

der Esterfraktion von Cholesterin sowie der Konzentration von Lysolecithin bei leichter Erhöhung der Lecithinfraktion deuten auf eine Hemmung des plasmatischen Acyltransfers auch bei der leichten Galaktosaminhepatose hin. Hierfür spricht weiter, dass Lysolecithin auf dem Höhepunkt der Leberschädigung statistisch signifikant gegenüber dem Basiskollektiv erniedrigt ist und zu diesem Zeitpunkt positiv mit dem veresterten Cholesterin korreliert.

Eine weitergehende Analyse der Ergebnisse zeigt jedoch, dass neben dem verminderten Acyltransfer auch andere gestörte Regulationsmechanismen für den Abfall des veresterten Cholesterins verantwortlich sein müssen. Wie die Figur zeigt, nimmt zwar das Molverhältnis zwischen Lysolecithin und Gesamtacylphosphatidylcholin ab, das molare Konzentrationsverhältnis zwischen Esterfraktion und Gesamtcholesterin dagegen zu. Hierbei sind auf dem Höhepunkt der Intoxikation die Unterschiede der beiden molaren Quotienten am grössten.

Die vorliegenden Ergebnisse, relative Erniedrigung von Lysolecithin bei relativer Erhöhung von Cholesterinestern im Ratten Serum, stehen nur dann nicht im Widerspruch zu einer gleichzeitigen Hemmung des plasmatischen Acyltransfers, wenn man berücksichtigt, dass die Cholesterinester des Plasmas nicht ausschliesslich im Blutplasma synthetisiert werden, sondern auch anderen extraplasmatischen Quellen entstammen. Nach neueren Untersuchungen von SWELL und LAW⁹ wird Cholesterin auch in der Rattenleber durch ein ähnliches Enzymsystem zu den im

Blutplasma vorkommenden Fraktionen verestert. Aus den im Perfusionsversuch gewonnenen Ergebnissen geht hervor, dass die in der Leber synthetisierten Cholesterinester ins Perfusat abgegeben werden. Die Bedeutung des hepatischen Syntheseweges der Plasmacholesterinester ist zur Zeit noch unbekannt.

Summary. After single i.p. application of 300 mg/kg D-galactosamine-hydrochloride in male conventional Wistar-II-rats, the concentration of serum cholesterol esters and serum lysolecithin decreases in statistical significance, serum lecithin increases slightly. Because the relation of esterified serum cholesterol to total serum cholesterol increases, it may be that the significant decrease of the cholesterol ester fraction, induced by the slight galactosamine-liver injury, is not only effected by transacylation-inhibition in plasma.

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⁹ L. SWELL und W. D. LAW, *Biochim. biophys. Acta* 237, 302 (1971).

¹⁰ Unter experimenteller Mitarbeit von cand. med. B. RIESE

Influence of Temperature on the Sensitivity of Adrenergic β -Receptors

Experiments on isolated rabbit ileum and guinea-pig tracheal chain, using the catecholamine isoprenaline as well as the resorcin derivative Th 1165a, showed on the ileum a shift of their dose-response curves to the right by increasing the temperature, indicating a diminution of their affinity¹. On the trachea, on the contrary, the affinity of isoprenaline was decreased to a considerably smaller degree, whereas that of Th 1165a (hydroxyphenyl- orciprenaline) was not changed at all¹.

In experiments on isolated electrically driven left atria of the guinea-pig, the elevation of the temperature resulted in a decrease of the affinities of isoprenaline as well as of Th 1165a and furthermore also of the resorcin derivative orciprenaline².

Since on the atrium the affinity of all three sympathomimetic drugs was diminished by increasing the temperature in a similar manner, while on the tracheal chain that of the resorcin derivative Th 1165a showed no alteration, we were interested to find out whether the resorcin configuration is responsible for this change in sensitivity or the prolongation of the side chain. Therefore, we investigated the resorcin analogue of isoprenaline, namely orciprenaline.

Methods and material. The experiments were performed on the isolated ileum of rabbit and the tracheal chain preparation of guinea-pig as described in a recent paper at 25°, 33°, 37° and 42°C¹. The preparations were kept in Krebs-Henseleit solution containing phentolamine 2×10^{-7} g/ml in order to block the α -receptors³. On ileum the dose-response curves of orciprenaline were carried out by adding single doses. On the tracheal chain they were made in a cumulative manner¹. The tracheal chain was contracted beforehand by adding carbachol 10^{-7} g/ml to the bath. The concentrations of given effects⁴ and pD_2 -values⁵ (mean $\pm$ S.E.) are calculated. Significant differences are calculated by means of Student's *t*-test.

¹ J. WAGNER, D. REINHARDT and H. J. SCHÜMMANN, *Archs. int. Pharmacodyn.* 197, 290 (1972).

² D. REINHARDT, J. WAGNER and H. J. SCHÜMMANN, *Naunyn-Schmiedeberg's Archs. Pharmac.* 275, 95 (1972).

³ R. F. FURCHGOTT, *Ann. N.Y. Acad. Sci.* 139, 553 (1967).

⁴ E. J. ARIENS, *Molecular Pharmacology I* (Academic Press, New York 1964).

⁵ J. M. VAN ROSSUM, *Archs. int. Pharmacodyn.* 143, 299 (1963).

Temperature dependency of pD_2 -values for orciprenaline on ileum and tracheal chain

	Temperature (°C)			
	25°	33°	37°	42°
Ileum	5.71 $\pm$ 0.12 (6)	5.00 $\pm$ 0.14 (4) ^a	4.80 $\pm$ 0.11 (4)	—
Tracheal chain	6.48 $\pm$ 0.09 (4)	6.40 $\pm$ 0.13 (6)	—	6.49 $\pm$ 0.06 (8)

^a $P < 0.01$ significant difference in comparison with the lower temperature.

Result. On ileum the elevation of the temperature from 25° to 33°C resulted in a pronounced shift of the dose-response curve of orciprenaline to the right, whereas a further increase of the temperature to 37°C did not cause a further shift (Figure). This diminution of the affinity of orciprenaline is indicated by the pD_2 -values (Table). The pD_2 -value 5.0 at 33°C is significantly lower than that of 5.71 at 25°C. The relatively small difference of temperature from 33°C to 37°C did not alter the affinity. At 42°C the loss of affinity was so high that it was impossible to get the required amounts of orciprenaline dissolved. — The elevation of temperature from 25° to 37°C decreased the affinity of the resorcin Th 1165a from 6.46 ± 0.06 ($n = 6$) to 5.87 ± 0.06 ($n = 8$).

On the tracheal chain the temperature was without any influence on the dose-response curve of orciprenaline as well as on its pD_2 -values (Figure and Table). Likewise the affinity of Th 1165a was not changed, as is indicated by the pD_2 -value of 8.13 ± 0.09 ($n = 7$) at 25°C and 8.05 ± 0.07 ($n = 5$) at 42°C.

Discussion. The present results show that on ileum the effect of orciprenaline is also dependent on the tempera-

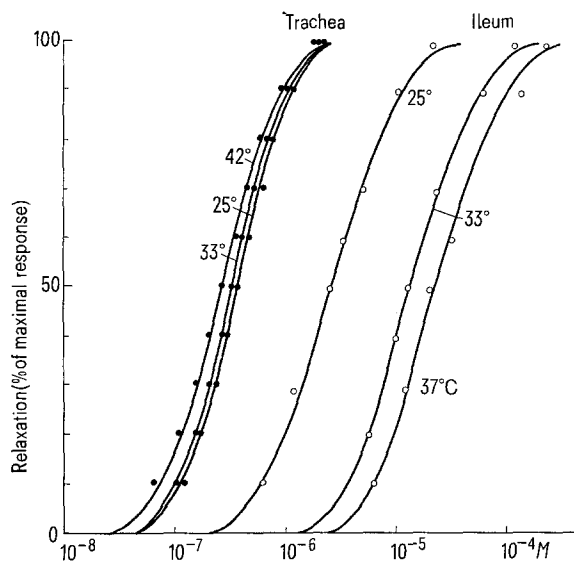
ture, as are the effects of isoprenaline and of Th 1165a. On the tracheal chain, on the contrary, the affinity of orciprenaline is not influenced by increasing the temperature. The resorcin derivatives Th 1165a and orciprenaline show the same effects on both organs, ileum and tracheal chain, under the influence of temperature alteration. This observation implies that the resorcin configuration determines the behaviour of both agents and that the prolongation of the side chain in the case of Th 1165a is exclusively responsible for the 20 to 40 times higher affinity obtained for Th 1165a compared with orciprenaline on ileum and trachea.

The different responsiveness of the trachea on the one hand and ileum on the other to the adrenergic drugs under the conditions of temperature changes might be explained by results from our laboratory using the metabolic inhibitor iodoacetic acid (IAA). IAA was able to re-shift the dose-response curves of all three amines mentioned to the left on ileum but not on trachea, indicating a relatively low metabolic activity of the trachea and a higher one of the ileum⁶. Temperature increase would, therefore, be expected to stimulate the metabolism to a much higher degree in the ileum than in the trachea. Consequently, the observed loss of affinity for amines in the ileum might be due to changes of the intracellular pH. If our assumption is correct lowering of the extracellular pH in the trachea should lead to lowering of the intracellular pH and concomitantly to a diminished affinity of the amines. Such a diminished affinity could indeed be obtained after lowering of the extracellular pH⁶, thus indicating the importance of the metabolic activity of the organs for the sensitivity of the β -receptors.

Zusammenfassung. Versuche am Ileum des Kaninchens und der Trachea des Meerschweinchens mit dem Resorcin-derivat Orciprenalin⁷ bei 25 bis 42°C führten zu folgenden Ergebnissen: Temperaturerhöhung verminderte am Ileum die Affinität des Orciprenalins, an der Trachea dagegen war sie ohne Einfluss⁸.

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Influence of temperature changes on the dose-response curves of orciprenaline on trachea and ileum. On tracheal chain (●—●) the increase of temperature from 25° up to 42°C did not alter the dose-response curve of orciprenaline. Note the strong shift to the right in the case of ileum (○—○) by increasing temperature. (Numbers of experiments are identical with those given in the Table).

⁶ H. J. SCHÜMANN, J. WAGNER and D. REINHARDT, Naunyn-Schmiedeberg's Arch. Pharmac. 275, 105 (1972).

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Long Term Retention of Colloidal Thorium Dioxide in the Liver and Spleen of *Xenopus laevis* Daudin

Colloidal thorium dioxide (ThO_2) can be used as a contrast medium in radiography and has been especially effective in demonstrating lymphatic movements and drainage in amphibians¹. Colloidal thorium dioxide is also useful as a tracer substance in ultrastructural studies owing to its easily identifiable electron-dense appearance²⁻⁴. It is well established in anurans¹ and in mammals including man that injected colloidal ThO_2 is rapidly removed from the circulating fluids and taken up by the reticulo-endothelial system (RES), in particular by phagocytic cells of the liver and spleen^{2,5}. With radioactive

tracers such as ThO_2 that have a slow biological half-life, prolonged deposition in cells of the RES can result eventually in a carcinogenic response⁶. An experiment was therefore performed to determine the long term retention capacities of liver and spleen in young *Xenopus* frogs receiving a single injection of colloidal ThO_2 in view of the fact that these animals possess a relatively simple RES even in comparison with other common anuran genera⁷.

Material and methods. 50 small *Xenopus laevis* frogs, 30–40 mm snout/vent length, weighing on average 2.65 g,