

EFFECT OF THIOTRIAZOLINE OINTMENT WITH SILVER NANOPARTICLES ON NITROGEN OXIDE METABOLISM IN ULTRAVIOLET-INDUCED SKIN LESIONS IN GUINEA PIGS

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Excessive amount of nitric oxide (NO) results in immunological disorders, known to play a crucial role in the development of both early and remote consequences of ultraviolet radiation (UVR). The aim of the study was to investigate the effect of ointment containing thiotriazoline and nanoparticles (NPs) of silver on NO metabolites in blood in albino guinea pigs exposed to local UVR. The study involved 42 animals, divided into 4 groups: 1 - intact; 2 – control group without treatment (UVR); 3 - reference drug (UVR + thiotriazoline ointment (TO), (JSC “Chemical pharmaceutical plant” “Krasnaya Zvezda”, Ukraine)), 4 – main group (UVR + TO containing silver NPs (obtained by electron-beam evaporation and condensation of substances in vacuum). Erythema was induced by irradiation of shaved skin area with a mercury-quartz lamp (2 minutes). Ointment was applied on the skin 1 hour prior, 2 hours following the exposure and on a daily basis for 3 days. The rate of damaging effect was evaluated by the intensity of erythema reaction. Total serum NO metabolites, nitrite anion, nitrates (V.A. Metelskaya, N.G. Gumanova, 2005), the activity of inducible NO-synthase (iNOS) (H. M. Golovchak et al., 2014) were determined in 4 hours and on the 3rd day. The results showed that all guinea pigs developed erythema following local UVR. In 4 hours after irradiation, all of the animals without treatment (group 2) were found to have maximum erythema reaction (total intensity comprised 9.2 points). During the 3rd day total intensity of erythema remained prominent (7.7 points). At that UVR of the skin caused intensification of NO synthesis, which was confirmed by an increase in all of its metabolites in blood. In 4 hours following irradiation the contents of total NO metabolites, nitrates and nitrite anion exceeded the indices registered in intact guinea pigs by 1.6 times, 1.5 times and 2.6 times respectively. During the third day the level of NO metabolites still remained high: total metabolites exceeded the norm by 2 times, nitrates by 1.9 times and nitrite anion by 2.6 times. In 4 hours after irradiation iNOS activity increased by 2.1 times and by 3.1 times on the 3rd day in comparison with intact animals. The abrupt increase in iNOS activity, resulting in the accumulation of NO metabolites in blood, is indicative of significant immunological changes occurring under the influence of local UVR of the skin.

In animals treated by TO (reference drug) the severity of erythema 4 hours after irradiation was less by 36% and by 28% on the third day, compared to the control group. There was a decrease only in the level of nitrite anion in 4 hours after irradiation, namely by 1.5 times in comparison to the control group. However, on the third day after irradiation the content of all NO metabolites and

inducible synthase was lower by 1.3 times (total metabolites and nitrates), 1.2 times (nitrite anion) and 1.4 times (iNOS) in comparison to control group.

TO with silver NPs (main group) showed higher pharmacological activity than the reference drug. This was evidenced by a decrease in erythema intensity by 2 times in comparison to the group without treatment and by 1.2 times in comparison to the group with the employment of TO. Significant immunoprotective effect exerted by TO containing silver NPs is indicative of a decrease in blood levels of NO metabolites and iNOS activity as early as in 4 hours after exposure: 1.4 times (total metabolites and nitrates), 1.7 times (nitrite anion), 1.5 times (iNOS activity) in comparison to the control. During this period the total concentration of metabolites and nitrates (by 1.4 times) and the activity of iNOS (by 1.8 times) were also lower than the indices in the group using the reference drug. On the 3rd day the directivity of changes in the level of NO metabolites was similar to that observed after 4 hours: the content of all NO metabolites and iNOS activity decreased in comparison to the control group, reaching values observed in intact animals and reference drug (total metabolites and nitrates by 1.6 times, iNOS activity by 1.8 times).

Thus, local UVR of the skin in guinea pigs results in an increase in blood concentration of NO (total nitrite anion, nitrate) during 3 days. The activity of iNOS increases within 3 days along with accumulation of NO metabolites in blood. The inclusion of silver NPs into Thiotriazoline substance enhances immunoprotective effect of ointment, accompanied by a decrease in the intensity of erythema reaction, normalization of NO metabolites and iNOS activity in blood.