TRITERPENE GLYCOSIDES OF PATRINIA SCABIOSOFOLIA; II

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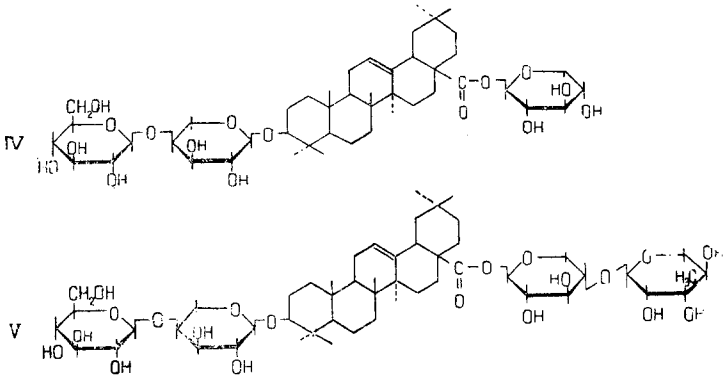
In a preceding communication the isolation of scabiosides A, B, and C from Patrinia scabiosofolia Fisch. et Link. and the establishment of their structure were described [1]. On further separation of the polar fractions, we isolated other glycosides, scabiosides D, E, F, and G, and we have established the structures of the first two of them. These glycosides are derivatives of oleanolic acid.

According to its molecular weight, scabioside D (IV) is a trioside the carbohydrate moiety of which consists of D-glucose, D-xylose, and L-arabinose. The latter form two carbohydrate chains, since when scabioside D is saponified xylose is split off and an acid glycoside is obtained that can be hydrolyzed by mineral acids to oleanolic acid, glucose, and arabinose.

The full methyl ether of scabioside D, synthesized by Kuhn's method [2], decomposes on being heated with hydrochloric acid into 2,3,4,6-tetra-O-methyl-D-glucopyranose, 2,3-di-O-methyl-L-arabopyranose, 2,3,4-tri-O-methyl-D-xylopyranose, and oleanolic acid.

What has been said above, and the results of a comparison of the constants of the acid glycoside and scabioside B [1] show that the structure of the carbohydrate chain of scabioside D attached to the hydroxyl of the genin is completely identical with that of the carbohydrate chain of scabioside B.

As a calculation by Klyne's method [3] shows, a β-glycosidic bond exists between the D-xylopyranose and the carboxyl of the oleanolic acid (table). On the basis of these facts, the complete structure of scabioside D can be shown in the following way:



On acid hydrolysis, scabioside E (V), a tetraoside of oleanolic acid, gives D-glucose, D-xylose, L-arabinose, and L-rhamnose. Just like scabioside D, it is saponified to scabioside B. The permethylated derivative is hydrolyzed by acids to form 2,3,4,6-tetra-O-methyl-D-glucopyranose, 2,3-di-O-methyl-L-arabopyranose, 2,3-di-O-methyl-D-xylopyranose, and 2,3,4-tri-O-methyl-L-rhamnopyranose. Thus, scabioside E is obtained from scabioside D by the addition of a L-rhamnose residue to the D-xylopyranose attached to the carboxyl of the genin, the terminal rhamnose being connected by an α-glycosidic bond (see table). The complete structure of scabioside E is shown in the scheme.

EXPERIMENTAL

Chromatography was carried out on type ASK silica gel and on Schleicher – Schüll No. 2043 paper. The glycosides were revealed either with antimony tri- or pentachloride, or with H_2SO_4. The following systems of solvents were used: 1) ethyl acetate-methanol-water (10 : 2 : 3), 2) butan-1-ol-ethanol-water (5 : 1 : 4 and 4 : 1 : 5), 3) chloroform–ethyl acetate (1 : 1), and 4) butanol–benzene–pyridine–water (5 : 1 : 3 : 3).

Isolation of the individual scabiosides. A 93 g amount of the dry butanolic extract [6] was transferred to a column of silica gel (5.5 × 120 cm) and was eluted with butan-1-ol (fractions 1–17) and then with water-saturated butanol (fractions 18–26), 1 liter fractions being collected.

Table

Glycosides of monosaccharides	$[M]_D$, deg		Glycosides	$[M]_D$ deg	Δc	Form of the bond
	α	β				
Methyl L-rhamnopyranoside [4]	−111	+170	Scabioside E	−115.0		
			Scabioside D	+120.0	−235,3	α
Methyl D-xylopyranoside [5]	+253	−108	Scabioside B[1]	− 52,4	+172,4	β

Fractions 1–7 (28.3 g) contained mainly scabiosides A, B, and C; fractions 8–13 (11.2 g) contained scabiosides D and E; fractions 14–18 (12.3 g) contained scabiosides D, E, and F; fractions 19–24 (15.8 g) contained scabiosides F and G; and fractions 25 and 26 (26 g) contained mainly the reserve sugars.

Fractions 8–13 were deposited on a column of silica gel (4.5 × 50 cm) and eluted with system 1, 100-ml fractions being collected. This gave 2.7 g of scabioside D and 4.3 g of scabioside E. On reseparation in a similar manner, fractions 19–24 gave 4 g of scabioside F and 2.4 g of scabioside G.

Scabioside D. The substance obtained had mp 224–226° C (from methanol–butan-1-ol), $[\alpha]_D^{20}$ +4 ± 3° (6.4; pyridine).

Found, %: C 60.17, 59.92; H 8.34, 8.28. Calculated for $C_{46}H_{74}O_{16} \cdot 2H_2O$, %: C 60.10; H 8.55.

Acid hydrolysis. Three 145-mg samples of scabioside D were heated with 6% HCl for 4 hr. They yielded 78.9, 72.4, and 74.7 mg, respectively, of oleanolic acid.

Found, %: mol wt 840, 926, and 889. Calculated, %: mol wt 883.

Alkaline hydrolysis. A solution of 0.15 g of scabioside D in 10 ml of water was deposited on a column of Dowex 1 × 4 ion-exchange resin (OH^- form) and left for a day. The column was washed with 500 ml of water and 200 ml of methanol containing 3% of acetic acid. The methanolic eluate was evaporated, giving 120 mg of an acid glycoside. After heating in aqueous methanolic solution with 5% hydrochloric acid, D-glucose and L-arabinose were identified by paper chromatography in system 4. The glycoside was identical in respect of its constants [mp 210–212° C; $[\alpha]_D^{20}$ −7° ± 3° (c 5.0; pyridine)] and chromatographic behavior with scabioside B.

Full methyl ether of scabioside D. A mixture of 0.48 g of scabioside D, 10 ml of methyl iodide, 5 g of barium oxide, and 30 ml of dimethylformamide was heated in the water bath for 25 hr. Fresh portions of reagents were added every 5 hr. The completeness of the methylation was checked by thin-layer chromatography in system 3. The reaction mixture was treated with 150 ml of aqueous sodium thiosulfate solution, the methylation product was extracted with 300 ml of chloroform, and the solvent was distilled off. The residue was transferred to a column of silica gel (2 × 30 cm) and eluted with 300 ml of chloroform. This gave 0.23 g of the full methyl ether.

The permethylated product was dissolved in a mixture of 30 ml of methanol and 5 ml of conc HCl and heated in the water bath for 6 hr. Then 15 ml of water was added and heating was continued for another 3 hr. The reaction mixture was diluted with butan-1-ol (30 ml), and the solvent was distilled off in vacuum. The hydrolysate was shown by paper chromatography in system 2 to contain 2, 3, 4, 6-tetra-O-methyl-D-glucopyranose (R_g 1.0) and 2, 3-di-O-methyl-D-xylopyranose (R_g 0.77). By absorption chromatography on silica gel (system 3) the mixture of methylated monosaccharides yielded 10.5 mg of 2, 3, 4-tri-O-methyl-D-xylopyranose (R_g 0.94), $[\alpha]_D^{20}$ +56 ± 3° (1.5; chloroform). Literature data: $[\alpha]_D^{20}$ +55.6° [7].

Scabioside E. The substance obtained had mp 224–227° C (from methanol–butan-1-ol) $[\alpha]_D^{20}$ −11.3 ± 3° (c 5.3; pyridine).

Found, %: C 60.24, 60.13; H 8.36, 8.19. Calculated for $C_{52}H_{86}O_{20}$, %: C 60.60; H 8.40.

Acid hydrolysis. Weighed samples of scabioside E (176.8 and 210 mg) were hydrolyzed with 6% HCl. They yielded 80.7 and 91.0 mg, respectively, of oleanolic acid.

Found, %: mol wt 1000 and 1060. Calculated, %: mol wt 1031.

The hydrolysate was shown by paper chromatography in system 4 to contain D-glucose, D-xylose, L-arabinose, and L-rhamnose.

Alkaline hydrolysis. 184 mg of scabioside E was hydrolyzed on ion-exchange resin as described above, giving 125 mg of scabioside B.

Full methyl ether. A mixture of 0.6 g of scabioside E, 16 ml of methyl iodide, 20 g of barium oxide, and 30 ml of dimethylformamide was heated and treated as described above. The yield of the permethylated product was 0.38 g. It was dissolved in a mixture of 60 ml of methanol and 10 ml of conc HCl and hydrolyzed in the same way as before. The hydrolysate was shown by paper chromatography in system 2 to contain 2,3,4,6-O-methyl-D-glucopyranose (R_g 1.0), 2,3-di-O-methyl-D-xylopyranose (R_g 0.77), and 2,3-di-O-methyl-L-arabopyranose (R_g 0.64). By absorption chromatography on silica gel as described above, the hydrolysate yielded 25 mg of 2,3,4-tri-O-methyl-L-rhamnopyranose (R_g 1.07), $[\alpha]_D^{20}$ +25 ± 3° (c 2.5; water). Literature data: $[\alpha]_D^{20}$ +25.9° [8].

CONCLUSIONS

The triterpene glycosides scabiosides D, E, F, and G have been isolated from the roots of Patrinia scabiosofolia Fisch. et Link. It has been established that scabioside D is O-β-D-glucopyranosyl-(1 → 4)-O-α-L-arabopyranosyl-(1 → 3)-O-oleanoloyl-(28 → 1)-β-D-xylopyranose, and scabioside E is O-β-D-glucopyranosyl-(1 → 4)-O-α-L-arabopyranosyl-(1 → 3)-O-oleanoloyl-(28 → 1)-O-β-D-xylopyranosyl-(4 → 1)-α-L-rhamnopyranose.

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