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Efficacity in experimental induced liver damage of a natural polypeptide

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TWO NINHYDRINPOSITIVE fractions were obtained from a liver extract through fractionation on a cation exchanger (of SE-Sephadex C 25). Characterisation of the fractions was done by ascending chromatography on paper (*n*-propanol : NH_3: H_2O = 6:3:1). One of the fractions was pure and, after total acid hydrolysis, was shown to contain nine amino acids: Glu, Asp, Gly, Lys, Leu, Thre, Ser, Isoleu, Ala. This fraction, after experimental demonstration of its liver-protective effect, was named hepatotrop factor 1 (FH 1).

The study of the liver protective effect was carried out in two ways: (1) acute allyl alcohol intoxication in rats. In three successive experiments on 180 Wistar male rats, 180–200 g, allyl alcohol was administered per os in amount of 0·4 ml(sol 1%)/100 g animal weight. Groups of animals were preventively treated with FH 1 (solution of 8μM/ml) given subcutaneously (s.c.) at the doses of 1 ml/100 g animal weight 48·24 and 1 hr before the intoxication. Other groups were treated curatively with the same doses of FH 1, but given 1, 6, 24 and 30 hr after allyl alcohol administration. All the groups were sacrificed 48 hr after the allyl alcohol administration, the results obtained are listed in Table 1 and Fig. 1.

(2) Chronic intoxication with CCl_4 in rats. In three successive experiments the CCl_4 was administered twice weekly (six administrations) s.c. in doses of 0·1 ml/100 g to 120 Wistar male rats, of 150–200 g, divided in lots of twenty animals. FH 1 was administered s.c. at a dose of 0·5 ml/100 g animal for 5 days after the end of CCl_4 administration. Twenty-four hr after the end of the FH 1

TABLE 1. THE EFFECT OF FH 1 ON THE LIVER DAMAGE INDUCED WITH ALLYL ALCOHOL IN RATS IN g OF DAMAGED LIVER TISSUE FOUND FOR A GROUP OF TWENTY RATS

No. of experiments	Denomination of group treated		
	control	preventively	curatively
I	8·328	0·720	1·300
II	7·070	0·608	1·560
III	7·955	0·570	1·648

FH 1 was administered preventively for an accumulation in liver and curatively (1–30 hr after intoxication) of the reason then the liver necrosis become clearly visible in allyl alcohol intoxication after 36 hr. Of every liver lobe the damaged tissues was weighed. In this way a total value of damaged tissues is found for twenty animals group which can be compared with that of a control group (allyl alcohol intoxicated).

FIG. 1. Macroscopic aspect of rat liver after intoxication with allyl alcohol (C = control) and treatment (curatively) with FH 1 (T = treated).

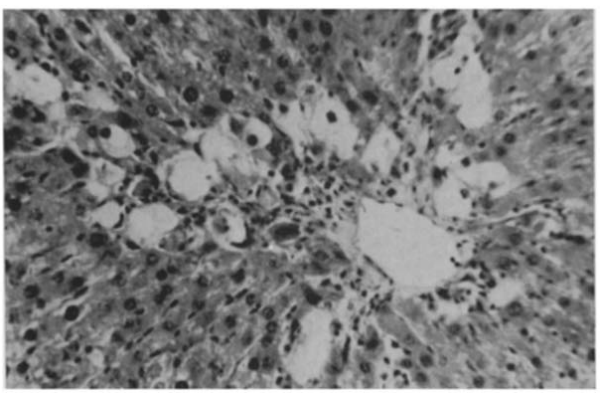

FIG. 2. Rat liver. Chronic intoxication with CCl_4. Hematoxylin–eosin. Magnification: ×200.

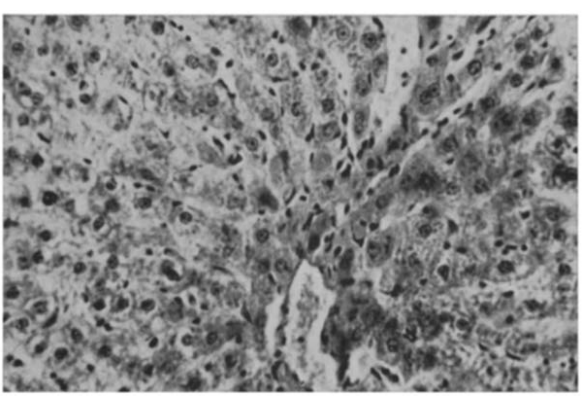

FIG. 3. Rat liver. Chronic intoxication with CCl_4 and treatment with FH 1. Hematoxylin–eosin. Magnification: ×200.

B.P.—*facing page 2278*

TABLE 2. THE BSP RETENTION VALUES (%) IN RATS, INTOXICATED WITH CCl_4 AND TREATED WITH FH 1

No. of experiments	Denomination of group					
	control	ES	CCl_4	ES	CCl_4 + FH 1	ES
I	14	±4	27	±6	19	±5
II	18	±3	36	±6	17	±1
III	18	±4	38	±4	18	±3

FH 1 was administered for 5 days after the last (6) injection of CCl_4. After this 5 days of treatment with FH 1, BSP (bromosulfophtalein) was administered all the groups i.v. in sol. 1% in amount of 5 mg/100 g A, blood samples was gathered in after 1 and 10 min. The quantity of BSP in serum was determined by the Shoemaker method and the retention values was calculated with the formula:

$$\frac{\text{Concentration BSP at 10 min}}{\text{Concentration BSP at 1 min}} \times 100$$

treatment the animals were sacrificed for microscopical and bromosulfophtalein (BSP) retention investigations. The results obtained are listed in Figs. 2 and 3 and Table 2.

The allyl alcohol intoxication is characterized by a perilobular liver necrosis. FH 1 diminishes the intensity of those lesions (Table 1 and Fig. 1). The administration the FH 1 in chronic liver damages induced by CCl_4 also re-establishes the metabolical function of the liver (BSP values return to normal—Table 1) and diminishes the centrolobular necrosis of hepatocytes (Figs. 2 and 3). On the basis of these results, it may be concluded that FH 1 is an efficient therapeutic agent in some forms of experimental liver damage.

Pharmacological Department
Chemical-Pharmaceutical Research Institute,
şos. Vitan 112,
Bucharest 4,
Rumania

M. TIMAR
I. HÄDRICH
GH. VREJOIU
M. TEODORESCU
G. SZEGLI
I. NITELEA

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The subcellular distribution of pancreatic kallikrein

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THE KALLIKREINS are a group of enzymes, probably isoenzymes, which occur in the submaxillary gland and the pancreas. Subcellular studies have shown that kallikrein occurs in granules which sediment at low *g* min values.[1–3] This finding has been recently confirmed.[4,5] In the present experiments the intracellular distribution of pancreatic kallikrein was studied and its distribution pattern compared with that of amylase and trypsin.

Cats and dogs, which had been allowed food *ad libitum*, were anaesthetised with intraperitoneal sodium phenobarbitone (45 mg/kg), exsanguinated and the pancreas removed, rinsed in 0·32M sucrose, dried on filter paper and weighed. The glands were cut into small pieces and homogenised