Effect of Penicillin on Growth and Pancreatic Amylase Levels of Rats Fed Soybean Diets

Soya beans contain heat-labile factors that inhibit tryptic digestion and growth and induce pathological effects, such as pancreatic enlargement and goitre1. Addition of antibiotics to a ration containing unheated soybean flour (SBF) enhances the growth of rats and chickens, although they are not quite able to catch up the weights gained by animals given heated SBF1. The growth-promoting action of antibiotics may not owe their activity entirely to a change of the intestinal flora. This conclusion was drawn from observations on the effect of penicillin on the pancreas of rats fed unheated SBF². Administration of a meal of unheated SBF reduced the amylolytic and the tryptic activities of the pancreas. The addition of 100 mg of penicillin to the meal, or its simultaneous parenteral injection, partly prevented enzyme depletion of the pancreas. It was believed that this effect of penicillin was not exerted by its action on the intestinal flora because it was already discernible 1 h after administration of the meal, before the intestinal flora could have been affected. This was especially true when penicillin was given parenterally. In the present study some effects of penicillin administered per os or by s.c. injection, on growth and pancreatic amylase of rats fed SBF are reported.

Materials and methods. Animals, SBF's, diets³ and the procedure for measuring amylase activity have been described4. The diet of some rats was supplemented with 200 mg of penicillin-G-sodium per kg. Animals that were to be injected s.c. with a long-acting penicillin preparation were treated with N: N'-dibenzyl-ethylenediamine dipenicillin G. 2 portions, each of 50 mg, were injected at the beginning of the experiment and after 2 weeks.

Results. The results obtained after 3 weeks are summarized in the Table. It can be seen that penicillin, administered either per os or s.c., significantly improved the weight gain in rats fed unheated SBF, whereas no such effect was observed when the diet contained heated SBF. As expected, pancreases of rats fed unheated SBF contained less amylase than those of rats fed heated SBF⁵⁻⁹. Administration of penicillin per os but not s.c. prevented depletion of pancreatic amylase, regardless of whether the diet contained heated or unheated SBF.

Comment. The effect of orally- or parenterally-administered penicillin on weight gain may be explained on the basis of fractionation studies on the heat-labile factors in SBF. The growth-inhibiting fraction appears to be devoid

Weight gain and pancreatic amylase of non-fasted rats subsisting for 3 weeks on soybean flour diets and treated with penicillin

Soybean	Penicillin	Weight gain (g)	Pancreatic amylase,	
			units per g pancreas	per 100 g body wt.
Heated	harrid.	96 ± 4	3366 ± 459	1709 ± 111
Heated	per os	107 ± 4	5051 ± 570	2778 ± 304
Heated	s.c.	85 ± 7	3158 ± 427	1583 ± 220
Unheated	_	44 ± 4	486 ± 77	341 ± 64
Unheated	per os	74 ± 3	765 ± 115	549 ± 75
Unheated	s.c.	72 ± 4	451 ± 61	339 ± 48

Figures indicate means ± S.E.M. of 9-18 rats.

of anti-trypsin activity and to reside in a water-soluble residue 10. A part of this activity was recently found to be associated with a compound of low molecular weight 11. It may be suggested that this substance can be absorbed by the intestinal wall and subsequently inactivated by circulating penicillin. The growth-promoting activities of both orally- and parenterally-administered penicillin are thus similar.

On the other hand, orally-given penicillin appears to affect the pancreas, regardless of the nature of the SBF given. Its action on the pancreas seems to be mediated by eliciting either humoral or nervous responses that inhibit pancreatic amylase depletion. The effect previously reported² of injected penicillin is not necessarily contradictory to the results presented here. It was obtained with a different technique by which a single massive dose (100 mg) of penicillin was administered in a short-term experiment. Small, but still active, amounts of this preparation may have been excreted with the bile, reached the duodenum and there exerted their slight but significant effect on the pancreas.

It appears that the growth-promoting effect of penicillin on rats fed unheated SBF is not necessarily due to its action on the pancreas. Pancreatic function is mainly affected by trypsin inhibitors 12, 13, whereas growth, by other heat-labile substances 11 , 14 .

Zusammenfassung. Die wachstumshemmende Wirkung von rohem Sojabohnenmehl wurde durch peroral oder subkutan verabreichtes Penizillin teilweise aufgehoben. Verfütterung von rohem Sojabohnenmehl verringerte den Amylase-Gehalt des Pankreas. Peroral verabreichtes Penizillin erhöhte den Amylase-Gehalt des Pankreas, unabhängig von der Art des Sojabohnenmehls des Futters.

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- ¹ O. Mickelsen and M. G. Yang, Federn. Proc. 25, 104 (1966).
- ² A. Goldberg and K. Guggenheim, Arch. Biochem. Biophys. 108, 250 (1964).
- ³ A. M. Konijn and K. Guggenheim, Proc. Soc. exp. Biol. Med. 126, 65 (1967).
- ⁴ A. M. Konijn, K. Guggenheim and Y. Birk, J. Nutr. 97, 265 (1969)
- ⁵ M. H. Pubols, H. C. Saxena and J. McGinnis, Proc. Soc. exp. Biol. Med. 117, 713 (1964).

 ⁶ A. J. Salman, G. Dal Borgo, M. H. Pubols and J. McGinnis,
- Proc. Soc. exp. Biol. Med. 126, 694 (1967).
- ⁷ S. Ma'ayani and R. G. Kulka, J. Nutr. 96, 363 (1968).
- ⁸ S. Lepkovsky, F. Furuta, T. Koike, N. Hasegava, M. K. DIMICK, K. KRAUSE and F. J. BARNES, Br. J. Nutr. 19, 41 (1965).
- ⁹ A. M. Konijn, Y. Birk and K. Guggenheim, J. Nutr., in press.
- 10 H. C. Saxena, L. S. Jensen and J. McGinnis, Proc. Soc. exp. Biol. Med. 112, 101 (1963).
- 11 D. J. Schingoethe, S. D. Aust and J. W. Thomas, Fedn. Proc. 28, 812 (1969).
- 12 A. M. Konijn, Y. Birk and K. Guggenheim, Am. J. Physiol., in
- ¹³ A. Gertler, Y. Birk and A. Bondi, J. Nutr. 91, 358 (1967).
- ¹⁴ Soybean flours were kindly supplied by Etz-Hazaith Ltd., Oil and Soap Factory, Petah-Tiqva (Israel).