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[8].

(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.

M. K. Paasonen* and A. Pletscher

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

[7] Standard error.

[8] A. Pletscher, Exper. *12*, 479 (1956).

* Guest worker from the Department of Pharmacology, University of Helsinki (Finland). Supported by a grant from the Finnish Medical Society *Duodecim*.

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

[1] H. Langendorff and R. Koch, Strahlentherapie *95*, 535 (1954).

[2] R. N. Feinstein, Amer. J. Physiol. *177*, 156 (1954).

[3] M. Quintiliani and M. Boccacci, R. C. Ist. sup. Sanità, in press.

[4] M. Quintiliani and M. Boccacci, II, U. N. Intern. Conference on the Peaceful Uses of Atomatic Energy A/Conf. 15/P/2252 (1958).

[5] H. Quastler, Rad. Res. *4*, 303 (1956).

[6] R. A. Conard, Rad. Res. *5*, 167 (1956).

[7] K. L. Jackson, R. Rhodes, and C. Entenman, Rad. Res. *8*, 361 (1958).

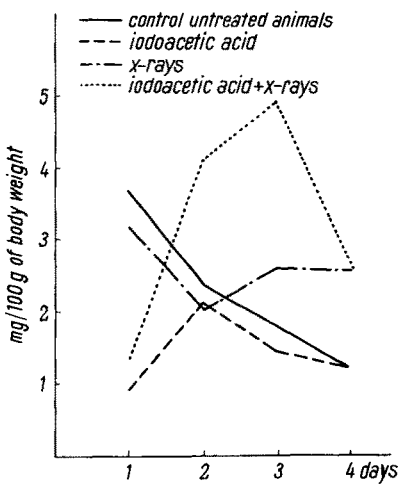
[8] K. L. Jackson and C. Entenman, Rad. Res. *10*, 67 (1959).

Total Excretion (Urine plus Feces) of Sodium and Potassium[1]
Mean values ± standard error of the mean

Treatment	Number of rats	Day 1	Day 2	Day 3	Day 4	Total over 4 days
		24 h sodium mg/100 g of body weight				
0	8	3·65 ± 0·96	2·36 ± 0·45	1·78 ± 0·21	1·20 ± 0·32	8·99 ± 0·75
Iodoacetic acid[2] . . .	8	0·90 ± 0·06	2·11 ± 0·30	1·43 ± 0·52	1·18 ± 0·52	5·62 ± 0·22
780 r[3]	12	3·18 ± 0·29	2·03 ± 0·55	2·58 ± 0·47	2·53 ± 0·40	10·32 ± 0·63
Iodoacetic acid[4] + 780 r	12	1·33 ± 0·17	4·02 ± 0·44	4·85 ± 0·33	2·68 ± 0·73	12·88 ± 0·93
		24 h potassium mg/100 g of body weight				
0	8	14·60 ± 1·26	8·07 ± 0·75	6·12 ± 0·07	5·18 ± 0·59	33·97 ± 0·83
Iodoacetic acid[2] . . .	8	11·60 ± 0·96	8·52 ± 1·06	7·72 ± 1·21	4·97 ± 0·68	32·90 ± 1·70
780 r[3]	12	20·45 ± 0·32	10·78 ± 0·79	12·96 ± 0·82	5·73 ± 0·59	49·90 ± 1·79
Iodoacetic acid[4] + 780 r	12	14·13 ± 0·37	14·26 ± 1·24	13·18 ± 0·61	7·53 ± 0·59	49·15 ± 1·40

[1] Adult female Wistar-Glaxo rats, 150 g mean body weight, mantained on the standard McCOLLUM diet until the beginning of the experiment.
[2] 25 mg/kg of body weight, injected intraperitoneally as neutralized solution.
[3] Whole body X irradiation delivered from a Picker therapy unit at 220 Kvp, 26 r/min.
[4] 25 mg/kg of body weight, 30 min before irradiation.

irradiated only rats, even at the dose level employed by us, agrees with that observed by JACKSON *et al.* In fact, during the first two days, the elimination of sodium shows no significant deviation from that observed in the untreated controls, whereas on the third day it is increased in the irradiated animals nearly double and is maintained rather high on the fourth day also. An increased elimination of potassium has been observed on the first and the third day.



Total excretion (urine plus feces) of sodium during the four days from the beginning of the experiments

Iodoacetic acid only determines a decrease of sodium and potassium excretion on the first day. During the following days, the excretion returns to normal. The decreased excretion during the first 24 h is due to the high degree of intestinal stasis induced by iodoacetic acid, which lasts about 24 h. This stasis is evidenced by the decrease of faeces of the treated animals as compared with the controls and can be better observed, in the laparactomized rats, by the enlargement of the intestinal tract and by the remarkable delay of the intestinal transit of a charcoal in arabic gum meal[9].

In the combined treatment with *iodoacetic acid plus radiations*, the excretion of sodium increases considerably on the second day, and even more on the third day, reaching average differences higly significant with respect to the irradiated only animals, while the excretion of potassium does not appear to be modified as compared with that observed in the animals treated with radiations only.

It appears, therefore, that the intestinal injury of the animals treated with iodoacetic acid and irratiated as well, is more serious than in rats irratiated only. As a matter of fact, as we have been able to observe in collateral tests, the amount of excretion of sodium is related, within certain limits, to the radiation doses received by the animals, and therefore to the severity of the gastrointestinal syndrome.

We have no sufficient elements, as yet, for advancing any hypothesis whatever on the mechanism of action of iodoacetic acid. We can only point out that in the course of recent research on the effect of iodoacetic acid on the incorporation of the P^{32} into the deoxyribonucleic acid of radio-sensitive organs of irratiated rats, we have observed that the incorporation of P^{32} is inhibited in the intestinal tract by iodoacetic acid[10].

M. BOCCACCI and M. QUINTILIANI

Istituto Superiore di Sanità, Roma, August 10, 1959.

Riassunto

Gli autori hanno studiato l'effetto dell'acido iodoacetico sulla escrezione totale di sodio e di potassio nel ratto irradiato. Essi hanno trovato che in seguito al trattamento combinato con acido iodoacetico e radiazioni l'escrezione di sodio risulta notevolmente aumentata rispetto a quella riscontrata negli animali soltanto irradiati.

[9] L. TENTORI, M. BOCCACCI, and M. QUINTILIANI, in preparation.
[10] M. BOCCACCI, M. QUINTILIANI, and L. TENTORI, in preparation.