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Development of phytodrug for gerontological practice

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It is known that in cases of widespread geriatric diseases there are violations of indicators of pro- and antioxidant systems of an organism. The aim of the work was the development of plant antioxidants used for gerontological practice. A unique technology of herbal oil balm "Yuvelaks" was developed. The preclinical studies of herbal remedies were conducted. The results of pre-clinical studies have demonstrated the safety of the drug and its use in gerontology practice.

Keywords: Gerontological practice, phytodrug, preclinical researches

It is known that in cases of widespread therapeutic diseases processes of aging are related to violation of balance of indicators of pro-and antioxidant system (Obukhova, 2002; Gilman, 2006). For the normalization of these processes antioxidant drugs are offered, which often have a synthetic origin (Byshevsky, Galyan, Ralchenko et al., 2005). Due to a wide range of pharmacological activity and the joint effect on the body, herbal remedies are more widely used in gerontological practice. Currently, attention is drawn to the fact of lack of preventive and curative properties of herbal medicines (Gumanova, Artyushkova, Metelskaya et al., 2007). Therefore, the phyto-composition "Yuvelaks" was developed, which shows antioxidant properties and can be a means of improving active longevity. The purpose of current work is the development of a vegetative antioxidant for gerontological practice.

An original technology of herbal oil balm based on established output of biologically active substances on technological factors, as well as a specification of quality and standardization of phyto-composition was developed (patent number 24,818 RK). Physical and chemical properties were studied by spectrophotometry phytodrug. Chronic toxicity studies of "Yuvelaks" on animals were carried out according to the "Rules on Preclinical Studies, Medical, and Biological Experiments and Clinical Trials in the Republic of Kazakhstan" approved by Decree of the Minister of Health of the Republic of Kazakhstan (No. 442) in accordance with the State Standard of the Republic of Kazakhstan "On Good Laboratory Practice. Main Principles" approved by Order of the Minister of Industry and Trade on December 29, 2006 (No.575 and No.557). Recommendations contained in the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Scientific Purposes" adopted in Strasbourg on 18 March 1986 were used as a guide when conducting experiments.

Tests were conducted on 124 white laboratory rats of both sexes to determine the toxicity of the drug (6 months). Animals were placed in quarantine for two weeks before the experiment. Daily inspection of animals was conducted during quarantine. Experimental animal groups were formed by random sampling with the body mass index being used as a determinant.

The study took into account the recommendations contained in the "Guide for Experimental (Pre-Clinical) Studies of New Pharmacological Substances" (Habriev, 2005). The body weight and weight of organs of all animals along with (scales BL 120S Sartorius, Germany) hematological, biochemical, macroscopic, and histological indices were determined (DM2500 Leica, Germany) in accordance with standard procedures for medical blood analyzers. Distributions, which were approximately normal, were marked as mean (M) and standard deviation (SD) for all animals in the group. A median and inter-quartile scope was applied to describe the distributions, which were not normal. Interquartile scale indicated 25% and 75%. Comparison with a normal distribution between the two groups was performed using two-sided t-test (Glants, 1999). For comparing groups that did not follow a normal distribution, the T-Mann-Whitney test was used. For processing the Microsoft Excel 97 program was used.

During the activities phyto-composition, which contained pumpkin oil, germs of wheat, a nettle, sea-buckthorn berries, and a palm tree in the corresponding concentration and proportions, was created by an original method. The effects of pumpkin oil were conditioned by the biologically active substances contained in it: tocopherols (alpha, beta, gamma, sigma-ısomers), carotenoids, phospholipids, sterols, phosphatides, flavonoids, vitamins A, E, F, B2, B6 , C, PP, saturated, unsaturated and polyunsaturated fatty acids (palmitic, stearic, oleic, linoleic, linolenic, arachidic), mineral compounds, and trace elements. Nettle oil contains chlorophyll, flavonoids, organic acids (oxalic acid, succinic acid, citric acid, etc.), vitamin C and carotene. Wheat germ oil contains three active complexes such as antioxidants - alpha-tocopherol, and carotenoids, polyunsaturated fatty acids (including linoleic and linolenic in optimal for lipid metabolism in the human body ratio of 3:1) and vitamins A, B, D, F, PP, pantothenic and folic acid. Palm oil is the source of ubiquinone, pro-vitamin A, vitamin E, which are antioxidants that protect the body from free radicals (Gilman, 2006).

The phyto-composition passed the state system of certification of the Republic of Kazakhstan and has the certificate of conformity (ST of SP 600811407767-01-2010) registered in the state register and corresponds to safety requirements and conditions established by ST of LLP of 01330509-02-2006, sub items 3.2.2, 3.2.3, 3.2.5. The phyto-composition passed the state registration in the Ministry of Health of the Republic of Kazakhstan, Committee of the State Sanitary and Epidemiologic Supervision, and Advisory Council on Registration of Biologically Active Additives to Food. It has been established that the phyto-composition corresponds to SanPin 4.01.071.03 "Hygienic Requirements to Safety and Food Value of Foodstuff".

The test report on organoleptic properties showed that the phyto-composition had corresponded to the State Standard Specification Requirements. It is liquid oil without a deposit, with color corresponding to used raw materials, with a reddish shade, with taste, and a smell peculiar to used raw materials, without a foreign smell and smack.

Researches on toxic elements, pesticides, mitoksinos, radionuclides, and microbiological indicators showed that levels of cesium of-137 Bq/kg (at norm 60) were not found and concentration oflatoxin B1 was not found.

Studies on physical and chemical properties of phyto-composition showed that the content of tocopherol of acetate in it was 47.5 mg on 100 g, beta carotene - 26.9 mg on 100 g, ascorbic acid - 5.7 mg on 100 g, and there were vitamin A traces. The density of phyto-composition was 0.914ú/cm3, solid - 72.4 %, the acid number corresponded 0.26 mg the GAME/g.

During the long-term oral intake of "Yuvelaks" the symptoms of intoxication and death of animals were not observed. Sexual distinctions in sensitivity of rats to preparation action was not revealed. Results of the taximeter, data of supervision

for 180 days after daily intake of "Yuvelaks" proves the absence of pathological changes in behavior and somatic indicators at animals.

Results of the research of "Yuvelaks" at its pre-oral intake once a day within a 60, 90, 120, 150, and 180 day-period in a dose of 0.3 ml/kg at rats of both sexes in comparison with control substance showed that sizes of changes of the physiological indicators caused by application of preparations, statistically authentically did not differ from each other. In all tests extent of change in indicators caused by control substance and a preparation of "Yuvelaks" was almost identical; authentic distinction between groups was not noted ($p>0.05$). During the study of the influence of applying "Yuvelaks" on hematological indicators, pathological changes were not revealed in all terms of supervision. Throughout the chronic experiment significant distinctions in number of erythrocytes, leukocytes, platelets, and hemoglobin level at the animals receiving "Yuvelaks" were not established statistically, in comparison with control animals. When taking "Yuvelaks" during a considerable period of time, essential changes in the level of general protein in blood serum was not revealed that pointed to stability of albuminiparous function of a liver ($p>0.05$). To identify possible damaging effects of "Yuvelaks" on a liver, the activity of aspartate transferase, alanine transferase, and the general lactate dehydrogenase blood serums were investigated. Throughout experiments a change in activity of these enzymes in serum of blood of all experimental animal groups did not fall beyond the limits physiological norm for this species of laboratory animals ($p>0.05$). Activity of aminotransferase, lactate dehydrogenase, and alkaline phosphatase on animals of both sexes receiving "Yuvelaks" during experiment did not differ essentially from the corresponding indicators in control ($p>0.05$). The findings of macro- and microscopic researches showed the absence of toxic effects of "Yuvelaks" at chronic six-month intake. Accordingly, the preclinical studies of the phytodrug were conducted, which did not show toxicity and that could be used in gerontological practice.

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