

EFFECT OF ELEUTHEROSIDES ON WEIGHT AND MITOTIC ACTIVITY OF THE REGENERATING MOUSE LIVER

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Eleutherosides (the glycoside fraction extracted from roots of the Far-Eastern medicinal plant Eleutherococcus senticosus Rupr. et Maxim), when injected into mice in a dose of 0.8 g/20 g body weight, do not alter the weight or mitotic activity of the liver. If injected in the same dose into mice from which two-thirds of the liver has been removed, they stimulate regeneration of the liver, increasing its weight and mitotic activity.

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Eleutherococcus and preparations made from it stimulate processes directly or indirectly connected with increased protein synthesis. Eleutherococcus has been shown, for instance, to increase activity of the adaptive liver enzyme tryptophan pyrrolase during stress [4], to stimulate hematopoiesis in human donors after withdrawal of blood [1] and in animals after single and repeated bleeding [5], to help in restoring the leukocyte count in rats receiving the maximal tolerated dose of ethimidine or cyclophosphane [6], and to accelerate adaptation of erythrocytes to hemolysis in newborn rats [2].

The object of the present investigation was to study the action of the glycoside fraction of eleutherosides—substances extracted from the roots of the Far-Eastern medicinal plant Eleutherococcus senticosus Rupr. et Maxim [3]—on the weight and mitotic activity of the intact and regenerating mouse liver.

EXPERIMENTAL METHOD

Experiments were carried out on 90 noninbred male mice with a mean weight of 26 g.

The experiments were divided into two series. In series I, 24 mice received an intraperitoneal injection of 0.4% solution of eleutherosides in a dose of 0.2 ml/20 g body weight, while the other 24 mice received 0.2 ml of distilled water. The preparations were injected daily for 3 days during the morning. At 7 a.m. 24 h after the last injection half of the mice were sacrificed, while the other half received an injection of 0.04% colchicine solution in a dose of 0.01 ml/g body weight; these animals were sacrificed 6 h later.

In the experiments of series II, two-thirds of the liver was resected by the method of Higgins and Anderson [7]. The animals of one group received an intraperitoneal injection of 0.4% solution of eleutherosides in a dose of 0.2 ml/20 g body weight, equal to 0.8 mg (experiment).^{*} The other group received an injection of 0.2 ml distilled water (control). The animals received three injections of the preparations: the first 1 h before operation, and then one injection each on the 2nd and 3rd day after operation. Some of the animals (9 experimental and 9 control) were sacrificed 86 h, and the rest (12 experimental and 12 control) 10 days after the operation. Decapitation was carried out at 7 a.m. The body weight and weight of the liver were determined. Pieces of liver were fixed in Carnoy's fluid. Paraffin sections were cut to a

^{*}A preliminary investigation showed that smaller doses of total eleutherosides (0.2 and 0.4 mg/20 g body weight) do not affect liver regeneration.

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TABLE 1. Effect of Eleutherosides on Weight and Mitotic Activity of Liver after Resection of Two-Thirds of the Organ

Time after operation	Group	No. of animals	Weight of liver		Mitotic index (in %)
			absolute (in g)	relative (in %)	
86 h	Control	9	0,78±0,047	3,83±0,26	13,2±2,29
	Exptl. P	9	1,19±0,034 0	5,30±0,140 0	38,5±7,31 0,005
10 days	Control	12	1,60±0,085	6,2±0,25	3,51±0,77
	Exptl. P	12	1,68±0,069 0,329	6,4±0,21 0,18	1,20±0,17 0,007

thickness of 6-7 μ and stained with hematoxylin-eosin. The mitotic index was obtained by counting mitoses in not less than 7000 interphase cells.

EXPERIMENTAL RESULTS

The results of the experiments of series I, in which eleutherosides were injected into intact mice, showed that during the 4 days of the experiment the preparation had no effect either on the weight of the liver or on mitotic activity of the hepatocytes. After injection of colchicine there was no significant change in the weight of the liver but the mitotic index was increased by 8 times. Eleutherosides had no effect on this action of colchicine.

The results of the experiments of series II in which eleutherosides were injected into mice undergoing partial hepatectomy are given in Table 1. The preparation increased the absolute and relative weight of the regenerating liver and also the mitotic activity of the hepatocytes 86 h after operation. Ten days after operation the weight of the liver was the same in the control and experimental animals, while the mitotic index was lower in animals receiving eleutherosides than in the control.

The results demonstrate that eleutherosides stimulate reparative regeneration of the mouse liver. This effect was seen most demonstratively in the experiment in which the animals were sacrificed 86 h after removal of two-thirds of the organ: the weight of the regenerating liver and mitotic activity of its cells were increased.

In the experiment lasting 10 days, no effect of the preparation was seen on the weight of the liver, but this could be attributed to the fact that by this time its weight was practically identical with that of the control organ.

However, the mitotic activity of the hepatocytes was still increased in the control animals. The decrease in this index in the experimental group could be taken as evidence that eleutherosides bring about a more rapid return of the normal number of mitoses in the late stages and, consequently, a more rapid completion of the regeneration processes.

It is an interesting fact that, while they exert a definite stimulant action on the regenerating liver, eleutherosides had no effect on the liver of the intact animals. The absence of difference between the mitotic index in the experimental and control series was also observed when colchicine was used.

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