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# EFFECT OF ELEUEROCOCCUS ON BIORHYTHMS OF PERIPHERAL BLOOD PARAMETERS IN DOGS

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KEY WORDS: biorhythms; peripheral blood; eleuterococcus.

A general biological law of the undulating course of all phases of adaptation, realized as an oscillating process, has been formulated and explains differences in biological effects obtained by acting on the living organism at different times [1, 4]. The chronobiological analysis of the effect of one of the most popular adaptogenic plant preparations in the Soviet Union, namely eleuterococcus, on peripheral blood parameters, which are known to undergo circadian and seasonal variations, is particularly interesting from this standpoint [3, 7, 8, 10, 11, 13, 15], being concerned with the temporal organization of the system [2, 9, 12]. The widespread use of eleuterococcus to optimize adaptive processes [5, 6, 14] under ordinary and stress situations requires knowledge of its chronotherapeutic action.

This paper describes the study of circadian rhythms of concentrations of erythrocyte, hemoglobin, and leukocytes in the peripheral blood of dogs and the effect on them of eleuterococcus, administered repeatedly at different times of day.

## EXPERIMENTAL METHOD

Experiments were carried out in winter on 12 inbred (beagles) and mongrel dogs closely similar in age and body weight, and kept for a long time under standard animal house conditions, with regular alternation of daylight (12 h) and darkness (12 h), and receiving similar diet and exercise. Blood for analysis was taken from the anterior Skachkov veins, keeping strictly to the order of their use for a period of 3 days. In each series tests were carried out in six time cuts: 6 and 10 a.m., 2, 6, and 10 p.m., and 2 a.m. The concentrations of erythrocytes and leukocytes were determined with a hemocytometer, and hemoglobin by a hemoglobinometer. A pharmacopoeial preparation of liquid extract of eleuterococcus was evaporated before use to one-quarter of its volume and diluted to the original volume with physiological saline, after which it was fed to dogs on bread in a dose of 1.5 ml/10 g body weight for 14 days; six dogs received only one dose of the preparation, at 9 a.m., the other six at 3 p.m., after which the program of tests was repeated. The experimental results were analyzed by a nonlinear method of least squares and by Student's statistical test, on a computer. There were two series of experiments In series I the initial rhythms of concentrations of erythrocytes, hemoglobin, and leukocytes were studied in winter in all 12 dogs. The dogs were then divided into two subgroups,

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TABLE 1. Effect of Eleuterococcus on Circadian Rhythms of Peripheral Blood Parameters of Dogs in Winter

| Blood parameters | Initially (n = 648) | After taking eleuterococcus | |
|---|---|---|---|
| | | 9 a.m. (n = 324) | 3 p.m. (n = 324) |
| Erythrocytes, $10^{12}$/liter | | | |
| period | 24,8 | 24,9 | 24,09 |
| mesor | 4,2 (3,0—5,1) | 4,35 (3,2—4,8) | 4,6 (3,8—5,2)* |
| amplitude | 0,17 (0,07—0,2) | 0,16 (0,06—0,22) | 0,25 (0,1—0,28)* |
| acrophase | 17,2 (13,5—18,6) | 17,0 (15,4—18,2) | 15,4 (12,1—16,6) |
| Hemoglobin, g/dl: | | | |
| period | 25,8 | 25,4 | 24,2 |
| mesor | 7,8 (3,5—10,2) | 7,5 (4,9—10,1) | 9,7 (4,7—10,6)* |
| amplitude | 0,13 (0,07—0,21) | 0,15 (0,08—0,18) | 0,23 (0,15—0,28)* |
| acrophase | 13,2 (12,5—16,7) | 13,0 (12,00—16,4) | 12,4 (11,0—14,6) |
| Leukocytes, $10^{9}$/liter: | | | |
| period | 24,48 | 24,09 | 23,85 |
| mesor | 9,4 (8,0—11,7) | 10,2 (9,4—11,9) | 10,8 (8,9—12,2)* |
| amplitude | 0,25 (0,16—0,65) | 0,31 (0,17—0,6) | 0,33 (0,18—0,72)* |
| acrophase | 19,4 (17,7—23,8) | 18,6 (17,2—20,4) | 18,0 (17,0—20,22) |

**Legend.** 95% Confidence intervals given within parentheses. *$p < 0.05$.

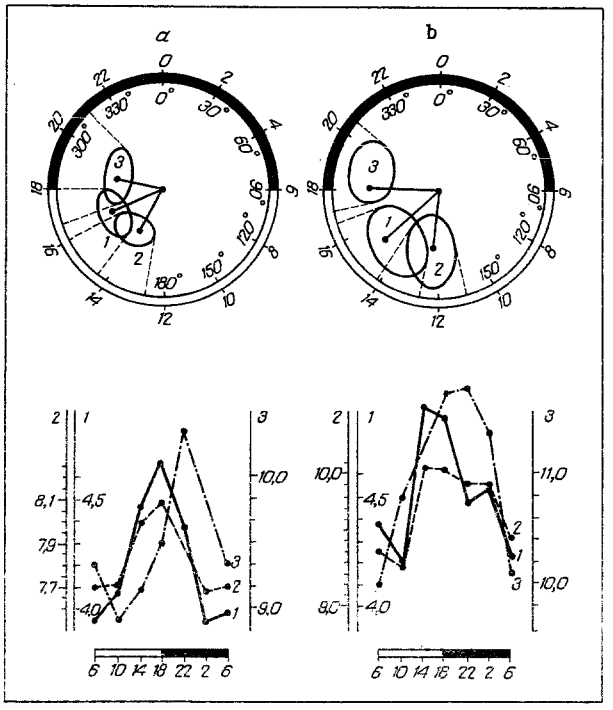


Fig. 1. Diagrams of circadian rhythms of erythrocytes (1), hemoglobin (2), and leukocytes (3) in peripheral blood of dogs during winter before (a) and after (b) repeated doses of eleuterococcus at 3 p.m.

with six animals in each subgroup, one of which received eleuterococcus in the morning the other in the afternoon; these constituted the experiments of series II, 1st and 2nd variants thereof respectively.

## EXPERIMENTAL RESULTS

Circadian fluctuations of erythrocyte, hemoglobin, and leukocyte concentrations were found in the intact animals (Table 1, Fig. 1), with a closely similar period (from 24.5 to 26.0 h). Prolonged administration of eleuterococcus, whether in the morning or in the afternoon, did not significantly change the duration of the periods of the biorhythms of these parameters, but significantly increased the mesor value and the amplitude if eleuterococcus was given at 3 p.m. The relative positions of the acrophases of the rhythms of these parameters was unaltered by eleuterococcus, but was shifted in the same sector of the

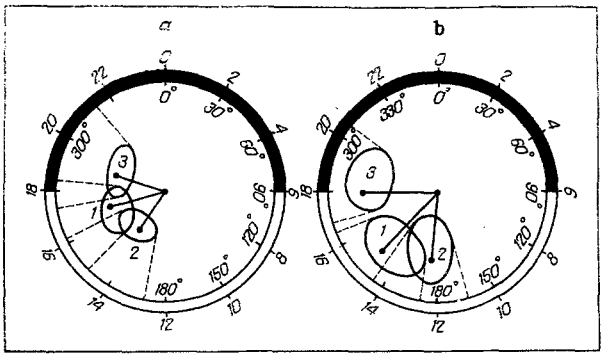


Fig. 2. Cosinor diagrams of circadian rhythms of erythrocytes (1), hemoglobin (2), and leukocytes (3) in peripheral blood of dogs during winter before (a) and after (b) repeated doses of eleuterococcus. Here and in Figs. 3 and 4: erythrocytes $10^{12}$/liter, hemoglobin mmoles/liter; leukocytes $10^{9}$/liter.

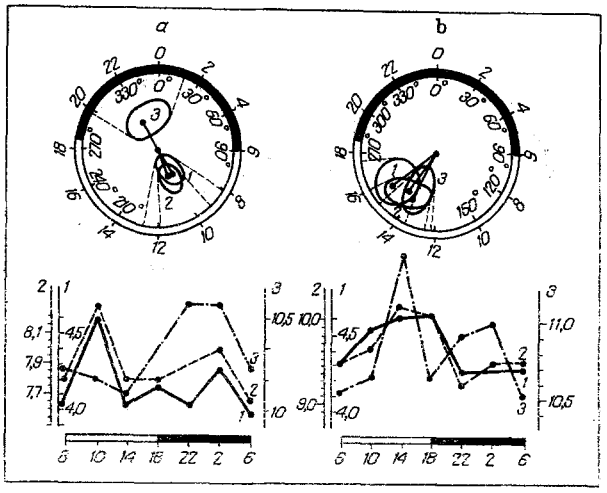


Fig. 3. Circadian rhythm of concentrations of peripheral erythrocytes (1), hemoglobin (2), and leukocytes (3) in dogs before (a) and after (b) repeated doses of eleuterococcus during the spring.

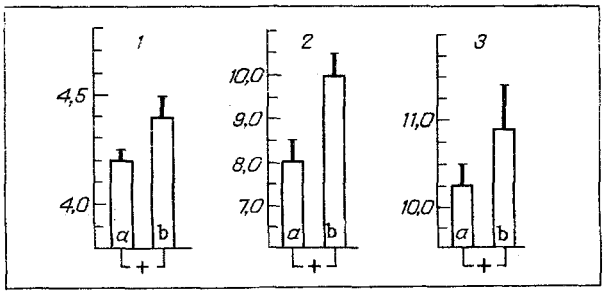


Fig. 4. Mesors of circadian rhythms of peripheral blood erythrocyte (1), hemoglobin (2), and leukocyte (3) concentrations in dogs before (a) and after (b) repeated doses of eleuterococcus in the spring.

diagram toward the beginning of the 24-hour period by 1-2 h, accompanied by a simultaneous decrease in the zone of confidence intervals of the mesors by 30 degrees (Figs. 2-4).

The result of the action of eleuterococcus on biological rhythms of erythrocyte, hemoglobin, and leukocyte concentrations thus depends on the time during the 24-hour period of its administration. Changes in the biological rhythms of these peripheral blood parameters took place only if the preparation was given to the animals in the afternoon.

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# EFFECT OF ENDOTOXIN ON OXIDATIVE METABOLISM OF POLYMORPHS


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**KEY WORDS:** endotoxin; neutrophils; active forms of oxygen; chemiluminescence.


The endotoxemia which often accompanies diseases of bacterial origin is connected with the appearance of an endotoxin (a fragment of the wall of Gram-negative bacteria) in the blood stream. The lungs are affected before other organs and most severely by endotoxemia. The primary target cells for endotoxin are considered to be the endotheliocytes of the alveolar capillaries. Results obtained in studies on cultures of endothelial cells indicate the absence of any direct cytotoxic action of the endotoxin over a wide range of concentrations [12]. However, another view also is widely held [2]. A characteristic feature of endotoxemia is the leukopenia which has already appeared by the end of the first hour [4]. Meanwhile, as has repeatedly been


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