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Research Article

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Plant-Based Dietary Supplements and Antler Products for Prevention and Treatment of Age-Related Diseases: Efficacy Study

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ABSTRACT

Since age-related diseases and conditions are a growing global concern and many scientists are searching for better approaches to enhancing the work performance of the aging population, it is important to find ways to prevent and treat age-related conditions, handle inadequate nourishment and increase work-related efficiency. Exploring plant-based dietary supplements and supplements with antler products, we selected two new supplements developed and manufactured by Biolit Science and Production Association (Tomsk city). For clinical trials, thirty participants (10 males and 20 females aged from 40 to 55) were divided into two groups and administered treatment with and without nutrition plans. For the assessment of the efficacy of treatment, we monitored the autonomic nervous system dynamics, hormonal changes, and immune system. The objective performance criteria included: (a) the data obtained upon the comprehensive assessment of the autonomic nervous system, mental and emotional states; (b) the neuroendocrine system functioning; (c) the levels of cytokines as they are useful biomarkers of inflammation; and (d) bone metabolism. The subjective performance criteria included monitoring participants' general well-being and the nature of their complaints.

Key words: *Dietary supplement, Age-related disease, Antler product, Nutrition*

INTRODUCTION

Age-related diseases and conditions are a universal matter of concern. On the one hand, many countries around the world are experiencing the growth of the aged population, while, on the other hand, there is a need to apply the experience and expertise of the older generation [1-4]. It is known that GDP can be increased if the life quality and, thus, the productivity of the older workforce are improved. The factors contributing to the development of age-related diseases (such as coronary artery disease, atherosclerosis, osteoarthritis and osteoporosis, metabolic disorders, and cognitive impairment) are oxidative stress which damages cells, the declining telomerase activity, endocrine disorders, and apoptosis.

It is scientifically proven (E.D. Goldberg *et al.*, Russia, 1996, G. Peters *et al.*, USA, 2005, Robert Levkovetc *et al.*, USA) that people's physical and social environments contribute to the way people age, induce psychosomatic disorders and age-related diseases. Most health conditions associated with aging can be successfully treated with the help of well-balanced nutrition plans which include functional foods like dietary supplements. Many researchers have explored the rationality and efficacy of functional foods studying both traditional and modern medicine and have established many beneficial effects [5-16].

MATERIALS AND METHODS

Two dietary supplements developed and manufactured by Biolit Science and Production Association (Tomsk city) were selected for the present study. Dietary supplement 1, berry syrup, contains Meadow geranium extract - 0.2 g, Kuril tea shoots - 0.2 g, Leuzea Safflower roots - 0.2 g, Rhodiola Rosea - 0.5 g, Manchurian aralia roots - 0.2 g, Echinacea purpurea - 0.8 g, Prickly Eleutherococcus roots - 0.5 g, lingonberries and cranberries - 5.0 g, antler - 0.3 g per 100 grams.

Dietary supplement 2 is manufactured in 600mg capsules. Each capsule includes (%) antler powder - 34.5, calcium hydroxyapatite - 50, dry extract of Hill Solyanka - 10, 'Isobel' biologically active additive (crystalline powder containing mineral salts and organic substances such as fulvic, humic, amino acids) - 5, and vitamin C - 0.5. Each capsule contains calcium - 80g; phosphorus - 40g; chondroitin sulfate -14g; and glucosamine sulfate - 6g.

For clinical trials, thirty participants (10 males and 20 females aged from 40 to 55) were divided into two groups. The participants of the first (experimental) group were prescribed 1 teaspoon of Dietary supplement 1 to be taken twice a day for a month (the supplement is to be dissolved before use) and 2 capsules of Dietary supplement 2 to be taken with food. The second (control) group received a placebo. Upon completion of the four-week treatment, 10 participants continued taking both dietary supplements for two more months.

As our research involved humans, the clinical trials were carried out following the EC and GCP guidelines, the ethical principles of the Declaration of Helsinki. The clinical trial was performed at the laboratory complex of Siberian State Medical University (Tomsk, Russia) and supervised by L.S. Sotninikova, Doctor of Medical Sciences, Professor.

To evaluate the efficacy of the dietary supplements, the autonomic nervous system dynamics, hormonal changes, and immune system were monitored. The objective performance criteria included: (a) the data obtained upon the comprehensive assessment of the autonomic nervous system, mental and emotional states; (b) the neuroendocrine system functioning; (c) the levels of cytokines as they are useful biomarkers of inflammation; and (d) bone metabolism. The subjective performance criteria included monitoring participants' general well-being and the nature of their complaints. For our study, we applied the following methods:

Adaptive immune response assessment

The assessment was carried out to determine the percentage of lymphocytes in the leukocyte formula and the neutrophil-to-lymphocyte ratio, applying the criteria described by E.D. Goldberg (E.D. Goldberg *et al*. 1996);

Screening and quantitative assessment of the vegetative dystonia syndrome

The assessment was based on the questionnaire developed by A.M. Vane and described in his paper 'A new approach to determining autonomic disorders' (2003).

Heart rate variability (HRV)

To assess HRV, spectral analysis with short recordings of the ECG signal was employed. To evaluate the central ergotropic or humoral metabolic effects on the heart rate, a very low-frequency range (VLF) was applied. The parasympathetic influence on heart rate was evaluated using a high-frequency range (HF), and the effects of the sympathetic nervous activity on heart rate were examined using a low-frequency range (LF). We also calculated the balance of sympathetic and parasympathetic influences (LF/HF, c.u.) according to V.M. Mikhailov (2002). Taking into account that many factors can influence HRV, we applied Orthostatic Test to establish baselines.

Cardiointervalography

We also used the Baevsky index (the sympathetic index). With this index, the most frequent RR interval in a given dynamic series is the Mode (Mo) with seconds as measuring units. The amplitude of mode (AMo) is the number of intervals of similar duration and is expressed in percentage to the sample size. The variation range demonstrates the difference between the shortest and the longest RR interval values and is expressed in seconds. The activity of central regulation is the index of regulation strain or stress index and is expressed in conventional units.

The vegetative tone

To identify signs of vegetative dystonia, we used the method of quantitative assessment developed by A.M. Vane (2003). Vegetative dystonia is a disorder with symptoms like shortness of breath, abdominal distension, sweating, diarrhea, tremor, cough, and hiccups which patients complain of.

The hormonal system

When assessing the functional state of the hormonal system functioning, sex steroid-binding globulin (SCBG), dehydroandrostenediol (DHAS), and prolactin (PL) were examined using radioimmunoassay and electrochemiluminescence analysis carried out with an automatic Elecsys analyzer with standard kits from Roche.

RESULTS AND DISCUSSION

The assessment of the autonomic nervous system functioning (ANS)

The results of diagnostic testing identified that most participants had autonomic nervous system disorders. The Cerdo vegetative index for both male and female participants amounted to 14.6±1.20 units, which indicates the increased activity of the sympathetic nervous system. The examination of participants' medical history also revealed symptoms of hyperactivity of the sympathetic nervous system. The heart rate variability examination demonstrated a statistically significant increase in the variation range, mode amplitude, and stress index when compared with normal values, which indicated a reduced activity of the parasympathetic nervous system. Female participants experienced the most stimulation from the sympathetic nervous system, and thus, a greater autonomic imbalance, with sympathicotonia resulting in the reduction of their functional feasibility.

As our assessment includes the subjective performance criteria, all the participants were asked about the changes in their well-being. The patients of the first (experimental) group acknowledged positive changes like better day-to-day functioning, increased productivity, better control over emotions, and, therefore, reduced emotional lability. Since periods of 4 and 12 weeks of treatment are generally considered to be sufficient for relieving the activated sympathetic nervous system, we assessed the heart rate variability to evaluate the overall functioning of the autonomic nervous system. It was recorded that the treatment plan with dietary supplements designed for the experimental group proved to be effective in correcting the autonomic dysfunction, while the treatment plan with placebo did not demonstrate any sufficient improvement in patients.

The increase in the total power (TP) compared with the data obtained before treatment should be noted. The changes in the sympathetic and parasympathetic nervous activity are reflected in the index of interaction LF/HF. The influence of the sympathetic nervous system decreases and the overall functioning of the autonomic nervous system improves **(Table 1)**.

Table 1. The results of the four-week treatment

Variables / Group	Before treatment	After four weeks of treatment		
		Experimental group	Placebo	Normal values (healthy people)
The Cerdo vegetative index, c.u.	34.25±2.32	0.22±0.02*	33.18±0.05*	0.23±0.04
Mode, sec	0.81±0.13	2.62±0.12*	0.98±0.11*	2.46±0.27
Mode amplitude, %	54.27±3.01	38.21±1.27*	55.74±2.38*	38.14±2.11
Variation range, sec	0.13±0.01	0.29±0.02*	0.12±0.03*	0.28±0.02
Stress index,c.u	193.25±4.04	136.35±2.05*	131.27±3.27*	138.23±5.12

The changes in the adaptive responses: Experimental and Placebo groups

Group / Condition	Experimental group		Placebo		Normal values (healthy people)
	Before treatment	After treatment (check-up 3)	Before treatment	After treatment (check-up 3)	
High intensity exercise	34.40	84.16*	39.56	38.64	100
Acute stress condition	17.35	1.51*	16.10	18.84	0
Chronic stress condition	48.25	13.33*	47.34	48.52	0

Note: * - significant difference (P <0.05) when compared with the data before treatment and with the Placebo group.

As we were interested in examining the progress made over shorter and longer treatment plans, we studied the impact the dietary supplements had on the autonomic nervous system during a continuous consumption for twelve weeks and four weeks of consumption with eight-week follow-up care **(Tables 2 and 3)**.

Table 2. The results of the twelve-week treatment

Variables / Group	Before treatment	After 12 weeks of treatment		
		Participants who took the dietary supplements for twelve weeks N=10	Participants who took the dietary supplements for four weeks with an eight-week follow-up care N=20	Normal values (healthy people)
The Cerdo vegetative index, c.u.	34.25±2.32	0.24±0.01*	0.37±0.05*	0.23±0.04
Mode, sec	0.81±0.13	2.33±0.10*	1.56±0.15*	2.46±0.27
Mode amplitude, %	54.27±3.01	38.44±1.15*	45.25±0.25*	38.14±2.11
Variation range, sec	0.13±0.01	0.31±0.06*	0.19±0.07*	0.28±0.02
Stress index,c.u	193.25±4.04	139.15±1.06*	151.15±1.03*	138.23±5.12

Note: * - significant difference (P <0.05) when compared with the data before treatment

Table 3. The changes in the adaptive responses: treatment plans of different duration

Group / Condition	Experimental group		Experimental group		Normal values (healthy people)
	A four-week treatment plan	A twelve-week treatment plan	A four-week treatment plan	A four-week treatment plan and eight-week follow-up care	
High intensity exercise	84.16*	92.15*	84.16*	75.15*	100
Acute stress condition	1.51*	0.55*	1.51*	1.05*	0
Chronic stress condition	13.33*	7.35*	13.33*	23.80*	0

Note: * - significant difference (P <0.05) when compared with the data before treatment

When analyzing the results, we concluded that the nutrition plans with dietary supplements contribute to adaptive responses and proper functioning of the ANS, help relieve stress and increase work productivity.

The assessment of the hormonal system

Hormonal changes in both men and women result in many age-related diseases and conditions, including osteoarthritis and osteoporosis, depression, metabolic syndrome, urogenital disorders, immunodeficiency, and cognitive impairments. With aging, men experience increased peripheral aromatization of testosterone, a decrease in the level of total and free testosterone in blood serum, and a relative rise in estrogen levels. Although both testosterone and estrogen are necessary for proper functioning, there should be a right balance. Insufficient testosterone is a primary cause of hypogonadism. Major hormonal changes in women during menopause originate from the decrease in the amount of estrogen and progesterone. As estrogens and androgens undertake the role of regulators of main biological processes in both men and women, they are essential for building, maintaining, and controlling reproductive systems. It should be noted that while with aging men experience a fall in testosterone, there is a simultaneous rise in sex steroid-binding globulin (SSBG) which is produced by the liver.

When examining the hormonal system, we were also interested in dehydroepiandrosterone, which is very important for the production of testosterone in men and estrogens in women. However, as people age, their dehydroepiandrosterone levels fall. While there are no similar or comparable precursor hormones like dehydroepiandrosterone in plants, antlers are known to contain substances similar to dehydroepiandrosterone, and when taken as a dietary supplement, allow successful use of their functional properties.

Comparing the results of hormone testing before treatment and after a four-week treatment, we observed a decrease in the level of prolactin, a hormone that hinders the production of other hormones in men and women, after four-week diet therapy. On the other hand, there was an increase in testosterone, dehydroepiandrosterone sulfate, and sex steroid-binding globulin **(Table 4)**. It is important to note the significance of sex steroid-binding globulin, as with aging the decreased production of SSBG results in a drop of freely circulating hormones in the bloodstream, which prevents hormones' access to target tissues even when the hormone levels are within the normal range.

Bearing in mind that most research indicates a correlation between treatment length and outcomes, treatment length is of particular interest. The changes in hormone levels of female patients administered four-week and twelve-week treatment plans are shown in **Table 5**.

Table 4. Hormone levels of male and female patients

Hormones	Experimental group (before treatment)	Experimental group (four-week treatment)	Control group
Hormone levels of male patients			
Prolactin (µg/L)	635 [780÷430]	501* [3470÷596]	405 [330÷419]
Testosterone (nmol/L)	6.2 [1.4÷ 6.6]	9.6 * [5.8÷ 10.2]	7.3 [1.4÷ 4.6]
Sex steroid-binding globulin (nmol/L)	65.5 [45÷100]	95.6* [80÷140]	98.5 [85÷135]
Dehydroepiandrostenediol sulphate (nmol/L)	1.5 [45÷100]	7.6* [2.80÷4.40]	6.5 [1.5÷3.0]
Hormone levels of female patients			
Prolactin (µg/L)	689 [780÷430]	391* [370÷596]	425 [305÷465]
Testosterone (nmol/L)	1.2 [1.4÷ 4.6]	2.6 * [2.2÷ 4.2]	3.3 [1.4÷ 4.6]
Sex steroid-binding globulin (nmol/L)	45.5 [45÷100]	75.6* [80÷140]	68.5 [85÷135]
Dehydroepiandrostenediol sulphate (nmol/L)	0.7 [0.5÷1.2]	3.8* [2.9÷4.5]	2.5 [1.8÷3.8]

Note: * - significant difference (P <0.05) when compared with the data before treatment

Table 5. Hormone levels of female patients: four-week and twelve-week treatment plans

Hormones	Experimental group (before treatment)	Experimental group (four-week treatment)	Experimental group (twelve-week treatment)	Control group
Prolactin (µg/L)	689 [780÷430]	391* [300÷596]	350* [310÷455]	425 [305÷465]
Testosterone (nmol/L)	1.2 [1.4÷ 4.6]	2.6 * [2.8÷ 4.2]	2.9 * [3.8÷ 4.0]	3.3 [1.4÷ 4.6]
Sex steroid-binding globulin (nmol/L)	45.5 [45÷100]	75.6* [80÷140]	70.5* [80÷145]	68.5 [85÷135]
Dehydroepiandrostenediol sulphate (nmol/L)	0.7 [0.5÷1.2]	3.8* [2.9÷4.5]	4.5* [3.5÷5.5]	2.5 [1.8÷3.8]

Note: * - significant difference (P <0.05) when compared with the data before treatment

As can be seen from the data above, diet therapy with antler products helps to reduce prolactin levels, and increase testosterone and dehydroepiandrostenediol sulfate. And the growth in levels of sex steroid-binding globulin creates a favorable environment for the sex steroid hormones which are responsible for efficient work performance, general well-being, and the quality of life.

The assessment of the immune system

Age-related diseases and conditions are associated with hormonal imbalance, manifest in declines in immune functioning, and cause immune deficiency. Various cellular and molecular damage, which occurs during the lifetime, results in decayed physical capacity. In elderly patients, inadequate immune functioning develops secondary immunodeficiency with a prolonged course of illness and low treatment response, thus, with aging, people are more likely to develop cancer. Intercellular messengers, which can regulate the activity and growth of cells and ensure the proper functioning of the immune, hormonal and nervous systems, are cytokines. Cytokines influence mental and emotional health; however, few studies have examined the benefits of antler products for the cytokine profile.

To evaluate the immune response, we determined the levels of IFN-γ, IL2, IL4, and IL10 cytokines in the supernatants using the enzyme-linked immunosorbent assay. The testing was performed in compliance with the instructions provided by the manufacturers of test systems (Procon, Russia and Cytimmune, USA). The results are presented in **Table 6**.

Table 6. TH1 and TH2 cytokine production by peripheral blood cells: Spontaneous and PHA-stimulated

Variable / Group	Before treatment	Follow-up care (1 month after treatment)			Follow-up care (3 months after treatment)
		Experimental group (four-week treatment) N=30	**Placebo**	**Normal values (healthy people)**	**Experimental group (twelve-week treatment) N=10**
INF-γ Spontaneous, pg/ml	77.24±5.15	102.44±18.25*	76.27±12.84	106.01±12.78	105.15±10.05*
INF-γ PHA-stimulated, pg/ml	183.14±18.76	278.97±21.04*	190.15±12.31	276.32±22.09	282.97±15.05*
INF-γ Stimulation index, c.u	2.31±0.20	2.58±0.10*	2.34±0.15	2.58±0.31	2.64±0.15*
IL2 Spontaneous, pg/ml	37.17±0.93	42.50±0.72*	38.31±0.93	42.70±8.35	44.50±0.55*
IL2 PHA-stimulated, pg/ml	81.73±15.59	146.73±13.83*	82.73±10.37	136.30±18.42	152.73±13.04*
IL2 Stimulation index, c.u	2.21±0.45	4.39±0.28*	2.48±0.26	3.23±1.06	3.15±0.34*
IL4 Spontaneous, pg/ml	116.63±12.03	58.84±10.25*	115.32±15.73	58.89±9.34	55.25±10.11*
IL4 PHA-stimulated, pg/ml	241.23±18.86	146.41±12.32*	235.92±15.73	146.05±18.04	148.33±12.05*
IL4 Stimulation index, c.u	2.03±0.05	2.68±0.16*	2.00±0.17	2.60±0.31	2.75±0.15*
IL10 Spontaneous, pg/ml	74.18±1.42	63.33±3.42*	72.21±9.35	64.21±7.85	65.35±3.15*
IL10 PHA-stimulated, pg/ml	165.53±6.18	156.15±5.18*	150.13±4.18	157.91±17.49	159.05±4.10*
IL10 Stimulation index, c.u	2.26±0.25	2.45±0.36	2.23±0.36	2.45±0.31	2.55±0.17

Note: * - significant difference (P <0.05) when compared with the data before treatment

As can be seen from the data above, the use of dietary supplements as part of combined therapy contributes to a significant activation of T cells and regulates the cytokine response with increased production of INF-γ and IL2 (both spontaneous and PHA-stimulated) and regularised production of IL4 and IL10.

The assessment of bone metabolism

Osteoporosis and osteoarthritis are among the most common age-related conditions. With aging, bones lose density and structure; therefore, there is a higher risk of fractures. Osteoporosis and osteoarthritis cause pain, reduce mobility and result in the need for regular medical care. Osteoporosis can cause prolonged or even permanent disability, leading to a significant decrease in the quality of life (L.I. Benevolenskaya, 2003, 2005, Schwartz G.Ya., 2005, Barlow D.H., 2007).

As these conditions affect many aging people, it is important to study the markers of bone remodeling and establish ways to reduce the risk of bone fractures (Garnero P., Delmas P.D. 2008). The data on the levels of calcium, phosphorus, alkaline phosphatase, and biochemical markers of osteoporosis (osteocalcin and C-terminal telopeptide of type I collagen) before and after treatment are shown in **Table 7**.

Table 7. The data on bone metabolism: nutrition plan with dietary supplements

Variables	Before treatment	Experimental group (four-week treatment)	Experimental group (twelve-week treatment)
Calcium, mmol/L	2.38±0.14	2.95±0.36	3.25±0.18*****

Phosphorus, mmol/L	1.45±0.10	1.97±0.12	2.05±0.09*
Alkaline phosphatase	196.93±28.21	201.05±34.72	205.14±30.05
CrossLaps, ng/mL	0.25±0.08	0.32±0.09	0.45±0.06*
Osteocalcin, ng/mL	13.02±2.76	21.42±3.42	35.05±2.15*

Note: * - significant difference (P <0.05) when compared with the data before treatment

Comparing the results of the tests, we can conclude that there are no significant changes in the levels of calcium, phosphorus, and alkaline phosphatase before and after a four-week treatment. However, after a four-week treatment with a dietary supplement C-terminal telopeptide of type I collagen levels were 1.3 times as high as those recorded before treatment (p=0.0013). At the same time, there was an increase in osteocalcin from 13.02±2.76 ng/mL to 21.42±3.42 ng/mL. The higher levels of C-terminal telopeptide of type I collagen and osteocalcin indicate positive biochemical changes in bone metabolism, as these two are now considered to be the markers of bone resorption and bone turnover.

CONCLUSION

Analyzing the findings of the clinical trials and assessing the efficiency of using dietary supplements in nutrition plans, we can draw the following conclusions:

1. A four-week treatment plan is sufficient for normalizing the functioning of the autonomic nervous system and the immune status.
2. A twelve-week treatment plan with dietary supplements is recommended for strengthening the hormonal system, in particular, for the increased production of dehydroepiandrostenediol.
3. A twelve-week treatment plan with dietary supplements is recommended when there is a need for improved bone metabolism.

Since the combined use of the tested dietary supplements has a positive potentiated effect on the autonomic nervous, hormonal, and immune systems as well as bone metabolism, we conclude that they can be successfully applied to prevent and treat age-related diseases and conditions. For example, they can be used to:

1. reduce anxiety and improve mental and emotional health.
2. minimize work fatigue, help recover from injuries, boost the immune system, assist in resisting and fighting infections in colder seasons, and get over jet lag.
3. treat neurological disorders that affect women during and after menopause and men during andropause.
4. treat acute and chronic conditions with a psychosomatic component, help maintain the functions of the cardiovascular system, manage blood pressure and anemia, and relieve gastric ulcers, chronic gastritis, and cholecystitis.
5. improve sports-related performance, prevent and beat fatigue and sickness, and help recover quicker after exercise.
6. restore vitamin and mineral deficiencies, enhance functional ability in unfriendly environments, and improve the quality of life.
7. suppress or stimulate the immune system to assist the body in fighting acute and chronic hepatitis, chronic bronchitis, and pulmonary tuberculosis.
8. accelerate the healing process after surgery, quicken fracture healing, and prevent adhesion formation.
9. improve sexual function in men and women.
10. prevent the signs of aging, help regenerate skin cells, rejuvenate the body and treat age-related conditions.

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REFERENCES

1. Gerasimenko NF, Poznyakovsky VM, Chelnakova NG. Healthy food and its role in ensuring the quality of life. Technologies of the food and processing industry of the agro-industrial complex-healthy food products. 2016;4(12):52-7.
2. Tutelyana VA, Nikityuk DB. Nutrition and Clinical Dietetics: National Guidelines. M.: GeoTAR-Media; 2020. 656 p.
3. Poznyakovsky VM, Chugunova OV, Tamova MYu. Food ingredients and biologically active additives. M .: INFRA-M; 2017. 143 p.
4. Khoroshilov IYe. Clinical nutrition and nutritional support. SPb .: ELBI – SPb; 2018. 192 p.
5. Stepanov KM, Lebedeva UM, Dyachkovskaya MP, Dokhunayeva AM, Zakharova LS. Development of innovative technology of a specialized drink of the functional purpose on a basis of Rosa acicularis. Yakut Med J. 2015;1(1):88-96.
6. Stepanov KM, Lebedeva UM. Fundamentals of rational nutrition in conditions of low temperatures. Yakut Med. 2018;6:70.
7. Stroev E, Krylov Y. Effect of the drugs changing the level of cyclic-nucleotides on acetylation. Farmakol Toksikol. 2017;42(4):402-6.
8. Sukhikh SA, Astakhova LA, Golubcova YV. Functional dairy products are enriched with plant ingredients. Foods Raw Mater. 2019;7(2):428-38.
9. Sunagawa Y. The therapeutic potency of natural products against heart failure. Yakugaku Zasshi. 2020;140(4):471-7.
10. Shim JO, Kim S, Choe BH, Seo JH, Yang HR. Effect of nutritional supplement formula on catch-up growth in young children with nonorganic faltering growth: a prospective multicenter study. Nutr Res Pract. 2020;14(3):230-41.
11. Shukla UN, Manju LM. Biofortification: Golden way to save a life from micronutrient deficiency. Indian J Agricu Rev. 2018;39(5):202-9.
12. Singh AK, Rana HK, Tshabalala T, Kumar R, Gupta A, Ndhlala AR, et al. Phytochemical, nutraceutical and pharmacological attributes of a functional crop Moringa oleifera Lam: An overview. S Afr J Bot. 2020;129:209-20.
13. Skoracka K, Eder P, Łykowska-Szuber L, Dobrowolska A, Krela-Kaźmierczak I. Diet and nutritional factors in male (in) fertility—underestimated factors. J Clin Med. 2020;9(5):1400.
14. Tokhiriyon B, Poznyakovsky VM, Beliaev NM. Biologically active complex for functional support of connective tissue: Scientific substantiation, clinical evidence. Int J Pharm Res Allied Sci. 2019;8(10):115-22.
15. Tokhiriyon B, Poznyakovsky VM, Andrievskikh S. Biologically active complex for multifactorial support of the central nervous system: new composition, efficacy. Carpathia J Food Sci Technol. 2020;12(1):52-60.
16. Tokhiriyon B, Poznyakovsky VM. Full-scale testing of a functional product in patients with vegetative-vascular dysfunction and chronic cerebrovascular disorder. Int J Pharm Res Allied Sci. 2019;8(3):91-7.