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EFFECT OF MELATONIN ON AGE-RELATED CHANGES OF GLYCATED HEMOGLOBIN CONTENT IN THE BLOOD OF ALLOXAN DIABETIC RATS

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Melatonin and its metabolites have potent antioxidant/anti-inflammatory properties, and they have proven to be highly effective in a variety of disorders linked to inflammation and oxidative stress. The increasing incidence of type 1 diabetes coupled with advances in treatment of type 1 diabetes has resulted in an unprecedented number of older adults living with and managing type 1 diabetes. Hyperglycemia-mediated oxidative stress plays a crucial role in diabetic complications. The consequence of the emergence of this shift can be the appearance of age features in the body's resistance to harmful factors of diabetes mellitus. Changes in the ontogenesis of sensitivity of the glycated hemoglobin content in the blood on the background of diabetes mellitus and melatonin injections are less studied.

The object of this experimental research was to ascertain the influence of melatonin on the background of aging on the level of glycemia and glycated hemoglobin content in the blood of alloxan diabetic rats. We used male Wistar rats, two age groups: the - 2-month (late puberty), and II - 4-month (adult). Alloxan diabetes was evoked via injecting the rats with a 5% solution of alloxan monohydrate intraperitoneally in a dose of 170 mg/kg. In each age group were control rats and diabetic animals which were introduced the melatonin ("Sigma", USA) preparation intraperitoneally in a dose of 10 mg/kg of body weight at 8 a.m. daily during 42 days starting with a 5-th 24 hour period after the injection of alloxan. Blood was taken from the tail vein to evaluate the glycemia level on 5-th and the 47-th day after the injection of alloxan. Rats were sacrificed on the 47-th day of the experiment in accordance with the ethical treatment of animals. Determination of the glycosylated hemoglobin content in whole blood (HbA_{1c}) was performed using a biochemical analyzer ("Bio-Rad Laboratory Inc.", France).

The level of glucose on the fifth day of the experiment in animals of both groups increased on average by 116% compared to control. However, on the 47-th day, this index was higher in the group of old rats by 22% more than in adult rats. HbA_{1c} content in erythrocytes of adult and old animals with overt diabetes increased by 177% and 190%, respectively compared with the control. The changes may be the result of age-related disorders of energy metabolism due to disturbances in free radical mechanisms. Moreover, hyperglycemia leads to increased free radical mechanism in old rats. We have reached the recovery of the HbA_{1c} content in the blood of diabetic rats of both age groups by melatonin injections. These results are consistent with the degenerative role of hyperglycemia on cellular reducing equivalent homeostasis and antioxidant defense, and provide further evidence that pharmacological intervention of antioxidants may have significant implications in the prevention of the prooxidant feature of diabetes and protects redox status of the cells. ROS reacts with some amino acid, producing anything from modified, denatured and non-functioning proteins that in further may be responsible for oxidative stress.

Thus, we have determined that there is a change in the course of ontogenesis the content of the HbA_{1c} in the blood to the effect of diabetes mellitus factors. According to the results we've got, melatonin shows its protective action against hyperglycemia-induced age-related changes of the HbA_{1c} content in the blood of alloxan diabetic rats.

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CHRONORYTHMS OF TOTAL ANTIOXIDANT ACTIVITY OF RAT SERUM UNDER DIFFERENT FUNCTIONAL ACTIVITY OF EPIPHYSIS CEREBRI

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The role of melatonin as a universal pacemaker of human biological rhythms has long been known. The physiological and biochemical parameters of the organism depend on the functional

state of the pineal gland. One of them is the state of antioxidant defense systems, the activity of which can be determined by the level of total antioxidant activity of blood serum (TAAS).

The goal of the study was to research the chronorhythmological features of TAAS in the serum of rats under conditions of different functional activity of the pineal gland.

Experimental studies were performed on white nonlinear adult male rats weighing 170 ± 10 g. For 14 days they were kept under different lighting conditions (simulation of different functional activity of the pineal gland): group A - normofunction - (12 hours of light: 12 hours of darkness); group B - hypofunction - (24 hours of light: 0 hours of darkness); group C - hyperfunction - (0 h of light: 24 h of darkness). The experiment used fluorescent lamps with an intensity of 1500 lux. Euthanasia, by decapitation under light ether anesthesia, was performed at 8.00, 12.00, 16.00 and 20.00. Serum TAAS was expressed as the percentage inhibition of spontaneous peroxidation of endogenous brain lipids (according to the content of malonic dialdehyde). Statistical processing of the obtained results was performed using the parametric Student's t-test. The difference in results at $p < 0.05$ was considered statistically significant.

It was investigated that in group A at 12.00 TAAS serum was the highest and amounted to 78.1%. The lowest rates were at 8.00. In animals of group B there were phenomena of desynchronosis with a shift of the peak of TAAS at 16.00 against the background of a decrease in absolute values by 13%; 27.3%; 11.4% and 15.75% at 8.00, 12.00, 16.00 and 20.00, respectively, compared to animals of group A. With hyperfunction of the pineal gland (group C), the chronorhythm of TAAS coincided with the rhythm in animals of group A. An increase in the level of TAAS have revealed in all hours of the experiment, especially at 16.00 (by 8.1%) and 20.00 (by 14.5%) compared with animals of group A.

The phenomena of desynchronosis against the background of hypofunction of the pineal gland are probably caused by suppression and disruption of the rhythm of melatonin synthesis. Normochronosis and an increase in serum TAAS when stimulating the pineal gland around the clock are probably caused by an increase in the production of melatonin, which is also a powerful antioxidant in the body.

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INFLUENCE OF THE PHENOMENON OF POLYMORPHISM ON THE PROPERTIES OF DRUGS

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The ability of solids to exist in two or more forms with different crystal structures, properties, and the same chemical composition describes the phenomenon of polymorphism. This turned out to be an extremely important factor that determines the therapeutic effect of pharmaceuticals (significantly affects the parameters of their biological activity).

Especially important for chemists-technologists and pharmacists were the detection and study of differences in chemical stability, solubility, hygroscopicity, phase transition temperature. Change of the modification of active pharmaceutical ingredients (API) can occur both during synthesis (when replacing the solvent, the introduction of additional substances), and during isolation, purification, drying, storage.

A large number of modern drugs are polymorphic in their physical structure with the same chemical composition, and in the process of transition from one form to another, significant changes in medicinal properties are possible.

Obtaining polymorphic forms of the same drug often occurs when changing the conditions of crystallization of substances. For this reason, medicinal substances obtained at different factories, and sometimes even within the same series at the same factory, may differ in physicochemical properties, which is determined by the peculiarity of its technology, in particular at the stage of crystallization, as well as the possibility of polymorphic transitions during transportation and storage. This can also occur during the production and storage of ready-made drugs with appropriate changes in the properties of drugs.