bergapten always per 1 million cells. (After approximately 1 month a few mice died, having developed only solid tumors.)

On the contrary, mice treated with cell suspensions irradiated in the presence of slightly larger amounts of furocoumarins did not develop tumors and appeared to be in normal health.

We have ascertained that the cell suspensions contained the same number of cells prior to and following irradiation in the presence of furocoumarins. Irradiated cells, Wright stained and microscopically observed, had a morphological aspect identical to that of normal tumor cells.

In this in vitro anti-tumor effect, as well as in skin-photosensitization, psoralen is more active than xanthotoxin, while xanthotoxin is more active than bergapten.

We recall here that BELLIN, MOHOS and OSTER[11] obtained inactivation of a wide variety of tumor cells by irradiating them in the presence of several dyes used as sensitizers.

This photodynamic effect may be interpreted as caused by a photooxydative reaction. In our case, on the contrary, we know that oxygen is not involved, and we must attribute the disappearance of the tumor-producing capacity now observed to the same mechanism that we have suggested for the explanation of the other photosensitizing effects of furocoumarins[10]; that is, to the photochemical linkage of the furocoumarins to DNA[12].

Riassunto. Il liquido ascitico del tumore di Ehrlich, irradiato a 3655 Å in presenza di furocumarine «fotosensibilizzatrici cutanee» e cioè di psoralene o xantotoxina o bergaptene, perde la capacità di trasmettere il tumore nel topo.

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[11] J. S. BELLIN, S. C. MOHOS and G. OSTER, Cancer Res. *21*, 1365 (1961).

[12] This work was aided by Consiglio Nazionale delle Ricerche, Roma.

Potentiation of Sympathetic Effects by a New Diphenylpropylamine Derivative[1]

The classical pharmacological tool for inducing supersensitivity in catecholamines is the administration of cocaine, which is a local anaesthetic and has marked central nervous system excitatory action, too. In this laboratory a new compound has recently been found in the course of a detailed research programme on diphenylalkyl derivatives which potentiates the effects of adrenalin and noradrenalin like cocaine but is devoid of other pharmacological actions of the latter. This compound is 1,1-*bis*-(4-amino-phenyl)-propyl-(3)-amine, to be referred to further as TK174.

TK174 increases the effects of exogenous catecholamines as well as that of the transmitter substance liberated by sympathetic nerve stimulation. The former was demonstrated in spinal cat and guinea-pig isolated vas deferens preparations. Pressor responses to i.v. administered catecholamines recorded by means of a mercury manometer on a smoked drum are tabulated in Table I. Some of the spinal cat preparations used (not included in Table I) had been subjected to bilateral adrenalectomy prior to blood pressure recordings. The enhancing influence of 2.5 mg/kg of TK174 on the pressor action of catecholamines was present, unaltered in these circumstances, too. Thus, the adrenal glands play no important role in this effect. The view of a peripheral action of TK174 is further confirmed by the results obtained on the isolated vas deferens, where TK174 potentiated the effect of noradrenalin (Table II) just as in vivo. Its activity is superior to that of cocaine.

[1] A detailed report will be published in the journal 'Drug Research' ('Arzneimittelforschung').

Table I. The influence of TK 174 on pressor responses to various drugs

Preparation used	Dose of TK174 mg/kg	Pressor substance	Dose/kg	No. of experiments	Pressor responses[a] recorded Before i.v. injection of TK174	After
Spinal cat	2.5	Adrenalin	0.25 µg	5	24.1 ± 4.5	56.8 ± 7.4
			0.5 µg	5	39.4 ± 7.0	86.4 ± 8.6
	2.5	Noradrenalin	0.25 µg	5	43.0 ± 7.4	85.2 ± 12.3
			0.5 µg	5	62.4 ± 11.5	105.8 ± 10.4
	2.5	Vasopressin	0.4 IU	8	46.1 ± 6.1	–
				9	–	56.8 ± .6.9
Narcotised rat	0.5	Tyramine	0.1 mg	5	23.2 ± 3.5	6.0 ± 1.7
			0.2 mg	6	31.3 ± 4.7	17.8 ± 4.0

[a] in mm Hg; mean values ± S.E.

The effect of TK174 on sympathetic nerve stimulation was tested on the guinea-pig isolated hypogastric nerve-vas deferens preparation[2]. Contractions were markedly increased by $5.0 \cdot 10^{-6}$ g/ml concentrations of both TK174 and cocaine, while those induced by direct muscular stimulation of the organ remained uninfluenced. Thus the effect of TK174 seems to be elicited specifically on the sympathetic nerve endings. This view is further supported by the fact that pressor responses of spinal cat preparations to vasopressin, which contracts vascular smooth muscle independently from sympathetic receptors[3], also failed to be increased significantly by 2.5 mg/kg of TK174 (Table I).

There are, however, exceptions to the potentiation of noradrenalin effects by TK174, inasmuch as direct cardiac actions such as the positive chronotropic action of noradrenalin failed to be enhanced by $5.0 \cdot 10^{-6}$ g/ml of TK174, a concentration highly effective in other tests mentioned.

The actions of tyramine, an indirectly acting sympathomimetic agent[4], are inhibited by TK174. This was demonstrated on pressor responses to this amine of rats under thiobarbiturate anaesthesia (Table I). From this point of view TK174 is also similar to cocaine[5].

The results obtained in our experiments suggest that the site of action of TK174 should be searched for in the peripheral sympathetic nerve endings supplying different organs, first of all those containing smooth muscle.

Table II. Effects of TK 174 and cocaine on guinea-pig isolated vas deferens preparations

A) Chemical stimulation by noradrenalin

Concentration of noradrenalin	No. of experiments	Contractions[a] recorded in the presence of		
		No other drug	TK 174 ($2.0 \cdot 10^{-7}$)	Cocaine ($2.0 \cdot 10^{-7}$)
$5.0 \cdot 10^{-7}$	6	3.2 ± 1.0	33.5 ± 14.5	14.8 ± 2.0
$2.0 \cdot 10^{-6}$	6	26.3 ± 2.8	100.3 ± 8.3	49.5 ± 5.2

(B) Electrical stimulation of the hypogastric nerve-vas deferens preparation

Drug to be tested	No. of experiments	Art of stimulation	Contractions[a] recorded	
			Before addition of the drug to be tested	After
TK 174 ($5.0 \cdot 10^{-6}$)	8	Muscular	22.9 ± 2.7	27.8 ± 2.1
		Neural	23.6 ± 4.4	44.1 ± 4.4
Cocaine ($5.0 \cdot 10^{-6}$)	6	Muscular	23.8 ± 5.3	23.1 ± 6.5
		Neural	18.8 ± 5.5	32.1 ± 6.0

[a] in mm; mean values $\pm$ S.E.

Résumé. Par le composé 1,1-*bis*-(4-amino-phényl)-propyl-(3)-amine (TK174), de même que par la cocaïne, les actions de la noradrénaline sont considérablement augmentées tandis que celles de la tyramine sont bloquées. Les autres effets pharmacodynamiques de la cocaïne ne sont pas produits par TK174.

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Effect of Secretin on Bicarbonate Secretion in Fluid Perfusing the Rat Ileum

Intravenous secretin increases the rate of bicarbonate secretion in both bile and pancreatic juice. Bicarbonate secretion also occurs in the rat ileum and colon[1]. The common embryologic origin of the liver, pancreas, and intestine suggested that secretin might also influence bicarbonate secretion in fluid perfusing the rat ileum. This study reports the effect of secretin on bicarbonate secretion and the net transport of sodium, potassium and chloride in the rat ileum.

Method. Sprague-Dawley rats of either sex, weighing 350–450 g, were anesthetized with 0.7 ml/kg of Dial-Urethane given i.p., and a femoral vein was cannulated for injections. The terminal 25 cm of the small intestine was cannulated at both ends, washed with 40 ml of perfusion fluid at a pressure of less than 10 cm of saline, and flushed with air. There followed two 30 min perfusion periods in which 8 ml of fluid was circulated from a reservoir at a rate of 2 ml/min with a Bowman pump (Process and Instruments Company, Brooklyn, New York). At the end of each period, the contents of the ileum and tubing were collected in the reservoir. After the first collection period, the system was washed for 5 min with fresh perfusion fluid and flushed with air. For the second period, 8 ml of fresh perfusion fluid was added to the system. 5 min after the start of each period, 2 ml of fluid was removed from the reservoir for determination of 'initial concentration' and was replaced with 2 ml of fresh perfusion fluid. 'Final concentration' was determined using the fluid collected in the reservoir at the end of each period. The perfusion fluid contained: NaCl 102.8 m*M*/l, KCl 4.7 m*M*/l, KH_2PO_4 0.8 m*M*/l, $NaHCO_3$ 28.2 m*M*/l,

[1] D. S. Parsons, Q. Jl exp. Physiol. *41*, 410 (1956).