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Ecdisten and Ecsumid as Effective Means of Preventing Negative Shifts in Certain Metabolic Processes of the Myocardium, Caused by Immobilization Stress

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Abstract The preparation of ecdisten, created based on the phytoecdysteroid 20-hydroxyecdysone, isolated from the rhizomes of *Rhaponticum carthamoides* and ecsumid (total ecdysteroid-containing drug, including 20-hydroxyecdysone, turkesterone, cyastron, etc.), obtained from the aerial part of *Ajuga turkestanica* was used in experiment. When it was administered to rats, exposed to prolonged immobilization stress, they effectively maintain the energy balance of the myocardium and prevent negative changes in the antioxidant and NO-ergic systems, observed under these conditions. In terms of the severity of its protective action on metabolic processes in the myocardium or stress, ecsumid surpasses the corresponding action of ecdisten. The study is an experimental animal study. The abilities of ecdisten and ecsumid as agents capable of preventing negative shifts in some metabolic processes of the heart muscle of rats developing under prolonged immobilization stress have been determined.

Keywords Phytoecdysteroids, Ecdisten, Ecsumid, Immobilization stress, Myocardial metabolism

1. Introduction

In recent years, it has been established that phytoecdysteroids are widespread in the plant kingdom. They are found both in lower plants: algae, fungi, and in higher ones: ferns, gymnosperms and angiosperms [1,2,3]. Numerous pharmacological studies on various experimental animals have shown that these compounds have the ability to increase the adaptive capacity to stressful environmental factors due to an optimizing effect on metabolic processes in their body in the complete absence of any toxic effects [2,4-9].

As a result, on the basis of phytoecdysteroids, drug preparations and biologically active food additives (ecdisten, ecsumid, serlisten, etc.) were created, which have a general strengthening and adaptogenic effect [10,11,12,13,14]. Considering that one of the most vulnerable systems of the body to the negative impact of stress (especially strong and long-term) is the cardiovascular system [15,16]. It seemed extremely important to determine the possibility of using ecdysteroid-containing agents to counteract this process, which is fraught with the subsequent development of diseases such as ischemic heart disease, myocardial infarction and others [15,17,18]. In this regard, this work presents the results of a study of two ecdysteroid-containing drugs - ecdisten and ecsumid.

Aim of the research. To determine the ability of ecdisten and ecsumid as a means of preventing negative changes in some metabolic processes of the rat cardiac muscle that develop under prolonged immobilization stress.

2. Materials and Methods

We used an ecdisten preparation containing purified ecdysterone (20-hydroxyecdysone), isolated from the rhizomes of *Rhaponticum carthamoides* (Willd.) Iljin and a total ecdysteroid-containing preparation ecsumid (the composition includes 20-hydroxyecdysone, turkesterone, casterone, etc.), obtained from the aerial part of *Ajuga turkestanica* (Rgl.) Brig [19,20,21]. We have used immobilization of male rats (130–140 g) as a model of severe long-term stress in the supine position for 16 hours [22], obtained from the vivarium at the Department of Pharmacology and Toxicology of the Institute of Chemistry of Plant Substances of the Academy of Sciences of the Republic of Uz. The contents and manipulations carried out with them corresponded to generally accepted international standards for the treatment of laboratory animals (Directive 2010/63/EU of the European Parliament. September 22, 2010). Ecdisten and Ecsumid were administered per os in the form of an aqueous emulsion with gummi arabicus (due to

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the poor solubility of the preparations) at a dose of 5.0 mg / kg (in preliminary experiments it was established as the most optimal), immediately before fixation of the animals. Control animals received an adequate amount of an aqueous emulsion of gummi arabicus. The animals were slaughtered by instant decapitation. A number of indicators assessed post-stress changes in myocardial metabolism. The content of glycogen was determined according to [23], adenine nucleotides according to [24], creatine phosphate according to [25] data. The energy charge was calculated using the formula: (adenosine triphosphate + 0.5 adenosine diphosphate) / sum of adenine nucleotides [26]. The content of malondialdehyde was determined according to [27], the activity of catalase according to [28] and superoxide dismutase according to [29] data. The activity of endothelial NO-synthase [30] and the main metabolites of nitric oxide [31] was also determined. The obtained data were subjected to statistical processing using the Student's t-test.

3. The Results of Research

As can be seen from the presented table, prolonged immobilization stress was accompanied by pronounced disorders of metabolic processes in the myocardium. The negative change in this case of energy metabolism was evidenced by the fact that stressful rats showed a lower preservation of the glycogen fund in the heart muscle, combined with a lower preservation of the adenosine triphosphate and creatine phosphate fund, as well as a significantly lower energy charge. The content of glycogen, ATP and creatine phosphate in control animals was lower than in intact animals by 53.7; 48.3 and 42.2%, respectively. The calculated value of the energy charge was 22.4% lower than the corresponding indicator in intact animals. The revealed changes seem to be very negative manifestations of the stress impact on the animal organism and the myocardium, in particular, since it is the decrease in the energy potential of cardiomyocytes that largely impairs their functional activity under these conditions [15]. In addition, free radical reactions increased in the heart, which play a significant role in myocardial damage during stress [13,15]. The products of these reactions, attacking unsaturated fatty acid residues of membrane phospholipids, change their polarity. This leads to disruption of the activity of enzymes, receptors, channel-forming proteins located on or inside membranes. As a result, the phospholipid layer becomes permeable to most cations (Ca^{2+}, Na^{+}), the accumulation of which in cardiomyocytes has a damaging effect [16].

Thus, under conditions of reproducible stress, an increase in the level of malondialdehyde, one of the products of lipid peroxidation, was revealed by 87.1%, which, apparently, could be due to a depression of the body's antioxidant defense by 47.3. In addition, catalase decreased the activity of superoxide dismutase by 42.9% (table 1).

Table 1. Effect of ecdistene and ecsumid on some parameters of cardiac muscle metabolism in rats under immobilization stress (M ± m, n=6-8)

Experimental conditions	Intact animals	Stress (control)	Stress + ecdisten	Stress + ecsumid
Glycogen, mg%	315±10,4	146±8,2 *	232±7,4 *,1	278±8,6 *,1,2
Adenosine triphosphate, microns M / g of tissue	2,28±0,06	1,18±0,04*	1,70±0,05*,1	2,08±0,06*,1,2
Adenosine diphosphate, microns M / g of tissue	0,66±0,05	0,50±0,02*	0,58±0,02 1	0,62±0,04 1
Adenosine monophosphate, microns M/ g of tissue	0,50 ± 0,03	0,74±0,03*	0,65±0,02*,1	0,56±0,02 1,2
The sum of adenine nucleotides	3,44 ±0,15	2,48±0,04*	2,93±0,05*,1	3,26±0,10 1,2
Energy charge	0,76	0,59	0,68	0,73
Creatine phosphate, microns M / g of tissue	4,22 ± 0,24	2,44±0,12*	3,18±0,16 *,1	3,52±0,18 *,1
Malondialdehyde, nmol / mg of protein	0,310±0,04	0,58±0,06*	0,380±0,04 1	0,352±0,02 1
Catalase, mcat/min / g of protein	12,6± 2,20	7,2±0,34*	9,2±0,42 1	10,6±0,46 1,2.
Superoxide Dismutase, CU / min/mg of protein	0,524±0,08	0,276±0,02*	0,398±0,04 1	0,452 ±0,06 1
NO-synthase nmol / min / mg of protein	2,12 ±0,20	1,10 ±0,06*	1,62 ±0,16 1	1,90±0,18 1
NO, mc M / g of protein	1,04±0,08	0,49±0,04*	0,750±0,05*,1	0,862 ±0,08 1

Note: * - Reliably to the indicators of intact animals, [1]- to the control, [2]-between two experimental groups (the confidence level is assumed at $p<0.05$)

The deficiency of the endogenous antioxidant system and a sharp increase in malondialdehyde in the experiments were accompanied by a significant inhibition of the NO-ergic system in the myocardium, which was manifested by a decrease in the activity of endothelial NO-synthase by 48.1 and a decrease in the level of the main NO metabolites in the heart by 52.9%. These changes indicate the developing endothelial dysfunction, characteristic of many pathological conditions of the cardiovascular system. Violation of NO-dependent vasodilation of blood vessels under stress is also one of the reasons for the development of myocardial ischemia [32,33].

Comparison of biochemical changes in the cardiac muscle of stressed rats in control and with the introduction of ecdisten and exumid showed their clear protective effect on the course of metabolic reactions aimed at maintaining homeostasis of energy production, as well as the normal functioning of the antioxidant and NO-ergic systems. The table shows that in experimental rats treated with ecdisten and ecsumid, the safety of energetically valuable myocardial products: glycogen, ATP, creatine phosphate was higher than in the control by 58.9 - 90.4; 44.1 - 76.3 and 30.3 -

44.3%. The energy charge of the system increased with the introduction of ecdysteroid-containing agents in relation to the control by 15.2 and 23.7% (lower than this indicator in intact animals only by 10.5 and 3.9%). The obtained data indicate that if under stress, as noted above, there is an excessive consumption of energy resources of the myocardium, then under the influence of ecdisten and ecsumid under these conditions, the corresponding metabolic shifts are aimed at adjusting the metabolism in cardiomyocytes towards an increase in the energy potential, which ultimately and determines the viability of the cell under extreme influences [15].

Ecdisten and ecsumid also markedly promoted the activation of key enzymes of the antioxidant system in the myocardium and inhibited lipid peroxidation reactions. Their introduction contributed to the fact that the activity of superoxide dismutase and catalase was higher than in the control by 44.2 - 63.8% and 27.8 - 47.2%, and the level of malondialdehyde decreased by 34.5 and 39.3%. Also, under stress conditions (see table), an optimizing effect of ecdisten and ecsumid on the NO-ergic system was revealed, leading to the restoration of NO-synthase activity and an increase in the level of NO in the myocardium.

For most of the indicators under consideration, reflecting the effect of the investigated ecdysteroid-containing drugs under stress, it is clear that ecsumid has a definite advantage over ecdisten. This may be due, on the one hand, to the synergism of the various ecdysteroids that make up the latter. On the other hand, this may be due to the fact that ecsumid contains turkesterone, one of the most active phytoecdysteroids in terms of its effect on the metabolism of higher animals [8].

Thus, ecdisten and ecsumid are of significant interest as a means of reducing pathological changes in the metabolic processes of the heart muscle under stress by changing the metabolism in the cell, aimed at reducing the consumption of energy resources, inhibiting lipid peroxidation processes and optimizing the functioning of the NO-ergic system of the myocardium.

4. Conclusions

1. Ecdisten and ecsumid in experiments on rats exposed to prolonged immobilization stress prevent negative changes in the metabolic processes of the myocardium.
2. By its ability to maintain homeostasis of energy production under stress, to optimize the state of the antioxidant and NO-ergic system of the heart muscle, ecdisten is inferior to the total ecdysteroid-containing drug ecsumid.

REFERENCES

[1] Ramazonov N.Sh., Bobaev I.D., Syrov V.N., Sagdullaev Sh.Sh., Mamatkhanov A.U. 2016. Chemistry, biology and technology of phytoecdysteroid production. – Tashkent: *Science and technology*. – 260 p.

[2] Dinan L., Lafont R. 2015. Phytoecdysteroid occurrence, distribution, biosynthesis, metabolism, mode of action and applications: developments from 2005 to 2015 // *Pharmaceutical Bulletin (Karaganda)*, – No. 3-4. – Pp. 9-37.

[3] Lafont R. 2012. Recent progress in Ecdysteroid Pharmacology // *Theoretical and Applied Ecology*, – No. 1. – Pp.6-12.

[4] Ashrafova R.A., Syrov V.N. 1979. General action, toxicity and changes in the microstructure of internal organs and tissues of experimental animals with prolonged administration of ecdysterone // *Pharmacology of natural compounds*. – Tashkent, – Pp. 147-153.

[5] Syrov V.N. 1984. To the mechanism of the anabolic action of phytoecdysteroids in mammals // *Biological sciences*,– No. 11. – Pp.16-20.

[6] Syrov V.N. 1994. Phytoecdysteroids: biological effects in the body of higher animals and prospects for use in medicine // *Experimental veterinarian pharmacology*, Vol. 57, No. 5. – Pp. 61-66.

[7] Syrov V.N. 1996. On the adaptogenic properties of phytoecdysteroids // *Reports of the Academy of Sciences of the Republic of Uzbekistan*, No. 11. – Pp. 61-64.

[8] Syrov V.N. Comparative study of the anabolic activity of phytoecdysteroids and steranabols in the experiment // *Chemical Pharmaceutical journal*, 2000. – Vol.34, No. 4. – Pp. 31-34.

[9] Phytoecdysteroids / Ed. V.V. Volodin. 2003. St. Petersburg: *Science*, 293 p.

[10] Volodin V.V., Volodina S.O. 2015. Phytoecdysteroids and adaptogens. New ecdysteroid-containing substance serpisten // *Pharmaceutical Bulletin (Karaganda)*, No. 3-4. – Pp. 69-82.

[11] Volodin V.V., Pchelenko L.D., Volodina S.O., Kudryasheva A.G., Shevchenko O.G., Zagorskaya N.V. 2006. Pharmacological evaluation of the new ecdysteroid-containing substance “Serpisten” // *Plant resource*, Vol. 42, Issue 3. – Pp.113-130.

[12] Volodin V.V., Syrov V.N., Khushbaktova Z.A., Volodina S.O. 2012. Stress-protective action of the ecdysteroid-containing substance Serpisten // *Theoretical and Applied Ecology*, No. 1. – Pp.18-24.

[13] Golikov A.P., Boytsov S.A., Mikhin V.P. 2003. Free radical oxidation and cardiovascular pathology: correction with antioxidants // *Attending physician*, No. 4. – Pp. 70-74.

[14] Syrov V.N. 2015. Experimental and clinical results of evaluating the effectiveness of ecdisten as a drug of metabolic type of action // *Pharmaceutical Bulletin (Karaganda)*, No. 3-4. – Pp.111-117.

[15] Merson F.Z. 1984. Pathogenesis and prevention of stress and ischemic damage to the heart. – Moscow: *Medicine*, 272 p.

[16] Merson F.Z., Kagan V.E., Archipenko Yu.V., Belkina L.M., Rozhitskaya I.I. 1981. Prevention of activation of lipid peroxidation and damage to antioxidant systems of the

myocardium during stress and experimental infarction // *Cardiology*, No. 12. – Pp.55-60.

[17] Abdullaev A.I., Abdullaev T.A., Prokhorova I.R., Ganieva N.P., Makhkamova Z.Z. 2001. Ecdisten in the complex therapy of patients with myocarditis // *Bulletin of the Association of Doctors of Uzbekistan*, No. 4. – Pp.61-63.

[18] Iskanderova S.D., 1992. Sharipova U.S. Influence of ecdisten on the physical performance of patients with myocardial infarction // *Medical journal of Uzbekistan*, No. 3. – Pp. 14-16.

[19] Mamatkhanov A.U., Shamsutdinov M., Shakirov T.T. 1980. Isolation of ecdisten from the roots of Rhaponticum carthamoides // *Chemistry of Nature*, No. 4. – Pp. 528-529.

[20] Ramazonov N.Sh., Syrov V.N, Soatov Z., Rakhmatullaev M.R. 2006. Method of producing ecdisten. *Patent IAP 03161*. The Republic of Uzbekistan.

[21] Turakhozhaev M.T., Mamatkhanov A.U., Abdukadyrov I.T., Syrov V.N., Khushbaktova Z.A., Sagdullaev Sh.Sh. 2015. A method of obtaining a remedy for stopping the phenomena of fatigue. *Patent IAP 05078*. The Republic of Uzbekistan.

[22] Dardymov N.V. 1976. Ginseng, Eleuthero coccus (to the mechanism of biological action). – Moscow: *Science*, 184 p.

[23] Lo S, Russell J.C., Taylor A.W. 1970. Determination of glycogen in small tissue samples // *Journal of Applied physiology*, V.28, No. 2. – Pp. 234-236.

[24] Venkstern T.V., Baev A.A. 1957. Nucleotide composition of nuclear erythrocytes // *Biochemistry journal*, No. 6. – Pp. 1043-1055.

[25] Ennor A.H., Rosenberg H. 1952. The determination and distribution of phosphocreatine in animal tissues // *Biochemistry journal*, Vol. 51. – Pp.606-610.

[26] Atkinson D.E. 1968. The energy charge of the adenylate pools as a regulatory parameter interaction with feedback modifiers // *Biochemistry journal*, Vol 7. – Pp. 4030-4031.

[27] Stalnaya I.D., Garishvili T.G. 1977. Method for the determination of malonic dialdehyde using thiobarbituloric acid // *Modern methods in biochemistry*. – Moscow: Medicine, Pp.66-68.

[28] Korolyuk M.A., Ivanova L.I., Mayorova I.T. et al. 1988. Method for determining the activity of catalase // *Laboratory work*, No. 1. – Pp.16-19.

[29] Dubinina E.E., Salnikova L.A., Yefimova L.F. 1983. Activity and isoenzyme spectrum of superoxide dismutase of erythrocytes and human blood plasma // *Laboratory work*, No. 10. – Pp. 30-33.

[30] Sumbayev V.V., Yasinskaya I.M. 2000. Effect of DDT on the activity of nitric oxide synthase in the liver, lungs and brain of rats // *Modern toxicological problems*, No. 3. – Pp.3-7.

[31] Green L.C., Wanger D.A., Glogowski J. et al. 1982. Analysis of nitrate, nitrite and [^{15}N] nitrate in biological fluids // *Analytical biochemistry*, Vol. 126. – Pp. 131-138.

[32] Vanin A.F. 2001. Nitric oxide is a regulator of cellular metabolism // *Sorovsky review journal*, No. 11 (7). – Pp.7-12.

[33] Markov Kh.M. 2005. Molecular mechanisms of vascular endothelial dysfunction // *Cardiology*, No. 12. – Pp. 62-72.