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Structural Changes of the Spleen Parenchyma Under the Action of Monosodium Glutamate and Their Correction by Melatonin

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ABSTRACT

Introduction: monosodium glutamate is one of the most common food additives in the world. Its effect on the organs of the lymphoid system, in particular on the spleen, has not been studied enough. The purpose of the research is to study the morphometric and submicroscopic changes of the spleen parenchyma of rats under the conditions of the action of monosodium glutamate and correction with melatonin.

Material and Methods: the study was conducted on 62 white female and male rats of reproductive age. Experimental animals are divided into 2 groups.

Results: after six weeks of monosodium glutamate exposure, a large number of cells with signs of apoptosis were found, the relative area of the white pulp is 9.04% in male rats and 12.05% in female rats less ($p<0.05$) than that of the intact group of animals, the relative area of the germinal center is, respectively, 13.97% and 13.45% more ($p<0.001$) than the parameters of the intact group of animals. After six weeks of exposure to monosodium glutamate followed by four weeks of melatonin, it was found that the number of changed cells significantly decreased, the relative area of the white pulp of the spleen and of the germinal center does not differ reliably from intact animals.

Conclusions: after six weeks of daily exposure to monosodium glutamate, destructive and degenerative changes develop in the parenchyma of the spleen. The four-week action of melatonin proved its effectiveness in correcting the changes caused by the influence of monosodium glutamate.

Keywords: Monosodium glutamate; Spleen; Lymphocytes; Blood capillaries; Melatonin.

Introduction

The spleen is a secondary lymphoid organ where antigen-dependent proliferation and differentiation of T- and B-lymphocytes takes place[1]. It is also a hematopoietic organ because it is here that the destruction of spent blood cells takes place[2]. The study of the influence of various external and internal factors on lymphoid organs has always had a place in morphology, because they provide the body's protection. Accordingly, if the functional capacity of immune organs suffers, the whole body will lose its protective mechanism and become sensitive to the action of both exoantigens and endoantigens[3].

Monosodium glutamate (MSG) is one of the most common food additives in the world[4]. It is used in the production of such foods as chips, croutons, soups, seasonings, sauces and much more. Belongs to taste enhancers, in addition to increasing appetite, it also improves the organoleptic properties of products[5,6]. The fact that not only adults, but also children consume this product poses a special danger. As you know, the result of increased appetite is an increase in the amount of food consumed, which causes a high-calorie diet (HCD). The consequence of the latter is the appearance of excess body weight and obesity, accompanied by metabolic syndrome[7]. Childhood obesity has been a serious problem for more than 10 years, which is quite difficult to fight. Despite this, there is too little information in the modern scientific literature regarding the possibilities of MSG's influence on the organs and tissues of the body. Further research is needed to study the effect of this supplement on the human body. Equally important is the issue of correcting the changes caused by the action of monosodium glutamate on the body, for which purpose we used melatonin.

Melatonin is a biogenic amine, mainly produced by the pineal gland, but there are studies that prove that it is also synthesized by the retina, respiratory epithelium, skin, intestine, liver, kidneys, thyroid gland, thymus, spleen, cells of the immune system and endothelium[8,9]. As a cytoprotector, melatonin serves to

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fight diseases such as diabetes, metabolic syndrome, as well as ischemic and non-ischemic cardiovascular diseases, which, by the way, even complicate the course of COVID-19[10].

The purpose of the study: to study the morphometric and submicroscopic changes in the parenchyma of the spleen of rats under the conditions of the action of monosodium glutamate and correction by melatonin.

Materials and Methods

The study was conducted on 62 white male and female rats of reproductive age (2.5–5.0 months) weighing 130–235 g.

The microanatomy of the structural components of the spleen of white rats under physiological conditions was studied on 10 intact animals. Experimental animals were divided into 2 groups: the first group (20 individuals) – animals that were on a high-calorie diet for six weeks; the second (20 individuals) - animals that were on a HCD for six weeks, followed by four weeks of melatonin correction and a standard vivarium diet. There were 10 male rats and 10 female rats in each group. A HCD was achieved by adding monosodium glutamate at a dose of 0.07 g/kg of rat body weight. It was administered through a pipette once a day (9-10 a.m.) with subsequent free access to food during the day. A dose of melatonin of 10 mg/kg of rat body weight was administered orally every day in the afternoon at the same time (4-5 p.m.). Controls were 12 white rats that received a standard vivarium diet instead of a high-calorie diet for six and ten week.

All experimental animals were kept in the vivarium of Lviv National Medical University named by Danylo Halytskyi. The research was conducted in accordance with the provisions of the European Convention on the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (Strasbourg, 1986), Council of Europe Directives 86/609/EEC (1986), Law of Ukraine No. 3447-IV «On the Protection of Animals from Cruelty handling», general ethical principles of experiments on animals, adopted by the First National Congress of Ukraine on Bioethics (2001), following the National Institutes of Health (NIH) Guide for the Care and Use of Laboratory Animals.

The Committee on the Ethics of Scientific Research, Experimental Development and Scientific Works of the Lviv National Medical University named by Danylo Halytskyi issued a positive opinion regarding the observance of humane, ethical and moral and legal principles when conducting scientific expe cacodylate at pH 7.2 for 2–2.5 hours in the cold. For dehydration and preparation for impregnation with water-insoluble resins, tissue blocks washed from the remains of fixatives were passed through alcohols of increasing concentration and absolute acetone.

Morphometric studies were carried out in the specified terms of the experiment on histological preparations stained with hematoxylin and eosin using VideoTest-5.0, KAARA Image Base, Stepanizer and Microsoft Excel programs on a personal computer. For all indicators, the values of the arithmetic mean (M) and the error of the arithmetic mean (m) were calculated. The reliability of the difference in values between independent quantitative values was determined with a normal distribution using the Student's t-test. Differences at $p<0.05$ are considered significant.

Results

The submicroscopic structure of the spleen of male and female white rats of reproductive age of the intact and control groups corresponds to the species norm. Supportive and contractile component of the spleen is represented by a capsule and trabeculae, which contain collagen and elastic fibers, bundles of smooth myocytes. The germinal center of lymphoid nodules mainly contains B-lymphocytes, and the periarterial zone contains T-lymphocytes. Small-sized lymphocytes have a small, rounded nucleus, which is surrounded by a thin area of cytoplasm. Medium-sized lymphocytes have a lower nuclear-cytoplasmic ratio than small lymphocytes, and the cytoplasm contains mitochondria and a granular endoplasmic reticulum. Large-sized lymphocytes contain a nucleus with a predominance of euchromatin. Reticular cells have elongated nuclei with clear contours of nuclear membrane. Plasma cells and macrophages have a characteristic structure (Figure 1).

After six weeks of monosodium glutamate exposure, both male and female rats show signs of destructive and degenerative changes. It was established by the morphometric method that the relative area of the white pulp of the spleen decreases after six weeks of the experiment, it is 9.04% and 12.05%, respectively, significantly less ($p<0.05$) than the indicator of the intact group of animals (Tables 1, 2).

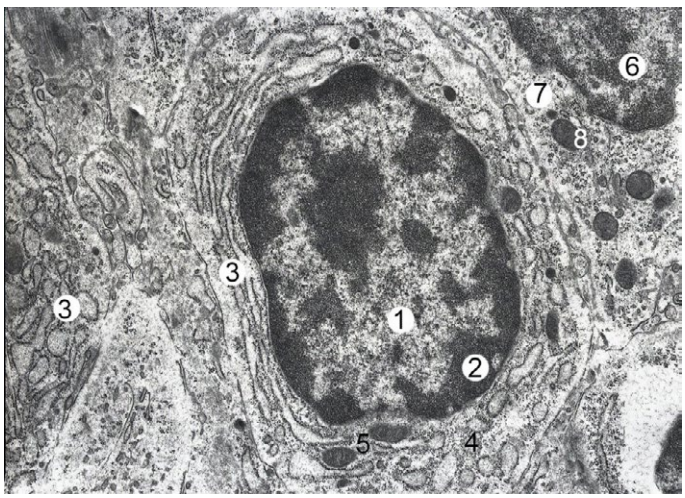

Figure 1. Ultrastructure organization of a fragment of the mantle zone of a lymphoid nodule of the white pulp of the spleen of a white male rat of the intact group. Electron micrograph. Magnification: ×8000. Symbols: 1 – euchromatin in the nucleus of a plasma cell, 2 – heterochromatin, 3 – cytoplasm of a plasma cell, 4 – granular endoplasmic reticulum in the cytoplasm of a plasma cell, 5 – mitochondria, 6 – nucleus of a medium-sized lymphocyte, 7 – cytoplasm of a medium-sized lymphocyte, 8 – mitochondrion in the cytoplasm of a medium-sized lymphocyte.

The relative area of lymphoid nodes of the spleen decreased, it is 8.42% and 11.51% significantly less ($p<0.05$) than the parameters of the intact group of animals. The relative area of lymphoid periarterial sheaths decreased, equal to 15.81% and 17.75%, respectively, significantly ($p<0.001$) less than the indicators of the intact group of animals. The relative area of the red pulp of the spleen increased by 1.79% and 3.64% more than the parameters of the intact group of animals (Tables 1, 2).

The relative area of the mantle and marginal zones on the histological preparation of the spleen section decreased, being 13.73% and 17.57% less than the indicator of the intact group of animals; of the germinal center increased, it is, respectively, 13.97% and 13.45% more parameters of the intact group of animals; of the periarterial zone decreased, equal to 7.46% in male rats and 9.62% in female rats, respectively, significantly less than the indicator of the intact group of animals (tables 1, 2). After six weeks of the experiment, the outer diameter of the central arteries increased and is 64.84% and 61.65%, respectively, significantly ($p<0.001$) more than the parameters of the intact group of animals. The inner diameter of the central arteries slightly decreased, it is 5.56% and 6.44% less than the indicator in animals of the intact group.

After six weeks of exposure to the food additive, when studying the ultrastructural organization of the spleen, deep changes in the cellular component and disturbances at the level of all links of the vascular bed were noted. A large number of lymphocytes had signs of apoptosis (Figure 2). It is important that there are few cells in the state of mitosis. The cytoplasm of cells in a state of karyopyknosis, karyorrhexis or karyolysis enlightened. The germinal center of lymphoid nodules contains a predominant number of small and medium-sized lymphocytes, as well as lymphoblasts. In the nuclei of lymphoblasts, condensation of heterochromatin is observed, lumps of which are located along the inner contour of the nuclear envelope. Dendritic cells often contain damaged organelles in the cytoplasm, and the nucleus is deformed.

Table 1. Morphometric parameters of the structural components of the spleen of the studied male rats (M ± m).

Parameter, units of measurement	The studied group of animals		
	Intact	First	Second
The relative area of the white pulp of the spleen, %	25.78 ± 1.18	23.45 ± 1.01*	25.21 ± 0.69
Lymphoid periarterial sheaths	2.15 ± 0.04	1.81 ± 0.04**	2.11 ± 0.04
Lymphoid nodules	23.63 ± 1.09	21.64 ± 0.64*	23.1 ± 0.62
Mantle and marginal zones	17.34 ± 1.06	14.96 ± 0.39**	17.01 ± 0.49
Germinal center	4.01 ± 0.31	4.57 ± 0.11**	4.11 ± 0.07
Periarterial zone	2.28 ± 0.09	2.11 ± 0.08*	2.23 ± 0.04
The relative area of the red pulp of the spleen, %	74.22 ± 1.33	76.55 ± 1.08*	74.79 ± 1.02
The outer diameter of the central artery of the spleen, d1, μm	14,02 ± 0,51	23,11 ± 0,27**	17,59 ± 0,33**
Internal diameter of the central artery of the spleen, d2, μm	6.11 ± 0.31	5.77 ± 0.1*	6.03 ± 0.06

Notes: * – values that are statistically significantly different from the indicators of the intact group of animals ($p<0.05$), ** – values that are statistically significantly different from the indicators of the intact group of animals ($p<0.001$).

Table 2. Morphometric parameters of the structural components of the spleen of the studied female rats (M ± m).

Parameter, units of measurement	The studied group of animals		
	Intact	Intact	Intact
The relative area of the white pulp of the spleen, %	26.38 ± 1.02	23.2 ± 0.76*	25.92 ± 0.65
Lymphoid periarterial sheaths	2.31 ± 0.06	1.9 ± 0.04**	2.26 ± 0.05
Lymphoid nodules	24.07 ± 1.11	21.3 ± 0.72*	23.66 ± 0.67
Mantle and marginal zones	17.59 ± 1.15	14.5 ± 0.44**	17.37 ± 0.42
Germinal center	4.09 ± 0.39	4.64 ± 0.09**	4.16 ± 0.11
Periarterial zone	2.39 ± 0.12	2.16 ± 0.07*	2.32 ± 0.05
The relative area of the red pulp of the spleen, %:	73.62 ± 1.4	76.8 ± 1.21*	74.08 ± 1.21
The outer diameter of the central artery of the spleen, d1, μm	14.21 ± 0.62	22.97 ± 0.31**	17.83 ± 0.39**
Internal diameter of the central artery of the spleen, d2, μm	6.21 ± 0.29	5.81 ± 0.11*	6.09 ± 0.06

Notes: * – values that are statistically significantly different from the indicators of the intact group of animals ($p<0.05$), ** – values that are statistically significantly different from the indicators of the intact group of animals ($p<0.001$).

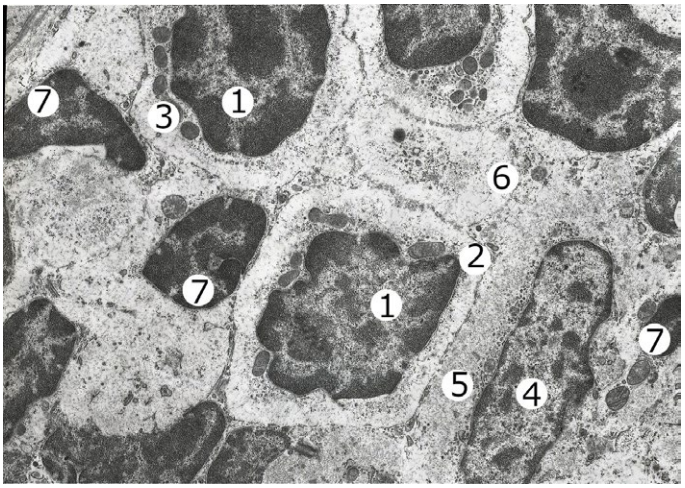

Figure 2. Apoptically altered lymphocytes in a white pulp fragment of the splenic white male rat after six weeks of monosodium glutamate exposure. Electron micrograph. Magnification: ×6000. Symbols: 1 – the nucleus of a lymphocyte with an uneven nuclear envelope; 2 – illuminated lymphocyte cytoplasm; 3 – swollen mitochondria; 4 – deformed nucleus of a reticular cell; 5 – enlightened organelle-free cytoplasm; 6 – area of destruction; 7 – lymphocyte karyopyknosis.

For the periarterial zone, signs of edema are characteristic at this time of the study, the intercellular spaces are expanded and contain vacuole-like structures. From the cellular component, small and medium-sized lymphocytes predominate. The mantle zone is also represented by small and medium lymphocytes. The nuclei of these cells are elongated, the nuclear envelope has a vague contour, contains both protrusions and depressions. There are many active macrophages in the marginal zone. Their cytoplasm contains numerous phagosomes and lysosomes, loaded with the remains of other cells and osmiophilic inclusions (Figure 3).

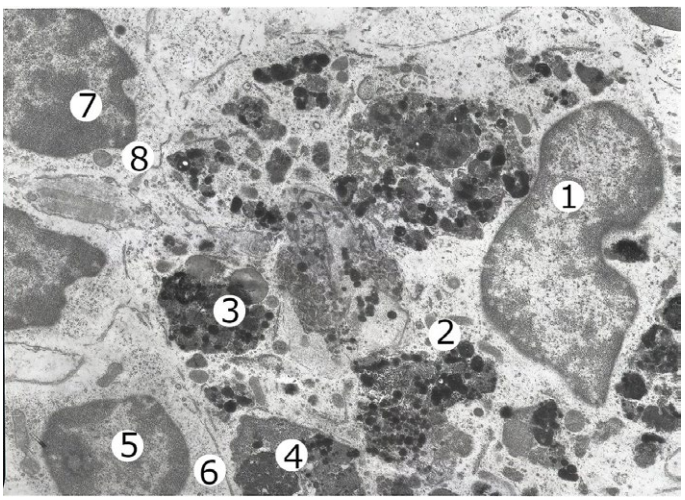

Figure 3. An active macrophage in the white pulp of the spleen of a white female rat after six weeks of monosodium glutamate exposure. Electron micrograph. Magnification: ×6000. Symbols: 1 – deformed nucleus of an active macrophage; 2 – the cytoplasm of a macrophage contains mitochondria, accumulation of hemosiderin (3); fragments of nuclear material of other cells (4); 5 – nucleus and cytoplasm (6) of a small lymphocyte; 7 – nucleus and cytoplasm (8) of a medium lymphocyte.

In the nuclei of small and medium-sized lymphocytes, heterochromatin condensed with lumps is clearly visualized, the nucleolus is not visualized. Cytoplasm of cells is clear, almost does not contain organelles, mitochondria with signs of matrix swelling and expanded deformed crypts. Large lymphocytes have nuclei with an uneven nuclear envelope that forms numerous protrusions and intussusceptions, the nucleolus is not clearly visualized, the cytoplasm is clear, and contains altered organelles. Some areas of the spleen parenchyma are represented by zones of destructively changed cells, fragments of cell nuclei, and in the red pulp also clusters of erythrocytes.

The red pulp is full-blooded, contains areas of accumulation of deformed shaped blood elements, polysegmented neutrophils and megakaryocytes. Many plasma cells, active macrophages, and myeloid cells at different stages of differentiation were detected. There are entire zones of neurophilic and basophilic granulocytes. Macrophage nuclei are slightly reduced, contain chromatin condensed in lumps, the cytoplasm is loaded with phagocytosed material and osmiophilic (fatty) inclusions (Figure 3). Their cytoplasmic processes are long, which increases the receptor surface of the cell. Hemocapillaries with a reduced lumen, which is associated with swelling of the nuclei of endotheliocytes and their protrusion into the lumen. Sinusoidal hemocapillaries are expanded, in their wall there are large gaps for the passage of cells. The basement membrane is swollen, stratified, swelling around the vessels.

After four weeks of melatonin correction, regression of the changes was found. It was established by the morphometric method that the relative area of the white pulp of the spleen after six weeks of a HCD followed by four weeks of melatonin use increases compared to the previous group of animals by 7.51% in male rats and by 11.72% in female rats and amounts to 2. 21% and 1.74%, respectively, less than the indicator of the intact group of animals (Tables 1, 2).

The relative area of lymphoid nodes of the spleen increased in comparison with the previous group of animals by 6.75% and 11.08%, which is 2.24% and 1.7% less than the parameters of the intact group of animals. The relative area of lymphoid periarterial sheaths increased compared to the previous group of animals by 16.57% and 18.95% and is 1.86% and 2.16% less than the values of the intact group of animals, respectively. The relative area of the red pulp of the spleen decreased compared to the previous group of animals by 2.3% in male rats and by 3.54% in female rats and is, respectively, 0.77% and 0.62% more than the parameters of the intact group of animals (Tables 1, 2).

The relative area of the mantle and marginal zones on the histological preparation of the spleen section increased compared to the previous group of animals by 13.7% in male rats and by 19.79% in female rats and is 3.34% and 2.33% less than the of the intact group of animals, the germinal center decreased by 10.07% and 10.34% and, respectively, by 2.49% and 1.71% more than the parameters of the intact group of animals,

the periarterial zone increased by 5.69% and 7.41% and, respectively by 2.19% in male rats and by 2.93% in female rats less than the indicator of the intact group of animals (Tables 1, 2).

The external diameter of the central arteries of spleen after six weeks of HCD followed by four weeks of melatonin administration was reduced compared to the previous group of animals by 23.89% in male rats and 22.38% in female rats, which was 25.46% and 25.48%, respectively significantly ($p<0.001$) more parameters of the intact group of animals. The inner diameter of the central arteries slightly increased compared to the previous group of animals by 4.51% in male rats and by 4.82% in female rats, which is 1.31% and 1.93% less than that of animals in the intact group (Tables 1, 2).

After six weeks of a HCD followed by four weeks of melatonin, it was found that the blood volume of the venous sinuses of the spleen decreased in comparison with the previous group of animals in both male and female rats. Rarely, macrophages are completely filled with elements of other cells and hemosiderin. The nuclear envelope of lymphocytes has clear contours, but the cytoplasm is clear and contains organelles with signs of damage and edema (Figure 4). The wall of the venous sinuses is not thickened, the lumen of the blood capillaries is narrowed.

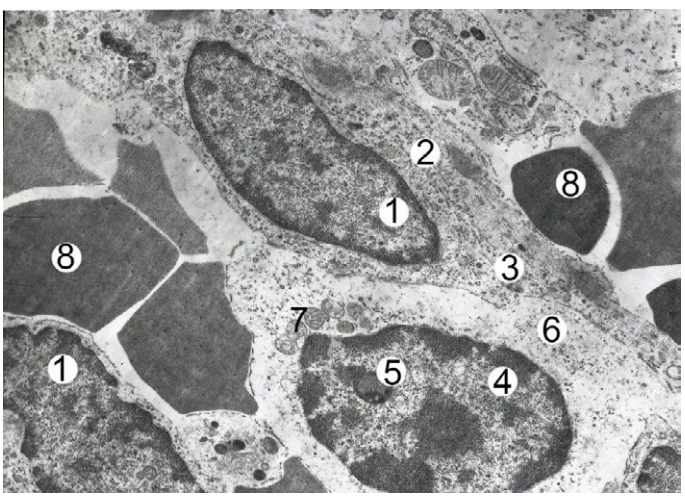

Figure 4. Illuminated cytoplasm of cells in the red pulp of the spleen of a white female rat after six weeks of MSG exposure followed by four weeks of melatonin. Electron micrograph. Magnification: ×6000. Symbols: 1 – nucleus of an interdigitating cell, 2 – cytoplasm, 3 – outgrowth of an interdigitating cell, 4 – nucleus of medium lymphocyte, 5 – nucleolus, 6 – illuminated cytoplasm of medium lymphocyte, 7 – enlarged mitochondria, 8 – erythrocytes in the lumen of the venous sinuses of the spleen.

The number of plasma cells and active macrophages in both the red and white pulp of the spleen is moderate (Figure 5). In relation to the previous group of animals, fewer lymphocytes in the state of apoptosis were found. The number of the latter is slightly more than in the intact group of animals. Intercellular spaces are slightly expanded. The number of osmiophilic (fatty) inclusions decreased both in the intercellular space and in the cytoplasm of cells.

Discussion

The results of a study conducted on experimental animals using this supplement showed that monosodium glutamate consumption leads to an increase in the peroxidation of lipids, nitric oxide, and neurotransmitters, accompanied by the accumulation of ß-amyloid peptides in the animal's body[11]. It was also found that the addition of monosodium glutamate to the diet of rats leads to a decrease in the excretion of Na, K and water from the body. NaCl retention leads to hypertension, accompanied by pathological changes in the kidneys, intrarenal oxidative stress and a decrease in the release of nitric oxide[12].

Numerous studies describe that a high-calorie diet leads to metabolic syndrome and obesity. insulin resistance, diabetes, splenomegaly, arterial hypertension, heart attacks, etc.[4].

Melatonin can partially correct the morpho-functional changes in the small intestine caused by obesity in the spring and autumn seasons. At the same time, evening administration of melatonin to obese animals is somewhat more effective, and also causes less changes in the small intestine of non-obese animals, compared to morning administration[13].

Experiments on rats with type 2 diabetes with resistant hypertension and rats with metabolic syndrome proved that melatonin administration significantly eases the course of arterial hypertension[14].

In modern literature, it is said that melatonin has the ability to synchronize not only central, but also peripheral (work of the adrenal glands, pancreas, liver, kidneys, heart, lungs, small and large intestines, etc.) biorhythms. This, in turn, ensures hemostasis of the body during periodic changes in the environment and, accordingly, contributes to the adaptation of the body. In order to objectify the indicator of the circadian time (clock) of a person, it is necessary to determine the level of melatonin in the blood. The impressive variety of melatonin's therapeutic effects opens up important prospects for measuring its level as a biomarker for clinical, prophylactic, and therapeutic use[15].

The therapeutic potential of melatonin due to its chronobiotic cytoprotective effect is significant in combating the consequences of COVID-19 infections. Due to its effect as an antioxidant, anti-inflammatory and immunomodulatory compound, melatonin may be a unique drug to reduce the effects of SARS-CoV-2 infection. Indirect evidence has been described indicating a possible antiviral effect of melatonin by affecting the SARS-CoV-2/angiotensin-converting enzyme 2 relationship. Melatonin is also an effective chronobiotic agent for overcoming the circadian disruption of social isolation and combating delirium in severely affected patients[10].

Conclusions

As a result of the study conducted on male and female rats, we found that after six weeks of exposure to monosodium glutamate, destructive and degenerative changes occur, in particular, stagnation phenomena are observed, numerous macrophages with remnants of hemosiderin in their cytoplasm, a large number of necrotized cells, vessels with damaged wall, which leads to the release of formed blood elements into the parenchyma of the organ, the relative area of the white pulp of the spleen is significantly less than that of intact animals.

After six weeks of exposure to monosodium glutamate followed by four weeks of melatonin, it was found that all changes in the structure of the spleen were less pronounced than in the previous group of animals. Of the morphometric parameters of the spleen, only the outer diameter of the central arteries remains 25.46% and 25.48%, respectively, significantly ($p<0.05$) more than the parameters of the intact group of animals.

References

1. El-Aziz R, Naguib M, Rashedb L. Spleen size in patients with metabolic syndrome and its relation to metabolic and inflammatory parameters. The Egyptian Journal of Internal Medicine. 2018;30:78–82. https://doi.org/10.4103/ejim.ejim_86_17.
2. Huang X, Lu Y, Li L, *et al*. Protective effect of acute splenic irradiation in rats with traumatic brain injury. NeuroReport. 2021;32,8:711–720. https://doi.org/10.1097/WNR.0000000000001650.
3. Habashy NH, Kodous AS, Abu-Serie MM. Targeting ROS/NF-κB signaling pathway by the seedless black Vitis vinifera polyphenols in CCl4-intoxicated kidney, lung, brain, and spleen in rats. Sci Rep. 2021;11:16575. https://doi.org/10.1038/s41598-021-96008-0.
4. Bautista RJH, Mahmoud AM, Konigsberg M, Guerrero NELD. Obesity: Pathophysiology, monosodium glutamate-induced model and anti-obesity medicinal plants. Biomedicine & Pharmacotherapy. 2019;111:503–516. doi: 10.1016/j.biopha.2018.12.108
5. Bhandari U. Effect of Embelin in Monosodium Glutamate Induced Obesity in Male Neonatal Wistar Rats. Atheroscler. Suppl. 2018;32:138. doi: 10.1016/j.atherosclerosissup.2018.04.423
6. Krynytska I, Marushchak M, Naumova L, Mazur L. The Toxic Impact of Monosodium Glutamate in Rats. J Med J. 2019;53(2):91–101.
7. Moneim WMA, Yassa HA, Makboul RA, Mohamed NA. Monosodium glutamate affects cognitive functions in male albino rats. Egypt J Forensic Sci. 2018;8:9. doi: 10.1186/s41935-018-0038-x
8. Souza CAPD, Gallo CC, Camargo LSD, *et al*. Melatonin multiple effects on brown adipose tissue molecular machinery. J Pineal Res. 2019;66(2):12549. doi: 10.1111/jpi.12549
9. Acuna-Castroviejo D, Escames G, Venegas C, *et al*. Extrapineal melatonin: sources, regulation, and potential functions. Cell Mol Life Sci. 2014;71(16):2997–3025. doi: 10.1007/s00018-014-1579-2.
10. Cardinali DP, Brown GM, Pandi-Perumal SR. Can Melatonin Be a Potential "Silver Bullet" in Treating COVID-19 Patients? Diseases. 2020;8(4):44. doi: 10.3390/diseases8040044
11. Hussein U, Hassan N, Elhalwagy M, *et al*. Ginger and Propolis Exert Neuroprotective Effects against Monosodium Glutamate-Induced Neurotoxicity in Rats. Molecules. 2017;22(11):1928. doi: 10.3390/molecules22111928.
12. Contini MC, Fabro A, Millen N, Benmelej A, Mahieu S. Adverse effects in kidney function, antioxidant systems and histopathology in rats receiving monosodium glutamate diet. Experimental and Toxicologic Pathology. 2017;69(7):547–556. doi: 10.1016/j.etp.2017.03.003
13. Vareniuk I, Shevchuk N, Roslova N, Dzerzhynskyi M. Vplyv rankovoho ta vechirnoho vvedennia melatoninu na stan slyzovoi obolonky ta krypt tonkoi kyshky u shchuriv z ozhyrinniam. [Effect of morning and evening administration of melatonin on the condition of the mucous membrane and crypts of the small intestine in obese rats]. Visnyk Kyivskoho natsionalnoho universytetu imeni Tarasa Shevchenka. 2019;1:50–53.
14. Rahman MM, Kwon HS, Kim MJ, Go HK, Oak MH, Kim DH. Melatonin supplementation plus exercise behavior ameliorate insulin resistance, hypertension and fatigue in a rat model of type 2 diabetes mellitus. Biomedicine & pharmacotherapy. 2017;92:606–614. doi: 10.1016/j.biopha.2017.05.035.
15. Tordjman S, Chokron S, Delorme R, *et al*. Melatonin: pharmacology, functions and therapeutic benefits. Current neuropharmacology. 2017;15(3):434–443. doi:10.2174/1570159X14666161228122115.

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