

PART III

Eleutherococcus Extract as an Agent Increasing the Biological Resistance of Man Exposed to Unfavourable Factors

USE OF ELEUTHROCOCCLUS EXTRACT FOR INCREASING THE BIOLOGICAL RESISTANCE OF MAN EXPOSED TO DIFFERENT UNFAVOURABLE ENVIRONMENTAL FACTORS (A REVIEW)

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This review discusses only certain aspects of potential uses of eleutherococcus extract, namely the use of this drug as an adaptogen (or resistance) that increases the adaptation potentialities and fitness for work of man under unfavourable conditions, including exposure to different chemical compounds with toxic effects. According to the manual of the drugs by M.D. Mashkovsky (1978), which is very popular in the USSR, eleutherococcus extract is used as a stimulant of the central nervous system though the mechanism of its action on this system is unknown and such a classification may be accepted only relatively.

By today eleutherococcus extract has been already successfully used for the treatment of various pathological conditions. We shall confine ourselves, however, to the title aspects as the closest ones to the formally accepted trend in the drug use.

We think it of importance to give in this review some examples illustrating the action of other similar drugs, to emphasize once more that there is a class of substances that prophylactically increase the biological resistance of man.

1. REDUCTION OF THE TOTAL DISEASE INCIDENCE

In 1973-1975, altogether 1200 drivers engaged at the Volga Automobile Plant (VAP) received eleutherococcus extract (8-12 mg) with tea annually for two months, in spring and

autumn. The control groups were represented by other professions.

After intake of eleutherococcus extract the total disease incidence decreased by 20-30% as compared with 1973. In 1975, for instance, the total disease incidence at the plant increased by 20%, whereas at the motor transport administration it reduced by 20%.

In 1975 (November and December), the mass pharmacoprophylaxis was carried out at the VAP. Eleutherococcus was included in the diet as eleutherococcus sugar (in a dose of 2 ml). Altogether 13,096 persons were engaged in experiments. The disease incidence dropped by 30-35% as compared to the control group. The reduction in the sick leave payments amounted 14,310 roubles (Schezhin et al., 1977).

A group of 54 miners working at the industrial association "Vorkuta-ugol" received eleutherococcus extract (2ml) before the shift daily over two months (June-July, 1976). The disease incidence dropped by 33.3% as regards the number of sick persons and by 45.6% as regards the number of disability days (Kalashnikov, 1977).

2. REDUCTION OF THE INCIDENCE OF INFLUENZA, ACUTE RESPIRATORY DISEASES (ARD) AND COLD-INDUCED DISEASES IN LARGE POPULATION GROUPS

According to the formally accepted definition, eleutherococcus extract is a stimulant and not an anti-influenzal agent. Nevertheless data have been accumulated by today on the anti-influenzal effect of

eleutherococcus. These facts which are described in detail below, may be explained in the following way:

- 1) either eleutherococcus extract possesses the invigorating and tonic action or
- 2) it has direct antiviral activity, which is manifested, in particular, in the capacity of the drug to retard the growth of viruses in mammalian cell cultures (Wacker and Eilmes, 1978).

In the Primorye Region, a group of young men (180) were given eleutherococcus liquid extract in a dose of 0.5 ml every other day during March. As compared to the control group, the influenza and ARD incidence decreased from 17 to 12.7% (Brekhman, 1976). In the winter of 1972-1973, about 1000 workers of the Norilsk mining and smelting plant received eleutherococcus extract (22ml) daily for two months. The influenza and ARD incidence reduced almost 2.4 times versus the same number of workers engaged at a shop with the same working conditions. The economic efficiency due to the reduction in manpower losses amounted to about 0.5 min. roubles (Gagarin, 1977; Brekhman, 1977).

Eleutherococcus is not the sole adaptogen having such properties. In the winter of 1965, dibazol, an adaptogen of the synthetic origin, was administered on a large scale during influenza epidemic in the city of Chelyabinsk. A total of 120 to 150 thousand persons covered by experiments received 15 kg of dibazol altogether, the total cost of the drug amounting to 1500 roubles.

The influenza incidence in Chelyabinsk was compared to that in Sverdlovsk. Both cities are similar with regard to the population number and are located in the same climatic zones. The disease incidence was previously the same. After prophylactic intake of dibazol in Chelyabinsk it turned out to be 15.9% lower among adults and 25.1% lower among children as compared to Sverdlovsk. As a result of the disease incidence reduction, the output of industrial goods rose by 15-16 min. roubles (Ebert et al., 1968).

3. REDUCTION OF THE INCIDENCE OF ESSENTIAL HYPERTENSION AND ISCHEMIC HEART DISEASE (OCCUPATIONAL DISEASES OF DRIVERS)

The prophylactic action of eleutherococcus extract in preventing relapses of essential hypertension and ischemic heart disease was confirmed in 1200 drivers of the VAP (Galanova, 1977).

From 1973 to 1975 the number of workers with high arterial blood pressure increased 2 times. In 1973, the number of cases of high arterial blood pressure at the motor transport administration was approximately the same as that at the whole plant. After prophylactic treatment with eleutherococcus performed in 1975, the number of hypertensive drivers reduced 3.5 times. As a result, the manpower losses decreased by 61% as compared with 1973. The number of cases with exacerbation of ischemic heart disease was 6.7 per 100 workers in 1973; in 1978 it dropped to 0.2. In 1973, the number of disability days was 282, which in 1978 decreased to 3. The experimental data obtained later (until 1979) are provided in the article by Shchezhin et al. (1981).

4. IMPROVEMENT OF VISION ACUITY, COLOUR PERCEPTION AND HEARING ACUITY

The effect of eleutherococcus on vision acuity was studied in healthy young subjects with normal vision. One hour after intake of eleutherococcus liquid extract, vision acuity increased from 1.15-1.16 to 1.26-1.32. Eight hours following intake of the drug vision acuity amounted to 1.46-1.52 and remained high (1.25) for 32 hours. By the end of the second day vision acuity returned to normal. Eleutherococcus extract was discovered to enhance function of color perception in persons with normal vision and in color-blind persons. In color-blind persons eleutherococcus extract given in a dose of 2 ml provides normal color vision for 36 hours (Sosnova, 1969).

On board the research ship "Akademik Korolev" the crew were given eleutherococcus for prophylaxis. The drug was administered in a daily dose of 36-40 drops for a month. The control group received alcohol diluted with stewed fruit. The crewmembers who were given eleutherococcus stopped complaining of a sharp pain sensation in the

eyes, photobia and rapid fatigability (Tikhomirova, 1977).

Twelve persons working for ship repair industry with the use of vibration tools received eleutherococcus extract for two months. The control group consisted of 4 persons. After intake of eleutherococcus vision acuity increased from 0.03 to 0.1 (Kalmykova, 1973).

Brekhman (1976) reported that hearing acuity improved in that half of the crewmembers of the ship under repair, who received eleutherococcus extract. The working operations were attended with noise (75 decibel). These crewmembers (19 persons) received eleutherococcus liquid extract at dinner in a dose of 2 ml for a month. The control group was given 2 ml of tinted alcohol.

5. INCREASE IN THE OUTPUT PER MAN-HOUR IN OPERATIONS REQUIRING ATTENTION AND NERVOUS TENSION

The telegraph operators aged 21-33 years relayed the text continuously for 5 minutes. On the day of experiment the relaying was performed twice: before and one hour after intake of eleutherococcus (in a dose of 2 ml in 30 ml of water); the control group received imitation of eleutherococcus extract in a dose of 30 ml. It appeared that eleutherococcus did not produce any effect on the number of the characters relayed but significantly reduced the number of errors.

In other cases, 19 radiotelegraph operators received eleutherococcus in a dose of 2 ml for 30 days, whereas 20 persons were given an imitation of the drug. The output per man-hour did not rise, but the operation quality improved: the number of errors noticeably decreased (Medvedev, 1963; Brekhman, 1980).

6. REDUCTION IN THE DISEASE INCIDENCE UNDER UNFAVOURABLE CLIMATIC CONDITIONS

During long-term navigation in the tropics where high temperature and moisture substantially restrict working capacity, the seamen were given an extract from the roots of eleutherococcus. The control group received an

imitation of eleutherococcus extract. It was demonstrated that eleutherococcus reduces unfavourable functional shifts on the part of the central nervous system, cardiovascular system and thermoregulation, promotes an increase in physical and mental working capacity, and improves vision analyser function (Berdysheva, 1977).

In operations under high-altitude conditions, daily single dose of eleutherococcus (30-40 ml) helps endure high physical effort (Kalashnikov, 1977).

During work performed under arctic conditions, the use of eleutherococcus may substantially reduce disease incidence (Gargarin, 1977; Brekhman, 1978; Kalashnikov, 1977).

Undoubtedly, eleutherococcus has competitors among the drugs administered in such situations. One of the adaptogens used under unfavourable climatic conditions is, for example, yellow sugar, intermediate product of sugar refinery industry. This sugar is sucrose with an admixture of molasses. The adaptogenic properties of yellow sugar were discovered for the first time by Brekhman. The effects of yellow sugar were studied in normal young men of the same age living in a high-altitude region (3600 m above the sea level). In the group of test subjects, 30 g of white sugar was replaced by 30 g of yellow sugar. The control group received only white sugar. The sleep, appetite, fatigability, the incidence of cold-induced diseases, weight, blood pressure and blood picture were checked for 3 months. Yellow sugar was found to promote more rapid adaptation to high-altitude conditions. Subjects of the control group applied for medical help 41 times, whereas those from the test group 31 times (Brekhman and Zharsky, 1980).

7. REDUCTION OF STRESS-INDUCED HARMFUL REACTIONS

It has been shown in animal experiments that adaptogens drastically reduce the stress-induced harmful effects. It is difficult enough to make an experiment on humans in a "pure form", i.e. to create a pure model of stress therefore no such data are available. However, positive results of experiments discussed in this review show that in assembly line operators, truck drivers, telegraph operators and people working under high-altitude conditions adaptogens undoubtedly demonstrated the protective action in stressful situations.

8. REDUCTION OF TOXICITY OF CHEMICAL COMPOUNDS BY ELEUTHEROCOCCUS EXTRACT

Positive results have been obtained in application of adaptogens for reducing toxicity of numerous chemical compounds, including drugs.

In 1967, Monakhov carried out 12 series of experiments on 418 white mongrel mice and 476 rats of both sexes with sarcomas 180 and 256. On days 4-6 after tumour transplantation the animals were divided into 4-6 groups to begin treatment with cytostatics. Eleutherococcus extract (1-5 ml/kg) was given daily with drink. Cytostatics were injected intraperitoneally: benzoteph (8-20 mg/kg) every 48 hours, cyclophosphamide (20-40 mg/kg) every 48 hours, and ethymidin (0.7-6 mg/kg) every 48 hours was injected daily. The animals' weight, tumour size, and leukocyte count were under control throughout the experiment. After it was completed the animals were sacrificed, tumors extricated and weighed to calculate the mean weight and tumour growth inhibition.

Eleutherococcus extract was shown to decrease the sensitivity of mice and rats to the toxic action of cyclophosphamide, ethymidin and benzoteph. In treatment with cytostatics combined with eleutherococcus the animals lost less weight and their leukocyte count was higher than in the animals treated with cytostatics alone.

Lethal doses of the cytostatics resulted in animals' death. In a group of mice given thiophosphamide in a dose of 16 mg/kg, 53% of the animals died. After administering combined eleutherococcus and thiophosphamide only 15% of the animals died.

Similar results were also obtained in experiments on rats with Walker's carcinoma. In a group of the animals given ethymidin in a dose of 1.5 mg/kg, 30% died. The rats which received ethymidin combined with eleutherococcus extract remained alive.

It has been demonstrated by Elkin (1981) that eleutherococcus extract can reduce the narcotic effects of hexenal, hydrogen chloride, sodium barbital and ether. The experiments were made on 1171 white mongrel mice of both sexes. Eleutherococcus extract was injected

intraperitoneally 30 minutes before administering the narcotics. Hexenal (80 mg/kg), sodium barbital (175 mg/kg) were dissolved in distilled water and injected subcutaneously. According to Elkin's data, eleutherococcus shortens the duration of the sleep induced in mice by the above drugs, i.e. it exerts an awakening effect under the action of both "cortical" and "intertrunkal" narcotics.

Other data obtained by the same author indicate that eleutherococcus extract may prove useful for prophylactic and therapeutic applications in acute and chronic poisoning with some insecticides (e.g. aniline, asymmetrical dimethyl-hydrazine, etc.).

Eleutherococcus as an antitoxic agent has high universal properties. This does not mean, however that it can reduce toxicity of all foreign chemical compounds. In the literature cited in part 1.8, one can find examples illustrating the lack of the effect of eleutherococcus on toxicity of individual compounds; there is also contradictory evidence: for instance, according to Elkin's data (1981), eleutherococcus extract reduces toxicity of sodium nitrite, whereas according to Mikhailova (1972), it makes it higher. In both cases the differences from the control are insignificant. In addition, it should be borne in mind that the authors of these and of many other similar works did not control the content of the active principle in eleutherococcus extract and dealt with the drug whose standards were determined under industrial conditions according to the indirect signs (the main indicator is the dry residue weight). It may be inferred that the new methods for drug standardization elaborated with one of the authors of this article will make it possible to improve the data reproducibility, to select the doses of eleutherococcus extract more accurately, thereby ensuring the reduction of toxicity of xenobiotics.

Attention is called to the fact that the overwhelming majority of the substances provided undergo metabolic inactivation in the body, i.e. chemical transformation provoked by special enzymes, which usually promotes elimination of foreign substances from the body and reduction of their toxicity. It might be assumed that this ability of eleutherococcus extract is linked with its property to activate the body's system of the metabolic inactivation of xenobiotics. As is known, this system includes a complex of specialized enzymes: the monooxygenase system with the terminal oxidase and cytochrome P-450. It has been

demonstrated recently that this system is closely linked with the immunological system, forming with the latter the total body's system that inactivates diverse exogenous and certain endogenous compounds, thereby maintaining the body's chemical homeostasis (Kovalev and Plevaya, 1981).

Other considerations about the antitoxic action of eleutherococcus with regard to antitumor drugs are provided in the work by Yaremenko (1981) that suggests a mechanism including the stressor action of these drugs and antistressor activity of eleutherococcus.

The antitoxic activity of eleutherococcus extract forms the basis for obtaining combined medicinal forms that include eleutherococcus extract as one of the components. It is advisable to use this extract in different formulae of food drinks, which can be used with some drugs to reduce their toxicity.

This review demonstrates that eleutherococcus extract can increase the man's resistance to diverse unfavourable factors: biological, physical, chemical, and psychological. In principle, it is possible to choose an effective drug that would counteract each of these factors, a drug that would be able to protect man, at least partly, against the given unfavourable factor and maintain the man's working capacity. However, eleutherococcus extract displays an extremely wide action range, which is essential, because in the majority of cases the action of unfavourable factors is manifested in the most diverse concurrent or successive combinations. Sometimes these factors remain completely unknown to man as is the case with environmental pollution induced by a complex mixture of chemical substances and (or) by different man-made physical exposures. The universal properties of eleutherococcus extract make it one of the most efficacious and promising pharmacological agents for increasing the non-specific resistance of man.

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