Presence of 5-Hydroxytryptamine after Raunescine in Blood Plasma *in vivo*

5-HYDROXYTRYPTAMINE is localized in the platelets of the blood, minimal amounts being found in platelet-free plasma[1–3]. *Rauwolfia* alkaloids are known to lower the content of 5-hydroxytryptamine in various tissues including blood both *in vivo* and *in vitro*[4,5]. Whether 5-hydroxytryptamine is released by *Rauwolfia* alkaloids from the cellular binding sites as such to the cytoplasma is still not clear. It has been stated that the incubation of rabbit platelet suspensions with reserpine in an atmosphere of nitrogen increases the amount of 5-hydroxytryptamine in plasma[5].

We have investigated whether 'free' 5-hydroxytryptamine can be found in plasma after a *Rauwolfia* alkaloid. As in the earlier experiments[6], which originally directed our attention to this problem, we have used raunescine, which is an alkaloid chemically and pharmacologically closely related to reserpine[7].

3 ml. of blood was collected by using a polyethylene cannula from the abdominal aorta of male rats (160–180 gm.) anæsthetized with ether. Each time one of the rats served as a control and the three others that received 5 mgm./kgm. of raunescine intraperitoneally were bled 1, 3 and 6 hr. after the injection. The blood was mixed with 1/10 vol. of 1 per cent disodium ethylenediamine tetraacetate and 30–50 int. units of heparin/ml. After separation of plasma and platelets[8] the platelet-poor plasma was extracted by 19 vol. of acetone[9] and the packed platelets, after suspension in acid saline, by 10 vol. of acetone. The samples were kept at around 0° C. during the whole pre-extraction period. The biological assay of 5-hydroxytryptamine was made by using the rat stomach preparation[10]. For collecting the blood from the rabbits a catheter was inserted into a cervical vein under light ether anæsthesia, from which the animals were allowed to recover before the withdrawal of blood. In half of the experiments the animals were pre-treated with 100 mgm. (as base)/kgm. of iproniazid phosphate subcutaneously about 16 hr. before raunescine.

The results from rats are presented in Fig. 1. There was a gradual fall in the platelet 5-hydroxytryptamine, and after 6 hr. about 10 per cent was left in the non-pretreated rats and 14 per cent in those receiving iproniazid. Platelets were counted in some tests and they had about 1 μgm. of 5-hydroxytryptamine/10^9 cells on both series. Raunescine did not change the number of them. In the plasma there was a rise in both groups when analysed 1 hr. after raunescine administration. The increase was more than 10-fold in the pre-treated rats, being less marked in the others. The return to normal was also faster in the animals that received raunescine only.

Essentially similar but less consistent results were obtained by using rabbits. The increase of plasma 5-hydroxytryptamine was not as marked as in rats and it was negligible without iproniazid pre-treatment.

The 5-hydroxytryptamine in plasma probably comes from the platelets; but the possible release from other tissues cannot be excluded. The highest amounts of amine in the plasma were found at the time of the most marked release from the platelets. It has been reported that human serum oxidizes 5-hydroxytryptamine[11]. This activity could be inhibited by iproniazid, ceruloplasmin being suspected as the enzyme involved. Therefore the effect

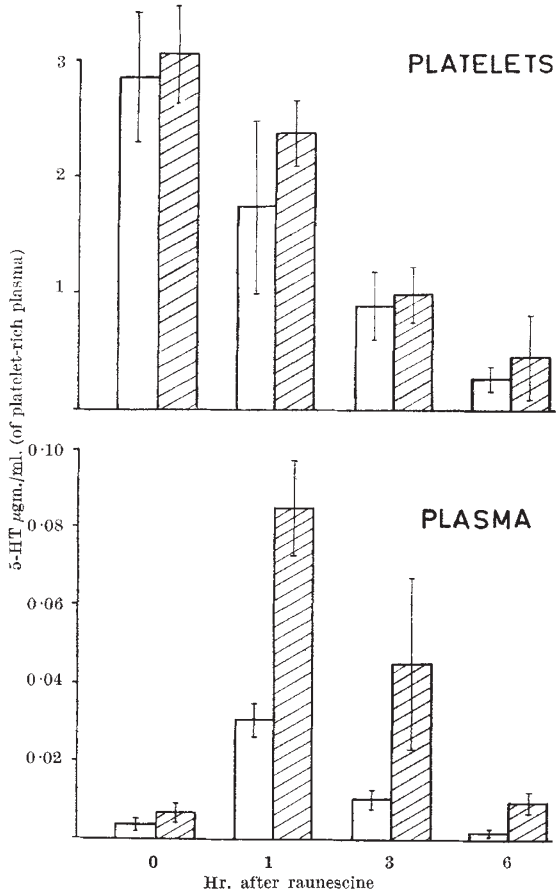

Fig. 1. The amounts of 5-hydroxytryptamine in platelets and platelet-free plasma of rats after raunescine. Each column represents the results from four experiments. Open columns, no pre-treatment; shaded columns, iproniazid pre-treatment; vertical lines, standard deviation

of iproniazid in our experiments may not be due to the inhibition of monoamine oxidase. It is interesting to note that the symptoms produced by raunescine become fully developed at a time when the plasma 5-hydroxytryptamine has returned to normal.

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