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THE INFLUENCE OF THE RARE-EARTH METALS NANOPARTICLES ON THE RAT'S MALES REPRODUCTIVE FUNCTION IN THE DESCENDING STAGE OF ONTOGENESIS

The anti-aging effects of the rare-earth metals nanoparticles have been studied on the 18-21-month-old rat males. It was shown that the nanoparticles of Gadolinium Ortovanadate activated by Europium ($GdVO_4 : Eu^{3+}$) in a dose of 0.33 mg/kg during chronic using (70 days) have demonstrated the anti-aging effects on the old male's reproductive function manifested by the increasing the sex hormone level and activating the spermatogenesis.

Key worlds: nanoparticles of Gadolinium Ortovanadate; reproductive function; spermatogenesis

INTRODUCTION

The increasing of the duration of human life in the high developed countries is often associated with the birth rate decreasing and with the changes of the population structure. The part of elderly men is increasing most rapidly. The manifestation of most elderly-aged-associating diseases is going after finishing reproductive period which is accompanied by the androgenic deficiency with men [3, 9]. These changes cause the increasing the amount of the old people with multiple pathologies, that, in its turn, causes the problem of prolonging an active life. The importance of the reproductive health can't be determined only by the care of the population strength.

There is natural slow decreasing of the sex hormone Ts (testosterone) level in the declining year's men. According to the data of the Massachusetts Adult Search (MMAS) the Ts level is decreasing approximately 0.8 % a year after 30-35 years to the end of life. The development of the age-associated hypogonadal state is closely connected with disturbances in the central hypothalamic-hypophysis system and in the testicles. The amount of the Leidig testosterone-synthesizing cells decreases in the testicles; the density of the luteinising hormone receptors and activity of the Ts synthesizing ferments are lowering. The concentration of the sex steroid binding globulin is increasing in blood, the fraction of the biologically active androgen is decreasing and the ratioTs/E_2 is changing, the estrogen activity is heightening [18].

Due to Ts versatile activity in the men's organism the decreasing of the androgen blood level determines not only sexual disturbances but different somatic changes too. It is considered that violation of the sex hormones ratio takes an important part in the age-associated diseases development such as DM (diabetes mellitus) and insulin resistance, determines the activity of the high nervous system, emotion sphere and so on [21]. In fact beginning from 50 years old the glucose blood level is gradually increasing – every 10 years by 0.055 mmol/l. The DM accompanies by the lowering of the total and free testosterone levels and oxidative stress is often developing [12]. There is lack of stimulating insulin action on the Leidig cells Ts production and decreasing those cells reaction to the chorionic gonadotropin introduction under the insulin resistance condition. All those facts quicken the involution of the reproductive function and make worse the quality of elderly life. Under the Ts deficiency the symptoms complex of the adult organism which requires varied therapy is developing. The polypragmasia may lead to the undesirable interaction between medicines, metabolic disturbances and developing of complications.

Nowadays there is lowered Ts concentration with the youngest men 8.0-12.0 nmol/l (subnormal indices). This accelerated involution of the reproductive function may be considered as civilization disease [6], which leads to the premature age androgen deficiency and hypofertility with difficult and often empirical treatment [2].

Taking into consideration mentioned facts the correction of the sex hormones disbalance for the decelera-

tion of the organism involution is an important part and expected positive effect of the anti-aging therapy. Moreover, the increasing of the middle-aged part of population requires for the prophylaxis and intensive control of the non-infectious diseases and determines the perceptivity of the innovational approaches and searches of the new nontoxic substances with positive effects on the age processes which would be able to stimulate reproductive function and fertility, to normalize age metabolism, to influence insulin resistance and to support full value of the β-cells function thus showing antidiabetic effects. The substances with endocrinological effects on the human organism might be the most perspective for the anti-aging therapy.

The substances of vanadium should be marked among ones. This element takes up an exceptional position among essential elements, because both of its forms – anionic and cationic – take part in the biological processes [13]. The element is a catalyst in the redox reactions. Vanadium is an inhibitor or regulator of the Na^+-K^+-ATF-ase, ribonuclease and others ferments. It intensifies the tissues oxygen absorption, catalyzes the phospholipids oxidation by liver ferments and influences the blood glucose level. In addition to their hypoglycemic effect, Vanadium compounds have anti-hypertensive anti-cholesterolemic activities, change food taking throw their influence the hypothalamic neuropeptide Y. This metal is an active to the different organism functions. On the base of animals' researches it was proven that vanadium using under the conditions of iodine deficiency or goitrogens activity has a positive effects on the thyroid functions. Vanadium inhibits the fat acids and cholesterol synthesis [11]. In experiments with the animal it has been shown that vanadium deficiency in the organism leads to the increasing of the abortion frequency, to thyroid disorders and decreasing lactation [17]. But in the big doses this metal is very toxic for the human organism [10], especially for the reproductive system [15], it may disturb spermatogenesis an initiate apoptosis of the spermatozoons [16]. The biological role of the vanadium is considered not to be enough studied.

The vanadium insulin-like activity carefully summarized in the reviews [14, 15] is the most interesting. At the same time the high toxicity of the soluble vanadium compound [5, 10] prevents it's using as insulin-like substance, although, its insoluble salts, especially gadolinium ortovanadate, are nontoxic, but have low bioavailability. It is expected that using the gadolinium ortovanadate in the form of nanocrystals would raise the solubility keeping safe its positive biological effects and nontoxicity. Analysing above-cited data we might allow that vanadium compounds have anti-aging effects especially with decreasing their toxicity in the form of nanoparticles (NP).
Purpose: the studying of the affectivity of the $GdVO_4$ nanoparticles using for age changes correction in rat males in the descending stage of ontogenesis as a potential medicines for prevention the age-associated conditions and involution of the reproductive function.

MATERIALS AND METHODS

The investigation has been carried out on the Wistar rat males from the vivarium of SI "Institute for endocrine pathology named after V. Ya. Danilevskyi NAMS of Ukraine". The animals have been kept in the standard conditions of natural light sources, recommended diet and water regime ad libitum. The experiment has been carried out according to the national ethic principles which correlated with thesis of European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes.

The model for natural aging replaying not only Ts level lowering but also expressive age androgen-depending processes has been used. The influence of the $GdVO_4 : Eu^{3+}$ nanoparticles on the reproductive function has been studied on the group of rats (21 males) with fixing age (18 months in the experiment beginning, descending stage of ontogenesis). According to [7] rats after 18 months are related to the pre-elderly period (18-23 months). During experiment the general condition, body weight and glucose blood level have been controlled. The animals have been taken away from the experiment throw the fast decapitation without using narcosis on the 71-st day. Fast decapitation allows avoiding changes of the sex hormone concentration in blood owing to anesthetics action. The indices of the reproductive function have been determined after course (70 days) intaking of the $GdVO_4 : Eu^{3+}$ nanoparticles (NP $GdVO_4$ group). The colloidal water solution of the NP $GdVO^4$ activated by Europium ($GdVO_4 : Eu^{3+}$) has been obtained at the Institute for scintillation materials NAS of Ukraine. NP $GdVO_4$ in dose of 0.33 mg/kg have been given with the feeding avoiding stress influence the long manipulations with sonde. During animals autopsy the visual inspection and determination of the eternal mass of organs have been carried out. The samples of blood preserving at – 18 °C for determining of sex hormone level (Ts and E_2) have been taken on the 30-th day (from tail vein) and on the 71-st day (during decapitation).

The condition of the reproductive system has been estimated using spermogram indices of the epididymal sperms during microscoping. The concentrations of the epididymal sperms, motility and pathological forms percentage have been determined [7]. The concentration of the morphologically normal sperms C_x has been calcula ted [8]. In order to study the morphological indices of the histological sections the testicles have been fixed in the 10 % formaldehyde solution of neutral pH, then cut sections have been dehydrated by passing the tissue trough the increasing concentrations of the ethylic alcohol (from 0 to 100 %). After that the tissue has been embedded into the celoidine-paraffin, cut using the microtome and colored with haematoxylin and eosin. On the cut sections of the testicles tissue the morphometric estimating of spermatogenesis indices, the relative quantity of the seminiferous tubules with the spermatogenic epithelium and with the spermatozoa in the metaphase of the second part

Table 1

ABSOLUTE MASS OF ORGANS OF THE EXPERIMENTAL RATS ($\bar{x} \pm S_{\bar{x}}$)

Mass	Group	
	Control (n = 7)	NP $GdVO^4$ (n = 6)
Testicles, mg	3557.1 ± 174.4	4100.0 ± 194.9*
Seminal vesicles, mg	828.6 ± 40.6	970.0 ± 88.9
Epididymis, mg	1278.6 ± 28.6	1320.0 ± 93.0
Ventral prostate gland, mg	628.6 ± 68.9	710.0 ± 64.0
Thymus gland, mg	235.1 ± 36.1	212.6 ± 31.0
Adrenal glands, mg	39.4 ± 2.3	41.0 ± 3.4
Spleen, mg	1171.4 ± 108.5	1480.0 ± 158.6
Pituitary gland, mg	10.0 ± 1.2	8.8 ± 1.3

Note: *– Differences between control group (0.05 < P < 0.1).

Table 2

SPERMOGRAMM OF THE INVESTIGATED RATS AFTER CHRONIC APPLICATION OF THE NP $GDVO_4$ ($\bar{x} \pm S_{\bar{x}}$)

Indices	Control (solvent) (n = 7)	NP $GdVO_4$ (n = 5)
Concentration, mil./ml	42.9 ± 4.4	56.2 ± 5.2*
Motility, %	73.1 ± 4.5	78.8 ± 4.9
Pathological form, %	14.4 ± 1.4	16.0 ± 2.7
Non-motile, %	8.1 ± 1.2	10.6 ± 1.0
C_N**, mil./ml	33.3 ± 3.8	41.2 ± 3.8
Duration of motility, min	218.7 ± 14.2	258.4 ± 20.9

Note: * – Statistical differences between Control group (P < 0.05); ** – The concentration of the morphologically normal and motile spermatozoons.

of ripening (with 12-th stage of meiosis), and the quantity of the normal spermatogonial sterm cells in the spermatic code have been carried out [7].

The blood glucose level has been estimated with all rats on 30-th, 50-th and 70-th days. The glucose concentration in blood obtained from rat's tale on empty stomach has been measured using glucometer "Exan-G" [7]. The concentrations of sex hormones in the blood serum have been determined by enzyme-linked immunosorbent assay (ELISA) method on ELISA Analyzer "StartFax-100" using commercial sets of agents "Testosterone-CHEMA" and "Estradiol-CHEMA" (Russia).

The results obtained from the rats of the similar age, which have been fed with the starch solution without any additional components, have been considered to be as control ones.

The statistical analyze has been carried out using Excel program 2003. The results have been calculated as an arithmetic mean ($\bar{x}$) and their statistical error ($\pm S_{\bar{x}}$) using the Q Dunn criterion for the polynomial equations [15]. The differences between groups have been considered to be a statistical probability according to statistical reliability $p < 0.05$.

RESULTS AND DISCUSSION

One of the main indices of the animal condition is a body weight control which has been carried out during the experiment with the interval of 10-15 days. On the beginning of the experiment all of animal groups have no ifferences; the average body weight of the sample was 361 ± 2.6g. In 2 month from the beginning of the experiment (20-month-old rats) all of rats have the statistically increased body weight by compared with 18 month-old rats. The difference was 7.1-8.7 %. This fact is evidence of the absence of the toxicity of the studying substances. Taking into the account the using of the standard diet it may be confirmed that an increasing body weight is due to natural aging processes [20]. At the same time it must be marked the difference in the changing rate of this index. The rats of control group have a statistically reliable exceeded body weight than initial ones beginning from the 45-th day of the experiment (20-21-month-old). In the NP $GdVO^4$ group the body weight has been growing slowly and only on the 60-th day of the experiment has exceeded the initial and has become such as the control group. Thus, the age-associated body weight increasing in the NP $GdVO_4$ group of animals was slower that may be considered to be positive effect. During the experiment the glucose blood concentration has been determined. There is no difference between groups of animals as to the initial glucose level; the concentration of the glucose in the whole sample was 5.1 ± 0.2 nmol/l. The glucose level in the control group animals has statistically reli-able increased up to 6.0 ± 0.2 nmol/l (135.2 % from initials meanings) when the rats were 19 months. On the 50-th day of the experiment the glucose level was exceeded the nitials meanings by the 33.5 % (P < 0.05) and on the 70-th day – by the 18.5 % (P < 0.05). After NP $GdVO_4$ using on the 50-th and 70-th days of the experiment the blood glucose concentration was at the initial level. On the 30-th day this index was smaller than in the control group but only on the 70-th day has reached the age level. The differences with the initial level on the 30-th, 50-th and 70-th days of the experiment were 11.5 (P < 0.05), 8.3 (P < 0.05) and 16.6 % (P < 0.05) accordingly. Thus, the inhibition of the age-depending hyperglycaemia is observed in the NP $GdVO_4$ group. It may by considered that long-term keeping the normal body weigh and normoglycaemia are connecting. The obtained data shows the necessity of the additional researches of the glucose decreasing properties of these substances on the proper models.

During visual examination the differences of the state of the internal organs between control and NP $GdVO_4$ group have been not determined. There are no differences between masses of the immune organs (thymus gland and spleen). The masses of the adrenal glands have no differences, too (Tab. 1).

The chronic using of the NP has no influence on the reproductive organs.

Only increasing the testicles masses has been observed in the NP $GdVO_4$ group (0.05 < P < 0.1).

The obtained results have shown that investigated substances have no toxic influence on both reproductive and immune systems of old rats.

Table 3

THE QUANTITATIVE CHARACTERISTIC OF THE RAT SPERMATOGENESIS, *ME (LQ; UQ)*

Indices	Control	$GdVO_4$	P_1 (according to Mann-Witney criterion)	P_2 (according to Student's criterion t)
Normal spermatogonial sterm cells, M ± m	61.04 ± 0.51	62.25 ± 0.10*	–	0.0014
Index of spermatogenesis, point, *Me (LQ; UQ)*	3.31 (3.25; 3.37)	3.35 (3.32; 3.37)*	0.0035	–
Tubules with 12-th stage of meiosis, %, *Me (LQ; UQ)*	4.0 (4.0; 5.0)	7.0 (6.0; 7.0)*	0.0023	–
Tubules with stratified epithelium, % *Me (LQ; UQ)*	0.0 (0.0; 1.0)	0.0 (0.0; 0.0)	0.8357	–

Note: * – Statistically significant differences between experimental and control groups on the significance level $p < 0.05$.

According to the Tab. 2, the increasing of the spermatozoon's concentration in the epididymal sperms suspension has been marked under the NP influence.

According to the prior investigations the spermatozoon's concentration with 10-month-old rat males is 35.3 ± 5.6 mil/ml, the part of motile sperms is 69.0 ± 5.4 %, abnormal forms – 17.5 ± 4.7 % and CN – 29.0 ± 5.0 mil/ml. Comparing these indices with the data in Tab. 2 it may be seen that spermogram's indices of control rat males group (20-20.5-month-old) are the similar.

The morphometrical characteristics of the spermogram of the rats which took the NP $GdVO_4$ confirmed the visual signs of the spermatogenic epithelium improvements (Tab. 3). The presented data show the evident increasing of the spermatogonial sterm cells, the spermatozoon's meioses activity and the index of spermatogenesis with the experimental males. The combination of these signs may be considered to be real stimulation of the spermatogenesis.

The main man's sex hormone is known to be Ts; it determines sex belonging, regulates the sex development and intensity and character of the sexual behavior with the adults; it regulates the spermatogenesis and metabolism. The level of its derivate E_2 synthesized in the target tissue cells by aromatization of the Ts is of great importance because the ratio between these steroids demonstrates the androgen-estrogen correlation and relative androgenization or estrogenization of the organism. Ts synthesizes in the gonads by Leidig cells and gets the blood straight away. Its synthesis is regulated by gonadotropic hormones and is characterized by specific daily rhythm. The blood samples were obtained at one and the same time in 20-th and 60-th day of the nanoparticle feeding. The measuring concentration of steroid showed no significant differences between experimental and control groups on the 20-th day of the experiment (Tab. 4).

The 72 % increasing of the Ts concentration was determined with the males in 60 days of the NP $GdVO_4$ feeding. This index was statistically higher than with the same males or with the control animals on the 20-th day of the experiment. The concentration of E_2 in all groups of the experimental animals has no significant differences. Such changes caused increasing the Ts/E_2 ratio, they weren't statistically reliable though. It means, the long lasting application of the NP $GdVO_4 : Eu^{3+}$ stimulate Ts synthesis which is demonstrated by the spermatogenesis activating.

Table 4

THE CONCENTRATION OF THE SEX HORMONES OF THE RAT ($\bar{x} \pm S_{\bar{x}}$)

Index	Day	Group	
		Control (n = 6)	NP $GdVO_4$ (n = 6)
Testosterone, nmol/l	20	10.3 ± 1.1	11.6 ± 2.5
	60	12.8 ± 1.8	20.0 ± 4.1*/**
Estradiol, pmol/l	20	127.0 ± 17.7	161.0 ± 19.5
	60	136.9 ± 23.5	162.2 ± 42.0
Testosteron/ Estradiol	20	66.1 ± 8.8	57.2 ± 9.8
	60	94.0 ± 12.9	154.6 ± 37.0

Note: * – Statistically significant differences from control group, 20 days ($P < 0.05$ due to Dunn criterion); ** – Statistically significant differences from group NP $GdVO_4 : Eu^{3+}$ 20 days ($P < 0.05$ due to Dunn criterion).

Thus, under the condition of the alimental chronic application in dose of 0.33 mg/kg stimulate the spermatogenesis. It has been proved by Ts level increasing, activating the testicles spermatogenic epithelium and by increasing the epididymal spermatozoons concentration.

The estimating of the obtained results confirms the anti-aging biological activity of the NP $GdVO_4$. Due to the anti-aging effect the NP $GdVO_4$ have hindered the age-depending hyperglycemia development, inhibited the age-depending increasing of body weight, have positive influence on the spermatogenesis intensity and Ts synthesis with the old rat males.

Indeed, it is very difficult to discuss the obtained results of the NP $GdVO_4 : Eu^{3+}$ investigations owing to the unique properties of the nanoparticles and used term

of the researching (70 days). The comparison between the well-known biological properties of vanadium and its salts might be incorrect. First of all, the researchers mark the high toxicity of the vanadium and its salts [5, 10]. In our case from 7 animals of the NP $GdVO^4$ experimental group only one male died on 67-th day without signs of the toxic injury. During autopsy the increasing of the adrenal glands and other internal organs masses were not obtained. The organs had a usual surface look. However, it is necessary to carry out subsequent experiments with the nanoparticles chronic application by younger animals that will allow to study NP chronic and gonads toxicity.

The vanadium has demonstrated a positive influence on the glucose metabolism during NP $GdVO_4$ application [19]. However, to make any conclusions as to any available kind of actions – insulin like or of the prolonging of the pancreas β-cells function is impossible. The answer to this question requires the subsequent specific investigations using the appropriate models.

The significant increasing of the spermatozoons production accompanied by the testicles mass growing under the influence of the NP $GdVO_4$ has been determined. It allows to suppose that NP $GdVO_4$ stimulating effect on the reproductive function will remain after stopping nanoparticles application. The data of spermogram have been proved by the light microscopying of the testicles tissues. The evident increasing of the spermatogonial quantity in the tubules, spermatozoons activity in the meiosis and index of the spermatogenesis has been detected after the NP $GdVO_4$ application. As for the possible mechanism of such action one may think that it is the consequence of the Ts production more than 30 % that has lead to the above-cited effects. The increasing of the androgenisation may also lead to other determined positive effects.

CONCLUSIONS

1. The nanoparticles of the $GdVO_4$ in dose of 0.33 mg/kg has demonstrated the significant and long-lasting effects as for glucose metabolism. The inhibition of the age-depending growing body weigh (up to 45-th day) and absence of the increasing glucose blood level (up to 50-th day) have been detected.
2. The positive effect of the nanoparticles of the gadolinium ortovanadate on the reproductive function of old animals by the increasing of the Ts concentration and spermatogenesis activating has been detected.

The experimental results obtained on the model of the aged organism involution which has summarized inhibition of the all organs and functions have been described. The reproductive system functions of full value in the young age when its different disturbances have another character and may lead to the fertility lost. This fact defines the perceptivity of the further investigations on the specific models of the hypo fertility in the young age which may appear due to different negative factors.

REFERENCES

1. Безруков В. П. Влияние старения населения на формирование потребностей в финансировании здравоохранения // Матер. консульт. междунар. семинара. – М.: МЗМП РФ, 1995. – С. 149.
2. Бондаренко В. А. Функция печени и андрогенный статус у мужчин с идиопатическими патоспермиями // В. А. Бондаренко, А. С. Минухин, Е. И. Скорняков // Пробл. ендокринол. патол. – 2012. – № 2. – С. 15-19.
3. Верткин А. Л. Возрастной андрогенный дефицит и эректильная дисфункция / А. Л. Верткин, Д. Ю. Пушкарь. – М.: Изд. группа «ГЭОТАР-Медиа», 2009 – 176 с.
4. Гланц С. А. Медико-биологическая статистика. – М.: Практика, 1998. – 459 с.
5. Голубев М. А. Сравнительная характеристика ванадий-содержащих соединений, обладающих инсулиноподобным действием / М. А. Голубев, В. К. Городецкий, А. П. Аниськина // Вопр. мед. химии. – 2000. – № 2. – С. 78-83.
6. Дедов И. И. Возрастной андрогенный дефицит у мужчин [Текст] / И. И. Дедов, С. Ю. Калинченко. – М.: Практ. медицина, 2006. – 240 с.
7. Доклінічні дослідження лікарських засобів: [метод. рекоменд.] // За ред. О. В. Стефанова. – К.: Авіценна, 2001. – 528 с.
8. Карпенко Н. О. Інтегральна оцінка репродуктивної функції самців лабораторних тварин / [Н. О. Карпенко, В. В. Талько, С. Т. Омельчук та ін.] // Укр. біофармац. журн. – 2011. – Т. 13, № 2. – С. 64-68.
9. Куликовский В. Ф. Частичный андрогенодефицит, остеопения и ранние нарушения микции у стареющих мужчин, связь явлений / В. Ф. Куликовский, Н. В. Олейник // Совр. наукоемкие технол. – 2009. – № 6. – С. 48-49.
10. Пат. 2341528 RU, МПК C 07 F 9/00. Оксованадиевый комплекс с глицином, проявляющий гипогликемическую активность [Електронний ресурс] / Е. Н. Вергейчик, О. В. Лапочкин, Л. Б. Губанова (RU); заявник та патентовласник ГОУ ВПО Пятигорская государственная фармацевтическая академия Федерального агентства по здравоохранению и социальному развитию (RU). – № 2007116481/04. – Заявл.: 02.05.07. Опубл.: 20.12.08. – Режим доступа: www.fips.ru
11. Скальный А. В. Химические элементы в физиологии и экологии человека [Електронний ресурс]. – Режим доступа: http://www.m-kat.ru/ebook.php?file=skalny.djvu&page=26
12. American Association of Clincal Endocrinologists. Medical Guidelines for Clinical Practice for the Management of Diabetes Mellitus: AACE Diabetes Mellitus Clinical Practice Guidelines Task Force // Endocrine Practice. – 2007. – Vol. 13, Suppl. 1. – P. 3-66.

13. Baran E. Oxovanadium (IV) and oxovanadium(V) complexes relevant to biological systems // J. Inorg. Biochem. – Vol. 80, Issues 1-2. – P. 1-10.
14. Cam M. C. Mechanisms of vanadium action: insulin-mimetic or insulin-enhancing agent? / M. C. Cam, R. W. Brownsey, J. H. McNeill // Canad. J. Physiol. Pharmacol. – 2000. – Vol. 78, № 10.– P. 829-847.
15. Chandra A. K. Effects of vanadate on male rat reproductive tract histology, oxidative stress markers and androgenic enzyme activities / A. K. Chandra, R. Ghosh, A. Chatterjee, M. Sarkar // J. Inorg. Biochem. – 2007. – Vol. 101, № 6. – P. 944-956.
16. Chandra A. K. Protection against vanadium-induced testicular toxicity by testosterone propionate in rats [Text] / A. K. Chandra, R. Ghosh, A. Chatterjee, M. Sarkar // Toxicol. Mech. Methods. – 2010. – Vol. 20, № 6. – P. 306-315.
17. Domingo J. L. Vanadium: a review of the reproductive and developmental toxicity // Reprod. Toxicol. – 1996. – Vol. 10, № 3. – P. 175-182.
18. Holland J. Testosterone levels and cognition in elderly men: [a review] // Maturitas. – 2011. – Vol. 69, № 4. – P. 322-337.
19. Marzban L. Insulin-Like Actions of Vanadium: Potential as a Therapeutic Agent / L. Marzban, J. H. McNeill // J. Trace Elements in Experim. Med. – 2003. – Vol. 16. – P. 253-267.
20. Thomas M. A. Effects of aging on food intake and body composition in rats / M. A. Thomas, H. B. Rice, D. Weinstock, R. L. Corwin // Physiol. Behav. – 2002. – Vol. 76, № 4-5. – P. 487-500.
21. Yeap B. B. Hormones and health outcomes in aging men // Exp. Gerontol. – 2013. – Vol. 11, № 2. – P. 251-270.

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ВПЛИВ НАНОЧАСТИНОК РІДКОЗЕМЕЛЬНИХ ЕЛЕМЕНТІВ НА РЕПРОДУКТИВНУ ФУНКЦІЮ САМЦІВ ЩУРІВ НА НИЗХІДНІЙ СТАДІЇ ОНТОГЕНЕЗУ

На самцях щурів віком 18-21 міс. досліджені антивікові ефекти наночастинок рідкоземельних металів. Показано, що наночастинки ґадолінію ортованадату активованого європієм ($GdVO_4$: Eu^{3+}) у дозі 0,33 мг/кг маси тіла при хронічному застосуванні (70 діб) чинять антивікову дію щодо репродуктивної функції старих тварин, у яких зросла концентрація чоловічого статевого гормону та активувався сперматогенез.

Ключові слова: наночастинки ґадолінію ортованадату; репродуктивна функція; сперматогенез

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ВЛИЯНИЕ НАНОЧАСТИЦ РЕДКОЗЕМЕЛЬНЫХ ЭЛЕМЕНТОВ НА РЕПРОДУКТИВНУЮ ФУНКЦИЮ САМЦОВ КРЫС НА НИСХОДЯЩЕЙ СТАДИИ ОНТОГЕНЕЗА

На самцах крыс возрастом 18-21 мес. исследованы антивозрастные эффекты наночастиц редкоземельных металлов. Показано, что наночастицы гадолиния ортованадата активированного европием ($GdVO_4$: Eu^{3+}) в дозе 0,33 мг/кг массы тела при хроническом применении (70 суток) замедляли возрастной рост массы тела и развитие гипергликемии (до 50-х суток) в сравнении с исходным уровнем. Установлено антивозрастное действие вещества относительно репродуктивной функции старых животных, у которых возросла концентрация мужского полового гормона, активировался сперматогенез.

Ключевые слова: наночастицы гадолиния ортованадата; репродуктивная функция; сперматогенез

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