THE STRUCTURE OF VERALOSINE

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We have previously isolated new bases (veralosine, veralosinine, and veralosidine) from the epigeal part of Veratrum lobelianum and have proposed a structure and configuration for veralosidine [1].

Veralosine, $C_{35}H_{55}O_8N$ (I), forms a crystalline hydrochloride and an acetyl derivative. It is known [1] that the IR spectrum of I has absorption bands at (cm^{-1}) 3450 (OH), 2900, 1460 (CH_3), 1725 (C=O of an ester), 1660 (> C=N−), and 1000–1100 (broad absorption band characteristic for glycoalkaloids), and the UV spectrum [λ_{max} 245 mμ (log ε 2.20)] is similar to those of verazine and veralosidine [1, 2].

Veralosine was hydrolyzed in 10% HCl in the presence of ethanol (1 : 1). By separation on a column of silica gel, the hydrolysis products yielded an aglycone identical with respect to mixed melting point and IR and UV spectra with veralosidine [1], and a base A.

The IR spectrum of the base A (II) exhibited absorption bands at (cm^{-1}) 3400 (OH), 2935, 1450 (CH_3), 1650 (> C=N−), and 1000–1100 (broad absorption band for glycoalkaloids), but lacks the band for a carbonyl group; UV spectrum: λ_{max} 242 mμ (log ε 2.45).

When veralosidine and base A had been isolated, a neutral substance was obtained which gave the silver mirror reaction characteristic of aldoses. On paper chromatography the neutral substance had the same R_f value as D-glucose. In addition, the osazone from the neutral substance was identical with a known sample of D-glucose osazone.

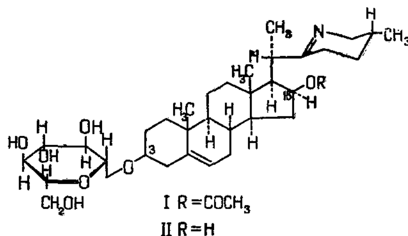
The saponification of veralosine in 5% ethanolic alkali yielded crystals with mp 229–231° C identical with base A. The alkaline solution was acidified with H_2SO_4 and extracted with ether. In the ethereal residue acetic acid was detected by paper chromatography.

The acetylation of veralosine with acetic anhydride in pyridine led to the formation of an acetyl derivative identical with the acetyl derivative of base A. Consequently base A is desacetylveralosine.

In the veralosine molecule, the D-glucose residue is present on carbon atom 3, since base A does not give a digitonide. The hydroxyl at C_3 is a glycosidic hydroxyl group [3–5]. Consequently, in the molecule of veralosine, the acetyl group is located at C_{16}.

A comparison of molecular rotations showed that, according to Klyne's rule [6], in veralosidine* the D-glucose is attached by a β-glycosidic bond. Hence, in veralosine (I), also, the D-glucose is attached to 16-acetylveralosidine by a β-glycosidic bond.

On the basis of the above facts, veralosine has the structure of 16-acetyl-3β-O-D-glucopyranosylveralosidine.



*Sic. Probably base A is meant [Translator].

EXPERIMENTAL

For thin-layer chromatography (TLC) we used KSK silica gel (10 mμ) and the following solvent systems: 1) chloroform–ethanol (9 : 1), 2) chloroform–ethanol (3 : 2), and 3) chloroform–ethyl acetate–methanol (4 : 4 : 3). The developer was Dragendorff's solution. The IR spectra were taken on a UR-10 double-beam spectrophotometer (molded tablets with KBr), and the UV spectra on an SF-4 spectrophotometer (ethanolic solutions).

Veralosine hydrochloride. When mixed with an ethanolic solution of HCl, an ethanolic solution of veralosine formed a hydrochloride with mp 221–222° C [ethanol–acetone (1 : 2)].

Hydrolysis of veralosine. A mixture of 6.3 g of veralosine, 320 ml of ethanol, and 320 ml of 10% HCl solution was boiled for 4 hr. After the elimination of the ethanol, the acid solution was made alkaline with sodium carbonate and extracted with chloroform. This gave 4.9 g of a mixture of the aglycone and base A.

Aglycone and base A. The mixture of aglycone and base A (4.9 g) was passed through a column filled with silica gel (150 g, 31-mμ sieve). It was eluted with 1100 ml of a chloroform–ethanol mixture (9 : 1). The first 400 ml of eluate yielded the aglycone, veralosidine (0.73 g) with mp 153–155° C [from methanol–acetone (1 : 3)], $[\alpha]_D^{26}$ −92.2° (c 0.466, ethanol), R_f 0.25 on TLC in system 1, identical with veralosidine according to a mixed melting point and UV and IR spectra. Then it was eluted with a chloroform–ethanol mixture (3 : 2). The eluate, 300 ml, yielded base A (0.86 g) with mp 229–231° C [from ethanol–acetone (1 : 1)], $[\alpha]_D^{26}$ −115.7° (c 0.432, ethanol), R_f 0.45 on TLC in system 2.

The alkaline solution after the removal of the aglycone and base A was neutralized with 5% H_2SO_4 and evaporated to dryness, and the residue was treated with absolute ethanol. The ethanolic solution was separated from the inorganic substances and evaporated in vacuo. This gave an oily neutral product which on ascending paper chromatography (Leningrad, slow) with a D-glucose marker in the acetone–butan-1-ol–water (7 : 2 : 1) system showed a spot with the same R_f value, 0.29; time of chromatography, 15 hr; developer, o-toluidine.

Osazone. A mixture of 4 ml of an aqueous solution of the neutral product, 0.16 g of phenylhydrazine hydrochloride, and 0.27 g of sodium acetate was heated in a water bath for 1 hr. The crystals that deposited, after recrystallization from ethanol, had mp 207–208° C. A mixed melting point test with D-glucose osazone gave no depression.

Saponification of veralosine. A solution of 0.10 g of veralosine in 10 ml of 5% ethanolic caustic potash was heated for 3 hr. The ethanol was driven off and the residue was diluted with water and extracted with chloroform. The substance obtained after the distillation of the chloroform (0.09 g) was recrystallized from an ethanol–acetone mixture (1 : 1), mp 229–231° C, R_f 0.45 on TLC in system 2. A mixture of the crystals with base A melted at 229–231° C.

The alkaline solution after the removal of the crystals was acidified with 1% H_2SO_4, extracted with ether, and the extract was made alakaline with ammonia and evaporated. The ethereal residue was chromatographed on paper (Leningrad, slow) for 15 hr with an acetic acid marker by the ascending method in butan-1-ol saturated with 1.5 N aqueous ammonia. The ethereal residue and the acetic acid had the same R_f value. The developer was an ethanolic solution of Bromophenol Blue.

Acetylation of veralosine. A mixture of 0.51 g of veralosine, 5 ml of pyridine, and 5 ml of acetic anhydride was kept at room temperature for 2 days. After elimination of the pyridine and the addition of 5% H_2SO_4 to the solution, the acetylation product was extracted with ether. The ethereal extract was made alkaline with ammonia and then washed repeatedly with water. The residue, after the ether had been distilled off, deposited acetylveralosine (0.68 g) with mp 248–250° C (from methanol), R_f 0.73 on TLC in system 3.

Acetylation of base A. Base A (0.30 g) was acetylated with acetic anhydride (3 ml) in pyridine (3 ml) in a manner similar to the acetylation of veralosine. This gave 0.46 g of acetyl-base A with mp 248–250° C (from methanol), R_f 0.73 on TLC in system 3.

CONCLUSIONS

Results of a study of the chemical and physical properties of the hydrolysis products of veralosine show that its most probable structure and configuration is 16-acetyl-3β-O-D-glucopyranosylveralosidine.