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## The Excretion of Scillaren A by Rats

SIR,—As part of a survey of the metabolism and excretion of cardiac glycosides being carried out in this department[1-4] we have examined the bile and urine of rats after doses of scillaren A. The excretory products have been separated by paper chromatography and estimated colorimetrically. The squill glycosides (bufadienolides) do not give colours with the reagents normally used to detect the unsaturated lactone ring in the cardenolides and we have therefore used the pink colour given by these glycosides with 80 per cent sulphuric acid to detect them on paper and to estimate them colorimetrically after elution of the glycoside areas from paper chromatograms.

The bile of male albino rats (150–300 g.) was collected for 6 hours after intravenous injection of doses of 1 μg./g. of body weight of scillaren A.[3] After dilution to about 15 ml. with water the bile from each rat was extracted with chloroform in a liquid-liquid extractor for 4 hours and the extracts streaked across strips of Whatman Paper No. 1 (1¼ in. × 18 in.) and the chromatograms developed with the solvent mixture chloroform : methanol : water (10 : 4 : 5) by the descending method. After 5 hours the papers were dried at 100° for 10 minutes and a longitudinal strip ¼ in. wide cut from the chromatogram and treated with 65 per cent v/v sulphuric acid. Under these conditions scillaren A gave a pink colour on the paper strip. The corresponding area on the remainder of the strip was cut and eluted with methanol. The methanol extracts were evaporated to dryness, 1·75 ml. of 65 per cent v/v sulphuric acid added and the optical density of the pink colour produced was measured in an EEL Colorimeter (green filter 624). The colour obtained reached a maximum intensity in 10 minutes and was stable for at least 25 minutes (5 μg. of scillaren A could be readily detected and with the quantities assayed an error of ± 2 per cent was possible).

Using this procedure, extraction of known quantities of scillaren A from bile gave mean recoveries of 82 per cent (79–85 per cent, P = 0·95) and this figure was used as a correction factor to obtain a close approximation of the scillaren A content of the bile collected in the excretion experiments.

Only one band was detected in the chromatograms of the bile extracts obtained after doses of 1 μg./g. This was eluted and identified as scillaren A by rechromatography on paper with the original glycoside using four different solvent systems for development: chloroform : methanol : water (10 : 8 : 5), toluene : butanol (8 : 2) saturated with water, ethyl acetate : butanol : chloroform (16 : 16 : 68) saturated with formamide, and chloroform : benzene : butanol (70 : 10 : 10) saturated with formamide.

Quantitative determination of the amount of glycoside present in bile showed that 84 per cent (79–90 per cent, P = 0·95) of the dose was excreted in 5 hours.

Chloroform extracts of urine collected for 12 hours after intraperitoneal doses of 1 μg. and 2 μg./g. of scillaren A were chromatographed but no glycosides or metabolites could be detected on the papers indicating urinary excretion was very low during this period.

It appears from these results that scillaren A is similar to the polar digitalis glycosides lanatoside A and lanatoside C[3] and to ouabain[4] in being excreted mainly in the bile and without chemical modification.

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## Carcinoid Tumours and Pineapples

SIR,—The presence of 5-hydroxytryptamine (5–HT) and its precursors in fruits has been reported in recent years[1,2]. The ingestion of large quantities of banana and tomato may lead to erroneous chemical diagnoses of carcinoid tumours by producing an increased urinary excretion of 5–HT and its metabolites. These fruits should be eliminated therefore from the diets of patients whose urinary indoles are being measured. To the list of forbidden fruits, Bruce[3] in Australia has recently added the pineapple. Firstly he showed that fresh and canned pineapple juice contain much 5–HT (12–25 μg./ml.), and secondly he found that the rate of excretion of 5-hydroxyindoleacetic acid (5–HIAA) was increased 10-fold after the ingestion of 500 ml. commercial canned pineapple juice.

During a systemmatic examination over 2 years ago of the presence of indole compounds in plants, we had detected only traces of indole derivatives in fresh pineapples, and Foy and Parratt[4] this year obtained a similar result using the fruit gathered from the trees in Nigeria. A re-investigation of the problem was thus needed.

Fresh pineapple, three brands of canned pineapple juices, and a sample of bottled juice were extracted with acetone, and after removal of the acetone the extracts were subjected to paper chromatographic analysis and to bioassay using the rat uterus preparation. The concentrations of 5–HT in no case exceeded 1·5 μg./ml. juice and there were only traces of tryptophan and indoleacetic acid. It seems unlikely therefore that the ingestion of much pineapple juice would increase the excretion of 5–HIAA above the range (2–10 mg./day) found in patients who do not have carcinoid tumours. It should be pointed out that none of the preparations of pineapple used in the present work was of Australian origin.

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