

### Zusammenfassung

Das synthetische Bradykinin H-L-Arg-L-Pro-L-Pro-Gly-L-Phe-L-Ser-L-Pro-L-Phe-L-Arg-OH hat (innerhalb der durch Unterschiede in der Methodik bedingten Fehlerbreite) die gleiche biologische Wirksamkeit wie natürliches, durch Einwirkung von Trypsin oder *Bothrops jararaca*-Gift aus Rinderplasma gewonnenes Bradykinin.

### The Effect of Uncoupling Agents on Metabolism of Insect Muscle

It was stated by SACKTOR and CHANCE<sup>1</sup> that uncoupling agents are without effect on oxygen consumption of isolated mitochondria of insect muscle. We found, however, that  $10^{-3}$  M 2,4-dinitrophenol has a pronounced effect on metabolism of the intact muscle of the American cockroach<sup>2</sup>. In denervated fibres, the effect was much smaller, which could not be accounted for by any changes in the activities of enzymes of different types. We will now present further data about the action of 2,4-dinitrophenol and another uncoupling agent dicumarol on muscles of *Periplaneta americana* L. and *Locusta migratoria* L.

The experiments were carried out on the intact muscle preparations described by GILMOUR<sup>3</sup> and KUBIŠTA<sup>4</sup>. The oxygen consumption was measured in Warburg respirometer and glycogen determined by anthron method. Both agents were prepared in physiological solution. The preparations were perfused with some drops of these solutions which were injected into the distal parts by means of a syringe. The oxygen consumption was measured for half an hour immediately on injection. In the case with high concentrations of 2,4-dinitrophenol, the oxygen consumption was highest at the beginning of the experiment and began to decrease after 10 min.

In anaerobic experiments, the uncoupling agents were injected 5 min after the beginning of the anaerobiosis; in this period, all oxygen is supposed to be removed.

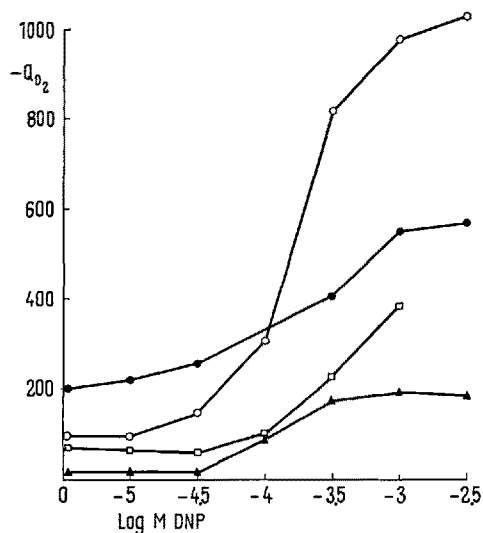
As may be seen from the Figure 2,4-dinitrophenol has a pronounced effect on the oxygen consumption of intact insect muscle preparations. The oxygen consumption is enhanced in both types of muscle fibres, i. e. in red muscles of the cockroach and also in white muscles of the locust which appear to have smaller resting values than cockroach muscles. The concentrations indicated in the Figure concern the injected solutions; the effective concentration within the muscle fibres was approximately calculated from the amount of 2,4-dinitrophenol determined analytically in the preparation and was found to be 50–60% of the concentration of the injected solution, provided that the dinitrophenol is equally distributed in the tissue.

24 days after nerve section, however, the effect of 2,4-dinitrophenol in the cockroach muscles is decreased. The differences of resting values between normal and denervated muscles are probably caused by the spontaneous activity observed in these muscles by BERÁNEK and NOVOTNÝ<sup>5</sup>.

Dicumarol, another uncoupling agent, also caused an increase in oxygen consumption, but its effect was smaller (Fig.) and no differences were observed between normal and denervated muscles as in the case of 2,4-dinitrophenol.

This effect of the uncoupling agents does not seem to be due solely to their action in the mechanism of oxidative phosphorylation, since both agents brought about an enhancement of metabolism in anaerobic condition (Table). The glycogen breakdown was increased particularly with 2,4-dinitrophenol. This corresponds to the findings of RONZONI and EHRENFEST<sup>6</sup> in frog muscle.

It appears, therefore, that the conditions for the action of uncoupling agents are more favorable in intact muscle fibres than in isolated mitochondria. Chronic denervation causes some unknown change in biochemical equipment of muscle which results in decreased sensitiveness to 2,4-dinitrophenol.



The effect of uncoupling agents on oxygen consumption. 2,4-Dinitrophenol: ○ = normal cockroach muscles; ● = denervated cockroach muscles; ▲ = locust muscles; dicumarol: ◻ = cockroach muscles. Oxygen consumption expressed in 100 mm<sup>3</sup>/g/h

The effect of uncoupling agents on anaerobic breakdown of glycogen in muscles of the cockroach. Temperature 22°C. Duration of anaerobiosis 20 min. Glycogen expressed in mg%

Uncoupling agent	Decrease of glycogen
None	172 ± 55
$10^{-4}$ M 2,4-Dinitrophenol	276 ± 45
$10^{-3}$ M 2,4-Dinitrophenol	346 ± 85
$10^{-3}$ M Dicumarol	246 ± 39

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Der Einfluss von 2,4-Dinitrophenol und Dicumarol auf intakte Präparate von Insektenmuskeln wurde geprüft. Beide Stoffe, besonders aber 2,4-Dinitrophenol, riefen eine erhebliche Steigerung des aeroben und anaeroben Stoffwechsels hervor. Dauernde Denervation der Muskeln führt zu erniedrigter Empfindlichkeit gegen 2,4-Dinitrophenol.

<sup>1</sup> B. CHANCE and B. SACKTOR, Arch. Biochem. Biophys. 76, 509 (1958).

<sup>2</sup> I. NOVOTNÝ, Physiol. bohemoslov. 8, 22 (1959).

<sup>3</sup> D. GILMOUR, Biol. Bull. 80, 45 (1941).

<sup>4</sup> V. KUBIŠTA, Acta Soc. zool. bohemoslov. 20, 188 (1956).

<sup>5</sup> R. BERÁNEK and I. NOVOTNÝ, Physiol. bohemoslov. 8, 87 (1959).

<sup>6</sup> E. RONZONI and E. EHRENFEST, J. biol. Chem. 115, 749 (1936).