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DEVELOPMENT OF A DIETARY SUPPLEMENT FOR IMPROVING THE COGNITIVE FUNCTIONS AND LOWERING THE HOMOCYSTEINE LEVELS

Introduction. *Hyperhomocysteinemia is a dangerous metabolic disorder that leads to a number of diseases.*

Problem Statement. *Urgent task is to develop pharmaceutical product for lowering the homocysteine levels without causing side effects.*

Purpose. *To develop the dietary supplement for reducing high homocysteine levels, which has a minimum content of components that may cause side effects; to test the supplement effect on the cognitive abilities of animals and to commercialize the product.*

Materials and Methods. *The developed dietary supplement Alfacognitin contains vitamins B6, B9, B12, C, and choline. For modelling experimental hyperhomocysteinemia in rats, the animals are kept on a diet rich in L-methionine. Blood homocysteine concentrations are determined by the ion exchange liquid column chromatography method with the use of an automatic amino acid analyzer. The behavioral responses and cognitive abilities of the rats have been studied with the use of behavioral tests (open field test, fear conditioning test, and social interaction test). The production of Alfacognitin dietary supplement has been launched with Nutrimed Ltd. (Kyiv).*

Results. *Alfacognitin has been shown to reduce homocysteine levels, to improve cognitive abilities, social interaction and communication skills, and to compensate functional memory and learning disorders in animals with hyperhomocysteinemia. Specifications for the dietary supplement have been approved, a pilot technology for obtaining the capsule form of the drug has been developed, and an experimental batch has been manufactured.*

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Conclusions. *Alfacognitin may reduce the homocysteine levels. Therefore, it may be used to normalize the functional state of the cardiovascular and nervous systems in patients with hyperhomocysteinemia, as well as to improve the cognitive functions, in particular in patients after COVID-19.*

Keywords: hyperhomocysteinemia, dietary supplement, vitamins B, vitamin C, choline, cardiovascular diseases, cognitive functions, and COVID-19.

Hyperhomocysteinemia (or homocysteinemia) is a pathological condition characterized by a significant increase in homocysteine levels in human blood (more than 15 μmol/l). It may lead to dangerous cardiovascular diseases (chronic heart failure, stroke, migraine, thrombophilia, blood fetoplacental disorders) and severe disorders of the central nervous system (neuropsychiatric disorders, neurodegenerative diseases, including multiple sclerosis, Alzheimer's and Parkinson's disease) [1].

Homocysteine is a representative of the so-called aproteinogenic amino acids that are not part of proteins and are contained in the cytoplasm of cells and intercellular substance. This amino acid is formed in the S-adenosyl-L-methionine cycle as a result of degradation of methionine that is an essential proteinogenic amino acid entering the human body mainly from products of animal origin and may be regenerated from homocysteine [2]. Homocysteine is toxic to vascular endothelial cells. Under normal conditions, homocysteine does not harm the body because it is rapidly metabolized by enzymes that require B vitamins for catalytic activity, namely B6 (pyridoxine), B9 (folic acid), and B12 (cyanocobalamin). When metabolism is impaired, excess homocysteine is oxidized to form large amounts of free radicals that damage vascular endothelial cells, which contributes to the formation of atherosclerotic plaques, the narrowing of vascular lumen, thrombosis or rupture of blood vessels [3].

Therefore, the development of new medical products and dietary supplements for reducing the homocysteine levels in the body without causing side effects, is an urgent task. The existing dietary supplements for reducing homocysteine levels usually contain vitamins B6 (or pyridoxal-5-phosphate), B9 (or L-5-methyltetrahydrofolate), B12 (or methylcobalamin), and sometimes B1 (thiamine), B2 (riboflavin), and calcium salts. The dosage of the main components of the supplements varies widely: B6 (2.5—100 mg), B9 (0.4—8.5 mg), B12 (0.5—5 mg), with the maximum doses of vitamins exceeding the reference daily intake (RDI) for a person tens or even thousands times. This gives rise to concern because high doses of some vitamins may cause side effects. Thus, several studies have confirmed that the consumption of high doses of vitamin B9 by women during pregnancy increases the risk of asthma in newborns [4, 5].

The spread of hyperhomocysteinemia is facilitated by factors such as sedentary lifestyle, smoking, abuse of coffee and alcohol, administration of a number of drugs (nitrous oxide, anticonvulsants, methotrexate, metformin, euphylline, etc.), certain diseases (leukemia, diabetes, renal and thyroid dysfunction), as well as hereditary mutations in the genes of synthesis and catabolism of homocysteine [1]. The most common genetic cause of hyperhomocysteinemia is C677T mutation in the 5,10-methylenetetrahydrofolic acid reductase (MTHFR) gene, which leads to decreased activity of this enzyme, and, in the case of insufficient folic acid intake, to decreased levels of 5-methyltetratenehydrofolate and accumulation of homocysteine to toxic levels [6].

Recently, it has been shown that high levels of homocysteine or the presence of C677T MTHFR genetic polymorphism may be used as a prognostic marker of severe COVID-19 [7, 8]. It is suggested that timely adjustment of the diet and the use of supplements that help reduce homocysteine levels may facilitate the course of this disease [9]. It is likely that the normalization of homocysteine levels may also help overcome the effects

of the so-called long-term COVID-19, when even 3—4 months after discharge from hospital, 60% of patients have neurological and long-term cognitive complications [10].

Therefore, the purpose of this research is to develop a dietary supplement for reducing the level of homocysteine with a minimum content of components that may cause side effects and may be used for the prevention and treatment of cardiovascular, cerebrovascular, neurodegenerative and other diseases; to study whether the developed supplement affects the cognitive abilities of animals, and to launch its production.

Developed *Alfacognitin* dietary supplement contains 3 mg vitamin B6, 400 μg vitamin B9, 5 μg vitamin B12, 300 mg choline, 50 mg vitamin C, as well as excipients: microcrystalline cellulose, calcium stearate, amorphous silicon dioxide (orisil) and maltodextrin.

The research has been conducted in compliance with the rules of the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes, the Rules of Performance of Experimental Animals approved by the Ministry of Healthcare of Ukraine and the Law of Ukraine on the Protection of Animals from Cruelty (No. 3447-IV dated 13.02.2020).

The experimental animals (adult male Wistar rats weighing 230—250 g) are divided into 4 groups (7 animals in each): the reference group (1); the animals taking *Alfacognitin* (2); the animals taking the L-methionine diet (with elevated homocysteine levels) (3); the animals taking the L-methionine diet and *Alfacognitin* (4). To simulate experimental hyperhomocysteinemia, L-methionine (from which homocysteine is formed in the body) was administered to rats for 50 days. L-methionine is dissolved in drinking water at a concentration of 10 mg/ml at a rate of 1 g per 1 kg body weight [11]. Prior to testing, the rats have a period of adaptation to the new environment, and during the experiments they were given free access to food and water. From the 30th day of methionine administration, the rats were given 0.5 ml *Alfacognitin* solution at a concentration of 24 mg/ml at a rate of 48.0 mg/kg/animal, per os, for 21 days. This dose corresponds to a dose of 7.76 mg/kg/person given the differences in the body surface area of different species as an indicator of the difference in metabolic activity (48.0 mg/kg × × (0.24 kg: 60 kg)$^{0.33}$ = 7.76 mg/kg) [12]. To obtain this dose, a person with a standard weight (70 kg) should take 1 capsule of dietary supplement *Alfacognitin* daily.

The behavioral tests on the animals of all the four groups after 50 days have been made: the open field test for measuring locomotor activity, research activity, and fear of environmental changes; the fear conditioning test for measuring the ability to associative emotional learning, short-term and long-term memory, and the social interaction test for measuring cognitive abilities, sociability, and level of interest in a new social object [13].

To determine the level of homocysteine in the blood serum of the rats of all groups, blood is taken from the eye retrobulbar venous sinus, under light ether anesthesia, in the morning, after fasting for 12 hours. The sera are obtained by incubation at 37 °C for 3 h and centrifugation of whole blood at 3000 *g* for 7 min. To hydrolyze proteins, the serum is diluted 1:1 with 3% sulfosalicylic acid, kept at 25 °C for 3 h, centrifuged for 30 min at 5000 *g*, with the supernatant used for analysis [14]. The content of homocysteine in the samples is determined by the ion exchange liquid column chromatography method with the use of an automatic amino acid analyzer T339 (*Mikrotechna*, Czech Republic) and standard homocysteine S 69453 (*Sigma*, USA).

The test process is recorded on video with the help of an IP camera, after which the necessary parameters are evaluated with the use of the *MATLAB* computer software package. The results have been statistically processed with the use of *GraphPad Prism* software, by the Kruskal-Wallis ANOVA and Unpaired t-test methods (the differences between the indicators with a value of $p < 0.05$ are considered statistically significant).

Medico-biological substantiation of functional properties of *Alfacognitin* dietary supplement

Researchers of the Palladin Institute of Biochemistry of the NAS of Ukraine (Department of Biochemistry of Vitamins and Coenzymes; Department of Molecular Immunology) have developed *Alfacognitin* for reducing elevated levels of homocysteine in humans. *Alfacognitin* is a complex of vitamins (B6, B9, B12, and C) and vitamin-like substance choline. Each component of the developed dietary supplement stimulates a certain biochemical pathway of homocysteine degradation, as well as has other important functions. The main components of *Alfacognitin* dietary supplement, which are also part of other dietary supplements to reduce homocysteine levels, are vitamins B6, B9, and B12.

Vitamin B6 in the form of pyridoxal phosphate is a cofactor of cystathionine-γ-lyase (CE 4.4.1.1), the most important enzyme of the first way of L-homocysteine degradation. In addition, vitamin B6 is involved in the metabolism of macronutrients, the synthesis of neurotransmitters, histamine, lipids, the synthesis and functioning of hemoglobin, gluconeogenesis, and gene expression [15].

Vitamins B9 (folic acid) and B12 (cyanocobalamin) are involved in the second pathway of L-homocysteine degradation: they ensure the efficient functioning of methionine synthase (CE 2.1.1.13) and the conversion of L-homocysteine to L-methionine in S-adenosyl-L-methionine cycle, due to L-homocysteine and N5-methyltetrahydrofolate (synthesized from vitamin B9) being the substrates of methionine synthase, and vitamin B12 being the cofactor of methionine synthase [16].

Vitamins B9 and B12 also stimulate the hematopoiesis process (the formation and maturation of megaloblasts, the formation of erythrocytes and leukocytes). Vitamin B9 lowers blood cholesterol, participates in choline metabolism, as well as in the synthesis of amino acids, nucleic acids, and their bases (pyrimidines and purines) [17]. Vitamin B12 plays an important role in the metabolism of proteins, fats, and carbohydrates (in close interaction with vitamin C, folic and pantothenic acids), provides the inclusion of carotenoids in the metabolic processes and their subsequent conversion into active vitamin A, plays an extremely important role in the nerve function thus affecting the functioning of all organs, promotes the synthesis of deoxyribonucleic and ribonucleic acids [18].

Choline (2-oxyethyltrimethylammonium hydroxide) is included in the developed dietary supplement as a precursor of betaine that is the main link in the third biochemical pathway of elimination of homocysteine. Betaine (like N5-methyltetrahydrofolate) is a methyl group donor that replaces the hydrogen atom at the sulfur atom of L-homocysteine during the conversion of betaine into dimethylglycine by the enzyme betaine-homocysteine S-methyltransferase (CE 2.1.1.5) [19, 20]. Choline is also required for the synthesis of neurotransmitter acetylcholine, phospholipids, and amino acid methionine. It is a hepatoprotector and lipotropic agent. In combination with lecithin, it promotes the transport and metabolism of fats in the liver, affects carbohydrate metabolism, regulates insulin levels, and improves memory. Choline is known to lower blood pressure in people with metabolic syndrome and is a prophylactic to prevent the development of cardiovascular diseases [21].

Vitamin C (L-ascorbic acid) is another component of the dietary supplement, as it has antioxidant properties and is able to reduce the oxidative activity and acute toxicity of homocysteine [22]. This vitamin helps neutralize the superoxide radical that transforms into hydrogen peroxide, reduces ubiquinone and vitamin E, participates in the synthesis of collagen, catecholamines, corticosteroids, and serotonin (from tryptophan), as well as in the conversion of cholesterol into bile acids, stimulates the synthesis of interferon and the immune system fight against viral infections

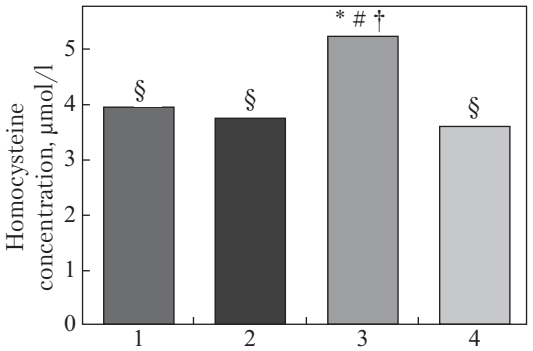

Fig. 1. The level of homocysteine in the serum samples of rats of the four groups: 1 — the reference group; 2 — the animals taking *Alfacognitin*; 3 — the animals taking L-methionine diet (with hyperhomocysteinemia); 4 — the animals taking L-methionine diet and *Alfacognitin*. Statistically significant differences: * — $p < 0.05$ as compared with the reference group (1); # — $p < 0.05$ as compared with the animals taking *Alfacognitin* (2); § — $p < 0.05$ as compared with the animals taking L-methionine diet (3); † — $p < 0.05$ as compared with the animals taking L-methionine diet and *Alfacognitin* (4)

[23, 24]. Vitamin C is necessary for the functioning of connective and bone tissues and provides the physiological detoxification processes in hepatocytes with the participation of cytochrome P450 [23]. There are data on the neuroprotective effect of vitamin C, in particular, its positive effects on the prevention of premature aging, age-related cognitive decline, and Alzheimer's disease [25].

The content of each active ingredient in *Alfacognitin* dietary supplement is determined on the basis of physiological norms of consumption of relevant biologically active substances by an adult, given the special needs of people with certain metabolic disorders and the risk of adverse reactions at excessive doses of dietary supplements. Table 1 presents the doses of components used in *Alfacognitin* and other dietary supplements to reduce homocysteine levels, as well as the reference daily intake (RDI) and maximum permissible dose for humans [26, 27]. The formulation of *Alfacognitin* dietary supplement in terms of its active ingredients includes 3 mg vitamin B6, 400 μg vitamin B9, 5 μg vitamin B12, 300 mg choline, and 50 mg vitamin C. One capsule of *Alfacognitin* contains 1—2 RDI of vitamins B6, B9, B12, and half of RDI of choline and vitamin C (given the recommendation to take 1—2 capsules daily). The finished pharma product is solid capsules as the best option given the compliance of consumers (patients), the target daily intake of relevant biologically active substances, as well as their physicochemical and technological features [28, 29, and 30].

Table 1. **Doses of Biologically Active Components Used in *Alfacognitin* Dietary Supplement and Other Dietary Supplements to Reduce Homocysteine Levels as Compared with Reference Daily Intake and Maximum Permissible Dose for Humans**

Biologically active components of *Alfacognitin*	Content in one capsule of *Alfacognitin*, μg and RDI *	Content in one capsule of similar dietary supplements **, μg and d.i.	Reference daily intake for humans, μg [26, 27]	Maximum permissible daily dose for humans, μg [26]
Vitamin B6	3 000 ≈ 1.8 d.i.	2 500 – 100 000 (≈ 1.5 d.i.– 59 d.i.)	1 700	100 000
Vitamin B9	400 = 1 d.i.	400 – 8 500 (≈ 1 d.i.– 21 d.i.)	400	1 000
Vitamin B12	5 ≈ 2 d.i.	500 – 5 000 (≈ 208 d.i. – 2083 d.i.)	2.4	Not established
Choline	300 000 ≈ 0.5 d.i.	—	550 000	3 500 000
Vitamin C	50 000 ≈ 0.5 d.i.	—	90 000	2 000 000

Note: * RDI — Reference Daily Intake for a person; ** information on the composition of dietary supplements for reducing the level of homocysteine presented on the Ukrainian market and produced by *Life Extension*, *Source Naturals, Thorne Research*, *Solgar*, *Metagenics*, and *Swanson* (USA) as specified in the instructions for use and freely available on the websites of relevant manufacturers.

Influence of *Alfacognitin* dietary supplement on the behavioral responses and cognitive abilities of animals

The content of homocysteine in the serum samples of rats is shown in Fig. 1. The studies have shown that in the animals taking the L-methionine diet, homocysteine levels increase as compared with the reference group, while in the animals taking the L-methionine diet and *Alfacognitin*, there has been reported a decrease its level to the normal one.

The open field test that determines the level of locomotor and research activity of animals, as well as the level of fear of the new environment has shown a tendency towards improving the locomotor activity and reducing the anxiety in the animals that take *Alfacognitin*, and declining activity in the rats taking the L-methionine diet and having hyperhomocysteinemia, regardless of whether they take *Alfacognitin* or not (Fig. 2).

The social interaction test for cognitive ability, sociability, and interest in a new social object has shown that the animals taking L-methionine diet and having hyperhomocysteinemia spend significantly less time near the left section with a new rat than near the right section with a familiar rat (Fig. 3). This is a sign of impaired social interaction and declined cognitive abilities. In contrast to this group, the rats taking *Alfacognitin* spend significantly more time near the left section with a new rat, which indicates greater social activity and better cognitive abilities. In the rats taking L-methionine diet and *Alfacognitin*, the social activity and cognitive abilities have been restored to the level of the reference group.

The fear conditioning test for measuring the ability to associative emotional learning, short- and long-term memory has shown that for the animals taking L-methionine diet and having hyperhomocysteinemia, the time of freezing behavior after stimulation of the limb decreases as compared with the reference animals (Fig. 4), which is an evidence of functional memory impairment. In the group of the rats taking L-methionine diet and *Alfacognitin*, the disorders have been partially remedied.

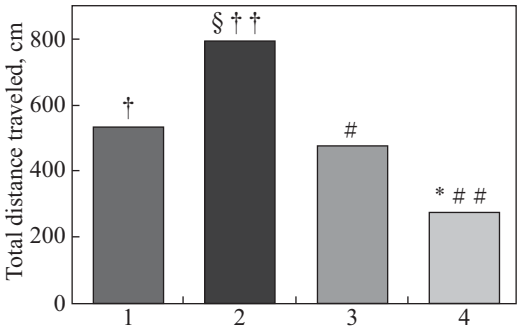

Fig. 2. The locomotor activity levels in the open field test in the rats of the four groups: *1* — the reference group; *2* — the animals taking *Alfacognitin*; *3* — the animals taking L-methionine diet (with hyperhomocysteinemia); *4* — the animals taking L-methionine diet and *Alfacognitin*. Statistically significant differences: * — $p < 0.05$ as compared with the reference group (1); # — $p < 0.05$ as compared with the animals taking *Alfacognitin* (2); § — $p < 0.05$ as compared with the animals taking L-methionine diet (3); † — $p < 0.05$, †† — $p < 0,01$ as compared with the animals taking L-methionine diet and *Alfacognitin* (4)

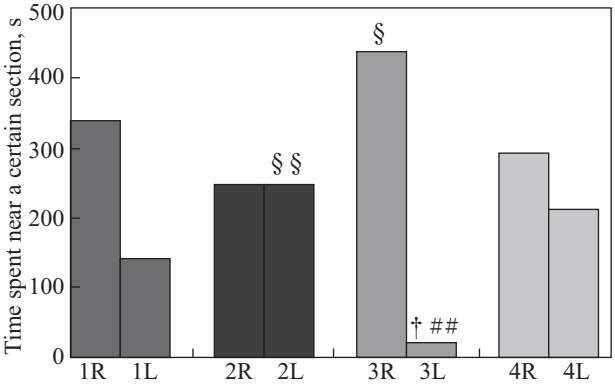

Fig. 3. Time spent near the right (R) section with a familiar rat and near the left (L) section with a new rat in the social interaction test in the rats of the four groups: *1* — the reference group; *2* — the animals taking *Alfacognitin*; *3* — the animals taking L-methionine diet (with hyperhomocysteinemia); *4* — the animals taking L-methionine diet and Alfacognitin. Statistically significant differences: ## — $p < 0.01$ as compared with the animals taking *Alfacognitin* and spending time near the section with a new rat (2L); ‡ — $p < 0.05$ as compared with the animals taking L-methionine diet and spending time near the section with a familiar rat (3R); § — $p < 0.05$, §§ — $p < 0.01$ as compared with the animals taking L-methionine diet and spending time near the section with a new rat (3L)

Hence, the tests have shown that keeping the rats on a diet enriched with L-methionine to induce hyperhomocysteinemia causes several disorders: declined locomotor activity and increased

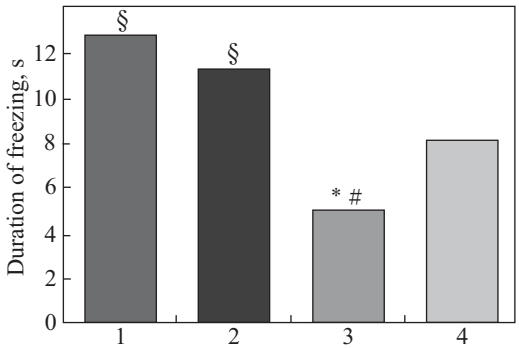

Fig. 4. Time of rat freezing behavior in the fear conditioning test in the the rats of the four groups: *1* — the reference group; *2* — the animals taking *Alfacognitin*; *3* — the animals taking L-methionine diet (with hyperhomocysteinemia); *4* — the animals taking L-methionine diet and *Alfacognitin*. Statistically significant differences: * — $p < 0.05$ as compared with the reference group (1); # — $p < 0.05$ as compared with the animals taking *Alfacognitin* (2); § — $p < 0.05$ as compared with the animals taking L-methionine diet (3)

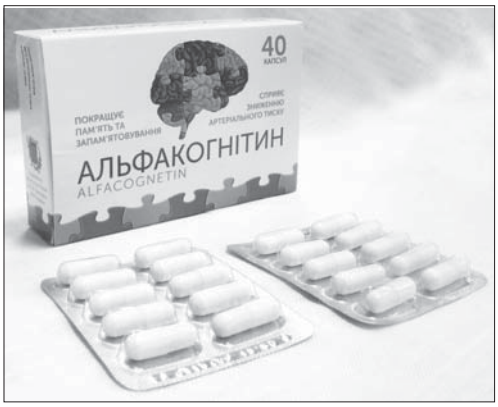

Fig. 5. Test sample of *Alfacognitin* dietary supplement developed at the Palladin Institute of Biochemistry of the NAS of Ukraine

anxiety (Fig. 2), declined cognitive abilities, sociability, and interest in a new social object (Fig. 3), as well as functional memory disorders (Fig. 4). The use of *Alfacognitin* by the animals with hyperhomocysteinemia helps improve their sociability, efficiency of the social interaction and cognitive abilities (Fig. 3), as well as normalize the functional disorders of memory and learning ability (Fig. 4), although does not affect their low locomotor activity and increased anxiety (Fig. 2).

Thus, the studies have shown that *Alfacognitin* dietary supplement has potential not only in terms of combating hyperhomocysteinemia, but also as a means to improve the cognitive abilities. Therefore, the dietary supplement has been introduced into production in order to make a test batch for further testing.

Launching the production of *Alfacognitin*

The production of *Alfacognitin* dietary supplement has been launched with *Nutrimed Ltd*. pharmaceutical company (Kyiv). Specifications for the production of *Alfacognitin* dietary supplement, package design, and draft instructions for use have been developed. A pilot technology for obtaining a ready-made product in the form of solid capsules has been developed (Fig. 5), and an experimental batch of dietary supplements has been manufactured.

One of the most important prerequisites for commercializing a dietary supplement is to substantiate and to establish indicators of its safety, which is one of the starting points for assessing and managing risks in the use of product by humans [31—34]. The maximum permissible levels of the active ingredients of the dietary supplement have been established according to the Norms of Physiological Needs of the Population of Ukraine in Basic Nutrients and Energy (Resolution of the Ministry of Healthcare of Ukraine No. 1073 dated 03.09.2017) and the Hygienic Requirements for Dietary Supplements (Resolution of the Ministry of Healthcare of Ukraine No. 1114 dated 19.12.2013). The following regulations have been used to regulate the safety indicators: the State Hygienic Rules and Regulations on Maximum Levels of Certain Contaminants in Foodstuffs (Resolution of the Ministry of Healthcare of Ukraine No. 368 dated 13.05.2013), the Provisional Hygienic Standards for Chemical Contaminants and Contaminants of the Biological Nature in Biologically Active Supplements (GN 4.4.8.073-2001), as well as the recommendations of the State Pharmacopoeia of Ukraine.

According to the results of the state sanitary and epidemiological examination made by the State Service of Ukraine for Food Safety and Con-

sumer Protection, TU U 10.8-05417288-004:2018 Dietary Nutraceutical Supplement, the specifications meet the requirements for safety for human health and life and the requirements of the applicable sanitary legislation of Ukraine. Based on the major research results, the patent has been issued [35].

As a result of this research, *Alfacognitin* dietary supplement for reducing homocysteine levels and normalizing the functional state of the cardiovascular and nervous systems in hyperhomocysteinemia, which is also an additional source of vitamins B6, B9, B12, C, and choline has been developed. The study of the central nervous system in rats with elevated homocysteine levels has shown that the use of *Alfacognitin* in the animals helps improve the cognitive abilities, the effectiveness of social interaction and communication and normalize the functional memory and learning abilities.

The ability of *Alfacognitin* dietary supplement to improve the brain cognitive function may be used in preventive and therapeutic measures to protect and support the most vulnerable groups of COVID-19 patients with a high risk of cognitive impairment.

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РОЗРОБЛЕННЯ ЗАСОБУ ДЛЯ ПОКРАЩЕННЯ КОГНІТИВНИХ ФУНКЦІЙ ТА ЗНИЖЕННЯ РІВНЯ ГОМОЦИСТЕЇНУ

Вступ. Гіпергомоцистеїнемія є небезпечним метаболічним порушенням, що призводить до виникнення низки захворювань.

Проблематика. Нагальним завданням є розроблення препаратів, які здатні знижувати рівень гомоцистеїну, не спричиняючи побічних ефектів.

Мета. Розробити дієтичну добавку, що при мінімальному вмісті компонентів, які здатні викликати побічні реакції, знижує рівень гомоцистеїну; а також дослідити, чи впливає розроблена добавка на когнітивні здібності тварин, та впровадити її у виробництво.

Матеріали й методи. До складу розробленої дієтичної добавки «Альфакогнітин» включено вітаміни B6, B9, B12, C і холін. Моделювання експериментальної гіпергомоцистенемії у щурів проводили шляхом утримання тварин на L-метіоніновій дієті. Вміст гомоцистеїну у крові визначали за допомогою іонообмінної рідинно-колонної хроматографії з використанням автоматичного аналізатору амінокислот. Поведінкові реакції та когнітивні здібності щурів досліджували за допомогою поведінкових тестів «Відкрите поле», «Електрична стимуляція кінцівки» і «Соціальна взаємодія». Роботи щодо впровадження у виробництво виконано за участі компанії ТОВ «Нутрімед» (Київ).

Результати. Показано, що у тварин із гіпергомоцистеїнемією «Альфакогнітин» знижував рівень гомоцистеїну, підвищував когнітивні здібності, ефективність соціальної взаємодії та комунікабельність, а також нормалізував функціональні порушення пам'яті та здатності до навчання. Затверджено технічні умови виробництва дієтичної добавки, відпрацьовано пілотну технологію отримання її капсульованої форми та виготовлено дослідну партію.

Висновки. «Альфакогнітин» може знижувати рівень гомоцистеїну, що дозволяє використовувати його з метою нормалізації функціонального стану серцево-судинної та нервової систем за гіпергомоцистеїнемії, а також для покращення когнітивних функцій, зокрема після захворювання на COVID-19.

Ключові слова: гіпергомоцистеїнемія, дієтична добавка, вітаміни групи B, вітамін C, холін, серцево-судинні захворювання, когнітивні функції, COVID-19.