Introduction to the biochemical effects of Fulvicherb – Synergy

Support your health with the power of natural ingredients

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Introduction

Humans are still connected to their environment, which has changed in the last 100 years. We do not live in the environment in which we evolved. Modern diseases are maladaptations resulting from a changed environment (changes in diet and eating habits, sedentary lifestyles). We use new food ingredients in enormous quantities. Experience shows that there is something wrong with the way we live and eat, with people's general health deteriorating and the incidence of cancer, cardiovascular, metabolic and autoimmune diseases increasing.

The blocked kynurenine pathway: mitochondrial disease in animals and humans

The pig (Sus scrofa) is an excellent biomedical model because of its similarity to humans in size, anatomy, physiology, metabolism, pathology and pharmacology. Alan Archibald, Professor of Medicine and Veterinary Science at the University of Edinburgh, Faculty of Medicine, believes that human studies in pigs give the best results in all cases (Alan Archibald et al; 2020).

Today there are more and more serious health problems in humans and animals. Increased incidence and new diseases are often not linked to changing environmental factors. Genetically modified feed and food crops, and the effects of additives used in feed and food over the past decades, have not been adequately studied.

Our livestock experience over the last four decades can be divided into two parts. Until about 1996, we had feed mixtures made from non-GM feed ingredients. They did not contain free amino acids, fermentation by-products or so-called single-cell proteins (SCP). After the 2000s, GMO feed crops and free amino acids increased in livestock production.

Farm animals and humans experience many similar effects through their diets because

- Plants grown in the same soil using the same technology
- Free amino acids (produced by GMO bacteria and used as additives in feed and processed foods)
- GMO feed and food crops.

It is no coincidence that the work of Alan Archibald, Professor of Medicine and Veterinary Science at the University of Edinburgh, draws attention to the need for a close link between human and veterinary science.

The mitochondria in pigs work in the same way as in humans. The hormone and enzyme systems are the same, and the immune system is very similar. The gastrointestinal and microbiome problems of humans are also typical of pigs. There are many similarities between pigs and humans, but one key difference is the generation interval. It is 14 months in pigs and 25 years in humans. Human mothers give birth to 1-4 children in their lifetime; sow mothers can have up to 100 offspring. This gain in time, and the fact that thousands of animals on a pig farm can eat the same feed composition, allows us to draw significant conclusions.

Impact of modern feed on farm animals and indirectly on humans

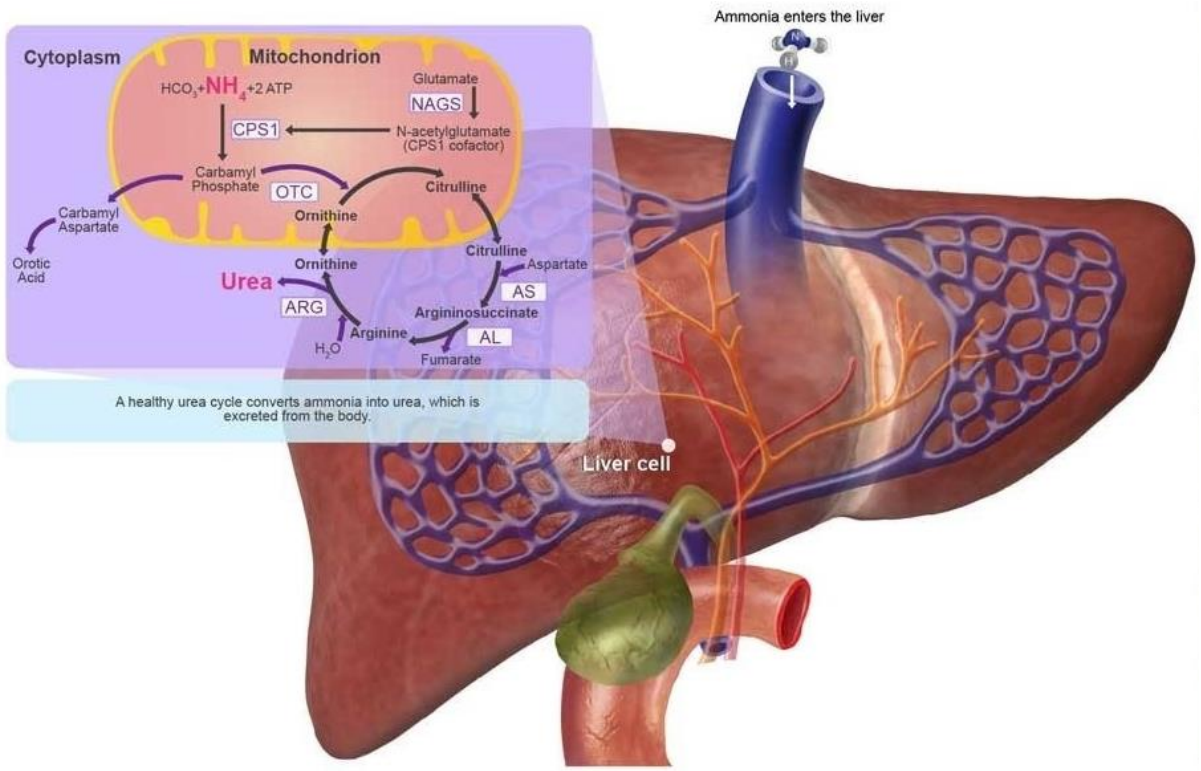
In industrially fed animals, the problem of tryptophan amino acid metabolism and consequent nicotinic acid (niacin) deficiency takes several forms.

Niacin deficiency results in inadequate energy production in the cells (due to NAD+ production). In the last 10-15 years we have seen more skin lesions in pigs fed industrial feed than we have seen before. The lesions caused by nicotinic acid (niacin) deficiency and pellagra symptoms are the scaly inflammation of the skin, neck and back. Necrosis of the upper flange of the curd and ulceration of the tongue and mucous membranes of the mouth are common. In addition to hyperkeratotic symptoms on the back and bone marrow, a bluish-green pigmented patch may occur on the back. The lesions affect the epithelial cells of the skin. A similar effect is seen in the epithelial cells of the intestinal mucosa. Necrotizing and ulcerative enteritis can also develop.

The researcher into the human background of pellagra was a Hungarian-born doctor of American origin, József Goldberger (1874-1929), a doctor in the US Public Health Service in New York. He hypothesised that the skin disease was not infectious but nutritional. According to Goldberger, pellagra was a disease of the four Ds: dermatitis, diarrhoea, dementia and death. In addition to skin pellagra in sows due to nicotinic acid deficiency, piglets have damaged intestinal mucosal epithelial cells during in utero development, known as PFTS syndrome. Piglets are born with gastric and intestinal mucosal damage and villous atrophy.

The blocked urea cycle

A characteristic symptom in pigs is foaming at the mouth, a sign of ammonia poisoning. This means that the urea cycle in the liver is not working. The blood has high levels of ammonia and the blood-brain barrier (BBB) allows ammonia to pass into the cerebrospinal fluid, blocking the motor cells and preventing the animal from swallowing.



There are two reasons for this:

- The first is lysine-arginine antagonism (resulting in local arginine deficiency). Local arginine deficiency interferes with the proper functioning of the urea cycle.

- Another reason is the so-called Krebs cycle phenomenon. The Szent-Györgyi - Krebs cycle, the final stage of biological oxidation, degradation (the most efficient process for energy production), is not working properly.

Glutamate inhibits the urea cycle in the absence of oxaloacetic acid

Fumarate uptake is inhibited because the NAD-supplying capacity of the kynurenine pathway is not continuous with the Szent-Györgyi Krebs cycle, so it cannot take up the fumaric acid of the urea cycle.

Glucose utilisation does not function properly in ammonia toxicosis, so a significant proportion of alpha-ketoglutaric acid in tissue cells is bound to ammonia. This phenomenon inhibits the citrate cycle.

It usually occurs in pigs after the first farrowing (endocrine and glucose metabolism disorders). Glucocorticoids regulate this process in the nicotinamide-dependent adrenal cortex (along with insulin, which is also nicotinamide-dependent).

The nicotinamide in Fulvicherb-Synergy is a specific source of vitamins. We have found that it can significantly reduce skin and other problems caused by nicotinamide deficiency in humans.

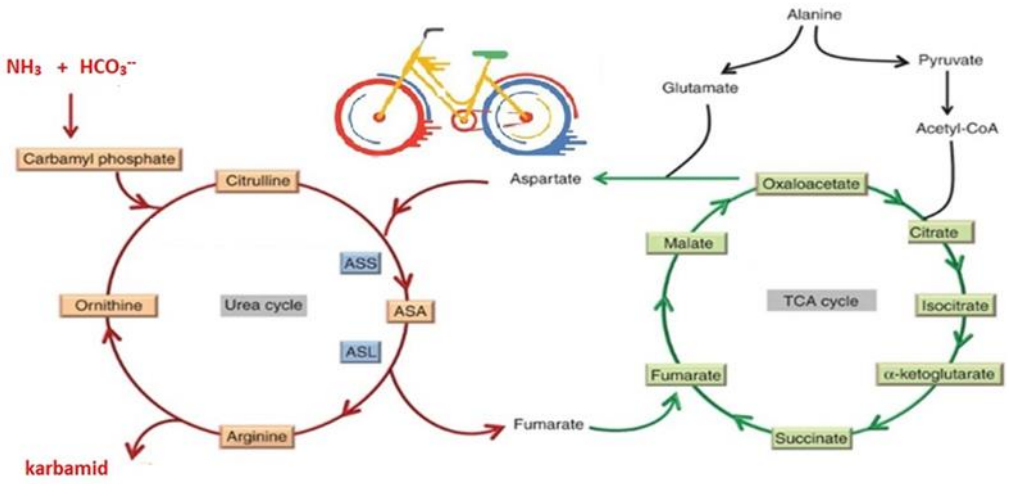
About nicotinamide in detail and the role of tryptophan

Vitamin B3 has several names, including nicotinic acid and niacin. Nicotinamide or niacinamide is the active form of niacin in the body. The liver makes this water-soluble vitamin from an amino acid called tryptophan. Bacteria in the beneficial gut flora can also produce niacin from tryptophan.

Plant-based foods contain nicotinic acid. Foods of animal origin contain nicotinamide (niacinamide).

Nicotinic acid is essential for the synthesis of sex hormones (oestrogen, progesterone, testosterone), cortisone, thyroxine and insulin. It is necessary for the healthy functioning of the brain and peripheral nervous system.

In animals and humans, nicotinic acid is converted to nicotinamide in the liver. The cytochrome p450 enzymes transport functional groups of various substrates (hydroxylation, carboxylation, decarboxylation, desaturation and amidation).



The amidation of nicotinic acid to nicotinamide is essential in the liver. In this process, the cytochrome p450 enzyme system is the biocatalyst.

Niacinamide is a component of nicotinamide adenine dinucleotide (NAD+). NAD+ is required by more than 100 enzymes involved in carbohydrate, fat, protein and alcohol metabolism, DNA repair and cell signalling. Tissues composed of rapidly proliferating cells (skin, intestinal epithelial cells, brain) have high energy requirements and rapid biochemical processes. These are the tissues most affected by pellagra.

Nicotinamide adenine dinucleotide (NAD+) is an essential cofactor found in all living cells. It plays an important role in the transport of electrons across the membranes of mitochondria. The operation of the electron transport chain results in the transfer of hydrogen across the membrane. This process creates a hydrogen gradient that drives oxidative phosphorylation of ADP, the synthesis of ATP.

The role of NAD+ is therefore critical for mitochondrial energy production and many enzymatic redox reactions. Several biochemical processes in the body require NAD+: cholesterol metabolism, neurotransmitter metabolism, free radical production and detoxification. Disturbances in NAD+ production are at the root of many diseases, including metabolic and neurodegenerative disorders and a lack of cellular defence mechanisms against oxidative stress.

The mitochondrial disease

Animal studies have shown that the tryptophan-nicotinamide conversion pathway (kynurenine pathway) influences homeostasis, the internal stability of the organism, and the ability to adapt to a changing environment.

Proper functioning of the kynurenine pathway is a prerequisite for good health. The presence of disease, the use of nutrients, hormones and the function of the immune system all depend on the kynurenine pathway. Human studies have shown that infants produce 1 mg of nicotinamide from 67 mg of tryptophan intake. The conversion rate of tryptophan to nicotinamide increases from mid to late pregnancy (Tsutomu Fukuwatari and Katsumi Shibata 2013). The conversion of tryptophan - nicotinic acid - nicotinamide is essential to provide niacin to the body.

In the liver, mitochondria are specialised in ammonia detoxification. The urea cycle takes place partly in the liver mitochondria. The final step of catabolism, terminal oxidation, also takes place in other mitochondria, where hydrogen bound to cofactors is oxidised to water. Nearly 95% of the energy released during biological oxidation is terminal oxidation. The body needs mitochondria for cholesterol metabolism, estrogen and testosterone synthesis, neurotransmitter metabolism, and free radical production and detoxification.

PFTS syndrome in pigs - a mitochondrial disease in humans

Peri-weaning failure-to-thrive syndrome (PFTS) is a poor growth syndrome in piglets around the time of birth. It occurs intermittently or continuously on virtually all pig farms. It affects 5-15% of the herd. Symptoms are lethargy, anorexia - feed refusal and death by starvation due to wasting - no infectious cause. Many studies in several countries have ruled out all potentially harmful infectious diseases. Specific pathogen free (SPF) herds with high animal health status have a similar susceptibility to disease as the average commodity herd. Piglets born by caesarean section in a gnotobiotic model and reared without colostrum also show PFTS. A typical symptom is polyserositis (the simultaneous inflammation of multiple acid membranes and the developmental abnormalities of rapidly proliferating mucosal epithelial, glandular and brain cells). It is also known as Concato's disease. The catabolic processes are damaged, depleting the body's reserves.

Types of lesions:

- Inflammation of the gastric mucosa and atrophy of the intestinal mucosa (villous atrophy)
- Atrophy of the serous cells that secrete gel-forming mucins in the colonic mucosa.
- Inflammation of the nasal mucosa
- Atrophy of the thymus (thymic atrophy)
- Meningitis of unknown origin (non-suppurative meningoencephalitis)When mitochondria malfunction, cells lack energy, and tissues and organs cannot function properly.

There is a link between arginine deficiency and thymus atrophy. In thymic atrophy, the production of T lymphocytes is inadequate. The result is that piglets die or are humanely euthanised due to severe debilitation. (Yanyun Huang, Henry Gauvreau, John Harding 2011; 2012).

The symptom complex is known in human medicine as mitochondrial disease and bears a strong resemblance to PFTS.

Niacin is found in every cell in the body. Nicotinic acid, or nicotinamide, is an active compound that builds up dehydrogenating and oxidising enzymes. Another active form is the reversible hydrogen carrier, nicotinamide adenine dinucleotide (NAD+). These enzymes play a crucial role in intermediary metabolism, which is essential for the function of enzymes involved in cellular respiration.

In the absence of nicotinamide, the processes that break down and synthesise fatty acids, carbohydrates and amino acids do not function properly.

Since most gut bacteria can synthesise nicotinic acid from the amino acid tryptophan, the gut must be in good condition. If the gut is in dysbiosis (lack of beneficial gut flora), it cannot synthesise niacin (nicotinic acid) from tryptophan. In this case, the intestinal lining is damaged. Not enough tryptophan and nicotinic acid are absorbed (60 mg tryptophan = 1 mg nicotinic acid).

Tryptophan and nicotinic acid are the precursors of nicotinamide. They are converted to active nicotinamide in the liver and play a role in the synthesis of sex hormones. The body needs nicotinamide to synthesise oestrogen, progesterone and testosterone.

Dr Judit Mária Molnár is a professor at the Semmelweis University of Medicine in Hungary, where she studies mitochondrial diseases. It can begin in childhood and can be very severe. In adulthood, the disease tends to be milder. Telltale signs can include drooping eyelids, muscle fatigue, muscle wasting, epilepsy, various endocrine disorders, anaemia of unknown cause, incoordination and psychiatric symptoms.

Mitochondria are cellular components whose primary function is to maintain the energy balance of cells. The more active the metabolism of a cell, the more mitochondria it contains. If they malfunction, cells develop an energy deficit and tissues and organs cannot perform their functions. Symptoms are most often manifested in the dysfunction of tissues with high energy demands, leading to neurological, psychiatric and medical disorders, as well as damage to the heart muscle, endocrine organs, liver and kidneys. Symptoms are usually not isolated. Several organs or organ systems are affected simultaneously (Zsófia Haszon, 2018).

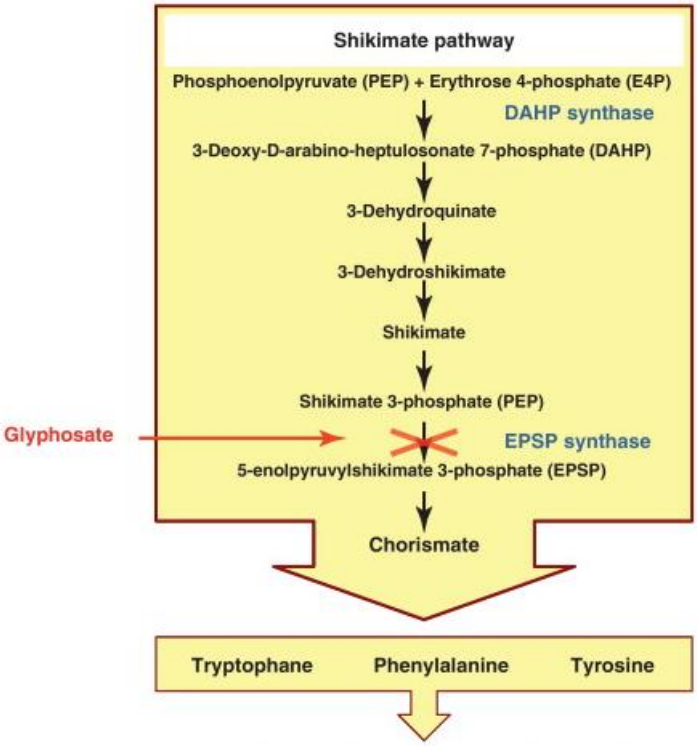
The dysfunction of cellular mitochondria is partly inherited, but acquired mitochondrial defects caused by environmental and dietary factors are becoming more common. According to researcher Douglas Wallace, the accumulation of mitochondrial damage is the cause of lifestyle diseases and ageing (Wallace, 2005).

Most of the diseases appear around the age of 40-50 years and the physical deterioration starts around the age of 50-60 years.

The daily human requirement of tryptophan is 250-500 mg, and 94% of this essential amino acid is converted into NAD+ production.

Environmental change affects the availability of the amino acid tryptophan

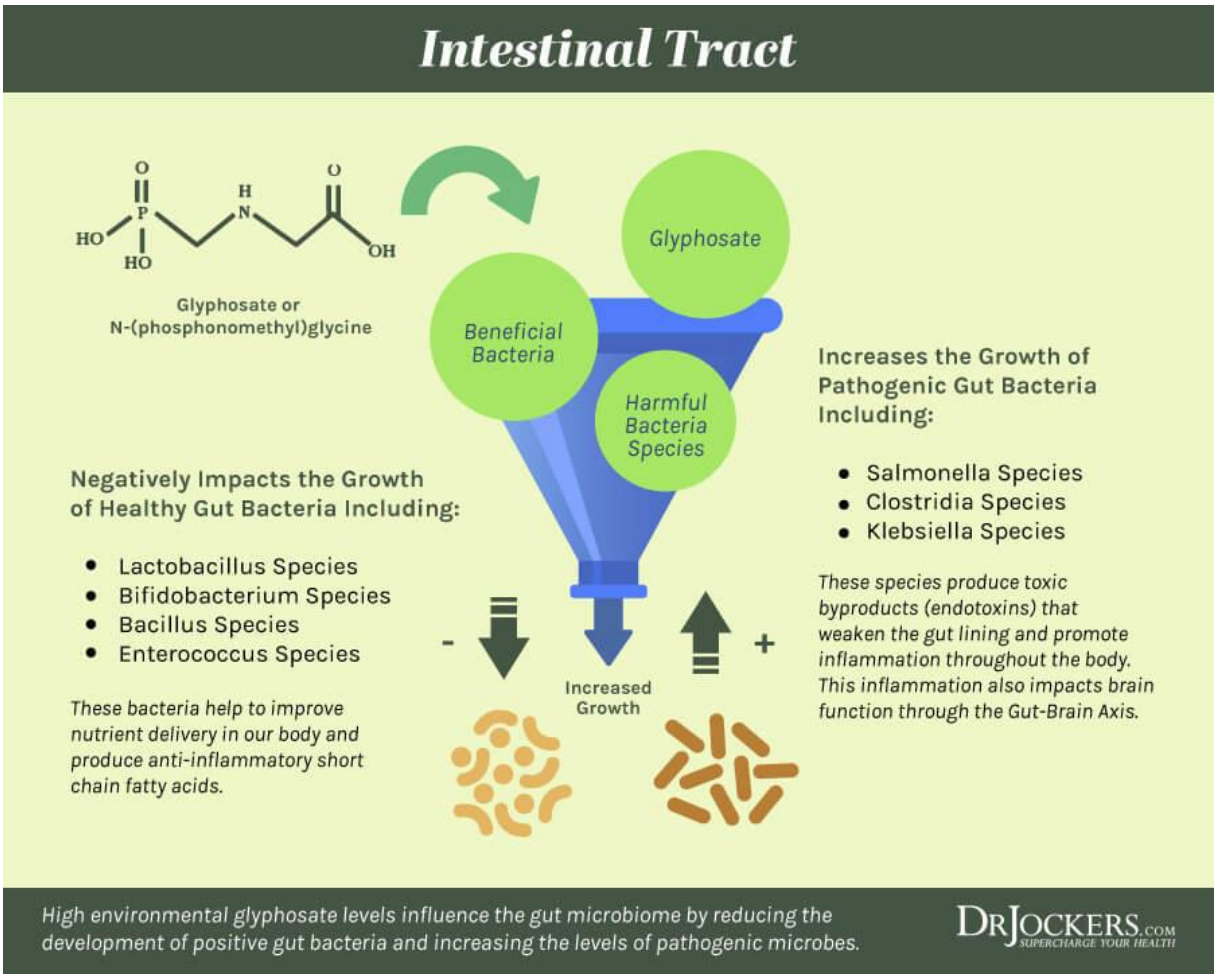
The most widely used herbicide in the world is glyphosate, which is used on GM crops. It inhibits the production of tryptophan and phenylalanine (aromatic essential amino acids). These are formed along the shikimate pathway in plants, bacteria and some fungi. Inhibits the enzyme EPSP-synthetase in the formation pathway of these two amino acids.



Gut bacteria also metabolise the essential amino acid tryptophan, improving the availability of tryptophan to the host. The action of glyphosate thwarts this possibility. (O'Mahony et al; 2015); (Martin et al; 2018); (Anthony Samsel and Stephanie Seneff 2013).

About glyphosate and its adverse effects

GM food crops and animal products derived from animals fed on GM feed crops contain glyphosate. Glyphosate kills beneficial gut bacteria (Enterococcus, Bacillus, Bifidobacteria, Lactobacillus) and inhibits the growth of tryptophan-producing gut bacteria. Clostridium, E. coli and Salmonella overgrow when exposed to glyphosate.

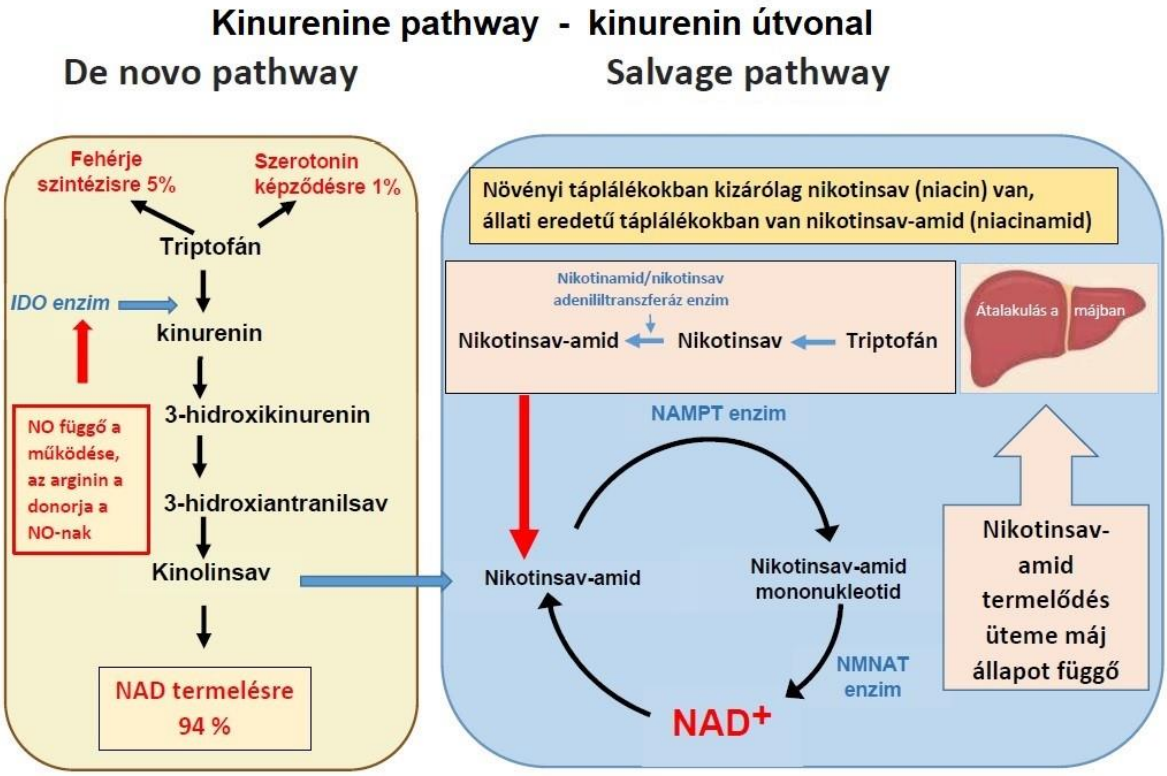


Enterotoxins cause intestinal inflammation. Neurotoxins damage the peripheral nervous system (PNS) and central nervous system (CNS), altering the permeability of the blood-brain barrier (BBB).

As a result of the physiological problems caused by 70 years of chemical agriculture and almost 30 years of GMO agriculture, feed materials and additives used by the feed industry, nicotinamide deficiency is evident in farm animals.

Today's diets, chemical and GMO food production and unnatural feed and food additives (such as free amino acids) cause physiological problems. These have caused the kynurenine pathway to malfunction.

For example, the free amino acid lysine causes local arginine deficiency due to lysine-arginine antagonism. The NO deficiency inhibits the first step of the kynurenine pathway (tryptophan-kinurenine conversion). Indoleamine 2 3-dioxygenase (IDO) catalyses this process. (Hao Wu Jianping and Gong Yong Liu, 2018).



Free amino acids in feed, food, and food supplements

Amino acid antagonism is the axiom behind the use of free amino acids. Threonine administered as a free amino acid inhibits the absorption and transport of tryptophan in the body.

The effects of lysine as a food additive have been studied by the Food and Nutrition Science Program of the Department of Biochemistry at Carleton University in Canada and the Canadian Food Directorate and its Bureau of Nutrition Science. "L-lysine is a popular food additive, but the physiological effects of excessive L-lysine supplementation are poorly understood and there are no upper limits for safe intake."

This study aimed to investigate the effects of increasing levels of L-lysine supplementation on body weight, food intake and various haematological and biochemical blood parameters.

Lysine supplementation above 1.5% of protein content was detrimental to the parameters studied (Chao-Wu Xiao, Carla Wood, Jesse Bertinato, 2019).

Glyphosate damages the animal microbiome through glyphosate residues in GM soy.

In a eubiotic gut flora, beneficial gut bacteria produce 1 mg of nicotinic acid from 60 mg of tryptophan. Humans also synthesise nicotinic acid (vitamin B3) from tryptophan in the liver.

The conversion of tryptophan to nicotinic acid in the liver is called the kynurenine pathway.

The first step in the kynurenine pathway is carried out by an enzyme called indoleamine 2, 3-dioxygenase (IDO). This enzyme is known as the rate-limiting enzyme because it determines the availability of NAD+ (the end product of the kynurenine pathway). The role of the liver in the function of tryptophan-nicotinamide metabolism is critical. The function of the IDO enzyme is dependent on

nitric oxide. The IDO enzyme is an essential part of the immune system and plays a role in the natural defence against various pathogens.

The availability of the amino acid tryptophan plays an essential role in modulating T-cell activity.

T cells are sensitive to tryptophan deprivation. An essential amino acid in their microenvironment confers strong immunomodulatory properties to active IDO in the expressing cell (Laura Vallius, 2011).

What might interfere with the function of the IDO enzyme?

IDO enzyme function is dependent on nitric oxide (NO). There is a NO deficit due to local arginine deficiency and lysine-arginine antagonism - NO limits the availability of tryptophan-nicotinamide conversion in the 'de novo' kynurenine pathway.

Healthy mitochondrial function is only possible when the kynurenine pathway is functioning normally. It affects several biochemical processes, including

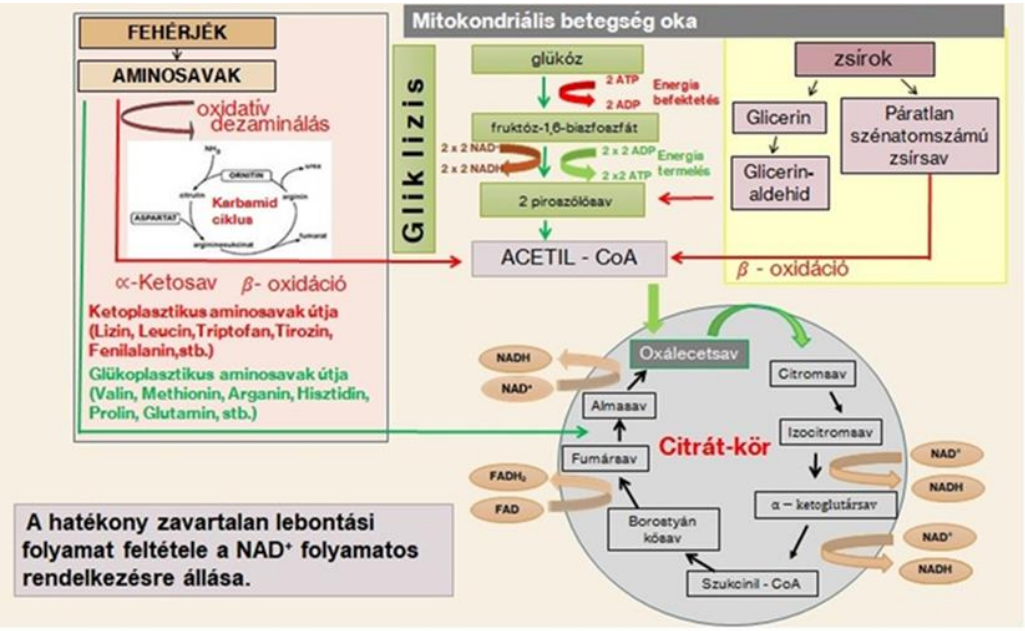
- Cholesterol metabolism
- Oestrogen and testosterone synthesis
- Neurotransmitter metabolism
- Free radical production
- Detoxification

The amidation of nicotinic acid takes place in the liver. The only precursor of NAD+ is nicotinamide. Nicotinamide is found in every cell in the body, not just liver cells.

Glyphosate residues damage the liver's cytochrome p450 enzyme system. It inhibits the enzyme adenylyltransferase, which is responsible for converting nicotinic acid to nicotinamide).

Amidated nicotinamide is present in all body cells, not just liver cells. Studies have shown that the liver plays a critical role in tryptophan-nicotinamide metabolism.

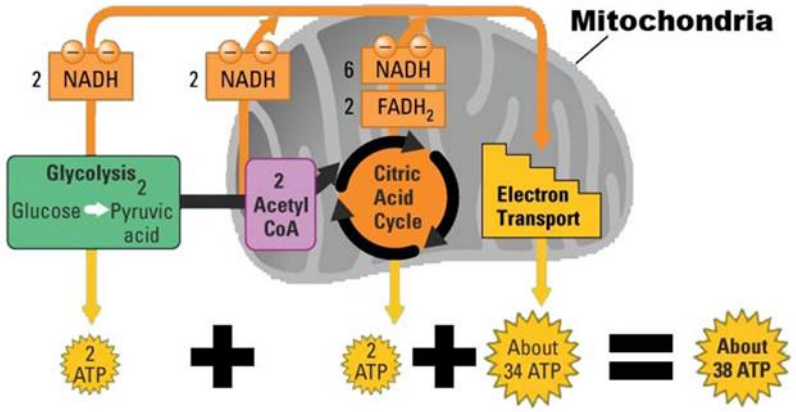
The Szent-Györgyi Krebs or citrate cycle is an essential metabolic process in all living cells that use oxygen in cellular respiration. The energy released during the oxidative steps of the process is transferred to NAD+ in the form of high-energy electrons. The result is NADH.



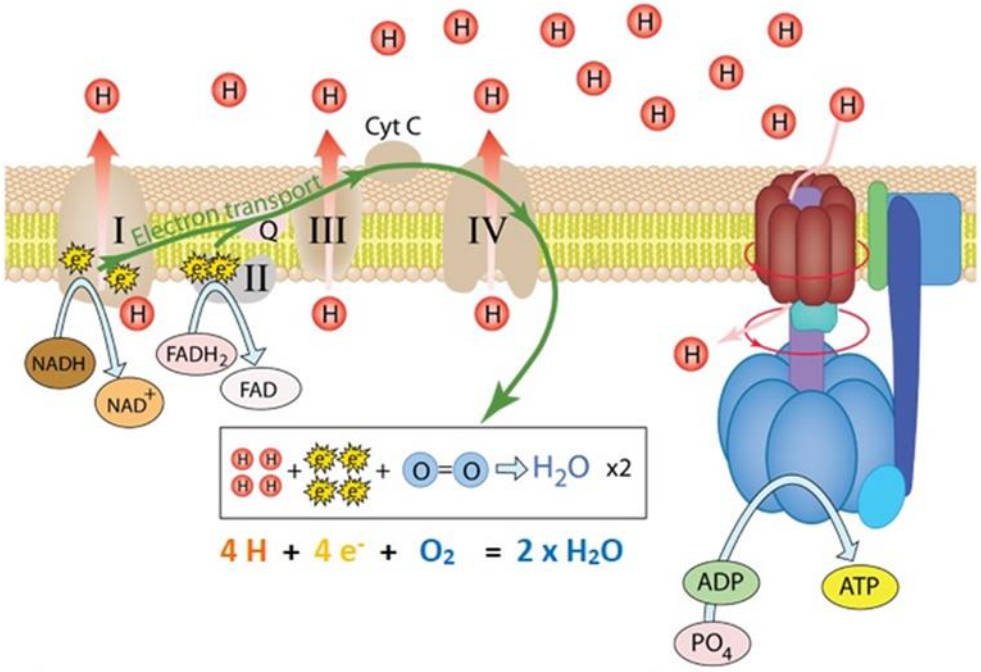
In the citric acid cycle, three molecules of NADH are formed alongside the electron acceptor FAD to form FADH2.

Nearly 90% of the energy ingested from food is produced in the citric acid cycle by the conversion of NAD+ to NADH via electron transport. NAD+ is converted to the reduced form NADH by the addition of a hydrogen atom and two electrons.

When NAD+ production is impaired, the citrate cycle is impaired and the energy-producing capacity of the mitochondria is reduced. The lack of NAD+ reduces cellular function, cell protection and energy production and is a central pathological factor in many diseases and ageing. The required level of NAD+ production is a prerequisite for the healthy functioning of the body.



The coenzyme NAD+ is loaded in the citrate cycle to form NADH. NAD+ is a central metabolic cofactor in eukaryotic cells that plays a critical role in the regulation of cellular metabolism and energy homeostasis. The reduced form of NAD+ (i.e. NADH) serves as the primary electron donor in the mitochondrial respiratory chain. The proton gradient generated by the electron transport chain drives the nanomotors, and the energy generated by the motors powers oxidative phosphorylation and ATP production.



The NAD+ / NADH ratio regulates the activity of enzymes involved in various metabolic pathways such as glycolysis, the citrate cycle and fatty acid oxidation. Both NAD+ / NADH and ADP / ATP interact through their conversion.

In equilibrium, this interaction is related to the essentiality of yin and yang, and they tend to be ordered, balanced and in equilibrium under different conditions.

The availability of precursors of NAD+ is also essential, especially for growth and development, to maintain the stability of the organism. According to a study by Sarika Srivastava, increasing intracellular NAD+ levels improves oxidative metabolism and prevents bioenergetic and functional decline, mitochondrial disease and age-related disorders (Srivastava, S. 2016).

One study reviews more than one hundred scientific articles published over the last ninety years. This comprehensive review shows that supplementation with NAD+ precursors improves health and longevity. The effect of NAD+ precursors is therapeutic in humans. These precursors have a curative role in pellagra and pellagra-like disorders; therefore, nicotinic acid amide supplementation is suggested to alleviate skin lesions.

Cholesterol levels and kidney disease

Nicotinic acid amide acts as a cholesterol-lowering agent in humans. These molecules also have potential benefits in chronic kidney disease. It supports the physiological function of mitochondria and therefore has a beneficial effect on the metabolism of patients with type 2 diabetes. Nicotinamide improves muscle performance in patients with mitochondrial myopathy, and NAD+ precursors improve muscle performance in humans (Ruben Zapata-Perez, 2021).

The adverse effects of certain chemicals used in crop production

The three most widely used herbicides are glyphosate, atrazine and 2,4-dichlorophenoxy-acetic acid. They have toxicological and hormonal effects on animals and humans via feed and food crops.

Insecticidal and fungicidal pesticides that act by inhibiting chitin synthesis affect human connective tissue. Chitin synthesis inhibitors inhibit the coenzyme uridine diphosphate-N-acetylglucosamine (UDP-GlcNAc). They thus inhibit chitin synthesis by insects and fungi and the formation of glycosaminoglycans from the extracellular matrix of human connective tissue (hyaluronic acid, chondroitin sulphate and N-acetylglucosamine polymer of chitinase-like proteins).

The GM soy herbicide glyphosate is harmful to the stomach and intestinal lining. It causes intestinal dysbiosis and plays a role in liver and kidney damage. By blocking the action of the enzyme aromatase, it has a herbicidal hormone-modulating effect. It prevents the conversion of testosterone to oestrogen in the female body. Excess testosterone leads to the development of polycystic ovaries (PCO). An indirect problem with GM soy is that the glyphosate content of pigs and poultry raised on industrial feed causes similar problems to the direct effects of GM soy.

Atrazine also affects the enzyme aromatase, which converts testosterone into oestrogen.

Atrazine disrupts the activity of the aromatase enzyme. It reduces testosterone levels in men and increases oestrogen levels in women. It causes problems in both sexes: testosterone deficiency in men and high oestrogen levels in women cause endometriosis.

Effects of unfermented foods and food additives

In the modern human diet, traditional fermented foods have disappeared, replaced by the use of food additives.

Wholemeal flours can be harmful: the wheat germ agglutinin protein (glycoprotein) is an inflammatory substance. Bran is not a healthy ingredient in many ways. It is high in lignin and low in pectin and hemicellulose. It is poorly fermentable by intestinal bacteria (poor quality fibre).

There is a potential risk of various fungal toxins or fungicide residues in bran. Most of the phytates ingested with bran are plant lectins, which can cause severe intestinal inflammation.

High fructose corn syrup (monosaccharide) is used everywhere instead of beet sugar (disaccharide). Thirty years ago, the daily intake of fructose was 0-10 grams. Today it can be as much as 250-300 grams. High fructose corn syrup interferes with metabolism and is a major cause of metabolic syndrome.

The food industry uses many additives to make food tastier, but certainly not healthier. Additives play a significant role in the development of high blood pressure.

Omega-3 and omega-6 fatty acids and their proportions play an essential role in maintaining homeostasis and preventing inflammatory processes. Our diet should contain the right balance of omega-3 and omega-6 fatty acids for our body to function optimally. Experience has shown that a healthy ratio of omega-3 to omega-6 fatty acids of between 1:1 and 1:3 is not uncommon, as opposed to a ratio of 1:30, which can cause serious problems.

We have created Fulvicherb - Synergy to draw on the rich resources of nature to provide adequate help to solve the above problems.

Fulvicherb - Synergy is the result of four decades of experience in animal husbandry. Our experience is complemented by naturopathic and phytotherapeutic knowledge.

Production technology

The production of Fulvicherb-Synergy is a semi-aseptic process where we adjust the pH of the supplement to 4.3. The product is sterilised and bottled at 84 degrees Celsius. This technology ensures that the product's natural and botanical ingredients retain their potency for one year. We do not use artificial preservatives and the product is microbiologically sterile.

The herbs in Fulvicherb - Synergy and their effects

The herbs in this product have bactericidal and bacteriostatic properties. The blend of herbs helps to eliminate gram and gram+ bacteria from the intestinal tract that cause dysbiosis.

They have a bacteriostatic effect on dysbiotic gut bacteria.

They do not prevent the proliferation of valuable species of eubiotic intestinal flora. In particular, the compounds in the seeds of Rumex acetosa inhibit the growth of harmful bacteria, destroy certain bacteria and protect tryptophan- and niacin-producing bacteria.

A microbiome researcher at Yale School of Medicine, Andrew Goodman, found that harmful gut bacteria consume vitamins in the diet, especially B vitamins. Beneficial bacteria produce large amounts of B vitamins and vitamin K2, crowding out harmful bacteria and preventing the proliferation of vitamin-consuming bacteria (Yoshii Ken et al; 2019).

Milk thistle - natural help for the liver and kidneys

Silybum marianum, also known as milk thistle, has been used to treat liver disease, including hepatitis and prostate cancer. This herb contains a number of lignans that have anti-inflammatory and anti-fibrotic effects and improve liver function.

The active ingredients are silymarin and water-soluble flavonoids (quercetin and taxifolin). They protect the cytochrome p450 enzyme system. These play an essential role in detoxification (breaking down harmful fungal toxins, xenobiotics and pesticides).

Glyphosate damages this enzyme system, which plays an essential role in regulating the body's metabolism and maintaining a healthy hormonal balance.

Milk Thistle protects and regenerates the liver and the epithelial cells of the renal tubules.

Fulvicherb contains a milk thistle module, including non-GMO and phytoestrogen-free sunflower lecithin, which facilitates the absorption of oily extracts such as silymarin.

Oral administration of silymarin has a highly beneficial effect on liver damage. It reduces lipid peroxidation and increases antioxidant enzyme activity to enhance the liver's antioxidant defence system. It reduces the overexpression of pro-inflammatory cytokines and inhibits inflammatory signalling. Liver enzyme levels of ALT, AST, ALP and GGTA in blood serum are improved by silymarin action. Silymarin increases liver antioxidant enzyme levels (catalase, superoxide dismutase, glutathione peroxidase, glutathione S-transferase) (Lan Wang et al; 2017).

Silymarin is concentrated in kidney cells. The epithelial cells of the renal tubule promote regeneration processes. Silymarin protects animals and humans from kidney damage caused by various toxins (Barbara L. et al; 2008).

The active constituents of milk thistle have poor bioavailability because they are insoluble in water. In experiments with rats, only 0.95% of the amount of silibinin is utilised orally (Jhy-Wen Wu et al; 2007). Fulvicherb-Synergy contains a silymarin complex absorption enhancer which, according to various literature sources, provides 4.6 to 10-fold drug absorption. The active ingredients (taxifolin, quercetin, kaempferol, apigenin) have different polarity properties. They act synergistically with the silymarin-type components of the flavonolignan complex. Milk thistle also contains sterols. Sterols are active substances with "amphiphilic" (double) properties. They have polar and apolar moieties and contain both a lipid-soluble and a water-soluble moiety. Both polar moieties are readily soluble in organic solvents (Kidd P. Head K. 2010).

The technology we use to extract the active ingredient is unique. In addition to cold-pressed oil, we use tinctured cold-pressed cake to extract active ingredients with different polarity properties. We also add a natural amphiphilic substance to aid absorption. We have developed the drug extraction using the pharmacognosy knowledge listed above. The result is good absorption and excellent silymarin activity.

Chamomile - nature's anti-inflammatory

Chamomile has anti-inflammatory properties and treats many ailments, including infections, bronchitis, fever and wounds. It treats digestive problems, menstrual pain, toothache, dizziness and headaches. Chamomile helps to improve sleep and breathing. It has a good effect on gastritis (inflammation of the stomach lining), enterocolitis (inflammation of the digestive tract) and colitis (inflammation of the inner lining of the colon). As a complementary therapy, it helps in the treatment of ulcerative colitis (Rácz, Rácz-Kotilla, Szabó 2012) and protects the stomach and intestinal mucosa.

Camomile contains two groups of active ingredients:

- Sesquiterpene hydrocarbons (chamazulene): essential oils with anti-inflammatory properties.
- Sesquiterpene alcohol (bisabolol): non-volatile flavonoids.

An aqueous solution of camomile flowers reduces the body's sensitivity to histamine. It is also an effective remedy for mucus diarrhoea.

European blueberry leaves - a natural enhancer for blood circulation

The decoction of blueberry leaves has a good effect on blood circulation. It also plays a role in blood pressure regulation. It has a good effect on tissue oxygenation by protecting the NO-producing function of endothelial cells in blood vessels. It plays an important role in the opening of small diameter arterioles and venules, thereby improving eye circulation and vision. Even in old age, blueberries improve endothelial function. Quercetin can prevent the production of histamine and other allergens and inflammatory substances. Quercetin inhibits platelet aggregation (blood clotting).

Rosehips - a natural source of vitamin C & P

Rosehips are a natural source of vitamin C and rutin (vitamin P), a natural stamina booster. Together, vitamin C and rutin are responsible for the structural integrity of connective tissue and are particularly important in maintaining the connective tissue structure of blood vessel walls. Vitamin C is a synergist of silymarin (the active ingredient in milk thistle), so we have added a naturally occurring form of vitamin C from rose hips to Fulvicherb. Due to the blood sugar regulating effect of rose hips, their consumption is recommended for people with diabetes.

Nettle - a natural source of quercetin

Nettle contains active ingredients that have a positive effect on the human body. Supports blood circulation and detoxification. Improves kidney, prostate and gastrointestinal health.

Nettle leaves contain many beneficial substances: chlorophyll, carotenoids, vitamins A, C, K, U, triterpenes, glucokinase, sterols and flavonoids (quercetin, kaempferol, isorhamnetin) and minerals.

Studies have confirmed the anti-diarrhoeal and anti-inflammatory effects of quercetin. It inhibits intestinal wall secretion (the excretion of beneficial substances into the extracellular or intercellular space) and the production of inflammatory neurotransmitters (such as histamine, serotonin and prostaglandins).

In the light of the above, the quercetin content of nettle leaves helps to stop secretory diarrhoea when it is not caused by a viral or bacterial infection.

Davidović, M. Joksimović Todorović, B. Stojanović and R. Relić V. (2012) studied the combined phytotherapeutic effect of Rumex acetosa L. and Urtica dioica L. The test results showed that both herbs have excellent anti-inflammatory and anti-diarrhoeal effects.

Broad-leaved sorrel - nature's anti-diarrheal

It contains a number of essential micronutrients such as vitamin C, an important antioxidant that helps the body fight infection.

Another essential nutrient in Rumex acetosa is vitamin A, a fat-soluble vitamin that supports eye health, immune function and reproductive health. For centuries, its fruit has been used in folk medicine as a natural remedy for diarrhoea in humans and animals.

Dr Andor Oláh, one of the founders and president of the Scientific Association of Hungarian Alternative Medicine Practitioners and Life Reformers, worked in Békés County in the 50s and 60s. In his book published in 1985, "Fűbe-fába az orvosság! Békés megye népi orvoslása (Medicinal plants and herbs: the folk medicine of Békés County), he gives ten references for the use of Rumex acetosa L; commonly known as field sorrel, to treat diarrhoea in humans and animals.

It is an essential herb in the complementary therapy of Crohn's disease.

The pharmacologists Z. Kisgyörgy and M. Péter from Cluj-Napoca (1982) were engaged in pharmacognosy. They studied the effects of species of the genus Rumex, commonly used in folk medicine. They confirmed the anti-diarrhoeal effect through experiments.

Rácz, Rácz-Kotilla and Szabó came to a similar conclusion (2012). Rumex acetosa L. does not affect the beneficial species and strains of bacteria within the gut microbiome. Its inhibitory effect on the development of enterobacteria has been experimentally demonstrated. The extract of the fruit of Rumex spp. has been shown to inhibit bacterial growth (Bernáth et al; 2001).

Serotonin-induced secretory diarrhoea was inhibited by a drug derived from Rumex maritimus (Rouf et al; 2003).

Yineger et al; (2007) noted that Far Eastern medicine uses species of the genus Rumex against Clostridium sp.

The drug extracted from the sorrel fruit (Rumicis Fructus) contains plant flavonoids, quercetin, vitexin, rutin, other polyphenols and tannin. It also contains astringents, which are useful in treating diarrhoea and intestinal inflammation, and tannins, which form a film on the surface of the intestinal mucosa, reducing local irritation and protecting the intestinal mucosa from the adhesion of harmful enterobacteria. These substances inhibit bacterial growth by damaging cell membranes (Rácz, Rácz-Kotilla, Szabó 2012).

Sage - a natural antioxidant with anti-inflammatory properties

Sage is rich in nutrients. Its antioxidants and anti-inflammatory compounds have anti-cancer properties and promote oral health and wound healing. The dried leaves contain essential oils, diterpene carboxylic acids, polyphenols, and rosmarinic acid. It contains an astringent substance (carnosol, also known as picrosalvin) which reduces the inflammation of mucous membranes and has anti-diarrhoeal and antibiotic properties.

Poracova, Taylorova, and Salamon (2009) studied the antimicrobial and anti-diarrhoeal effects of common sage at the Universities of Nitra and Prešov. Phytotherapy had a positive antimicrobial effect, resulting in a significant reduction in the number of harmful Enterobacteriaceae in the intestinal contents.

Fennel - nature's antibacterial diuretic

Foeniculum vulgare has antibacterial properties and is rich in nutrients, such as B vitamins and dietary minerals, including calcium, iron, magnesium, and manganese. It supports a healthy heart, blood cell formation, and weight management and helps reduce inflammation.

The achene of fennel, which contains 3–7% essential oils, is used medicinally. Its active ingredient is anthenol, and it also contains fencon and methyl chavicol. Sweet fennel has a mild antispasmodic and antibacterial effect in the urinary tract and increases the formation of protective urinary colloids (Rácz, Rácz-Kotilla, Szabó 2012).

Fennel and anise fruit increase urinary excretion; the active ingredients of their essential oils have an inhibitory effect on bacterial growth in the urinary tract and prevent the formation of kidney stones. They also support the production of digestive juices.

Anise - Fennel's natural companion

The primary use of anise in traditional European herbal medicine was for its carminative (flatulence-reducing) properties.

The plant's schizocarp (diachaenium) is used medicinally. The active principles of anise are similar to those of fennel and reinforce each other (synergistic effect). Its active ingredient is an essential oil (3.0-6.0%) containing 80-90% anethole and estragole (or methyl chavicol). This active ingredient is also eliminated by the respiratory and excretory systems.

Anise acts on the gastrointestinal tract. It inhibits the growth of harmful bacteria, promotes the secretion of digestive juices and increases appetite (Rácz, Rácz-Kotilla, Szabó 2012).

Natural ingredients

Inulin - the most valuable prebiotic

Fulvicherb - Synergy contains high levels of inulin: a sweet-tasting dietary fibre that human digestive enzymes cannot break down. It is a very useful prebiotic, a so-called resistant carbohydrate.

The inulin used in this product is from Jerusalem artichokes but, unlike other products, has very high purity. It does not contain simple sugars or sugar alcohol and avoids the bloating effect of regular Jerusalem artichoke syrup. (Jerusalem artichokes contain approximately 24% inulin, 14% monosaccharides, fructose and glucose, and 3% sugar alcohol).

Pectin - the most valuable natural fibre

Fermentable fibres resist digestion and absorption in the small intestine; we digest them in the large intestine.

The gut flora typically consists of the following beneficial bacteria

- Lactic acid producing bacteria (gram-positive lactobacilli and bifidobacteria)
- Butyric acid-producing bacteria (Gram-negative Fusobacteria and members of the genus Bacteroides)
- Short-chain fatty acid-producing bacteria (acetic acid and propionic acid producers)

Their food source is fermentable fibre. Fermentation in the large intestine is most dependent on the water solubility of the fibre component.

Pectin substances are 100% fermentable and are the most valuable fermentable fibres and natural detoxifiers. Pectin is a linear galacturonic acid chain. Beneficial intestinal bacteria ferment galacturonic acid into butyric acid (the best nutrient for colon cells).

Butyric acid (also known as butyrate) is an essential nutrient for liver cell mitochondria. Butyrate is also critical for mental health, acting along the gut-brain axis in the brain.

Pectin's other healing property is its coating and protective effect. Because pectins are high molecular weight polysaccharides, they can form a gel on the surface of the stomach and mucous membranes, protecting them from the irritating effects of aggressive factors.

L-rhamnose is also related to pectin. Pectin contains varying amounts of free carboxyl and hydroxyl radicals. Many other natural sugars, such as fructose and glucose, can be linked to rhamnose. It therefore has complexing properties, which reduce the osmotic concentration of the intestinal contents, helping to prevent osmotic diarrhoea.

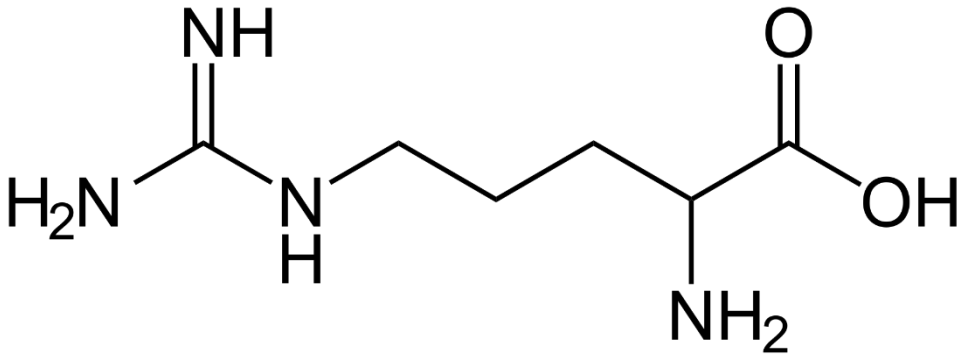
Fulvic acid - nature's carrier molecule

Fulvic acid is a natural chelating and complexing agent that helps the absorption of nutrients. Fulvic acid has been in the human body continuously as long as we have drunk water from natural sources, streams, or rivers.

The molecule's acidic carboxyl and aromatic hydroxyl groups can form chelate and complex bonds with metals, especially with essential organic molecules. Since fulvic acid is low molecular weight, it is easily soluble in water and absorbed in chelate and complex forms in the small intestine. Without loss, complexes formed with fulvic acid absorb rapidly in the small intestine.

Fulvic acid is so powerful that a single fulvic acid molecule can deliver more than 60 elements to the body.

L-Arginine - a key to adequate nitric oxide (NO) production



Fulvicherb - Synergy contains arginine in the form of a fulvic-acid-arginine complex that is 100% absorbed.

- Arginine is necessary for optimal angiogenesis and helps blood vessel formation
- It is essential in wound healing.

- Quickly absorbed by the fulvic acid-arginine complex, arginine promotes NO production by the enzyme iNOS.
- It is involved in the immune response by producing apoptosis-inducing NO in humoral and cellular immune cells as part of the immune defence mechanism.
- It plays an essential role in the neurons of the respiratory, digestive, and urogenital systems.
- As a signal transducer, it plays a role in learning and memory processes.

The wide-ranging effects of nitric oxide

- Nitric oxide synthases (NOS) catalyse the production of nitric oxide (NO) from L-arginine.
- NO is an important cell-signalling molecule.
- Nitric oxide (NO) production improves blood circulation, opens capillaries, and helps maintain optimal blood pressure.
- NO produced by the endothelium (eNOS) mediates smooth muscle movements.
- It has beneficial effects on visceral smooth muscle function and improves intestinal peristalsis, respiration, and cardiac function.
- It helps vasodilatation, regulates blood sugar and insulin levels and plays an essential role in modulating respiration.
- It improves renal capacity and permeability (ischemia).
- NO is a physiological regulator of mitochondrial respiration and regulates mitochondrial ATP synthesis and oxygen consumption.
- It has beneficial effects on insulin resistance and improves blood glucose levels and HgbA1C.

Electrolytes bound by fulvic acid - a natural Ringer's solution

The product contains natural unrefined rock salt from Praid. In the composition of the macro-and microelements of Praid salt, the ratio of each element is the same as the composition of the extracellular fluid space of a healthy body.

It is a natural electrolyte bound by fulvic acid as a chelate and the most natural medical infusion (Ringer's) solution. It contains 84 macro-and microelements in the natural state of salt evaporated in ancient seas over millions of years. The importance of chelates lies in their perfect absorption at the beginning of the small intestine, helping to maintain the body in an optimal osmotic state.

Niacinamide (vitamin B3) - no skin redness

Unlike niacin, niacinamide has no unpleasant effects (niacin causes a rapidly disappearing skin redness above a 50 mg/day dose).

Nicotinic acid amide (niacinamide, vitamin B3) is a precursor for forming the coenzyme nicotinamide adenine dinucleotide (NAD+). It is essential in the kynurenine pathway.

In many cases, the production of NAD+ is not appropriately paced or stops - a result of our modern-day diet. The kynurenine pathway is compromised.

Fulvicherb-Synergy unblocks the kynurenine pathway.

Natural protection for the cytochrome p450 enzyme system

Milk thistle (Silybum marianum) has a flavonolignan complex in its fruit, collectively known as silymarin. The substances in the silymarin complex bind to liver cells, effectively preventing toxins from entering the liver.

Silymarin has a neutralising effect and helps liver cells to fight xenobiotics and biogenic amines more effectively. The silymarin complex has a substantial protective effect on various cytochrome p450 enzymes.

In endometriosis and endothelial hyperplasia, cytochrome p450 enzymes restore the body's hormonal balance through their role in estrogen regulation (Karimi G. et al; 2011).

Restoration of nitric oxide (NO) production in the normal functioning of the kynurenine pathway

In the liver, the conversion of tryptophan to nicotinic acid is the kynurenine pathway. The enzyme IDO (indoleamine 2, 3-dioxygenase) plays a critical role in the first step of the kynurenine pathway. IDO is also known as the rate-limiting enzyme because it ensures the continued availability of the end product of NAD+ in the kynurenine pathway. The production of the enzyme IDO depends on the availability of nitric oxide.

A natural solution for lysine-arginine antagonism

Fulvicherb - Synergy's Arginine-Fulvic Acid Complex is 100% absorbed so arginine, the NO donor, is continuously available.

Nowadays, lysine is present in large amounts in processed foods in the form of free amino acids. This substance causes lysine-arginine antagonism in humans, known as local arginine deficiency. The solution to this antagonism is fulvic acid, which is present in the product. The complexing effect of fulvic acid helps to ensure 100% absorption of lysine, thus avoiding lysine-arginine antagonism.

Helping the NAD+ production on the saved route

Because of our modern diet, the production of NAD+ from tryptophan is inadequate and the 'de novo' pathway does not work properly. With nicotinamide we can support the production of NAD+ via the salvage pathway. The amidating enzyme is nicotinamide adenylyl transferase. The problem is that glyphosate prevents it from working properly. As a result, vitamin B3, which is provided as nicotinic acid (niacin) in most products, is not absorbed.

An excellent example of this is that despite the presence of nicotinic acid (niacin) in animal feed, we find many cases of skin pellagra caused by niacin deficiency! The addition of nicotinamide eliminates this problem.

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