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MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

Azerosides A and B: Two new phloroacetophenone glycosides from the roots of *Dorema glabrum* Fisch. & C.A. Mey

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Abstract *Dorema glabrum* (Apiaceae) is a monocarpic plant distributed in southern Caucasus. The gum-resin of this species is traditionally used as diuretic and anti-diarrheal and for the treatment of bronchitis and catarrh. In the present study, free radical-scavenging activity and total phenolic content of the essential oil together with *n*-hexane, chloroform, ethyl acetate, and methanol extracts of *D. glabrum* roots were evaluated in DPPH and Folin-Ciocalteu assays, respectively. Methanol extract with the highest free radical-scavenging activity ($IC_{50} = 74.2 \pm 6.6$ μg ml^{-1}) and total phenolic content (186.7 ± 8.6 mg GAE/g) was subjected to phytochemical investigation using different chromatographic methods on the Si gel (normal and reversed-phase) and Sephadex LH-20 columns. Chemical constituents of the roots oil were also analyzed using GC and GC–MS. Two new phloroacetophenone glycosides, azerosides A (**1**) and azerosides B (**7**), along with nine known phenolic compounds, echisoside (**2**), pleoside (**3**), hyrcanoside (**4**), 7,8-dihydroferulic acid-4-O-β-D-glucopyranoside (**5**), Lavandoside (**6**), 6,7,8-trihydroxycoumarin (**8**), chlorogenic acid (**9**), 4,5-Di-O-caffeoylquinic acid (**10**), and cynarin (**11**), were isolated and identified from *D. glabrum* roots. Among the isolated compounds, **8–11** exhibited potent free radical-scavenging activity (IC_{50} values of 1.8–2.7 μg ml^{-1}) in comparison with BHT ($IC_{50} = 19.5 \pm 0.8$ μg ml^{-1}). Twenty-six compounds were also identified in the roots oil, among them myristicin (14.1 %) and elemicin (11.7 %), two bioactive phenylpropanoid derivatives, were main compounds. This study introduces *D. glabrum* as a source of phloroacetophenone glycosides and caffeoylquinic acid derivatives and suggests it as an appropriate candidate for further pharmacological and toxicological studies.

Keywords *Dorema glabrum* · Phenolic compounds · Essential oil · DPPH assay · Folin-Ciocalteu assay

Introduction

Iran with about 120 genera is one of the main distribution centers of the Apiaceae (*alt*. Umbelliferae) family plants in the world (Ghahreman, 2002; Mozaffarian, 2007). The genus *Dorema* from this family comprises about 12–14 species, mainly distributed in southwestern and central Asia (Rechinger, 1987; Pimenov, 1988). Some of *Dorema* species exude gum-resins with medicinal properties, among them the gum-resin "ammoniacum" from *D. ammoniacum* is a well-known therapeutic agent which is used as an antispasmodic and expectorant and for the treatment of skin inflammatory diseases (Amanzadeh, 2002).

Dorema glabrum Fisch. & C.A. Mey. is one of the seven *Dorema* species from the flora of Iran which is also found in Azerbaijan Republic and Armenia (Mozaffarian, 2007). In Nakhichevan region (Azerbaijan Republic), the gum-resin of this species is used by Azeri people as a diuretic and anti-diarrheal agent, as well as for the treatment of bronchitis and catarrh (Mirbabayev *et al*., 1993).

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Previous biological surveys have shown anti-lipidemic and antioxidant effects of the aerial parts (Dehghan *et al*., 2009) and cytotoxic activity of the fruits of *D. glabrum* (Amirkhiz *et al*., 2013). The essential oil of the roots of this plant has also been reported to contain δ-cadinene and β-bisabolene as the main compounds with a weak free radical-scavenging activity ($IC_{50} = 2.2$ mg ml^{-1}) (Asnaashari *et al*., 2011).

Unfortunately, decrease in natural population of *D. glabrum* during recent decades, which is most likely caused by extensive medicinal uses and seed germination problems in *Dorema* genus plants, has led it to be considered as an endangered species (Ibadullayeva *et al*., 2011; Irvani *et al*., 2012).

Previous reports on phytochemical constituents of *Dorema* species roots are limited to the isolation of some sesquiterpene derivatives from *D. kopetdaghense* (Iranshahi *et al*., 2007) and some phloroacetophenone glycosides from *D. hyrcanum* (Nurmukhamedova and Nikonov, 1976) and *D. aitchisonii* (Bukreeva and Pimenov, 1991). In this study, we report essential oil composition and isolation of the eleven free radical-scavenging compounds from *D. glabrum* roots including two new phloroacetophenone glycosides, namely azerosides A and B.

Experimental section

Plant material

The roots of *D. glabrum* were collected from the rocky slopes of "Ghaflankuh" mountains located in East-Azerbaijan (northwest of Iran) in June 2012. A voucher specimen of the plant (No. 2120 MPIH) was deposited in the herbarium of Institute of Medicinal Plants, ACECR, Karaj, Iran.

Extraction

The air-dried and ground roots (2.4 kg) were macerated successively with n-hexane, chloroform, ethyl acetate, and methanol (3 × 5 L each) at the room temperature. The obtained extracts were then concentrated using a rotary evaporator under 45 °C.

Essential oil extraction

The air-dried and comminuted roots (100 g) were subjected to hydrodistillation for 4 h using a Clevenger-type apparatus to produce pale yellow oil in 0.3 % (v/w) yield. The obtained oil was dried over anhydrous sodium sulfate and stored in 4 °C until analysis.

DPPH free radical-scavenging activity assay

Free radical-scavenging potentials of the samples were evaluated using 2, 2-diphenyl-1-picryl-hydrazyl (DPPH) method described by Delazar *et al*., (2012). Briefly, the stock sample solution (5 mg ml^{-1} in methanol) was diluted twofold with methanol to get concentrations ranging from 5 to 9.5 × 10^{-3} mg ml^{-1}. DPPH (Sigma) was prepared in the concentration of 80 μg ml^{-1} in methanol. Diluted solutions (1 ml each) were mixed with 1 ml of DPPH solution and were kept 30 min at 25 °C in dark for any reaction to take place.

UV absorptions of the solutions were recorded on a Cecil CE7250 spectrophotometer at 517 nm. Butylated hydroxytoluene (BHT), a synthetic antioxidant, was used as a positive control. All tests were performed in triplicate, and IC_{50} values were reported as Mean ± SD.

Determination of total phenolic content

Total phenolic content (TPC) of the extracts was measured by a colorimetric method using Folin-Ciocalteu reagent as described by Moradi-afrapoli *et al*., (2012). Briefly, 1.5 ml of tenfold distilled-water diluted Folin-Ciocalteu reagent (Merck) was added to 200 μl of extract solution (500 μg ml^{-1} in methanol) and allowed to stand at the room temperature for 5 min. Sodium bicarbonate solution (60 g l^{-1}, 1.5 ml) was then added to the mixture and stored 90 min at 22 °C. The absorptions of the final solution were recorded on a Cecil CE7250 spectrophotometer at 725 nm.

The TPCs were quantified using a calibration curve obtained from absorbance measuring of the known gallic acid concentrations (50–200 μg ml^{-1} in methanol) as standard. The experiment was performed in triplicate, and the results were expressed as milligrams of gallic acid equivalents (GAE) per gram of dry extracts as Mean ± SD.

Isolation and purification of compounds

Methanol extract having the highest free radical-scavenging activity and TPC (Table 1) was subjected to phytochemical analysis to identify the compounds involved in its free radical-scavenging activity.

Insoluble white precipitate was appeared after adding the methanol (100 ml) to the methanol extract (100 g). One gram of the filtered insoluble material (7 g in total) was moved on a reversed-phase (RP-18) column (230–400 mesh, fully endcapped, Fluka) and eluted with CH_3CN-H_2O (1:9) to get one (12 mg) and two (680 mg). Fifty grams of the concentrated supernatant (the soluble part) was chromatographed on a Sephadex LH-20 (Fluka) column, eluted with MeOH to afford four fractions (A–D). Si gel column chromatography (230–400 mesh, Merck) of the

fraction A (10 g) eluted with a gradient mixture of MeOH-$CHCl_3$ (2:8 → 4:6) yielded twelve fractions ($A_{1–12}$). Compound **3** (58 mg) was obtained from the fraction A_1 (173 mg) by chromatography on a RP-18 column, eluted with CH_3CN-H_2O (2:8). RP-18 column chromatography of the fraction A_4 (360 mg) (CH_3CN-H_2O, 2:8) afforded three fractions ($A_{4a–4c}$). Fraction A_{4b} (60 mg) was purified on a RP-18 column (CH_3CN-H_2O, 1.5:8.5) to get **4** (53 mg). Si gel column chromatography of the fraction A_5 (435 mg) eluted with MeOH-$CHCl_3$ (2.5:7.5) yielded four fractions ($A_{5a–5d}$). Fraction A_{5a} (77 mg) was moved on a RP-18 column (CH_3CN-H_2O, 2:8) to get **5** (35 mg) and **6** (7 mg). RP-18 column chromatography of the fraction A_{11} (270 mg) with CH_3CN:H_2O (0.5:9.5 → 1.5:8.5) resulted in the isolation of **7** (36 mg). A portion of fraction B (2 g) was moved on a RP-18 column (CH_3CN-H_2O, 0.5:9.5 → 2:8) to obtain nine fractions ($B_{1–9}$). Fraction B_1 (415 mg) was rechromatographed over a RP-18 column (CH_3CN-H_2O, 0.5:9.5) to get **8** (8 mg) and **9** (162 mg). Fraction B_6 (320 mg) moved on a Sephadex LH-20 column and eluted with MeOH-H_2O (8:2) gave **10** (110 mg). Compound **11** (94 mg) was obtained from the fraction B_7 (360 mg) by chromatography on Si gel column, eluted with H_2O-HCOOH-CH_3COOH-EtOAc (2.4:1:1:63).

In all steps, column chromatography was monitored by thin layer chromatography (Pre-coated Si gel GF_{254} and Si gel 60 RP-18 F_{254}s plates, Merck), and fractions with similar spots detected under UV (254 and 366 nm) or after spraying anisaldehyde/sulfuric acid reagent were combined.

The structures of the isolated compounds were elucidated by ^{1}H-NMR, ^{13}C-NMR, HMBC, and HSQC spectral analysis (Bruker Avance 400 DRX, 400 MHz for ^{1}H and 100 MHz for ^{13}C), as well as by comparing with data published in the literature. In the case of new compounds, melting points were measured on an Electro-thermal melting point apparatus. The optical rotations were determined on a Perkin-Elmer 241 polarimeter. UV spectra were recorded on a Cecil CE7250 spectrophotometer. IR spectra were obtained on a Nicolet Magna 550-FT-IR spectrometer. EIMS spectra were acquired on a Hewlett-Packard model 5973 HP system. Elemental analyses were carried out on Costech 4010 CHNS/O Elemental Combustion System.

Sugar analysis

The type of sugar moieties was confirmed, if needed, by a chromatographic method described by Yassa *et al*., (2007). Briefly, about 10 mg of compound was hydrolyzed in acidic condition (HCl (2 N), 10 ml) with heating for 45 min on a steam bath. The obtained solution was cooled and extracted by diethyl ether to remove aglycon portion. The aqueous phase was then chromatographed alongside with glucose, galactose, rhamnose, mannose, and xylose on paper (Whatman, No. 1) in ethyl acetate-pyridine-water (12:5:4) as solvent system. The chromatogram was then sprayed with a solution of *p*-anisidine hydrochloride/sodium hydrosulfite reagent and heated for 10 min until the appearance of brown spots of sugars.

GC and GC–MS analysis of the essential oil

The essential oil was analyzed on a Hewlett-Packard 6890 gas chromatograph with HP-5MS column (30 m × 0.25 mm id, 0.25 μm film thickness) equipped with a mass detector (Hewlett-Packard model 5973 HP). The flow rate of helium (carrier gas) was 1 ml min^{-1}. The initial oven temperature was 40 °C and was then raised at a rate of 3 °C per minute to 250 °C. The injection temperature was 250 °C, and the oil sample (1 μl) was injected with a split ratio of 1:90. The mass spectra were obtained by electron ionization at 70 eV. The retention indices (RI) of the compounds were calculated using a homologous series of *n*-alkanes injected in conditions equal to the samples.

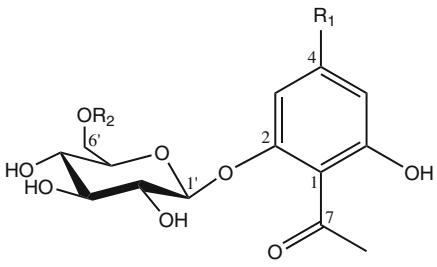
Identification of the compounds was carried out using computer matching with the Wiley7n.L library, and also by comparison of the RI and fragmentation pattern of the mass spectra with those for standard compounds published in the literature (Adams, 2007).

The essential oil was also analyzed on an Agilent HP-6890 gas chromatograph coupled with a FID detector for calculation of the relative amounts of the separated compounds. The FID detector temperature was 290 °C, and the operation was performed under the same conditions as described for GC–MS analysis.

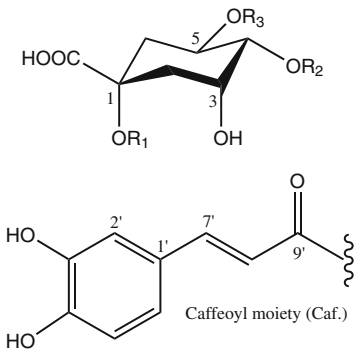
Results and discussion

Among the tested extracts, methanol extract was found to contain the highest free radical-scavenging capacity (IC_{50} = 74.2 ± 6.6 μg ml^{-1}) and TPC (186.7 ± 8.6 mg GAE/g) in DPPH and Folin-Ciocalteu assays, respectively (Table 1).

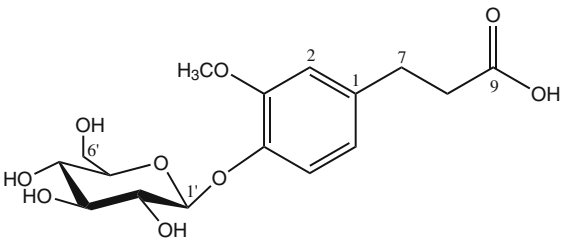
Phytochemical analysis of this bioactive extract using different chromatographic methods yielded to the isolation of eleven phenolic compounds. The isolated compounds were identified as 2-O-[β-D-glucopyranosyl-(1″ → 6′)-β-D-glucopyranosyl]-phloroacetophenone (azeroside A) (**1**), 2-O-[β-D-glucopyranosyl-(1″ → 6′)-β-D-glucopyranosyl]-4-O-methyl-phloroacetophenone (echisoside) (**2**) (Bukreeva and Pimenov, 1991), 2-O-β-D-glucopyranosyl-4-O-methyl-phloroacetophenone (pleoside) (**3**) (Nurmukhamedova and Nikonov, 1976; Chevalley *et al*., 2001), 2-O-[α-D-glucopyranosyl-(1″ → 6′)-β-D-glucopyranosyl]-4-O-methyl-phloroacetophenone (hyrcanoside) (**4**) (Nurmukhamedova and Nikonov, 1976; Singh and Bharate, 2006), 7,8-dihydroferulic acid-4-O-β-D-



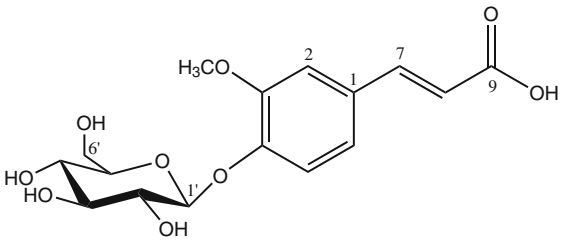
	R_1	R_2
Azeroside A (**1**)	OH	β-D-glucopyranosyl
Echisoside (**2**)	OCH_3	β-D-glucopyranosyl
Pleoside (**3**)	OCH_3	H
Hyrcanoside (**4**)	OCH_3	α-D-glucopyranosyl
Azeroside B (**7**)	OCH_3	β-D-glucopyranosyl-(6",1'")-β-D-glucopyranosyl



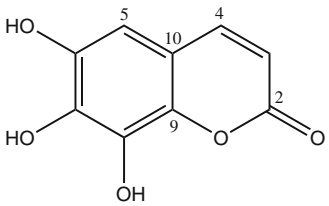
	R_1	R_2	R_3
Chlorogenic acid (**9**)	H	H	Caf.
4,5-diCQA (**10**)	H	Caf.	Caf.
Cynarin (**11**)	Caf.	H	Caf.



7,8-dihydroferulic acid-4-O-β-D-glucopyranoside (**5**)



Ferulic acid-4-O-β-D-glucopyranoside (**6**)



6,7,8-trihydroxycoumarin (**8**)

Fig. 1 Structures of the isolated compounds from the methanol extract of *D. glabrum* roots

glucopyranoside (**5**) (Kraus and Spiteller, 1997; Tezuka *et al.*, 2001), Ferulic acid-4-O-β-D-glucopyranoside (**6**) (Kurkin *et al.*, 2008; Morikawa *et al.*, 2012), 2-O-[β-D-glucopyranosyl-(1″ → 6′)-β-D-glucopyranosyl-(1‴ → 6″)-β-D-glucopyranosyl]-4-O-methyl-phloroacetophenone (azeroside B) (**7**), 6,7,8-trihydroxycoumarin (**8**) (Nykolov *et al.*, 1993; Kayser and Kolodziej, 1995), 5-O-caffeoylquinic acid (5-CQA, chlorogenic acid) (**9**) (Chan *et al.*, 2009), 4,5-Di-O-caffeoylquinic acid (4,5-diCQA) (**10**) (Basnet *et al.*, 1996), and 1,5-Di-O-caffeoylquinic acid (1,5-diCQA, cynarin) (**11**) (Carnat et al., 2000).

The structures of these compounds were elucidated using their NMR spectroscopic data (^{1}H-NMR, ^{13}C-NMR, HMBC, and HSQC) and by comparing with those reported in the literature (Fig. 1).

Among the isolated compounds, azeroside A (**1**) and azeroside B (**7**) report in this study for the first time. This is also the first report on the isolation of **5**–**11** from *Dorema* genus plants. Compounds **5** and **8** are two rare compounds which have been reported from few natural sources (Nykolov *et al.*, 1993; Kayser and Kolodziej, 1995; Kraus and Spiteller, 1997; Tezuka *et al.*, 2001).

The ^{1}H-NMR spectrum of **1** was found similar to echisoside (**2**), a known phloroacetophenone glycoside previously reported from the roots of *D. aitchisonii* (Bukreeva and Pimenov, 1991), with an additional broad singlet resonance at δ 8.38 and without any resonance characteristic for methoxy group at δ 3.7–4. These differences suggested that the methoxy group of **2** has been substituted by a hydroxy group in **1**. Therefore, structure of 1-{2-[β-D-glucopyranosyl-(1 → 6)-β-

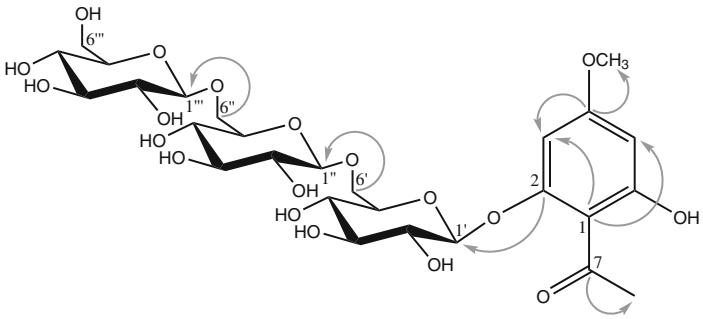


Fig. 2 Selected HMBC correlations (C → H) for Azeroside B (**7**)

D-glucopyranosyloxy]-4,6-dihydroxyphenyl}-1-ethanone was suggested for compound **1** (Fig. 1), supporting with ^{13}C-NMR spectral data, and was named azeroside A. The EIMS spectrum of 1 revealed $[M + H]^+$ ion peak at *m/z* 493, corresponding to the molecular formula $C_{20}H_{28}O_{14}$ (M = 492). An ion peak at *m/z* 168 was also found in EIMS spectrum of **1**, assignable to the 1-[2,4,6-trihydroxyphenyl]-1-ethanone (phloroacetophenone) fragment as aglycon of **1**. The monoglycoside analog of azeroside A, Myrciaphenone A, has been reported from *Curcuma comosa* and *Corymbia maculata* with choleretic and antileishmanial activities (Suksamrarn *et al*., 1997; Sidana *et al*., 2013).

Pleoside (domesticoside) (3) has previously been isolated from the roots of *D. hyrcanum* (Nurmukhamedova and Nikonov, 1976). This compound has also been identified as an antifungal principle of the roots of *Ribes rubrum* (Chevalley *et al*., 2001).

Hyrcanoside (**4**) is a stereoisomer of **2**, previously reported from the roots of *D. hyrcanum* (Nurmukhamedova and Nikonov, 1976). The appearance of the anomeric proton resonances at δ 5.00 (1H, *d*, $J = 7.1$ Hz) and 4.81 (1H, *d*, $J = 2.8$ Hz) in ^{1}H-NMR spectra of this compound and identification of only glucose as a result of paper chromatography following acidic hydrolyses of this compound were indicative of α (1 → 6) linkage of its two glucopyranosyl moieties.

^{1}H and ^{13}C-NMR spectra of **7** showed a methoxy phloroacetophenone derivative structure similar to **2**–**4**, containing three glucopyranosyl moieties. The 4-O-methyl-phloroacetophenone skeleton was confirmed as aglycon of **7** from long-range correlations ($^2J_{HC}$ or $^3J_{HC}$) of δ 3.81 (3H, *s*, OCH_3) and δ 6.37 (1H, *d*, $J = 2$, H_3) with δ 165.73 (C_4), δ 2.66 (3H, *s*, H_8) with δ 203.46 (C_7), as well as δ 6.37 (1H, *d*, $J = 2$, H_3) and δ 6.12 (1H, *d*, $J = 2$, H_5) with δ 105.71 (C_1) in HMBC spectrum of **7** (Fig. 2). The EIMS spectrum of **7** also displayed an ion peak at *m/z* 182, representing the 4-O-methyl-phloroacetophenone ($C_9H_2O_4$) fragment as aglycon of **7**. The anomeric carbon resonances of glucosyl moieties were assigned at δ 100.8 ($C_{1'}$), 103.31 ($C_{1''}$), and 103.61($C_{1'''}$) from their direct correlations ($^1J_{HC}$) with δ 5.04 (1H, *d*, $J = 7.3$, $H_{1'}$), 4.20 (1H, *d*, $J = 7.7$, $H_{1''}$), 4.18 (1H, *d*, $J = 7.7$, $H_{1'''}$), respectively, observed in HSQC spectrum of **7**. Finally, detection of $^3J_{H,C}$ correlations of $H_{1''}$ (δ 4.20) with $C_{6'}$ (δ 68.70), and $H_{1'''}$ (δ 4.18) with $C_{6''}$ (δ 69.18) in HMBC spectrum of **7** resulted in elucidation of 1-{2-[β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyloxy]-6-hydroxy-4-methoxyphenyl}-1-ethanone structure for compound **7**, a new compound which was named azeroside B (Fig. 1).

All of the five isolated phloroacetophenone glycosides (**1**–**4**, **7**) exhibited a moderate free radical-scavenging activity in DPPH assay, which reports in this study for the first time (Table 1).

7,8-dihydroferulic acid-4-O-β-D-glucopyranoside (**5**) is a rare phenolic compound with anti-inflammatory activity reported from *Zanthoxylum bungeanum* (Kraus and Spiteller, 1997) and *Picea glauca* (Tezuka *et al*., 2001). This compound was differentiated from **6** by the resonance patterns of H_7 and H_8 in their ^{1}H-NMR spectra. The resonances of these two protons were assigned at δ 7.72 (1H, *d*, $J = 16.2$ Hz, H_7) and 6.32 (1H, *d*, $J = 16.2$ Hz, H_8) for **6**, whereas they were revealed as two multiplets at lower chemical shifts at δ 2.75 (2H, *m*, H_7) and 2.45 (2H, *m*, H_8) in the ^{1}H-NMR spectrum of **5**.

6,7,8-trihydroxycoumarin (**8**) is another isolated rare compound previously reported from *Pelargonium sidoides* (Nykolov *et al*., 1993) and *Fraxinus ornus* (Kayser and Kolodziej, 1995). This compound has also been isolated in glycoside form (6,7,8-trihydroxycoumarin-O-rhamnopyranoside) from *Sarcandra glabra* (Li *et al*., 2011).

Compounds **9**–**11** are classified as caffeoylquinic acid derivatives. These natural polyphenolic compounds are widely distributed in plant families and have been considered for their various biological effects such as antioxidant, hepatoprotective, hypocholesterolemic, anti-carcinogenic, anti-inflammatory, and anti-PAF activity (Schutz *et al*., 2004; Zhao *et al*., 2006).

Isolated caffeoylquinic acid derivatives (**9**–**11**), along with 6,7,8-trihydroxycoumarin (**8**) exhibited potent free radical-scavenging activity in DPPH assay (IC_{50} values of 1.8–2.7 μg ml^{-1}), about nine to ten times stronger than BHT ($IC_{50} = 19.5 \pm 0.8$ μg ml^{-1}), a synthetic

Table 1 Total phenolic content (TPC) of the extracts and free radical-scavenging activity of the oil, extracts and compounds obtained from the *D. glabrum* roots

Sample	TPC (mg GAE/g)[b]	FRS activity[a] IC_{50} (μg ml^{-1})[c]
Essential oil	–	1,830 ± 23.1
n-Hexane extract	51.6 ± 4.7	277.3 ± 9.8
Chloroform extract	59.1 ± 4.2	241.8 ± 7.2
Ethyl acetate extract	83.5 ± 6.1	157.2 ± 8.1
Methanol extract	186.7 ± 8.6	74.2 ± 6.6
Azeroside A (**1**)	–	25.6 ± 3.2
Echisoside (**2**)	–	47.8 ± 5.5
Pleoside (**3**)	–	34.1 ± 2.0
Hyrcanoside (**4**)	–	44.6 ± 2.8
Dihydroferulic acid glucoside (**5**)	–	38.8 ± 5.1
Ferulic acid glucoside (**6**)	–	31.4 ± 3.7
Azeroside B (**7**)	–	56.0 ± 6.9
6,7,8-trihydroxycoumarin (**8**)	–	1.8 ± 0.3
Chlorogenic acid (**9**)	–	2.2 ± 0.5
4,5-diCQA (**10**)	–	2.7 ± 0.3
Cynarin (**11**)	–	2.6 ± 0.4
BHT	–	19.5 ± 0.8

[a] Free radical-scavenging activity

[b] Milligrams of gallic acid equivalent per gram of dry extract

[c] Concentration providing 50 % inhibition

commercial antioxidant (Table 1). Considering to the well-recognized role of free radicals and reactive oxygen species (ROS) in pathogenesis of many diseases such as cancers, atherosclerosis, rheumatoid arthritis, and neurodegenerative diseases, natural antioxidants (either in diet or in supplement form) have recently received special attention for their potential role in the prevention of such diseases (Valko *et al*., 2007). In food industries, natural antioxidants could also be appropriate substitutes for synthetic antioxidants such as BHT and butylated hydroxyanisole (BHA), which have been questioned for their safety (Barlow, 1990).

Chromatographic and spectroscopic data

*1-{2-[β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyloxy]-4,6-dihydroxyphenyl}-1-ethanone; 2-O-[β-D-glucopyranosyl-(1″ → 6′)-β-D-glucopyranosyl]-phloroacetophenone; azeroside A (**1**)*

White solid; mp 209–210 °C; R_f: 0.40 ($CHCl_3$-MeOH, 8:2); $[\alpha]_D^{25}$ −62.5 (c 0.002, MeOH); UV (MeOH) λ max (log ε): 205 (0.75), 282.5 (0.43) nm; IR (KBr) ν max: 3,473, 3,406, 2,926, 1,626, 1,596, 1,428, 1,398, 1,290–1,029, 929, 594 cm^{-1}; ^{1}H-NMR (DMSO-d_6, δ/ppm, *J*/Hz): 13.78 (1H, *s*, OH_6), 8.38 (1H, *s*, OH_4), 6.22 (1H, *d*, $J = 2$, H_3), 5.87 (1H, *d*, $J = 2$, H_5), 4.92 (1H, *d*, $J = 7.3$, $H_{1'}$), 4.25 (1H, *d*, $J = 7.1$, $H_{1''}$), 3–4 (12H, *m*, $H_{2'-6',2''-6''}$), 2.64 (3H, *s*, H_8); ^{13}C-NMR (DMSO-d_6, δ/ppm): 202.44 (C_7), 165.82 (C_4), 165.82 (C_6), 160.96 (C_2), 104.35 (C_1), 103.26 ($C_{1''}$), 100.64 ($C_{1'}$), 96.93 (C_5), 94.71 (C_3), 76.83 ($C_{3''}$), 76.61 ($C_{3'}$), 76.36 ($C_{5''}$), 75.94 ($C_{5'}$), 73.59 ($C_{2''}$), 73.07 ($C_{2'}$), 69.98 ($C_{4''}$), 69.30 ($C_{4'}$), 68.03 ($C_{6'}$), 60.87 ($C_{6''}$), 32.84 (C_8); EIMS, 40 eV, *m/z* (%): 493 $[M + H]^+$ (2), 168 [Aglycon] (40), 153 [Aglycon -CH_3] (100); Anal. Calcd. for $C_{20}H_{28}O_{14}$: C, 48.78; H, 5.73; O, 45.49. Found: C, 47.13; H, 5.48; O, 44.81.

*2-O-[β-D-glucopyranosyl-(1″ → 6′)-β-D-glucopyranosyl]-4-O-methyl-phloroacetophenone; echisoside (**2**)*

White amorphous solid; R_f: 0.45 ($CHCl_3$-MeOH, 8:2); ^{1}H-NMR (DMSO-d_6, δ/ppm, *J*/Hz): 13.67 (1H, *s*, OH_6), 6.34 (1H, *d*, $J = 2$, H_3), 6.12 (1H, *d*, $J = 2$, H_5), 5.04 (1H, *d*, $J = 7.3$, $H_{1'}$), 3.99 (1H, *d*, $J = 7.0$, $H_{1''}$), 3.81 (3H, *s*, OCH_3), 2.90–3.75 (12H, *m*, $H_{2'-6',2''-6''}$), 2.66 (3H, *s*, H_8); ^{13}C-NMR (DMSO-d_6, δ/ppm): 203.50 (C_7), 165.72 (C_4), 165.53 (C_6), 160.54 (C_2), 105.82 (C_1), 103.65 ($C_{1''}$), 100.45 ($C_{1'}$), 95.05 (C_5), 93.50 (C_3), 76.90 ($C_{3''}$), 76.72 ($C_{3'}$), 76.63 ($C_{5''}$), 75.55 ($C_{5'}$), 73.53 ($C_{2''}$), 73.11 ($C_{2'}$), 70.06 ($C_{4''}$), 69.66 ($C_{4'}$), 68.89 ($C_{6'}$), 61.03 ($C_{6''}$), 55.72 (OCH_3), 33.13 (C_8) (Bukreeva and Pimenov, 1991).

*2-O-β-D-glucopyranosyl-4-O-methyl-phloroacetophenone; pleoside (**3**)*

White amorphous solid; R_f: 0.85 ($CHCl_3$-MeOH, 8:2); ^{1}H-NMR (DMSO-d_6, δ/ppm, *J*/Hz): 13.72 (1H, *s*, OH_6), 6.28 (1H, *d*, $J = 2$, H_3), 6.13 (1H, *d*, $J = 2$, H_5), 5.00 (1H, *d*, $J = 7.4$, $H_{1'}$), 3.80 (3H, *s*, OCH_3), 3.10–3.75 (6H, *m*, $H_{2'-6'}$), 2.66 (3H, *s*, H_8); ^{13}C-NMR (DMSO-d_6, δ/ppm): 203.47 (C_7), 165.60 (C_4), 165.53 (C_6), 160.59 (C_2), 106.12 (C_1), 100.64 ($C_{1'}$), 94.96 (C_5), 93.43 (C_3), 77.26 ($C_{3'}$), 76.70 ($C_{5'}$), 73.09 ($C_{2'}$), 69.64 ($C_{4'}$), 60.62 ($C_{6'}$), 55.59 (OCH_3), 33.09 (C_8) (Chevalley *et al*., 2001).

*2-O-[α-D-glucopyranosyl-(1″ → 6′)-β-D-glucopyranosyl]-4-O-methyl-phloroacetophenone; hyrcanoside (**4**)*

White solid; R_f: 0.65 ($CHCl_3$-MeOH, 8:2); ^{1}H-NMR (DMSO-d_6, δ/ppm, *J*/Hz): 6.27 (1H, *br s*, H_3), 6.13 (1H, *br s*, H_5), 5.00 (1H, *d*, $J = 7.1$, $H_{1'}$), 4.81 (1H, *d*, $J = 2.8$, $H_{1''}$), 3.80 (3H, *s*, OCH_3), 3–4 (12H, *m*, $H_{2'-6',2''-6''}$), 2.66 (3H, *s*, H_8); ^{13}C-NMR (DMSO-d_6, δ/ppm): 203.46 (C_7), 165.61 (C_4), 165.47 (C_6), 160.56 (C_2), 109.23 ($C_{1''}$), 105.83 (C_1), 100.60 ($C_{1'}$), 95.08 (C_5), 93.36 (C_3), 78.69 ($C_{3''}$),

76.59 ($C_{3'}$), 75.88 ($C_{5'}$), 75.53 ($C_{5''}$), 73.28 ($C_{2''}$), 73.01 ($C_{2'}$), 69.83 ($C_{4''}$), 69.83 ($C_{4'}$), 67.65 ($C_{6'}$), 63.13 ($C_{6''}$), 55.63 (OCH_3), 33.06 (C_8) (Nurmukhamedova and Nikonov, 1976).

*7,8-dihydroferulic acid-4-O-β-D-glucopyranoside (**5**)*

White crystals; R_f: 0.70 ($CHCl_3$-MeOH, 8:2); ^{1}H-NMR (DMSO-d_6, δ/ppm, *J*/Hz): 7.04 (1H, *d*, $J = 8.5$, H_5), 6.07 (1H, *d*, $J = 2.5$, H_2), 6.49 (1H, *dd*, $J = 8.5, 2.5$, H_6), 4.80 (1H, *d*, $J = 7.3$, $H_{1'}$), 3.70 (3H, *s*, OCH_3), 3.0–3.6 (6H, *m*, $H_{2'\text{-}6'}$), 2.75 (2H, *m*, H_7), 2.45 (2H, *m*, H_8); ^{13}C-NMR (DMSO-d_6, δ/ppm): 174.64 (C_9), 158.70 (C_4), 156.14 (C_3), 129.82 (C_5), 121.70 (C_1), 106.53 (C_2), 101.54 (C_6), 100.90 ($C_{1'}$), 77.12 ($C_{3'}$), 76.73 ($C_{5'}$), 73.34 ($C_{2'}$), 69.88 ($C_{4'}$), 60.77 ($C_{6'}$), 54.96 (OCH_3), 34.33 (C_7), 24.76 (C_8) (Kraus and Spiteller, 1997; Tezuka *et al*., 2001).

*Ferulic acid-4-O-β-D-glucopyranoside; lavandoside (**6**)*

White crystals; R_f: 0.70 ($CHCl_3$-MeOH, 8:2); ^{1}H-NMR (DMSO-d_6, δ/ppm, *J*/Hz): 7.72 (1H, *d*, $J = 16.2$, H_7), 7.53 (1H, *d*, $J = 8.7$, H_5), 6.68 (1H, *d*, $J = 2.4$, H_2), 6.53 (1H, *dd*, $J = 8.7, 2.4$, H_6), 6.32 (1H, *d*, $J = 16.2$, H_8), 4.92 (1H, *d*, $J = 7.3$, $H_{1'}$), 3.70 (3H, *s*, OCH_3), 3.0–3.6 (6H, *m*, $H_{2'\text{-}6'}$); ^{13}C-NMR (DMSO-d_6, δ/ppm): 168.65 (C_9), 161.97 (C_3), 161.97 (C_4), 156.99 (C_7), 138.25 (C_1), 129.21 (C_6), 116.16 (C_8), 107.99 (C_5), 77.21 ($C_{3'}$), 76.83 ($C_{5'}$), 73.27 ($C_{2'}$), 69.77 ($C_{4'}$), 60.67 ($C_{6'}$), 55.31 (OCH_3) (Kurkin *et al*., 2008).

*1-{2-[β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyloxy]-6-hydroxy-4-methoxyphenyl}-1-ethanone; 2-O-[β-D-glucopyranosyl-(1″ → 6′)-β-D-glucopyranosyl-(1‴ → 6″)-β-D-glucopyranosyl]-4-O-methyl-phloroacetophenone; azeroside B (**7**)*

White solid; mp 156–157 °C; R_f: 0.20 ($CHCl_3$-MeOH, 8:2); $[\alpha]_D^{25}$ −42.5 (c 0.002, MeOH); UV (MeOH) λmax (log ε): 223.1 (0.5), 282.5 (0.6) nm; IR (KBr) ν max: 3,483, 3,437, 2,926, 1,635, 1,590, 1,401, 1,295-1,082, 987, 853 cm^{-1}; ^{1}H-NMR (DMSO-d_6, δ/ppm, *J*/Hz): 13.69 (1H, *s*, OH_6), 6.37 (1H, *d*, $J = 2$, H_3), 6.12 (1H, *d*, $J = 2$, H_5), 5.04 (1H, *d*, $J = 7.3$, $H_{1'}$), 4.20 (1H, *d*, $J = 7.7$, $H_{1''}$), 4.18 (1H, *d*, $J = 7.7$, $H_{1'''}$), 3.81 (3H, *s*, OCH_3), 2.9–4 (18H, *m*, $H_{2'-6',2''-6'',2'''-6'''}$), 2.66 (3H, *s*, H_8); ^{13}C-NMR (DMSO-d_6, δ/ppm): 203.46 (C_7), 165.73 (C_4), 165.52 (C_6), 160.47 (C_2), 105.71 (C_1), 103.61 ($C_{1'''}$), 103.31 ($C_{1''}$), 100.38 ($C_{1'}$), 94.89 (C_5), 93.64 (C_3), 67–77($C_{2'-5',\ 2''-5'',\ 2'''-5'''}$), 69.18 ($C_{6''}$), 68.70 ($C_{6'}$), 60.92 ($C_{6'''}$), 55.67 ($OCH_3$), 33.08 ($C_8$); EIMS, 40 eV, *m/z* (%): 182 [Aglycon] (35), 167 [Aglycon - CH_3] (100); Anal. Calcd. for $C_{27}H_{40}O_{19}$: C, 48.50; H, 6.03; O, 45.46. Found: C, 47.24; H, 6.87; O, 44.76.

*6,7,8-trihydroxycoumarin (**8**)*

Brown solid; R_f: 0.90 ($CHCl_3$-MeOH, 8:2); 1H-NMR (DMSO-d_6, δ/ppm, *J*/Hz): 7.47 (1H, *d*, $J = 8.3$, H_4), 6.05 (1H, *d*, $J = 8.3$, H_3), 6.02 (1H, *s*, H_5); ^{13}C-NMR (DMSO-d_6, δ/ppm): 172.76 (C_2), 166.81 (C_7), 164.79 (C_9), 161.25 (C_6), 161.25 (C_8), 131.47 (C_4), 112.54 (C_{10}), 104.87 (C_3), 102.11 (C_5) (Nykolov *et al*., 1993; Kayser and Kolodziej, 1995).

*5-O-caffeoylquinic acid; chlorogenic acid (**9**)*

Yellow amorphous solid; R_f: 0.55 ($CHCl_3$-MeOH, 8:2); ^{1}H-NMR (DMSO-d_6, δ/ppm, *J*/Hz): 7.45 (1H, *d*, $J = 15.8$, $H_{7'}$), 7.05 (1H, *d*, $J = 2.0$, $H_{2'}$), 6.98 (1H, *dd*, $J = 8.3, 2.0$, $H_{6'}$), 6.76 (1H, *d*, $J = 8.3$, $H_{5'}$), 6.26 (1H, *d*, $J = 15.8$, $H_{7'}$), 5.16 (1H, *m*, H_5), 3.93 (1H, *m*, H_3), 3.48 (1H, *dd*, $J = 9.8, 2.7$, H_4), 1.6–2.0 (4H, *m*, $H_{2,6}$); ^{13}C-NMR (DMSO-d_6, δ/ppm): 176.29 (C_7), 166.36 ($C_{9'}$), 148.60 ($C_{4'}$), 145.76 ($C_{3'}$), 144.65 ($C_{7'}$), 125.39 ($C_{1'}$), 121.21 ($C_{6'}$), 115.79 ($C_{5'}$), 114.65 ($C_{2'}$), 114.48 ($C_{8'}$), 75.18 (C_1), 73.34 (C_4), 71.63 (C_3), 71.48 (C_5), 38.10 ($C_{2,6}$) (Chan *et al*., 2009).

*4,5-Di-O-caffeoylquinic acid (**10**)*

Yellow amorphous solid; R_f: 0.75 ($CHCl_3$-MeOH, 8:2); ^{1}H-NMR (DMSO-d_6, δ/ppm, *J*/Hz): δ 7.48 (1H, *d*, $J = 16.0$, $H_{7''}$), 7.43 (1H, *d*, $J = 16.0$, $H_{7'}$), 7.02 (1H, *d*, $J = 2.0$, $H_{2'}$), 7.03 (1H, *d*, $J = 2.0$, $H_{2''}$), 6.97 (1H, *dd*, $J = 8.0, 2.0$, $H_{6'}$), 6.95 (1H, *dd*, $J = 8.0, 2.0$, $H_{6''}$), 6.75 (1H, *d*, $J = 8.1$, $H_{5'}$), 6.74 (1H, *d*, $J = 8.1$, $H_{5''}$), 6.25 (1H, *d*, $J = 16.0$, $H_{8'}$), 6.16 (1H, *d*, $J = 16.0$, $H_{8''}$), 5.36 (1H, *m*, H_5), 4.97 (1H, *dd*, $J = 7.7, 2.8$, H_4), 4.19 (1H, *m*, H3), 1.8–2.2 (4H, *m*, $H_{2,6}$); ^{13}C-NMR (DMSO-d_6, δ/ppm): 174.87 (C_7), 166.03 ($C_{9''}$), 165.61 ($C_{9'}$), 148.44 ($C_{4',4''}$), 145.53 ($C_{7',7''}$), 145.50 ($C_{3',3''}$), 125.37 ($C_{1',1''}$), 121.54 ($C_{''}$), 121.45 ($C_{6'}$), 115.75 ($C_{5''}$), 115.69 ($C_{5'}$), 114.65 ($C_{2''}$), 114.62 ($C_{2'}$), 113.77 ($C_{8''}$), 113.55 ($C_{8'}$), 73.66 (C_1), 73.46 (C_4), 67.64 (C_3), 66.50 (C_5), 37.44 (C_2), 37.40 (C_6) (Basnet *et al*., 1996).

*1,5-Di-O-caffeoylquinic acid; cynarin (**11**)*

Yellow amorphous solid; R_f: 0.70 ($CHCl_3$-MeOH, 8:2); ^{1}H-NMR (DMSO-d_6, δ/ppm, *J*/Hz): δ 7.48 (1H, *d*, $J = 16.0$, $H_{7'}$), 7.45 (1H, *d*, $J = 16.0$, $H_{7''}$), 7.07 (1H, *d*, $J = 2.0$, $H_{2'}$), 7.04 (1H, *d*, $J = 2.0$, $H_{8''}$), 6.99 (2H, *dd*, $J = 8.1, 2.0$, $H_{6',6''}$), 6.78 (1H, *d*, $J = 8.0$, $H_{5'}$), 6.77 (1H, *d*, $J = 8.0$, $H_{5''}$), 6.22 (2H, *d*, $J = 16.0$, $H_{8'}$), 6.20 (2H, *d*, $J = 16.0$, $H_{8''}$), 5.23 (1H, *m*, H_5), 4.06 (1H, *m*, H_3), 3.60

Table 2 Chemical composition of the essential oil of *D. glabrum* roots

No.	Compounds[a]	RI[b]	Methods of identification	%
1	Hexanal	804	MS	1.2
2	α-Pinene	935	MS	4.1
3	Camphene	949	MS/RI	2.2
4	2-Pentyl furan	987	MS/RI	1.7
5	β-Myrcene	991	MS	2.0
6	Limonene	1,027	MS/RI	1.9
7	(Z)-β-Ocimene	1,035	MS/RI	4.8
8	(E)-β-Ocimene	1,047	MS/RI	1.7
9	Terpinolene	1,089	MS/RI	0.3
10	(2E)-Nonenal	1,161	MS/RI	1.8
11	Exo-Fenchyl acetate	1,232	MS	6.6
12	Carvacrol methyl ether	1,244	MS/RI	0.4
13	Bornyl acetate	1,286	MS/RI	1.7
14	Undecanal	1,309	MS/RI	0.3
15	(E,E)-2,4-decadienal	1,318	MS	1.1
16	α-Ylangene	1,377	MS	0.8
17	Methyl eugenol	1,406	MS/RI	0.5
18	α-Cedrene	1,416	MS/RI	7.7
19	β-Cedrene	1,425	MS/RI	4.2
20	Aromadendrene	1,445	MS	2.0
21	(Z)-β-Farnesene	1,447	MS/RI	2.1
22	β-Chamigrene	1,483	MS	1.6
23	Myristicin	1,524	MS/RI	14.1
24	(E)-γ-Bisabolene	1,536	MS/RI	1.2
25	Elemicin	1,561	MS/RI	11.7
26	Tetradecanal	1,619	MS/RI	5.1
	Hydrocarbon monoterpenes			17.0
	Hydrocarbon sesquiterpenes			19.6
	Oxygenated monoterpenes			8.3
	Oxygenated non-terpenes			37.9
	Total identified			82.8

[a] Identified compounds listed in order of elution from HP-5MS column

[b] Retention indices to C_8–C_{24} n-alkanes on HP-5MS column

(1H, *dd*, $J = 8.1, 2.8$, H_4), 2.0–2.4 (4H, *m*, $H_{2,6}$); ^{13}C-NMR (DMSO-d_6, δ/ppm): 173.76 (C_7), 166.38 ($C_{9'}$), 165.20 ($C_{9''}$), 148.76 ($C_{4'}$), 148.12 ($C_{4''}$), 145.87 ($C_{3'}$), 145.83($C_{3''}$), 144.87 ($C_{7'}$), 143.74 ($C_{7''}$), 125.74 ($C_{1''}$), 125.37 ($C_{1'}$), 121.33 ($C_{6'}$), 120.31 ($C_{6''}$), 115.96 ($C_{8''}$), 115.96 ($C_{5'}$), 115.84 ($C_{5''}$), 114.84 ($C_{2'}$), 114.81 ($C_{2''}$), 114.33 ($C_{8'}$), 82.06 (C_1), 72.35 (C_4), 70.41 (C_5), 68.83 (C_3), 37.82 (C_6), 34.86 (C_2) (Carnat *et al.*, 2000).

GC and GC–MS analyses of the essential oil obtained from the roots of *D. glabrum* resulted in identification of twenty-six compounds, representing 82.8 % of the total oil. The results showed that the oil was dominated by the presence of oxygenated non-terpenes (37.9 %), of which myristicin (14.1 %) and elemicin (11.7 %) were main compounds (Table 2).

Myristicin and elemicin have been identified as responsible for hallucinogenic effects of *Myristica fragrans* (nutmeg) (Braun and Kalbhen, 1973). Furthermore, hepatoprotective (Srivastava *et al.*, 2001), anti-inflammatory (Morita *et al.*, 2003), and insecticidal (Lee and Park, 2011) properties of myristicin, and antifungal (Rossi *et al.*, 2007) and antibacterial (Tavares *et al.*, 2008) activities of elemicin have previously been shown during biological investigations.

Our study reports these two bioactive phenylpropanoid derivatives as the main compounds of the essential oil of *D. glabrum* roots, whereas a previous study on the essential oil of this species roots collected from the Jolfa region (northwest of Iran) has reported δ-cadinene (12.8 %) and β-bisabolene (7.5 %) as its main compounds, without the detection of any myristicin and elemicin in its chemical composition (Asnaashari *et al.*, 2011). Myristicin and elemicin, however, have been identified in high levels in essential oils of the roots of *Ferula* species, the genus classified in the same tribe (Scandiaceae) as *Dorema* genus (Kurzyna-Młynik *et al.*, 2008; Sahebkar and Iranshahi, 2011).

In DPPH assay, the oil showed very weak free radical-scavenging activity ($IC_{50} = 1{,}830 \pm 23.1$ μg ml^{-1}) which seems to be related to the absence or low concentrations of antioxidant principles such as oxygenated mono/sesquiterpenes and phenolic compounds in its composition.

Conclusion

The results of our study introduce *D. glabrum* as a source of natural phenolic antioxidants, specially phloroacetophenone glycosides and caffeoylquinic acid derivatives.

This report also emphasizes the necessity of conservation of *D. glabrum*, as a valuable genetic source of potentially active natural products and highlights it as an appropriate candidate for further biological and pharmacological studies.

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