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# Assessment of Cytokine Levels in The Blood and Correction with the New Anti-Obesity Drug "Bronchotus Forte"

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**Annotation.** The article presents studies of the effectiveness of a new anti-cough drug "Bronchotus forte" by the method of determining the level of cytokines in the blood. White male rats in which acute inflammation was reproduced were used for the experiment. The amount of cytokines IL -1β, IL-6 and TNFα was determined in the blood of healthy and experimental rats by enzyme immunoassay. As a result of the studies it was revealed that the investigated preparation "Bronchotus forte - eleksir" reduced the severity of the inflammatory process caused by carageenin and provided an adaptive response in inflammation, and surpassed the effect of the branded comparison preparation "Codelac® Broncho with thyme - eleksir", produced by "Pharmstandart - Leksredstva" OJSC, Russia.

**Key words:** herbal preparations, cytokines, cough, inflammation.

**Relevance.** Cough is one of the most severe symptoms of coronavirus infection (COVID-19).

The occurrence of cough during acute infection may result from damage to epithelial cells, leading to the release of anti-inflammatory cytokines that may cause cough or sensitize the airway to mucosal irritation [1]. At the same time, it is known that inflammatory and immune reactions, both normally and in pathology, are the result of regulatory interactions of numerous body systems, the connecting link between which are cytokines.

Cytokines are protein-peptide factors produced by cells that carry out short-distance regulation of intercellular and intersystem interactions. Cytokines determine cell survival, stimulation or inhibition of cell growth, differentiation, functional activation and cell apoptosis.

Currently, there are several models for studying the effectiveness of antitussive drugs, but in the literature there is no data on determining the activity of the cytokine component when using antitussive drugs.

Therefore, to uncover the currently unknown pathogenetic mechanisms of the formation of the inflammatory process in bronchopulmonary tissue and the protective effect of anti-inflammatory and antitussive drugs, it is important to study the level of cytokines in the blood serum.

This article presents the data obtained from studying the effectiveness of the antitussive drug “Bronchotus-Forte” - elixir by determining the level of cytokines in the venous blood of rats.

**Purpose:** Determination of the level of cytokines in the venous blood of rats under the influence of a new domestic medicinal product of plant origin "Bronchotus forte - elixir for carrageenan inflammation.

**Material and research methods:** the study drug "BRONCHOTUS FORTE" is an elixir, developed by employees of the Tashkent Pharmaceutical Institute, which included ambroxol hydrochloride - 0.2 g and dry extract of licorice roots - 1 g. The effect of the drug is due to the active substances included in its composition.

The experiments were carried out in an ISO 17025 accredited testing laboratory at NEW INNOVATION PHARM GROUP LLC. Experimental animals were kept in conditions that met the requirements for keeping laboratory animals on a standard diet with free access to drinking water. The experiment involved healthy, sexually mature rats of both sexes, which were quarantined for 14 days and after preliminary adaptation to the vivarium conditions and monitoring their condition for 4–5 days.

**Determination of cytokine levels.**

The experiment was carried out on white outbred mature male rats, weighing 180 - 200 g, which were divided into 4 groups. Reproduction of acute edema of inflammation was carried out by subcutaneous injection into the oral cavity of a phlegnic agent, in the form of a 2% aqueous solution of carrageenan [2,3]. Immediately after the manipulation and then for 5 days (once a day), the experimental groups of rats were injected with aqueous solutions of the compared drugs. On the 5th day, the rats were decapitated and blood was collected. Next, the blood was centrifuged, the serum was used to determine the concentration of the main cytokines: IL-1β, IL-6 and TNFα using the enzyme-linked immunosorbent assay (ELISA) on the MR-96 A Mindray enzyme-linked immunosorbent analyzer, in accordance with the instructions for the use of reagent kits produced by Vector Best CJSC , (RF). With this method, the cytokine is detected due to the ability to bind to monoclonal antibodies directed against two different antigenic epitopes in the cytokine molecule.

The compared drugs were administered as follows:

Group I – intact; no manipulations were performed with the animals of this group;

Group II - control, the animals of which, after reproducing acute inflammation, were injected intramuscularly for 7 days with physiological sodium chloride solution in a dose of 0.4 ml (n = 15);

Group III – experiment, rats were intragastrically injected with 0.5 ml of the drug "Bronchotus forte - elixir" for 5 days.

Group IV – experiment, rats were intragastrically injected with 0.5 ml of the drug "Codelac® Broncho with thyme – elixir" for 5 days.

The intensity of inflammation was judged by the percentage increase in the weight of the rat's paw and the suppression of edema at the peak of inflammation.

The research results were processed statistically using the Microsoft Excel 2007 software package (for Windows 7), the reliability of the data obtained was assessed using the Student's test.

**Results:**

During experimental inflammation in the "carrageenan edema of the rat paw" model, changes in the content of cytokines were observed in the form of a decrease in the concentration of the anti-inflammatory interleukin IL-1β and an increase in the level of IL-6 (Fig.). The level of interleukin IL-1β in the control group with inflammation was 2.1 times lower compared to the intact group, and the level of interleukin IL-6 was 2.4 times higher compared to the intact group. This indicates that during carrageenan inflammation, secondary immunodeficiency develops, which is based on the inhibition of the immunoregulatory functions of cytokines responsible for the development of inflammation [4]. In addition, the severity of inflammation is indicated by an increase in the serum level of TNFα by 1.8 times compared to the control, which is a factor of excessive proliferation and increased apoptosis (table).

Table

**The level of cytokines in the blood serum of experimental rats in dynamics under the influence of the drugs "Bronchotus forte - elixir", JSC "O'zkimyofarm", Uzbekistan and "Codelac® Broncho with thyme - elixir", JSC "Pharmstandard - Leksredstva", Russia (M ± m)**

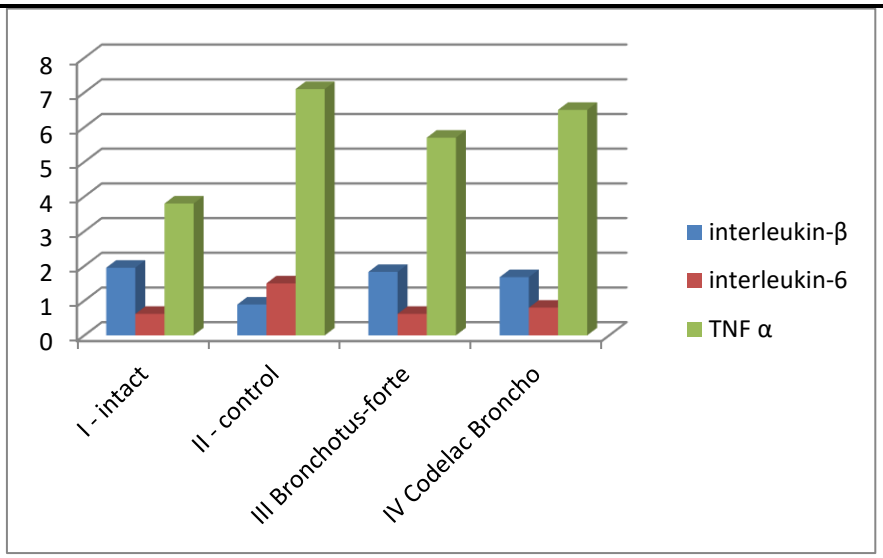
| **Group of animals** | **Indicator under study** | | |
|---|---|---|---|
| | **Interleukin-1β, pg/ml** | **Interleukin-6, pg/ml** | **TNFα, pg/ml** |
| Group I – intact | 1,95 ± 0,1 | 0,62 ± 0,05 | 3,8 ± 0,4 |
| Group II – control | 0,89 ± 0,06<br>$P_1$ = 0,0001 | 1,5 ± 0,03<br>$P_1$ = 0,0001 | 7,1 ± 0,4<br>$P_1$ = 0,0001 |
| Group III – "Ortof-S" experiment | 1,83 ± 0,1<br>$P_2$ = 0,0001 | 0,62 ± 0,03<br>$P_2$ = 0,0001 | 5,7 ± 0,3<br>$P_2$ = 0,0001 |
| Group IV – "Ketaneim" experiment | 1,68 ± 0,07<br>$P_3$ = 0,0001 | 0,8 ± 0,05<br>$P_3$ = 0,0001 | 6,5 ± 0,3<br>$P_3$ = 0,0001 |

***Markings: P1 – intact compared to control;***

*P2 - "Bronchotus forte – elexi" regarding control:*

*P3- "Bronchotus forte - elixir compared with "Codelac® Broncho with thyme"*

**The level of cytokines in the blood serum of experimental rats in dynamics under the influence of the drugs "Bronchotus forte - elixir", JSC "O'zkimyofarm", Uzbekistan and "Codelac® Broncho with thyme - elixir", JSC "Pharmstandard - Leksredstva", Russia (M ± m)**




As can be seen from the graph, the administration of the drug "Bronchotus forte - elixir" limited the influence of the pathological process on the content of cytokines in the blood of rats. In the blood serum of the experimental group of rats, when modeling "carrageenan inflammation" against the background of drug administration, an increase in Interleukin-1β by 2 times and a decrease in Interleukin-6 by 2.4 times were observed compared with the data of the control group of rats with "carageenin inflammation". The amount of TNFα, pg/ml, decreased by 20% compared to the control.

Similar data were obtained with the administration of the drug "Codelac® Broncho with thyme - elixir", JSC "Pharmstandard - Leksredstva", Russia against the background of "carrageenan inflammation". Those. In the blood serum of rats, there was an increase in Interleukin-1β by 1.8 times and a decrease in Interleukin-6 by 1.8 times compared to the data of the control group of rats with "carrageenan inflammation". The amount of TNFα, pg/ml, decreased by 8.5% compared to the control.

**Conclusion:**

Herbal medicines have unique potential as promising agents for the treatment of viral diseases. The results obtained indicate that the study drug "Bronchotus forte - elixir" reduced the severity of the inflammatory process caused by carrageenan and provided an adaptive response to inflammation, and at the same time surpassed the effect of the branded comparison drug "Codelac® Broncho with thyme - elixir", produced by Pharmstandard OJSC - Leksredstva", Russia.

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