TRITERPENE GLYCOSIDES OF Astragalus AND THEIR GENINS.

XXIX. CYCLOARTANES OF Astragalus kuhitangi

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Continuing a study of cycloartane methylsteroids and their glycosides from plants of the genus Astragalus (Leguminosae), we have investigated the epigeal part of A. kuhitangi (Nevski) Sirj., collected in July 1986, in the flood plain of the R. Tupalang (Uzbek SSR, Hissar range). The comminuted lignified branches several years old with their cores (4.5 kg) were exhaustively extracted with methanol (4 × 16 liters). The methanolic extract was evaporated to a viscous consistency and was diluted with 2 liters of water. The precipitate that deposited was filtered off. It did not contain the substances sought. The filtrate was treated with butanol. The butanolic extract was evaporated to dryness, giving 237 g of combined triterpenoids. Part of this material (150 g) was chromatographed on a column of type KSK silica gel with successive elution by chloroform in the following solvent systems: 1) chloroform–ethanol (20:1) and 2) chloroform–methanol–water (70:12:1) (a) and (70:23:4) (b). Four compounds were isolated which were designated in order of increasing polarity as substances (1)-(4).

Elution by system 1 gave 200 mg of substance (1) (0.007%; the yield here and below is calculated on the air-dry raw material), mp 239-241°C (from methanol), $[\alpha]_D^{23}$ +50 ± 2° (c 1.2; methanol), which was identified as cycloseversigenin [1, 2].

Elution of the column with system 2a gave 29 g (1%) of substance (2) and 1.4 g (0.049%) of substance (3).

Substance (2), mp 280-284°C (from methanol), $[\alpha]_D^{23}$ +28.5 ± 2° (c 0.49; methanol), was identified as cyclosieversioside F [2, 3].

Substance (3), mp 292-293°C (from methanol), $[\alpha]_D^{21}$ +9 ± 2° (c 0.9; pyridine) was identified as cyclocanthoside D [4].

The fractions collected when the column was eluted with system 2b yielded 5.5 g (0.19%) of substance (4), mp 272-273°C (from methanol), $[\alpha]_D^{23}$ −8 ± 2° (c 0.73; pyridine). Compound (4) was a glycoside containing, according to GLC, D-glucose and D-xylose residues in a ratio of 2:1. The Smith degradation [5] of glycoside (4) (200 mg) gave 60 mg of cyclosieversigenin.

The trioside (4) (400 mg) was subjected to partial hydrolysis in 20 ml of a 0.25% methanolic solution of sulfuric acid at 70°C. After the working up of the reaction mixture and chromatography of the reaction products on a column in systems 1 and 2a, 10 mg of cyclosieversigenin, 8 mg of cyclosieversigenin 3-O-β-D-xylopyranoside, mp 263-265°C (from methanol), $[\alpha]_D^{24}$ +41.5 ± 2° (c 0.5; methanol), 27 mg of amorphous cyclosieversigenin 6-O-β-glucopyranoside, $[\alpha]_D^{23}$ +46.6 ± 2° (c 0.6; methanol) [2, 3], and 34 mg of cyclosieversioside F were isolated.

Thus, substance (4) was a derivative of cyclosieversioside F and differed from it by the presence of an additional D-glucose residue. The anomeric proton of the latter gave a signal in the PMR spectrum at 4.88 ppm in the form of a doublet with the SSCC ^3J = 8 Hz. Consequently, this D-glucose residue was also attached by a β-bond. The position of the D-glucose residue under consideration followed unambiguously from the ^{13}C NMR spectrum of trioside (4).

The chemical shift of the anomeric carbon atom of the second D-glucose residue (98.67 ppm) showed that it was attached to tertiary hydroxy group [7]. In actual fact, the C-25

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atom of the genin underwent the effect of glycosylation and resonated at 78.66 ppm. The other carbon atoms of the D-glucose residue under consideration resonated at (ppm): 74.92 (C-2), 78.28 (C-3), 71.26 (C-4), 77.68 (C-5), and 62.97 (C-6).

The facts presented determined substance (4) as 20R,24S-epoxycycloartane-3β,6α,25-tetraol 6,25-di-O-β-D-glucopyranoside 3-O-β-D-xylopyranoside. Astragalaoside VII isolated from Astragalus membranaceus Bunge has an identical structure [8].

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LINK BETWEEN CHEMICAL STRUCTURE AND MEMBRANOTROPIC ACTIVITY OF GLYCOSIDES OF BETULAFOLIENETRIOL AND ITS 3-EPIMER

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Triterpene glycosides of ginseng are attracting the attention of research workers by the unique nature of their medicobiological action [1]. Analogs of ginseng glycosides have been synthesized from betulafolienetriol, isolated from the leaves of Far Eastern birches, and its 3-epimer – 20(S)-protopanaxadiol [2]. We have studied the membranotropic activity of ginsenoside Rb_1, isolated from ginseng roots, and its synthetic analogs.

Experiments on bilayer lipid membranes were performed by a method described previously [3], except that in place of α-monoolein we used Span-80 (Loba-Chemie). The results (Fig. 1) showed that ginsenoside Rb_1 (I), the molecule of which contains two glycosidic residues, at C-3 and C-20, exerts a destabilizing action on a lipid bilayer. The presence of cholesterol in the membrane decreases the efficacy of the action of the glycoside. With a decrease in the number of glycoside residues in the glycoside molecules, their activity rises. The most active glycoside was (VIII), in which a glucose residue is attached to the aglycon at C-3. It was approximately 20 times more active than glucoside (I). The configuration (α or β) of the 3-OH group had no appreciable influence on the membranotropic activity of the glycosides in relation to a lipid bilayer. The introduction of cholesterol into the membrane substantially decreased the efficacy of the action of the ginsenoside Rb_1 (I) and its synthetic analogs – glycosides of 3-epibetulafolienediol (II, IV, VI, and VIII), while the efficacy of the glycosides on betulafolienetriol (III, V, VII, and IX) rose substantially. The results obtained on model lipid membranes correlate with those for biological activity.

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