# EFFECT OF MELATONIN ON FIBRINOUS AND PROTEOLYTIC ACTIVITY OF TISSUES OF INTERNAL ORGANS AND BLOOD PLASMA OF WHEAT RATS

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***Abstract.*** *Questions of fibrinolysis attract the attention of a wide range of medical specialists in the clinical and theoretical areas. Depression of fibrinolytic activity is one of the pathogenetic factors in the development of thrombosis. Statistics on the occurrence of myocardial infarctions clearly demonstrate the daily dependence of this pathology, which may be due to circadian oscillations of the fibrinolytic potential. However, the effect of melatonin on the fibrinolytic activity of tissues is not sufficiently studied. In conducted experimental studies on non-linear males of white rats, it was found that melatonin causes an increase in the intensity of enzymatic and non-enzymatic fibrinolysis in plasma of blood and tissue of the heart. At the same time, in the lungs, liver, spleen and kidneys there is a decrease in total fibrinolytic activity due to inhibition of the enzymatic fibrin lysis and increased intensity of proteolytic destruction of low and high molecular proteins and collagen.*
***Keywords:*** *melatonine, plasma fibrinolysis, fibrinolytic activity of the tissues, proteolysis.*

It is known that the pineal gland is a producer of the methoxindol family, of which N-acetyl-5-methoxy tryptamine (melatonin) and 5-methoxytryptamine have hormonal properties, which is clearly proven [1, 5, 10, 11]. As a gland that has very broad integrative properties, the epiphysis through melatonin, on the one hand, modulates neuroendocrine functions, on the other hand, it is the object of control of various hormonal and humoral signals [4]. There are some reports of increased levels of melatonin in patients with cirrhosis of the liver with chronic renal and cardiovascular disease [2, 5, 8, 11]. In addition, it is known that melatonin is a major component of the body's pacemaker system. He participates in the formation of circadian and circadian rhythms both directly acting on cells, and by changing the secretion of other hormones and biologically active substances, the concentration of which varies depending on the time of day.

Questions of fibrinolysis attract the attention of a wide range of medical specialists in the clinical and theoretical areas. Depression of fibrinolytic activity is one of the pathogenetic factors in the development of thrombosis. Statistics on the occurrence of myocardial infarctions clearly show the daily dependence of this pathology, which may be due to circadian oscillations of the fibrinolytic potential [3, 4, 5, 6]. It is known that the fibrinolytic potential of blood is regulated by inhibitors and plasminogen activators. Among the latter, great importance belongs to urokinase, which is injected by the kidneys and increases the intensity of fibrinolysis [1, 6]. The photoperiodic dependence of the excretory, acid-dependent and ion-regulating functions of the kidneys is clearly proven. The influence of melatonin on the homeostatic activity of the kidneys was revealed [9, 12]. However, the effect of this indolamine on the fibrinolytic activity of tissues is not sufficiently studied.

**Purpose of the study.** To find out the role of melatonin in the mechanisms of regulation of fibrin and proteolytic processes in the tissues of the internal organs of white rats.

**Material and methods.** Experiments were performed on 15 males of nonlinear white rats with a body weight of 0.12-0.14 kg. Melatonin was administered once intraperitoneally at a dose of 6 mg / kg body weight. The control group consisted of 11 rats, which were administered solvent melatonin in appropriate volumes. One year later, the rats were decapitated with etheric anesthesia. Blood stabilized with 3.8% solution of sodium citrate. Inequalities of the internal organs (heart, kidneys, lungs, liver, spleen) were triturated in a glass homogenizer with borate buffer (pH 9.0). For the determination of

fibrinolytic and proteolytic activity, homogenates and blood plasma were incubated for 30 minutes with the azo-fibrin company Simko Ltd (Ukraine) [7]. The obtained results are statistically processed using the method of variation statistics with the definition of the Student's t criterion.

Experiments have been carried out in compliance with the European Convention for the Protection of Vertebrate Animals, Used for Experimental and Other Scientific Purposes (Strasbourg, 1986).

**Discussion of research results.** It has been established that melatonin causes changes in plasma fibrinolysis, more than double the increase in total fibrinolytic activity due to the growth of both enzymatic and non-enzymatic fibrinolysis (Table 1).

Table 1. Characteristics of changes in plasma fibrinolysis and proteolysis when melatonin is administered to intact rats (x+Sx)

| **Indicators studied** ***E440/g of fabric per hour*** | **Control** ***n=11*** | **Experience** ***n=15*** |
|---|---|---|
| **Asoalbumin lysis** | 3,13±0,28 | 0,85± 0,08 *p<0,001* |
| **Asocasein lysis** | 2,08±0,06 | 1,41± 0,20 *p<0,001* |
| **Asocole lysis** | 0,20±0,03 | 0,21+0,01 |
| **Total fibrinolytic activity** | 0,45±0,03 | 1,06±0,06 *p<0,001* |
| **Non-enzymatic fibrinolytic activity** | 0,24±0,01 | 0,56+ 0,04 *p<0,001* |
| **Enzymatic fibrinolytic activity** | 0,21+0,02 | 0,50+0,04 *p<0,001* |

Notes: *p* – the degree of reliability of differences in indicators, relative to the control;
*n* – is the number of observations.

In the heart, an increase in total fibrinolytic activity was observed as a result of an increase in enzymatic fibrinolysis (by 37%) and non-minimum lysis of fibrin (by 31%). In the liver, total fibrinolytic activity decreased due to inhibition of enzymatic fibrinolysis and a decrease in non-enzymatic fibrinolytic activity. In the kidneys, there was also a decrease in total fibrinolysis due to inhibition of the enzymatic lysis of fibrin, the intensity of which decreased 2.5 times. Analysis of changes in tissue fibrinolysis in the spleen revealed a decrease in total fibrinolytic activity by 25%, which was due to inhibition of the enzymatic fibrin lysis, since non-enzymatic fibrinolytic activity practically did not differ from the control level. In the lungs, inhibition of the enzymatic fibrinolytic activity by 13% was observed in the absence of significant changes in the intensity of total and non-enzymatic fibrinolysis (Table 2).

Table 2. Characterization of changes in tissue fibrinolysis and proteolysis with the introduction of melatonin intact rats (x+Sx)

| **Indicators studied** ***E440/g of fabric per hour*** | **Asoalbumin lysis** | **Asocasein lysis** | **Asocole lysis** | **Total fibrinolytic activity** | **Non-enzymatic fibrinolytic activity** | **Enzymatic fibrinolytic activity** |
|---|---|---|---|---|---|---|
| *1* | *2* | *3* | *4* | *5* | *6* | *7* |
| **Liver** | | | | | | |
| **Control** ***n=11*** | 21.75±0.88 | 21.3+ 0.91 | 12.2± 0.61 | 12.03+0.62 | 6.01+0.29 | 5.95+0.36 |
| **Experience** ***n=15*** | 28.0+1.60 *p<0.005* | 20.41±1.52 | 11.03+0.93 | 8.56+0.47 | 4.70+0.32 *p<0.05* | 3.81+0.18 *p<0.005* |
| **Heart** | | | | | | |
| **Control** ***n=11*** | 14.79+0.55 | 14.79+0.55 | 14.79+0.55 | 14.79+0.55 | 14.79+0.55 | 14.79+0.55 |
| **Experience** ***n=15*** | 24.29+1.63 *p<0.001* | 24.93±1.85 *p<0.001* | 13.65+1.00 *p<0.001* | 11.47+0.62*p<0.005* | 6.05±0.33 *p<0.01* | 5.42+0.40 *p<0.005* |

Continuation of table 2

| *1* | *2* | *3* | *4* | *5* | *6* | *7* |
|---|---|---|---|---|---|---|
| **Lungs** | | | | | | |
| **Control *n=11*** | 14.35+1.08 | 15.33+0.66 | 6.96+0.33 | 6.96+0.33 | 4.76+0.24 | 4.75+0.10 |
| **Experience *n=15*** | 22.72+1.31 *p<0.001* | 27.88+0.67 *p<0.001* | 16.22+0.65 *p<0.001* | 9.63±0.66 | 5.48±0.50 | 4.15±0.20 *p<0.01* |
| **Kidneys** | | | | | | |
| **Control *n=11*** | 18.09+0.64 | 18.63+0.81 | 7.02+0.22 | 8.61+0.24 | 4.29+0.18 | 4.33+0.17 |
| **Experience *n=15*** | 18.09+0.64 | 28.22±1.06 *p<0.001* | 8.78+0.81 *p<0.05* | 4.47±1.00 *p<0.001* | 3.06±0.88 | 1.76+0.59 *p<0.001* |
| **Spleen** | | | | | | |
| **Control *n=11*** | 16.08+1.13 | 9.83+0.86 | 6.91+0.28 | 6.37+0.29 | 4.76+0.50 *p<0.01* | 1.76+0.59 *p<0.001* |
| **Experience *n=15*** | 19.58±0.90 | 15.81+1.0 *p<0.001* | 8.01+0.75 | 3.19+0.14 | 2.69±0.24 | 2.07+0.30 *p<0.005* |

Notes: *p* – the degree of reliability of differences in indicators, relative to the control;
*n* – is the number of observations.

It is known that the distribution of exogenous melatonin in the body has features: the highest concentrations of this hormone are registered in organs of the gastrointestinal tract, heart and blood plasma [5]. In addition, each target organ has its own rhythm of sensitivity to melatonin [11], which can determine the features of the latter's effect on tissue fibrinolysis. According to the results of our study, in organs where tissue macrophages are concentrated (the liver is Kupffer cells, the kidneys are mesangial cells, the spleen are fixed lacunar macrophages, lung – alveolar macrophages), melatonin inhibits enzymatic fibrinolysis, whereas in plasma of blood and in the heart tissue, the enzymatic intensity The lysis of fibrin under the influence of this indolamine, on the contrary, is increasing. This can be explained by the different phase of chronotropy of these organs to melatonin.

**Conclusions.** Exogenous melatonin activates enzymatic and non-enzymatic fibrinolysis and suppresses lysis in the blood plasma of low- and high-molecular proteins. The activity of melatonin in the heart is a total activation of fibrinolysis, proteolysis and collagenolysis, and in the tissues of the liver, lungs, kidneys and spleen, the inhibition of the enzymatic lysis of fibrin is combined with an increase in the intensity of proteolytic destruction of low-, high-molecular-weight proteins and collagen.

**Prospects for further research.** The research in the chosen scientific direction will be continued in order to further develop ways of the chronic correction of disorders on the body and organ level.

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