

## Collagen in Experimental Lathyrism<sup>1</sup>

Since lathyrism has been known mainly from the morphological aspect, we wish to report here the effect of sweet pea diet on the synthesis of collagen in growing rats. MIELKE, LALICH, and ANGEVINE<sup>2</sup> found recently, that the administration of the toxic agent ( $\beta$ -amino-propionitrile) decreased the synthesis of hydroxyproline in croton oil pouches. The findings reported below agree well with their results.

The experimental diet<sup>3</sup> contained 56% sweet peas and the control diet ordinary peas respectively. The rats (Wistar stock, both males and females) were fed with diet *ad libitum* in individual cages. The weanling animals weighed in the beginning 40 g (mean) and after 2 months in the control group 135 g (mean) and in the lathyrus group 100 g (mean).

Wounds of about 1 cm length were cut (in local anaesthesia) in the backs of the animals and closed with continuous silk suture. No infections occurred. After five days the animals were killed. Strips (1 cm broad), containing the scar transversely in the middle, were cut from the skins and the tensile strength up to the rupture was measured with a simple system of hanging weights. In the control group (5 rats), the tensile strength of the scars was on the average 140 g (range 106–181 g) and in lathyrus-group (4 rats) 57 g (33–87 g). The thickness of the corium was 0.25 mm (mean) in the control group and in the lathyrus group 0.15 mm (mean).

To check the stability of the collagen, the thermal shrinking point was determined from 4 samples of tail tendon in each group. It was identical and normal in both groups (61°–62°C).

The skin samples were cleaned mechanically from hair and fat, ground and finally extracted with ether and acetone. The amount of hydroxyproline was estimated (after conversion of the collagen to gelatine) according to NEUMANN and LOGAN<sup>4</sup> and tyrosine according to

HEIDELBERGER and MACPHERSON<sup>5</sup>. The respective bone samples were similarly obtained from the thigh-bones. Bone salts were not removed.

The 'tyrosine'-content differed in bone gelatine between the lathyrus and control groups (means 0.28% and 0.17%,  $P < 0.01$ ). This was not found in skin samples.

The non-collagenous residues contained very little hydroxyproline. There was no differences in the amount of 'tyrosine' in the skin samples, but again in the bone it was higher in the lathyrus than in the control group (means 0.35% and 0.25% respectively,  $P < 0.10$ ). Against this background the decrease in the hydroxyproline in the bones is still more significant.

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### Zusammenfassung

Mit Wickendiät synthetisieren wachsende Ratten weniger Hydroxyprolin als Kontrollen, und die Zugfestigkeit des Narbengewebes ist vermindert. Der Wärmeschrumpfungspunkt des Collagens ist unverändert. In der Haut bleibt die Menge des Gelatin«tyrosins» gleich, während sie im Knochen anscheinend vermehrt ist.

<sup>5</sup> M. HEIDELBERGER and C. F. M. MACPHERSON, *Science* 97, 405 (1943).

## Ein neuer vorteilhafter Substitutionstypus der Lokalanästhetika

Auf Grund von Erwägungen über die Bedeutung physikalisch-chemischer Eigenschaften für den Wirkungsmechanismus von Arzneimitteln wird bei der rationalen Synthese von Lokalanästhetika oft die Alkoxy-Substitution angewandt. Es soll durch Vergrößerung der Lipoidlöslichkeit die Wirksamkeit erhöht werden. Die geeignetste Länge der Alkoxykette liegt gewöhnlich bei C<sub>2</sub> bis C<sub>4</sub>, höhere Derivate sind meist zu stark hydrophob (geringe Wasserlöslichkeit, Hydrolyse der Salze in Wasserlösung).

In Fortsetzung unserer Studien über lokalanästhetisch wirksame basische Ester der alkoxy-substituierten Arylcarbaminsäuren<sup>1</sup> haben wir im Bestreben, lipophile Derivate herzustellen, ohne ihre unvorteilhaften Eigenschaften, eine Reihe von Diäthylaminoäthylestern isomerer Phenoxy-, Benzyloxy- und Phenyläthoxycarb-

<sup>1</sup> A. SEKERA, A. BOROVANSKÝ, I. JAKUBEC, K. PALÁT und Č. VRBA, *Českoslov. farm.* 5, 388 (1956). – K. PALÁT, A. SEKERA und Č. VRBA, *Chem. listy* 51, 563 (1957); *Exper.* 12, 273 (1956).

<sup>1</sup> This work forms a part of a program which has been aided by Reumaliitto (Society for Campaign against Rheumatic Diseases in Finland) and, technically, by the pharmaceutical manufacturers, Lääke Oy. Their help is gratefully acknowledged.

<sup>2</sup> J. E. MIELKE, J. J. LALICH, and D. M. ANGEVINE, *Proc. Soc. exp. Biol. Med. N. Y.* 94, 673 (1957).

<sup>3</sup> Sweet pea meal (*Lathyrus odoratus* Spencer) . . . . . 56.0%  
Casein . . . . . 5.8%  
Wet yeast (containing 27% dry matter) . . . . . 5.8%  
Sodium chloride . . . . . 2.3%  
Calcium carbonate . . . . . 2.3%  
Sucrose . . . . . 27.7%  
Each rat received daily 1 ml of following solution: 100 ml of olive oil, 1000 I.U. vitamin A, 30 I.A. vitamin D, 50 mg tocopherol and 6 mg vitamin K.

<sup>4</sup> R. E. NEUMANN and M. A. LOGAN, *J. biol. Chem.* 186, 549 (1950); 184, 299 (1950).

	Hydroxyproline in % of defatted tissue	
	Skin	Bone
	Mean (range)	Mean (range)
Lathyrus group (5 rats) . . . . .	7.80 (7.35–8.55)	1.84 (1.50–2.40)
Control group (4 rats) . . . . .	8.51 (8.05–9.05)	2.31 (1.89–2.43)
<i>P</i> of change occurrence of the difference	< 0.10	< 0.05