EFFECT OF ADAPTOGENS ON ACTIVITY OF THE PITUITARY-ADRENOCORTICAL SYSTEM IN RATS

A. A. Filaretov, T. S. Bogdanova,
M. I. Mityushov, T. T. Podvigina,
and G. T. Srailova

UDC 612.014.49-06:[612-432+612.453].014.46:615.241

KEY WORDS: corticosteroids; stress; adaptogens.

The adaptive powers of the body near physiological conditions are regulated by the pituitary-adrenocortical system (PACS) and pharmacologic regulation is linked with the use of adaptogens. The question arises whether the action of adaptogens is effected through the PACS. Data in the literature on the effect of these preparations on the PACS are few in number and contradictory in nature [2, 3, 8, 9].

Investigation of the effects of adaptogens on evoked activity of the PACS, which is a constant and reliable indicator of stress [4, 6] — this most characteristic adaptive reaction — is particularly interesting. The aim of this investigation was to study the effect of ginseng (*Panax ginseng* C. A. Mey), *Polyscias filicifolia* Bailey, and *Eleutherococcus* Maxim on function of the PACS at rest and during stress.

EXPERIMENTAL METHODS

Experiments were carried out on 130 male Wistar albino rats weighing 160-200 g. PACS activity was determined by measuring the corticosterone concentration in blood taken after decapitation of the animals. Preparations of the adaptogens were injected intraperitoneally, once or repeatedly.

Corticosterone was assayed 60 min after a single injection of the adaptogens. Basal and stress-induced concentrations of the hormones were tested. In the latter case, 30 min after injection of the adaptogens the animals were immobilized, and decapitated at the 30th minute of immobilization.

For long-term administration the adaptogens were given daily for 7 days. On the 7th day (60 min after the last injection) the animals were killed and basal or stress-induced corticosterone concentrations were determined. The course of the experiments was the same as when a single injection of the adaptogens was given. A special frame, to the base of which the rats were pressed by a piece of wood, served for immobilization.

Tinctures (1:10) of cultures of ginseng and *Polyscias folicifolia*, obtained at the Leningrad Pharmaceutical Chemical Institute, a pharmaceutical preparation of tincture (1:10) of ginseng, and a pharmaceutical preparation of *Eleutherococcus* extract (1:1) were used. Before use, the preparations were evaporated to one-third of their volume and diluted with physiological saline. The dose of the preparations given to the animals was not more than 2 ml/200 g body weight. The following doses were investigated (calculated as the original preparation): 1) tincture of ginseng 0.75, 1.5, 3.0, and 6.0 ml/200 g body weight, 2) pharmaceutical preparation of tincture of ginseng 0.75 and 1.5 ml/200 g body weight, 3) tincture of *Polyscias filicifolia* 1.5 ml/200 g body weight, 4) pharmaceutical preparation of *Eleutherococcus* extract 0.04 ml/200 g body weight. The plasma corticosterone level was determined fluorometrically [10]. The experimental results were subjected to statistical analysis by Student's test.

Laboratory of Experimental Endocrinology, I. P. Pavlov Institute of Physiology, Academy of Sciences of the USSR, Leningrad. (Presented by Academician of the Academy of Medical Sciences of the USSR V. G. Baranov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 101, No. 5, pp. 573-574, May, 1986. Original article submitted July 10, 1985.

0007-4888/86/0005-0627$12.50

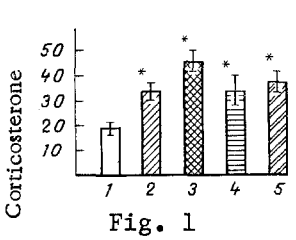

Fig. 1

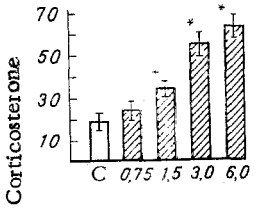

Fig. 2

Fig. 1. Effect of a single injection of adaptogens on basal blood corticosterone concentration (in μg %): 1) control (injection of Ringer's solution into animals); 2) injection of tincture of ginseng in a dose of 1.5 ml/200 g; 3) injection of pharmaceutical preparation of tincture of ginseng in a dose of 1.5 ml/200 g; 4) injection of tincture of *Polyscias filicifolia* in a dose of 1.5 ml/200 g; 5) injection of *Eleutherococcus* extract in a dose of 0.04 ml/200 g. Each group contains 7-10 animals. Asterisk indicates significance of difference from control at $P < 0.05$ level.

Fig. 2. Dependence of basal corticosterone concentration (in μg %) on dose of tincture of ginseng, given by a single injection. C) Control, injection of Ringer's solution into animals). Numbers beneath columns indicate dose of ginseng (in ml/200 g), calculated in the original tincture.

RESULTS

A single injection of tincture of ginseng, of the pharmaceutical preparation of tincture of ginseng, of tincture of *Polyscias filicifolia*, and of the pharmaceutical preparation of *Eleutherococcus* extract led to an increase in the basal blood corticosterone concentration (Fig. 1). Injection of increasing doses of the adaptogens caused the blood corticosterone level to rise. Direct dependence of the blood corticosterone level on the dose of ginseng is shown in Fig. 2. Similar dependence of the corticosterone level on the dose of the adaptogens was demonstrated previously for a purified fraction of ginseng glucosides [8, 9]. Prolonged administration of ginseng, *Polyscias filicifolia*, and *Eleutherococcus* did not affect the basal blood corticosterone level.

The next investigations were to study the effect of adaptogens on response of the PACS to stress. Immobilization of the rats led to an increase in the blood corticosterone concentration. Changes in the response of PACS to stress were observed during long-term administration of the adaptogens. Injection of ginseng and of *Polyscias filicifolia* for 7 days caused enhancement of the stress-induced rise of the blood corticosterone level (Fig. 3).

In these experiments, enhancement of the response of the PACS to stress was thus observed under the influence of ginseng and of *Polyscias filicifolia*, in agreement with our previous data [7]. Similar intensification of the response to stress under the influence of *Eleutherococcus* was described by Brekhman and Dardymov [1]. These results which are evidence of increased stressor activity of the PACS during the action of adaptogens contradict those of investigations in which a decrease was found [2, 3], and also to views that the effect of adaptogens is connected with inhibition of the stressor response. The contradictory nature of the results can be explained on the following grounds: 1) Function of the PACS was determined mainly on the basis of indirect parameters (weight of the adrenals, concentrations of ascorbic acid and cholesterol in the adrenals) [2, 3], 2) more powerful stressors were used than in the present experiments, and 3) the response to stressors in the present experiments was tested at different time intervals from those used by other workers.

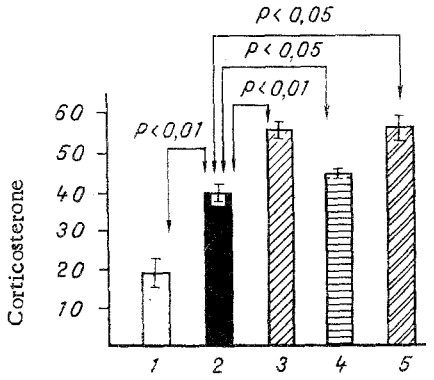

Fig. 3. Effect of 7-day course of adaptogens on blood corticosterone concentration (in μg %) during immobilization: 1) control (injection of Ringer's solution), 2) immobilization; 3) injection of tincture of ginseng (1.5 ml/200 g) for 7 days plus immobilization; 4) injection of tincture of *Polyscias filicifolia* (1.5 ml/200 g) daily for 7 days plus immobilization; 5) injection of pharmaceutical preparation of tincture of ginseng (0.75 ml/200 g) daily for 7 days plus immobilization. Each group contains 7-12 animals.

Since the stress reaction is one of adaptation, its intensification by adaptogens must be regarded as enhancement of the body's powers of adaptation. One of the mechanisms of the action of adaptogens is thus their effect on the PACS, which stimulates the reaction to stress.

LITERATURE CITED

1. I. I. Brekhman and I. V. Dardymov, in: Physiological Sciences — Medicine [in Russian], Leningrad (1983), pp. 84-95.
2. I. V. Dardymov, Ginseng, Eleutherococcus [in Russian], Moscow (1976), pp. 49-55.
3. O. I. Kirillov, in: Experience of Pharmacologic Control of Stress [in Russian], Vladivostok (1966), pp. 63-71.
4. T. Cox, Stress [Russian translation], Moscow (1981).
5. H. Selye, Essays on the Adaptation Syndrome [Russian translation], Moscow (1960).
6. A. A. Filaretov, Nervous Regulation of the Pituitary-Adrenocortical System [in Russian], Leningrad (1979).
7. A. A. Filaretov, T. S. Bogdanova, T. T. Podvigina, and G. T. Srailova, in: Problems in the Exploitation of the Medicinal Resources of Siberia and the Far East [in Russian], Novosibirsk (1983), pp. 230-231.
8. S. Hiai, H. Yokoyama, H. Gura, and S. Yano, Endocr. Jap., 26, 661 (1979).
9. S. Hiai, H. Yokoyama, and H. Gura, Endocr. Jap., 26, 737 (1979).
10. J. Van der Vies, R. F. M. Bakker, and D. De Wied, Acta Endocrinol. (Copenhagen), 34, 513 (1960).