New Glycosides from Senna

SIR,—The letter by Vickers in the August issue of this Journal (1961) has stimulated us to report the isolation of five anthracene glycosides from senna since our report of the separation of an active primary glycoside (Fairbairn, Friedmann and Ryan, 1958).

Rhein-8-glucoside. This has been isolated from Alexandrian senna pod and appears to be similar to that reported by Vickers. We have shown it to be a rhein-monoglucoside by chemical analysis. Ultra-violet absorption measurements indicate that the compound is identical with synthetic rhein-8-glucoside, prepared from authentic rhein anthrone-8-glucoside by aerial oxidation in sodium borate solution at pH 9·2, and differs from a sample of synthetic rhein-1-glucoside, kindly supplied by Dr. A. C. Bellaart. Our experience is that the glucoside isolated by us is not readily decomposed by sodium bicarbonate solution with the formation of rhein, which does not accord with the inference that can be drawn from Vickers' letter.

Rhein-8-diglucoside. A second glycoside isolated has been shown to be rhein-8-diglucoside. This glycoside, is much more soluble in water than the 1- or 8-monoglucosides. It can be converted into the 8-monoglucoside by treatment with 0·1N hydrochloric acid at room temperature.

Rhein anthrone-8-glucoside, which is virtually half a sennoside molecule, was also found by us to be present in senna pod. This has been identified by hydrolysis to rhein anthrone, which was characterised spectroscopically, and by the formation of a green compound (λ_{max} 640 mμ) with *p*-nitrosodimethylaniline in pyridine (Tsukida and Suzuki, 1954). The conversion of rhein anthrone-8-glucoside to rhein-8-glucoside has been shown to proceed slowly in sodium bicarbonate solution. Rhein anthrone-8-glucoside, in alkaline solution, can give end-products other than rhein-8-glucoside: for example, Stoll, Becker and Helfenstein (1950) were able to obtain sennosides, and under more vigorous conditions, rhein. We are investigating the reaction conditions and the mechanisms which produce these different oxidation products.

Primary glycoside. Fairbairn and others (1958) have already described an active primary glycoside (related to the sennosides) having a molecular weight of 1164. We now report the discovery of a further primary glycoside having a molecuar weight of about 2000. It is characterised by a greater solubility in water than any of the other substances we have isolated and can be degraded to the sennosides by mild hydrolysis.

Aloe-emodin glycoside. This has been isolated from the non-rhein fraction of senna-leaf glycosides. It occurs as a pale-orange substance, soluble in water and methanol. Hydrolysis produces aloe-emodin and glucose, and quantitative work suggests it is a monoglucoside. We have good evidence also for the presence in the leaf of an aloe-emodin anthrone glucoside.

The important question raised by the discovery of these new glycosides is what contribution they make to the total activity of senna. Experiments on mice show that the new primary glycoside (MW 2000) is more active than the primary glycoside described by Fairbairn and others (1958), and significantly more active than the sennosides. Rhein anthrone-8-glucoside is about as active as the sennosides whereas Vickers' rhein glucoside, according to his results, appears to be much less active. Our experience with Alexandrian senna pod indicates that the less active rhein glucoside it contains constitutes only about 4 to 8 per cent of the total acidic anthracene glycosides, and that the aloe-emodin glycosides are present only in insignificant quantities. As the result of routine assays on many samples, we confirm the earlier findings (Fairbairn, 1959) that the pharmacological activity as determined by bioassay (Lou, 1949) runs

parallel with the sennoside content determined by the chemical assay (Fairbairn and Michaels, 1950). Both assay procedures have been shown to reflect adequately the laxative activity in man (Browne, Edmunds, Fairbairn and Reid, 1957).

When dealing with other varieties of senna or with extracts this satisfactory relationship between chemical and biological assays may not hold owing to varying proportions of active glycosides and the presence of breakdown products.

School of Pharmacy,
University of London,
Brunswick Square,
London, W.C.1.

J. K. CRELLIN.
J. W. FAIRBAIRN.
C. A. FRIEDMANN.
H. A. RYAN.

Westminster Laboratories Ltd.,
Regents Park,
London, N.W.1.
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