

PART I

Eleutherococcus Extract: Action Range

STUDY OF THE RANGE OF THE ADAPTOGENIC ACTION OF ELEUTHEROCOCCUS SENTICOSUS RUPR. ET MAXIM

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Over the past years much attention has been paid in the Soviet medicine to the problems of increasing the total body's resistance to diverse unfavorable conditions and to the prophylaxis of different diseases. One of the most important trends in disease prophylaxis and in the increasing of the man's adaptation possibilities lies in the use of resistance of the body can be increased by administering enzymes, hormones and other biologically active substances (Yakovlev, 1969; Rusin and Trefilov, 1971; Wolf and Ransberger, 1976). The encouraging results have also been obtained thanks to the use of nucleic acid precursors, bacterial polysaccharides, and a number of other substances (Berzins et al., 1965; Ermolyeva, 1966; Lazarev, 1969; Belenky, 1971; Nikolaeva et al., 1971; Sokolov et al., 1980).

Of considerable interest in this respect is the use of natural plant compounds. They include, in particular, the plants belonging to the Aralia family, among which *Eleutherococcus senticosus* ranks the first as regards its medical importance.

A large body of literature exists on the adaptogenic activity of *Eleutherococcus senticosus* (Blokhin, 1966; Brekhman, 1969; Dardymov, 1976). However, since these data were obtained under different and inadequate conditions, on different objects, and with the use of different drug doses, they did not always correlate and were sometimes contradictory.

These facts make it necessary to carry out research under similar conditions with the use of the same objects.

The purpose of the given work was to specify the range of the drug adaptogenic action under external conditions.

1. GENERAL CHARACTERISTICS OF THE MATERIALS AND RESEARCH METHODS

A study was made of the capacity of *eleutherococcus* extract to exhibit different types of biological activity:

- 1) the ability to increase physical endurance under intense physical loads;
- 2) the ability to prevent reduction of physical endurance after exposure to hypodynamia combined with painful stress;
- 3) the protective action in hypoxia;
- 4) the antihyperthermal action;
- 5) the protective action in radiation;
- 6) the protective action in microbial intoxication.

Prior to the study an alcoholic tincture prepared from *eleutherococcus* liquid extract was evaporated on a rotor evaporator at 30°C to exclude the effect of alcohol, after which distilled water was added to the residue to make up the initial volume. The aqueous solution of the drug thus obtained was conditionally referred to as extract.

Experiments were made on mongrel white mice and rats. The drug was administered intragastrically in different concentrations depending on the experimental conditions. In experiments for studying radioprotective activity the drugs were injected intraperitoneally.

Ten animals at a time were used in the same experiment. With the exception of experiments for studying the radioprotective action of *eleutherococcus* extract during X-ray radiation and microbial intoxication, the drug was administered intragastrically in a single dose 1 or 24 h before exposure, or in the same dose for 3 or 7 days at rest or after functional load.

Animals of the control group received physiological solution in the same dose as that of the extract (0.2ml per 20g b/w).

2. EFFECT ON PHYSICAL ENDURANCE

2.1. The Total Physical Endurance

Experiments were made on white mongrel male mice weighing 18-20 g. The animals' working capacity was assessed according to the duration (min) of their climbing along an "endless" cord until complete exhaustion. This method was found to be most adequate for evaluating the total physical endurance. The drug was administered one hour before the experiment. Each dose of the drug was tested on a new group of animals in which the conditioned reflex of climbing along an "endless" cord was first elaborated.

The data obtained show that eleutherococcus extract (2.5 ml/kg) significantly increases the duration of the animals' running, while a higher dose increases the animals' working capacity to 145.8% as compare to control. Further increase of the dose to 7.5 ml/kg does not bring about any progressive growth in the duration of the animals' climbing.

2.2 High-Speed Physical Endurance

In addition to the study of the action of eleutherococcus on the total physical endurance (performance of the work of a "styer" under conditions of a sufficient oxygen supply) action of the drug on physical endurance was also studied under oxygen deficiency (work of a "sprinter").

Experiments were made on white mongrel male mice weighing 16-20 g. High-speed endurance was determined in a 10-track tretbahn, with the rate of the tape movement amounting to 40 m/min. The experiment was regarded as completed after 30 s of the animals' sojourn on the tretbahn electrical netting under a voltage of 90 V.

The effect of eleutherococcus extract on the animals' endurance of the forced running

in a tretbahn was studies in two functional states: at rest and after graded physical load. Physical load included forced running in a tretbahn for 5 min, the rate of the tape movement being 28 m/min. Multiple load was performed for 7 days. On the first day the duration of running was 5 minutes, later it was progressively increased (by 1 min a day).

Eleutherococcus extract (2.5 ml/kg) administered 1 h or 24 h before stress full effect did not promote any significant increase in the duration of the animals' running.

Analogous data were obtained in other series of experiments where eleutherococcus extract was administered at rest for 7 days, producing no substantial effect on the characteristics under study.

Mice exposed to a single physical load manifested, as compared with control, an increase in the duration of the running in a tretbahn not only 1 hour but also 24 hours after administration of eleutherococcus extract in a dose of 2.5 ml/kg.

It should be noted that at the end of the experimental period the most overt stimulating effect was seen in mice, which were trained daily for 7 days.

2.3 Physical Endurance After Exposure to Hypodynamia Combined with Painful Stress

In a series of experiments conducted on male mice weighing 18-22 g, the combined exposure to hypodynamia and painful stress was induced by suspending mice buy the neck fold with the aid of assayers' tongs for 18 hours daily for 3 days. Within an interval between experimental suspensions (6h), the animals were fed a full-value diet under animal house conditions. Intact mice not exposed to hypodynamia were deprived of water and food for the period of the suspending of experimental mice. The extract was administered intragastrically in a dose of 5 ml/kg.

It has been demonstrated that eleutherococcus has a marked protective action on the physical endurance, which was manifested in the reduction of the animals' running as compared with control. Administration of eleutherococcus extract in a dose of 5

ml/kg was conducive to a significant preservation of physical endurance in mice exposed to the described complex of adverse actions. The magnitude of physical endurance remained almost the same as that in intact animals.

3. ANTIHYPOXIC ACTIVITY

Acute hypobaric hypoxia in mice was produced in a special flow-exhaust pressure chamber. The animals were "raised" to the 6000m altitude, the rate of the lifting being 20 m/s. At this altitude the animals were kept for 2 min whereupon they were lifted at the same rate to the 10,000m altitude, where they were kept until the lethal outcome.

The animals' lifespan served as the criterion for the appraisal of the drug efficacy in acute hypobaric hypoxia.

A single administration of eleutherococcus extract at rest did not change the duration of the mouse lifespan as compared to the same characteristics in the control group. A single administration of eleutherococcus 1 or 24 hours after physical loads did not increase the animals' resistance to acute hypobaric hypoxia.

An opposite effect was seen after a 7-day prophylactic administration of the drug. Under such conditions eleutherococcus provoked a significant increase in the lifespan of experimental animals exposed to hypoxia. Long-term administration of eleutherococcus extract to the animals exposed to multiple incremental loads brought about a significant rise in the lifespan of mice.

4. ANTIHYPERTHERMAL ACTIVITY

Experiments were performed on mongrel while male mice weighing 16-20 g. The animals were overheated in a dry air chamber at a constant temperature of 50°C where they were kept until death.

The lifespan of the animals exposed to high environmental temperature served, as compared with control, as the criterion for

the appraisal of the drug efficacy in overheating.

Eleutherococcus (2.5 ml/kg) practically does not change the animals' endurance of overheating under relative rest and physical load.

An opposite effect was observed after a 7-day administration of eleutherococcus extract in combination with exercise over the same period. The drug administered to the animals exposed to exercise for 7 days favored a significant increase in the lifespan of the overheated mice.

5. RADIOPROTECTIVE ACTIVITY

Experiments were made on H₃ mice weighing 19-23 g. The animals were irradiated on PYM-13 unit at 180 kV, 15 A, filters: Al—1 mm+ Cu—0.5 mm, with the dosage amounting to 50 R/min.

The 30-day survival of the animals and the mean lifespan of the dead animals served as criteria of the radioprotective action of the drug.

It has been demonstrated that intraperitoneal injection of eleutherococcus to irradiated mice exerts a moderate radio-protective action.

The data indicated, in particular, that at a dose of 450 R the survival rate of experimental mice amounts to 20-30%, with the death rate in the control being equal to 100%. As the radiation dose is raised, the protective efficacy declines, completely disappearing at a dose of 600 R.

6. STUDY OF THE PROTECTIVE ACTION OF ELEUTHEROCOCCUS IN MICROBIAL INTOXICATION

The body's non-specific resistance to tetanus toxoid was examined in white mongrel male mice weighing 18-20 g. Tetanus toxoid was injected intraperitoneally in a dose of 1 mg/kg in a volume amounting to 0.2 ml.

The protective action of eleutherococcus was evaluated from the number of survived mice (%) 24, 48, 72 and 96 h after tetanus toxoid injection

Eleutherococcus substantially increases the survival of animals exposed to the lethal doses of tetanus toxoid (48 hours before drug administration). After 96 hours 20% of animals

of this group survive. Whereas in the control group, all the animals die by the third day.

The data provided in this article attest to a broad adaptogenic action range of *Eleutherococcus senticosus* Rupr. Et Maxim extract. We think it necessary to emphasize that the phenomenon of pretension occurs at a multiple drug intake.

Of no less importance is the finding that the drug exhibits a more marked action after graded functional loads. It may be assumed that eleutherococcus extract enhances the super-compensation phase after exhausting loads, specified by Weichert — Volbert — Pavlov

BIBLIOGRAPHY

- Belenky, E.E., Sokolov, I.K., Tunitskaya, T.A. Effect of potassium orotate, inosin and other purines on the development of heart hypertrophy in experimental aortal stenosis. *Famakologia I toskologia*, 1971, 4, 472-475.
- Berzins, V.K., Blumberg, M.Ya., Zvirgzda, A. Yu. Effect of zymozan on complement properdin levels in rabbits. In: *Biochemical Factors and Body Reactivity*. Zintane Publishers. Riga, 1965, 63-73.
- Blokhin, B.N. Effect of extracts from the roots and leaves of eleutherococcus on the working capacity of athletes. In: *Materials of the 3rd Conference of the Central Research Laboratory of the Tomsk Medical Institute*. Tomsk, 1966, 134-135.
- Brehkman, I.I. *Eleutherococcus*. A new Stimulant and Tonic. The V.I. Lenin Military Institute of Physical Culture and Sports. Leningrad, 1960, 22 pp.
- Dardymov, I.V. *Ginseng, Eleutherococcus*. Nauka Publishers, Moscow, 1976, 184 pp.
- Ermolaeva, Z.V. *Biologically Active Substances*. Znanie Publishers. Moscow, 1966, 32 pp.
- Lazarev, N.V. Prerequisites for the use of purines and pyrimidines in the treatment of respiratory diseases. In: *Materials of the Conference of Pyrimidine and Purine Derivatives for Respiratory Diseases and Some General Aspects of the Therapeutic Action of These Drugs*. The Gorky Research Institute of Industrial Hygiene and Occupational Diseases, the RSFSR Ministry of Health. Gorky, 1969, 3-6.
- Nikolaeva, A.F., Chernichenko, N.M., Sokolova, R.I. Effect of inosin on myocardial metabolism outside the infarction zone. *Kardiologia*, 1971, 11, 8, 111-118.
- Rusin, V. Ya., Trefilov, G.V. Comparative assessment of the adaptogenic efficacy of dibazol and certain other biologically active substances. *Materials of the Yaroslavl*, 1971, 77, 9-17.
- Sokolova, I.K., Kaplan, E.Ya., Airapetyan, G.M. The adaptogenic effect of riboxine. *Khimiko-farmatsevtichesky zhurnal*, 1980, 1, 40-50.
- Wolf, M., Ransberger, K. *Treatment with Enzymes*. Mir Publishers. Moscow, 1976, 121 pp.
- Yakovlev, N.N. Goal-oriented regulation of metabolism in muscle activity. In: *Materials of the 2nd Symposium on the Pharmacology of Motor Activity*. All-Union Research Institute of Physical Culture and Sports. Moscow, 1969, 27.