

THE INHIBITION BY SODIUM SALICYLATE OF OEDEMA OF THE HIND-PAW OF THE RAT INDUCED BY 5-HYDROXYTRYPTAMINE

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The subcutaneous administration of 600 mg./kg. body weight of sodium salicylate to adult rats 3 to 4 hr. previously inhibited the development of hind-paw oedema following the injection of 2.5 μ g. of 5-hydroxytryptamine. This effect was more pronounced in normal than in adrenalectomized rats.

The inhibitory effect of large doses of salicylate on rat hind-paw oedema induced with testicular extract has been previously described (Kelemen, Majoros, Ivanyi, and Kovacs, 1950). Other types of oedema of the hind-paw, such as those produced by the histamine liberator 48/80, dextran, human sera with enhanced activity to induce oedema, or the animal protein permeability factor of Miles and Wilhelm (1955) were also inhibited by subcutaneous administration of salicylate. The present experiments are concerned with the inhibition of oedema induced with 5-hydroxytryptamine.

METHOD

Injection of 0.3 to 0.8 mg. of crude testicular extract, dissolved in 0.11 ml. saline, into the plantar side of the hind-paw of the rat caused a gross acute oedema. Each animal served as its own control immediately before injecting sodium salicylate (600 mg./kg.). The acute oedema reached its maximum within 10 to 20 min. Details of reading the grade of oedema formation have been given previously (Kelemen, 1956). The inhibition of oedema was recorded as "good" if no marked oedema developed around the tibia.

In the present experiments, 2.5 μ g. of 5-hydroxytryptamine (Upjohn) was used to provoke topical oedema, by the same technique and with similar results, except for the slower effect of the 5-hydroxytryptamine. Similar observations on 5-hydroxytryptamine oedema have been made by Benditt and Rowley (1956). A dose of 0.5 to 1.0 μ g. was also effective in our young rats.

RESULTS

Results of our attempts to influence this type of oedema with systemic sodium salicylate are presented in Table I. Sixty-eight rats of 165 to 200 g. body weight were used in this series. As shown, the 5-hydroxytryptamine oedema investigated 3 to 4 hr. after subcutaneous administration of 600 mg./kg. body weight of sodium salicylate was inhibited in the normal rat. A less pronounced inhibition was obtained with sodium salicylate in

TABLE I

INHIBITION OF TESTICULAR-EXTRACT-INDUCED AND OF 5-HYDROXYTRYPTAMINE OEDEMA OF THE HIND PAW BY SUBCUTANEOUS ADMINISTRATION OF 600 MG./KG. BODY WEIGHT OF SODIUM SALICYLATE IN THE NORMAL AND IN THE ADRENALECTOMIZED RAT

As untreated adrenalectomized rats usually died shortly after the administration of 600 mg./kg. of sodium salicylate, the groups of adrenalectomized animals marked thus * received two doses of 8 mg. of cortisone 8 to 18 days before being given sodium salicylate. This dose of cortisone was without effect on permeability.

	No. of Animals in Each Group	No. of Animals Showing Inhibition of Oedema Formation 3 to 4 Hr. after Sodium Salicylate		
		Good	Moderate	None
<i>Testicular Extract</i>				
Normal	17	14	3	0
*Adrenalectomized 8 to 18 days before	17	2	2	13
<i>5-Hydroxytryptamine</i>				
Normal	17	15	2	0
Adrenalectomized 2 months before	5	1	3	1
*Adrenalectomized 8 to 18 days before	12	6	3	3

the same dose in the adrenalectomized rat treated for several days with an amount of cortisone that had no effect on permeability (see Table I).

DISCUSSION

As far as I know, no substance other than 5-hydroxytryptamine initiates gross acute transitory oedema in such a minute dose and volume. Histamine, for example, which is often said to cause oedema, does not initiate a similar state in doses of less than 100 μ g. The effect in the adrenalectomized rats with 5-hydroxytryptamine-

induced oedema contrasts with those in which the oedema was induced by testicular extract. The reason for this difference is at present unknown.

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