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APPLICATION OF DIHYDROQUERCETIN IN THE PRODUCTION OF FUNCTIONAL NUTRITION

The effect of adverse environmental factors on the human body is combined with the activation of free radicals and the formation of the "oxidative" stress that can cause the development of several diseases. Thus, modern views on therapeutic and prophylactic nutrition were expanded with new concepts and ideas about food additives possessing antioxidant, anti-carcinogenic and tonic properties.

Dihydroquercetin is an antioxidant of natural origin with a high biological activity and a whole range of positive effects on metabolic reactions and the dynamics of different pathological processes. Due to its properties, the presence of dihydroquercetin in the composition of foods will ensure the prevention of several diseases and will also help to protect the body from harmful free radicals.

Moreover, dihydroquercetin can be recommended as a component of functional food for the prevention of dysbacteriosis of various etiology, secondary, immune deficiencies, cardiovascular diseases, protection from exposure to radiation, electromagnetic fields, and chemical pollution.

Currently the use of dihydroquercetin as a component in the diet of athletes is becoming increasingly popular.

Dihydroquercetin promotes the acceleration of regenerative processes of the body; normalize its functions after exercise.



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PROPERTIES OF DIHYDROQUERCETIN

Properties of Dihydroquercetin (DHQ)

1) Antioxidant properties

Dihydroquercetin is an antioxidant of direct action which binds free radicals. Dihydroquercetin inhibits free radical oxidation of both water soluble (luminol, ABTS) and fat-soluble substrates. Dihydroquercetin as antioxidant could function as (1) the "catcher" of active forms of oxygen, (2) chelator of metal with variable valency, (3) chainformative agent.

2) Capillary-protective

Dihydroquercetin decreases the pathological capillary fragility and increases the resistance of normal capillaries to trauma. Dihydroquercetin tends to maintain the normal tensile strength of capillary walls.

3) Anti-inflammatory

Dihydroquercetin reduces capillary permeability, inhibits action of many enzyme systems involved in the development of inflammation and allergy, reduces release of histamine and other mediators of inflammation from mast cells and basophils, limits action of kinins and anti-inflammatory prostaglandins to tissues.

4) Radioprotective

Dihydroquercetin slows the development of free radical oxidation, decreases lipid peroxidation activity induced by gamma irradiation. Some studies reveal the possible use of dihydroquercetin as pharmaceutical to defend the human organism from a lipid peroxidation effects which are activated under various pathologic conditions including general irradiation by gamma rays.

5) Detoxifying properties

Detoxifying properties of Dihydroquercetin are related to the direct interaction with toxins. Dihydroquercetin binds toxins into a stable form with the subsequent excretion from the organism.

6) Hepatoprotective

Dihydroquercetin has the positive effect on the liver function: normalizes the cell membrane and the structure of hepatocytes, has an antioxidant effect, accelerates the regeneration of damaged liver parenchyma, thereby enhances its detoxifying function.

Dihydroquercetin and atherosclerosis

- Combined with ascorbic acid and complex therapy DHQ improves hemoroheological indicators: viscosity of the blood due to the decrease of aggregation and increase of erythrocyte deformability, content of products of lipid peroxidation in erythrocytes and blood plasma reduces. (*Plotnikov M.B., Plotnikov D.M. // Journal of neurology and psychiatry, 2004*).

- Dihydroquercetin, as an adjunct to the basic therapy for patients with atherosclerosis and cerebrovascular pathology leads to the reduction in the frequency of the headache, noise in the head, dizziness, impaired coordination of movements. (*Britov A.I., Aparina T.V. // Doctor, 2006*).

- DHQ has a positive influence on the body functioning, resulting in reducing of the blood glucose level and the activity of transaminases. (*Tikhonov V.I., 2008*).

- Dihydroquercetin, as an adjunct to the basic therapy of peripheral atherosclerosis, leads to normalization of cholesterol metabolism. (*Tihonov V.I., 2008*).

DHQ and arterial hypertension

- DHQ contributes to the significant reduction of SBP, DBP, normalization of the night SBP variability, pulse pressure decrease. (*Belyakin S., 2007*).

- DHQ, as an adjust to the complex rehabilitation programs for patients with hypertension, has a positive influence on the subjective condition of patients, improves psychophysiological indexes (reducing the frequency of headaches, head noises, dizziness, improving health conditions, activity and mood enhancing). (*Belyakin S., 2007*).

- Dihydroquercetin, as an adjunct to the basic therapy, leads to a decrease of the concentration of NO₂ and NO₃ indicators in blood serum, that states the normalizing effect in endothelial function. (*Otanov R.G., 2005*).

PROPERTIES OF DIHYDROQUERCETIN

Dihydroquercetin κ Ischemic Heart Disease

•DHQ in combination with ascorbic acid and complex therapy helps to reduce the blood level of fibrinogen, decrease LPO processes. The reception of the DHQ is accompanied by the reduction of the blood viscosity among patients with the increased viscosity. (Plotnikov M.B., Pavlyukova E.N. // *Tromboz, gomostaz, reology*, [Thrombosis, Homeostasis, Rheology], 2005).

•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. (Plotnikov, M.B., Tyukavkina, N.A., et al. 2005).

•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 (Sakula A.V., Belyakin S.A. // *Vrach* [Physician], 5, 2007).

•DHQ affects the central and peripheral hemodynamics, improves intracardiac hemodynamics, improves external respiration` functions. DHQ eliminates the spasm of arteries, including coronary spasm, relieves spasm both in normal and atherosclerotic coronary arteries, which leads to the elimination of the microangiopathy. (Shakula A.V., Belyakin S.A.// *Vrach*, [Physician, 2007]).

Dihydroquercetin and Chronic Venous Insufficiency

•Topical application of DHQ normalized microcirculation, stabilized the barrier function of the capillaries, increased erythrocyte deformability, decreased intracapillary blood viscosity; decreased the feeling of heaviness and tiredness in the legs. (Kozlov, V., et al. 2008).

•DHQ leads to the improvement of rheological blood properties, disappearance of pain and discomfort in the lower extremities. (Kozlov, V., Azizov G.// *Vrach*, [Physician, 2007]).

•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. (Kozlov, V., et al. 2008).

DHQ and diabetes

•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 complex therapy of patients with the type II diabetes, leads to the reduction of the activity of the Na⁺/H⁺-exchanger in the membrane of erythrocyte and the increase of the NO production, which indicates of the DHQ influence on the functional activity of the valuable elements and the blood rheology. (Bslsbokin M.I., Nedosugova L.V. // *Problems of endocrinology*, 2003).

•DHQ leads to the significant decrease of the HbA1c level. (Nedosugova L.V. // *Vrach* [Physician]).

•Dihydroquercetin, as an adjunct to the basic therapy, decreased lipid peroxidation (LPO) in membranes of erythrocytes, lowered malondialdehyde (MDA) levels. (Dzuntceva E.I., Culagin V.I., 2003).

PROPERTIES OF DIHYDROQUERCETIN

DHQ and cholesterol

- Dihydroquercetin, as an adjunct to the basic therapy, decreased the levels of total cholesterol and triglycerides (*Nedosugova, L.V. Vrach [Physician], 7 (2006)*).
- 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*).
- DHQ and vitamin C, as an adjunct to the complex atherosclerosis therapy, leads to normalization of indicators of cholesterol metabolism, reduction the level of VLDL-cholesterol, decrease in coefficients of efficient blood atherogenic by increasing HDL-cholesterol. (*Tikhonov V.I. Report, 2008*)
- Dihydroquercetin, as an adjunct to the complex therapy of patients with the type II diabetes, leads to the reduction of the activity of the Na⁺/H⁺-exchanger in the membrane of erythrocyte and the increase of the NO production, which indicates of the DHQ influence on the functional activity of the valuable elements and the blood rheology. (*Bslsbokin M.I., Nedosugova L.V. // Problems of endocrinology, 2003*).

Antitumor effect of DHQ

- DHQ shows antitumor activity on cultures of malignant tumor cells (HEP-2 (epidermal larynx carcinoma) and Hela (carcinoma of cervix), connected with the activation of lipid peroxidation processes in malignant cells. (*Kontorschikova K.N., Alyasova A.V., 2008*).
- DHQ, as an adjunct to the complex therapy of patients with breast cancer can improve the quality of their lives, reduce the appearance of toxic side effects of chemotherapy drugs, regulate the process of formation and elimination of peroxides and exerts the immunomodulatory effect on the immune responsiveness of these patients. (*Alyasova A.V., Maikoparova S.Ch., Kontorschikova K.N., 2006*).
- DHQ as an adjunct to the complex therapy, allows to maintain a high level of functioning of the endogenous antioxidant mechanisms and strengthen body's detoxication abilities of patients with breast cancer, which is clinically showed by a decrease in the occurrence and severity of side toxicokinetics cytostatics. (*Maikoparova S.S. Abstract, 2010*)
- DHQ has a favorable effect on the immune status of patients with breast cancer, consists in increasing in the level of CD+16 cells and in immunoregulatory index and preventing a significant increase in CD+25 and CD+95 cells, contributes to the reduction of the immunosuppressive action of cytotoxic drugs, reduction the incidence of Staphylococcus. (*Maikoparova S.S. Abstract, 2010*)

EFFECTIVENESS OF DHQ IN THE PRODUCTION OF FUNCTIONAL NUTRITION

Effectiveness of the DHQ in the production of dry mixes for beverages of functional direction

- Addition of the DHQ in the powdered mixture for beverages contributes to the pharmaceutical features of the product: correlation of the blood pressure, strengthening of the capillary walls, increase immunity, normalization of the gastrointestinal track.
- Powdered mixtures for beverages on the basis of the DHQ make a positive impact on the dynamic of the body weight, biochemical and immunological status, functional resources of the body. (*Makrov P.P., Dantsev V.V., 2011*).
- Enrichment of the tea with the DHQ leads to the increase of the antioxidant activity of the beverage, its tonic features. (*Livshyc V.B., Shymanovsky N.L., 2008 (Patent)*).
- Addition of the DHQ in tea leads to increase its shelf life from 24 to 36 months, conservation of the maximum quantity of the nutrients, contained in tea. (*Livshyc V.B., Shymanovsky N.L., 2008 (Patent)*).

Confectionery

- During the animal experiments it was shown that addition of the DHQ in the confectionery protects the liver from pathology, caused by the various poisons, ionizing radiation, etc.
- Addition of the DHQ in the confectionery recipes slows lipid peroxidation in rats liver under the effect of CCl₄ (*Tyukavkina N.A., Rulenko I.A., Kolesnik Yu.A., 1997*)
- Normative-technical documentation for such products as "Chocolate with antioxidant" and "Chocolate for prophylactic use with dihydroquercetin" was intended on the basis of various researches for prevention a number of diseases associated with insufficient levels of antioxidants in the body and the disorder of permeability of capillaries (atherosclerosis, coronary heart disease, bronical diseases, etc.), (*Kondakova I.A., Tyukavkina N.A., 1997*)

Meat semi-finished products

- Addition of the DHQ to the beef mince for the production of semi-finished products leads to the decrease in cholesterol, also there is a downward trend in the blood viscosity and increase in hemoglobin levels. (*Ustinova A.V., Khvylya S.I., Belyakina N.E., 2006*)

Dairy products

- Enrichment of dry milk with the DHQ contributes to the optimization of the daily diet of a wide range of individuals, who are particularly exposed to a adverse environmental factors, including high physical activity and psycho-emotional stresses.
- Dairy products, enriched with the DHQ are to be recommended as an antioxidant therapy for people, living in areas with the adverse environmental conditions, including high radiation level.

Effectiveness of DHQ in the production of functional nutrition

Drinking and mineral water

- "Cosmetology clinic "Beauty Institute" CJSC carried out clinical trials on the "Aqua Minerale Beauty" drinking water, containing dihydroquercetin - 2 mg/ 100 ml. Four groups of patients were examined (each group contained 10 healthy patients). As a result of trials it was stated that the "Aqua Minerale Beauty" drinking water has a pleasant organoleptic properties, does not cause allergies and dyspepsia. There was a decrease in body weight among the patients of all 4 groups. The improvement in skin microcirculation was noted. A tendency to restore the hydro-lipid mantle of the skin was marked, the increase of skin moisture and turgor and restores the microrelief of the skin, increase epidermal thickness and decrease of its echogenicity were clinically revealed. (Dolzhenikova E.M., 2006).

Sparkling beverages

-Preliminary experiments, which were performed on animals, have revealed the potential of application of dihydroquercetin in the composition of carbonated soft drinks. Thus, the use of drinks made with the technology of kvass by fermenting baking yeast wort with the addition of a concentrate of kvass wort, juice of wild-growing raw materials and Taxifolin in a concentration of 6 mg/100 cm³ for 3 weeks contributed to the decrease fatigue, increase activity, improve psycho-emotional status. There was also an improvement of appetite and weight gain in experimental animals. Also, there was an increase in hemoglobin levels, decrease in cholesterol. (Pomozova V.A., Babij N.V., Bibik I.V., 2008).

- The analysis of the observation results on rats, which were subjected to cold exposure and received drinks containing dihydroquercetin, indicates an improvement of regulatory processes with respect to vascular tone, nerve conduction and muscle processes (improvement of processes repolarization of the ventricles). (Pomozova V.A., Babij N.V., Bibik I.V., 2008).

Regulations for the use of DHQ in food industry

The application of Dihydroquercetin in the food industry is regulated by the following normative documentations in the Russian Federation:

- According to the Decision of the State Chief Medical Officer dated November 14, 2001 No 36 "About the application of the Sanitary and Epidemiological Conclusion (SEC) 2.3.2.1078-01", dihydroquercetin is classified as an antioxidant;
- The Decision of the State Chief Medical Officer dated April 18, 2003 No 59 "About the application of SEC 2.3.2.1293-03" allows using dihydroquercetin for manufacturing of cream, chocolate, dry milk. The maximal content of Dihydroquercetin in these products is 200 mg/kg fat of the product;
- In the Technical regulations of the Custom Union TR CU 029/2012 «Safety Requirements for food additives, flavorings and technological auxiliary means" dated 20.07.2012, the hygienic standard of application of Taxifolin in concentrated cream, powdered milk, processed cheese and chocolate in the among of 200 mg/kg fat product is stated.
- GOST R 52791-2007. Canned milk. Dry milk. Specifications. Date of introduction: January 1, 2009;
- GOST R 53436-2009. Canned milk. Milk and cream sweetened condensed. Specifications. Date of introduction: January 1, 2011.
- GOST 53507-2009. Canned condensed milk with sugar. General technical conditions. Date of introduction: January 1, 2011.
- GOST R 54661-2011. Canned dairy products. Dry cream. Technical Requirements. Date of introduction: January 1, 2013.

PRACTICAL APPLICATION

Practical application of DHQ in the production of the functional products

-«Majeric-Ultra» biscuits with дигидрохверцетином («Rushleb» Ltd., Yaroslavl Sity).

Ingredients: wheat flour, salt, sugar, vegetable fat, milk whey, condensed, BAD CPD, yeast, vitamin E, dihydroquercetin (T. M. Flucol-D), lactulose, acidity regulator). Biscuits are intended for the prevention and correction of dysbacteriosis, proctology and gastrointestinal inflammatory and functional diseases, protection of the body exposed to chemical toxicants. Biscuits help to improve digestion, heal damaged mucous membranes, prevents the development of allergic reactions. (Uzefov I.V., Sheremet I.M., 2007).

- «Zdraviya zhelayu» chocolate («Russian biscuits» CJSC, Cherepovetsck Sity).

It is recommended at increased physical, and emotional stress. Ingredients: sugar, cocoa mass, cocoa butter, emulsifier lecithin, whey, condensed fermented, antioxidant dihydroquercetin, dry cow colostrum, vitamin E, dietary Supplement Kissel, flavour vanillin.

- «Profilakt 120/80» Fermented milk drink («Vimm-Bill`-Dann» JSC).

Ingredients: skimmed milk, whole milk, water, sugar, glucose-fructose syrup, concentrated purées, premix Vegetans, dihydroquercetin (60 mg per 100g), pectin, flavourings, dye - beta-carotene, acidity regulator, starter, probiotic cultures.

- «Vitagen - Blueberry with fructose» chocolate bar («Fakel-design » JSC).

Recommended as an additional source of bioflavonoids. The main effect of using dietary supplements is to maintain the permeability and structure of blood vessels, the prevention of sclerotic lesions.

Effectiveness of application of DHQ in the production of the beverage for functional purpose

- «Aqua Minerale Beauty» mineral water («PepsiCo Holdings» Ltd.)., Aqua Minerale Beauty is an innovative product for the Russian market: this clear sparkling water contains vitamin and mineral complex with plant extracts dihydroquercetin, which helps strengthen skin capillaries and helps to maintain its health, youth and beauty. Composition: purified potable water, carbon dioxide, dihydroquercetin - 2 mg/100 ml, natural mineral complex (sodium, potassium, magnesium, chlorine, calcium, sulfate), D-Biotin, B6, calcium Pantothenate)

- «Normoprotein» Cocktails («Maslyaninsky Food Factory» CJSC).

«Normoprotein» is recommended for: people whose food intake is insufficient and unbalanced; vegetarians who do not consume the vital proteins; smokers experiencing an increased need for vitamins b and C; at elevated physical and mental stress.

- Low-fat, diet cherry, pear, sea buckthorn, red rowan, aronia, black currant, apples fruit drinks («Michurinsk experimental center «M-Concl»).

It is used as a dietary product for patients with diabetes, in the prevention of overweight, cardiovascular diseases, Hypo - and avitaminosis. Composition: 1 gram of compote contains: ascorbic acid - 30 mg, dihydroquercetin - 10 mg, pectin - 0.5 mg., fresh or frozen fruits and berries.

EFFECTIVENESS OF APPLICATION OF DHQ IN THE PRODUCTION OF THE PRODUCTS FOR ATHLETES

DHQ does not contain doping components and can be recommended for widespread use in sports medicine (Bazaev V.V., Ledovskoy S.M. Centre of sport medicine Restart. Review, 2007).

The introduction of dihydroquercetin in the form of dietary supplements in the diet of highly trained athletes contributes to the improvement of speed-power capabilities of the neuromuscular system, aerobic and anaerobic performance. (Ordzhonikidze Z.G. Report, 2011).

The introduction of dihydroquercetin in the diet of athletes, involved in sports with a cyclic character of activity, during the "re" training technique, contributes to the inhibition of the process of "acidification" of the muscles, increase the number of repetitions at a given pace or to maintain a higher speed exercises. (Portnov Yu.M., Tkachuk A.P., Semyonov V.A., Report, 2006).

The inclusion of dihydroquercetin in the composition of products for athletes helps to normalize the functional state of body systems, to stimulate processes of cellular respiration and increase emotional stability and physical performance of athletes. (Tokaev E.S., Manukyan G.G., Titova M.E., 2009).

Course application of dihydroquercetin during 4 months promotes the preservation and overall athletic performance, positively affecting the factors limiting required physical activity, prevents chronic overexertion of individual organs and body systems. DHQ supports appetite during the training process, allowing you to maintain body mass during extreme physical exertion without the use of steroids and banned MK IOC. (Bazaev V.V., Ledovskoy S.M. Centre of sport medicine Restart. Review, 2007).

Efficiency of DHQ in dietary supplements for sports nutrition

Application of the dietary supplement on the basis of DHQ (Ingredients: L-carnosine 50 mg, dihydroquercetin - 10 mg, zinc 2.5 mg, selenium - 20 µg, Vitamin C - 20 mg, 5 mg, And 0.25 mg) provides the body's resistance to heavy physical activity and shortens the period of adaptation to extreme environmental factors, slows the aging process of cells and tissues of the body, has beneficial effects on the cardiovascular system.

Application of the antioxidant complex (dihydroquercetin 50 mg, L-carnosine 300 mg, selenium 40 mcg, zinc 15 mg, vitamin C 40 mg, vitamin E 10 mg, vitamin a - 0,5 mg) in the diet of athletes promotes health and reduce the negative effects of intense physical exertion (Manukyan G.G., Abstract, 2009)

Recommendations for application of DHQ for athletes

- Methodical recommendations of the State sanitary-epidemiological standardization of the Russian Federation No. 2.3.1.1915-04 of 2004 "Recommended levels of consumption of food and biologically active substances" establish adequate and top admissible levels of consumption of dihydroquercetin in quantities of 25 and 100 mg per day;
- The competitive intensity workouts dose of dihydroquercetin should be raised and on the eve of an important start can be up to 300 mg per day (for example: 50 mg at bedtime, 50mg in the morning after charging, 100 mg to 1 hour before the start and 100 mg after 10 minutes after the competition). Duration of the course is 4 months.