

## NON – NUTRITIONAL NATURAL ANTIOXIDANTS

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**Abstract.** *Within this group are framed the substances which are found in vegetal and animal organisms, but do not represent components of human alimentation, not being edible. They are found in great quantities, especially in the vegetal regnum.*

**Key words:** *antioxidants, non-nutrition, alpha-tocopherol.*

### Non-Nutritional Natural Antioxidants

Antioxidants	Sources	Roles
Ubiquinone (Coenzyme Q <sub>10</sub> )	In all cells of the body of animal origin: fish (salmon, macro, sardines), heart and liver of bovines	–participates in the chain of electronic transport –antioxidant role in reduced form: it protects the cellular membranes, together with vitamin E; it directly acts upon the radicals R-OO or reduces the tocopheroxyl radical to tocopherol –ubiquinolol-10, reduced form of ubiquinone-10 is a strong lipophilic AO –ubiquinolol-10 protects human LDL against lipoperoxidation much more efficiently than vitamin E; the plasmatic level of ubiquinolol represents a faithful index for the oxidative stress <i>in vivo</i> –CoQ <sub>10</sub> protects the ventricular function from lesions through ischemia-reperfusion in animals and in humans

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Flavonoids	<p>- medicinal tree Ginkgo Biloba contains ginkgoflavonoids (quercetin, cumaroil, kemferol, glucoramnosides)</p> <p>- rind of the maritime pine tree contains pycnogenol (procyanidins)</p> <p>- propolis contains the natural balsam prepared from honey</p>	<p>-strong AO agent <i>in vitro</i>, depurates <math>\text{OH}^\bullet</math>, <math>\text{O}_2^{\bullet-}</math>, <math>\text{H}_2\text{O}_2</math>, <math>\text{NO}</math></p> <p>-<i>in vivo</i> were tracked the effects of the therapy with the extract Egb 761; it diminishes platelet aggregation and stimulates the synthesis of prostacyclin.</p> <p>-it protects the myocardium from lesions through ischemia -reperfusion</p> <p>-tonic, role in increasing intellectual capacity, tranquilizing, antitumoral, antiviral, anti-inflammatory</p> <p>-it diminishes the cholesterol level and the formation of uric acid</p> <p>-chronic treatment with ginseng raises the HDL fraction, cAMP, stimulates the biosynthesis of phospholipids and of corticosteroid hormones.</p> <p>-it depurates the free radicals (<math>^1\text{O}_2</math>, <math>\text{O}_2^{\bullet-}</math>, <math>\text{OH}^\bullet</math>, lipoperoxides, <math>\text{NO}</math>)</p> <p>-it recycles the radicals ascorbyl/tocopheryl economizing the reserves of vitamin C and E</p> <p>-it amplifies the activity of AO enzymes (SOD, CAT, GSH)</p> <p>-it stimulates endothelium-dependent vasodilatation and it inhibits platelet aggregation.</p> <p>-it raises resistance to physical effort through economizing the reserves of AO, is cytoprotector, immunomodulator, anti-inflammatory, anti-edematous, it protects the skin from UV radiations, has a venotonic action in chronic venous insufficiency with static oedema</p> <p>-it has been proved that the ethanolic propolis extract protects mice from irradiation with <math>\gamma</math> rays</p> <p>-bactericide properties, bacteriostatic properties, antiseptic, cicatrisation properties, haemostatic, anesthetic, anti-inflammatory properties</p> <p>- strong antioxidant effect: depuration <math>\text{H}_2\text{O}_2</math>, <math>^1\text{O}_2</math>, lipoperoxides</p> <p>-depuration <math>\text{O}_2^{\bullet-}</math> is proportional to the degree of polymerization of the taniures</p>

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	<ul style="list-style-type: none"> <li>- the oak rind contains tannins</li> <li>- tea leaves, persimmon leaves contain tannins and phenylpropanoids (cumarins)</li> </ul>	<ul style="list-style-type: none"> <li>- cumarins exercise anti-inflammatory effects, through the inhibition of the lipo-oxygenase path and cyclo-oxygenase path of the arachidonic acid and blocks the generation of <math>O_2^{\bullet -}</math></li> </ul>
Metallothionein (MT)	<ul style="list-style-type: none"> <li>- ubiquitous proteins fixating transition metals Cd, Zn, Cu, Hg, Bi</li> <li>Obs. They occur under the action of exogenous inductive factors of SO: radiations, hyperoxia, cold, isolation, inanition, physical effort</li> </ul>	<ul style="list-style-type: none"> <li>-MT are involved in numerous intracellular functions: regulation of the mineral homeostasis for Cu, Zn, Cd through: control upon the expression of the genes for the regulation, synthesis and functional activity of the proteins (metalloproteins) and of the metal-dependent transcription factors especially for Zn (Zn MT prevail in the blood); control of the absorption of Zn and Cu; deposit for essential metals such as Zn and Cu and thereby contributes to the prevention of toxicity of the metals in case of antioxidants (Bi, Co, Cu, Zn, Hg, Cd; donation of metals for water-metal-proteins in physiological conditions, a process which is facilitated by GSH; control of the hepatic metabolism of Zn and Cu; antioxidant against SRO and SRN, with direct action <i>in vitro</i> and indirect <i>in vivo</i>.</li> <li>- <i>in vivo</i> the protective action of MT has been indirectly, experimentally proved: through the supra-expression of MT in transgenic mice they offer a direct model for the physiological role of MT; through the protection offered against lesions induced by the oxidative stress in cultures of epithelial human cells (HE) and mouse fibroblasts (C1 1D); through protection against the oxidative stress induced by radiations: ZnMT and CdMT are deparators of <math>OH^{\bullet}</math> and <math>O_2^{\bullet -}</math>; in the protective action are involved 20 atoms SH of cysteine; the effect is predominantly AO against <math>OH^{\bullet}</math> and is 340-800 times superior to GSH; through the inhibition of the lipoperoxidation in erythrocytes incubated with ZnMT and CdMT</li> </ul>

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		<ul style="list-style-type: none"> <li>- in humans, there have been evinced high values of MT in the liver and in the kidneys, in some congenital diseases such as Wilson disease and Menke disease, during the gestation and postnatal period, in some pulmonary tumours and in cardiac affections (ischemia-reperfusion lesions, cardiac hypertrophy)</li> </ul>
<p>Superoxide-dismutase (SOD)</p> <p><i>CuZnSOD (SOD-1)</i></p> <p><i>Extra-cellular CuZnSOD (EC-SOD or SOD-3)</i></p>	<ul style="list-style-type: none"> <li>- liver, brain, lungs, hematies</li> <li>- plasma, lymph, synovial liquid</li> </ul>	<ul style="list-style-type: none"> <li>-CuZnSOD plays a major role in the first antioxidant line of defence, through catalyzing the dismutation of the radicals <math>O_2^{\bullet-}</math></li> <li>-antioxidant action, ensured by the enzymatic couple SOD + CAT; both enzymes have high reaction speeds</li> <li>-pharmacological effects depending on the administered dose; small doses have moderated protective effect upon the extension of infarct in rabbits; high doses (50 <math>\mu\text{g}/\text{kg}</math>) raise the dimension of the infarct</li> <li>-prevention of the formation of the chemotactic factor for neutrophils, the formation depending on <math>O_2^{\bullet-}</math></li> <li>-the modification (inversion) of the inhibiting effect of MDA upon the relaxation of the arterial wall, induced by Ach, on precontracted veins with NA)</li> <li>-protection of dehydrases, inhibition of the formation of methHb through the anions of <math>O_2^{\bullet-}</math>, inhibition of the peroxidation PUFA</li> <li>-anti-apoptotic role (SOD exercises an indirect anti-apoptotic effect, through the inhibition of the apoptotic effect of <math>H_2O_2</math>)</li> <li>-rise of the production of NO on the endothelial level of its activity</li> <li>-role upon the neurobehavioral functions; EC-SOD was involved in the learning process: in mice, the phenotypic expression of the genotypic alterations of the production of EC-SOD is characteristic for spatial learning and memory</li> </ul>

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		<ul style="list-style-type: none"> <li>-daily administration ameliorates inflammatory cutaneous reactions</li> <li>- SOD is involved in: allergy, cancer, cardiovascular and arteriosclerosis ischemic lesions, infections with <i>Helicobacter pylori</i>, infections with viruses, genetic diseases (Down syndrome), neurodegenerative diseases: Alzheimer disease, amyotrophic lateral sclerosis, Huntington disease, Prion disease; cataract</li> </ul>
Catalase (CAT)	- liver	<ul style="list-style-type: none"> <li>-detoxification H<sub>2</sub>O<sub>2</sub></li> <li>-role in growth and development</li> <li>-oxidation of ethanol</li> <li>-tumour protection evinced through experimental studies</li> <li>-inhibition of apoptosis</li> <li>-CAT has been involved in cancer, infections with viruses, genetic diseases: chronic granulomatous disease, diabetes, cataract</li> </ul>
Glutathione (GSH)	- liver	<ul style="list-style-type: none"> <li>-important depurator of OH<sup>•</sup> and <sup>1</sup>O<sub>2</sub></li> <li>-regulation of the cellular sulphhydryl redox status</li> <li>-role in growth and development</li> <li>-regulation of the metabolism of the leukotrienes and PG</li> <li>-immune function</li> <li>- it is involved in viral, neurodegenerative, pulmonary diseases</li> </ul>
Ceruloplasmin		<ul style="list-style-type: none"> <li>-protein of acute phase, with an anti-inflammatory role, against SRO liberated by the macrophages and as inhibitor of the reactions mediated by SRO, through blocking the formation of hydroxylanions and of lipoperoxides</li> <li>-it fixes Cu ions and prevents reinitiating the reactions</li> <li>- it acts as feroxidase, transforming Fe<sup>2+</sup> into Fe<sup>3+</sup></li> </ul>
Melatonin (ML)		<ul style="list-style-type: none"> <li>-the protective determinant role of ML in oxidative stress may be:</li> <li>-primary, direct, as direct depurator OH<sup>•</sup>; secondary, indirect through: stimulating effect upon GSH-Px,</li> </ul>

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		<p>which decomposes <math>H_2O_2</math>; stimulating effect upon SOD, inhibiting the formation of <math>^1O_2</math> and <math>H_2O_2</math>; inhibitor of lipoperoxidation</p> <ul style="list-style-type: none"> <li>-anti-apoptotic effect proved through the reduction of the DNA fragmentation</li> <li>-inhibitor of 5-lipoxygenase, enzyme involved in the synthesis of the leukotrienes</li> <li>-it suppresses the NOS activity, probably through coupling the calmodulin</li> <li>-favorable effects in neurodegenerative diseases, protective effects towards paraquat and <math>CCl_4</math>, ionizing radiations</li> <li>-potential remedy for HIV due to the inhibiting action against NF-<math>\kappa</math>B induced by the cytokines, mitogens and ionizing reactions</li> <li>-it inhibits the LDL oxidation at supra-physiological concentrations</li> <li>-favourable effects upon cardiac arrhythmia, the nephrotoxicity induced by cyclosporine A and gentamicin</li> <li>- favourable influences upon the cellular and humoral immune response</li> </ul>
Estrogens		<ul style="list-style-type: none"> <li>-it inhibits the peroxidation of fats (lipids: estrona 11, estradiol 12 and 2-OH-<math>E_2</math>13)</li> <li>-17 <math>\beta</math>-estradiol has AO activity at physiological concentrations</li> <li>- the administration at supra-physiological concentrations reduces the lipoperoxidation lesions in the myocardium and in the skeletal muscle both <i>in vitro</i> and <i>in vivo</i></li> </ul>
Polyamines	- liver: putresceine, spermidine, spermine	<ul style="list-style-type: none"> <li>-antilipoperoxidating action through the capacity to fix on the membranal phospholipid</li> <li>-spermine stabilizes <math>\alpha</math>-tocopherol 1, carotenoids</li> <li>-anti-inflammatory action (it chelates the metals, it inhibits the proliferation of lymphocytes, diminishing the secretion of IL-2)</li> </ul>

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		<ul style="list-style-type: none"> <li>-high affinity for Fe, protecting the tissues in inflammatory processes</li> <li>-anti-radiation action</li> <li>-anti-mutagenous action (protector effect of spermine upon DNA exposed to SO)</li> <li>- useful in neurodegenerative diseases, they prevent the toxicity of the paraquat</li> </ul>
$\alpha$ -lipoic acid	<p>- it was evinced in the form of lipoil-lysine in different natural sources, especially in vegetal stuff: spinach &gt; flower buds of broccoli &gt; tomatoes &gt; peas and Brussels cabbage &gt; rice bran; in animal tissues, lipoil-lysine has been evinced in bovines, in kidneys &gt; heart &gt; liver &gt; spleen &gt; brain &gt; pancreas &gt; lungs</p>	<ul style="list-style-type: none"> <li>-depuration effect of the free radicals (<math>\text{OH}^*</math>, <math>\text{HOCl}</math>, chelation of the transition metals, especially Fe and Cu)</li> <li>-regeneration of other AO (C vitamin, <math>\alpha</math>-tocopherol, GSH, ubiquinolol)</li> <li>-inhibition of NF-kB activation, with favorable effects in HIV, arteriosclerosis, diabetes</li> <li>-lipoate presents in clinics a special importance as tiol regenerator and redox modulator agent; it intervenes in producing energy and in reducing equivalents</li> <li>-it has been evinced that the treatment with lipoate selectively facilitates the death of the cancerous cells through intensifying the inductible activity of capsase 3, the protease of death</li> <li>- the unique property of the lipoate is <i>metabolic AO</i></li> </ul>
Adenosine		<ul style="list-style-type: none"> <li>-it inhibits the production of <math>\text{O}_2^{\bullet-}</math> by the human neutrophils in culture with FMLP</li> <li>- protective against lesions with postischemic re-oxygenation</li> </ul>
Nicotinamide		<ul style="list-style-type: none"> <li>- prolonged ingestion of the nicotinic acid leads to the rise of <math>\text{NAD}^+</math> in the circulating lymphocytes, determining resistance to the oxidative aggression</li> </ul>
Lactoferrin	- human secretions (milk, saliva, tears, nasal secretions)	<ul style="list-style-type: none"> <li>- protein fixating the Fe ions, is an endogeneous acid AO on the level of the mucous membranes</li> </ul>
Arginine		<ul style="list-style-type: none"> <li>-it is the precursor of NO</li> <li>-Arginine ameliorates the reperfusion lesions after the ischemia of the myocardium</li> <li>- inhibits the liberation of <math>\text{O}_2^{\bullet-}</math></li> </ul>

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Potassium		–it inhibits the generation of $O_2^{\bullet -}$ by monocyit-macrophage cells and PMN circulation
Copper		– organic complexes of Cu, they have anti-inflammatory, analgesic, anti-diabetic, anticonvulsive, anti-ulcerous, anti-carcinogeneous effects

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