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IMPACT OF MELATONIN ON THE ACTIVITY OF GLUCOSE-6-PHOSPHATASE IN THE LIVER OF ALLOXANDIABETIC AND TETRACHLORMETHANE-INTOXICATED RATS EXPOSED TO LIGHT DEPRIVATION

Summary. *The paper demonstrates that the level of basal glycemia in the blood and the activity of glucose-6-phosphatase in the liver of alloxan diabetic rats with overt diabetes increase respectively compared with the control value. Toxic hepatitis decreases glucose-6-phosphatase activity in the liver. Rats exposed to light deprivation during the experiment room lighting (500Lk, fluorescent lighting), and the absolute round the clock darkness and under photoperiod 12 hour light : 12 hours dark. Exogenous melatonin normalizes impaired due alloxan diabetes and tetrachlormethane hepatitis glucose-6-phosphatase activity in rat liver independent from type of illumination.*

Key words: *melatonin, alloxan diabetes, toxic hepatitis, glucose-6-phosphatase, liver, rats, photoperiod.*

Introduction.

Glucose-6-phosphatase (EC 3.1.3.9, G6Pase) is an enzyme that hydrolyzes glucose-6-phosphate, resulting in the creation of a phosphate group and free glucose. Glucose is then exported from the cell via glucose transporter membrane proteins [12]. This catalysis completes the final step in gluconeogenesis and glycogenolysis and therefore plays a key role in the homeostatic regulation of blood glucose levels [10].

Nanoparticles were designed to promote insulin intestinal absorption via the oral route, to increase portal insulin levels to better mimic the physiological pathway, providing enhanced glucose control through glycogenolysis and gluconeogenesis. This important enzyme in gluconeogenesis and glycogenolysis are known to be inhibited by insulin and a shortage of the latter has increased activity [5].

Due to peculiarities of the molecular mechanisms of tetrachlormethan (CCl4) action upon the hepatocyte subcellular membranes (microsomal activation, lipid peroxide oxidation as the mechanism of catalytic peculiarities disorders of the membrane-linked enzymes) toxic hepatitis is considered to be as a model of molecular pathology of the membranous structures. Disturbance of the membrane structure and functions is a key intracellular process in the development of aetiologically different pathological processes [6].

Information from light and melatonin appear to be combined by the human circadian clock. The ability to combine circadian time cues has important implications for

Results and discussion.

According to the results obtained in the liver of alloxan diabetic rats, whose fasting glucose exceeded 8.9 mmol/l (overt diabetes), activity of the G6Pase (Fig. 1) for 12 days after alloxan administration increased compared with intact rats (175% during their stay in full light, at 157% in a photoperiod of 12 hours light : 12 hours darkness and 138% in absolute darkness).

G6Pase activity indicators in the group of rats with the passage of latent diabetes (blood glucose level on an empty stomach does not exceed 6,0 mmol/l) in conditions under day and night illumination in the term of observation was 50% higher than that of intact control parameters contained in the conditions of the equinox. The results (Figure 1) indicate that the maximum increase in G6Pase activity observed in the liver of diabetic rats with hyperglycemia levels greater than 8.9 mmol / l, and contained within a week, in full light.

So, diabetes in rat liver is accompanied by increase phosphorolysis of glycogen and gluconeogenesis; by decrease – glycolysis and characterized by reduction in the activity of antioxidant enzymes [4, 11]. Activation of gluconeogenesis explains the relative benefit of glucocorticoids, which induce the synthesis of key enzymes of gluconeogenesis. Histological examination of diabetic liver showed necrosis and degenerative changes of hepatocytes [1].

Daily, during the week, intraperitoneal administration of melatonin to alloxan diabetic rats decreases G6Pase activity in rat liver, both overt and latent diabetes, independently of the mode of illumination. The level of its activity was only on 35% respectively higher than control, means on 30% less than indexes of untreated diabetes rats.

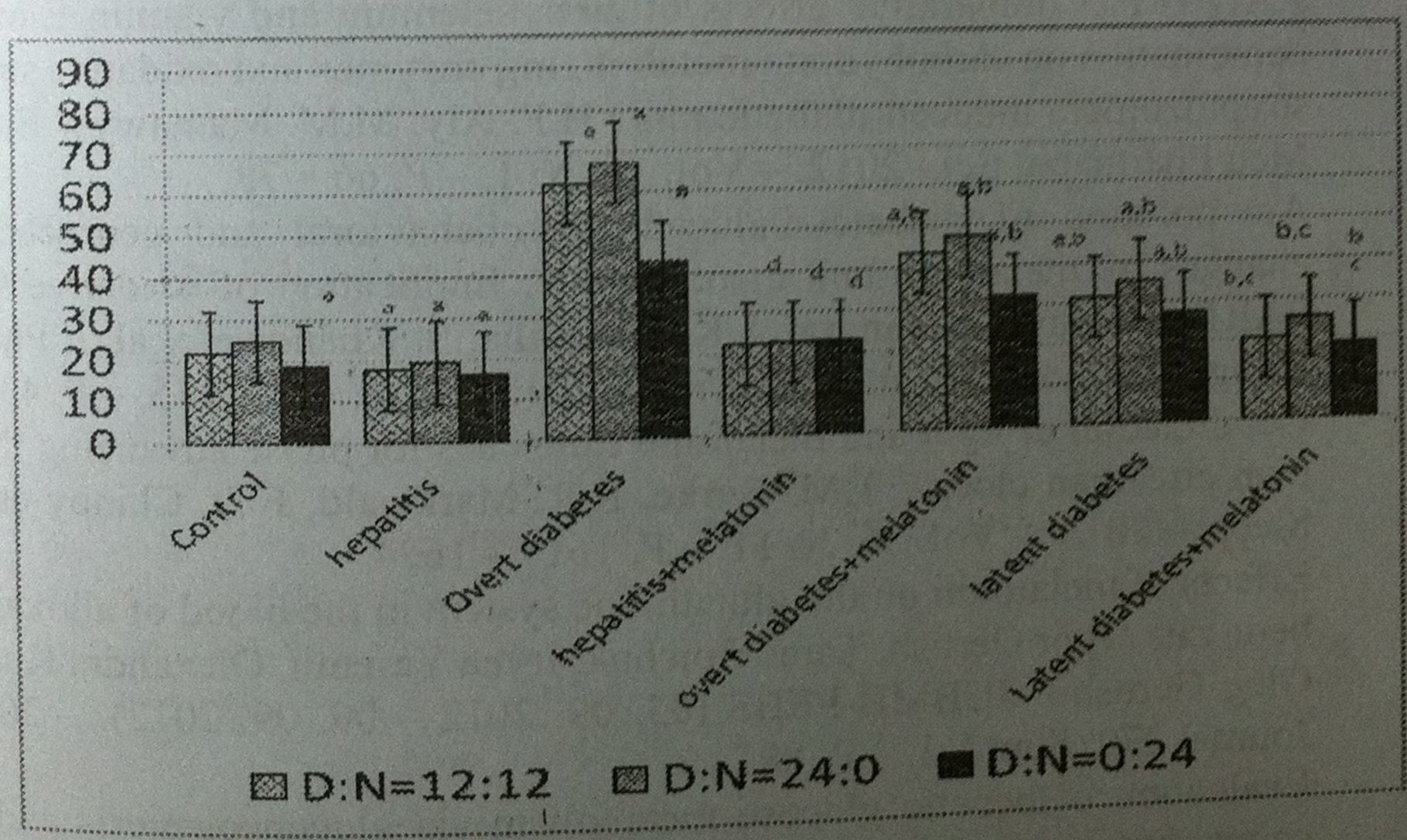

Fig. 1. Effect of melatonin on the activity of glucose-6-phosphatase in the liver (mkg/min×mg), (n=6, x±Sx): 1. a, b, c, – reliable changes (p≤0,05). 2. a – relative to a control under equinox; b – relative to overt diabetes mellitus; c – relative to latent diabetes mellitus; d – relative to hepatitis.

In CCl4-intoxicated liver of rats on the 7th day after the last administration of CCl4 recorded decreased activity of G6Pase: 22% in the complete illumination; 18% in a 12 hour light : 12 hour dark and 12% under the conditions of absolute darkness. As in the previous series of experiments, the maximum changes in the activity of the G6Pase there is a shortage of melatonin (pineal gland hypo function around the clock on the background lighting).

G6Pase activity in the liver of CCl4-intoxicated rats, which during the week daily orally administered melatonin, did not differ from that of the corresponding control and indices of intact rats, as in the previous experiment does not depend greatly on the nature of light deprivation.

Melatonin is an effective scavenger of different ROS, such as hydroxyl and peroxyl radicals cross all morphophysiological barriers, is distributed throughout all cells and also has a powerful capacity to scavenge free radicals and prevents tissue damage. In a recent study, melatonin was showed to decrease oxidative stress in diabetic patients [7].

Conclusion.

Thus, exogenous melatonin normalizes impaired due alloxan diabetes and tetrachlormethane hepatitis glucose-6phosphatase activity in rat liver.

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