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THE STRUCTURE AND ABSOLUTE CONFIGURATION OF SODOPONIN AND EPINODOSINOL, NEW MINOR DITERPENOIDS OF ISODON JAPONICUS

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We had isolated enmein[1], enmein-3-acetate[1], isodocarpin[2a,2b], nodosin[2a,3], isodotricin[2a], ponicidin[2a], and oridonin[4] from the dried leaves of Isodon japonicus Hara ("Hikiokoshi"), and clarified their structures except ponicidin.

Now, we isolated the other four components from the same plant source, two of which were shown to be identical with isodonal[5] and epinodosin[6]. The other two minor components were new diterpenoids and named sodoponin and epinodosinol.

Sodoponin [$C_{22}H_{32}O_7$, M^+ 408, m.p. 229 ∿ 231.5°, $[\alpha]_D^{28}$ + 45.7° (c,1 ; pyridine)] was indicated to possess three secondary hydroxy-, a tertiary hydroxy-, a secondary acetoxy-, an ether-type methylene, an exocyclic methylene, and two tertiary methyl groups, by the spectroscopic data. Consideration of the fact that sodoponin contains neither a five-membered ring hemiacetal nor a δ-lactone, but does bear a tertiary hydroxy-group, together with the number of site of unsaturation and biogenesis led to an assumption that it may have a kaurene-type 7-hemiketal structure I.

Figure 1 shows the NMR spectrum (100MHz) of sodoponin and spin-spin decouplings. The protons Ha, Hb, Hc, and He were shown to be hydroxy protons. The protons Hi and Hj can be assigned to C-20 methylene protons, which allows the assignment of Hn to C-9 proton, because of its long-range coupling to Hj. The Hd quartet was assigned to a proton on the acetoxylated carbon from its

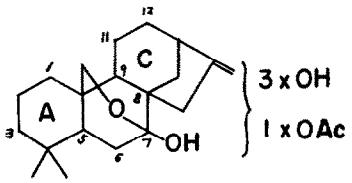
chemical shift and it was shown to be coupled to Hn and Hm by decoupling experiments. Consequently, the acetoxy-group was found to be located in C-11, and Hm is located in C-12. Consideration of the coupling constant (J = 9, 9, and 9 Hz) of Hd quartet and the boat form of the C-ring in the skeleton I led to the quasi-equatorial conformation of the acetoxy-group. Then, the relationship among protons Hm, Ho, and Hp was checked by irradiations, and now the C-ring moiety can be shown as A.

On the basis of comparison of NMR of sodoponin with those of oridonin and trichokaurin[7], OHa was assigned to β-oriented group at C-6, OHc to β at C-15, and OHe to α at C-1. Thus, structure II was proposed for sodoponin.

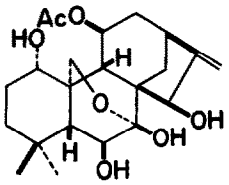
Now, sodoponin was treated with 15% methanolic hydrochloric acid to give a ketone III, $C_{20}H_{30}O_6$ (M^+ 366.205), m.p. 227 ∿ 231° [ν_{max}(KBr) : 3320 and 1715 cm^{-1}], by Garryfoline-Cuauchichicine rearrangement[7,8] accompanied by hydrolysis. The compound was allowed to react with metaperiodate in acetic acid to yield a hemiacetal lactone, $C_{20}H_{28}O_6$ (M^+-H_2O 346.176), m.p. 227 ∿ 232° [ν_{max}(KBr) : 3380, 3320, 1760, and 1720 cm^{-1}], which was proved to be identical with epinodosin dihydro-derivative IV[6], m.p. 229 ∿ 231°. Thus, the structure and absolute configuration of sodoponin were chemically confirmed as II.

Epinodosinol [$C_{20}H_{28}O_6$ (M^+ 364.188), m.p. 244 ∿ 247° (263 ∿ 265°), $[\alpha]_D^{28}$ -87.5° (c,1 ; pyridine)] has two tertiary methyl, two secondary hydroxy-groups, an exocyclic methylene, a five-membered ring hemiacetal, and a δ-lactone, as supported by spectroscopic data. The mass spectrum gave a strong fragment peak at m/e 149 assignable to V. In addition, the NMR* and IR spectra are very similar to those of epinodosin tetrahydro-derivative (VI), except signals of C-15 proton [δ : 5.45 ppm (1H, d, J = 11 Hz)] and C-16 methyl protons [δ : 1.18 ppm (3H, d, J = 7 Hz)]. Epinodosinol on hydrogenation over Adams' catalyst gave a dihydro-derivative, m.p. 243 ∿ 245° [$C_{20}H_{30}O_6$ (M^+ 366.205), ν_{max}(KBr) : 3340, 3200, and 1710 cm^{-1}], and a ketone, m.p. 228 ∿ 232° [$C_{20}H_{28}O_6$ (M^+ 364.187), ν_{max} (KBr) : 3380, 3320, 1760, and 1720 cm^{-1}]. The former proved to be identical with epinodosin tetrahydro-derivative (VI), m.p. 242 ∿ 246° [$C_{20}H_{30}O_6$ (M^+ 366.206), ν_{max}(KBr) : 3340, 3200, and 1710 cm^{-1}].

* Taken for solutions in D_5-pyridine on a Varian A-60 spectrometer.



(I)



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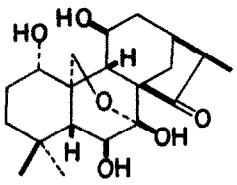

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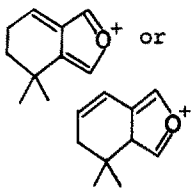
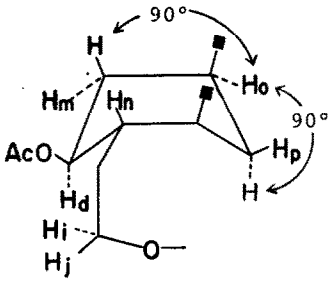
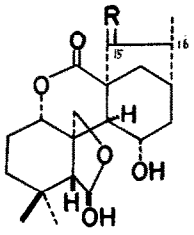


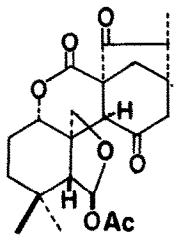
(V)



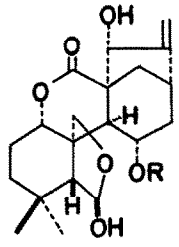
(A)



(IV) R=O
(VI) R=α-OH,βH



(VII)



(VIII) R=H
(IX) R=Ac

On the other hand, the known diketolactone acetate VII[3] derived from nodosin, on reduction with $NaBH_4$ in isopropyl alcohol, also gave epinodosin tetrahydro-derivative (VI). The cis-relationship between C-15 OH and C-16

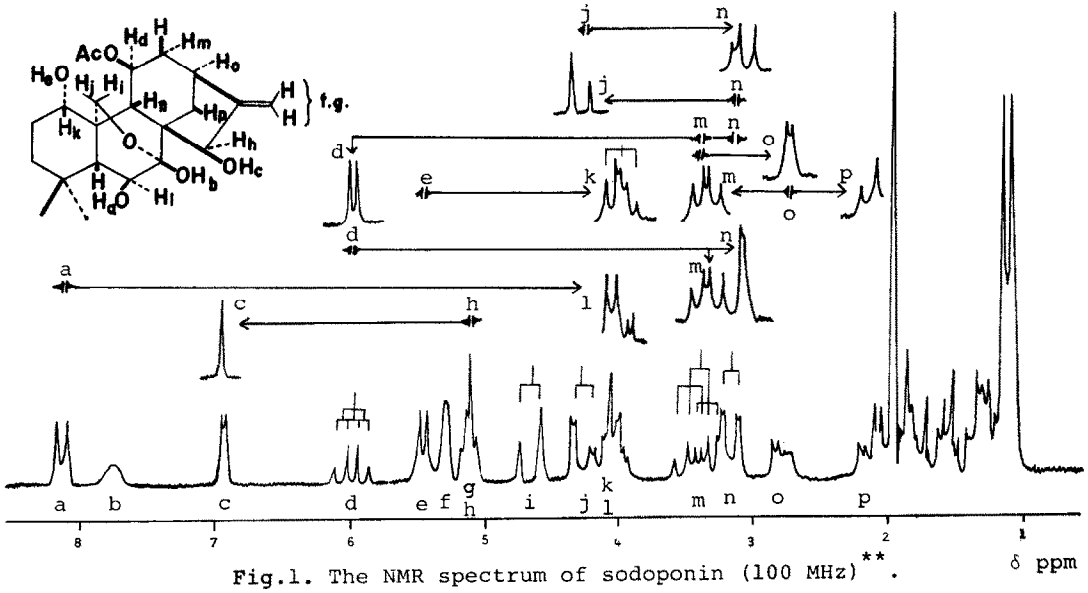


Fig.1. The NMR spectrum of sodoponin (100 MHz)**.

** Taken for solutions in D_5-pyridine with TMS as an internal standard on a Varian HA-100 spectrometer.

methyl groups in VI was recognized from C-15 PMR* [δ : 5.45 ppm (1H, d, J = 11 Hz)]. On the basis of the established C-16 methyl group of VII[3], the absolute configurations of C-16 methyl and C-15 OH groups of VI, and hence, that of C-15 OH of epinodosinol are established.

The foregoing ketone proved to be epinodosin dihydro-derivative IV[6]. It seemed to be formed by Garryfoline-Cuauchichicine rearrangement[8] during hydrogenation.

An exhaustive evidence was provided by the following chemical conversion. Sodoponin (II) was treated with metaperiodate in acetic acid to give a lactone hemiacetal IX, m.p. 230 ∿ 241° [ν_{max}(KBr) : 3380, 3320, 1718, 1693, and 1280 cm^{-1}], which was hydrolyzed in methanol with aqueous potassium carbonate to afford a crystalline product VIII, m.p. 242 ∿ 246° [$C_{20}H_{28}O_6$ (M^+ 364.190), ν_{max}(KBr) : 3400, 3230, 1715, 1663, and 890 cm^{-1}]. The complete identity of the latter with epinodosinol was indicated by direct comparison of both substances.

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