Ametis Joint Stock Company

APPLICATION OF **DIHYDROQUERCETIN** IN PRODUCTION OF DIETARY SUPPLEMENTS

Dihydroquercetin is the natural antioxidant of plant origin, bioflavonoid. Dihydroquercetin as an ingredient of phenolic compounds is found in many kinds of herbs and shrubs, but only in several kinds of trees dihydroquercetin is found to a greater extend. Dihydroquercetin, produced by Ametis JSC under the trade mark **"Lavitol",** is a flavonoid, derived from Dahurian Larch (Larix gmelinii) by a water-ethanol extraction method.

Dihydroquercetin extract is an active antioxidant that could slow down oxidative reactions. The level of antioxidative activity allows to put dihydroquercetin on the first positions among the substances with similar spectrum of action.

Dihydroquercetin has a wide range of pharmacological properties. All these activities support the use of Dihydroquercetin **in manufacturing of bioactive food additives**.

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This document was made by managers of Ametis JSC

Health-Related Benefits of Dihydroquercetin

(based on studies, researches, reports)

Dihydroquercetin as Antioxidant

- Dihydroquercetin exhibited protective actions against the oxidative injury induced by xanthine/xanthine-oxidase in primary cultured rat cortical cells. The protective effect Dihydroquercetin was maintained at 300 mcg/ml *(Dok-Go, H., Lee, K.H., et al. Brain Research, 965 (2003) 130-136).*
- Dihydroquercetin showed high inhibitory activity toward nicotinamide adenine dinucleotide phosphate (NADPH) oxidation and xanthine oxidase-dependent superoxide ion degeneration *(Steffen, Y., Gruber, C., et al. Archives of biochemistry and Biphysics, 469 (200) 209-219).*
- Dihydroquercetin showed the highest peroxyl radical [generated by thermal decomposition of DPPH scavenging properties (stoichiometric factor 4.7 mole/mole)] among the tested compounds. The effect of Trolox was much less (stoichiometric factor 2.0 mole/mole) *(Willfor, S.M., Ahotupa, M.O., et al. J Agric Food Chem, 51 (2003) 7600-7606).*
- Dihydroquercetin significantly increased the resistance of rat liver microsomes to lipid peroxidation induced by NADPH-Fe^{2+} (*Kravchenko, L.V., Morozov, S.V., Tutel'yan, V.A. Bulletin of Experimental Biology and Medicine, 6 (2003) 572-575*).
- Dihydroquercetin significantly lowered the amount of MDA in the homogenate with Fe2+ and NADPH- induced lipid peroxidation (*Kolhir, V.K., Bykov, V.A., Baginskaja, A.I., et al. Phytotherapy Research, 10 (1996) 478-482*).
- Dihydroquercetin inhibited brain mitochondrial lipid peroxidation induced by ferrous sulfate *(Ratty, A.K., Das, N.P. Biochemical Medicine and Metabolic Biology, 38 (1988) 69-79)*.
- Dihydroquercetin dose-dependently inhibited phorone (diisopropylidene acetone)-induced spontaneous lipid peroxidation in phenobarbital-induced rats (*Younes, M., Siegers, C.-P. Planta Medica, 43 (1981) 240-244)*
- Dihydroquercetin at 100 mg/kg significantly lowered MDA levels in a liver homogenate of rats with tetracycline-elicited hepatitis (*Kolhir, V.K., Bykov, V.A., Baginskaja, A.I., et al. Phytotherapy Research, 10 (1996) 478-482*).
- Dihydroquercetin significantly decreased the levels of the primary and secondary products of lipid peroxidation in patients with arterial hypertension of the II and III degree *(Plotnikov, M.B., Tyukavkina, N.A. 2005).*
- Dihydroquercetin significantly decreased the primary and secondary products of lipid peroxidation in patients with cerebral atherosclerosis in a randomized, controlled study (*Plotnikov, M.B., Tyukavkina, N.A. 2005*).
- Dihydroquercetin as an adjunct to the basic therapy, significantly decreased the levels of MDA in cell membranes and increased activity of SOD, catalase and glutathione peroxidase in erythrocytes in patients with type 2 diabetes mellitus (*Plotnikov, M.B., Tyukavkina, N.A. 2005*).
- Dihydroquercetin, as an adjunct to the basic therapy, decreased the levels of primary products of lipid peroxidation in patients with ischemic heart disease in a randomized, open, placebo-controlled, parallel study *(Plotnikov, M.B., Tyukavkina, N.A., et al. 2005).*
- Dihydroquercetin, as an adjunct to the basic therapy, decreased the levels of the primary and secondary products of lipid peroxidation in patients with type 2 diabetes mellitus *Plotnikov, M.B., Tyukavkina, N.A., et al. 2005).*
- Dihydroquercetin, as an adjunct to the basic therapy, significantly decreased the levels of MDA in cell membranes and increased activity of SOD, catalase and glutathione peroxidase in erythrocytes in patients with type 2 diabetes mellitus *(Nedosugova, L.V., Volkova, A.K., et al. Klinicheskaya Farmacologiya I Therapiya [Clinical Pharmacology and Therapy, 4 (2000) 65-67]).*
- Dihydroquercetin, as an adjunct to the basic therapy, lowered the MDA, increased the levels of catalase and SOD in patients that underwent an operation on ovaries *(Plotnikov, M.B., Tyukavkina, N.A. 2005).*
- Dihydroquercetin, as an adjunct to the basic therapy, decreased levels of the secondary products of lipid peroxidation and increased levels of plasma catalase, glutathione peroxidase and SOD in women with Lyme disease (*Plotnikov, M.B., Tyukavkina, N.A. 2005*).
- Dihydroquercetin as an adjunct to the basic therapy, lowered the content of diene conjugates and of TBARS [thiobarbituric acid reactive substances] in blood plasma; decreased serum levels of ceruplasmin, and elevated serum levels of α-tocopherol in patients with acute pneumonia in a controlled study *(Kolhir, V.K., Bykov, V.A., Teselkin, Yu.O., et al. Phytotherapy Research, 12 (1998) 606-608).*

HEALTH-RELATED BENEFITS OF DIHYDROQUERCETIN

Dihydroquercetin as Cardioprotective Agent

Circulation Enhancer

- Dihydroquercetin, as an adjunct to the basic therapy, strengthened the capillary walls, decreased capillary permeability, and increased number of capillaries in patients with chronic microcirculatory disturbances due to arterial hypertension, atherosclerosis, ischemic heart disease, diabetes, etc (*Kozlov, V., Azizov, G., et al. Capilar in correction of microcirculatory disturbances. Vrach [Physician] 6 (2006)).*
- Combined with ascorbic acid, Dihydroquercetin improved hemorheological indices in a model of high viscosity syndrome developed after myocardial infarction in Wistar rats. Improved deformability of erythrocytes resulted in a decrease in blood viscosity *(Plotnikov, M.B., Aliev, O.I., Maslov, M.Ju., et al. Phytotherapy Research, 17 (2003) 86-88.)*
- Dihydroquercetin, as an adjunct to the basic therapy, increased deformability of erythrocytes and decreased the level of fibrinogen in patients with ischemic heart disease and decreased blood viscosity in patients with ischemic heart disease after myocardial infarction in a randomized, open, placebo-controlled, parallel study (*Plotnikov, M.B., Tyukavkina, N.A. 2005*).
- Dihydroquercetin, as an adjunct to the basic therapy, had positive effects on the haemorheological status in people with ischemic heart disease in a randomized, controlled study (*Tyukavkina, N., Pavlyukova, E., Bogach, E., et al.)*.
- Dihydroquercetin, as an adjunct therapy, showed vasotrophic action, stimulated blood microcirculation and rheological indices, decreased arterioles' constriction, and stabilized barrier function in patients with chronic microcirculatory disturbances due to arterial hypertension, atherosclerosis, ischemic heart disease, diabetes, etc. *(Kozlov, V., Azizov, G.,et al. Vrach [Physician] 6 (2006)).*
- Dihydroquercetin, as an adjunct to the basic therapy, enhanced microcirculation and lowered levels of fibrinogen in patients with peripheral atherosclerosis, in randomized, controlled study *(Tikhonov, V.I. , Tomsk (2008)).*
- Dihydroquercetin, as an adjunct to the basic therapy, improved microcirculation in patients with atherosclerosis of the lower extremities (*Koshkin, V.M., Nastavsheva, O.D. Spravochnik Policlinicheskogo Vracha [Reference Book of the Out-Patient Physician] 5 (2008))*
- Dihydroquercetin, as an adjunct therapy significantly improved microcirculation, increased number of capillaries, decreased arteriole constriction, and improved central and peripheral hemodynamic and blood oxygenation in patients with ischemic heart disease after aorta-coronary shunting surgery *(Shakula, A., Belyakin, C.A., et al. Vrach [Physician], 5 (2007)).*
- Dihydroquercetin normalized the indices of tissue and organs' microcirculation, increased blood oxygenation, and improved rheological blood parameters in patients with chronic pulmonary obstructive disease *(Shakula, A., Shegol'kov, A., et al. Vrach [Physician] November 2008).*

Simultaneous administration of Dihydroquercetin and acetylsalicylic acid to rats with cerebral ischemia lowered blood viscosity, aggregation of erythrocytes and the level of fibrinogen in the plasma while preserving the anti-aggregating effect of the drug (*Plotnikov, M.B., Yamkin, A.B., et al. [Experimental'naya i clinicheskaya pharmacologiya], 68(2) (2005) 33-35.*)

Dihydroquercetin and Blood Pressure Control

- Dihydroquercetin significantly decreased the frequency of headaches, lightheadedness, sleep disturbances and the number of complaints on disturbance in coordination, and improved cerebral microcirculation in the group of hypertensive patients with atherosclerosis in a randomized, double-blind, placebo-controlled study *(Britov, A.N., Aparina, T.V., 5 (2006) 46-53)*.
- Dihydroquercetin decreased the levels of the primary and secondary products of lipid peroxidation; increased deformability of erythrocytes and their aggregation and moderately decreased the level of fibrinogen; significantly decreased blood pressure, increased the systolic index, decreased to total peripheral resistance, decreased the frequency of headaches and fatigue, and improved short-term memory and psychomotor functioning of the cerebrum in patients with arterial hypertension of the II and III degree (*Plotnikov, M.B., Tyukavkina, N.A. 2005*).

HEALTH-RELATED BENEFITS OF DIHYDROQUERCETIN

Dihydroquercetin and Diabetes Mellitus

- Dihydroquercetin decreased functional activity of polymorphonuclear neutrophils (PMN) from non-insulin-dependent diabetes mellitus (NIDDM) patients. Dihydroquercetin decreased activities of protein kinase C and myeloperoxidase in activated polymorphonuclear neutrophils (PMN) and could bind Fe^{2+} ions *(Fedosova, N.F., Alisievich, S.V., et al. Bull Epx Biol Med, 2 (2004) 143-146).*
- Dihydroquercetin, as an adjunct to the basic therapy, decreased lipid peroxidation (LPO) in membranes of erythrocytes, lowered malondialdehyde (MDA) levels, increased the activities of superoxide dismutase (SOD), catalase, and glutathione peroxidase in red blood cells (RBC), and lowered antiaggregatory activity of thrombocytes in patients with type 2 diabetes mellitus in a controlled study *(Nedosugova, L.V., et al. Clinical Pharmacology and Therapy, 4 (2000) 65-67).*
- Dihydroquercetin, as an adjunct to the basic therapy, significantly decreased HbA1c levels and improved sensitivity to insulin in patients with type 2 diabetes mellitus in a randomized, placebo-controlled Study *(Nedosugova, L.V. Vrach [Physician], 7 (2006)).*
- Dihydroquercetin, as an adjunct to the basic therapy, significantly decreased malondialdehyde levels and coefficient of intoxication, as determined by the level and value of oligopeptides in patients with diabetes-related onychomycosis of feet and hands in a controlled study *(Davudova, T.B., Zoloeva, E.I., 7 (2009)).*
- Supplemented to patients with diabetic retinopathy with Dihydroquercetin inhibited the development and progression of diabetes related complications in the blood vessels *(Nedosugova, L.V. Vrach [Physician], 7 (2006)).*
- Dihydroquercetin, as an adjunct to the basic therapy, improved vision and stabilized the eye fundus in patients with diabetic retinopathy in a controlled study (*Plotnikov, M.B., Tyukavkina, N.A. 2005*).
- Dihydroquercetin increased deformability of erythrocytes and their aggregation and moderately decreased the level of fibrinogen in patients with arterial hypertension of the II and III degree *(Plotnikov, M.B., Tyukavkina, N.A., et al. 2005).*
- Dihydroquercetin reliably decreased the levels of both base and adenosine 5'diphosphate (ADP)- or thrombin-induced cytoplasmic Ca^{2+} in a thrombocyte suspension *(Kubatiev, A.A., Yadigarova, Z.T., et al. Pharmaceutical Chemistry Journal, 33 (1999) 629-630).*
- Dihydroquercetin at 5 mcM increased the content of cyclic nucleotides- adenosine monophosphate (cAMP) and cyclic guansoside monophosphate (cGMP) in native and thrombin-activated human platelets due to inhibition of phosphodiesterases *(Kubatiev, A.A., Yadigarova, Z.T., et al. Pharmaceutical Chemistry Journal, 33 (1999) 629-630).*
- Combined with ascorbic acid, Dihydroquercetin decreased the content of plasma fibrinogen and erythrocyte aggregation in a model of high viscosity syndrome developed after myocardial infarction in Wistar rats *(Plotnikov, M., Aliev, O.I., et al. Phytotherapy Research, 17 (2003) 86-88).*
- Dihydroquercetin, as an adjunct to the basic therapy, lowered antiaggregatory activity of thrombocytes in patients with type 2 diabetes mellitus *(Nedosugova, L.V., Volkova, A.K., et al. Clinical Pharmacology and Therapy, 4 (2000) 65-67).*
- Dihydroquercetin reduced hemolysis in red blood cells (RBC) induced by 2,2'-azobis(2-amidinopropane) dihydrochloride (AAPH) when measured by the hemoglobin content in the solution *(Chen, Y., Deuster, P. Chemico-Biological Interactions, 182 (2009) 7-12).*
- Dihydroquercetin protected human erythrocytes against oxidative hemolysis *(Haraguchi, H., Mochida, Y., et al. Biosci. Biotech. Biochem, 60(6) (1996) 945-948).*

Cholesterol Reduction

- Pretreatment of human hepatoma cell line, HepG2 cells, with Dihydroquercetin led to inhibition of cholesterol synthesis in a dose- and time-dependent manner, with an 86±3% inhibition at 200 μM observed within 24 hr. Dihydroquercetin was show to inhibit the activity of hydroxymethyl-glutaryl (HMG) CoA reductase reductase by 47±7%. Additionally, cellular cholesterol esterification, triacylglycerol and phospholipid synthesis were also significantly suppressed in the presence of Dihydroquercetin. ApoA-I secretion was found to increase by 36±10%, while there was an average reduction of 61±8% in labeled apoB in the medium (*Theriault, A., Wang, Q., et al. J Lipid Res, 41 (2000) 1969-1979.)*
- Dihydroquercetin, as an adjunct to the basic therapy, decreased very-low-density lipoprotein (VLDL-C) levels and increased HDL-C levels in patients with atherosclerosis in a randomized, controlled study (*Tikhonov, V.I. Tomsk, 2008*)
- Dihydroquercetin, as an adjunct to the basic therapy, decreased total cholesterol levels, VLDL-C levels, LDL-C levels, and triglyceride levels in patients with chronic venous insufficiency, in a randomized, controlled study (*Tikhonov, V.I. Tomsk, 2008*)
- Dihydroquercetin, as an adjunct to the basic therapy, decreased the levels of total cholesterol and triglycerides and increased the levels of HDL-C in patients with type 2 diabetes mellitus *(Nedosugova, L.V. Vrach [Physician], 7 (2006)).*

HEALTH-RELATED BENEFITS OF DIHYDROQUERCETIN

• Dihydroquercetin markedly reduced apoB secretion under basal and lipid-rich conditions up to 63% at 200 mcmol/L in HepG2 cells. Dihydroquercetin also inhibited microsomal triglyceride synthesis by 37% and its subsequent transfer into the lumen. The reduction of synthesis was due to a decrease in diacylglycerol acyltransferase (DGAT) activity *(Casaschi, A., Rubio, B.K., Maiyoh, G.K, et al Atherosclerosis, 176 (2004) 247-253).*

• Dihydroquercetin caused a 30-40% decrease in serum concentrations of β-lipoproteins and triglycerides in animals fed atherogenic diet. This effect was comparable to the effect of polysponin, an antilipidaemic agent *(Kolhir, V.K., Bykov, V.A., et al. Phytotherapy Research, 10 (1996) 478-482).*

Dihydroquercetin and Atherosclerosis

• Dihydroquercetin showed good protective activity toward oxidation of human low-density lipoproteins (LDL) *(Vuorela, S., Kreander, K., et al. J Agreic Food Chem, 53 (2005) 5922-5931).*

• Dihydroquercetin protected LDL against neutrophil-mediated modification [phorbol 12-myristate 13-acetate (PMA) –activated neutrophils] appears to act by inhibiting myeloperoxidase (MPO)-catalyzed oxidation.

•Dihydroquercetin inhibited copper ion- and 2,2'-azobis(2-amidinopropane) dihydrochloride (AAPH)-induced low-density lipoproteins (LDL) oxidation (Loke, W.M., Proudfoot, J.M., et al. J Agric Food Chem, 56 (2008) 3609-3615).

•Dihydroquercetin, as an adjunct to the basic therapy, improved microcirculation, significantly improved ability to walk longer distances without pain, and decreased the ischemic pain in the damaged extremity in patients with atherosclerosis of the lower extremities *(Koshkin, V.M., Nastavsheva, O.D. Reference Book of the Out-Patient Physician. 5 (2008)).*

•Dihydroquercetin, as an adjunct to the basic therapy, enhanced microcirculation, lowered fibrinogen levels, lowered VLDL-C, increased HDL-C, lowered glucose levels, lowered the coefficient of atherogenicity and lowered plasma C-reactive proteins (CRP) to undetectable levels in patients with atherosclerosis, in randomized, controlled study *(Tikhonov, V.I. Tomsk, 2008).*

• Dihydroquercetin significantly decreased the primary and secondary products of lipid peroxidation, increased erythrocyte deformability and the time of erythrocyte aggregation, decreased the number of complaints on headache, fatigue and sleep disturbance, and improved short-term memory and ability to concentrate in patients with cerebral atherosclerosis *(Plotnikov, M.B., Tyukavkina, N.A., et al. 2005).*

Dihydroquercetin and Ischemic Heart Disease

• Dihydroquercetin, as an adjunct therapy, improved microcirculation, increased number of capillaries, decreased arteriole constriction, improved central and peripheral hemodynamic and blood oxygenation, increased tolerance to exercise, and improved psycho-emotional conditions in patients with ischemic heart disease after aorta-coronary shunting surgery *(Shakula, A., Belyakin, C.A., et al.. Vrach [Physician], 5 (2007).*

• Dihydroquercetin, as an adjunct to the basic therapy, significantly decreased the number of anginal episodes/week in people with ischemic heart disease in a placebo-controlled study *(Tyukavkina, N., Pavlyukova, E., Bogach, E., et al., 2008).*

Dihydroquercetin and Chronic Venous Insufficiency

• Dihydroquercetin, as an adjunct to the basic therapy, enhanced microcirculation, lowered fibrinogen levels, lowered total cholesterol, increased HDL-C, lowered VLDL-C, LDL-C, and triglyceride levels, lowered coefficient of atherogenicity, and lowered AST and ALT levels in patients with chronic venous insufficiency, in a randomized, controlled study (*Tikhonov, V.I. Tomsk, 2008*).

• Administration of Dihydroquercetin excerpted vasotrophic effect; specifically, it stimulated the flow of blood in the tissues, stabilized functions of the microvessels, and decreased the capillary permeability in patients with chronic venous insufficiency *(Kozlov, V., Azizov, G., et al. Vrach [Physician], 7 (2006))*.

• Topical application of Dihydroquercetin normalized microcirculation, stabilized he barrier function of the capillaries, increased erythrocyte deformability, decreased intracapillary blood viscosity; decreased the feeling of heaviness and tiredness in the legs, decreased edema in the ankles and feet, led to disappearance of nighttime muscle spasms, increased the rate of capillary circulation, decreased the index of microcirculation, and improved overall well-being in patients with chronic venous insufficiency *(Kozlov, V., et al. Vrach [Physician], 7 (2008))*.

HEALTH-RELATED BENEFITS OF DIHYDROQUERCETIN

Dihydroquercetin as Anticarcinogenic Agent

Breast cancer

- Dihydroquercetin exhibited significant antiandrogenic and antiprogestational activity as revealed by its ability to block prostate specific antigen (PSA) production by more than 50% as indicated in the steroid hormone receptor-positive breast carcinoma cell line T-47D and BT-474 *(Rosenberg, R.S., Grass,L., et al., (1998) 939-939)*.

Colon cancer

- Dihydroquercetin induced significant quinone reductase activity, but displayed relatively low cytotoxicity to human colonic HCT116 cells. Sixty-five genes, including a few detoxification enzymes (phase I detoxification enzymes) and an antioxidant enzyme were up-regulated and 363 genes and the phase I detoxification enzyme were down-regulated in the presence of 60 mcM Dihydroquercetin. Moreover, Dihydroquercetin was shown to significantly activate antioxidant response element (ARE), but not xenobiotic response element (XRE), suggesting that Dihydroquercetin acts as a potential chemopreventive agent by regulating genes via an ARE-dependent mechanism (*Lee, S.B., Cha, K.H., et al. Biol Pharm Bull, 30(6) (2007) 1074-1079)*

Ovarian cancer

- Dihydroquercetin inhibited cell growth of the human ovarian cancer cell line OVCAR-3 *(Luo, H., Jiang, B.-H.,et al. Nutrition and Cancer, 60(6) (2008) 800-809).*

Prostate cancer

- Taxifolin inhibited cell growth and cell death in LNCaP prostate cancer cell lines via blockage of the enzymatic activity of FAS *(Brusselmans, K, Vrolix, R.,et al. J Biol Chem, 280 (2005) 5636-5645).*

- Dihydroquercetin, as an adjunct to the basic therapy, decreased the number of episodes of stenocardia, decreased the number of administered nitroglyceride, and moderately increased tolerability to physical exercise in patients with ischemic heart disease after myocardial infarction in a randomized, open placebo-controlled, parallel study *(Plotnikov, M.B., Tyukavkina, N.A., et al. 2005).*
- Dihydroquercetin in combination with ascorbic acid significantly attenuated ischemic damaged induced by circulatory disturbances in rats with experimental cerebral ischemia. Specifically, Dihydroquercetin decreased the number of irreversibly changed neurons, lowered the number of cells with increased levels of granular endoplasmic reticulum, promoted less marked increase in specific volume of lysosymes and lipofuscin, and improved functional activity of the brain cortex *(Plotnikov, M.B., Logvinov, S.V., et al. Bulletin of Experimental Biology and Medicine, 11 (2000) 1080-1083).*

Dihydroquercetin as Immunomodulating Agent

- Dihydroquercetin decreased the amount of inflammatory exudates in the peritoneum of rats *(Kolhir, V.K., Bykov, V.A., et al. Phytotherapy Research, 10 (1996) 478-482).*
- Dihydroquercetin showed significant anti-inflammatory activities similar to hydrocortisone in carrageenan-induced edema, formaldehyde-induced arthritis, and granulation tissue formation by cotton pellet implantation in albino rats *(Gupta, et al. Japan J Pharmacol, 21 (1971) 377-382).*
- Dihydroquercetin at 0.7 μM decreased peroxidase activity of the complex of cytochrome c with dioleyl cardiolipin by 50% as estimated by chemiluminescence with luminol. Additionally, Dihydroquercetin decreased the lipid production in a dose-dependent manner as was evident by coumarin C-525-activated chemiluminescence. Experiments performed on liver slices and mash showed that Dihydroquercetin has a low inhibitory effect on the lucigenin-dependent chemiluminescence in the tissue at concentrations higher than 100 μM. The authors concluded that the flavonoid decelerate radical production at the three stages that lead to apoptosis: superoxide radical production by the mitochondrial respiratory chain; formation of lipid radicals by the cytochrome c-cardiolipin complex; and chain oxidation of lipids initiated by these radicals (*Vladimirov, Yu.A., et al. Biochemistry, 74(3) (2009) 301-307*).
- Dihydroquercetin reduced nitric oxide production in a dose-dependent manner in activated macrophages *(Vuorela, S., Kreander, K., et al. J Agric Food Chem, 53 (2005) 5922-5931).*
- Dihydroquercetin has shown activity against herpes simplex virus, poliovirus, Sindibis virus, and respiratory syncytial virus, possibly by inhibition of viral polymerase and binding of viral nucleic acid or viral capsid protein (*International Journal of Antimicrobial agents, 26 (2005) 343-356*).
- Dihydroquercetin was shown to exhibit antibacterial properties against Enterococcus faecali, with high-scoring functions and good binding affinities, docked well with β-ketoacyl carrier protein synthase (efKAS III), resulting in MIC values of 128 μg/ml. Interestingly enough, the reference molecule, thiolactomycin, a known antibiotic inhibitor of ecKAS III has MIC value of 256 μg/ml *(Jeong, et al. J Nat Prod, 72 (2009) 719-724).*

HEALTH-RELATED BENEFITS OF DIHYDROQUERCETIN

Dihydroquercetin as Neuroprotective Agent

• Dihydroquercetin exhibited protective actions against the oxidative injury induced by hydrogen peroxide in primary cultured rat cortical cells. Moreover, the protective effect of Dihydroquercetin was maintained at 300 μg/ml (*Dok-Go, H., Lee, K.H., Kim, H.J, et al. Brain Research, 965 (2003) 130-136*).

• Dihydroquercetin exhibited a dose-dependent suppression effect of nitric oxide production from lipopolysaccharide (LPS)/gamma-interferon (INF-γ) stimulated C6 astrocyte cells *(Soliman, K.F.A., Mazzio, E.A. P.S.E.B.M., 218 (1998) 390-397).*

• Dihydroquercetin significantly decreased the primary and secondary products of lipid peroxidation, increased erythrocyte deformability and the time of erythrocyte aggregation, decreased the number of complaints on headache, fatigue, and sleep disturbances, and improved
short-term memory and ability to concentrate in patients with cerebral atherosclerosis in a randomized, controlled study (*Plotnikov, M.B., Tyukavkina, N.A. 2005*)

• Dihydroquercetin in combination with ascorbic acid significantly attenuated ischemic damaged induced by circulatory
disturbances in rats with experimental cerebral ischemia. Specifically, Dihydroquercetin decreased the number of irreversibly changed neurons, lowered the number of cells with increased levels of granular endoplasmic reticulum, promoted less marked increase in specific volume of lysosymes and lipofuscin, and improved functional activity of the brain cortex (*Plotnikov, M.B., Logvinov, S.V., Pugachenko, N.V. Bulletin of Experimental Biology and Medicine, 11 (2000) 1080-1083).*

•Dihydroquercetin, as an adjunct to the basic therapy, decreased the frequency of headaches, improved memory, optimized the state of awakening, and significantly improved psycho-emotional state in patients with discirculatory encephalopathy (*Zavolokov, I.G., Ilyuhina, B.A. Report. 2001*).

• Dihydroquercetin in combination with ascorbic acid relived headache, reduced vertigo and fatigability, and improved cognitive function in patients with stages I and II vascular encephalopathy (Plotnikov, M.B., Plotnikov, D.M., et al., 104(12) (2004)33-37).

Dihydroquercetin as Ophthalmoprotective Agent

• Dihydroquercetin inhibited cell death induced by glutathione (GSH) depletion and t-butyl peroxide (tBOOH) treatment in stress in the immortalized retinal ganglion cell line, RGC-5 cells *(Maher, P. & Hanneken, A. Invest Ophthalm Vis Sci, 46 (2005) 4796-4803)*

•Dihydroquercetin [+ Ascorbic acid, 1:2.5] led to disappearance of foci of injuries and limited blood supply disorders in the retina and destruction of neurosensory and glial cells in rats exposed to high-intensity light *(Logvinov, S.V., Plotnikov, M.B., et al. Bulletin of Experimental Biology and Medicine, 140(5) (2005) 578-581).*

•In combination with other antioxidants, Dihydroquercetin reduced destruction of the pigment epithelium and radial glia and reduced the area of lesion foci in rats exposed to high-intensity light *(Logvinov, S.V, et al. Bulletin of Experimental Biology and Medicine, 144(1) 100-102).*

•Dihydroquercetin in combination with standard pharmaceutical drugs improved regeneration of eye tissue in rabbits with chemical eye burn (*Gakhramanov, F.S. Bulletin of Experimental Biology and Medicine, 140(3) (2005) 289-291*)

•Dihydroquercetin, as an adjunct to the basic therapy, improved vision and stabilization of the eye fundus in patients with diabetic retinopathy in a controlled study (*Plotnikov, M.B., Tyukavkina, N.A. 2005*)

Dihydroquercetin as Radioprotective agent

• Introduced by intraperitoneal injection at 24 mg/kg in the form of a solution in an ethanol-physiological solution (1:12) mixture 15-20 minutes before irradiation, Dihydroquercetin significantly reduced the radiation damage (10-100 cGY) in mice; specifically the cytogenic damage by approximately 45% similar to the effect of the reference drug aminoethyl-isothiuronium bromide (AETB)
(Zaichkina, S.I., Kondakova, N.V. et al. Pharmaceutical Chemistry Journal, 38(8) (2004) 405-410.).

• Dihydroquercetin administered per os at 100 mg/kg during the first 40 days after irradiation and 5 mg/kg during the
remaining 115 days of the experiment enhanced the endogenous antioxidant system and retarded the accumulation of reactive oxygen species in the plasma and liver of in the female BALB strain mice subjected to 4 Gy irradiation (*Teselkin, Yu.O., Babenkova, I.V., et al. Phytotherapy Research, 12 (1998) 517-519*)

DHQ IN PRODUCTION OF DIETARY SUPPLEMENTS

In spite of its relative novelty, the application of Dihydroquercetin is widespread in the manufacturing of different categories of products. By the end of December 2013, over 400 products with Dihydroquercetin were registered with the regulatory organs of the Russian Federation. Among these products, more than 170 were bioactive food supplements.

Food Supplements containing Dihydroquercetin

cardio - vascular diseases

- "Aronodiquertin" (Balzam, JSC)
- "Ardial" (Natyropharm, Co., Ltd)
- "Antitrombin" (MiraxBioPharm, JSC)
- "Divimet" (Inter-Service, Co., Ltd)
- "Dihydroquercetin" (Evalar, JSC)
- "Dihydroquercetin plus" (Parapharm, Co., Ltd)
- "Kapilar" (Diod, PC)
- "Novomegin" (Art Life, Co., Ltd)
- "Flavopectin" (Demetra-Product, Co., Ltd)

Strengthens the capillary walls, enhances the blood flow, prevents the formation of blood clots

protection of immunity

- "Antiorvin" (Balzam, JSC)
- "Araglin - D" (Diod, PC)
- "Mirra-Diovit" (Mirra-M, JSC)
- "Oxi Grissent" (Bios, Co., Ltd)
- "Rockilar immuno"
- "Flavocon-100" (Yalma, PC)
- "Ecopam Time" (Pharm Panto, Co., Ltd)

Increases resistance to viral infections and colds

eye diseases

- "Vizi Max" (Alina-Pharm)
- "Vizus" (Art Life, PC)
- "Oculist" (Diod, PC)

Improves the vision, strengths the walls, improves the blood vessels, prevents dystrophic changes in eyes

joint diseases

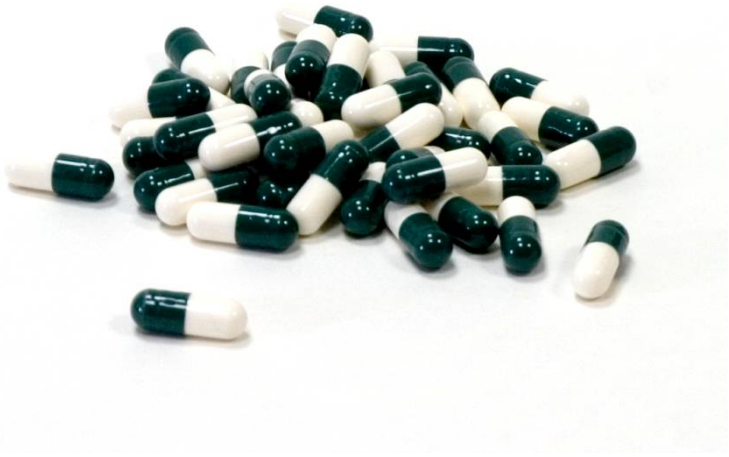
- "Artrocin" (Vis, Co., Ltd)
- "Regepart" (Pharma, JSC)
- "Sustadol" (Biotica-C, Co., Ltd)

Improves joint mobility, reduces the risk of developing osteoarthritis and osteochondrosis

weight loss and cellulite treatment

- "Gracio Plus" (Biofit, JSC)
- "Cellecaps" (Pharma, JSC)

Enhances lymphatic drainage function; reduces the risk of appearance and progression of cellulite



DIETARY SUPPLEMENTS PRODUCED BY AMETIS JSC

LAVIOCARD+

FOR CARDIO-VASCULAR SYSTEM

Composition:
Dihydroquercetin (extract of Dahurian larch wood) – 30 mg
Ascorbic acid – 70 mg
Other ingredients: lactose as filler material

Laviocard+:
- normalizes blood pressure;
- strengthens blood vessels and capillary walls;
- lowers levels of cholesterol;
- improves rheological blood properties

VitaLAG

IMMUNE BOOSTER

Composition:
Dihydroquercetin (extract of Dahurian larch wood) – 30 mg
Larch arabinogalactan – 230 mg

VitaLAG
- has restorative (immunostimulating) effect
- improves the regeneration of the mucous membrane of the stomach
- normalizes the intestine microflora
- promotes gastric and duodenal ulcer healing

LavitoForte

ADVANCED ANTIOXIDANT COMPLEX

LavitoForte:
- enhances body's resistance to negative factors, strengthens the natural defence mechanism of the organism.
- decreases the level of sugar in blood;
- improves cerebral circulation;
- inhibits inflammatory processes in the body

Composition:
Chaga extract – 270 mg
Resveratrol – 30 mg
Dihydroquercetin – 30 mg

FLUKOL SLIM

WEIGHT AND APPETITE CONTROL

Flukol SLIM:
- suppresses hunger;
- stimulates lipid and energy metabolism;
- accelerates fat oxidation and stimulates detoxification system;
- improves the efficiency of the digestive process.

Composition:
Garcinia extract – 150 mg
Larch arabinogalactan – 100 mg

LAVIOCARD Extra

BLOOD PRESSURE SUPPORT

Composition:
99% Lavitol (Dihydroquercetin) -100 mg
ascorbic acid – 70 mg

Laviocard Extra:
- normalizes blood pressure;
- relieves headaches, reduces the symptoms of vertigo;
- improves a functional condition of the cardiovascular system;
- normalizes cerebral circulation.

HEPATOLAG

RESTORE LIVER HEALTH

HepatoLAG:
- increases the liver resistance to adverse external factors;
- stimulates metabolic processes in liver and helps in the regeneration process of damaged liver cells;
- normalizes biliation and increases the intensity of bile secretion;
- enhances the strength and detoxification power of the liver.

Composition:
Milk thistle extract – 100 mg
Bark birch extract (betulin) – 30 mg

LAVIO SPORT

FOR ATHLETES

Composition:
Dihydroquercetin – 30 mg
L-carnitine-L-tartrate – 350 mg

- accelerates regeneration of the body after intensive exercise
- improves endurance and stamina
- supports the process of cellular respiration
- reduces tiredness and physiological strain
- strengthens the immune system

CHAGA MUSHROOM EXTRACT

ANTIOXIDANT IMMUNE SUPPORT

Chaga mushroom extract:
- improves metabolism and metabolic processes;
- restores normal intestinal flora;
- helps to remove toxins;
- improves cerebral circulation;
- normalizes blood pressure;
- boosts body resistance.

Composition: chaga extract - 50 g