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ISOLATION OF SAIKOGENIN F, ANOTHER GENUINE SAPOGENIN FROM BUPLEURUM FALCATUM L.

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Previously, we have described (1) that acid hydrolysis of the crude saponin obtained from the root of Bupleurum falcatum L. afforded saikogenins A (I), isolation of which was first reported by Shibata et al. (2), B (II), C (III) and D (IV) and longispinogenin. Recently, Aimi and Shibata (3) and the present authors (4) independently succeeded in isolating saikogenin E (V), a genuine sapogenin corresponding to saikogenins C (III) and B (II). We wish now to describe isolation of another sapogenin, named saikogenin F (VI), which is shown to be a genuine sapogenin corresponding to saikogenin A (I).

The crude saponin consists of three main fractions, which seem to be equivalent to, in order of chromatographic mobility, saikosides Ia, Ib and II* named by Shibata et al. (2). Saikogenin E (V) has been obtained from the saikoside II fraction (3,4). Shibata et al. (2) have previously reported that both saikosides Ia and Ib showed strong UV absorption at 242, 251 and 260 mμ characteristic of a heteroannular diene. However, in our determination, only the Ib fraction shows the strong absorption and

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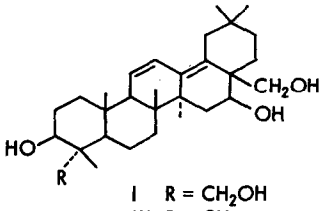
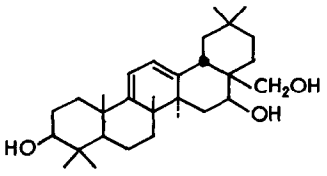
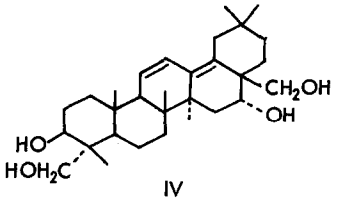
* Although Shibata et al. have described (2) that saikogenin A (I) was obtained from acid hydrolysis of both saikosides Ia and Ib, it was indicated in a private communication from Prof. Shibata that saikoside Ia gave saikogenin A (I), but that saikoside Ib afforded saikogenin D (IV). Their amended results were traced by us.



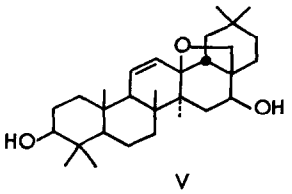
I R = CH_2OH
III R = CH_3



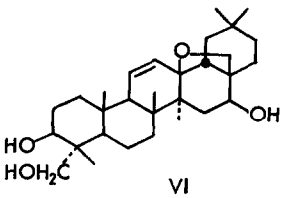
II



IV



V



VI

the Ia fraction exhibits only a very weak absorption at those region in comparison with that at 205 mμ.

The Ia fraction is subjected to the reaction sequence, which was successful for the isolation of saikogenin E (V) (4). The product which is obtained by oxidation with sodium metaperiodate followed by treatment with ethanolic KOH is shown to be much more polar than saikogenin A (I) on thin layer chromatography. Its analytical value, $C_{36}H_{58}O_9$, indicates that the product still has a hexose in addition to the expected aglycone through partial degradation of the saponin. Although the structure of the saponin is not elucidated yet, the above results suggest that, in the saponin, a sugar

molecule linked to an aglycone has no vicinal glycol owing to linkages with additional sugar molecules. The remaining sugar molecule in the product should now have a vicinal glycol through release from the linkages with the adjoining sugar molecules and should be cleft with periodate. The intermediate is again treated with sodium metaperiodate, which is consumed as expected. Treatment of the oxidation product with boiling ethanolic KOH gives saikogenin F (VI), which on recrystallization from chloroform is obtained as plates combined with chloroform, $C_{30}H_{48}O_4 \cdot \frac{1}{2} CHCl_3$, m.p. 265-273°, $[\alpha]_D$ +95.7° (+107.8° on calculation as $CHCl_3$-free). The combined chloroform is not lost by heating in vacuo at 100° for 5 hrs. Saikogenin F (VI) on the UV spectrum shows no absorption except at 205 mμ and its IR spectrum (Nujol) exhibits a broad hydroxyl absorption, and sharp bands at 977, 904 and 884 cm^{-1} indicative of an oxide linkage and at 763 and 754 cm^{-1} due to $CHCl_3$.

Mild acetylation of VI affords the triacetate, $C_{36}H_{54}O_7$, m.p. 205-208.5°, $[\alpha]_D$ +109.6°, which displays no hydroxyl band in the IR spectrum. Its NMR spectrum (60 Mc, in $CDCl_3$) shows signals at τ 9.17-8.88 (6 Me), 7.98 and 7.94 (1 Me and 2 Me, respectively, of acetoxy groups), 6.80 and 6.01 (CH_2 at C_{28} being involved in the ether bridge; AB quartet, J=7.5 cps, with small split in the former signal), 6.22 (CH_2 of CH_2OAc at C_{23}; singlet), 5.22 and 4.55 (1H each at C_3 and C_{16} bearing the acetoxy groups; two quartets), and 4.56 and 4.12 (2H of the two-substituted double bond at Δ^{11}; AB quartet, J=10 cps, with small splits in each of the signals).

Since saikogenin F (VI) on heating with H_2SO_4 in aqueous ethanol readily affords saikogenin A (I), the former (VI) is shown to be the genuine sapogenin corresponding to the latter (I), which has been obtained as a major sapogenin of this plant (1,2). From the above-mentioned results, the structure of saikogenin F has now been established as 13β:28-epoxyolean-11-ene-3β,16β,23-triol (VI), in connection with the

structure of saikogenin A (I) and with the correlation (4) between saikogenins C (III) and E (V).

On the other hand, the saikoside Ib fraction exhibits a strong UV absorption due to the conjugated diene, as already mentioned, and even on treatment with the same procedure which yielded saikogenin F (VI) affords saikogenin D (IV). From these facts, it is supposed that saikogenin D (IV) itself exists as a genuine sapogenin in the plant, but it should be noted that an imaginative genuine sapogenin corresponding to IV may be so unstable, owing to its axial hydroxy group at C_{16}, that it might be transformed during extraction from the plant. The fact that the repeated treatments of the periodate-alkali sequence are required for isolation of saikogenins F (VI) and D (IV) suggests that the saikosides Ia and Ib may contain the same type of a sugar moiety branched at sugar molecules linked to the aglycones.

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