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EFFECTS ON AMINE OXIDASE OF SUBSTANCES WHICH ANTAGONIZE 5-HYDROXYTRYPTAMINE MORE THAN TRYPTAMINE ON THE RAT FUNDUS STRIP

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Certain substances, 2-bromolysergic acid diethylamide, dimethyltryptamine (3-(2-dimethylaminoethyl)indole), 2-methyldimethyltryptamine (3-(2-dimethylaminoethyl)-2-methylindole), and 5-benzyloxydimethyltryptamine (5-benzyloxy-3-(2-dimethylaminoethyl)indole), antagonize the effects of 5-hydroxytryptamine on the rat fundus strip more than those of tryptamine. These substances have been tested for their ability to inhibit the oxidation of tryptamine and 5-hydroxytryptamine by suspensions of guinea-pig liver and rat fundus. 2-Bromolysergic acid diethylamide has virtually no inhibitory activity and it is doubtful if the others produce any significant inhibition of amine oxidase in the concentrations which antagonize the effects of 5-hydroxytryptamine more than those of tryptamine. It seems that the differential character of the blocking action of these compounds should be ascribed either to interference with the transport of tryptamine (but not 5-hydroxytryptamine) through the cell wall, coupled with the block of a receptor common to both tryptamine and 5-hydroxytryptamine, or to the existence of separate tryptamine and 5-hydroxytryptamine receptors.

The amine oxidases of the guinea-pig liver and rat fundus appear to be a mixture of at least two types of enzyme, one of which has a higher affinity for 5-hydroxytryptamine than the other and is more susceptible to inhibition by 2-methyldimethyltryptamine.

Woolley & Shaw (1957) found that certain compounds (notably 1-benzyl-3-(2-dimethylaminoethyl)-5-methoxy-2-methylindole, " BAS ") antagonized the effects of 5-hydroxytryptamine more than those of tryptamine on the blood-pressure of the anaesthetized dog. They suggested that this substance blocked " serotonin-receptors " more than " tryptamine-receptors."

Barlow & Khan (1959a and b) found that certain analogues of tryptamine (notably 3-(2-dimethylamininoethyl)indole " dimethyltryptamine," 3-(2-dimethylaminoethyl)-2-methylindole " 2-methyldimethyltryptamine " and 5-benzyloxy-3-(2-dimethylaminoethyl)indole " 5-benzyloxydimethyltryptamine ") and also 2-bromolysergic acid diethylamide antagonized the effects of 5-hydroxytryptamine more than those of tryptamine on the rat fundus strip preparation described by Vane (1957).

Vane (1959) suggested that in the rat fundus strip tryptamine was destroyed inside the cell by amine oxidase because its action was potentiated by iproniazid (which he assumed to be acting specifically as an inhibitor of amine oxidase). The action of 5-hydroxytryptamine, however, was not potentiated by iproniazid, and it was suggested that this substance, unlike tryptamine, did not penetrate the cell.

Vane demonstrated the destruction of tryptamine and 5-hydroxytryptamine by ground rat fundus and the relative insolubility of 5-hydroxytryptamine in olive oil.

The greater antagonism of 5-hydroxytryptamine than of tryptamine, observed by Barlow & Khan, might be explained by supposing the existence of separate tryptamine and 5-hydroxytryptamine receptors: another possibility might, however, be that the differential blocking substances act at a common receptor and simultaneously penetrate the cell and inhibit amine oxidase (so preserving tryptamine from destruction). Govier, Howes & Gibbons (1953) had tested some analogues of 5-hydroxytryptamine, rather similar to those studied by Barlow & Khan, as substrates of the oxidases of guinea-pig liver and as inhibitors of the oxidation of tyramine. Although their results suggested that these differential blocking compounds might be inhibitors of amine oxidase, there was insufficient information to be certain about this.

This paper describes an attempt to investigate the problem manometrically. It was recognized that it would not be sufficient merely to demonstrate the ability or inability of the compounds to inhibit amine oxidase; it would be necessary to establish whether or not the substances were likely to have any effects on the particular enzyme (or enzymes) present in the rat fundus at the concentrations used in the pharmacological experiments. In manometric experiments the amounts of both enzyme and substrate are necessarily much larger than those in pharmacological experiments. If the degree of saturation of the enzyme is the same in both situations, however, the effects of inhibitors will be comparable. The experimental work began, therefore, with a study of the effects of substrate concentration on the rate of uptake of oxygen. Unfortunately the rat fundus is a poor source of oxidizing enzymes; usually almost a whole fundus was required per manometer flask and the range of substrate concentrations which could be tested was small. The effects of the substrates (tyramine, tryptamine and 5-hydroxytryptamine), and of the inhibitors, have consequently been studied mostly with acetone-powdered guinea-pig liver suspensions. Selected experiments, regarded as the most important, were then repeated using suspensions of ground rat fundus.

Ground rat uterus in oestrus has also been tested as an enzyme source. On the isolated rat uterus preparation, in contrast to the rat fundus, the effects of 5-hydroxytryptamine and of tryptamine were blocked to an equal extent by all the compounds (Barlow & Khan, 1959b), and it was expected that this tissue would be deficient in amine oxidase activity.

METHODS

Compounds

Tryptamine hydrochloride and tyramine hydrochloride were obtained from British Drug Houses, 5-hydroxytryptamine creatinine sulphate monohydrate from May & Baker, iproniazid (Marsilid phosphate) from Roche Products, 2-bromolysergic acid diethylamide from Sandoz, and the remaining compounds were synthesized (Barlow & Khan, 1959a, b).

Tissues

Guinea-pig liver. An acetone-powder was made from the livers of a number of guinea-pigs and stored at room temperature and atmospheric pressure over calcium chloride. When required for use, a quantity was weighed out, suspended in phosphate buffer (0.067 M; *p*H

7.4) and centrifuged for a few min in a "Wifug" bench centrifuge at 3,500 rev/min. The supernatant was decanted off and the sediment re-suspended and centrifuged again. After further re-suspension and centrifugation the sediment was suspended once more and the volume made up to the desired amount (usually 100 mg/ml. or 50 mg/ml.).

Rat fundus. This is a tough structure which cannot be broken up easily. An "Atomix" blender only reduced it to a fibrous mat and it was extremely tedious to break down any appreciable quantity of material by hand in an all-glass homogenizer (the only other equipment available). The fundus was therefore dissected, washed in phosphate buffer (0.06 M, *p*H 7.4), dried with filter paper, weighed, cut as small as possible with scissors and ground with sand in phosphate buffer. The suspension was made up to a measured volume and used directly.

Rat uterus. On the day before the experiment, the rats received an injection of stilboestrol (10 μg/0.1 ml. arachis oil/100 g body weight) in order to induce oestrus. The rat uterus was dissected out and ground with sand in phosphate buffer exactly as with the rat fundus (it was much easier to break down than the fundus).

Variation in the activity of the enzyme source

In experiments with the guinea-pig liver suspensions, the acetone powder should provide a homogeneous source of enzyme for use in a number of experiments. Different batches of powder, however, varied in activity. In this work only 4 batches were used; the last, in particular, was less active than the others. The suspensions of liver in phosphate buffer, even when stored at 4°, deteriorated detectably in 24 hr, and usually a fresh suspension was made every day.

In experiments with ground rat fundus, sufficient material (usually from 5 to 10 funduses) was ground together to provide a source for a particular experiment, but fresh material (possibly, therefore, of different activity) had to be employed each day. This was also necessary in experiments with rat uterus.

Procedure

In all the manometric experiments standard procedures were employed. The flasks contained 0.3 ml. N potassium hydroxide in the centre well, pure oxygen was used and, unless otherwise stated, the temperature was 37° C. Thermobarometers, and suitable blank experiments incorporating cell fragment suspensions but no substrate, or cell fragments and inhibitor but no substrate, were included whenever necessary. The quantity of tissue per flask and the time during which the inhibitor and enzyme were left in contact was recorded.

In experiments with guinea-pig liver the amount of tissue per flask was usually 50 mg, but in some experiments it was greater (up to 100 mg). In experiments with rat fundus the amount varied from 180 mg to 320 mg/flask (being the same for each flask in any one set of experiments and usually around 220 mg); with the uterus it varied from 170 to 260 mg (usually around 220 mg). The actual quantity used depended partly on the efficiency of the material as a catalyst of oxidation; the aim was to obtain constant results with the standard concentrations of substrate.

In experiments with substrates at a concentration of 10^{-3} M the total volume in the flask was 4.0 ml.; at a concentration of 2×10^{-3} M it was 3.0 ml.; and at higher concentrations, 2.0 ml.

Evaluation of results

Rate of oxidation. In experiments with guinea-pig liver, readings were taken 3, 6, 9, 12, 15, 20, 25 and 30 min after tipping. A graph of the net oxygen uptake (deducting blank values for uptake in the absence of substrate) was plotted for each flask containing substrate. In the early part of the experiment, this graph should be linear and indicate only the reaction of oxygen with amine rather than any further oxidation of products such as aldehydes. From the slope of this line the uptake (in μl.) over a period of 9 min was calculated.

In experiments with ground rat fundus and rat uterus the reaction was much slower. Readings were taken 5, 10, 15, 30, 45 and 60 min after tipping and the oxygen uptake was expressed as μl./g tissue (wet weight)/hr.

Effects of inhibitors. The effect of (a particular concentration of) an inhibitor was estimated as the percentage inhibition of the oxidation of (a particular concentration of) substrate. The net oxygen uptake of the flask containing inhibitor was compared with the net oxygen uptake of the flask containing the same concentration of substrate without the inhibitor. The average was usually taken of the values obtained from the figures 15 and 30 min after tipping. When, however, these values differed considerably (as they did when only small volumes of oxygen were involved as in the experiments with rat fundus) it was necessary to plot the two graphs of oxygen uptake against time and to estimate the percentage inhibition by comparing their slopes.

RESULTS

Variation of rate of uptake of oxygen with substrate concentration

Guinea-pig liver. Table 1 and Fig. 1 summarize the results of the first group of experiments. The curve for tyramine indicates that it is the best substrate. The curves for tryptamine and 5-hydroxytryptamine are indistinguishable and flatter than the curve for tyramine. It was concluded that a concentration of 10^{-3} M of any of these substrates would produce something approaching half-saturation of the enzyme. This conclusion was reasonably well confirmed on repetition: Table 2 shows results of similar experiments with a less active acetone-powder performed

TABLE 1

OXIDATION OF SUBSTRATES BY SUSPENSIONS OF GUINEA-PIG LIVER CELL FRAGMENTS

Figures show the oxygen uptake in μl. from the 3rd to the 12th min after tipping. The number of experiments is shown in brackets and the mean value is given with the standard error. The oxygen uptake has been corrected for thermobarometer changes and uptake by tissue in the absence of substrate. In all experiments each flask contained 50 mg tissue. The acetone powder used was dated September 16, 1959

	Molar concentration				
Substrate	10^{-3}	2×10^{-3}	5×10^{-3}	10^{-2}	2×10^{-2}
Tyramine	18·2±1·1 (5)	22·6±0·9 (5)	28·8±2·3 (5)	31·6±2·8 (5)	28·8±2·2 (6)
Tryptamine	12·8±0·7 (6)	13·6±1·4 (5)	19·2±1·5 (5)	21·6±1·2 (5)	22·8±1·0 (5)
5-Hydroxytryptamine	12·1±0·7 (8)	14·1±0·6 (8)	19·0±1·3 (6)	19·2±1·2 (6)	

TABLE 2

OXIDATION OF SUBSTRATES BY SUSPENSIONS OF GUINEA-PIG LIVER CELL FRAGMENTS

As Table 1, but in all experiments each flask contained 70 mg tissue and the acetone powder was dated September 7, 1960

	Molar concentration				
Substrate	10^{-3}	2×10^{-3}	5×10^{-3}	10^{-2}	2×10^{-2}
Tyramine	18·4±1·4 (4)	21·0±3·7 (3)	23·1±0·4 (3)	25·9±2·3 (5)	25·9±1·9 (4)
Tryptamine	9·4±0·6 (6)	12·0±2·0 (2)	13·2±0·6 (6)	14·0±1·5 (2)	13·2±0·2 (2)
5-Hydroxytryptamine	9·3±0·7 (6)	9·5±0·5 (2)	13·1±0·6 (6)	13·3±0·3 (3)	7·7±1·2 (2)

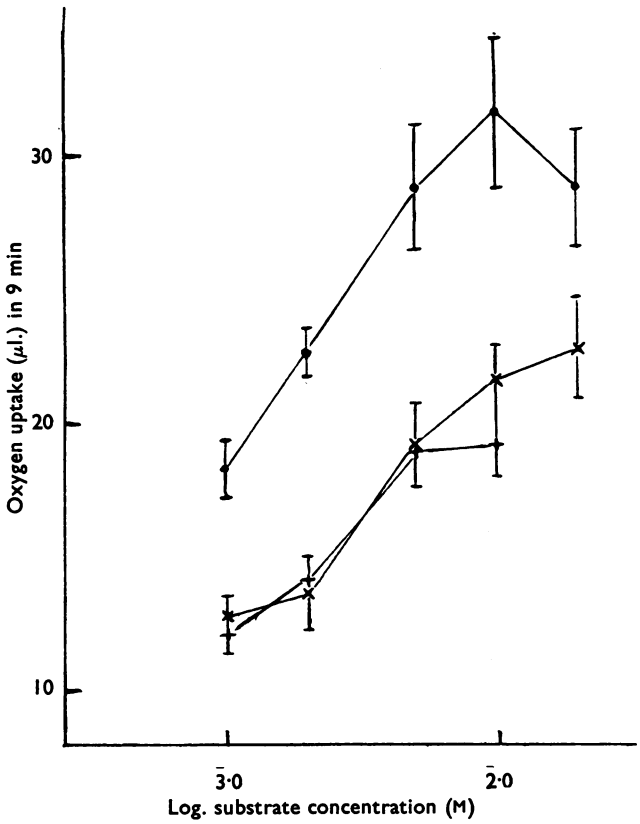

Fig. 1. Effect of substrate concentration on rate of oxygen uptake with suspensions of acetone-powdered guinea-pig liver. Each flask contained 50 mg tissue. Ordinate: oxygen uptake μl. in 9 min. Abscissa: log. molar concentration of substrate. ● Tyramine. X Tryptamine. + 5-Hydroxytryptamine.

12 months later. 5-Hydroxytryptamine was tested as the creatinine sulphate, but creatinine itself, even in a concentration of 10^{-2} M, did not take up oxygen in the presence of guinea-pig liver suspension, nor did it inhibit at all the oxidation of tyramine.

TABLE 3

OXIDATION OF SUBSTRATES BY SUSPENSIONS OF GROUND RAT FUNDUS

Figures show the oxygen uptake in μl./g tissue (wet weight)/hr. The number of experiments is shown in brackets and the mean value is given with the standard error. The oxygen uptake has been corrected for thermobarometer changes and uptake by tissue in the absence of substrate. Results of Vane (1959) using a substrate concentration of $7{\cdot}5\times10^{-3}$ M were : tryptamine, 124; 5-hydroxytryptamine, 142; tyramine, 207

	Molar concentration	
Substrate	5×10^{-3}	10^{-2}
Tryptamine	73·5±7·7 (6)	124±15·4 (9)
5-Hydroxytryptamine	224±12·9 (6)	196±14·3 (4)
Tyramine		271±16·9 (9)

Ground rat fundus. The results of experiments with the ground rat fundus are summarized in Table 3. Only 2 substrate concentrations were used. When the concentration was less than 5×10^{-3} M the oxygen uptake was too small to be estimated accurately: a concentration of 5-hydroxytryptamine greater than 10^{-2} M was difficult to obtain because a 2×10^{-1} M solution of this compound is almost saturated and this had to be diluted by the volume of the suspension of tissue.

The results suggest that a concentration of 10^{-2} M 5-hydroxytryptamine saturates the amount of enzyme in these experiments but that tryptamine at this concentration does not. The decrease in oxygen uptake with the higher concentration of 5-hydroxytryptamine resembles the results with the guinea-pig liver, particularly those shown in Table 2, where a 5×10^{-2} M solution was tested.

Inhibitory activity

Guinea-pig liver. Preliminary experiments, summarized in Table 4, produced two surprising results. First, 2-bromolysergic acid diethylamide appeared to be almost inactive, and, second, the tryptamine analogues appeared to inhibit the oxidation of tyramine more than that of tryptamine. It was because of these results that it was realized that the effect of concentration on the rate of oxygen uptake would have to be studied for each particular substrate.

TABLE 4

EFFECTS OF INHIBITORS ON OXIDATIONS BY SUSPENSIONS OF GUINEA-PIG LIVER AT 37° C

Figures in brackets indicate the number of experiments: the mean is given with the standard error

Compound	Molar concn.	% Inhibition of oxidation of Tyramine (10^{-2} M)	% Inhibition of oxidation of Tryptamine (10^{-2} M)
2-Bromolysergic acid diethylamide	5×10^{-4}	28	
	10^{-4}	0	
Iproniazid	10^{-5}	23	
Dimethyltryptamine	10^{-3}	79·7±8·1 (3)	44·0±3·5 (3)
2-Methyldimethyltryptamine	10^{-3}	58·3±12·0 (3)	28·7±14·1 (3)
5-Benzyloxydimethyltryptamine	10^{-3}	50·7±2·7 (3)	16·3±3·3 (3)

The results of the main group of experiments are summarized in Table 5. While the accuracy of single experiments is uncertain, it should be noted that with two exceptions (marked) the antagonists were less effective when diluted and that they were more effective in inhibiting the oxidation of 10^{-3} M substrate than of 5×10^{-3} M. From these results it was concluded that the tryptamine analogues, particularly 2-methyldimethyltryptamine, but not iproniazid, really did inhibit the oxidation of 5-hydroxytryptamine more than that of tryptamine. These results were confirmed when checked subsequently (Table 5) and 2-bromolysergic acid diethylamide was found to be completely without effect on the oxidation of tryptamine, 5-hydroxytryptamine, or tyramine in the highest concentrations which could be tested (5×10^{-3} M), even when left in contact with the suspension more than 30 min before adding the substrate.

TABLE 5

EFFECTS OF INHIBITORS ON OXIDATIONS BY SUSPENSIONS OF GUINEA-PIG LIVER AT 37° C

Figures in brackets indicate the number of experiments: the mean is given with the standard error. An asterisk indicates that the result does not conform with the expectation that inhibition should increase as the inhibitor concentration is increased or the substrate concentration decreased. The second set of results for 2-methyldimethyltryptamine and 2-bromolysergic acid diethylamide were obtained approximately twelve months after the results in the rest of this table

		% Inhibition of oxidation of			
		Tryptamine		5-Hydroxytryptamine	
	Molar concn.	10^{-3} M	5×10^{-3} M	10^{-3} M	5×10^{-3} M
Dimethyltryptamine	10^{-3}	65	46	100	94
	2×10^{-4}	52·7±16·2 (3)	0	89·7±10·3 (3)	50
2-Methyldimethyltryptamine	10^{-3}	20*	27	99	100
	2×10^{-4}	20·3±10·7 (3)	0	88·0±7·1 (3)	42
5-Benzyloxydimethyltryptamine	10^{-3}	28*	26	60	46
	2×10^{-4}	36·5±2·5 (2)	—	49·5±9·5 (2)	—
Iproniazid	3×10^{-5}	71·0±12·4 (3)	58·7±12·9 (3)	52·0±23·7 (3)	36·3±5·7 (3)
2-Methyldimethyltryptamine	10^{-3}	27±7 (2)*	28±10 (2)	95±4 (2)	91±8 (2)
	2×10^{-4}	6±6 (2)	10±10 (2)	86±1 (2)	64±1 (2)
2-Bromolysergic acid diethylamide	5×10^{-4}	0	0	0	0

Ground rat fundus. Results of experiments with 2-methyldimethyltryptamine, iproniazid and 2-bromolysergic acid diethylamide on suspensions of ground rat fundus are shown in Table 6. As in the experiments with guinea-pig liver, 2-methyldimethyltryptamine inhibited the oxidation of 5-hydroxytryptamine more

TABLE 6

EFFECTS OF INHIBITORS ON OXIDATIONS BY SUSPENSIONS OF GROUND RAT FUNDUS AT 37° C

Figures in brackets indicate the number of experiments : the mean is given with the standard error

		% Inhibition of oxidation of			
		Tryptamine		5-Hydroxytryptamine	
	Molar concn.	5×10^{-3} M	10^{-2} M	5×10^{-3} M	10^{-2} M
2-Methyldimethyltryptamine	2×10^{-4}	(9±9 (3)	3±3 (2)	91±5 (3)	75±7 (2)
Iproniazid	3×10^{-5}	56		63±15 (2)	
	10^{-5}	15±1 (2)		38±3 (2)	
2-Bromolysergic acid diethylamide	5×10^{-4}	0		22	

than that of tryptamine. In the highest concentration which could be tested, 5×10^{-4} M, 2-bromolysergic acid had little effect on the oxidation of tryptamine or 5-hydroxytryptamine even when left in contact with the suspension more than 30 min before adding the substrate.

Experiments with ground rat uterus

The results of these experiments are summarized in Table 7. Because the considerable ability of this tissue to catalyse the oxidation of tyramine and tryptamine was unexpected, the experiments were repeated at 30° C, the temperature at which the tissue is used in pharmacological experiments. Even at this temperature the oxygen uptake was considerably greater than with ground rat fundus (weight for weight). In two experiments at 37° C the oxidation of both tyramine and tryptamine (10^{-2} M) was completely inhibited by 10^{-5} M iproniazid.

TABLE 7

OXIDATION OF SUBSTRATES BY SUSPENSIONS OF RAT UTERUS IN OESTRUS

Figures show the oxygen uptake in μl./g tissue (wet weight)/hr. The number of experiments is shown in brackets and the mean value is given with the standard error. Compare these results with those in Table 3

Substrate		37° C	30° C
Tryptamine	10^{-2} M	378·9±22·9 (8)	240·8±41·4 (6)
Tyramine	10^{-2} M	602·2±27·2 (9)	427·3±6·9 (6)

DISCUSSION

In Table 8 are set out the approximate concentrations of the compounds which are effective in the pharmacological experiments and in inhibiting the oxidation of tryptamine by ground tissues. The figures for pharmacological experiments with iproniazid are based on the observations of Vane (1959), Barlow and Khan (1959b) and Khan (1959). Vane found that 3×10^{-5} M iproniazid potentiated the effects of tryptamine 12.7 times on the rat fundus strip ; Khan recorded a 36-fold potentiation at this concentration. Barlow and Khan reported that 3×10^{-5} M iproniazid did not potentiate the action of tryptamine or 5-hydroxytryptamine on the rat uterus, but Khan recorded slight effects (not greater than a factor of 2) on the responses

TABLE 8

EFFECTIVE MOLAR CONCENTRATIONS

	Modification of effects of tryptamine on:		Inhibition of destruction of tryptamine by oxidases of:	
Compound	Rat fundus	Rat uterus	Guinea-pig liver suspensions	Rat fundus suspensions
Dimethyltryptamine	3×10^{-7}	100×10^{-7}	$1{,}000 \times 10^{-7}$	
2-Methyldimethyltryptamine	20	100	1,000	$1{,}000 \times 10^{-7}$
5-Benzyloxydimethyltryptamine	6	90	1,000	
Iproniazid	300	30–300	100	100
2-Bromolysergic acid diethylamide	1	0·1	>5,000	>5,000

to tryptamine with concentrations of iproniazid varying from 3×10^{-6} M to 3×10^{-5} M (allowed to act for 45 min). Because the figures in Table 8 showing the concentrations inhibiting the oxidation of tryptamine by ground tissues were obtained from experiments in which the enzyme or enzymes should not have been saturated it should be justifiable to assume that they would be comparable with the concentrations effective inside the cell in the pharmacological experiments. This

assumption receives support from the figures for iproniazid: the concentrations effective in inhibiting the oxidation of tryptamine by ground rat fundus are comparable with those which potentiate the action of tryptamine on the rat fundus strip.

2-Bromolysergic acid diethylamide, however, cannot have any effect on amine oxidase in the experiments with the rat fundus strip unless it is being concentrated inside the cell to a fantastic extent (to such an extent that it must almost form a saturated solution). For this reason the differential blocking action of 2-bromolysergic acid diethylamide cannot be ascribed to block of a common receptor coupled with a simultaneous inhibition of amine oxidase, although it might be supposed that potentiation of tryptamine is brought about by blocking its entry through the cell wall.

The results for the tryptamine analogues are more ambiguous. It is possible to suppose that these may be concentrated inside the cell and produce a differential block by, simultaneously, blocking a process activated by both tryptamine and 5-hydroxytryptamine, and inhibiting the destruction of tryptamine by amine oxidase. There are, however, objections to this idea: (1) The compounds would have to be concentrated about 100-fold inside the cell (that is, to a very much greater extent than iproniazid; there seems no reason why this should be so). (2) In the rat uterus conditions are more favourable to inhibition of amine oxidase than in the fundus (see Table 8), but the compounds antagonize tryptamine and 5-hydroxytryptamine to the same extent.

These results draw attention to the need for information about the effects of these compounds on the transport of tryptamine across the cell membrane. If 2-bromolysergic acid diethylamide, for instance, does not affect this, it seems unlikely that tryptamine and 5-hydroxytryptamine can be acting on a common receptor. It would also be gratifying to have direct evidence that 5-hydroxytryptamine does not penetrate the cells of the rat fundus, for if it does penetrate to any extent the tryptamine analogues used in this work should inhibit its destruction more than that of tryptamine. It appears, from the results, that the intracellular destruction of tryptamine by amine oxidase may be peculiar to the rat fundus; it does not seem likely to occur in the rat uterus.

The greater inhibition of the oxidation of 5-hydroxytryptamine than of tryptamine by suspensions of guinea-pig liver and ground rat fundus is an unexpected finding. It does not appear to be an artefact caused by working at different levels of saturation of the enzyme, for in the experiments with suspensions of guinea-pig liver the degree of saturation should be the same for both substrates. Hope & Smith (1960) have studied the substrate specificity of amine oxidases obtained from a variety of tissues of the mouse and deduced the existence of more than one species of enzyme. From the results of our experiments it would seem that the enzymes in guinea-pig liver and rat fundus are not exactly the same (compare the results for tryptamine and 5-hydroxytryptamine in Tables 1, 2 and 3). If there are different types of amine oxidase, it is conceivable that the enzymes in the liver and fundus are not homogeneous. It appears possible to distinguish 2 types; one, for which 5-hydroxytryptamine has a higher affinity than tryptamine, is more readily inhibited by 2-methyldimethyltryptamine than the other. The existence of

2 such types might account for the variation in the activity of different acetone-powders of guinea-pig liver or of suspensions of rat fundus and also for the impression that the ability of these to oxidize tryptamine seems to deteriorate more rapidly than ability to oxidize 5-hydroxytryptamine or tyramine.

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