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Antifatty Liver Action of Papain and Ficin in Insulin-Treated, Depancreatized Dogs.* (19555)

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Previous work from this laboratory has shown that the fatty liver that develops in insulin-treated, depancreatized dogs can be prevented by the feeding of either methionine, choline. or hydrolysed casein(1,2). On the basis of these findings, it was proposed that the prevention of the fatty liver by raw pancreas, pancreatic juice and certain fractions derived from raw pancreas was the result of proteolytic enzymes furnished by the pancreatic substances(3). This view was later substantiated by the finding that crystalline trypsin, when added to the diet, also prevented the development of fatty livers(4).

The present report shows that prevention of fatty livers in depancreatized dogs can be achieved with plant preparations—papain and ficin—substances rich in proteolytic activity.

Experimental. The methods for assay of antifatty liver activity have been described elsewhere(5). Papain and ficin were fed twice daily to depancreatized dogs, for periods of 18-21 weeks, along with a diet consisting of 250 g of lean meat, 50 g of sucrose, 5 g of bone ash, and 1.5 g of salt mixture(4). Vitamin supplements(4) were fed once daily. Eight units of insulin were injected at each time of feeding. During the 3-4-week interval between pancreatectomy and the initiation of papain and ficin administration, the dogs were fed 25 g of raw pancreas with each meal in order to insure normal livers at the start of the assay period. At the end of the assay period, the dogs were anesthetized with nembutal. The entire liver was removed and thoroughly ground and mixed. Several samples were taken for the determination of total fatty acids(6).

Results. The fatty acid content of the livers of the control dogs fed no supplement ranged from 13.2 to 21.5% (Table I). The livers of the dogs fed papain were well within the normal range, *i.e.*, from 2.2 to 4.7%. Similar results were obtained with ficin-fed dogs; in these, the total fatty acid content of the liver varied from 1.6 to 2.5%. Throughout the course of the experiment the animals displayed a vigorous appetite. Ficin and papain did not prevent a loss in weight in these dogs.

Discussion. The capacity of papain to digest protein is well established(7), and its specificity, as determined on certain peptide linkages, is apparently similar to that of trypsin; indeed, papain is classified as a trypsinase (8). It is of interest to note that papain shows proteolytic activity over a wide range of temperature (10°-70°) and pH (3-12)(7). Although ficin has not been so extensively studied, it is nevertheless considered a papain-like enzyme(9).

Procedures for preventing the accumulation of fat in the liver of insulin-treated, depancreatized dogs can be classified into 1) those furnishing lipotropic substances in the free

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TABLE I. Effect of Papain and Ficin Feeding on Fatty Acid Content of Liver of 16 Insulin-Treated Depancreatized Dogs.

Pre-operative wt, kg	Final wt, kg	Supplement: Type	Supplement: Amt daily, g*	Supplement: Period fed, wk	Liver: Wt, g	Liver: Total fatty acids, % wet wt
9.5	7.2	None	—	20	670	21.5
6	5.5	"	—	24	580	13.3
7.9	6.5	"	—	19	310	37.3
9.2	8.2	"	—	12	720	17.2
13.1	9.2	Papain	.5	18	433	2.4
13.1	7.2	"	.5	18	443	4.5
12.8	9	"	1	21	433	3.1
12.8	11	"	1	21	382	2.5
10	9.4	"	1	21	432	3.1
9.7	6.3	"	1	21	356	3.5
13.8	10.7	"	4	21	630	4.7
6.4	6.6	"	4	20	463	2.2
14	8.7	"	4	20	495	2.8
8.3	6.6	Ficin	.5	21	400	1.6
9.1	7.8	"	.5	21	390	2.6
9.1	11.4	"	.5	18	420	2.5

* One-half of the amount recorded was fed with each meal.

form, and 2) those providing a means of liberating lipotropic substances from their bound form. There can be little doubt that the two plant enzymes, papain and ficin, act by replacing the loss of digestive capacity of the depancreatized dog. These results indicate that restoration of adequate digestive function, even with substances not specific to the animal organism, can prevent fat deposition in the liver.

Summary. It is shown that the development of fatty liver in insulin-maintained, depancreatized dogs can be prevented by the daily administration of the plant proteolytic enzymes, papain and ficin.

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Effect of β-propiolactone on Metabolism of *Pseudomonas aeruginosa* and Growth of Certain Fungi. (19556)

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β-propiolactone has been shown to be both bactericidal and virucidal and to have a relatively low toxicity(1-5). One of the organisms it is effective against, *Pseudomonas aeruginosa,* has been used in the following to study its possible mode of action. In aqueous solution the lactone hydrolyzes to β-hydroxpropionic acid, a fairly strong acid. This