

Dihydroquercetin in the complex treatment of obesity in children

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and the creation of drugs based on it is due to the wide interest in the biological action of dihydroquercetin (DHQ). For the first time, DKV was isolated from flax in 1948 [1]. Chopped Siberian larch wood containing up to 3.5% flavonoids is used as a raw material source. In experimental studies in vitro and in vivo

antioxidant, anti-inflammatory, hepatoprotector, angioprotective, antiaggregant, hypolipidemic, antiarrhythmic, hypotensive, antiischemic effects of DHQ [1–3]. Developed and since 2000 registered in the Russian pharmaceutical market, a biologically active food supplement (BAA) for food Kapilar (10 mg of dihydroquercetin in 1 tablet).

To date, the effectiveness of DHQ has also been confirmed in a number of clinical studies in which dietary supplements Kapilar or pre-Diquertin was included in the standard therapy regimen for patients with exertional angina [2, 4, 5], in the early post-infarction period [6], patients with post-infarction cardioclerosis [7], patients undergoing reconstructive surgery on the coronary vessels [8], patients with hypertension and neurocirculatory dystonia of hypertonic type [9, 10], patients with chronic obliterating

diseases of the arteries of the lower extremities [11], patients with chronic obstructive pulmonary disease [12], acute pneumonia [13], patients with type 2 diabetes mellitus [14, 15].

It has been shown that the inclusion of DHQ in the regimens of standard therapy for various diseases led to a significant improvement in the parameters of external respiration functions, central and peripheral hemodynamics, oxygen blood generation, improvement of microcirculation, increase of tolerant to physical activity, improve the psycho-emotional state of patients and increase the therapeutic and rehabilitation effect

treatment, improve long-term results. Positive impact The effect of DHQ on microcirculation was expressed in an improvement in the rheological properties of blood and an increase in the active vasomotor mechanisms of microcirculation regulation. There was also a positive effect of the drug on the neurological condition of patients, which manifested itself in a significant reduction in the incidence of headache, the symptom of "noise in the head" and the frequency of cases of impaired coordination of movements.

In our study, we used DHQ in the treatment of obesity. In all countries of the world, there is an increase in the number of children and adolescents suffering from obese people [16]. Increasing prevalence of this disease

accompanied by a change in the structure of morbidity in childhood those and an increase in the number of adolescents with metabolic syndrome, arterial hypertension, non-alcoholic fatty liver disease and type 2 diabetes mellitus, which further leads to an increase in the disease risk of death in young adults [17, 18].

In the development of the above complications of obesity, an important role is played by there is oxidative stress [19, 20]. This process is accompanied by an increase in the level of free radicals, activation of lipid peroxidation, impaired metabolism of proteins and nucleic acids, suppression of glycolysis, inhibition of the activity of a number of enzymes (glucose-6-phosphatase, adenylatcyclase, etc.), which leads to dysfunction of many tissues [21]. An increase in the formation of free radicals is accompanied by a violation the work of antioxidant enzymes in the body, such as glutathione, superoxide dismutase, catalase, glutathione peroxidase.

The main goal of treating obese children is to gradually weight loss, leading to a decrease in the risk of developing diabetes mellitus and cardiovascular diseases [22]. For the prevention of complications neniya, along with the reduction of body weight, significant importance is attached to the treatment of associated disorders, such as violation of tolerance carbohydrate tolerance, dyslipidemia, insulin resistance, arterial hypertension, etc. To reduce the risk of metabolic complications, it is necessary it is also possible to carry out a complex of therapeutic measures aimed at for the correction of oxidative stress in this group of patients. One of the dietary approaches to increase antioxidant protection you of the body is the inclusion in the standard diet therapy of the source biologically active substances of plant origin with antioxidant action (flavonoids) [23].

We have conducted a study of the effectiveness of prescribing dietary supplement Kapilar in complex therapy in obese children. We observed 50 obese patients aged 10 to 17 years 11 months (average 13.03 ± 0.3 years), of which: 17 boys, 33 girls. By the principle of random sampling, all patients were divided

lines into two groups. The main group consisted of 35 patients aged 13.2 ± 0.4 years, including 12 (34.3%) boys and 23 (65.7%) girls. The control group included 15 children aged 12.6 ± 0.5 years (10 girls check - 66.7% and 5 boys - 33.3%). The groups did not differ significantly in the main clinical and laboratory parameters (Table 1).

During 21 days of observation, the children of both groups did not present any complaints. lyali. All children received a low-calorie diet, patients of the main group received dietary supplements Kapilar. The dynamics of body weight during the hospitalization was comparable in both groups: there was a decrease in weight by 6.7 ± 0.4 and 6.1 ± 0.7 kg, respectively, in the main and control groups, which was comparable to a loss of $7.3 \pm 0.2\%$ and $7.4 \pm 0.4\%$

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Table 1

The main clinical and laboratory parameters of children obese

Indicator	Main group (n = 35)	Control group (n = 15)
Gender (male/female)	12/23	5/10
Age, years BP	12.6±0.5	13.2±0.4
system, mm Hg Art.	121.6 ± 3.1	115.4 ± 1.9
BP diast., mm Hg Art.	75.5 ± 1.2	76.7 ± 2.5
heart rate	79.9 ± 2.3	74.0±2.3
BH	19.1±0.3	24.3 ± 3.7
Weight, kg	91.9 ± 4.9	83.7 ± 9.2
Height, cm	156.6 ± 6.1	152.1 ± 9.0
BMI	39.02 ± 3.6	36.7 ± 3.6

initial body weight. Body mass index (BMI) in the 1st group at the beginning The follow-up period was 39.02 ± 3.6 (97.9 ± 0.2 percentile), after 21 days it was 36.7 ± 3.6 (96.9 ± 0.4 percentile). In the control group, the same indicator was 31.4 ± 2.8 (96.7 ± 0.5 percentile) before treatment and 29.4 ± 2.9 (94.1 ± 0.8 percentile, p < 0.05) at the end of the study. At the same time, there was a decrease in

waist (from 100.8 ± 3.2 to 94.3 ± 2.8 cm) and hips (from 110.6 ± 2.2 to 104, 7 ± 2.09 cm) in the main group. In the control group, a positive dynamics of anthropometric indicators was also observed (decrease waist circumference from 95.1 ± 5.6 to 89.8 ± 5.7 cm, hip circumference from 103.9 ± 3.7 to 98.8 ± 3.3 cm).

All the average values of the general and biochemical blood tests, determined at the beginning of hospitalization and 21 days after the start of therapy, remained within normal limits.

Carrying out a standard glucose tolerance test revealed a violation decrease in glucose tolerance (IGT) in 11 patients (31.4%) of the 1st group and 3 (20%) patients of the 2nd group (Table 2). A repeat test after 21 days showed that impaired glucose tolerance persisted only in 6 (17.1%) patients of the 1st group and in none of the children.

ka 2nd group.

The mean HOMA-IR (Homeostasis Model Assessment of Insulin Resistance) index before treatment was 5.14 ± 1.1 (with a normal value of up to 2.85) in the main group and 4.77 ± 1.15 in the control group. At the same time, insulin resistance was detected in 22 (62.8%) children of the first group and 11 (73.3%) children of the second group. After 3 weeks of treatment, the HOMA-IR index was 3.3 ± 0.3 and 3.6 ± 0.7 in the main and control groups, respectively.

responsible. Insulin resistance persisted in 11 (31.4%) patients in the main group and in all children of the second group.

In the study of the content of peroxidation products lipids - diene conjugates and malondialdehyde in plasma blood and the main antioxidant enzymes of erythrocytes - glutathione peroxidase and superoxide dimutase are the only reliable

significant (p < 0.05) difference should be considered an increase in superoxide dismutase of erythrocytes in patients of the main group. The same applies to the auxiliary index of enzymatic antioxidant protection (AOI farm.) (p < 0.05). This effect is also manifested at the level of total antioxidant index (AOI total) (p < 0.01). In general, a significant antioxidant effect of the drug was proved in the main group, directed on the reduction of oxidative stress according to the AOI index total. (values changed from -1.33 to -1.07 at normal = 0, p < 0.01), while in the group no comparison of the dynamics of the indicator was noted (-0.97 and -1.00). These changes were caused mainly by the hematopoietic component associated with the appearance of new erythrocytes with an increased content of superoxide dismutase (or an increase in its activity).

Initially, microcirculation parameters did not differ significantly between patients of different groups. On average, the linear blood flow velocity (Vas) was 2.73 cm/s, the volumetric blood ka (Qas) - 1.29 ml / s, the pulsation index (Pi) was 3.09, and the resistance index (Ri) - 0.39.

Already after 7 days of taking the drug Kapilar, an improvement in microcirculation parameters was recorded in most patients: the linear blood flow rate increased by 1.2 times compared to baseline, the volumetric blood flow rate - by 1.2 times, the pulsation index - by 1.3 times, and the resistance index - 1.2 times. Microhemodynamic parameters reached their peak on the 21st day of the study.

dovaniya (Fig. 1).

In the control group, on the contrary, there was a tendency to slow down decrease in blood flow and decrease in the elastic properties of blood vessels by the 8th day of the study, which persisted throughout the entire observation period, which may be associated with active weight loss, especially in the first days of diet therapy, a decrease in the amount of total fluid in the body of patients and a decrease in circulatory blood (Fig. 2).

Thus, after taking a course of dihydroquercetin, by the end of the study, the linear blood flow velocity in patients of the main group was 1.34 times higher than the same parameters recorded in the control group, the volumetric blood flow velocity was 1.32 times higher, the pulsation index was 2 times higher, resistance index - 1.58 times.

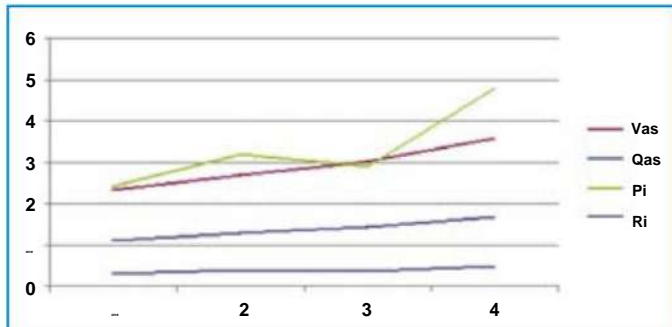
Summarizing the data obtained, it can be argued that regular The regular intake of dietary supplement Kapilar promotes a rapid and complete response of the microcirculatory bed, which is expressed in an increase in the speed and volume indicators of blood flow, as well as an improvement in the elastic properties of the vessels of the microcirculatory bed, which persists throughout the study (21 days).

The results of the study showed a good tolerability and absence of side effects of dietary supplement Kapilar in obese children. None of the patients had any adverse events associated with the use of the drug. Dietary supplement Kapilar does not adversely affect the functional state of the liver and biliary system in obese children.

table 2

Indicators of glucose tolerance test and insulin resistance

Time	1st day of observation		21st day of observation	
	0 min	120 min	0 min	120 min
Main group, mmol/l	5.3 ± 0.1 7.3 ± 0.2 11 children (31.4%)		5.2 ± 0.07 7.06 ± 0.2	
NTG			6 children (17.1%)	
HOMA-IR Index	5.14 ± 1.1		3.3±0.3	
insulin resistance	22 children (62.8%)		11 children (31.4%)	
Control group, mmol/l	5.1 ± 0.09	6.5±0.4	5.3±0.1	6.5±0.2
NTG	3 children (20%)		0	
HOMA-IR Index	4.77 ± 1.15 11		3.6±0.7	
insulin resistance	children (73.3%)		11 children (73.3%)	



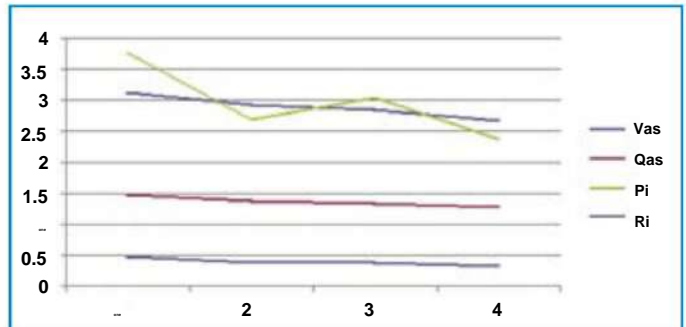
Rice. 1. Indicators of microcirculation in children with obesity while taking the dietary supplement Kapilar

Thus, in children with obesity, the use of dietary supplement Kapilar for 21 days was accompanied by a reduction in body weight, a decrease in the percentage of adipose tissue and anthropometric indicators.

indicators (circumferences of the abdomen and hips) comparable with those control group. The main differences in the groups were related to zany with indicators of microcirculation and antioxidant status. The inclusion of dietary supplements Kapilar in the standard hypocaloric diet leads to the normalization of the antioxidant status of patients, is associated with a decrease in oxidative stress, which is accompanied by an improvement I eat microcirculation and indicators of carbohydrate metabolism: an increase in speed and volume indicators of blood flow, an improvement in the elastic properties of the vessels of the microvasculature and, ultimately,

as a result, a decrease in the number of patients with impaired glucose tolerance and insulin resistance. Considering the constant increase and peak values of microhemodynamics by the 21st day in the main study group, we can conclude that the effectiveness of the drug is directly

proportional to the duration of the reception.



Rice. 2. Indicators of microcirculation in children with obesity - control group

All of the above is important in the prevention of development of such complications of obesity as arterial hypertension, impaired glucose tolerance, type 2 diabetes mellitus, metabolic syndrome.

The results of the study, as well as the absence of side effects effects allow us to recommend the inclusion of the tablet form of dietary supplement Kapilar in the complex therapy of children with obesity in the grow older than 10 years. \bar{y}

Literature

1. Plotnikov M.B., Tyukavkina N.A., Plotnikova T.M. Medications based on divertin. Tomsk University Press. 2005. 222 p.
2. Belaya O.L., Baider L.M., Kuropteva Z.V., Artamoshina N.E. Antioxidant properties of the bioflavonoid diquertin. Proceedings of the XVI Congress Russian National Congress "Man and Medicine". Moscow, April 6–10, 2009 Abstracts of reports. S. 37.
3. Kubatiev A.A., Yadigarova Z.T., Rudko I.A. and others. Diquertin is an effective

ВНИМАНИЮ ПЕДИАТРОВ!

ОЖИРЕНИЕ У ДЕТЕЙ. ЧТО ДЕЛАТЬ?

Использование «Капилара» при ожирении у детей*

Клинические исследования в НИИ питания РАМН доказали целесообразность и эффективность использования «Капилара» в клиническом лечении ожирения у детей. «Капилар» обладает выраженным антиоксидантным, капилляропротекторным и ангиопротективным действиями, что способствует:



- уменьшению окислительного стресса и нормализации антиоксидантного статуса организма в период снижения веса;
- улучшению микроциркуляции и снижению проницаемости сосудистой стенки;
- снижению инсулинорезистентности периферических тканей и печени.

*Исследование по оценке влияния диетотерапии с включением к пище дигидрокверцетина (ДКВ) (активное действующее вещество биологически активной добавки (БАД) «Капилар») на клинико-метаболические показатели детей с избыточной массой тела и ожирением проводилось в контролируемых условиях стационара на базе отделения педиатрической диетологии клиники НИИ питания РАМН. В исследование были включены 50 детей, страдающих избыточной массой тела и ожирением в возрасте от 10 лет до 17 лет 11 мес.

Коррекция веса

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СГР №РЛУ/77/99.11.003.Е.017.042.04.11 БАД. Не является лекарством. РЕКЛАМА

- inhibitor of platelet aggregation // *Vopr. biol., med. and pharmaceutical. chemistry.* 1999. No. 3. S. 47–50.
4. *Schegolkov AM, Dergacheva LI* The Efficiency of Biologically Active Substance CAPILAR Used in Medical Rehabilitation of Cardiosurgical Patients // *International journal of immunorehabilitation.* 2007 Vol. 9. No. 2. P. 92–93.
5. *Belaya O.L., Fomina I.G., Baider L.M., Kuropteva Z.V., Tyukavkina N.A.* Effect of the bioflavonoid diquertin on the antioxidant system ceruloplasmin/transferritin and lipid peroxidation in patients with stable forms of coronary heart disease with dyslipidemia // *Clinical medicine.* 2006. No. 7. P. 46–50.
6. *A. V. Shakula, A. M. Shchegolkov, V. V. Klimko, V. P. Yaroshenko, and V. I. Nekrasov, Dergacheva L.I.* The use of dihydroquercetin in complex medical rehabilitation of patients with coronary heart disease in the hospital and outpatient polyclinic stages // *Consilium medicum.* 2008. V. 10. No. 12. S. 44–48.
7. *Schegolkov AM, Dergacheva LI* The Efficiency of Biologically Active Substance CAPILAR Used in Medical Rehabilitation of Cardiosurgical Patients // *International journal of immunorehabilitation.* 2007 Vol. 9. No. 2. P. 92–93.
8. *Shchegolkov A.M., Belyakin S.A., Shakula A.V., Klimko V.V., Yaroshenko V.P., Dergacheva L.I.* Medical rehabilitation of patients with ischemic disease heart after coronary artery bypass surgery using dihydroquercetin // *Bulletin of restorative medicine.* 2007. No. 3 (21). pp. 93–96.
9. *Shakula A.V., Nekrasov V.I., Shchegolkov A.M., Klimko V.V., Yaroshenko V.P., Dergacheva L.I.* The use of dihydroquercetin in the complex treatment of patients hypertension // *Doctor.* 2008. No. 4. S. 42–46.
10. *Skedina M.A., Belozeroval I.N., Dergacheva L.I.* Comprehensive study dynamics of the state of the cardiovascular system when using drugs dihydroquercetin in patients with hypertension // *Vestnik vosstanovitel'noy medicine.* 2008. No. 6 (28). pp. 32–35.
11. *Shakula A.V., Shchegolkov A.M., Klimko V.V., Yaroshenko V.P., Nekrasov V.I., Dergacheva L.I.* Comprehensive treatment of patients with coronary heart disease in polyclinic conditions: the use of dihydroquercetin // *Handbook polyclinic doctor* 2008. No. 3. S. 36–39.
12. *Shakula A.V., Shchegolkov A.M., Budko A.A., Yaroshenko V.P., Marochkina E.I., Dergacheva L.I.* Comprehensive medical rehabilitation of patients with chronic obstructive pulmonary disease // *Vrach.* 2008. No. 11. S. 67–71
13. *Teselkin Yu.O., Babenkova I.V., Novozhenov V.G.* etc. Using the new antioxidant agent diquertin in the treatment of patients with acute pneumonia // *Vopr. biol., med. and a pharmacist. chemistry.* 1999. No. 1. S. 36–40.
14. *Balabolkin M.I., Nikishova M.S., Volkova A.K.* etc. The use of antioxidants from the group of flavonoids in the treatment of diabetic retinopathy with diabetes type 2 diabetes // *Problems of endocrinology.* 2003. No. 3. V. 49. S. 3–6.
15. *Nedosugova L.V., Nikishova M.S., Volkovoy A.K., Balabolkin M.I., Rudko I.A., Kubatiev A.A., Dergacheva L.I.* Correction of free-radical processes oxidation against the background of the use of the bioflavonoid dihydroquercetin in diabetes type 2 diabetes // *Bulletin of restorative medicine.* 2006. No. 4 (18). pp. 51–54.
16. The problem of obesity in the WHO European Region and strategies to address it. WHO European Ministerial Conference on Combating Obesity "Nutrition and physical activity for health". Istanbul, Turkey, November 15–17 2006 World Health Organization. European Regional Office.
17. *Ebbeling CB, Pawlak DB, Ludwig DS* Childhood obesity: public-health crisis, common sense cure // *Lancet.* 2002, 360: 473–482.
18. *Nathan BM, Moran A.* Metabolic complications of obesity in childhood and adolescence: more than just diabetes // *Curr Opin Endocrinol Diabetes Obes.* Feb 2008; 15(1):21–29.
19. A Clinical Guide to Pediatric Weight Management and Obesity. Hassink SGLippincott Williams&Wilkins, 2007, pp. 114–129.
20. Non-alcoholic steatohepatitis (NASH). U.Leuscher. 5th edition. 2006. Dr. Falk Pharma GmbH.
21. *Dedov I.I., Balabolkin M.I., Mamaeva G.G.* etc. Diabetes mellitus: angiopathy and oxidative stress. A guide for doctors. M.: MZ RF, GU ENTS RAMN, 2003. 85 p.
22. *Egger B.* Helping patients lose weight - what works? // *Aust Fam Physician.* 2008 Jan-Feb; 37(1–2): 20–23.
23. *Maltsev G.Yu., Vasiliev A.V.* RBC antioxidant index in the monitoring of clinical nutrition // *Problems of nutrition.* 1999. No. 2, pp. 41–43.