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Chemical Studies on Chinese Traditional Medicine, Dangshen. I. Isolation of (*Z*)-3- and (*E*)-2-Hexenyl β-D-Glucosides

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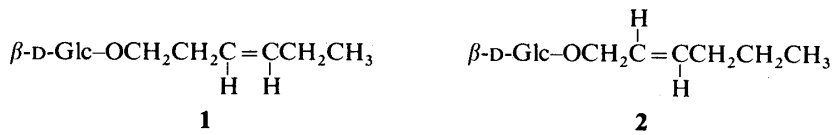
Two alkene glucosides were isolated from Dangshen (Codonopsis Radix) purchased in Chengdu, Sichuan, China. On the basis of proton and carbon-13 nuclear magnetic resonance spectral data, the structures were characterized as (*Z*)-3-hexenyl β-D-glucopyranoside (**1**) and (*E*)-2-hexenyl β-D-glucopyranoside (**2**).

Keywords——Dangshen; Codonopsis Radix; Campanulaceae; Chinese traditional crude drug; (*Z*)-3-hexenyl β-D-glucopyranoside; (*E*)-2-hexenyl β-D-glucopyranoside

Dangshen (党参), Codonopsis Radix, is a very important Chinese traditional crude drug. This drug is believed to be a hematonic and has been used for treatment of spleen and stomach disorders as well as anemia, fatigue and anorexia.[1] Dangshen has been described as the roots of *Codonopsis pilosula* (FRANCH.) NANNF. (Campanulaceae), (Lu-Dangshen, Xi-Dangshen or Dong-Dangshen) or *C. tangshen* OLIV. (Chuan-Dangshen).[1] However, it is also stated that roots of *C. tubulosa* KOM., *C. viridiflora* MAXIM., *C. tsinlingensis* PAX. *et* K. HOFFM., *C. clematidea* (SCHRENK.) CLARKE and *C. nervosa* (CHIPP.) NANNF. are sometimes used as Dangshen.[1]

This drug contains a large amount of sucrose and other carbohydrates.[1] With regard to secondary metabolites in this drug, isolation of three triterpenoids, two phytosterols and their mono-glucosides[2] as well as the presence of a trace of alkaloids[1] have been reported. As a part of our China–Japan cooperative studies on oriental traditional medicines, we have examined this drug. Such work should be valuable for the chemical identification of the source of the drug. The present paper deals with the isolation and identification of two alkene glucosides from Dangshen purchased in Chengdu, Sichuan, China.

An aqueous solution of the MeOH extract of the drug was subjected to chromatography on highly porous polymer to remove sucrose and other carbohydrates by eluting with water, and the fraction eluted with MeOH was rechromatographed on silica gel and then on reversed-phase silica gel, affording two glycosides (**1** and **2**).



1 **2**

Chart 1

Acid hydrolysis of **1** and **2** afforded glucose. The carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectrum of both **1** and **2** showed signals attributable to a β-D-glucopyranosyl moiety and six signals (–CH_3 × 1, –CH_2– × 2, –CH_2O– × 1 and –CH= × 2) due to the aglycone moiety. By means of a proton decoupling experiment in the proton nuclear magnetic resonance (^{1}H-NMR) spectrum, the aglycone moieties of **1** and **2** were established to be (*Z*)-3- and (*E*)-2-hexen-1-ol, respectively. It follows that **1** and **2** can be formulated as (*Z*)-3-hexenyl β-D-glucopyranoside and (*E*)-2-hexenyl β-D-glucopyranoside, respectively. Glycoside **1** has already been isolated from the leaves of *Pertya glabrescens* SCH. BIP. (Compositae) by Nagumo *et al.*[3] Based on the ^{13}C-NMR data for the aglycone alkenols[4] and glycosylation shifts,[5] the carbon signals of **1** and **2** were assigned as indicated in Experimental.

Investigation of other chemical constituents of this specimen as well as a variety of other specimens of Dangshen is in progress.

Experimental

Optical rotations were measured with a Union PM-101 automatic digital polarimeter. NMR spectra were recorded on a JEOL FX-100 spectrometer at 25.00 MHz for ^{13}C-NMR and at 99.55 MHz for ^{1}H-NMR using Me_4Si as an internal standard. For gas liquid chromatography (GLC), a Shimadzu GC-6A was used (dual flame ionization detector); carrier gas, N_2 (40 ml/min); column, 5% silicone GE SE-52 on Chromosorb W (2.6 mm × 2 m); column temperature, 170 °C; injection temperature, 230 °C. For column chromatography, Kieselgel 60 (70—230 mesh, Merck), LiChroprep RP-8 (40—63 μm, Merck) and Diaion HP-20 (Mitsubishi Chem. Ind. Co., Ltd.) were used. High performance liquid chromatography (HPLC) was carried out with a Tosoh CCPM pump, and a Tosoh RI-8000 differential refractometer was used as a detector. All solvent systems for chromatography were homogeneous.

Extraction and Separation——The Dangshen was purchased in Chengdu, Sichuan, China, and pharmacognosically identified as Codonopsis Radix by M.-R. Jia, Y.-K. Ling and X.-F. Pu. The dried material (2.3 kg) was extracted with MeOH (4 l × 4) under reflux and the extract was concentrated to dryness. The MeOH extract (770 g) was chromatographed on a column of highly porous polymer (Diaion HP-20) and eluted with H_2O, MeOH and Me_2CO, successively. The MeOH eluate (22.36 g) was subjected to chromatography on a silica gel column with $CHCl_3$–MeOH–H_2O (gradient elution, from a ratio of 60 : 10 : 1 to 60 : 50 : 10) to give twelve fractions (frs. 1—12 in order of elution). Fraction 7 was chromatographed on a reversed-phase (LiChroprep RP-8) column with 40% MeOH and further purified by HPLC on TSKgel ODS-120T (21.5 × 300 mm, Tosoh Co., Ltd.) with 50% MeOH to give **1** and **2** in yields of 0.0008% and 0.001%, respectively.

(*Z*)-3-Hexenyl β-D-Glucopyranoside (1)——A colorless syrup, $[\alpha]_D^{21}$ −38.0° (*c* = 0.48, EtOH) (lit. (3) −36.5°). ^{13}C-NMR (in CD_3OD) δ: 104.2 (Glc-1), 74.9 (Glc-2), 77.8 (Glc-3 or −5), 71.5 (Glc-4), 78.0 (Glc-5 or −3), 62.7 (Glc-6), 70.3 (C-1), 28.7 (C-2), 134.4 (C-3), 125.7 (C-4), 21.4 (C-5), 14.5 (C-6). ^{1}H-NMR (in CD_3OD) δ: 4.28 (1H, d, *J* = 7 Hz, anomeric H of Glc), 2.39 (2H, q, *J* = 7 Hz, 2-H_2), 5.38 (1H, dt, *J* = 10, 7 Hz, 3-H), 5.49 (1H, dt, *J* = 10, 7 Hz, 4-H), 2.07 (2H, quintet, *J* = 7 Hz, 5-H_2), 0.96 (3H, t, *J* = 7 Hz, 6-H_3). On acid hydrolysis, **1** yielded glucose.

(*E*)-2-Hexenyl β-D-Glucopyranoside (2)——A colorless syrup, $[\alpha]_D^{21}$ −28.3° (*c* = 0.43, EtOH). ^{13}C-NMR (in CD_3OD) δ: 102.9 (Glc-1), 75.6 (Glc-2), 77.9 (Glc-3 or -5), 71.6 (Glc-4), 78.0 (Glc-5 or -3), 62.7 (Glc-6), 70.8 (C-1), 135.7 (C-2), 127.3 (C-3), 35.4 (C-4), 23.3 (C-5), 14.0 (C-6). ^{1}H-NMR (in CD_3OD) δ: 4.27 (1H, d, *J* = 7 Hz, anomeric H of Glc), 5.56 (1H, dt, *J* = 16, 7 Hz, 2-H), 5.82 (1H, dt, *J* = 16, 7 Hz, 3-H), 2.06 (2H, q, *J* = 7 Hz, 4-H_2), 1.39 (2H, sextet, *J* = 7 Hz, 5-H_2), 0.91 (3H, t, *J* = 7 Hz, 6-H_3). On acid hydrolysis, **2** yielded glucose.

Acid Hydrolysis of 1 and 2, and Identification of Resulting Monosaccharides——Compound **1** or **2** (1 mg) was heated with 3.5% HCl in H_2O–dioxane (1 : 1) (several drops) in a sealed microtube at 80 °C for 4 h. The reaction mixture was diluted with H_2O and washed with $CHCl_3$. The H_2O layer was neutralized with Amberlite MB-3 resin and concentrated to dryness. The residue was heated with a few drops of *N*-trimethylsilylimidazole in a sealed microtube at 80 °C for 30 min. The reaction mixture was diluted with H_2O and extracted with *n*-C_6H_{14}. The *n*-C_6H_{14} layer was subjected to GLC analysis (t_R min: 23.1, 36.5 (glucose)).

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