Studies on Hydrangea Species. I.\(^1\) Phenolic Components of Hydrangea serrata Seringe var. thunbergii Sugimoto

AKIRA YAGI, YUKO WASHIDA, NAOE TAKATA and ITSUO NISHIKA

Faculty of Pharmaceutical Sciences, Kyushu University\(^4\)

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Phenolic components in the plant were investigated to give phyllodulcin, phyllodulcin-8-O-β-D-glucoside, hydrangenol, umbelliferone, p-hydroxybenzoic acid, protocatechuic acid, gallic acid, methyl chlorogenate, chlorogenic acid, kaempferol, quercetin, isoquercitin, rutin and three new components, hydrangea glucosides A, B, and C. On the basis of chemical and spectral data hydrangea glucosides A(I), B(II), and C(III) were characterized to 2-[β-(4′-hydroxyphenyl)-β-hydroxyethyl]-6-hydroxybenzoic acid-6-O-β-D-glucopyranoside, 2-[β-(4′-hydroxyphenyl)-β-hydroxyethyl]-6-hydroxybenzoic acid-β-O-β-D-glucoside and p-hydroxybenzaldehyde-O-β-D-glucopyranoside, respectively.

As a sweetening component in Hydrangea serrata Seringe var. thunbergii Sugimoto (Japanese name: Amacha) phyllodulcin was isolated and identified by Asahina and Asano\(^3\) and its absolute configuration was determined by Arakawa\(^4\) to 3(R)-(3′-hydroxy-4′-methoxyphenyl)-8-hydroxydihydroisocoumarin. Recently, Kimura, et al.,\(^5\) reported the isolation of phyllodulcin-8-O-β-D-glucoside from the fresh leaves and suggested that phyllodulcin occurred as phyllodulcin-8-O-β-D-glucoside in the plant. For the purpose of studying on biosynthesis of phyllodulcin and its related compounds the investigation of phenolic constituents connected with phyllodulcin in the fresh leaves was of importance. The work reported in this paper deals with the isolation of phenolic components and the structural elucidation of new compounds, hydrangea glucosides A, B, and C.

Isolation

The concentrated methanol extract of fresh leaves was suspended in water and fractionated to the water soluble portion and the benzene soluble portion. The water soluble portion was extracted with butanol and the solvent was evaporated to dryness. The residue was subjected to chromatography on silica gel column using benzene–methanol (99: 1 to 85: 15 v/v) as the solvent and the following components were isolated: p-hydroxybenzoic acid, protocatechuic acid, gallic acid, chlorogenic acid, methyl chlorogenate, phyllodulcin-8-O-β-D-glucoside, hydrangea glucosides A, B, and C, kaempferol, quercetin, isoquercitin and rutin. After alkaline hydrolysis of benzene soluble portion an unsaponifiable fraction was excluded by extracting with ether and the alkaline layer was acidified and extracted with ether. The ether extract was chromatographed on silica gel column using benzene as the solvent and phyllodulcin, hydrangenol and umbelliferone were isolated. The known

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2) Location: Katakasu, Fukuoka.
compounds isolated in the procedure were identified by mixed melting point, cochromatography and by comparison of spectral data with those of the authentic sample.

**Hydrangea Glucoside A (I)**—Upon acid and enzymic hydrolysis (I), mp 180—182°, $C_{31}H_{32}O_{18}$, $[\alpha]D^2$ = 40°, yielded b-glucose and hydragenol as aglycon. I was assumed the glucoside of hydragenol. However, I was soluble in sodium bicarbonate solution at room temperature, showing an acidic character and the infrared (IR) spectral bands at 2600, 1720 cm$^{-1}$ revealed the presence of carboxyl group in this glucoside. I gave hexacetate (I-a), mp 269—271°, $C_{35}H_{36}O_{16}$, on acetylation with $C_2H_5-O-ACONa$ or $C_2H_5-O-pyridine$. The nuclear magnetic resonance (NMR) spectrum of I-a$^6$ indicated the signal corresponding to a phenol acetate at 2.30 ppm, an alcoholic acetate at 2.15 ppm and glucose tetraacetate at 2.00—2.10 ppm. Additionally, the NMR spectrum of I-a showed ABX-type signals of bibenzyl at 2.98 and 3.30 ppm. From the spectral data I-a differed from hydragenol-8-$O$-$\beta$-$D$-glucoside pentaacetate$^7$, mp 246—248°, $C_{31}H_{32}O_{14}$, and I was characterized to the glucoside of hydragenol whose lactone ring opened.

To clarify the site of glucose to the aglycon the methylation followed by acid hydrolysis was carried out. I was methylated by Hakomori's procedure$^8$ to give hexamethylylate I-b, $C_{37}H_{33}O_9$, which exhibited a methoxycarbonyl (1740 cm$^{-1}$) in IR spectrum and a methoxy-carbonyl (3.90 ppm), a phenolic methoxy (3.75 ppm), four alcoholic methoxy signals (3.35—3.62 ppm) and an anomeric proton of the sugar moiety at 4.85 ppm as a doublet ($J=6$ Hz) in NMR spectrum. I-b was subjected to methanalysis to give a phenolic substance I-c, mp 45°, $C_{17}H_{16}O_4$, showing an unstable purple coloration by FeCl$_3$ reagent.$^9$-10 I-c showed an associated phenol with carbonyl group at 12.8 ppm$^9$ in NMR spectrum and the carbonyl

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6) NMR spectra of hydragenol, 4$'$-acetylhydragenol and 4$'$,8-diacetylhydragenol-Hydragenol (C$_2$D$_2$N): 2.94 (1H, d, $J=17.5$), 3.32 (1H, d, $J=17.11$), 5.52 (1H, d, $J=11.5$); 4$'$-acetylhydragenol: 2.30 (3H, s, $4$'Ac), 3.02 (1H, d, $J=17.5$), 3.32 (1H, d, $J=17.11$), 5.55 (1H, d, $J=11.5$), 6.70—7.45 (7H, aromatic), 10.88 (1H, s, OH); 4$'$,8-diacetylhydragenol: 2.30 (3H, s, $4$'Ac), 2.36 (3H, s, $8$'Ac), 3.02 (1H, d, $J=17.5$), 3.38 (1H, d, $J=17.11$), 5.50 (1H, d, $J=11.5$), 7.02—7.58 (7H, aromatic). Abbreviation: s = singlet, d = doublet, m = multiplet


group at 1660 cm$^{-1}$ in IR spectrum and was identified with 2-methoxy carbonyl-3-hydroxy-4'-methoxystilbene, mp 45$^\circ$, which was synthesized by partial methylation of hydrangeaic acid by diazomethane.

Consequently, the site of sugar linkage in (I) must be the phenol at C-6 and hydrangea glucoside A (I) is defined as 2-[β-(4'-hydroxyphenyl)-β-hydroxyethyl]6-hydroxybenzoic acid 6-O-β-D-glucopyranoside.

**Hydrangea Glucoside B** (II) — II, mp 214—216$^\circ$, [α]$_D$$^\	ext{589}$ = -30$^\circ$, C$_{21}$H$_{21}$O$_{10}$, was soluble in sodium bicarbonate solution at room temperature and showed a stable purple coloration for FeCl$_3$ reagent. II was suggested to have an orthophenol carboxylic acid character by IR spectrum (1690 cm$^{-1}$). From the spectral data of NMR at 2.98, 3.15, 5.68 ppm corresponding to ABX type proton of dibenzyl, ultraviolet (UV) absorption at 303 m$_{	ext{u}}$ and of mass fragment pattern, II was assigned to be a substance like I. Acid hydrolysis of II afforded hydrangelenol, together with II-a, mp 220—221$^\circ$, C$_{12}$H$_{14}$O$_3$ and D-glucose. By the deficiency of a stable purple coloration for FeCl$_3$ reagent and of the IR band at 1690 cm$^{-1}$, II-a was characterized to the decarboxylated phenol. Methylation of II-a by Hakomori's method gave II-c, mp 101—102$^\circ$, which was identical with 3,4'-dimethoxystilbene synthesized by the decarboxylation of hydrangeaic acid by methylation. When hydrolyzed with β-glucosidase (II) gave hydrangolenol, II-a and II-b on thin-layer chromatography (TLC). By a stable coloring for FeCl$_3$ reagent and by cochromatography with an authentic sample II-b was deduced to 2-[β-(4'-hydroxy phenyl)-β-hydroxyethyl]-6-hydroxybenzoic acid. In order to determine the site of glucose in II the acetylation and the methylation of II were carried out. Hexaacetate, oily substance II-d, C$_{38}$H$_{38}$O$_{16}$·1½H$_2$O, showed two signals corresponding to phenol acetate at 2.30 ppm in addition to glucose tetraacetate at 2.08 ppm in NMR spectrum. II was methylated by Hakomori's method to give heptamethoxylate, oily substance II-e, C$_{38}$H$_{38}$O$_{10}$·½H$_2$O. II-e showed the absorption at 280, 285 m$_{	ext{u}}$ in UV spectrum and indicated two methoxy groups of phenol at 3.80 ppm, a methoxycarbonyl group at 3.90 ppm and tetramethoxyl signals of sugar moiety at 3.38—3.64 ppm in NMR spectrum. Accordingly, II-e was confirmed not to be a stilbene derivative as I-b.

On the basis of chemical and the spectral data it was concluded that D-glucose attached to an alcoholic function in II-b. The structure of hydrangea glucoside B (II), therefore, was established to 2-[β-(4'-hydroxyphenyl)-β-hydroxyethyl]-6-hydroxybenzoic acid-β-O-β-D-glucoside.

**Hydrangea Glucoside C** (III) — III, mp 168—170$^\circ$, [α]$_D$$^\text{81-3}$ = 81.3$^\circ$, C$_{12}$H$_{10}$O$_7$·H$_2$O, presented the carbonyl band at 1660 cm$^{-1}$ in IR spectrum and showed the positive coloring test for 2,4-dinitrophenylhydrazine solution. Hydrolysis of III with β-glucosidase afforded an

aglycon III-a, mp 112—114°, C₇H₆O₂ and D-glucose. As III-a revealed the carbonyl band at 1670 cm⁻¹ in IR spectrum and signals of an aldehyde at 9.90 ppm, a phenol at 6.40 ppm and AB type four protons at 6.95 and 7.50 ppm in NMR spectrum, III-a was deduced to \(\beta\)-hydroxybenzaldehyde. III-a was identified by mixed melting point and by comparison of IR and NMR spectra with those of an authentic sample.

Consequently, III was proved to the glucoside of \(\beta\)-hydroxybenzaldehyde. The structure of III was confirmed by comparison of its acetate III-c with tetraacetate of \(\beta\)-hydroxybenzaldehyde-\(\alpha\)-\(\beta\)-D-glucoside as follow. By standing \(\alpha\)-D-tetraacetylchryoglucose, mp 88—89°, \([\alpha]_D^{199.5}\)°, with sodium salt of \(\beta\)-hydroxybenzaldehyde in acetone for 24 hr at room temperature, \(\beta\)-hydroxybenzaldehyde-\(\alpha\)-\(\beta\)-D-glucopyranoside tetraacetate III-b, mp 143—145°, C₂₅H₂₄O₁₁·1.5H₂O, \([\alpha]_D^{26}\)° was synthesized in the yield of 25% by the conventional method. Acetate of III, III-c, mp 143—145°, \([\alpha]_D^{29}\)°—29° was identical with III-b by mixed melting point and by comparison of IR spectrum.

The presence of hydrangea glucosides A and B, the prototype of natural occurring dihydroisocoumarin, together with phyllodulin-S-O-\(\beta\)-D-glucoside in the plant is of biogenetical significance. Further studies on biosynthesis of phyllodulin are in progress.

**Experimental**

Melting points were determined on a Kofler block and are uncorrected. IR spectra were obtained with a KOKEN DS-301 and UV spectra were recorded with a Shimadzu SV-50A. NMR spectra were taken with a Nihonenshi C-60H in CDCl₃ unless otherwise specified. Chemical shifts were expressed in ppm from Me₄Si as internal reference and coupling constants (J) in cps. Mass spectral data were determined on a JEOL-01 double focus high resolution spectrometer. TLC were performed on silica gel G (Kiesel gel G, Merck), polyamide (Wako, E-10) and cellulose powder (MN Cellulose powder 300) employing the following solvent system: TLC (1): C₅H₅·MeOH·AcOH (45—8—4 v/v), C₅H₅·isoPrOH·AcOH (45—8—4 v/v) on silica gel for phenols and phenolic acids, TLC (2): AcOEt·MeCOEt·HCOOH·H₂O (5—3—1—1 v/v), AcOEt·MeCOEt·HCOOH·H₂O·C₅H₅ (4—3—1—1 v/v) on silica gel or polyamide for glycosides of phenol and phenol carboxylic acids, TLC (3): 30% AcOH, BuOH·AcOH·H₂O (4—1—5 v/v) on cellulose powder for flavonoids. 1% FeCl₃, 1% 2,4-dinitrophenylhydrazine in dil. HCl and 10% H₂SO₄ (spraying followed by heating) were used as

coloring reagents. Paper chromatography (PCP) for sugar was run on Toyo Roshi No. 50 using the upper layer of BuOH–AcOH–H₂O (4:1:5 v/v) and BuOH–Pyridine–H₂O (6:4:3 v/v) by ascending method with double development technique and a coloring reagent was aniline hydrogenphthalate.

**Isolation (Chart 1)**—The fresh leaves of the plant (7 kg) collected in Fukuoka (May, 1968 and 1970) were extracted with MeOH at room temperature. MeOH extract was concentrated and evaporated to dryness in vacuo. The residue (490 g) was suspended in water and fractionated to the water soluble portion and the benzene soluble portion. The water soluble portion was extracted with BuOH and the solvent was evaporated to dryness. The residue (58 g) was subjected to chromatography on silica gel column using C₂H₅OH–MeOH (99:1 to 85:15 v/v) as solvent and phenolic compounds were isolated. The C₂H₅OH soluble matters (98 g) were refluxed with 5% alc, KOH (700 ml) for 1 hr and the solvent was evaporated. The alkaline layer was extracted with ether and the solvent was evaporated to give unsaponifiable matters (6.3 g). The alkaline layer was acidified with 10% HCl and extracted with ether. The ether extract (50 g) was subjected to chromatography on silica gel column using C₂H₅OH as the solvent to give phyllodulcin (22 g), hydromenol (2 g) and umbelliferone. The known compounds isolated and their derivatives were identified with the authentic sample by mixed melting point, cochromatography and by comparison of spectral data.

**Hydrangea Glucoside A(I)**—Colorless needles (from MeOH–H₂O) (4.2 g), mp 180—182°, [α]₀ = -40° (EtOH, c = 0.1). Anal. Calcd. for C₃₉H₄₃O₁₅: C, 57.79; H, 5.54. Found: C, 57.43; H, 5.69. IR ν_max cm⁻¹: 2600 (OH), 1720 (C=O), 1610 (C=C). UV λ_max nm (log e): 286, 304 (3.77, 3.81).

**Acid Hydrolysis of (I)**—I (100 mg) was treated with 5% H₂SO₄ (5 ml) on a steam bath for 1 hr to yield precipitate. It was collected by filtration, washed with water and recrystallized from MeOH–H₂O to give colorless needles (66 mg), mp 180—181°, identified with an authentic sample of hydromenol, mp 176°, IR ν_max cm⁻¹: 3230 (OH), 1670 (C=O), 1620 (C=C). UV λ_max nm (log e): 285, 315 (3.63, 3.91), by mixed melting point and by comparison of IR spectrum. The filtrate was neutralized with barium carbonate filtered and concentrated in vacuo. After removal of salt the filtrate was evaporated in vacuo to give syrup and it was examined by PCP to give n-glucose.

**Enzymic hydrolysis of (I)**—I (20 mg) suspended in water (10 ml) was stirred with β-glucosidase (Sigma Chemical Co., U.S.A.) (20 mg) for 5 days at 30°. The reaction mixture was evaporated with EtOAc, evaporated and the residue was recrystallized from MeOH–H₂O to give hydromenol.

**Acetylation of (I)**—I (1.4 g) in pyridine (5 ml) was acetylated with Ac₂O (10 ml) for 5 days at room temperature, and treated with ice water to give precipitate. It was collected by filtration, washed with water and recrystallized from MeOH–CHCl₃ to give colorless fine needles (I-a) (1.6 g), mp 209—217° (decomp.). Anal. Calcd. for C₃₉H₄₃O₁₅: C, 57.56; H, 5.29. Mass spectrum m/e: 644 (M⁺-CO₂), 331 (glucose tetraacetate). IR ν_max cm⁻¹: 3440 (OH), 1758 (C=O), 1610 (C=C). UV λ_max nm (log e): 296 (3.41), 390, 320 (4.1, 4.1). NMR: 3.35—3.62 (12H, sugar, 4 × CH₂), 2.15 (3H, s, acetyl), 2.30 (3H, s, 4'-Ac), 2.08 (1H, d, J = 15.5), 3.30 (1H, d, J = 15.9), 4.30—5.50 (6H, m, sugar), 7.00—7.48 (7H, aromatic).

**Methylation of (I)**—According to the Hakomori's method NaH (0.4 g) was mixed with dimethyl sulfoxide (DMSO) (4 ml) at room temperature for 0.5 hr and to his reagent the solution of (I) (0.4 g) in DMSO (4 ml) was added and the reaction mixture was kept for 1 hr at room temperature. Then CH₃I (2 ml) was added and the reaction mixture was allowed to stand for 1 hr at room temperature. After dilution with water the reaction mixture was extracted with CHCl₃ and CHCl₃ layer was washed with water, dried and evaporated to dryness. The oily residue was chromatographed on silica gel column using C₂H₅OH and CHCl₃ as the solvent. The fraction eluted with CHCl₃ afforded oily substance (I-b) (0.3 g). Anal. Calcd. for C₃₉H₄₃O₁₅: C, 64.53; H, 6.82. Found: C, 64.82; H, 6.98. IR ν_max cm⁻¹: 1740 (C=O), 1610 (C=O), 1100 (CH₂O). UV λ_max nm (log e): 306, 320 (4.1, 4.1). NMR: 3.35—3.62 (12H, sugar, 4 × CH₂O), 3.75 (3H, s, CH₂O), 3.90 (3H, s, COOCH₃), 4.85 (1H, d, anomic H, J = 6), 6.62—7.35 (9H, aromatic).

**Methanolysis of (I-b)**—I-b (50 mg) was hydrolyzed with 1N HCl-MeOH (10 ml) for 2 hr under refluxing on water bath. The reaction mixture was diluted with water and extracted with ether. The ether layer was washed with water, dried and the solvent was evaporated to dryness. The residue was subjected to chromatography on silica gel column using hexane and hexane–C₂H₅OH (1:1 v/v) as the solvent. The fraction eluted with hexane–C₂H₅OH (1:1 v/v) was crystallized from MeOH to give colorless needles, mp 45°, (I-c). I-c was identical with 2-methoxybenzyl-3-hydroxy-4-methoxyxystilbene, mp 45°. Anal. Calcd. for C₃₉H₆₃O₁₅: C, 71.82; H, 5.67. Found: C, 71.82; H, 5.71. IR ν_max cm⁻¹: 3100 (OH), 1660 (C=O), 1600 (C=C). UV λ_max nm (log e): 300, 338 (3.1, 3.2). NMR: 3.84 (3H, s, CH₂O), 3.90 (3H, s, COOCH₃), 6.65—7.60 (9H, aromatic), 12.8 (1H, s, OH). It was synthesized by partial methylation of hydrangeaic acid with diazomethane and was identified by mixed melting point and comparison of IR spectrum.

**Hydrangea Glucoside B (II)**—Colorless needles (from MeOH–H₂O) (0.42 g), mp 214—216°, [α]₀ = -30° (EtOH, c = 0.1). Anal. Calcd. for C₃₉H₄₃O₁₅: C, 57.79; H, 5.54. Found: C, 57.95; H, 5.58. IR ν_max cm⁻¹: 3450 (OH), 1600 (C=O). Mass Spectrum m/e: 456 (M⁺), 256 (M⁺-C₃H₅O₃; hydromenol), 230 (M⁺-C₃H₅O₃, -CO₂H; II-a). UV λ_max nm (log e): 290, 303 (3.65, sh.). NMR (C₆D₅N): 2.08 (1H, d, J = 12.3), 3.15 (1H, d, d, J = 12.9), 5.68 (1H, d, J = 9.5), 5.50—4.50 (6H, m, sugar), 6.85 (2H, d, d, J = 9.2), 7.40 (2H, d, d, J = 9.2).

**Acid Hydrolysis of (II)**—II (50 mg) was treated with 5% H₂SO₄ (10 ml) on a steam bath for 1 hr. The reaction mixture diluted with water was extracted with EtOAc and the solvent was evaporated to dryness.
The residue was subjected to chromatography on silica gel column using C6H6 as the solvent to afford hydralgenol which was identical with an authentic sample by mixed melting point and cochromatography. The following fraction eluted with C6H6-MeOH (99:1 v/v) was recrystallized from C6H6-acetone to afford (II-a), mp 220–221°, [α]D° 45° (MeOH, ε = 0.05). Anal. Calcd. for C49H44O8: C, 73.02; H, 6.13. Found: C, 72.49; H, 6.16. Mass Spectrum m/e: 230 (M+), 124 (HO-C8H8(CHOH)2), 108 (HO-C8H8(CH2)), IR v_max cm⁻¹: 3500 (OH), 1613 (C=C). UV λ_max nm (log e): 280 (2.71). The water layer was neutralized with barium carbonate and worked up as usual to give n-glucose by PCC.

Methylation of (II-a) (20 mg) was methylated by Hakomori's method as previously described and the product was subjected to chromatography on silica gel column using hexane and hexane-C6H6 (1:1 v/v) as the solvent to give (II-c). II-c was identified to 3,4'-dimethoxy stilbene, mp 101–102°. Mass Spectrum: Calcd. for C14H12O2: 240.115; Found: 240.118, IR v_max cm⁻¹: 1600 (C=C), 1450 (C=O). UV λ_max nm (log e): 305, 324 (5.55, 3.55). NMR: 3.80 (3H, s, CH3O), 3.82 (3H, s, CH3O), 6.84–7.80 (10H, aromatic). It was synthesized by the decarbonylation of hydralgenol according to methylation with diazomethane and was identified by comparison of IR spectrum.

Enzymic Hydrolysis of (II)—II (30 mg) dissolved in water (30 ml) was stirred with β-glucosidase (30 mg) for 4 days at 28°. The reaction mixture was extracted with EtOAc and the solvent was evaporated to dryness. Along with hydralgenol and (II-a), (II-b) was detected on TLC. By coloring for FeCl3 reagent and by cochromatography with an authentic sample (II-b) was deduced to 2-[β-(4'-hydroxyphenyl)-β-hydroxyethyl]-6-hydroxybenzoic acid.

Acetylation of (II)—II (50 mg) was acetylated with Ac2O (5 ml), Ac2OAc (50 mg) under refluxing for 2 hr. The reaction mixture was worked up as usual to give colorless oily substance (II-d) (58 mg). Anal. Calcd. for C25H25O3: 1/12H2O: C, 55.38; M, 5.49. Found: C, 55.44; H, 5.71. Mass Spectrum m/e: 644 (M+CO2), 331 (glucose tetraacetate), 312 (M+CO3-glucose tetraacetate). IR v_max cm⁻¹: 1760–1740 (C=O), 1600 (C=C). UV λ_max nm (log e): 302 (3.36). NMR: 2.08 (12H, s, 4 × Ac2), 2.30 (6H, s, 2 × Ac), 2.98 (1H, d, J = 15.5), 3.03 (1H, d, d, J = 15.9), 4.30–5.50 (6H, m, sugar), 6.55–7.25 (7H, aromatic H).

Methylation of (II) (80 mg) dissolved in DMSO (8 ml) was methylated by Hakomori's method as previously described and oily product was subjected to chromatography on silica gel column using C6H6 and CHCl3 as the solvent to afford oily substance, heptamethyl ether (II-e). Anal. Calcd. for C25H25O3·1/2H2O: C, 61.86; H, 7.23. Found: C, 61.93; H, 7.09. IR v_max cm⁻¹: 1740 (C=O), 1600 (C=C). UV λ_max nm (log e): 280, 285 (3.3, 3.0). NMR: 3.38, 3.55, 3.63, 3.64 (3H, s, 4 × CH₂O, resp.), 3.80 (6H, s, 2 × CH₂O), 3.90 (3H, s, COOCH₂), 6.32–7.08 (7H, aromatic H).

Synthesis of 2-[β-(4'-Hydroxyphenyl)-β-hydroxyethyl]-6-hydroxybenzoic Acid (II-b) and 3,4'-Dimethoxy-stilbene (II-c)—Hydralgenol (1 g) in 10% aceton–H2O (300 ml) was refluxed for 1 hr on a steam bath. The reaction mixture was extracted with ether and the solvent was evaporated to dryness. The residue was subjected to chromatography on silica gel column using C6H6 and C6H6-MeOH (99:1 v/v) as the solvent to give the starting material, pale yellow hydralgenic acid (0.5 g), mp 180–181°, IR v_max cm⁻¹: 3300 (OH), 1690 (C=O), 1600 (C=C). UV λ_max nm (log e): 302, 326 (4.13, 4.06) and colorless needles, 2-[β-(4'-hydroxyphenyl)-β-hydroxyethyl]-6-hydroxybenzoic acid, mp 216–218°, [α]D° 20° (MeOH, ε = 0.05). Anal. Calcd. for C25H25O3·1/2H2O: C, 65.69; H, 5.15. Found: C, 65.76; H, 4.66. IR v_max cm⁻¹: 3300 (OH), 1690 (C=O), 1620 (C=C). UV λ_max nm (log e): 286, 302 (sh, 3.0), indicating a stable purple coloration for FeCl3 reagent. To the solution of hydralgenic acid (0.1 g) dissolved in glycerol (3 ml) potassium hydroxide (0.1 g) was added and heated at 200° for 3 hr. The reaction mixture was diluted with water, extracted with ether and the solvent was evaporated to dryness. The residue was subjected to chromatography on silica gel column using CHCl3 as the solvent to give colorless needles, 3,4'-dihydroxy-stilbene (40 mg), mp 210–212° (from C6H6). Anal. Calcd. for C14H12O2: C, 79.22; H, 5.70. Found: C, 79.18; H, 5.83. IR v_max cm⁻¹: 3300 (OH), 1610 (C=C). UV λ_max nm (log e): 308, 326 (3.24, 3.24). 3,4'-Dihydroxy-stilbene (20 mg) was methylated with CH3NH2 and the product was subjected to chromatography on silica gel column using C6H6 as the solvent to give colorless needles, 3,4'-dimethoxy-stilbene.

Hydrangea Glucoside C (III)—Colorless needles (from EtOH) (0.2 g), mp 168–170° (decomp.). Anal. Calcd. for C18H20O2·2H2O: C, 51.65; H, 6.60. Found: C, 51.28; H, 6.59. [α]D° 81.3° (MeOH, ε = 0.12). UV λ_max nm (log e): 275, 292 (3.64, sh). IR v_max cm⁻¹: 3540 (OH), 1600 (C=O), 1610 (C=C). (III) showed reddish yellow for 2,4-dinitrophenylhydrazine reagent.

Enzymic Hydrolysis of (III)—III (50 mg) suspended in water (10 ml) was stirred with β-glucosidase (50 mg) for 10 hr at 27° and worked up as usual to give an aglycon, III-a (15 mg), mp 119–114° (from EtOH-C6H6). Anal. Calcd. for C18H16O2·2H2O: C, 58.84; H, 4.95. Found: C, 59.00; H, 5.22. IR v_max cm⁻¹: 3200 (OH), 1670 (C=O), 1600 (C=C). UV λ_max nm (log e): 285 (4.10). NMR: 6.40 (1H, m, OH, exchanged with D₂O), 6.95 (2H, d, d, J = 9.2), 7.80 (2F, d, d, J = 9.2), 9.90 (1H, s, CHO) and showed reddish yellow for 2,4-dinitrophenylhydrazine reagent. III-a was identified by mixed melting point and by comparison of IR and NMR spectra with those of the authentic 3-hydroxybenzaldehyde. The water layer was concentrated in vacuo to afford syrup which was examined by PCC to give n-glucose.

Acetylation of (III)—III (0.01 g) in pyridine (1 ml) was acetylated with Ac2O (2 ml) for 24 hr at room temperature and worked up as usual to give (III-c), mp 143–145° (from MeOH), [α]D° 22° (CHCl₃), ε =...
Synthesis of $\beta$-Hydroxybenzaldehyde-$\beta$-d-glucopyranoside Tetraacetate(III-b)—To the solution of $\beta$-hydroxybenzaldehyde (1.7 g) dissolved in 4% NaOH (20 ml) a solution of $\alpha$-n-tetraacetylglucosamine, mp 88—89°, $[\alpha]_D^20$ 199.5° (CHCl₃, $c=0.1$) (4 g) in acetone (30 ml) was added and the reaction mixture was kept for 24 hr at room temperature. The solvent was evaporated in vacuo at 25—30° and the residue was diluted with water, extracted with CHCl₃ and evaporated to dryness in vacuo. The residue (4 g) was subjected to chromatography on silica gel column using C₄H₆ and C₅H₆-EtOAc as the solvent. The fraction eluted with C₅H₆-EtOAc (85:15 v/v) was crystallized from MeOH to give colorless needles (1.2 g), $\beta$-hydroxybenzaldehyde-$\beta$-d-glucopyranoside tetraacetate(III-b), mp 143—145°, $[\alpha]_D^20$ —23° (CHCl₃, $c=0.3$). Anal. Calcd. for C₂₄H₃₅O₁₁·½H₂O: C, 54.66; H, 5.46. Found: C, 55.08; H, 5.17. UV $\lambda_{max}^{nO}$ m$\mu$ ($\log e$): 284 (4.0), IR $\nu_{max}$ cm$^{-1}$: 1760 (AcO), 1700 (CO). NMR: 2.04 (12H, s, 4×Ac), 4.0—5.5 (7H, m, sugar), 7.10 (2H, d.d, $J=9.2$) 7.85 (2H, d.d, $J=9.2$) 9.90 (1H, s, CHO), indicating reddish yellow for 2,4-dinitrophenylhydrazine reagent. III-c was identical with III-b by mixed melting point and by comparison of UV and IR spectra.

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