

Influence of Trametin based on of basidiomycete *Trametes pubescens* (Shumach.: Fr.) Pilat. on the biosynthesis of α - and γ -interferons in laboratory animals

Chkhenkeli V.A.

Siberian Federal Scientific Center of Agrobiotechnologies RAS, 4, Botkina st., Irkutsk, 664005, Russian Federation

ABSTRACT. The work investigated the effect of Trametin obtained using biotechnology methods. It was shown that a single oral administration of Trametin in doses from 15 to 60 mg / kg caused a dose-dependent induction and production of γ -interferon (IFN - γ) in the blood serum of mice, the maximum content of which in 48 hours after the administration at a dose of 30 mg / kg was 1337.0 ± 93.0 pg / ml. The level of production of IFN- γ , under the effect of Cycloferon at a dose of 4.5 mg / kg, slightly exceeded that content and amounted to 1447.0 ± 90.0 pg / ml. With an increase in the dose of Trametin from 15 to 30 mg / kg, the level of production of IFN- α increased more than 7.5 times, and compared with the control level, more than 49 times.

Keywords: Trametin, Cycloferon, interferon, interferon status

1. Introduction

Today, the use of both drugs with the properties of immunomodulators that exhibit antiviral and antibacterial effects directly or indirectly due to stimulation of the immune system and drugs that increase the immunogenicity of existing vaccines is gaining popularity.

Such a drug is Trametin. The concept of the existence of a highly competent system of interferon formed during evolution in animals, and the variety of physiological functions of interferon discovered and studied to date, undoubtedly indicate their control and regulatory role in maintaining homeostasis (Ershov and Zhdanov, 1982; 1985). The system of interferons is close to the system of immunity in its importance, and in universality even surpasses it (Grigoryan et al., 2015). The goal of the work was to study the biosynthesis of α - and γ -interferons when using the drug Trametin in laboratory animals.

2. Material and methods

Trametin is prepared using a deep cultivation of the tree-destroying fungus *Trametes pubescens* (Shumach.: Fr.) Pilat., followed by separation of the culture fluid and its treatment (Chkhenkeli et al., 2011; Chkhenkeli, 2014). Experiments to determine the interferonogenic properties of the drug Trametin

were performed in vitro experiments on outbred white mice in a comparative aspect with the drug Cycloferon. The quantitative content of IFN- α , - γ in serum per 1 ml was determined by ELISA using the following commercial test systems according to the manufacturer's instructions: Mouse Interferon Alpha ELISA Kit; R & D Systems; USA; Mouse IFN- γ ELISA Kit; R&D Systems Europe LTD, UK; Great Britain. The ELISA used for the measurements, was the Human complex (Germany). The measurements were carried out at a wavelength of 450 nm.

The results were subjected to statistical processing by calculating the arithmetic mean value (M) and the standard error to it ($\pm \sigma$). Assessment of the statistical significance of differences in intergroup comparisons was performed according to the two-tailed Student t-test for independent groups. For statistical calculations, the computer program Microsoft Excel 2009 was used. The differences were considered reliable at $p \leq 0.05$.

3. Results

After 6, 24, 48 and 72 hours, the mice were decapitated and blood serum samples of laboratory animals were obtained in which the level of α - and γ -interferons was tested by the method of solid-phase ELISA. Mice were kept under mild ether anesthesia until nociceptive reflexes disappeared. Blood sampling was performed by decapitation under sterile conditions.

*Corresponding author.

E-mail address: chkhenkeli@rambler.ru (V.A. Chkhenkeli)

Blood samples obtained at each study period consisted of a pool (mixture) of blood from 2 mice with a volume of 2 ml (1 ml from each individual), from which, after centrifugation at 5000 rpm for 15 min, 1,0 ml of supernatant serum was taken. The content of IFN- α , - γ in serum samples was determined in 4 time periods (6, 24, 48, 72, 96 hours - 2 mice each time) after a single oral (intra-gastric) administration of drugs – Trametin, and a comparison drug - Cycloferon.

To determine the optimal concentration of Trametin for the formation of both α -interferon and γ -interferon in mice, 6 groups were created according to the principle of analogues of 8 animals: group 1 - control; Group 2 - control - with the oral introduction of 0.2 ml of saline (placebo); group 3 - experimental - with the introduction of 0.2 ml of the drug Trametin orally (1:20); Group 4 - experimental - 0.2 ml of the drug Trametin diluted (1:10); Group 5 - experimental - 0.2 ml of the drug Trametin diluted (1: 5); 6 group - experimental - 0.2 ml of the drug Cycloferon diluted (1:30), with a content of 125 mg / ml meglumine acridone acetate in 1 ml of Cycloferon. The calculation of the optical density of the studied samples was carried out with subsequent processing and conversion of the optical density data into picograms in ml (pcg/ml).

4. Discussion

A single oral administration of Trametin in doses of 15 to 60 mg / kg caused a dose-dependent induction and production of IFN - α , - γ in the blood serum of mice, the maximum content of which was 48 mg at a dose of 30 mg / kg 48 hours after the administration of Trametin and amounted to 1338 ± 84.0 pg / ml for IFN- α , and 1337 ± 93.0 pg / ml for IFN- γ . The level of production of IFN- α , - γ in the blood serum of mice under the effect of cycloferon at a dose of 4.5 mg / kg was slightly higher than that and amounted to 1455.47 ± 84.2 pcg / ml for INF- α , and $1447.0 \pm 90, 0$ PCG / ml in IFN- γ . With an increase in the dose of Trametin from 15 to 30 mg / kg, the level of production of IFN- α increased more than 3 times, and compared with the control, more than 46 times, and for IFN- γ the

level of production increased more than 7.5 times, and compared with the control, more than 49 times.

5. Conclusion

The obtained data on the interferonogenic properties of the drug Trametin on the example of α - and γ -interferons contained in the serum with the action of the well-known drug Cycloferon (when diluted 10 times) with a dose of 0.2 mg/ml meglumine acridone acetate (in terms of acridone acetic acid) indicate that the greatest effect is achieved with the introduction of the drug Trametin at a dilution of 1:10 (30 mg / kg) after 48 hours.

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