REVISED STRUCTURE OF ISOTERCHEBIN, ISOLATED FROM CORNUS OFFICINALIS[1]

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Abstract —— A dehydroellagitannin isolated from the fruit of Cornus officinalis, whose structure is assigned as 1,2,3-tri-O-galloyl-4,6-O-dehydrohexahydroxydiphenoyl-β-D-glucopyranose (I), is considered to be identical as isoterchebin which had been presumed to have structure (V).

Tannin-rich fruit of Cornus officinalis Sieb. et Zucc. has been used as an ingredient in several prescriptions of Chinese medicine. We have isolated three tannins temporarily named Cornus-tannin 1, 2 and 3.

Cornus-tannin 2 and 3 have been identified as 1,2,3-tri-O-galloyl-4,6-O-hexahydroxydiphenoyl-β-D-glucopyranose (II)[2], and 2,3-di-O-galloyl-4,6-O-hexahydroxydiphenoyl-D-glucopyranose (III)[2], by comparison of physical properties and spectral data. The absolute configuration of the biphenyl group in II has been newly determined to be S based on the specific rotation of dimethyl hexamethoxydiphenoate, $[\alpha]_D^{23}$ -29°(c 1.0, $CHCl_3$), obtained by methanolysis of pentadecamethyl derivative of II. The absolute configuration of biphenyl in III is also S as III has been identified with Alnus-tannin 2, whose structure was determined to be 2,3-di-O-galloyl-4,6-O-(S)-hexahydroxydiphenoyl-D-glucopyranose[3].

Cornus-tannin 1 (I), which is obtained in a larger amount than the other two tannins, forms yellow crystals, $C_{41}H_{30}O_{27}\cdot 4H_2O$, $[\alpha]_D^{23}$ +103° (c 1.0, EtOH), and showed a spot on the paper chromatogram (Rf 0.70, by n-BuOH-AcOH-H_2O, 4:1:5, upper. Rf 0.28, by 7% AcOH). The ^{1}H-NMR spectrum (acetone-d_6) showed proton peaks due to three galloyl groups at δ7.17, 7.16 and 7.08 (2H each), and those assignable to a dehydrohexahydroxydiphenoyl (DHHDP) group at δ6.85, 6.43 and 4.69. The proton peaks attributable to glucopyranose were also exhibited at δ6.35(d, 9Hz, H-1), 5.99(t, 9Hz, H-3), 5.80(t, 9Hz, H-2), 5.76(t, 9Hz, H-4), 5.16(dd, 4 and 10Hz, H-6), 4.48(m, H-5) and 4.16(d, 10Hz, H-6'). The ^{13}C-NMR spectrum (acetone-d_6)

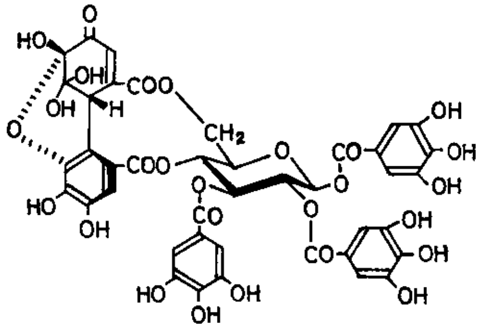
showed that Cornus-tannin 1 is composed of the groups described above, and also that the DHHDP group forms the hydrated hemiacetal structure in analogous way as that of crystalline geraniin (six-membered hemiacetal structure)[4], by the carbon peaks as follows: δ43.4(methine); 66.2, 69.7, 71.5, 73.4, 73.8 and 93.5 (glucose); 92.3(gem-diol); 97.2(hemiacetal); 111.0(6C), 120.5, 121.4(2C), 140.2(2C) and 140.7 (galloyl); 108.5, 113.5, 124.5, 131.9, 136.5, 143.2, 152.4 and 193.2 (DHHDP); 146.9(7C, six galloyl carbons and a DHHDP carbon); 165.5, 166.0, 166.7, 167.3 and 169.0 (ester). However, formation of the equilibrium mixture in the presence of water, which occurred for geraniin, was not observed for Cornus-tannin 1.

The pattern and the chemical shifts of the H-6 and H-6' peaks of the glucose moiety in Cornus-tannin 1, which are analogous to those of II and III[2], indicate that one of the two ester linkages between glucose and DHHDP group is on C-6 of glucose. As the ^{1}H-NMR spectrum shows that glucopyranose in Cornus-tannin 1 forms C1 conformation, another ester linkage should be on O-4 of glucose. Three galloyl groups in Cornus-tannin 1 are then on O-1, O-2 and O-3 of glucose.

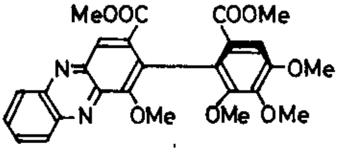
Cornus-tannin 1 condensed with o-phenylenediamine to give a phenazine derivative which showed protons at δ6.73(s, 1H), 7.94(s, 1H) and 7.8-8.4(m, 4H) in the ^{1}H-NMR spectrum (acetone-d_6). Upon methylation with diazomethane, this phenazine derivative yielded tridecamethyl derivative, $C_{60}H_{58}O_{24}N_2 \cdot H_2O$, $[\alpha]_D^{23}$ +84°(c 1.0, acetone). This derivative was subjected to methanolysis, and the acetone soluble fraction of the product was methylated with diazomethane. By preparative TLC (silica gel, ligroin-dichloromethane-acetone, 6:3:1), methyl 4-methoxy-3-(4,5,6-trimethoxy-2-methoxycarbonylphenyl)phenazine-2-carboxylate (IV), $[\alpha]_D^{14}$ -38°(c 0.5, EtOH), was obtained and was identified with the authentic specimen produced from granatin B[5], by the IR spectra and the specific rotations. Methyl tri-O-methylgallate was also isolated from the products mixture, and glucose in the mixture was identified by the gas chromatography of trimethylsilyl ether.

The specific rotation of IV indicates that the absolute configuration of the biphenyl group in the phenazine derivative from Cornus-tannin 1 is S. The absolute configuration at the methine carbon of the DHHDP group in Cornus-tannin 1 is then assigned S in analogous way as that in granatin B.

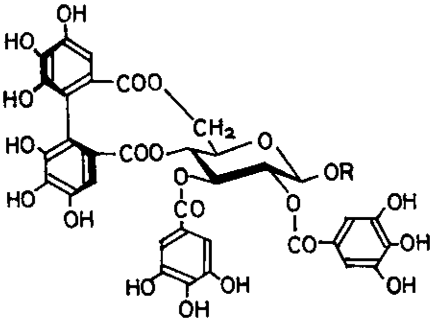
The structure of Cornus-tannin 1 is therefore 1,2,3-tri-O-galloyl-4,6-O-dehydrohexahydroxydiphenoyl-β-D-glucopyranose which forms a hydrated six-membered

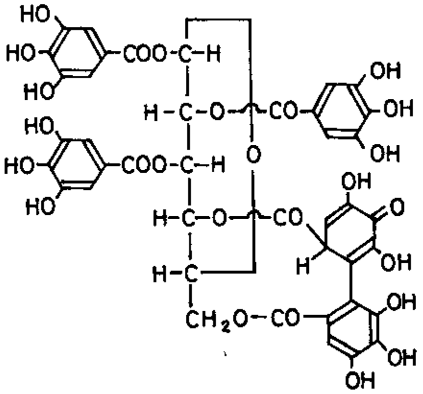


(I)



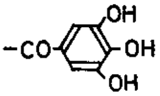
(IV)



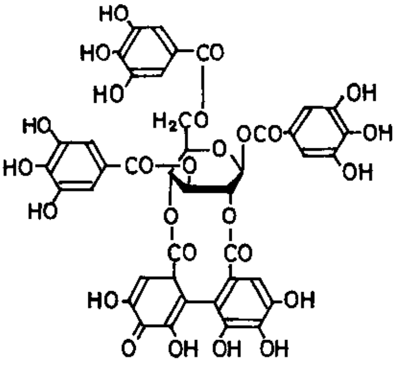


(V)

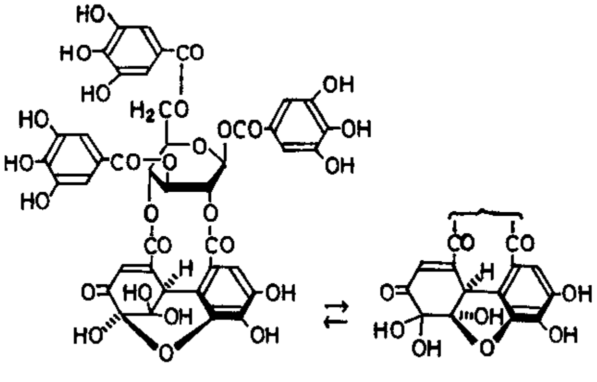
(II) R: —CO



(III) R: H



(VI)



(VII)

hemiacetal structure (I).

In the ^{1}H-NMR spectra, H_4 peak of glucose in Cornus-tannin 1 shifts upfield upon the formation of the phenazine derivative, from δ5.76 to δ5.38, while H_6 shifts downfield from δ5.16 to δ5.42. These shifts may be due to the shielding and deshielding effects by the newly formed aromatic ring in the phenazine derivative. However, inspection of the molecular models also indicates that such shifts may be induced by the conformational change of the aromatic ring originally present in the DHHDP group, upon the formation of the phenazine derivative. The ^{13}C-NMR spectra show that C_6 is the only carbon for which marked upfield shift (1.3 ppm), comparable to the difference of shifts of the same carbon in Cornus-tannin 1 and 2 (2.5 ppm), occurs upon the formation of the phenazine derivative. These ^{13}C-NMR spectral data are rather indicative of the orientation of the DHHDP group in Cornus-tannin 1 as in the structure (I).

Isoterchebin, isolated from Cytinus hypocistis, was reported to have structure (V)[6] having an enol form of cyclohexanetrione (named "isohexahydroxydiphenoyl" group[7]), based on the analogy of the properties and the ^{1}H-NMR spectral pattern to those of terchebin for which structure (VI) had been proposed[7]. However, the structure of terchebin has recently been revised to (VII) which has the DHHDP group in place of the "isohexahydroxydiphenoyl" group[5]. As the reported properties and the ^{1}H-NMR spectrum of isoterchebin practically coincide with those of Cornus-tannin 1, the structure of isoterchebin should be revised to (I).

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