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PRAECOXIN B, C, D AND E, NOVEL ELLAGITANNINS FROM *STACHYURUS PRAECOX*

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Praecoxin C (6), D (7) and E (8), ellagitannins having depside linkage, and praecoxin B (9), an isomer of tellimagrandin I (1), were isolated from *Stachyurus praecox*.

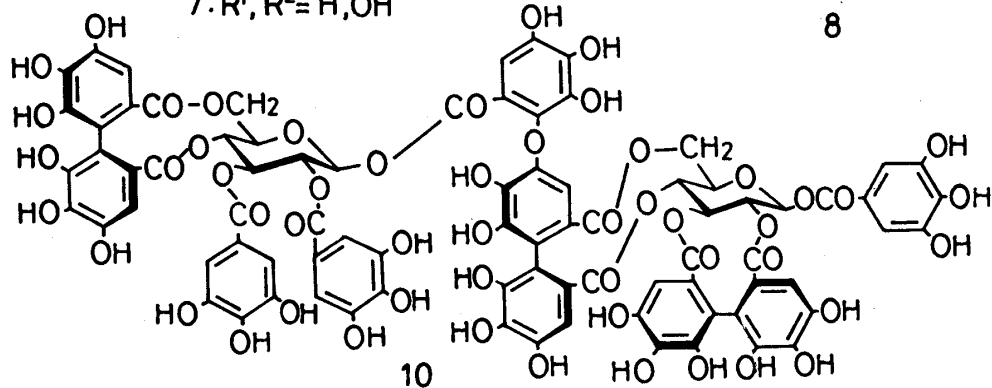
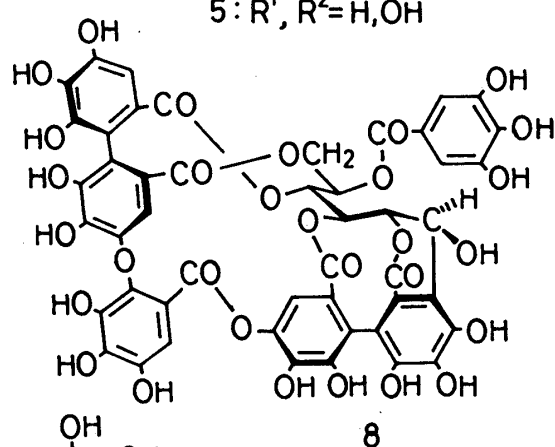
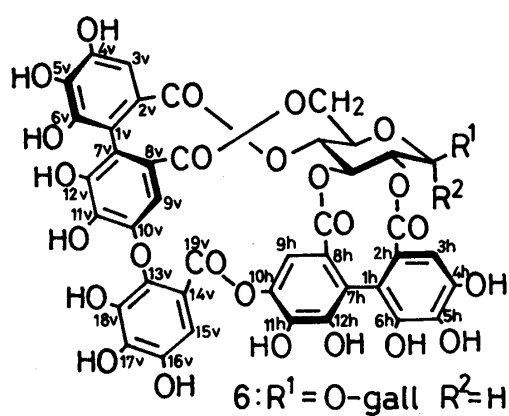
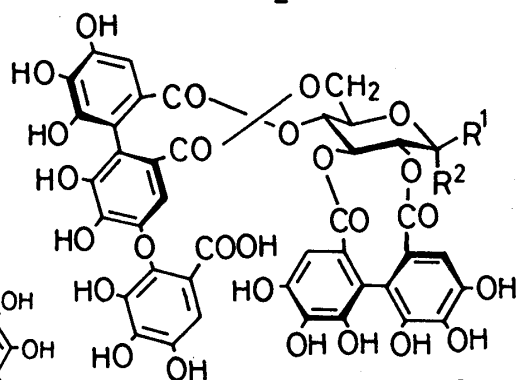
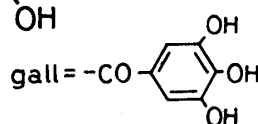
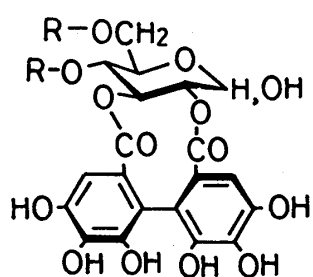
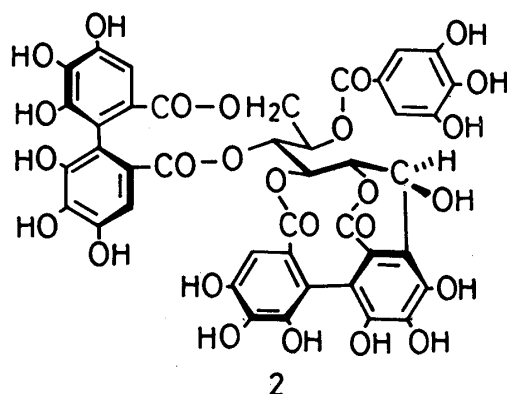
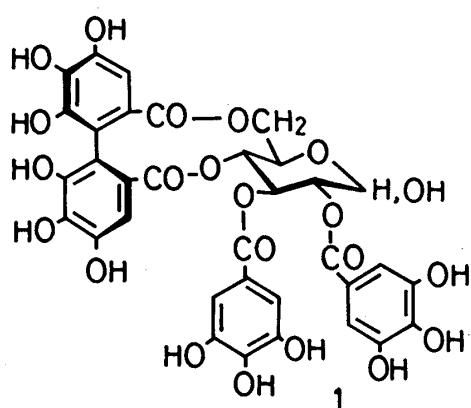
KEYWORDS — *Stachyurus praecox*; Stachyuraceae; ellagitannin; valoneoyl group; depside linkage; C-glucosidic tannin; praecoxin B; praecoxin C; praecoxin D; praecoxin E

The leaves of *Stachyurus praecox* Sieb. et Zucc. (Japanese name: kibushi, Stachyuraceae) are rich tannin sources, and also have been used as diuretics in Japan. Recently, we found tannins and related compounds, namely casuarictin, pedunculagin, tellimagrandin I (1), strictinin, casuarinin (2), stachyurin, casuariin, 2,3-O-[(S)-hexahydroxydiphenoyl]-D-glucose (3), rugosin C (4) and praecoxin A (5) in the leaf of *S. praecox*.¹⁻³⁾ We now report the isolation and the structure of three ellagitannins of novel type from the leaf, named praecoxin C (6), D (7) and E (8), and an additional new tannin named praecoxin B (9), and also the isolation of 1,2,6-tri-O-galloyl-β-D-glucose and rugosin F (10),⁴⁾ a dimeric ellagitannin.

These tannins have been isolated from the ethyl acetate extract of the crude extract of the leaf collected in August, by centrifugal countercurrent chromatography⁵⁾ combined with the chromatography on Sephadex LH-20 and cellulose column.

Praecoxin B (9), C₃₄H₂₆O₂₂·3H₂O, [α]_D +49° (c=0.5, MeOH), UV λ_{max}^{MeOH} nm (log ε) 210 (4.85) and 297 (4.34), was obtained as a light tan amorphous powder. The ¹H-NMR spectrum (200 MHz, in acetone-d₆) shows that 9 forms an anomer mixture (α:β=1:1), and possesses two galloyl groups [δ7.17 (s, 2H), 7.14 (s, 1H) and 7.11 (s, 1H)], a hexahydroxydiphenoyl (HHDP) group [δ6.62 (s, 1H) and 6.39 (s, 1H)], and a glucose core [δ5.66 (t, J=9.5 Hz, α-anomer, H-3), 5.52 (d, J=3.5 Hz, α, H-1), 5.51 (t, J=7 Hz, β, H-3), 5.40 (d, J=9 Hz, β, H-1), 5.21 (dd, J=7, 9 Hz, β, H-2), 5.10 (dd, J=3.5, 9.5 Hz, α, H-2), 4.90 (t, J=9.5 Hz, α, H-4), 4.90 (dd, J=7, 9 Hz, β, H-4), 4.61-4.44 (m, H-5 and H-6), 4.31 (d, J=12 Hz, β, H-6') and 4.29 (d, J=12 Hz, α, H-6')]. The HHDP group should be on O-2 and O-3, since partial hydrolysis of 9 with tannase yielded 3. The two galloyl groups then should be on O-4 and O-6 of the glucose moiety. Therefore, praecoxin B is 4,6-di-O-galloyl-2,3-O-[(S)-HHDP]-D-glucose (9),⁶⁾ an isomer of 1.

Praecoxin C (6), C₄₈H₃₀O₃₀·5H₂O, [α]_D +41° (c=0.5, MeOH), UV λ_{max}^{MeOH} nm (log ε)



209 (4.93) and 302 (4.47), was obtained as a light tan amorphous powder. Its $^1\text{H-NMR}$ spectrum (200 MHz, in acetone- d_6) showed the presence of a galloyl group (δ 7.19, s, 2H), and a HHDP and a valoneoyl group [δ 7.21 (s, 1H), 6.96 (s, 1H), 6.60 (s, 1H), 6.46 (s, 1H) and 6.37 (s, 1H)]. Chemical shifts and coupling constants of glucose protons [δ 6.21 (d, J =9 Hz, H-1), 5.46 (dd, J =9, 10 Hz, H-3), 5.26 (t, J =10 Hz, H-4), 5.25 (dd, J =7, 13 Hz, H-6), 5.21 (t, J =9 Hz, H-2), 4.51 (dd, J =7, 10 Hz, H-5) and 3.97 (d, J =13 Hz, H-6')] which are similar to those of **4**,³⁾ indicate the $C1$ conformation of β -D-glucopyranose.

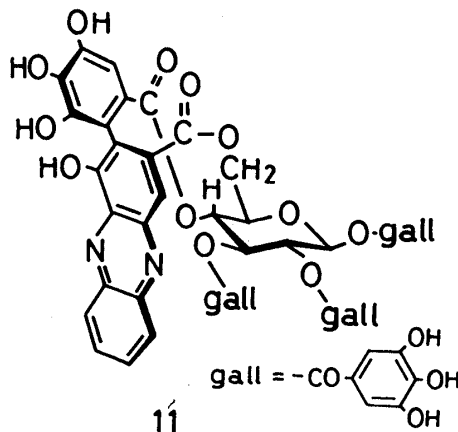
The treatment of **6** with water (37°C, three days) afforded **4**, quantitatively, and that with diazomethane in methanol gave heptadeca-*O*-methylrugosin C methyl ester, to show close correlation of **4** and **6**.

When an aqueous solution of a mixture of **4** and **6** was extracted with ethyl acetate at pH 6.5, and then at pH 2.5, most of **6** was extracted at pH 6.5, while most of **4** was found in the extract obtained at pH 2.5. This difference in the behavior between **4** and **6** is similar to that between the tannins having a free carboxyl group such as mallotusinic acid⁷⁾ and chebulinic acid,⁸⁾ and the tannins which lack a free carboxyl group. These results show that the relationship of **4** to **6** is that the free carboxyl group of the valoneoyl group in **4** forms an ester linkage in **6**. The position of the depside linkage between the carboxyl group of the valoneoyl group and the hydroxyl group at C-10h of the HHDP group was indicated by the comparison of the $^{13}\text{C-NMR}$ spectra of **4** and **6** [δ 164.8 (C-19v in **6**, shifted 4.0 ppm higher from the corresponding carbon in **4**), 152.6 (C-10h, >5.9 ppm lower), 133.7 (C-11h, >3.4 ppm higher), 122.9 (C-14v, 4.4 ppm lower) and 108.1 (C-15v, 1.3 ppm lower)]. The occurrence of an aromatic proton in the low field (δ 6.96) assignable to H-9h in the $^1\text{H-NMR}$ spectrum of **6** indicate that the hydroxyl group at C-10h, and not the group at C-12h, is linked to the valoneoyl group.

These facts and the molecular model show that the orientation of the valoneoyl group at O-4-O-6 of glucose as in the structure **6** allows the carboxyl group of the valoneoyl group to approach spatially to the HHDP group at O-2-O-3 of glucose, in a way analogous to the phenazine moiety of the phenazine derivative (**11**) of isoterchebin.⁹⁾

The structure of praecoxin C, including the absolute configurations of the HHDP group and the valoneoyl group, is therefore assigned as **6**. This is the first example of ellagitannin forming a depside by the valoneoyl group.

Praecoxin D (**7**), $\text{C}_{41}\text{H}_{26}\text{O}_{26} \cdot 5\text{H}_2\text{O}$, $[\alpha]_D +81^\circ$ ($c=0.5$, MeOH), UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ) 206 (4.85), 235 (sh.) (4.77) and 293 (4.46), was obtained as a light tan amorphous powder. Its $^1\text{H-NMR}$ spectrum (200 MHz, in acetone- d_6) shows that **7** forms an anomer mixture ($\alpha:\beta=4:3$), and possesses five aromatic protons [δ 7.19 (s, 3/7H), 7.17 (s, 4/7H), 6.97 (s, 1H), 6.63 (s, 3/7H), 6.62 (s, 4/7H), 6.61 (s, 4/7H), 6.58 (s, 3/7H) and 6.35 (s, 1H)]. Among them, an aromatic proton in the low field (δ 6.97) indicates the presence of a depside linkage in **7**, which is analogous to that in **6**.



The partial hydrolysis of **6** with tannase afforded **7**, and prolonged treatment gave **3**. The treatment of **7** with water yielded **5**, in a way analogous to the hydrolysis of **6** to **4**. Therefore, the structure **7** is assigned to praecoxin D.

These tannins having a depside linkage are not artefacts produced upon the treatment of the extract, since they were detected by HPLC carried out immediately after homogenizing the fresh plant. Concentration of the solutions and desiccation of **4** and **5** at various temperature did not produce **6** and **7**.

Praecoxin E (**8**), $C_{48}H_{30}O_{30} \cdot 4H_2O$, $[\alpha]_D +17^\circ$ ($c=0.8$, MeOH), UV λ_{max}^{MeOH} nm (log ϵ) 205 (4.88) and 276 (4.34), was obtained as a light tan amorphous powder. The glucose protons show a pattern analogous to that of *C*-glucosidic casuarinin (**2**)¹⁾ in the 1H -NMR spectrum (200 MHz, in acetone- d_6 - D_2O). The spectrum also shows the protons assignable to a galloyl group ($\delta 7.11$, s, 2H) and to a valoneoyl group [$\delta 7.09$, 6.87 and 6.54 (s, 1H each)], and a proton in the low field ($\delta 7.00$, s, 1H), which is attributable to a *C*-glucosidic HHDP group forming a depside linkage. The *C*-glucosidic tannins can be regarded biogenetically as the products of a C-C bond formation between C-1 of glucose and a carbon in the aromatic ring of the tannins which have a glucopyranose ring.^{1,2)} Co-occurrence of several tannins of these two types in *S. praecox* and other species of plant is also known.²⁾ Combined with the spectral data shown above, the structure of praecoxin E is accordingly assumed to be **8**.

Two additional tannins were identified as 1,2,6-tri-*O*-galloyl- β -D-glucose and rugosin F (**10**)⁴⁾ which is one of the dimeric ellagitannins recently isolated from *Rosa rugosa* Thunb.

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