EFFECT OF THE SEEDS OF Trichodesma incanum ON THE DEVELOPMENT OF FATTY DEGENERATION OF THE LIVER

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Administration of seeds of the weed $\underline{\text{Trichodesma}}$ incanum in conjunction with a low protein diet and during CCl_4 poisoning leads to marked inhibition of fatty degeneration of the liver and is accompanied in all cases by an increase in the autolipolytic activity of the organ. Lipolysis in the fatty tissue is reduced in some cases, while in others (if fatty degeneration of the liver is inhibited) it is increased. Experiments in vitro showed that the increase in lipolysis is due to the direct action of alkaloids of the $\underline{\text{Trichodesma}}$ incanum seeds and also, evidently, to the appearance of metabolically active substances capable of stimulating the lipolytic activity of these tissues in the serum of animals receiving the $\underline{\text{Trichodesma}}$ seeds.

To examine the mechanisms of the unique action of seeds of <u>Trichodesma incanum</u> in inhibiting the development of fatty degeneration of the liver, demonstrated previously by the writers [1], experiments were carried out on 149 male albino rats weighing 180-200 g.

EXPERIMENTAL METHOD

The animals of one group received a normal synthetic diet (18% protein in calorific value), those of the second group received a low-protein synthetic diet (10% protein), while those of the third group, which received a normal diet, were poisoned with CCl₄ (0.3 ml/100 g body weight, three doses on alternate days). The experimental animals received the seeds of Trichodesma incanum by mouth in doses of 10 and 20 mg/100 g body weight on alternate days for 30 days. Indices of carbohydrate and lipid metabolism were determined in the blood, liver, and fatty tissue of all the animals [1].

EXPERIMENTAL RESULTS

The glycogen content in the liver of the animals receiving a low-protein diet was reduced (to 0.96 ± 0.06 compared with 2.1 ± 0.1 g% in the control; P<0.001), while the content of total lipids was increased (from 16.2 ± 0.2 to 28.9 ± 1.2 g%; P<0.001). Lipolysis in the fatty tissue was increased, while autolipolysis in the liver was reduced (to 6.3 ± 0.2 and 2.6 ± 0.1 from normal values of 3.9 ± 0.2 and 4.1 ± 0.2 $\mu eq/ml$ per gram tissue, respectively; P<0.001). The formation and output of β -lipoproteins and phospholipids were disturbed. When Trichodesma incanum seeds were administered under these conditions, although a further decrease was observed in the glycogen and β -lipoprotein content in the liver, the lipid content in the liver fell regularly (to 19.9 ± 0.8 compared with 28.9 ± 1.2 g% in the control; P<0.001). Meanwhile the autolipolytic activity of the liver was increased (to 7.3 ± 0.5 ; P<0.001), while the rate of lipolysis in the fatty tissue was reduced (to 2.3 ± 0.1 ; P<0.001). Morphologically, the signs of fatty degeneration in the hepatocytes decreased in intensity or even disappeared.

In the animals receiving CCl_4 , the glycogen content in the liver was reduced (to 0.8 ± 0.06 g%; P < 0.001), the formation and output of β -lipoproteins and the accumulation of lipids in the liver were disturbed

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 $(27.7 \pm 1.0 \text{ g}\%; P < 0.001)$, and the intensity of lipolysis in the fatty tissue also was increased $(6.0 \pm 0.3; P < 0.001)$ [2, 3]. Administration of Trichodesma incanum seeds under these conditions also led to a marked decrease in the lipid content in the liver $(18.6 \pm 0.6 \text{ g}\%; P < 0.001)$ and to an increase in its autolipolytic activity (to 3.9 ± 0.2 compared with 1.0 ± 0.08 in the control; P < 0.001). During administration of the Trichodesma incanum alkaloids the intensity of lipolysis in the fatty tissue decreased. A decrease in the lipid content in the hepatocytes also was found morphologically.

The results of the experiments in vitro showed that addition of the Trichodesma incanum alkaloids (trichodesmine, incanine, and the n-oxide form of incanine), both separately and as a mixture, to the incubation medium containing the fatty tissue of normal rats led to a marked increase in its lipolytic activity (up to 60%) in every case regardless of the quantity. Large doses of incanine and of its n-oxide form appreciably inhibited, while small doses increased the autolipolytic activity of the liver tissue. Trichodesmine and a mixture of alkaloids in comparatively large doses potentiated this activity of the organ. It is interesting to note that the serum of animals receiving Trichodesma incanum alkaloids for a period of 15 days, if added to the incubation medium inhibited lipolysis in the fatty tissue of normal animals (by 44%). By the 30th day of poisoning this effect disappeared, and by the 45th day, conversely, lipolysis in the fatty tissue was increased (by 31%). This serum was added to the incubation medium containing normal liver tissue, its autolipolytic activity was increased (up to 60%). These results suggest that during poisoning with Trichodesma incanum alkaloids, metabolically active substances with a marked action on the lipolytic activity of fatty and liver tissue appear in the serum of the animals.

Administration of <u>Trichodesma incanum</u> seeds whether in conjunction with a low-protein diet or during CCl₄ poisoning, when marked fatty degeneration of the liver develops, thus leads to a decrease in the lipid content of the liver which is due primarily to the direct action of the <u>Trichodesma incanum</u> alkaloids on the lipolytic activity of the fatty and liver tissues.

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