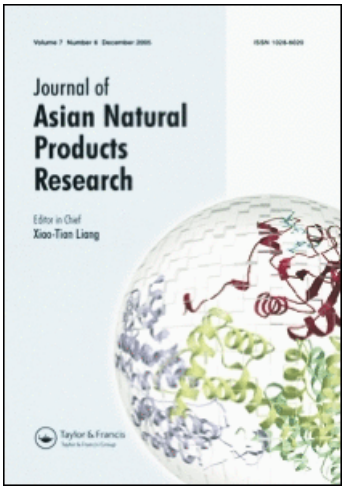

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Pervosides A and B, new isoferulyl glucosides from *Perovskia atriplicifolia*

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Pervosides A (**1**) and B (**2**), two new isoferulyl glucosides, have been isolated from the ethyl acetate soluble fraction of *Perovskia atriplicifolia* and their structures have been assigned on the basis of spectroscopic data. 3-Hydroxyestragole β-D-glucopyranoside (**3**) has also been isolated and characterized for the first time from this species.

Keywords: *Perovskia atriplicifolia*; Labiatae; pervosides A and B

1. Introduction

The genus *Perovskia* belonging to the family Labiatae comprises seven species. One of these is *Perovskia atriplicifolia* Benth., commonly known as Russian sage, which is a shrubby plant found in central Asia, Pakistan, Afghanistan, and Iran [1]. The plant has antibacterial activity and is also used as a cooling medicine in the treatment of fever [2]. Essential oils, phenolic compounds, flavonones, triterpenes, steroid, and their glycosides have so far been reported from this species [3–5]. The ethnopharmacological and chemotaxonomic importance of the genus *Perovskia* prompted us to reinvestigate the chemical constituents of *P. atriplicifolia.* As a result of studies on polar constituents, we herein report the isolation and structure elucidation of two new isoferulyl glucosides named as pervosides A (**1**) and B (**2**) (Figure 1), besides 3-hydroxyestragole β-D-glucopyranoside (**3**), which is isolated for the first time from this species [8].

2. Results and discussion

The ethyl acetate soluble fraction of the whole plant of *P. atriplicifolia* was subjected to column chromatography over silica gel eluting with different mobile phases. Compounds **1**–**3** were finally obtained and their structures established by IR, mass, and NMR spectroscopy, including 2D NMR techniques.

Pervoside A (**1**) was isolated as a white amorphous powder, $[\alpha]_D^{25} = -40.2$. Its molecular formula was established by field desorption and HRFABMS as $C_{16}H_{20}O_8$. The presence of hydroxyl, α,β-unsaturated aldehyde moiety and aromatic ring in **1** was indicated by IR bands at ν_{max} 3365, 2720, 1670, 1600, 1550, and 1465 cm^{-1}. The EIMS showed a peak at *m*/*z* 178 due to the loss of hexose moiety. The ^{1}H-NMR spectrum showed the presence of α,β-unsaturated aldehyde moiety [δ 9.60 (d, $J = 7.8$ Hz, 1H), 7.60 (d, $J = 15.8$ Hz, 1H), and 6.70 (dd, $J = 15.8$, 7.8 Hz, 1H)]. The larger coupling constant of the olefinic protons

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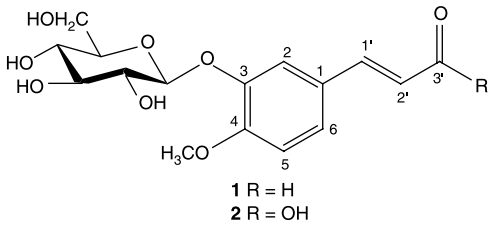

Figure 1. Structures of pervosides A (**1**) and B (**2**).

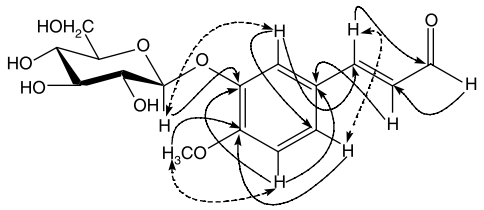

Figure 2. HMBC (→) and NOESY (→) correlations of pervoside A (**1**).

was in conformity with *E* configuration. A 1,3,4-trisubstituted aromatic ring was also evident from characteristic signals at δ 7.40 (d, $J = 1.6$ Hz, 1H), 7.02 (d, $J = 8.4$ Hz, 1H), and 6.91 (dd, $J = 8.4$, 1.6 Hz, 1H). A three-proton signal at δ 3.91 could be ascribed to a methoxyl group. The presence of hexose moiety was inferred by EIMS and further confirmed by the signal of an anomeric proton at δ 5.01 (d, $J = 7.1$ Hz, 1H). Its larger coupling constant of the anomeric proton allowed us to assign β-configuration to the sugar moiety. The other signals of the sugar moiety were observed at δ 3.53, 3.50, 3.48, and 3.44 (oxymethine protons). The oxymethylene protons were observed at δ 3.92 (dd, $J = 10.1$, 4.7 Hz, 1H) and 3.68 (dd, $J = 10.1$, 2.6 Hz, 1H). The broad band and distortionless enhancement by polarization transfer (DEPT) ^{13}C NMR spectrum showed signals at δ 151.2, 150.9, 130.4, 123.4, 118.2, and 114.6 for aromatic carbons while the α,β-unsaturated aldehyde carbons appeared at δ 196.0, 155.1, 128.2. The signals for hexose moiety appeared at δ 102.1, 78.4, 77.9, 74.8, 71.3, and 62.4. The signal at δ 56.8 was attributed to methoxy carbon.

Acid hydrolysis of **1** provided the aglycone and the sugar which could be identified as D-glucose through TLC comparison and sign of its optical rotation. The identity of the sugar was further confirmed by comparing the retention time of its trimethylsilyl (TMS) ether with that of the standard in gas chromatography (GC). The aglycone was identified as isoferulylaldehyde through comparison of physical and spectral data with those reported in literature [6]. The position of the glucose moiety was confirmed by HMBC correlations between anomeric proton at δ 5.01 and C-3 at δ 150.9. Further HMBC, HMQC and NOESY correlations were in complete agreement with the assigned structure of pervoside A (**1**) as (*E*)-isoferulylaldehyde-3-*O*-β-D-glucopyranoside (Figure 2).

Pervoside B (**2**) was obtained as colorless amorphous solid and the molecular formula $C_{16}H_{19}O_9$ was deduced by HRFABMS showing $[M - H]^-$ peak at *m/z* 355.1022. The IR and ^{1}H-NMR spectra were similar to **1**, except for the absence of signals of aldehyde group. It gave brisk effervescence with dilute $NaHCO_3$ solution, revealing the presence of free carboxylic group. The broad band and DEPT ^{13}C NMR spectra showed carbonyl signal of the carboxylic moiety at δ 172.1, while other peaks were similar to those of **1**. Acid hydrolysis of **2** provided D-glucose and the aglycone, the latter identified as isoferulic acid through comparison of physical and spectral data with literature [7]. Based on these evidences, the structure of pervoside B could be assigned as (*E*)-isoferulic acid-3-*O*-β-D-glucopyranoside (**2**).

3-Hydroxyestragole-β-D-glucopyranoside (**3**) was isolated for the first time from this genera and its structure was established by mass spectrometry, 1D and 2D NMR techniques and by comparison with previously reported data [8].

3. Experimental

3.1 General experimental procedures

The melting points were recorded on a Buchi melting point apparatus and are uncorrected. Optical rotations were measured on a Jasco

DIP-360 digital polarimeter using a 10 cm cell tube. The UV spectra were recorded on Hitachi-UV-3200 spectrometer. The IR spectra were recorded on Jasco-320-A spectrometer. The ^{1}H, ^{13}C NMR, and the 2D NMR spectra were recorded on a Bruker AMX-400,100 spectrometer in methanol-d_4. Chemical shifts are in ppm (δ), relative to tetramethylsilane as an internal standard, and scalar coupling constants are reported in Hz. Mass spectra were measured on Finnigan MAT 12 and MAT 312 spectrometers and ions are given in *m/z* (%).Column chromatography was carried out using silica gel 70–220 mesh and flash chromatography on silica gel 220–440 mesh. Alumina sheets precoated with silica gel 60 F_{254} (20 × 20 cm, 0.2 mm thick; E-Merck, Darmstadt, Germany) were used for TLC to check the purity and were visualized under UV light (254 and 366 nm) or sprayed with ceric sulfate solution.

3.2 Plant material

The whole plant of *P. atriplicifolia* Benth. (Labiatae) was collected from Quetta (Pakistan) and identified by Professor Rasool Bakhsh Tareen, Department of Botany, University of Baluchistan, where a voucher specimen has been deposited (BU-68).

3.3 Extraction and isolation

The shade-dried plant material (20 kg) was extracted with methanol (3 × 50 l) at room temperature. The extract was evaporated to yield residue (780 g), which was divided into *n*-hexane (65 g), chloroform (60 g), ethyl acetate (48 g), *n*-butanol (70 g), and water-soluble fractions (41 g). The EtOAc-soluble fraction was subjected to column chromatography over silica gel eluting with $CHCl_3$, $CHCl_3$/MeOH, and MeOH in increasing order of polarity. The fractions obtained from chloroform–methanol 9.5:0.5 were combined and further subjected to column chromatography using chloroform–methanol (9.0:1.0) as eluent and 100 fractions (10 ml each) were collected. Compound **3** was obtained from fractions 5–30 (23 mg), compound **1** from fractions 37–65 (20 mg), and compound **2** from fractions 70–98 (18 mg), respectively.

3.3.1 Compound (*1*)

White amorphous powder; mp 207–209°C; $[\alpha]_D^{25} = -40.2$ ($c = 0.3$ in CH_3OH). UV λ_{max} nm: 340, 310, 250. IR (KBr) ν_{max} cm^{-1}: 3365, 2720, 1670, 1600, 1550, 1465. ^{1}H-NMR (300 MHz) δ_H: 9.60 (d, $J = 7.8$ Hz, H-3′), 7.60 (d, $J = 15.8$ Hz, H-1′), 7.40 (d, $J = 1.6$ Hz, H-2), 7.02 (d, $J = 8.4$ Hz, H-5), 6.91 (dd, $J = 8.4$, 1.6 Hz, H-6), 6.70 (dd, $J = 15.8$, 7.8 Hz, H-2′), 5.01 (d, $J = 7.1$ Hz, glc-H-1), 3.92 (dd, $J = 10.1$, 4.7 Hz, glc-H-6a), 3.91 (s, 4-OCH_3), 3.68 (dd, $J = 10.1$, 2.6 Hz, glc-H-6b), 3.53 (m, glc-H-5), 3.50 (m, glc-H-2), 3.48 (m, glc-H-3), 3.44 (m, glc-H-4). ^{13}C-NMR (100 MHz) δ_C: 196.0 (C-3′), 155.1 (C-1′), 151.2 (C-4), 150.9 (C-3), 130.4 (C-1), 128.2 (C-2′), 123.4 (C-6), 118.2 (C-2), 114.6 (C-5), 102.1 (glc-C-1), 78.4 (glc-C-3), 77.9 (glc-C-5), 74.8 (glc-C-2), 71.3 (glc-C-4), 62.4 (glc-C-6), 56.8 (OMe). EIMS: *m/z* (%) 178 (10), 162 (18), 150 (15), 147 (20), 135 (22). HRFABMS *m/z* 339.1071 $[M - H]^-$ (calcd for $C_{16}H_{19}O_8$, 339.1079).

3.3.2 Compound (*2*)

White amorphous powder; mp 240–242°C; $[\alpha]_D^{25} = -46.5$ ($c = 0.2$ in CH_3OH). UV λ_{max} nm: 205, 218, 230, 285, 315. IR (KBr) ν_{max} cm^{-1}: 3510, 3190, 1680, 1545, 1475, 1110. ^{1}H-NMR (300 MHz) δ_H: 7.53 (d, $J = 15.3$ Hz, H-1′), 7.37 (d, $J = 1.8$ Hz, H-2), 6.98 (d, $J = 8.2$ Hz, H-5), 6.87 (dd, $J = 8.2$, 1.8 Hz, H-6), 6.81 (d, $J = 15.3$ Hz, H-2′), 4.84 (d, $J = 7.4$ Hz, glc-H-1), 3.73 (s, 4-OCH_3), 3.70 (1H, m, glc-H-6a), 3.61 (1H, m, glc-H-6b), 3.51 (m, glc-H-5), 3.50 (m, glc-H-2), 3.45 (m, glc-H-3), 3.42 (m, glc-H-4). ^{13} C-NMR (100 MHz) δ_C: 172.1 (C-3′), 153.7 (C-1′), 150.5 (C-4), 149.3 (C-3), 131.2 (C-1), 125.5 (C-2′), 122.1 (C-6), 117.8 (C-2), 115.1 (C-5), 103.1 (glc-C-1), 78.0 (glc-C-3), 77.8 (glc-C-5), 74.9 (glc-C-2), 71.3 (glc-C-4), 62.5

(glc-C-6), 56.6 (OMe). EIMS: *m/z* (%) 194 (20), 148 (15), 130 (10). HRFABMS: *m/z* 355.1022 $[M - H]^-$ (calcd for $C_{16}H_{19}O_9$, 355.1029).

*3.3.3 Acid hydrolysis of compounds **1** and **2***

Solutions of **1** and **2** (each 9 mg) in MeOH (6 ml) containing 1 N HCl (4 ml) were refluxed for 4 h, concentrated under reduced pressure, and diluted with H_2O (8 ml). It was extracted with EtOAc and the residue recovered from the organic phase provided isoferulylaldehyde through preparative TLC from **1** and isoferulic acid from **2**. The aqueous phase was concentrated and D-glucose was identified by the sign of its optical rotation ($[\alpha]_D^{25} = +52$ from **1** and $[\alpha]_D^{25} = +51$ from **2**). The identity of the sugar was further confirmed by comparing the retention time of its TMS ether with that of the standard in GC.

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