Notes

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Studies on Saponin-bearing Drugs. III.[*3] Sapogenins of Domestic Senega and Polygala, a Chinese Drug "Yuan chi" (遠志).

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It is pointed out that there are two species of the botanical origin of senega, one of which is *Polygala senega* L. and the other is its variety, var. *latifolia* TORR. *et* GRAY.[1] The foreign senega (I) has its origin in the root of the former, while the latter is cultivated in Japan for supplying the domestic drug (II). In addition to them, it is said that a Chinese drug, "Yuan chi" (遠志) (III) originates in *P. tenuifolia* WILLD. All the saponin-bearing drugs are popularly used as expectorant in Japan. However, no investigations have been made on the saponin behaviour of (II), and also the structure of sapogenins obtained from (I) and (II) has not yet been clarified.

Quevenne[2] first isolated a saponin from (I) and named senegin and then, Kobert, *et al.*[3] isolated senegin as a neutral saponin and an acidic one named polygalic acid, later it is decided by Dafert and Kalman[4] that it contains solely senegin as the saponin and its hydrolysate yields glucose, methylpentose and arabinose.

Further, Wedekind and Krecke[5] isolated a saponin which gave an endosapogenin, $C_{26}H_{44}O_6$, m.p. 272°, as the hydrolysate named senegenin. Also, the isolation of senegenin was reported by Jacobs and Isler,[6] which corresponds to a formula, $C_{30}H_{46}O_8$ or $C_{30}H_{44}O_8$, m.p. 290~292°, is dibasic, and has one lactone and two hydroxyl groups. Recently, Shamma and Reiff[7] presented a partial structure of senegenin by using the nuclear magnetic resonance spectrum.

On the other hand, Chou, *et al.*[8] isolated tenuigenin A and B from (III), and reported that A has the formula, $C_{27}H_{40}O_3$ and melts at 272°, while B has the formula $C_{30}H_{46}O_8$, m.p. 248°, and both are dibasic and have one lactone and two hydroxyl groups in their molecule.

The present paper concerns with the identification of sapogenins obtained from (II) and (III).

The authors isolated an amorphous saponin from the root of 4-year plant(II), collected at Nagano Prefecture. This compound gives a crystalline sapogenin after hydrolysis and it corresponds with a formula $C_{30}H_{46}O_8$ or $C_{30}H_{44}O_8$, m.p. 274°(decomp.) which affords a diacetyl derivative, m.p. 288°(decomp.) by acetylation, and this indicates the presence of two

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hydroxyl groups in the molecule and also, its infrared absorption spectrum showed the presence of hydroxyl and carboxyl groups.

On the other hand, a sapogenin, $C_{30}H_{46}O_8$, m.p. 274° (decomp.) was obtained from (III). It forms a diacetate, m.p. 288° (decomp.). The sapogenin was confirmed to be identical with the sapogenin obtained from (II) by admixture and by comparison of infrared spectra.

Recently, it was reported on a saponin which was obtained from *Bredemeyera floribunda* WILLD.,[9] which might be considered to be identical with the present one from (II) and (III). This species is closely related with that of a genus, *Polygala* and its crude saponin was first isolated from the root by Wasicky and his co-worker.[10]

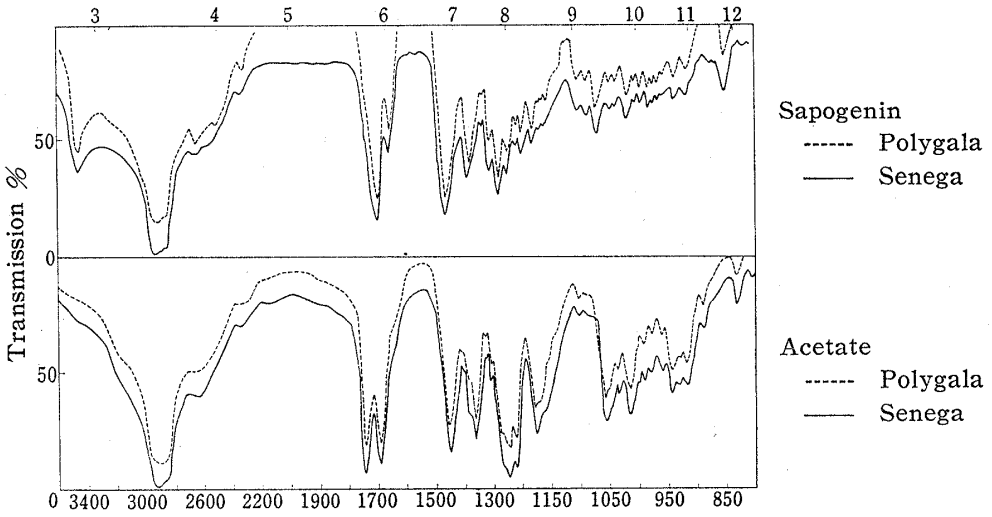

Fig. 1. Infrared Absorption Spectra (in Nujol)

Experimental

Isolation of Saponin from (III)——One kg. of dried powder of (III) was refluxed 3 times with 2 L. of 95% EtOH for 4 hr. and the reaction mixture was filtered while hot. After standing overnight, the combined EtOH filtrates afforded a large amount of precipitate of crude saponin which was filtered out and the mother liquor was concentrated to recover the further amount. The resulting brownish syrup was dissolved in 3% HCl and warmed on a water bath for 15 min., from which crude saponin was deposited. When the combined saponins (IV) were air-dried, the yield was ca. 40 g.

Hydrolysis of Crude Saponin (IV)——One part of (IV) was dissolved in a mixture of 3 parts of 50% EtOH and 2 parts of conc. HCl and then warmed on a water bath for 1 hr., from which an amorphous prosapogenin was obtained, then it was refluxed for 6 hr. with a mixture of 8 parts of 75% EtOH and 2 parts of conc. HCl. After cool, resulting precipitate was filtered and extracted with Et_2O, thus, a crude sapogenin was obtained from the Et_2O soluble fraction. This sapogenin was dissolved in 50% EtOH, treated with active carbon, and the filtrate was evaporated, crystals separated, which were repeatedly recrystallized from 50% EtOH to colorless fine needles, m.p. 274° (decomp.) (V). *Anal.* Calcd. for $C_{30}H_{46}O_8$: C, 67.38; H, 8.67. $C_{30}H_{44}O_8$: C, 67.64; H, 8.58. Found: C, 67.32; H, 8.55. On direct titration, 30 mg. of (V) required 1.11 cc. of 0.1*N* NaOH (indicator, Phenolphthalein). Eqiv. Weight. Calcd. (2-COOH) 267, 266. Found : 269. IR ν_{max}^{Nujol} cm^{-1} : 3415 (-OH), 1690 (=CO of -COOH).

Acetylation of Sapogenin (V)——Three hundred mg. of (V) was refluxed on a water bath for 2 hr. with 3 cc. of glacial AcOH and 0.15 g. of AcONa and therefrom crystals were obtained, collected which on recystallization from Et_2O by usual procedure gave colorless fine plates, m.p. 288° (decomp.) (VI). *Anal.* Calcd. for $C_{30}H_{46}O_8(CH_2CO)_2$: C, 65.99; H, 8.14. $C_{30}H_{44}O_8(CH_2CO)_2$: C, 66.21; H, 7.85. Found : C, 65.77; H, 7.92. When titrated with alkali, 30 mg. of (VI) required 0.95 cc. of 0.1*N* NaOH

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(indicator, Phenolphthalein). Eqiv. Weight Calcd.: (2 COOH) 309, 308. Found: 313. IR ν_{max}^{Nujol} cm^{-1}: 1753 (ester), 1701 (=CO of -COOH).

Isolation and Determination of Sapogenin from (II)——Crude saponin was obtained from 700 g. of (II), from which above-mentioned sapogenin and its diacetate were prepared by the same way as in the case of (III). This sapogenin was identified with (V).

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Summary

Comparative studies were made on the chemical nature of the sapogenins obtained by hydrolysis of two kinds of the saponins isolated from the roots of *Polygala senega* var. *latifolia* et *P. tenuifolia*. As the results, it was confirmed that the sapogenin of the former is completely identical with that of the latter and it is possible consider that both the compounds are the same as one of those obtained by Tschesche and Gupta from a Polygalaceous plant, *Bredemeyera floribunda*.

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Raymond N. Castle[*1] and Masayuki Onda[*2]: Cinnoline Chemistry. VIII. α-(ω-Dialkylaminoalkyl)-α-phenyl-4-cinnolineacetonitriles and Related Compounds.[1,2]

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The purpose of the present investigation was the synthesis of a variety of α-(ω-dialkylaminoalkyl)-α-phenyl-4-cinnolineacetonitriles and 4-[(1-phenyl-ω-dialkylamino)-alkyl]cinnotines for pharmacological screening.

The methods of Cutler, Surrey and Cloke[3] were used in the present work with some modification. Phenylacetonitrile (I) was alkylated with the ω-dialkylaminoalkyl halide (II) in dry benzene solution using sodium amide as the base to form the reactive carbanion. All of the (ω-dialkylaminoalkyl)phenylacetonitriles (III) that have not previously been reported in the literature are recorded in Table I. These were identified and analyzed as the picrates.

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2) The authors are grateful to Dr. S. Yamada and Dr. K. Abe of Tanabe Seiyaku Company, Ltd., Tokyo, for the carbon, hydrogen and nitrogen analyses.

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