The Sapogenins of the Chinese Drug, Yüan Chih, *Polygala Tenuifolia*, Willd.*

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An amorphous saponin has been isolated from *Polygala tenuifolia*, Willd. By hydrolysis of this saponin two crystalline sapogenins were obtained and some of their characteristics which were determined are reported.

THE Chinese drug Yüan Chih, identified in 1932 by Stuart (1) as *Polygala tenuifolia, Willd.* comes from the northern provinces of China and is usually prescribed in Chinese medicine in cough and as a stimulant. Its active constituents have not so far been much investigated. The present work deals with the isolation from the roots of the drug of an amorphous saponin which is acid in nature. On hydrolysis, this amorphous principle gives rise to the formation of two crystalline sapogenins to which the names tenuigenin A and B are respectively assigned. Tenuigenin A has the composition $C_{27}H_{40}O_8$ and melts at 272°, while tenuigenin B has the formula $C_{30}H_{46}O_8$ and a melting point of 248°. They are very similar in their chemical constitution and form readily a diacetyl derivative, indicating the presence in each molecule of two OH groups. Titration with alkali shows them to be dibasic and on heating with alkali, a third equivalent is consumed in both cases, undoubtedly owing to cleavage of a lactone group. In 1937 Jacobs and Isler (2) reported the isolation from the *Polygala senega* of a seneginin which possesses the formula $C_{30}H_{46}O_8$ or $C_{30}H_{44}O_8$ and a melting point of 290–292°, being also dibasic and having in its molecule one lactone and two OH groups. Consequently tenuigenin B is very similar to seneginin in its chemical composition and general properties, but differs from the latter in its melting point.

EXPERIMENTAL

Isolation of the Saponin.—One kilogram of the finely powdered drug was warmed on the water bath with 2 liters of light petroleum ether for six hours. After standing overnight it was filtered with suction and washed thoroughly with the same solvent. The petroleum ether extract, when distilled, left behind about 120 Gm. of oily residue. The defatted material was then dried, refluxed with 3 liters of 93% alcohol for three hours, and filtered hot. The extraction was repeated twice, each time with 2 liters of alcohol. The combined alcoholic filtrates, when kept in an ice chest for two days, deposited a copious precipitate of crude saponin which weighed about 40 Gm. when air-dried. It was dissolved in about 10 parts of methyl alcohol, refluxed with bone-black, and filtered. On cooling, there separated out a small amount of brownish precipitate which was filtered and discarded. The saponin was recovered from the methyl alcoholic solution by concentrating to one-third volume and adding an equal volume of acetone and this was repeated several times until finally the purified saponin had a melting point of about 230–240°. Further purification through its lead compound by precipitating its aqueous solution with basic lead acetate gave no better product. The saponin so obtained forms a colorless amorphous powder, is optically inactive, and dissolves in water with foaming to an acid solution.

Hydrolysis of Saponin.—Tenuigenin A: One gram of saponin obtained as above was dissolved in a mixture consisting of 12 cc. of 95% alcohol, 4 cc. of concentrated hydrochloric acid and 4 cc. of water and warmed on the water bath for eight hours. Tenuigenin A began to separate out after two to three hours' heating. After standing overnight, the crystalline precipitate was filtered, washed with little water, and dried in a desiccator over sulfuric acid. Its mother liquor was set aside for working up tenuigenin B. When recrystallized pure from acetone tenuigenin A formed colorless fine needles, melting at 272°. It was easily soluble in alcohol or ether, but much less so in acetone or ethyl acetate. Its composition was determined to be $C_{27}H_{40}O_8$ according to the following analysis:

Anal.—Calcd. for $C_{27}H_{40}O_8$: C, 65.85; H, 8.20. Found: C, 65.90, 65.72; H, 8.29, 8.39.

Titration with alkali showed the substance to be dibasic with the presence of one lactone group: 8.955 mg. of the substance was dissolved in 2 cc. of alcohol and titrated against phenolphthalein with 0.01 *N* NaOH. Calculated for 2 equivalents for 2 COOH groups, 3.64 cc.; found, 3.68 cc. After addition of 2 cc. of 0.1 *N* NaOH, the mixture was boiled for two hours and titrated back. Calculated for 1 equivalent for one lactone group: 1.82 cc. (based on 0.01 *N* NaOH); found, 2.13 cc.

On direct titration, 8.105 mg. of substance required 3.27 cc. of 0.01 *N* NaOH. Calculated for 2

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equivalents, 3.30 cc. When saponified as above, an additional 1.79 cc. of alkali was consumed.

Tenuigenin A diacetate: Twelve hundredths gram of tenuigenin A was warmed on the water bath for five hours with 2 cc. of acetic anhydride and a trace of pyridine. When cooled to the room temperature, the reddish solution was treated with a sufficient quantity of powdered ice under shaking. The diacetate separated out at first as an oil which solidified on standing. It was taken up with ether in which it was easily soluble. The ethereal solution was dried with anhydrous sodium sulfate and distilled and the residue taken up with little ethyl acetate. On addition of light petroleum ether, it crystallized out in colorless rhombic prisms, which, on exposure to air, became opaque and fell into a white powder, m. p. 280°. The analytical data indicated the compound to be a diacetyl derivative.

Anal.—Calcd. for $C_{27}H_{38}O_8(CH_3CO)_2$: C, 64.58; H, 7.70. Found: C, 64.30, 64.26; H, 7.68, 7.71.

When titrated with alkali, the following results were obtained: 9.210 mg. of substance dissolved in alcohol was titrated with 0.01 *N* NaOH against phenolphthalein. Calculated for 2 equivalents, 3.20 cc., found: 3.23 cc. The mixture was then refluxed for two hours after addition of 2 cc. of 0.1 *N* NaOH and titrated back. Calculated for 3 equivalents (lactone and 2 acetyl groups), 4.80 cc.; found 4.87 cc.

Tenuigenin B: The alcoholic hydrochloric acid mother liquor of tenuigenin A obtained above was diluted with water when a voluminous precipitate resulted. It was filtered, washed with water, and dried. On repeated crystallization from a mixture of acetone and ethyl acetate, tenuigenin B was obtained as colorless fine needles, m. p. 248°. It was more soluble in acetone than tenuigenin A. When analyzed, its composition agreed with the formula $C_{30}H_{46}O_8$:

Anal.—Calcd. for the formula $C_{30}H_{46}O_8$: C, 67.42; H, 8.67. Found: C, 67.82, 67.88; H, 9.07, 8.68.

On direct titration with alkali against phenolphthalein, 7.78 mg. of the substance dissolved in 2 cc. of alcohol required 2.93 cc. of 0.01 *N* NaOH; calculated for 2 equivalents, 2.91 cc. Two cubic centimeters of 0.1 *N* NaOH were added and, after boiling for two hours, the mixture was titrated back. Calculated for 1 equivalent, 1.45 cc.; found, 1.32 cc.

A second titration with 6.188 mg. of substance required 2.41 cc. of 0.01 *N* NaOH instead of 2.32 cc. theoretical. On saponification as indicated above, an additional 1.28 cc. of alkali was consumed.

Tenuigenin B diacetate was prepared in a similar way as in the case of tenuigenin A acetate. When crystallized pure from a mixture of ethyl acetate and petroleum ether, it formed shining plates, m. p. 272°. When intimately mixed with tenuigenin A acetate, it melted at 262°. Unlike tenuigenin A diacetate, its crystalline form remained unchanged on exposure to the air. Analytical results showed the substance to be a diacetate:

Anal.—Calcd. for $C_{30}H_{44}O_8(CH_3CO)_2$: C, 66.02; H, 8.15. Found: C, 65.73, 65.45; H, 8.42, 8.36.

Eight and twenty-eight hundredths milligrams of the substance was titrated with 0.01 *N* NaOH against phenolphthalein. Calculated for 2 equivalents, 2.68 cc.; found: 2.72 cc. After adding 2 cc. of 0.1 *N* alkali and refluxing for two hours, the mixture was again titrated. Calculated for 3 equivalents (lactone and 2 acetyl groups): 4.02 cc.; found: 3.72 cc.

SUMMARY

An amorphous saponin has been isolated from the Chinese drug, Yüan Chih which is botanically *Polygala tenuifolia* Willd. On hydrolysis with alcoholic hydrochloric acid, this amorphous principle gives rise to two crystalline sapogenins which are named tenuigenin A and tenuigenin B. Tenuigenin A has the composition $C_{27}H_{40}O_8$, melting at 272°, and tenuigenin B has the formula $C_{30}H_{46}O_8$ and a melting point of 248°. Both genins are found to be dibasic and contain in each molecule one lactone and two OH groups. Their diacetyl derivatives have been prepared.

REFERENCES

(1) Stuart, G. H., "Chinese Materia Medica," 1932, p. 328.
(2) Jacobs, W. A., and Isler, O., *J. Biol. Chem.*, **119**, 155 (1937).