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RUGOSIN A, B, C AND PRAECOXIN A, TANNINS HAVING A VALONEOYL GROUP

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New hydrolyzable tannins, rugosin A (**1**), B (**2**), C (**3**) from *Rosa rugosa*, and **3** and praecoxin A (**7**) from *Stachyurus praecox*, were isolated, and their structures, including the valoneoyl group, were elucidated.

KEYWORDS —— *Rosa rugosa*; Rosaceae; *Stachyurus praecox*; Stachyuraceae; tannin; valoneoyl group; rugosin A; rugosin B; rugosin C; praecoxin A

The flower of *Rosa rugosa* Thunb. (Japanese name: hama-nasu, Rosaceae) has been used as an antidiarrheic and a haemostatic in the northern part of Japan. We have isolated from the flower petal of this plant, three new tannins, named rugosin A (**1**), rugosin B (**2**) and rugosin C (**3**), and also 1,2,3-tri-*O*-galloyl-β-D-glucose, 1,2,6-tri-*O*-galloyl-β-D-glucose, strictinin,[1] isostrictinin,[2] pedunculagin,[3,4] casuaricitn (**4**),[3] tellimagrandin I (**5**)[3,5] and tellimagrandin II (**6**).[3,5,6] We have also isolated **3** and a new tannin named praecoxin A (**7**), from the leaf of *Stachyurus praecox* Sieb. et Zucc. (Japanese name: kibushi, Stachyuraceae).

The tannins of *R. rugosa* have been isolated from ethyl acetate extract obtained from the concentrate of an acetone-water (7:3) homogenate of the flower petal, by column chromatography on Sephadex LH-20 combined with preparative TLC on cellulose plate.

Rugosin A (**1**), $C_{48}H_{34}O_{31}\cdot 5H_2O$, $[\alpha]_D$ +110° (c=1, acetone), UV λ_{max}^{MeOH} nm (log ε) 218 (5.01) and 275 (4.65), forms a light tan amorphous powder. Its ^{1}H-NMR spectrum[7] shows nine aromatic protons [δ7.11 (s), 7.01 (s), 6.99 (s) (2H each, galloyl), 7.16 (s), 6.50 (s) and 6.37 (s) (1H each, valoneoyl)] and seven glucose protons [δ6.18 (d, *J*=8 Hz, H-1), 5.85 (t, *J*=10 Hz, H-3), 5.58 (dd, *J*=8, 10 Hz, H-2), 5.31 (dd, *J*=6, 14 Hz, H-6), 5.17 (t, *J*=10 Hz, H-4), 4.48 (dd, *J*=6, 10 Hz, H-5) and 3.80 (d, *J*=14 Hz, H-6')] which are analogous to those of **6**,[5] except for the presence of valoneoyl protons in **1** in place of hexahydroxydiphenoyl (HHDP) protons of **6**. The large difference between the chemical shifts of H-6 and H-6', and *C1* conformation of the glucose core indicate that the ester linkage of valoneoyl group should be on O-4 and O-6 of the glucose moiety. The three galloyl groups then should be on O-1, O-2 and O-3. The β-configuration at the anomeric carbon is then assigned by large coupling constant (8 Hz) of H-1. Both

of the two ester linkages between the valoneoyl group and the glucose core are presumed to be on the biphenyl part of the former, since the valoneoyl group is not lactonized,[8] as indicated by the production of optically active valoneate (**8**) from **1** as follows. Methylation of **1** with dimethyl sulfate and potassium carbonate afforded heptadeca-*O*-methylrugosin A methyl ester, $C_{66}H_{70}O_{31}\cdot H_2O$, $[\alpha]_D$ +46° (c=1, acetone), whose mass spectrum shows the peaks of the methylated valoneoyl (m/z 660, 614 and 570) and trimethylgalloyl (m/z 212, 197 and 195) groups. The treatment of the methylate with sodium methoxide in methanol gave trimethyl (*S*)-octa-*O*-methylvaloneate (**8**), $[\alpha]_D$ -17° (c=1, acetone), methyl tri-*O*-methylgallate (**9**) and glucose [by gas chromatography of trimethylsilyl derivative].

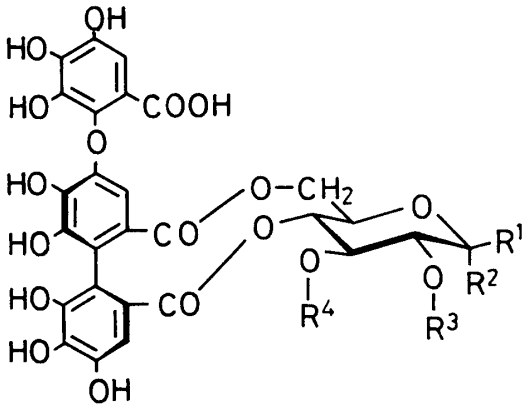
Degalloylation of **1** with tannase gave 4,6-*O*-[(*S*)-valoneoyl]-D-glucose (**10**), $C_{27}H_{22}O_{19}\cdot 3H_2O$, $[\alpha]_D$ +3° (c=1, MeOH), UV λ_{max}^{MeOH} nm (log ε) 216 (4.59) and 254 (infl.) (4.36), whose ^{1}H-NMR spectrum shows valoneoyl protons at δ7.13 (s), 6.75 (s) (1H each), 6.23 (s, 1/2H) and 6.21 (s, 1/2H), and the glucose protons of the pattern analogous to that of 4,6-*O*-[(*S*)-HHDP]-D-glucose. These data show that rugosin A is 1,2,3-tri-*O*-galloyl-4,6-*O*-[(*S*)-valoneoyl]-β-D-glucose (**1**).

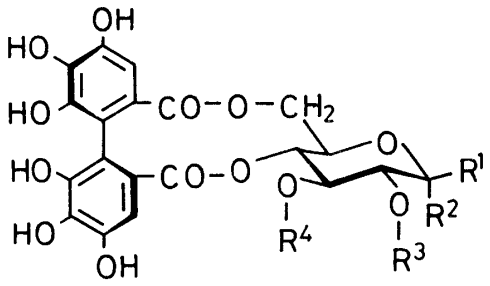
Rugosin B (**2**), $C_{41}H_{30}O_{27}\cdot 4H_2O$, $[\alpha]_D$ +124° (c=1, EtOH), UV λ_{max}^{MeOH} nm (log ε) 217 (4.91) and 269 (4.55), was obtained as a light tan amorphous powder. The ^{1}H-NMR spectrum (200 MHz) shows that **2** forms a mixture of anomers (α:β=2:1), by the peaks at δ7.07 (s, 4/3H), 7.06 (s, 2/3H), 7.00 (s, 4/3H) and 6.96 (s, 2/3H) (two galloyl groups); 7.18 (s, 1H), 6.48 (s, 2/3H), 6.46 (s, 1/3H), 6.32 (s, 2/3H) and 6.31 (s, 1/3H) (a valoneoyl group); 5.86 (t, *J*=10 Hz, 2/3H, α-anomer, H-3), 5.60 (t, *J*=10 Hz, 1/3H, β-anomer, H-3), 5.52 (d, *J*=3.5 Hz, 2/3H, α, H-1), 5.24 (dd, *J*=7.5, 9.5 Hz, 1/3H, β, H-2), 5.23 (dd, *J*=6.5, 13 Hz, 1/3H, β, H-6), 5.21 (dd, *J*=6.5, 13 Hz, 2/3H, α, H-6), 5.12 (dd, *J*=3.5, 10 Hz, 2/3H, α, H-2), 5.10 (d, *J*=7.5 Hz, 1/3H, β, H-1), 5.06 (t, *J*=10 Hz, 1H, α,β, H-4), 4.63 (ddd, *J*=1, 6.5, 10 Hz, 2/3H, α, H-5), 4.23 (ddd, *J*=1, 6.5, 10 Hz, 1/3H, β, H-5), 3.76 (dd, *J*=1, 13 Hz, 1/3H, β, H-6') and 3.68 (dd, *J*=1, 13 Hz, 2/3H, α, H-6') (glucose). Production of **2** was also effected by partial hydrolysis of **1** with trifluoroacetic acid, in a way analogous to the hydrolysis of **6** to **5**.[5] The structure of rugosin B is thus 2,3-di-*O*-galloyl-4,6-*O*-[(*S*)-valoneoyl]-D-glucose (**2**).

Rugosin C (**3**), $C_{48}H_{32}O_{31}\cdot 7H_2O$, $[\alpha]_D$ +90° (c=1, acetone), UV λ_{max}^{MeOH} nm (log ε) 218 (4.92) and 263 (4.60), forms a light tan amorphous powder. Its ^{1}H-NMR spectrum shows seven aromatic protons [δ7.15 (s, 2H, galloyl), 7.14, 6.54, 6.46, 6.40 and 6.34 (s, 1H each, HHDP and valoneoyl)] and seven glucose protons [δ6.18 (d, *J*=9 Hz, H-1), 5.44 (dd, *J*=9, 10 Hz, H-3), 5.28 (dd, *J*=7, 13 Hz, H-6), 5.14 (t, *J*=9 Hz, H-2), 5.07 (t, *J*=10 Hz, H-4), 4.46 (dd, *J*=7, 10 Hz, H-5) and 3.79 (d, *J*=13 Hz, H-6')]. The coupling constants of the glucose protons are in accord with the *C1* conformation and the β-anomer.

Heptadeca-*O*-methylrugosin C methyl ester, $C_{66}H_{68}O_{31}\cdot 3/2H_2O$, $[\alpha]_D$ +12° (c=0.9, acetone) obtained by the methylation of **3** with dimethyl sulfate and potassium carbonate [mass spectrum: m/z 660, 614 and 570 (methylated valoneoyl group); 450, 404 and 360 (methylated HHDP group); 212, 197 and 195 (trimethylgalloyl group)] was methanolyzed to give dimethyl (*S*)-hexamethoxydiphenate, $[\alpha]_D$ -35° (c=1.1, EtOH), **8**, **9** and glucose.

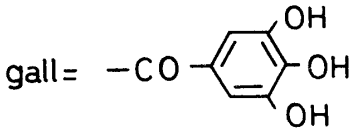
Partial hydrolysis of **3** by tannase gave a degalloylated compound (**7**), $C_{41}H_{28}O_{27}\cdot 3H_2O$, $[\alpha]_D$ +45° (c=0.5, MeOH), UV λ_{max}^{MeOH} nm (log ε) 205 (4.75) and 240

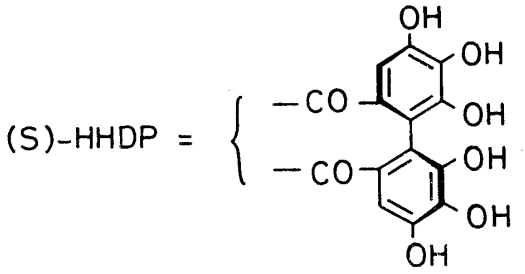


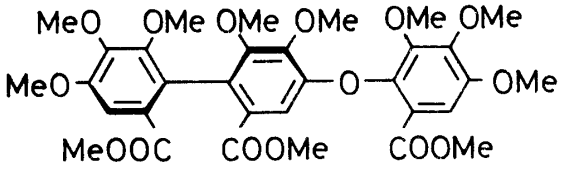


	R^1	R^2	R^3	R^4
1	O-gall	H	gall	gall
2	H, OH		gall	gall
3	O-gall	H	(S)-HHDP	
7	H, OH		(S)-HHDP	
10	H, OH		H	H

	R^1	R^2	R^3	R^4
4	O-gall	H	(S)-HHDP	
5	H,OH		gall	gall
6	O-gall	H	gall	gall







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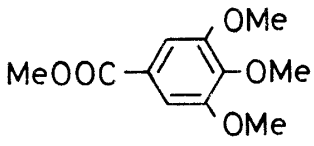

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(sh.) (4.59). The ^{1}H-NMR spectrum of **7** showed a large upfield shift of H-1 of glucose from that of **3** (> 0.6 ppm), and presence of anomers [δ7.17 (1H), 6.60 (1H), 6.56 (2/3H), 6.51 (1/3H), 6.37 (1H), 6.32 (1/3H) and 6.30 (2/3H) (valoneoyl and HHDP groups); δ5.56 – 3.60 (glucose protons)]. The galloyl group in **3** is then on O-1 of glucose.

The ^{1}H-NMR spectrum of **3** shows a distinct upfield shift of H-4, H-6 and H-6' (~ 0.1 ppm) and small shifts (≦ 0.04 ppm) of the other glucose protons from those of **4**.[3,9] The valoneoyl group is therefore presumed to be on O-4 and O-6 of the glucose core, and this presumption was proved by the production of 2,3-*O*-[(*S*)-HHDP]-D-glucose upon the prolonged treatment of **3** with tannase. Therefore **3** and

7 are 1-*O*-galloyl-2,3-*O*-[(*S*)-HHDP]-4,6-*O*-[(*S*)-valoneoyl]-β-D-glucose and 2,3-*O*-[(*S*)-HHDP]-4,6-*O*-[(*S*)-valoneoyl]-D-glucose, respectively.

Analogous fractionation combined with the droplet countercurrent chromatography of the tannins of the leaf of *S. praecox* yielded two tannins in addition to the six tannins previously reported.[1,2] One was identified as **3**, and the other one, named praecoxin A, was identified as **7**.

The present study and the investigation of tannins of *Mallotus japonicus* Muell. Arg.[8] showed that the tannins having a valoneoyl group coexist with their analogs having an HHDP group in several species of plant.

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7) ^{1}H-NMR spectra were measured with a Hitachi R22-FTS instrument (90 MHz) in acetone-d_6, unless mentioned otherwise.
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9) 200 MHz ^{1}H-NMR spectrum of **4** shows glucose protons as follows: δ6.22 (d, J=9 Hz, H-1), 5.45 (dd, J=9, 10 Hz, H-3), 5.37 (dd, J=7, 13 Hz, H-6), 5.18 (t, J=9 Hz, H-2), 5.17 (t, J=10 Hz, H-4), 4.50 (dd, J=7, 10 Hz, H-5) and 3.88 (d, J=13 Hz, H-6').

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