microbiota, refers to the collection of friendly bacteria that live in our gut. This review goes over the evidence that dietary polyphenols (one specific type of antioxidant, found mostly in plants) have beneficial effects on the gut flora:

- Polyphenol antioxidants can encourage helpful bacteria to grow.
- Polyphenol antioxidants can also discourage dangerous bacteria [6 - 8].

NM504. NEW ORLEANS NuMe Health LLC filed a patent application covering a proprietary formulation of its "cobiotic" product, NM504. NM504 is designed to help prediabetic individuals achieve and maintain normal blood glucose levels and a healthy body weight by altering the gastrointestinal (GI) microbiota and its environment. NM504 contains a blend of ingredients that can alter the composition of the GI microbiota in specific ways that promote improved control of glucose levels for prediabetics with an unhealthy weight. It acts by stimulating certain bacteria that inhibit appetite signals and stimulate satiety signals and also by inhibiting the ability of other bacteria to capture energy from undigested fat and protein and convert them into calories that are absorbed by the body.

NuMes cobiotics are designed to encourage healthy bacteria, discourage unhealthy bacteria and create a healthy GI environment. Cobiotics are combinations of prebiotics and other food components that cannot be digested, but that act to control the GI microbiota and its environment in specific beneficial ways. NuMe's initial cobiotic products are derived from bioactive ingredients in edible plants that

promote the growth of specific beneficial bacteria with the potential to positively affect metabolic conditions.

Another promising cobiotic is MT303. MT303 is made from molecules in soy cells that protect against infections [9, 10].

Conclusion. Cobiotics are more functional than synbiotics, since they are a combination of probiotics, prebiotics and digestive enzymes. Cobiotics are a catalyst that helps the body break down food into small pieces that feed on probiotics and intestinal cells. Cobiotics encourage the growth of good bacteria, discourage the growth of bad bacteria and help create an overall healthy microbiota environment in the gastrointestinal tract. Cobiotics show their effect in the small intestine, and in the fat. As a result of its action, cobiotics create optimal conditions for the development of intestinal microflora and create the necessary conditions for activating the renewal of the epithelium of the small and large intestines.

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