unimpaired. Increasing the dose to 100 μg/ml often depressed responses to all agonists. The bradykinin-induced vasodilation in the dog femoral vascular bed and the relaxation of the rat duodenum were affected by dimethothiazine to the same extent as the contraction responses of the other varieties of smooth muscle studied. If the bradykinin blockade can be interpreted as some sort of interaction with kinin receptors, these observations provide no evidence of the sort of heterogeneity revealed by antagonists in the case of catecholamines.

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October 17, 1968

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5-Hydroxyindole compounds in the perfusates from frog head

A series of investigations on the significance and role of 5-hydroxytryptamine (5-HT) have been made *in vitro*, in which the content of 5-HT and its metabolites in the brain of dead animals was measured. We have now made experiments with the perfused frog head, with the object of detecting whether there are in the perfusate any substances with properties of 5-hydroxyindoles (5-OH indoles) and also whether their content changes after administration of substances which interfere with biosynthesis, liberation or metabolism of 5-HT.

Male frogs (*Rana esculenta*, L.) were perfused as described by Trendelenburg (1938) with slight modifications: the perfusion fluid was administered through the truncus arteriosus and the collection of the perfusion fluid was via a polyethylene tube inserted in the sinus venosus. After a 1 h washing period, the specimens of perfusate were collected during the next 2 h. In these samples 5-OH indoles were estimated fluorimetrically (Ashcroft & Sharman, 1962). The following substances were used: 5-hydroxytryptophan (DL-5-hydroxytryptophan, Aldrich Chemical Co.), reserpine (Serpasil, Ciba), α-methyldopa (Aldomet, Merck), chlorpromazine (Largactil, Specia) and iproniazid (Marsilid, Roche). The doses of chlorpromazine and iproniazid are expressed as the free base, and the substances were administered subcutaneously.

In the perfusates of untreated animals we found substances with fluorescent properties of 5-OH indoles, the content of which was altered by administration of the above mentioned drugs. The results are summarized in Table 1. 5-Hydroxytryptophan induced a remarkable increase of the concentration of the total 5-OH indoles. After reserpine there was also a significant rise of 5-OH indole compounds in the perfusion fluid. α-Methyldopa lowered the content of total 5-OH indoles. Perfusion fluid from frogs pretreated with chlorpromazine showed an increased amount of 5-OH indoles. Samples from frogs treated with iproniazid showed no measurable fluorescence.

Our results with experiments *in vivo* obtained after administration of 5-hydroxytryptophan, reserpine and α-methyldopa are in good agreement with the results of related experiments *in vitro* (Udenfriend, Weissbach & Bogdanski, 1957; Pletscher,

Table 1. *Concentration of total 5-OH indoles in the perfusates of male frog head* (concentration expressed as μg 5-hydroxyindoleacetic acid/ml perfusate)

Drug	Dose (mg/kg)	Administered before perfusion	5-OH indoles	P (*t*-test)
Control	Isotonic saline	2 h	0·110 ± 0·007* (8)†	
5-Hydroxytryptophan	100	2 h	1·970 ± 0·290 (8)	<0·001
Control	Isotonic saline	2 h	0·071 ± 0·008 (11)	
Reserpine	20	2 h	0·180 ± 0·010 (10)	<0·001
Control	Isotonic saline	1 h	0·071 ± 0·004 (6)	
α-Methyldopa	75	1 h	0·026 ± 0·001 (6)	<0·001
Control	Isotonic saline	1 h 15 min	0·084 ± 0·004 (7)	
Chlorpromazine	25	1 h 15 min	0·106 ± 0·003 (8)	<0·001
Control	Isotonic saline	12 h	0·079 ± 0·005 (6)	
Iproniazid	100	12 h	no measurable fluorescence	—

* Values represent the means ± standard error of the mean.

† The figures in parentheses are numbers of experiments.

Shore & Brodie, 1955; Giarman & Schanberg, 1961). Opinions differ about the action of chlorpromazine on brain 5-HT (Bartlet, 1960; Pletscher & Gey, 1960). Our findings may be related to the action of chlorpromazine in decreasing the permeability of the storage site for 5-HT and this may be the reason why we obtained an increase of 5-OH indoles in the perfusates. Our results with iproniazid are unusual in that we failed to find any detectable fluorescence in the perfusates. On the other hand Gertner, Paasonen & Giarman (1957) observed an increased amount of 5-HT in the perfusion fluid of the isolated cervical ganglion.

Two questions arise. Firstly, which of the 5-OH indoles are present in perfusates, and secondly, is the brain the only source of these compounds.

This investigation was supported, in part, by the Federal Fund for Scientific Research, Grant No. 1819/2.

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