

INFLUENCE OF AESCUSAN ON PRO- AND ANTIOXIDANT SYSTEMS OF KIDNEYS IN CASE OF EXPERIMENTAL HYPOTHYROIDISM

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Summary. The experiments, carried out on 38 rats with hypothyroidism, demonstrated that *Aescusan* not only normalizes the activity of antioxidant protection enzymes in the renal tissue of hypothyroid rats, but significantly reduces the content of primary and secondary end-products of lipoperoxidation as well as neutral and basic end-products of protein peroxidation, limiting oxidative modification of the renal tissue.

Резюме. Эксперименты выполненные на 18 крысах с гипотиреозом, показали, что Эскузан не только нормализует активность ферментов антиоксидантной защиты, но и существенно снижает содержание первичных и вторичных продуктов липопероксидации, а также нейтральных и основных продуктов протеинопероксидации, ограничивая тем самым окислительную модификацию почечной ткани.

Introduction. Nowadays a great attention is paid to the study of free radical oxidation processes, which can be considered both as adaptational body reaction and as universal mechanism of alteration of biostructures in case of pathology, including thyropathies [2]. Pluripotent influence and universality of biologic effects of thyroid hormones determines the close connection between their level and the intensity of free radical oxidation, lipid and protein peroxidation processes – non-specific markers of the dysfunction of inner organs, including kidneys [6, 7]. Functional condition of the latest is known to influence all metabolic processes in the body. The fact of mutual influence of thyroid status of the body, lipid and protein peroxidation processes and renal function status is undisputed [5]. The investigation of peroxidation processes and antioxidant system state (AOS) in renal tissue in case of thyropathy will widen the possibilities of targeted pathogenic corrective influence on the initial stages of renal dysfunction in order to prevent its chronization [4]. This substantiates the search of therapeutic methods, regulating antioxidant status disturbances. Horse chestnut seed extract preparations, known to demonstrate significant antioxidant properties as well as vasoprotective and vasotonic, anti-inflammatory and anti-edematous, anticoagulant and fibrinolytic effects, were found to be perspective in this concern [1, 3].

The **objective** of this study was to establish the character of influence of thyroid hormone deficiency on the processes of lipid and protein peroxidation in the renal tissue and to assess the possibility of *Aescusan* administration in complex treatment of hypothyroidism for the improvement of its efficacy.

Material and methods. The experiments were carried out on 38 matured nonlinear male rats under the standard conditions of vivarium. For the experimental modeling of hypothyroidism 28 animals were administered mercazolil (*Mercazolilum*, LLC

«Pharmaceutical company «Zdorovye», Ukraine) intraperitoneally in a dose of 10 mg/kg. 14 days after the beginning of pathology formation 18 hypothyroid rats and 10 animals of control group were euthanized by decapitation under the slight diethyl ether anesthesia, the rest 10 hypothyroid rats were administered *Aescusan* in the dose of 100 mg of α -aescinum/kg. The object of the research was renal tissue, removed, washed out of blood and homogenized for the further investigations right after animals' decapitation [4].

The state of lipid peroxidation (LPO) was assessed by quantification of malondialdehyde (MDA) and diene conjugates (DC), antioxidant protection – by the contents of enzymatic (superoxide dismutase (SOD), catalase (CT), glutathione peroxidase (GPO)) and non-enzymatic systems (glutathione S-transferase (GST), sulfhydryl groups (SH-groups). Dinitrophenylhydrazones (DPH) concentration was determined to assess the intensity of protein oxidative modification (POM) [4].

Statistical processing of the obtained data was performed with the establishment of Student's coefficient (t).

Results. As the results of investigation showed (table), MDA level in renal tissue of hypothyroidal rats was twice higher as compared with control parameters, DC contents was found to be increased by 38,1% despite the reliable increase (by 28,6%) of SOD activity. Such biochemical changes were possible under the excessive intensity of reactive oxygen species generation, confirmed by the increase of CT activity by 58,5% and two-fold reduction of the basic intrarenal antiradical enzyme – GPO. The elevation of GST activity by 21,0%, probably, hasn't compensated these changes, since the level of free SH-groups in renal tissue was reliably decreased. On this background the intensive peroxidation has involved protein molecules of renal structures – the contents of neutral and basic DPH in renal tissue was found to be elevated by 82,5 и 81,4% respectively.

In the renal tissue of hypothyroid rats MDA contents was found to be twice decreased under the influence of natural antioxidant *Aescusan*, the level of DC decreased by 33,7% and was even 8,5% lower than the control values; SOD activity decreased by 25,0% and did not differ from that in control animals. The activity of CT was decreased by 27,1%, remaining 15,5% higher than control level. *Aescusan* practically did not affect the activity of GST and did not change the amount of SH-group in the renal tissue, but improved of GPO activity by 2,6 times. The content of neutral and basic DPH in renal tissue under the influence of *Aescusan* decreased by 47,3 and 38,5%, respectively, and the level of POM did not differ from that in the control group.

Conclusion. The obtained findings evidence, that due to the exhaustion and failure of compensatory intrarenal antioxidant system, the intensity of accumulation of nephrotoxic lipid and protein peroxidation end-products in the renal tissue of hypothyroid rats tends to become excessive, causing renal dysfunction, leading to the ischemic, toxic or immunologic damage of renal tissue. *Aescusan* not only normalizes the activity of antioxidant protection enzymes in the renal tissue of hypothyroid rats, but significantly reduces the content of primary and secondary end-products of lipoperoxidation as well as neutral and basic end-products of protein peroxidation, limiting oxidative modification of the renal tissue. Mentioned positive effects of *Aescusan* enable its practical usage for optimization of prooxidant-antioxidant balance in renal tissue in case of hypothyroidism.

Table

Influence of *Aescusan* on the intensity of lipid and protein peroxidation and antioxidant activity in renal tissue of rats with experimental hypothyroidism (X±Sx)

Indices	Group, number of animals		
	Control, n=10	Hypothyroidism, n=18	Hypothyroidism + <i>Aescusan</i> , n=10
Malondialdehyde, $\mu\text{mol}/1 \text{ mg of tissue}$	83,71±0,76	168,23±2,78 p<0,001	79,40±2,01 p=0,06 p ₁ <0,001
Diene conjugates, nmol/1 mg of protein	1,18±0,03	1,63±0,06 p<0,001	1,08±0,03 p<0,05 p ₁ <0,001
Superoxide dismutase activity, un./1 min./1 mg of protein	0,28±0,01	0,36±0,02 p<0,01	0,27±0,01 p>0,4 p ₁ <0,01
Catalase activity, $\mu\text{mol}/1 \text{ min./1 mg of tissue}$	94,80±0,89	150,31±4,52 p<0,001	109,50±3,18 p<0,001 p ₁ <0,001 p ₂ <0,001
Glutathione S-transferase activity, $\mu\text{mol}/1 \text{ min./1 mg of tissue}$	14,30±0,53	17,30±0,45 p<0,001	15,80±0,48 p=0,05 p ₁ <0,05
Glutathione peroxidase activity, $\mu\text{mol}/1 \text{ min./1 mg of protein}$	87,31±1,08	42,02±1,31 p<0,001	109,80±5,83 p<0,01 p ₁ <0,001
Level of SH-groups, mmol/1 mg of tissue	0,029±0,001	0,021±0,001 p<0,001	0,026±0,003 p>0,5 p ₁ >0,2
Neutral dinitrophenylhydrazones, mmol/1 g of protein, 370 nm	1,03±0,06	1,88±0,01 p<0,001	0,99±0,06 p>0,6 p ₁ <0,001
Basic dinitrophenylhydrazones, un.o.d./1 g of protein, 430 nm	9,14±0,49	16,58±0,56 p<0,001	10,20±0,93 p>0,3 p ₁ <0,001

Note: p – statistically significant difference in comparison with control group;
p₁ – statistically significant difference in comparison with the group of hypothyroid animals;
n – number of experimental animals.

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