

40 Action of Leptodactylin on the Isolated Vagus-Auricle Preparation of the Guinea Pig.

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Leptodactylin (*m*-hydroxyphenethyl) trimethyl ammonium, is a naturally occurring quaternary ammonium base recently isolated from *Leptodactylus* by Erspamer. Since he has shown it to possess marked nicotinic actions and neuromuscular blocking properties, its effects were studied on the isolated vagus-auricle preparation of the guinea pig and in the rat phrenic-diaphragm preparation. The findings were as follows: (1) Leptodactylin at concentrations of 1–10 $\mu\text{g/ml}$ induces a marked negative inotropic effect on the contractions of the isolated guinea-pig auricle, suspended in Tyrode solution at 28°C. (2) This response is abolished by atropine (0.1 $\mu\text{g/ml}$). After atropinization, larger doses of leptodactylin (10–25 $\mu\text{g/ml}$) induced a 50 to 75 per cent increase in amplitude and a 10 per cent increase in the rate of contraction of the auricular muscle. This response was blocked by large doses of hexamethonium (100–200 $\mu\text{g/ml}$). (3) The threshold to vagal stimulation of the auricle was not appreciably changed by the presence of leptodactylin in the bath (1–50 $\mu\text{g/ml}$). (4) Total neuromuscular blockade was observed on the isolated phrenic-diaphragm preparation of the rat only after very large doses of leptodactylin (50–500 $\mu\text{g/ml}$). It therefore appears, under these circumstances, that the nicotinic effects of leptodactylin are more readily elicited than its neuromuscular blocking actions.

41a Über die Foerderung der Energiegewinnung am erschöpften Herzmuskel durch ein Pyrimidinderivat. W. KUNZ and M. SIESS (Germany).

Strophanthin führt am überlasteten Herzvorhof des Meerschweinchens nach positiv inotroper Wirkung zu diastolischem Erschöpfungsstillstand, der mit einem Schwund der energiereichen Phosphate um etwa 30 Prozent verbunden ist. Dabei findet eine Na^+ -Aufnahme und eine K^+ -Abgabe in der Muskelfaser statt. Eine erneute Ansprechbarkeit auf positiv inotrop wirkende Stoffe wie Adrenalin oder Strophanthin findet sich erst nach einer Erholungszeit von etwa einer Stunde, in der das $\sim\text{PO}_4$ wieder aufgebaut und die Na^+ - K^+ -Verhältnisse wieder normalisiert werden. Diese Erholungszeit wird durch 2:6-Bis (diäthanolamino)-4:8-dipiperidino-pyrimido-5:4-d-pyrimidin (Persantin, Thomae) (P.) um etwa 75 Prozent verkürzt unter Beschleunigung der Resynthese der $\sim\text{PO}_4$. P. verlängert die positiv inotrope Wirkung von Strophanthin am überlasteten Vorhof.

Auch der durch Anaerobiose hervorgerufene Energiemangelstillstand wird durch P. unter Restitution des $\sim\text{PO}_4$ aufgehoben. Adrenalin und Strophanthin wirken im Gegensatz zu reiner

Anoxie bei P.-Anwesenheit sogar noch positiv inotrop.

Die biochemische Untersuchung ergab, dass eine Anreicherung von DPNH, welche durch Anaerobiose und gleichzeitige Ausschaltung der wasserstoffverbrauchenden Brenztraubensäurehydrierung mittels NaF erzeugt wurde, durch P beseitigt wird. Die Analyse mit ^{14}C markierter Glucose (C_1 oder C_6) ergibt eine Beschleunigung der C_6 -Dekarboxylierung bei unveränderter Geschwindigkeit des Glukose-6-Phosphatshunts. In Verbindung mit Metabolitanalysen und Untersuchungen der Atmung und Glykolyse ergibt sich der Schluss, dass die Übertragung des aus dem Tricarbonsäurecyclus stammenden Wasserstoffs durch P als Wasserstoffakzeptor unter Energiegewinnung katalysiert wird.

41b Energy Gains by the Exhausted Heart Muscle with the Aid of a Pyrimidine Derivative.

W. KUNZ and M. SIESS (Germany)

Strophanthin causes diastolic exhaustion-arrest of the overloaded guinea-pig atrium following a positive inotropic effect; this is due to the loss of approx. 30 per cent of the energy-rich phosphates. There is an uptake of Na^+ and a loss of K^+ by the muscle fibres. Renewed reactivity to positively inotropic substances such as adrenalin or Strophanthin only occurs after a recovery period of approximately 1 hour during which the $\sim\text{PO}_4$ is again built up and the Na^+ and K^+ relationship has returned to normal. This recovery period is shortened by about 75 per cent by 2:6-bis (diethanol amino)-4:8-dipiperidino-pyrimido-5:4-d-pyrimidin (Persantin, Thomae) (P) with acceleration of $\sim\text{PO}_4$ resynthesis. P prolongs the positively inotropic effect of Strophanthin on the overloaded atrium.

Arrest, due to lack of energy caused by anaerobiosis is also abolished by P, through the restitution of $\sim\text{PO}_4$. Adrenalin and Strophanthin, in contrast with pure anoxia, have an even positive inotropic effect in the presence of P. The biochemical investigation showed that the accumulation of DPNH, which was caused by anaerobiosis and the simultaneous inhibition of the hydrogen-accepting pyruvic acid by means of NaF, was eliminated by P. Analysis by means of ^{14}C , labelled glucose (C_1 or C_6) results in acceleration of C_6 -decarboxylation without change in the rate of the glucose-6-phosphate transfer. The conclusion reached, after combined analysis of metabolites and investigation of respiration and glycolysis, was that the transfer of hydrogen derived from the tricarboxylic acid cycle is catalysed by means of P which acts as a hydrogen-acceptor with a gain of energy.

42 Mechanism of Action of Histamine on the Heart. M. F. MURNAGHAN (Canada).

Isolated guinea-pig auricles were accelerated with a continuous infusion of histamine and the amount of veratramine require to cause a 50 per cent inhibition of acceleration, i.e. I_{50} dose, deter-