progressed, the inhibitory power of the homogenate declined (Figure). Heating the homogenate in a boiling water-bath for 10 min did not diminish its inhibitory activity. Dialysis through a cellophane membrane against 0·15 *M* phosphate buffer resulted in a partial removal of inhibitory activity (see Table). However, even prolonged dialysis (48 h) against constantly renewed buffer solution failed to remove the inhibitory material entirely, suggesting that more than one substance may be involved in this inhibition.

Even after prolonged dialysis, no IAA-oxidizing activity could be detected in the lettuce homogenates.

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Résumé

Des extraits de graines et de plantules de laitue (*Lactuca sativa*) var. Grand Rapids inhibent l'auxine-oxydase des homogénats de racine de pois Alaska. L'effet inhibiteur de ces extraits de laitue n'est pas détruit par la chaleur, et n'est que partiellement réduit par dialyse.

Inhibition of 5-Hydroxytryptamine Release from Blood Platelets by N²-Isopropyl Isonicotinic Acid Hydrazide

It has been shown that reserpine and 2-oxo-3-isobutyl-9, 10-dimethoxy-1, 2, 3, 4, 6, 7-hexahydro-benzo[a]quinolizine[1] cause a decrease of 5-hydroxytryptamine (5HT) in isolated blood platelets of rabbits[2]. Thereby the concentration of the free 5HT in the plasma increases if the animals have been pretreated with a monoamine oxidase (MAO) inhibitor [1-benzyl-2-(5-methyl-3-isoxazolylcarbonyl) hydrazine[3]]. This probably shows that although MAO is inhibited, reserpine and the benzoquinolizine derivative are still capable to release 5HT from platelets. On the other hand there exists some evidence that in the intestine and the brain the MAO inhibitor N²-isopropyl isonicotinic acid hydrazide (iproniazid)[4]) inhibits the reserpine induced release of 5HT from tissue structures[5]. A definite proof for this hypothesis has, however, not been presented up to now.

The following work was undertaken to investigate whether iproniazid inhibits the reserpine induced 5HT release in isolated blood platelets.

Method. Using a procedure previously described[6] 5HT determinations in platelets and platelet poor plasma were carried out after incubation of platelet rich rabbit plasma with reserpine for 3 h. Part of the samples were incubated with iproniazid alone or with iproniazid and reserpine (reserpine added 15 min after iproniazid, final iproniazid

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[4] Trade name Marsilid.

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Incubation	Undiluted platelet suspension (platelet rich plasma)			Diluted platelet suspension			Significance *p*
	No Iproniazid (1)	With Iproniazid (2)	% Difference (3)	No Iproniazid (1)	With Iproniazid (2)	% Difference (3)	
None	12·7	11·8	− 7	13·4	11·8	−12	
	13·6	13·6	0	7·7	7·8	+ 1	
	11·1	10·8	− 3	12·3	12·6	+ 2	
	18·6	19·4	+ 4				
Mean	14·0 ± 1·7 VI	13·9	−1·5 ± 2·5 I	11·1	10·7	− 3 ± 4·5 II	
							III/I < 0·01
	6·3	7·4	+18				IV/I < 0·01
Reserpine	5·5	8·6	+57				V/I < 0·01
1 μg/cm³	1·5	2·4	+60				V/II < 0·01
	11·6	15·3	+32				V/IV > 0·05
	8·8	10·8	+23				I/II > 0·05
							VI/VII < 0·01
Mean	6·7 ± 1·6 VII	8·9	+38 ± 8·5 III				VI/VIII < 0·01
	11·0	12·0	+ 9	12·5	14·0	+12	
Reserpine	6·5	7·8	+20	3·6	4·9	+36	
0·3 μg/cm³	8·2	10·8	+32	7·6	8·7	+15	
				5·7	7·8	+37	
Mean	8·6 ± 1·3 VIII	10·2	+20 ± 6·5 IV	7·4	8·9	+25 ± 6·5 V	

5HT content of rabbit platelets with and without iproniazid preincubation *in vitro*. The figures in columns 1 and 2 indicate the 5HT in μg contained in platelets from 1 cm³ platelet rich plasma. Reserpine incubation for 3 h; addition of iproniazid 1/4 h before reserpine. Standard errors.

concentration 10^{-3} M/l). Furthermore in some experiments the platelet rich plasma was diluted by adding 7 parts of saline before incubation with reserpine and/or iproniazid.

Results

(1) Incubation with iproniazid alone for 3 h did not change the 5HT content of the platelets (in % of the total 5HT of the platelet suspension) as compared to non incubated platelets (difference $-$ 1·5 $\pm$ 2·5%[7]). The 5HT content of the platelets was significantly lower after reserpine incubation than without reserpine. The mean 5HT concentration of platelets incubated with 1 and 0·3 μg/cm^3 reserpine for 3 h was, however, greater after preincubation with iproniazid than without (difference 38·5 $\pm$ 8·5% and 20 $\pm$ 6·5 respectively). These latter values are significantly different from the first one ($p < 0{\cdot}01$) (Table).

(2) After dilution of the platelet suspensions iproniazid preincubation had a similar influence on the 5HT content of reserpine treated platelets (difference of reserpine treated platelets with and without iproniazid preincubation: 25 $\pm$ 6·5%; difference with and without iproniazid incubation alone: $-$ 3 $\pm$ 4·5%; $p < 0{\cdot}01$) (Table).

(3) After incubation with reserpine alone the 5HT concentration in the plasma (in % of the total 5HT content of the platelet suspension) was not significantly higher than that of controls without reserpine (5·47 $\pm$ 2·56% with, 1·37 $\pm$ 0·81% without reserpine; $p > 0{\cdot}05$). In the plasma of undiluted platelet suspensions after iproniazid-reserpine incubation the 5HT amounted to 18·6 $\pm$ 2·73%. This value is significantly different from that of controls ($p < 0{\cdot}01$).

Discussion

The present results indicate that iproniazid modifies the effect of reserpine on 5HT in platelet suspensions in two ways:

(a) Iproniazid pretreatment causes an increase of the free 5HT in the plasma after reserpine incubation. This is probably due to inhibition of the enzymatic degradation of the amine released from platelets. A similar effect of another MAO inhibitor has been described in a previous paper[6].

(b) Iproniazid inhibits the reserpine induced 5HT decrease in the platelets. This is also the case in highly diluted platelet suspensions.

The 5HT content of the plasma might possibly influence the 5HT concentration in the platelets. Thus, one could assume that the reduction of the reserpine induced decrease of 5HT in the platelets by iproniazid is due to the increase of free plasma-5HT. This can, however, be excluded by the experiments with diluted platelet suspensions in which the concentration of free 5HT is negligible. In such suspensions iproniazid has indeed a similar inhibitory effect on the reserpine induced 5HT decrease of the platelets as in undiluted platelet rich plasma.

These findings add more evidence to the previously expressed hypothesis that iproniazid inhibits the reserpine induced 5HT release from the tissue[5,8]. It remains to be shown whether this effect is related to MAO inhibition.

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Medizinische Forschungsabteilung der F. Hoffmann-La Roche & Co., A.G., Basel, 4. November 1959.

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Zusammenfassung

In Thrombozyten-reichem Blutplasma von Kaninchen vermindert Vorinkubation mit Iproniazid den durch Reserpin bedingten 5HT-Abfall der Thrombozyten. Dieser Iproniazid-Effekt ist auch in stark verdünnten Plättchen-Suspensionen vorhanden.

Effect of Iodoacetic Acid on the Total Excretion of Sodium and Potassium in Rats Exposed to X-Rays

It is known that treatment with iodoacetic acid brings about an increase in the lethal action of ionizing radiations in mice[1] as well as in rats[2].

In the course of our research on the mechanism through which iodoacetic acid induces this sensitizing effect, we have confirmed the results of the previous authors and we have found moreover that this effect is common also to bromoacetic acid[3]. We have undertaken the study of the metabolic fate of this substance, having at our disposal a sample of C^{14}-bromoacetic acid[4].

We have at the same time started to study the influence of iodoacetic acid on the response to radiations of some radiosensitive organs. We have thus observed that the involution of thymus in mice treated with iodoacetic acid plus X-rays is slightly but constantly more marked than in those irradiated only (unpublished data).

In the present work we have studied the effects of iodoacetic acid on the gastro-intestinal syndrome of rats exposed to X-rays.

The effects of the ionizing radiations on the gastro-intestinal tract have been studied by numerous authors, and the extensive literature on this subject has been reviewed, among others, by Quastler[5], and by Conard[6]. Among the immediate causes of death of the animals irradiated with doses apt to determine the gastro-intestinal syndrome, the loss of water and of electrolytes through the intestinal wall, stripped of its mucous coating, is thought to be of primary importance. Recently Jackson *et al.*[7,8] have thoroughly studied the excretion of sodium and potassium in rats subjected to an X-ray dose that would kill the animals within 4–5 days. Jackson *et al.*, confirming other authors' results, have found that the damage of the intestinal wall involves a serious loss of water and of sodium, and they consider that the loss of sodium is of sufficient importance to justify by itself the death of the animals. The authors consider the loss of potassium to be less important.

Following the technique of Jackson *et al.*[7], we have studied the effect of iodoacetic acid on the total excretion of sodium and potassium in rats exposed to X-rays.

As shown by the Table and Figure, the course followed by the excretion of both sodium and potassium in the

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