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LEUCOGLYCODRIN, A GLYCOSIDE FROM LEUCADENDRON ADSCENDENS

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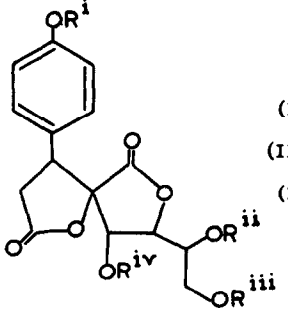
Following reports by Meiring-Beck (1,2) of the isolation of an amorphous grey substance, proteacin, from a species of Leucadendron plant, Merck (3) succeeded in separating two compounds from Leucadendron concinnum, the bitter principle, leucodrin, whose structure (I) has recently been determined by physical (4,5) and chemical (6) methods, and the compound for which he proposed the name leucoglycodrin. Merck's investigation of leucoglycodrin by acid hydrolyses, furnished an oil, the phenylosazone of which appeared to be the derivative of either D-galactose or D-glucose or a mixture of both compounds.



(I) $R^{i} = R^{ii} = R^{iii} = R^{iv} = H$

(II) $R^{i} = C_6H_{11}O_5$; $R^{ii} = R^{iii} = R^{iv} = H$

(III) $R^{iv} = C_6H_{11}O_5$; $R^{i} = R^{ii} = R^{iii} = H$

(IV) $R^{ii} = C_6H_{11}O_5$; $R^{i} = R^{iii} = R^{iv} = H$

(V) $R^{iii} = C_6H_{11}O_5$; $R^{i} = R^{ii} = R^{iv} = H$

In view of the lack of information on the nature of this apparent glycoside, the extracts of Leucadendron adscendens from which we had isolated considerable quantities of leucodrin [up to 20% on the weight of dried leaves (7)] were investigated in the hope that leucoglycodrin might also be present in this species.

Careful methanol extraction of the oily residue obtained by evaporation of the aqueous plant extracts from which leucodrin had been removed, and trituration of the concentrated methanolic solution with ether, yielded leucoglycodrin (9.2%) as an amorphous solid, $C_{21}H_{26}O_{15}.\frac{1}{2}H_2O$, m.p. 220-222°, $\nu_{max.}$ 1802, 1780, 1620, 1110, 1252 and 783 cm.$^{-1}$. Both the infrared spectrum and the ultraviolet spectrum are strikingly similar to those obtained for leucodrin (6) - the ultraviolet spectrum, $\lambda_{max.}$ 201 mu (ϵ 19,880), 226 mu (ϵ 9,240), 276 mu (ϵ 2,100) and at 280-284 mu (ϵ 1,960-1,820) showing only a slight bathochromic effect to that characteristic of the leucodrin chromophore. Leucoglycodrin was further characterised as its hepta-acetate, $C_{35}H_{40}O_{20}$, m.p. 262-264°, $\nu_{max.}$ 1802, 1780, 1744, 1730 and 1250 cm.$^{-1}$.

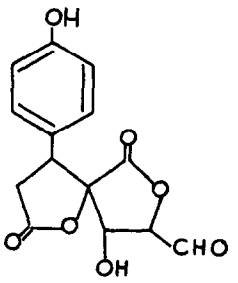
The speculation, inferred from spectral and analytical data, that leucodrin is the aglycone moiety present in leucoglycodrin, was substantiated by mild acid hydrolysis of the glycoside. The resulting mixture of products, on acetylation, yielded leucodrin tetra-acetate, identical in all respects with an authentic specimen. Paper chromatographic separation of the neutralised hydrolysis mixture established that the only sugar present in the mixture was glucose (R_F value 0.15) (8), its identity being corroborated by the preparation of glucosazone and the isolation of 2,3,4,6-tetramethylglucose from the acid hydrolysate of completely methylated leucoglycodrin.

That the glucose isolated must be D-glucose followed from the fact that the hydrolysis mixture was more dextrorotatory, $[\alpha]_D^{20}$ + 23.2°, than leucodrin itself (9) and in confirmation it has been observed that the rotation of a mixture of leucodrin and D-glucose under the above hydrolysis conditions has a value of +29.6 for $[\alpha]_D^{20}$.

The four possible sites of attachment of the carbohydrate residue to the leucodrin skeleton are shown in structures (II) - (V). However, structures (III) and (IV) are precluded on the grounds that completely methylated leucoglycodrin on mild acid hydrolysis, yielded a methyl ether derivative of leucodrin which showed no uptake of alkaline periodate. The leucodrin fragments obtained on acid hydrolysis of structures of the type (III) and (IV) would, on alkaline treatment, furnish a vicinal triol and a vicinal diol respectively. Moreover, the above mentioned, partially methylated leucodrin derivative, on treatment with ethereal diazomethane (a reagent which would not be expected to react with alcoholic OH groups but only with phenolic OH functions under these conditions) yielded leucodrin tetramethyl ether, identical in all respects with an authentic sample. These observations require that leucoglycodrin be formulated as (II).

Further evidence which convincingly demonstrated that the .CHOH.CH_2OH system in the leucodrin skeleton is not involved in attachment to the glucose residue followed from the isolation of an aldehyde, $C_{14}H_{12}O_7$, m.p. 178-179°, on periodate oxidation and subsequent acid hydrolysis of leucoglycodrin. This aldehyde which showed $\nu_{max.}$ 3500, 3300, 3180, 1300, 1768 and 1620 $cm.^{-1}$, and τ (dimethyl sulphoxide) C<u>H</u>O 0.48 (1H,s), aromatic protons 2.71, 2.87,

3.20, 3.33 (4H, A_2B_2 spectrum), CHOH 3.50, 3.60 (1H,d), phenolic OH 3.72, 3.81, 3.91 (1H,t), CH_2.CH 5.16, 5.49, 5.69 (3H, ABC spectrum), .CH.CHO 6.61, 6.68, 6.75, 6.81 (1H,q.) and CHOH 7.1, 7.2 (1H,d), furnished a p-nitrophenylhydrazone derivative, $C_{20}H_{17}N_3O_8$, m.p. 193-195°, and was identical in all respects with leucodrin noraldehyde, the structure of which has been unambiguously established as (VI) in our chemical investigation of the structure of leucodrin (6).



(VI)

The above evidence indicates that leucoglycodrin may be assigned the structure (II).

The role of leucoglycodrin in the leucadendron species is hard to envisage, since in general, no single explanation is sufficient to account for the presence of glycosides in plants. It may be that leucoglycodrin is formed from leucodrin itself at certain sites of development during the growth of the plant, in order to remove the phenolic compound in some kind of detoxification mechanism (10). Another possibility is that the antiseptic quality of the parent phenol could be a means of protection against bacterial invasion, by release of the aglycone at infected points. However, in the case of leucodrin it is difficult to envisage such a function, since leucodrin itself is

present in much higher concentration than leucoglycodrin, and therefore it seems more probable that leucoglycodrin is formed at development sites in the plant, where the presence of phenolic compounds may be harmful to anabolism.

It may also be possible that leucoglycodrin is formed as a storage compound for quick release of sugars at some stage in development (11) and it is interesting to note that in our examination of the extractives from Leucadendron adscendens, the presence of the oligosaccharides, sucrose, raffinose and stachyose were tentatively suspected, while the monosaccharides, glucose, arabinose, galactose, mannose, fructose and sedoheptulose were positively identified.

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