LETTERS TO THE EDITOR

Effects of Gentisate on the Urinary Excretion of Salicylate in the Rat

SIR,—Salicylates are among the commoner causes of poisoning either taken for suicidal purposes by adults or after accidental ingestion by children. The treatment of salicylate intoxication attempts either to control the more dangerous symptoms (for example, by using external cooling for hyperthermia) or to remove salicylate from the body. In the latter category are included such mechanical measures as gastric lavage, exchange transfusion, the use of the artificial kidney, and the administration of alkaline fluids to promote an alkaline urine because the renal excretion of salicylate is significantly increased as the urine pH rises above 7.

After salicylate has entered the cells it may react with a number of enzyme systems particularly those concerned with oxidative phosphorylation reactions, and many of the toxic effects of the drug are explicable in terms of its uncoupling action[1]. The use of a non-toxic substance which could displace salicylate from its intracellular combination would therefore be a valuable adjunct in the treatment of salicylate poisoning. A possible candidate for this role appeared to be

TABLE I

CUMULATIVE ^{14}C EXCRETION IN URINE EXPRESSED AS PERCENTAGES OF THE INJECTED DOSE OF SODIUM [*carboxy*-^{14}C] SALICYLATE

Group	Urine collection (hr.)				
	0–8	8–15	15–24	24–32	32–48
Saline (6)**	36·2*	61·4	75·9	80·5	85·9
	24·9–42·1	52·6–70·8	68·1–86·7	72·4–91·5	76·8– 96·7
Gentisate (6)	40·8	61·0	78·4	83·2	87·3
	34·0–44·0	56·3–72·9	73·0–83·8	77·5–98·4	79·4–102·5

* Results are given as means and ranges.

** Number of animals in each group.

Comparison of the results of the saline and gentisate groups by the *t*-test showed that the values of P exceeded 0·2 in every case.

the closely related gentisic acid (2,5-dihydroxybenzoic acid) which is devoid of uncoupling activity in mitochondrial suspensions[2] and does not produce toxic symptoms in large doses in man[3]. We have therefore studied the effects of the repeated administration of gentisate on the urinary excretion of radioactivity after the injection of [*carboxy*-^{14}C] salicylate in the rat.

6 male Wistar rats (280–310 g.) were given an intraperitoneal injection of 1 ml. of 10 per cent (w/v) sodium salicylate containing about 7 μc of sodium [*carboxy*-^{14}C] salicylate at 0 hours. Three rats subsequently received intraperitoneal injections of 0·5 ml. of 20 per cent (w/v) sodium gentisate at 2, 4, 6 and 8 hours, and the remaining three animals were given injections of 0·5 ml. of 5 per cent (w/v) sodium chloride at similar times. Urine collections were made at the following time intervals: 0–8; 8–15; 15–24; 24–32 and 32–48 hours. No fluid or dietary restrictions were imposed during the experiment. After measurement of the volume of each urine specimen, 1 ml. samples were counted in dished aluminium planchettes (1·0 mm. deep; 2·45 cm. diameter) using an end-window Geiger-Muller tube[4], which was flushed with helium containing 1·6 per cent (v/v) ethanol, and connected to a scaler. The distance between the end-window of the counting tube and the bottom of the planchette was 3·75 mm. Counts (5 minutes) were recorded and the background (60 counts/minute) was deducted. Under these conditions 1 ml. of sodium salicylate used

for the initial injection gave 40,515 counts/minute. The experiment was repeated after an interval of 4 weeks except that the rats which had received the gentisate injections in the previous experiment now received the saline, and vice versa.

The results are given in Table I and show that the administration of the gentisate produced no significant effects on either the rate or the total cumulative excretion of ^{14}C in the urine. The rats receiving gentisate showed an initial diuresis during the first 15 hours of the experiment but this did not alter the urinary excretion of radiocarbon. Thus, it must be concluded that despite the close chemical similarity of salicylate and gentisate it is unlikely that the latter substance displaces salicylate from its intracellular binding sites.

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New Possibilities for the Biological Assay of Digitalis

SIR,—In the research of cardiotonic-glycoside plants it is essential to determine the biological value of preparations containing glycoside mixtures or glycosides in the pure state, and it often happens that only a minimal quantity is available. Thus, biological titrations on larger animals or animals of a relatively high resistance to cardiotonic glycoside activity may be impossible.

Presuming that birds other than pigeons could be used to evaluate cardiotonic glycosides, attempts were made to use turtle-doves (*Streptopelia roseogrisea*) and sparrows (*Passer domesticus*). Since both the turtle-doves and especially the sparrows weigh less than pigeons, smaller quantities of the active materials have been thought to be needed.

The titrations on turtle-doves and sparrows were made by the method prescribed in the B.P. 1953 for pigeons, ignoring the sex of the birds. The solution to be examined was injected into sparrows by means of a microsyringe connected to a plastic tube and intracutaneous canula. The weight of the turtle-doves varied between 133 and 205 g., whereas that of sparrows varied between 12·5 and 18·5 g.

Experiments were carried out with *Digitalis purpurea* from two different sources (Preparations A and B) on pigeons, turtle-doves and sparrows comparing the results with the Yugoslav Digitalis standard preparation. Results of these experiments are given in Table I. As can be seen, these were not significantly different for the three species used.

Titrations of the Yugoslav Digitalis standard preparation were repeated at intervals of 3–6 months to check the reproducibility of the results. These results are given in Table II.

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