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# THE STRUCTURE OF PANAXADIOL

## A SAPOGENIN OF GINSENG

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THE roots of Panax ginseng C.A. Mey. is well-known as a Chinese drug which is widely employed as a tonic and other remedies.

Since earlier times, numerous studies have been reported concerning with the principles of Ginseng roots, nevertheless any available evidences have not yet been given for the chemical structure. The existence of a saponin, named panaquilon, in North American Ginseng roots (Panax quinquefolium L.) was reported by Garriques,[1] and the isolation of saponin as well as sapogenin from Ginseng roots of Japanese and Korean origin was reported by some Japanese workers.[2-6]

We have now obtained a crystalline sapogenin named panaxadiol from saponin of Ginseng roots. The same sapogenin has been isolated, though in a lower yield, from the roots of Panax japonicus C.A. Mey.(: P. ginseng

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C.A. Mey. var. japonicum Makino).

Panaxadiol (I), m.p. 250°, $[\alpha]_D^{18.5}$ +1.0° (c: 1.02, chloroform), is represented by the formula, $C_{30}H_{52}O_3$ (Found: C, 78.22; H, 11.32. Calc. for $C_{30}H_{52}O_3$: C, 78.20; H, 11.38) having two hydroxyls, one inactive oxygen, and no double bond. On acetylation with acetic anhydride and pyridine, only one of the hydroxyls of panaxadiol was acetylated to give monoacetate (II), m.p. 215°, $[\alpha]_D^{19}$ +12.0° (c: 1.37, chloroform), (Found: C, 76.35; H, 10.76. Calc. for $C_{32}H_{54}O_4$: C, 76.44; H, 10.83). The oxidation of the monoacetate (II) with chromic acid afforded a ketonic compound, panaxanolone acetate (III), m.p. 172°, $[\alpha]_D^{19}$ +57.0° (c: 1.39, chloroform), I.R. $\nu_{max}^{CS_2}$ $cm^{-1}$:1743 ($CH_3CO$); 1720 (six-membered ring C=O), (Found: C, 76.35; H, 10.40. Calc. for $C_{32}H_{52}O_4$: C, 76.75; H, 10.47). The Wolff-Kishner reduction modified by Barton[7] converted panaxanolone acetate (III) into a deacetyl-deoxo-compound, panaxanol (IV), m.p. 154°, $[\alpha]_D^{20}$ +18.2° (c: 1.10, chloroform), (Found: C, 80.91; H, 11.41. Calc. for $C_{30}H_{52}O_2$: C, 81.02; H, 11.79). Monoacetate, m.p. 198°, (Found: C, 79.19; H, 11.20. Calc. for $C_{32}H_{54}O_3$: C, 78.96; H, 11.18).

The inactive oxygen in the molecule of panaxadiol (I) which is retained in the compounds II, III and IV was shown to be present as an ether linkage by the infra-red absorption maxima at 1112-1122 and 1066-1067 $cm^{-1}$ (KBr or Nujol). The characteristic infra-red absorption bands of ether linkage disappeared when the compound IV was treated with hydrochloric acid in glacial acetic acid.

The resulted O-acetyl compound (V), m.p. 100° (Found: C, 81.98; H, 11.07. Calc. for $C_{32}H_{52}O_2$: C, 81.99; H, 11.18) was hydrolysed with methanolic potash to give anhydropanaxanol (VI), m.p. 141°-144° (Found: C, 83.86; H, 11.54. Calc. for $C_{30}H_{50}O$: C, 84.44; H, 11.81).

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A close similarity of the structure of VI and isotirucallenol[8,9,10] was suggested by the infra-red spectra with a slight difference at 885 $cm^{-1}$ band (KBr) that was given by the former suggesting the presence of vinyl group in the end of side chain.

The catalytic hydrogenation of V and VI resulted isotirucallenyl acetate (VII), and isotirucallenol (VIII), respectively, which was proved by the mixed fusion and the comparison of infra-red spectra as well as by the gas chromatogram developed on the silicone polymer SE-30 and QF-1.

Thus panaxadiol was formulated as (I), and the above reactions are illustrated by the scheme (I-VIII).

The hindered hydroxyl in panaxadiol was suggested to be at C-12 by the formation of an αβ-unsaturated ketonic compound (IX)* [U.V. $\lambda_{max}^{EtOH}$: 267.5 mμ, log ε 3.85; I.R. $\overset{CS_2}{\underset{max}{}}$ $cm^{-1}$: 1737 ($CH_3CO$); 1677 (C=O); 1608 (double bond)] from panaxanolone acetate (III) by the action of sulphuric acid in acetic acid.

The mass spectrum of panaxadiol (I) showed m/e 127 as a base peak which would correspond to the fragment (X), and the peak m/e 341 must be the fragment (XI). The parent peak appeared at 460 showed that the molecular formula of panaxadiol, $C_{30}H_{52}O_3$ (Calc. mol. wt.: 460), is correct.

Panaxadiol (I) has now been shown as being a tetracyclic triterpene of dammarane series having a characteristic trimethyltetrahydropyrane ring at C-17. The configurations at C-12, C-13, C-17 and C-20 are being studied.

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* An analogous structure of 12-keto-$\Delta^{13(17)}$ has been shown in betulafolien (13,17)-dione(3,12) giving U.V. $\lambda_{max}^{CS_2}$: 265 mμ, log ε 3.88 [F.G. Fischer and N. Seiler, Liebigs Ann. 626, 185 (1959); cf. Ibid. 644, 162 (1961)].

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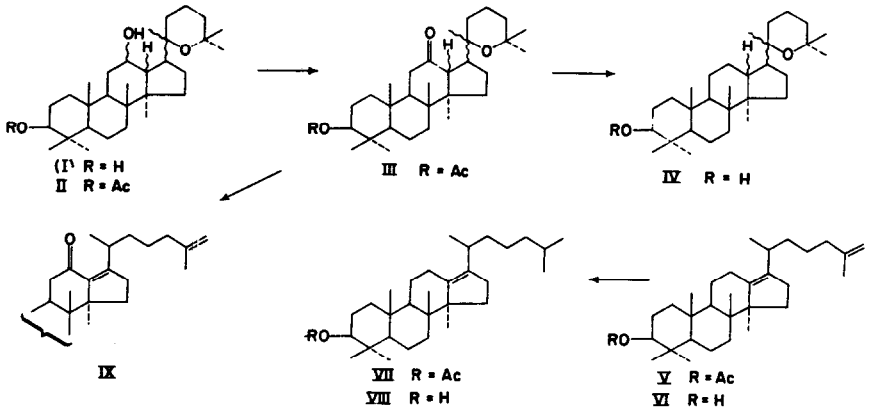


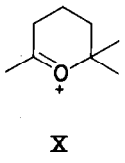
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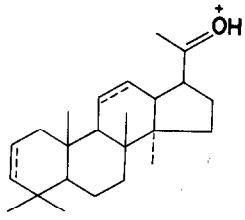

XI

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