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**Key words:** leiomyoma, matrix metalloproteinases, gene polymorphism.

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## THE INFLUENCE OF IMMUNE ACTIVITY COMPOUNDS TO THE BLOOD SERUM CYTOTOXICITY AND THE LEPTIN LEVEL IN THE CONDITIONS OF HYPOESTROGENIA

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The estrogen activity decrease during the menopause causes changes in metabolic processes and is the principal pathogen factor of post-menopause metabolic syndrome (MS) development. In turn, MS is the risk factor of diabetes mellitus, cardiovascular, autoimmune and other chronic diseases with women at menopause [1]. The level of adipose tissue hormones, in particular, of leptin, correlates with the main components of MS, including obesity, insulin resistance, low intensity inflammation, enhancement of atherogenesis processes [2]. We showed the positive impact of immunotropic pharmacological compounds to the metabolic status with ovariectomized (OVE) rats with MS on the model of estrogen deficiency.

The purpose of the work was to study the changes of blood serum cytotoxicity and leptin concentration with the ovariectomized rats with MS and in the conditions of levamisole immune activity compounds application and its derivate PL-308.

**Materials and Methods.** The MS with OVE rats was modeled with the high carbohydrate diet (HCD) which was administrated 2 weeks after of surgery for 5 weeks. 5 groups of animals were created: 1st group – intact control; 2nd group – OVE rats ("OVE"); 3rd group – OVE rats which received 30 % sucrose solution and placebo ("OVE+HCD+placebo"); 4th group – OVE rats which were administrated with levamisole (L) through probe on the background of HCD in the dose 2.5 mg / kg of body weight ("OVE+HCD+L"); 5th group – OVE rats which were administrated with PL-308 on the background of HCD in the dose 4.0 mg / kg of body weight ("OVE+HCD+PL-308"). We evaluated the rat blood serum cytotoxicity (BSC) in the reaction of lymphocytolysis (G. Friemel, 1987), the leptin concentration was established by the method of enzyme immunoassay on the analyzer Stat Fax 2100 (USA) with the kit of «Diameb» (USA). The material treatment statistics is made with the calculation of arithmetic mean and its error. The evaluation of null hypotheses is made at the level of significance not more than 0.05.

**Results.** It is established that OVE is accompanied by the BSC increase almost threefold in the comparison with intact control (respectively  $9.80 \pm 0.80$  % against  $3.20 \pm 0.60$  %,  $p \leq 0.05$ ). The presence of MS enhances significantly the BSC both compared to OVE control and intact rats (respectively  $20.00 \pm 1.40$  % against  $9.80 \pm 0.80$  %, i.e. 2 and 6 times,  $p \leq 0.05$ ). It is known that the cytotoxic reactions can be mediated by cellular or antibody mechanisms, their increase is observed in various inflammatory, in particular, autoimmune processes. An increase in BSC under hypoestrogenia as such may indicate, in particular, the activation of the humoral immunity level and testify to the possibility of increasing the proinflammatory state and the level of autoantibodies in the early stages of estrogen deficiency. The combination of OVE and MS enhances the imbalance

of humoral immunity which may be a trigger for the development of autoimmune diseases and other inflammation-induced processes. Given the introduction of L and PL-308 a significant decrease of BSC was observed (respectively for L –  $6.70 \pm 0.80$  %, PL-308 –  $2.50 \pm 0.50$  %,  $p \leq 0.05$ ). It should be noted that the compound PL-308 was more effective because it credibly reduced BSC even with respect to the comparator of L. The leptin level in the conditions of OVE and in the combination of OVE with MS tended to decrease compared to the intact group (respectively  $8.20 \pm 0.15$  ng / ml and  $8.10 \pm 0.10$  ng / ml against  $9.00 \pm 0.30$  ng / ml,  $0.05 < p < 0.1$ ) which may be due to the short duration of the experiment and, as we stated already, may be associated with the formation of insulin resistance at this stage [3]. The compounds L and PL-308 credibly increased the leptin level in comparison with OVE and OVE+MS (respectively L  $11.30 \pm 0.80$  ng / ml, PL-308 –  $10.00 \pm 0.80$  ng / ml,  $p \leq 0.05$ ), herewith the PL-308 indicators were not significantly different from intact control. It should be noted that L has a thymomimetic, cholinergic and nicotinic effect which promotes the increase of insulin receptors on insulin-dependent cells to which adipocytes belong, and they affect the intensification of metabolic processes and the reduction of manifestations of the state of insulin resistance in conditions of estrogen deficiency. Thus, the reduction of cytotoxicity and the increase / normalization of leptin level under the influence of immunomodulatory compounds indicate the feasibility of immunocorrection application during menopause to reduce the manifestations of MS. Prospects for further scientific research. The obtained data indicate the prospect of further study of the compound PL-308 especially given the fact that acute toxicity estimation of the compound PL-308 is considered as class 5 (almost non-toxic compounds) while levamisole is considered as class 4 (low-toxic compounds).

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**Key words:** serum cytotoxicity, leptin, hypoestrogenia, levamisole, levamisole derivate PL-308.

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## FEATURES OF DISTRIBUTION OF SOYBEAN AGGLUTININ (SBA) RECEPTORS IN THE EXTRACELLULAR MATRIX OF THE MENISCI OF RAT KNEE JOINT AFTER INTRAFETAL INJECTION OF ANTIGENS

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**Relevance.** The results of previous investigations at the Department of Human Anatomy of Zaporizhzhia State Medical University have shown that intrafetal injection of antigens leads to changes in the rates of morphogenesis of fetal organs and tissues, that can be used for the modeling of the syndrome of undifferentiated connective tissue dysplasia in rats [3]. Lectins are informative molecular probes that can detect glycoconjugates in cells and tissues. Lectins and their receptors provide extracellular, cell-matrix interactions, participate in the regulation of proliferation, differentiation and apoptosis of cells [1, 2]. Previously we have shown that distribution of the receptors to other lectins (WGA, VSA) differs in intact knee joint menisci and after intrauterine antigenic effect [4, 5].