

# Kienergy® – Scientific Research Dossier

Comprehensive review of bioactive ingredients and their clinical evidence

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#### Coenzima Q10

The discovery of coenzyme q represented the key link between the different complexes of the electron transport chain (\*) and energy production. Coenzyme q10 is a lipid molecule known mainly for its role in the mitochondrial respiratory chain, oxidative phosphorylation and its antioxidant properties. Coenzyme q10 is critical in transporting nutrients through mitochondrial membranes and is involved in processes that produce energy from food. It acts as a phenolic antioxidant and its role in protecting the different structures of our body from oxidation is fundamental, especially by reactive oxygen species and free radicals in general. It is an adjuvant in the physiological mechanisms responsible for the regularization of blood pressure and the contraction of the heart muscle. Our body is equipped with antioxidant mechanisms represented by enzymatic molecules or smaller molecules, the so-called soluble antioxidants, including coenzyme q10 which plays a fundamental role. One of the main functions is, therefore, precisely that of intervening in the chemical reactions internal to these organelles, making it possible to recover the energy contained in the food and accumulate it in adenosine triphosphate (atp) molecules indispensable for the energy activity of the cell. Coenzyme q 10, also called vit. Q, is produced by the body, aging significantly reduces its concentration. Statins, a drug used in case of hypercholesterolemia, are also responsible for reducing coenzyme q 10 in the body. Other diseases such as diseases of the cardiovascular system and neurovegetative diseases such as Parkinson's and diabetes, lead to a sharp reduction in the coenzyme q 10 in the body. Excellent for which, some studies have shown that, in case of a heart attack, the intake of coenzyme g 10 reduces the possibility of suffering subsequent heart attacks. Most studies have recommended that the dose of the supplement be between 100 and 300 mg/day (e.g. 100 mg 3 times a day). Specific indications include an antitumor effect mediated by immune stimulation, a decrease in insulin requirement in patients with diabetes, a slowdown in the progression of Parkinson's disease, efficacy in the treatment of heart failure and protection against anthracycline cardiotoxicity. The most important statement may be the improvement in endothelial cell dysfunction that contributes to cardiovascular disease. Although some preliminary studies suggest that coq10 may be useful in the treatment of these disorders, the results are not clear and further testing is necessary. A 2012 meta-analysis evaluated 5 randomized, controlled trials with a total of 194 patients and found a significant improvement in endothelial function, measured by flow-mediated peripheral arterial dilation (1). A 2013 meta-analysis of randomized controlled trials suggested that coq10 may improve functional status in patients with heart failure (2). However, this meta-analysis consisted of mainly small, short-term studies. A 2014 randomized, controlled, multicentred study of 420 patients with heart failure showed that coq10, 100 mg orally 3 times a day, when added to standard therapy, was safe, alleviated symptoms and reduced major cardiovascular events (3). A Cochrane review of 11 studies (1573 subjects) concluded that there was moderate quality evidence that coq10 reduces all-cause mortality and hospitalization for heart failure; however, there was no convincing evidence to support or refute the use of cog10 for heart failure (4). However, a 2017 meta-analysis of 14 randomized controlled trials (2149 subjects) stated that coq10 users had greater exercise capacity and lower mortality than those treated with placebo (5). A clinical controversy is whether coq10 supplementation decreases muscle symptoms associated with statins. Some studies have shown decreases, while others have not. A 2018 meta-analysis of 100 to 600 mg per day of coq10 for 30 days to 3 months reported significant decreases in muscle symptoms of pain, weakness, cramps and fatigue, compared to placebo. One limitation was the heterogeneity of the included studies (6). Adverse effects there are relatively few reported cases of gastrointestinal symptoms (e.g., loss of appetite, abdominal pain, nausea, vomiting) and central nervous system symptoms (e.g., dizziness, photophobia, irritability, headache). Other adverse effects include itching, rash, fatigue and flu-like symptoms. Drug interaction coq10 can reduce the response to warfarin. Coq10 can interact with some antihypertensive and chemotherapy drugs.

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# Spermidine

Researchers from the institute of biochemistry and cell biology of the national research council (CNR-IBBC) of Monterotondo, have shown that spermidine, a substance naturally present in many foods, is able to correct memory defects, resetting neurons in motion, in middle-aged subjects predisposed to cognitive decline thanks to its "cleaning" action of the toxic protein aggregates accumulated in the brain. The study is published in the journal aging cell spermidine is a polyamine capable of promoting longevity through a protective action on the heart system and has also been tested on neurodegeneration in drosophila. Symptoms of mental decline are associated with the accumulation, in neurons, of protein aggregates of alpha-synuclein\* and beta amyloid\*\* that can lead to fibrils or filaments that are potentially toxic to cells. In a young cell these aggregates, considered cell waste, are enclosed within a vesicle (autophagosome) that takes care of carrying them into the lysosome, an organelle that breaks them down and recycles their constituents there where possible. With aging, the

aggregates increase and the degrading capacity of the lysosomes decreases. Recent studies have shown that spermidine, naturally present in many foods, stimulates autophagy, the process of internal cleaning of cells, and thus improves their degrading abilities. The engulfing of lysosomes is accompanied by a defect in activating those processes of communication between neurons that are necessary in young people to form new memories and that are mediated by synapses through the glutamate receptor, AMPA. These processes are instead unaltered in young subjects, or in those aged but with intact memory. The study showed that a one month treatment with spermidine stimulates the expression of transcription factor TFEB (discovered in the laboratory of Andrea Ballabio at TIGEM) which controls the genes responsible for autophagy degradation and thereby promotes the cleansing of the cell from alpha-synuclein and beta-amyloid aggregates. Once the cell is freed from these aggregates, it is observed that synaptic communication, through the AMPA receptor, is restored so that memory can function even under high information load conditions in subjects who had the defect. Searches related to "spermidine".

# Senolytic

Spermidine is a naturally occurring polyamine compound, contained in several foods and generally abundant in the mediterranean diet in fact, wheat germ, whole grains, cheeses, mushrooms, pears and numerous vegetables, such as broccoli, cauliflower, green peppers, fermented soybeans and peas, are rich in spermidine. It is also present in the human body, particularly in sperm, from which it was isolated for the first time and from which its particular name derives. Another source of synthesis within the human body is represented by the intestinal microbiota.

## Physiological role

Spermidine intervenes in the metabolic control of cells, participating in numerous functions within the human body, including:

- Protection from oxidative stress; anti-inflammatory action;
- Proteostasis, i.e. The maintenance of normal functional levels of proteins within the cell;
- Cellular homeostasis, regulating the growth, proliferation and death of cells;
- The stabilization of DNA and RNA;
- The preservation of mitochondrial function;
- The prevention of stem cell senescence;
- Spermidine would also be able to have interesting cardioprotective and neuroprotective effects.

# Spermidine and autophagy

Some scientific evidence highlights the ability of spermidine to activate autophagy and slow age-related decline. Autophagy is a self-degrading process that induces the destruction of aged, damaged or dysfunctional intracellular components by lysosomes. In fact, it represents a process of cell renewal, by which cells develop greater resistance to oxidative stress and are induced to degrade poorly folded proteins and other dysfunctional cellular components, such as aged mitochondria, which produce an excess of reactive oxygen species, deleterious and dangerous to the health of the cell itself.

The correlation between spermidine and autophagic activity has also been demonstrated by the use of genetically modified animal models with silenced autophagic mechanisms, in which spermidine has not been shown to have any beneficial effect.

Autophagy appears to play an important role in the prevention of neurodegenerative diseases and related to early aging. A study conducted on centenary subjects has shown that these individuals possess genes that significantly over-regulate the autophagic-lysosomal pathways and that this genetic heritage can be transmitted to the offspring.

Pathological conditions associated with aging, such as neurodegeneration and cardiovascular disease, are directly linked to the intracellular accumulation of 'toxic debris'. The removal of cellular waste and dysfunctional components through autophagy is a well-documented way for the prevention of aging and the main diseases related to it.

# Spermidine and longevity

Due to its ability to regulate gene expression, spermidine could be called a real "molecule of longevity". Preliminary studies, conducted in both in vitro and in vivo in animals, have highlighted the ability of spermidine to prolong the lifespan of certain organisms, such as yeasts, nematodes, flies and mice. Depending on the species, the increase was from 15 to 25% and involved the activation of cellular autophagy processes. Spermidine also reduces oxidative stress and helps cells eliminate harmful components, optimizing metabolic processes. Some researchers have therefore hypothesized that it could induce such activity even in humans, delaying their aging. In fact, a correlation has emerged between spermidine and the various markers of aging since its levels decrease with advancing age. In humans, spermidine-rich diets have been associated with reduced overall mortality, both cardiovascular and cancer-related. In these studies, the high dietary intake of spermidine recorded a reduction in the incidence of death, even after correction with possible confounding factors, including age, body mass index, alcohol consumption, diabetes, metabolic syndrome, physical activity, sex, socioeconomic status and eating habits. This supports the idea that spermidine could actually be involved in the reduction of many factors involved in morbidity and proposes interesting preventive and health applications.

#### Hair health

The potential beneficial effects of spermidine on capillary follicles had already emerged in some previous animal model studies. These studies, conducted both in vitro and in vivo, showed the ability of spermidine to promote both the elongation of the hair shaft and to prolong its growth phase (anagen phase), as it is able to stimulate the stem cells leading to hair growth. In two recent in vitro studies carried out on cell cultures of human follicles, the efficacy of spermidine in improving hair shaft elongation and prolonging the anagen phase was evaluated by increasing the proliferation of epidermal keratinocytes in the dermal matrix. The anti-apoptotic effects and the promotion of anagen have also been confirmed, also in vitro, with the use of n1-methylspermidine, a stable metabolite of it. The exact mechanism by which spermidine exerts its beneficial effects on the human follicle is not yet entirely clear. It has previously been shown that spermidine can modulate the gene expression profile of follicles, potentially relevant to the growth cycle of human hair. In addition, its metabolite n1-methylspermidine exerts antioxidant and anti-inflammatory effects on the follicles. A clinical study conducted in 100 healthy people demonstrated the effectiveness of a spermidine-based dietary supplement in prolonging the "anagen" phase, and reversing the transition from this to the catagen and telogen phases. These effects could be attributed to both an increase in proliferation and a reduction in hair bulb cell apoptosis, as emerged from the determination of ki-67 (cell proliferation marker) and c-kit (apoptosis marker) levels.

# Immune system

Some scientific evidence obtained from in vivo studies conducted in laboratory animals, has shown the effectiveness of spermidine in the prevention of immune senescence, i.e. The aging process of the immune system, and in the formation of memory t lymphocytes. A study in elderly mice highlighted the ability of spermidine to increase the production of antibodies, particularly b lymphocytes, whose function is often reduced in the elderly. Spermidine also appears to be able to improve the generation and function of memory lymphocytes, similar to what is known for other molecules capable of inducing autophagy (such as, for example, metformin and rapamycin). In another study conducted on elderly mice, it emerged that the response of cd8+ t lymphocytes to influenza vaccination was increased following oral treatment with spermidine, in an autophagy-dependent way, emphasizing the important role of this mechanism underlying the process of formation of memory immune cells. In addition, further studies have found anti-inflammatory effects in spermidine, also partly related to the stimulation of autophagy in different pathophysiological contexts. Dietary supplementation of spermidine in mice has in fact reduced plasma concentrations of tumor-alpha necrosis factor (TNF-A) and other pro-inflammatory cytokines.

## Metabolic syndrome

In an in vivo study in mice, oral spermidine intake induced a significant reduction in weight gain, visceral fat, glucose intolerance and insulin-resistance compared to the control group, despite the animals being fed a high-fat diet. In addition, in some in vitro and in vivo animal studies, spermidine administration has been shown to have complementary pathway-mediated cardioprotective effects, such as autophagy, blood pressure reduction and atherosclerosis. Similarly, a high dietary intake of spermidine is associated with a reduction in blood pressure and, consequently, with a lower cardiovascular risk. La spermidine, in fact, in addition to suppressing the expression of pro-inflammatory cytokines, increases the availability of nitric oxide (no) at the endothelial level and reduces the processes of cellular oxidation.

# Regulatory status and recommended dosages

Spermidine can be used as an ingredient in food supplements, as it is included in the ministerial list 'other nutrients and other substances with a nutritive or physiological effect'. In 2017, the new food "spermidine rich wheat germ extract" was also authorised by the European commission. The maximum permitted dosages are 6 mg of spermidine per day.

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#### D-Ribosium

D-ribose is a glucide monosaccharide, or a simple carbohydrate, with molecular formula c5h10o5 and linear composition h-(c=o)-(CHOH)4-h. D-ribose is a component of ribonucleotides, from which RNA is constructed; it is therefore necessary for the coding, decoding, regulation and expression of genes. Its structural analogue, deoxyribose, which is an equally essential component of DNA. The most "metabolically" important factors that include phosphorylated ribose are: ATP, ADP, coenzyme a, and NADH; CAMP and CGMP are also ribose derivatives, and act as secondary messengers in some signalling pathways. Ribose also appears in some pharmaceutical agents, including the antibiotics neomycin and paromomycin. D-ribose has an ergogenic function due to the increase in the availability of ATP and therefore of energy. ATP, by extension adenosine triphosphate, is the fundamental molecule for the release of cellular energy; we could define it, in simple terms, as "pure biological energy". Under normal conditions, ATP levels are constant and fall within a range of equilibrium. For pathological

reasons, a reduction in ATP levels can be seen in the heart tissue – classically after myocardial infarction. A deficiency of ATP in myocardial cells can, however, result in very serious dysfunctions, such as functional insufficiency – inability to pump blood properly. Supplementing with d-ribose under conditions of low ATP levels could lead to energy benefits.

As mentioned above, d-ribose is a substance that allows the production of atp and nucleic acids.

This is partly metabolized into purines\* and pyrimidines\*\*, substances indispensable for the synthesis of nucleic acids (RNG). The latter is the precursor of protein synthesis and adenine nucleotides, mediated by ATP, allowing energy reserves to be obtained. Another main function of d ribose, is to be the direct precursor of amino acids such as histidine, glutamine, glutamate, proline and arginine. Ribose is the starting point and the compound that limits the speed in the synthesis of these fundamental cellular compounds. No other compound can replace ribose, which is the vital structural backbone of critical cellular compounds called purines and pyrimidines, which our bodies need to form our DNA and RNA, as well as some vitamins and numerous cofactors.

Ribose is produced in the cells of our bodies by glucose, but this process is slow in the heart and muscle tissue. Although ribose is present in all living matter, only a small amount can be ingested through the diet. In many clinical trials in the U.S. And Europe, the supply of additional bioenergy to ribose has been shown to significantly improve endurance during intense exercise, reduces recovery time, reduces cramps and pain, and reduces fatigue in people suffering from energy depletion.

Ribose plays a key role in the maintenance of cellular and tissue homeostasis, intervening in different reactions of both an energetic and metabolic and plastic nature.

#### Its main functions concern:

- Energy production, through the non-oxidative phase of the pentose phosphate pathway, which allows the conversion of pentoses such as ribose into metabolites interspersed in the neo glucogenic pathway, indispensable for the production of glucose during periods of fasting or increased demand;
- Synthesis of ATP, a fundamental ribonucleotide in energy processes, able to release energy through its hydrolysis;
- Protein synthesis and cell division, constituting the essential sugar for the synthesis of nucleic acids;
- Synthesis of valuable amino acids both structurally and metabolically, such as histidine, glutamine, glutamate, proline and arginine;
- Regulation of the state of cellular oxidation-reduction, important in protecting the cell from damaging stimuli induced by reactive oxygen species.

#### Resveratrole

Resveratrol reduces the anti-inflammatory effect due to its ability to inhibit certain reactions, such as cyclo-oxygenase, just like the most classic anti-inflammatory drugs do. In addition, resveratrol can interfere with the inflammatory process at various levels: from the activation of white blood cells and tissues (main protagonists of the immune response) to the inhibition of the production of inflammatory proteins by these same cells. Its protective action can also be executed against influenza viruses by preventing the virus itself from replicating within the cells. Resveratrol regulates the level of glucose in the blood by reducing its production at the hepatic level and encouraging its transport to the skeletal muscle level. It has been seen that resveratrol has a neuroprotective effect and it seems that this is due to its ability to stimulate AMPK kinase, a protein that has the task of monitoring the energy status of the cell. This kinase represents a real cellular sensor as its activity depends directly on the levels of energy that the cell has available. Stimulating the aforementioned kinase means restoring the energy necessary for the cells of our body to survive. Several studies have shown that moderate daily consumption of wine can reduce neurodegenerative diseases such as Alzheimer's and Parkinson's. There are also studies mainly in vitro at the level of cell lines that demonstrate an anticancer activity of resveratrol although at the moment it is suggested at most as an adjuvant in chemotherapy therapies.

Numerous publications enhance its activity such as:

- Immunostimulants
- Vascular system activator
- Anti-inflammatory
- Anti-aging
- Metabolic syndrome

# DI phosphoserine

It is a substance that is formed from the amino acid serine bound with phosphoric acid. It is contained in several phosphoproteins, and is a decisive molecule for the activity of certain enzymes and operates in processes of our metabolism at the brain level. It is a constituent of the phospholipids present within our body.

The ministry of health categorizes it as a physiological nutrient, and stimulates the abilities of our memory, helps cognitive deficit disorders, increases longevity and attenuates the predisposition to neurocognitive decline linked to increasing age, in fact increases concentration and attention and chronic stress conditions.

Along with vitamins b6, b9 and b12 they are very important for the brain and are considered vitamins for memory.

#### Griffonia

Griffonia (Griffonia Simplicifolia), also called African bean for the characteristic shape of its pods, is a tree typical of the tropical areas of west Africa, belonging to the Leguminosae family. From the seeds contained in these pods is extracted 5-hydroxytryptophan (5-htp), a precursor of serotonin – the neurotransmitter of good mood (also involved in the mechanism of inhibition of hunger). 5-htp is able to cross the blood-brain barrier, the narrow network of capillaries that separates the brain from the rest of the body, and once reached the central nervous system it can be transformed into serotonin, increasing the amounts available. Pharmacological uses and activities the drug contains fair amounts of 5-htp, which in the human body is a precursor of serotonin (5-hydroxytryptamine) very important neurotransmitter involved in various physiological functions including sleep, appetite and mood functions. Numerous studies have demonstrated the marked antidepressant action of 5-htp in vivo and this represents the main use of the drug. Considering the role of serotonin at the level of the hypothalamus, 5-htp has been shown to induce an inhibitory effect on the hunger centre at this level. In the subject there is an increase in the sense of satiety with a consequent decrease in appetite and decrease in body weight. The drug is therefore used in the treatment of obesity in adult subjects. Interesting actions of 5-htp in the treatment of insomnia and migraine have also been observed. Serotonin, in turn, is a precursor to another important neurotransmitter, melatonin, involved in the sleep-wake control mechanism. The integration of 5 HTP, therefore, can be applied in the field of

- Adjusting the sleep rhythm wakefulness
- Control of mood tone, in mild depressions
- Mild states of anxiety
- Control of obesity and bulimia natural products of relevance in the prevention and supportive treatment of depression.
- Biological activity and metabolomics of Griffonia Simplicifolia seeds extracted with different methodologies
- Relationship between the absorption of 5-hydroxytryptophan from an integrated diet, by means of Griffonia Simplicifolia extract, and the effect on satiety in overweight females after oral spray administration.
- An open-label trial of I-5-hydroxytryptophan in subjects with romantic stress

## Bacopa Monnieri

Bacopa Monnieri is a small plant containing bacosides (bacoside a and b or saponins), apigenin (relaxing alkaloid), plant sterols, quercetin, Luteonin and other flavonoids with the following functions:

- Protecting the brain from oxidative stress and chronic inflammation interacting with the serotonin system
- Reduce the aggregation and toxicity of fibrilla amyloids
- Stimulating the growth of nerve endings

- Improve signalling in the hippocampus, the area of the brain where memories are processed, through the enhancement of dendric proliferation
- Increase acetyl cline levels in the brain, inhibiting its degradation and increasing its synthesis
- Affecting GABA and serotonin increase dendritic connections to neurons

Bacopa Monnieri extract (Haematococcus Pluvialis) in a randomized, double-blind, controlled study of elderly subjects showed to: (9)

- Improve working memory;
- Improve attention;
- Improve cognitive processing;
- Suppress the activity of acetylcholinesterase in plasma. In a double-blind placebo-controlled clinical trial in subjects aged 18 to 60 years, bacopa monnieri extract was shown to be effective in increasing higher-order cognitive processes, which are critically dependent on the flow of information from the environment, such as learning and memory. The extract significantly improved visual information processing speed, level of learning and memory consolidation (p<0.05), and anxiety status (p<0.001) compared to placebo, with more marked effects after 12 weeks of treatment. (10) in another randomised, double-blind, placebo-controlled clinical trial, Bacopa Monnieri extract was shown to be effective in improving the ability to retain new information by means of the deferred recall test of word pairs, in subjects aged 40 to 65 years.
  - (11) a randomised double-blind placebo-controlled clinical trial demonstrates that Bacopa Monnieri extract has positive effects on memory, cognitive function, mental well-being and cognitive performance of the elderly subject. (12) Bacopa Monnieri is a perennial herb that commonly grows in wetlands in many areas of the world. This plant is also known as Brahmi, Indian pennywort, water hyssop, and herb of grace.

# Claims

Bacopa is said to improve or maintain memory, learning retention, concentration, focus, and overall cognitive function and performance. Some people take bacopa to help relieve or delay symptoms of Alzheimer disease and attention deficit-hyperactivity disorder (ADHD).

#### **Evidence**

There are no high-quality studies demonstrating that bacopa is effective for improving memory or cognitive function or treating any disorder. However, some small studies are worth noting.

A randomized study of 60 medical students in India who were treated with either 150 mg of standardized extract of bacopa or matching placebo twice a day for 6 weeks reported a significant improvement in memory and cognitive function testing (1).

In a randomized study, 54 participants 65 years or older (mean age 73.5 years) without clinical signs of dementia were treated with bacopa 300 mg a day or placebo for 12 weeks. The patients treated with bacopa had improvement in memory tests from baseline significantly more than those treated with placebo (2).

In a randomized study, 98 healthy Australian adults over 55 years of age were treated with bacopa 300 mg a day or placebo for 12 weeks. Bacopa significantly improved verbal learning, memory acquisition, and delayed recall compared to placebo (3).

# Adverse effect

Common adverse effects of bacopa include gastrointestinal upset, nausea, and dry mouth.

# **Drugs interactions**

Bacopa can increase acetylcholine and, therefore, may decrease the effect of anticholinergic drugs or increase the adverse effects of cholinergic drugs that increase acetylcholine (e.g., glaucoma or Alzheimer disease drugs).

Bacopa may increase thyroid hormone levels; therefore, people taking thyroid hormone drugs should not take bacopa.

Bacopa may change the blood levels of medications metabolized by the cytochrome p450 system (e.g., warfarin, some calcium channel blockers, antiseizure medications).

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## Vitamin B1

Thiamine (B1): necessary in carbohydrate metabolism, it promotes the general state of nutrition of nerve tissues. The deficiency causes damage to the nervous system, general wasting and some specific conditions such as Beri Beri, which is widespread among populations that feed mainly on bright rice, and Wernicke's syndrome, a severe form of confusional state. Thiamine is widespread in both plant and animal foods, such as cereals, legumes, pork, brewer's yeast, and is also partly produced by the intestinal flora but its requirement, which is at least 0.8 mg per day (0.4 mg per 1000 kcal taken) is barely covered by a normal diet.

#### Vitamin B2

Riboflavin (B2): important for the state of nutrition of the skin and mucous membranes, riboflavin is rarely poor in the diet of the populations of rich countries. Its deficiency is evident in poor populations, where associated with a general state of malnutrition, it causes skin alterations, injuries to the mucous membranes and the digestive tract. It is widespread in brewer's yeast, wheat germ, whole grains, liver, meat, milk and eggs and is also produced by the intestinal flora. However, a certain part is lost with the cooking of food. The daily requirement is 0.6 mg for every 1000 kcal taken.

# Vitamin B3 (vitamin pp)

Vitamin pp takes part in the reactions of cellular respiration, the synthesis and demolition of amino acids, fatty acids and cholesterol. The deficiency of niacin causes pellagra, a very widespread condition in poor areas of our country until the beginning of the '900, due to a diet

mainly consisting of corn, low in niacin and rich in antivitamin pp, a substance that combines with vitamin pp and makes it unavailable to the body. Typical symptoms of pellagra are dermatitis, epidermal spots and peeling, intestinal disorders, diarrhoea, up to neurological alterations, such as dementia. Niacin is widespread in foods of animal origin, and is synthesized by the body from the amino acid tryptophan so a protein-based diet guarantees a sufficient intake. The daily requirement is 6.6 mg per 1000 kcal taken.

#### Vitamin B5

Pantothenic acid (B5): very important vitamin in the protection from a series of pathological conditions, it is very common in all animal and plant foods, especially in the liver, egg yolk, legumes and brewer's yeast. It is deficient only in states of severe malnutrition, and its daily requirement is 3-12 mg per day.

#### Vitamin B6

Pyridoxine (B6): precursor of an important enzyme in the metabolism of nitrogen compounds, the presence of vitamin B6 influences the efficiency in the use of proteins by the body, but also the synthesis of haemoglobin and the metabolism of carbohydrates and lipids. B6 deficiency is quite rare, and usually causes apathy and weakness, and in some cases a form of hypochromic anaemia, where red blood cells are clearer than usual. It is very common among foods, in meat, fish, legumes and is also resistant to many industrial treatments. The daily requirement is estimated at least 1.1 mg per day for women and 1.5 mg per day for men.

#### Vitamin B12

Cobalamin (B12): is a group of substances containing cobalt, involved in the metabolism of fatty acids, amino acids and nucleic acids. The deficiency condition is quite rare, and can only occur in cases of a strict vegetarian diet. In this case, the stage of pregnancy is particularly delicate, where the deficiency in the mother can have very dangerous effects for the unborn child. However, the deficiency can also result from the absence of the factor that facilitates its absorption in the intestine, resulting in disorders of the nervous system and the production of blood cells, up to a form of anaemia defined as 'pernicious'. It is present in all animal foods in small quantities, particularly in liver, meat, fish in milk and eggs, and is resistant to cooking. Your minimum daily requirement, normally covered by your diet, is at least 2 mg per day.

# Vitamin B9

Vitamin B9 (folate) as a nootropic helps the brain produce dopamine, epinephrine, norepinephrine and serotonin. As a coenzyme, folate participates in the transfers of a carbon in

DNA and RNA synthesis. And it converts homocysteine into methionine which is used in the synthesis of s adenosyl-methionine (same). Folate is involved in gene expression, in the synthesis of amino acids and in the synthesis and repair of myelin. Green leafy vegetables, or "foliage", are rich sources of folate. And like "Folato" it took the name. You can also get folate from citrus juice, legumes, fortified foods (more on this controversy in the extended article) and liver.

Many neuro hackers, including doctors and other health professionals, confuse folate with folic acid.

They are not the same thing.

In the extended article, we explore the differences between folate and folic acid. And how vitamin B9 (folate) is essential for a fully optimized brain.

Being a nootropic, the dosage of vitamin b9 (folate) is 400 mcg per day.

Vitamin B9 is known to improve mood, energy, initiative, vigilance, concentration, psychomotor speed and social activity. Vitamin B9 (folate, folic acid, 5-methylenetrahydrofolate) is soluble in water and is one of the 8 B vitamins.

Folate works as a coenzyme in single carbon transfers in DNA and RNA synthesis. And it converts homocysteine into methionine which is used in the synthesis of s-adenosyl-methionine (same). [io]

As a nootropic, folate is also involved in gene expression, in the synthesis of amino acids, in the synthesis of myelin and is necessary for the synthesis of the neurotransmitters dopamine, epinephrin, norepinephrine and serotonin.

Many neuro hackers, including doctors and other health professionals, confuse folate with folic acid.

They are not the same thing.

In this article we will explore the differences between folate and folic acid. And how vitamin b9 (folate) is essential for a fully optimized brain.

Vitamin B9 (folate) helps:

- Brain optimization: folate is involved in DNA and RNA synthesis, genetic expression, amino acid synthesis and metabolism, as well as myelin synthesis and repair;
- Neurotransmitters: folate is necessary for the synthesis of dopamine, epinephrin and serotonin:
- Mood: in research environments it is believed that the involvement of folates in the synthesis of neurotransmitters is the main responsible for mood and cognitive functions. Also increasing the effect of SSRIS in subjects being treated for depression.

# Vitamin E (tocopherol)

Vitamin E is a necessary element for our body and is of considerable importance, as it has as its main characteristic of the anti-aging function because it has antioxidant properties, it is therefore a molecule that protects against free radicals, preventing aging. It also has the

function of strengthening our body's immune system. It is being studied if the activity of life. And can prevent or delay chronic diseases associated with the presence of free radicals. Vitamin E is also useful for preventing arteriosclerosis, thereby reducing the risk of heart attacks and cardio-vascular disease,. It also has the ability to lower the level of LDL, that is, that cholesterol considered 'bad' and harmful to our body.

#### **Functions:**

- Protects the skin from free radicals;
- Counteracts skin aging;
- Counteracts the onset of cardiovascular diseases;
- Protection of blood clots;
- · Reduces the formation of acne or eczema;
- Activity as an antioxidant;
- Reduces negative effects due to pollution and UV protection;

#### Selenium

Similar to Zinc, selenium is able to effectively counteract free radicals, implementing a defensive action against oxidative stress. In fact, selenium is involved in the activity of enzymes capable of combating oxidative stress, such as glutathione peroxidase. Like Zinc, selenium performs multiple beneficial actions in the body, including the regulation of the immune defences. Selenium:

- Is one of the components of glutathione peroxidase, an enzyme with antioxidant action;
- Is essential for the conversion of thyroid hormone t4 into its active form t3;
- Keeps the skin elastic by promoting the formation of collagen;
- We find it, like selenium-cysteine, in numerous proteins;
- Binds to heavy metals such as lead and mercury facilitating their elimination;
- Improves sperm motility;
- Protects against hypertension.

#### Zinc

Zinc has powerful antioxidant and anti-inflammatory effects. It is essential to combat autoimmune diseases, support healthy sexual and reproductive activity, increase cognitive function and muscle growth.

In athletes it has been shown that a fair value of Zinc present in the body, determines an increase in muscle performance by carrying out the task of promoting the production of hormones. Zinc also has an effect for post-workout recovery, affecting the metabolism due to the increased energy availability it provides to the muscle. Another relevant effect of zinc is to fight bacterial and viral infections. Another activity is at the level of the brain, in fact it is found in

high concentrations at the level of the hippocampus, which plays a fundamental role in though
and memory.