Kopetdaghins A−E, Sesquiterpene Derivatives from the Aerial Parts and the Roots of *Dorema kopetdaghense*

Mehrdad Iranshahi,*[,†] Fatemeh Shaki,[†] Ali Mashlab,[†] Andrea Porzel,[‡] and Ludger A. Wessjohann[‡]

Department of Pharmacognosy and Biotechnology, Faculty of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran, and Department of Bio-organic Chemistry (NWC), Leibniz Institute of Plant Biochemistry, Weinberg 3, D-06120, Halle (Saale), Germany

Received January 28, 2007

Three new sesquiterpene derivatives, kopetdaghins A−C (**1**−**3**), one known prenylated coumarin (**7**), and two known steroid glucosides, sitosterol 3-*O*-glucoside and stigmasterol 3-*O*-glucoside, were isolated from the aerial parts of *Dorema kopetdaghense*. In addition, two new sesquiterpene derivatives, kopetdaghin D (**4)** and kopetdaghin E (**5**), together with kopetdaghins A−C and one known sesquiterpene coumarin (**6**), were isolated from the roots of the plant. The structures of these compounds were elucidated by various 1D and 2D NMR techniques as well as high-resolution positive-ion ESIMS.

In Iran, the genus *Dorema* (Apiaceae) is represented by eight species, namely, *D. ammoniacum*, *D. aitchisonii*, *D. gummiferum*, *D. aucheri*, *D. aureum*, *D. glabrum*, *D. hyrcanum*, and *D. kopetdaghense*.[1] Among the mentioned species, the oleogumresin of *D. ammoniacum* was used in ancient medicine for treatment of dermatitis and as an anti-inflammatory and antispasmodic agents.[2] A recent article reported that the extract of ammoniacum gum has broad spectrum antimicrobial activity.[3] The oleogum resin, ammoniacum, is also obtained from some related plants from Central Asia and Iran.[4]

D. kopetdaghense is endemic to Iran and Turkmenistan. The plant is massive, over 2 m tall. When the fresh roots are cut or separated from the aerial parts, the roots exude a resin, which becomes brown on contact with air.

There are only a few reports about the chemical constituents of plants in the genus *Dorema*. Attempts to identify the chemical constituents of ammoniacum led to the finding of chroman-2,4-diones, of which only a few examples are reported.[4,5] In other work, flavone methyl esters have been isolated from the resin of *D. aucheri*,[6] and a new acetophenone derivative has been reported from *D. aitchisonii* roots.[7] In this paper we report new compounds including a 2-prenyldihydrofurochromone-type sesquiterpenoid and sesquiterpene derivatives from *D. kopetdaghense*.

The plant *D. kopetdaghense* was collected north of Mashhad in the Hezarmasjed Mountains. The dried aerial parts and roots were extracted separately.

Results and Discussion

Normal-phase column chromatography of the acetone extract of aerial parts, followed by preparative TLC, afforded kopetdaghin A (**1**), kopetdaghin B (**2**), kopetdaghin C (**3**), a known prenylated coumarin (**7**), and the two known compounds, sitosterol 3-*O*-glucoside and stigmasterol 3-*O*-glucoside. In addition, Si column chromatography of the root extract followed by preparative TLC afforded kopetdaghins A−E (**1**−**3**, **5**, and **6**) and a known sesquiterpene coumarin (**6**). TLC analysis of the two extracts revealed that the chromatographic profiles of the aerial parts and the roots were qualitatively identical but quantitatively different, with a higher amount of sesquiterpene derivatives in the roots.

Compound **1** was obtained as a yellow oil, and its molecular formula, $C_{24}H_{32}O_4$, was established by HREIMS ([M + Na]$^+$, *m*/*z* 407.21858, calcd 407.2198 and [M + H]$^+$, *m*/*z* 385.23679, calcd 385.23788). The ^{1}H and ^{13}C NMR resonances (Table 1) of **1** were assigned by different 2D NMR experiments. The ^{1}H NMR spectrum of **1** showed resonances characteristic for four methyl singlets at δ 1.21, 1.64, 1.90, and 2.17, a methoxy singlet at δ 3.86, and five olefinic resonances at δ 5.25 (1H, t, J = 6.7 Hz), 4.97 (1H, d, J = 17.4), 5.01 (1H, d, J = 10.8 Hz), 5.88 (1H, dd, J = 17.4 and 10.8 Hz), and 6.13 (1H, s). Three aromatic protons at δ 6.44 (1H, s), 6.45 (1H, d, J = 9.5 Hz), and 7.66 (1H, d, J = 9.5 Hz) suggested the presence of a 1,2,4-trisubstituted benzene ring, which was supported by the ^{13}C NMR spectrum. The side chain of this ring was also assigned through ^{13}C NMR, HMQC, ^{1}H−^{1}H COSY, and HMBC experiments. In the HMBC spectrum of **1**, the correlations of H-2 (δ_H 2.93) with C-1 (δ_C 204.2), C-3 (40.5), and C-13 (146.2); δ_H H-8 (3.05) with δ_C C-7 (130.1) and C-9 (199.5); H-13 (δ_H 5.88) and H-14 (4.97) with C-3 (40.5); OH (δ_H 13.07) with C-3′ (δ_C 101.4), C-1′ (115.2), and C-2′ (166.4); and H-6′ (δ_H 7.66) with C-1 (δ_C 204.2) and C-4′ (166.2) confirmed the structure of compound **1** (Figure 2). In addition, ROESY cross-peaks between H-12 and H-11, between H-2 and OH, H-6′, Me-3, and H-4, between H-14 and Me-3, and between H-8 and H-6, Me-7, and H-10 all supported the relative configuration of **1**. The configuration of the double bond at C-6 was determined as *E* on the basis of the ROESY experiment, in which a cross-peak was observed from H-6/H-8 pairs. Therefore, the structure of compound **1** was elucidated as 1-(2-hydroxy-4-methoxyphenyl)-3,7,-11-trimethyl-3-ethenyl-6(*E*),10-dodecadiene-1,9-dione and was named kopetdaghin A.

Kopetdaghin A showed no optical rotation, so it must either be racemic at C-3 or have accidentally no optical activity. Similar compounds[9,10] also showed no optical rotation and were considered to be racemic.

Compound **2** was also obtained as a yellow oil, and its molecular formula $C_{24}H_{34}O_4$ was established by HREIMS ([M + Na]$^+$, *m*/*z* 409.23547, calcd 409.23547). The ^{1}H and ^{13}C NMR data of **2** were similar to those of **1** (Table 1), and only slight differences were observed in the resonances of the farnesyl moiety. The ^{1}H NMR spectrum showed the presence of two equivalent methyl groups as a doublet (δ_H 0.9, 6H, J = 6.6 Hz), two methyl singlets (δ_H 1.14 and 1.84), and four olefinic protons (δ_H 6.02, s; δ_H 4.89, d, J = 17.4 Hz; δ_H 4.96, d, J = 10.8 Hz; δ_H 5.80, dd, J = 17.4 and 10.8 Hz). The ^{13}C NMR spectrum showed in addition two characteristic ketone carbonyl resonances (δ_C 200.6 and 203.9) in the farnesyl moiety. Inspection of the HSQC spectrum permitted correlation of all the proton resonances to the relevant carbon atoms, while examination of the HMBC spectrum gave useful information for assigning all the quaternary carbons. H-8 (δ_H 6.02) showed ^2J correlation with a quaternary carbon at δ_C 200.6. The ^3J connectivites of this proton with C-6 (δ_C 33.8) and Me-7 (δ_C 25.0) suggested the position of the double bond at C-7−C-8. On the other hand, the ^2J connectivites of the methyl group at δ_H 1.84 and methylene group at δ_H 2.54 with C-7 (δ_C 158.6) corroborated the position of the double bond. The ^2J and ^3J connectivities of the methylene group at δ_H 2.24 and the methine group at δ_H 2.12 (H-11) with C-9 (δ_C 200.6) also confirmed the position of the carbonyl group (C-9). Other correlations in the HMBC experiment were identical to those of **1**

* To whom correspondence should be addressed. Tel: +98-511-8823255-66. Fax: +98-511-8823251. E-mail: iransham@sina.tums.ac.ir.
† Mashhad University of Medical Sciences.
‡ Leibniz Institute of Plant Biochemistry.

10.1021/np070043u CCC: $37.00 © 2007 American Chemical Society and American Society of Pharmacognosy
Published on Web 07/11/2007

Table 1. ^{1}H NMR and ^{13}C NMR Data for Compounds **1**−**4** ($CDCl_3$, 500 MHz)[a]

	1		**2**		**3**		**4**	
position	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
1		204.2		203.9				
2	2.93 d (16.2)	47.3	2.87 d (16.2)	47.1		171.4		171.4
3		40.5		40.2	4.27 d (11.8)	54.9	4.29 d (12.0)	54.8
4	1.58 m[b]	40.9	1.51 m[b]	40.9	3.18 dq (11.8, 6.6)	41.6	3.15 dq (12.0, 6.9)	44.4
5	2.03 m	23.5	1.44 m	22.8		88.4		87.7
6	5.25 t (6.7)	129.6	2.54 m	33.8	1.83 m	39.8	1.67 m[b]	35.5
7		130.1		158.6	2.32 m	22.9	2.30 m	22.6
8	3.05	55.8	6.02 s	124.3	5.28 t (6.6)	128.1	5.28 t (6.1)	128.2
9		199.5		200.6		131.3		131.4
10	6.13 s	123.3	2.24 d (11)	53.4	3.10 s	55.6	3.11 s	55.4
11		155.7	2.12 m	25.4		199.5		199.4
12	1.90 s	27.9	0.9 d (6.6)	22.6	6.15 s	123.3	6.15 s	123.4
13	5.88 dd (10.8, 17.4)	146.2	5.80 dd (10.8, 17.4)	145.1		156.4		156.5
14	4.97 d (17.4) 5.01 d (10.8)	112.5	4.89 d (17.4) 4.96 d (10.8)	112.1	1.92 s	28.1	1.94 s	28.1
1′		115.2		114.7		114.3		114.3
2′		166.4		165.8		167.4		167.4
3′	6.44 s	101.4	6.39 s	100.8	6.48 d (2.1)	101.3	6.48 d (2.1)	101.3
4′		166.2		165.7		166.7		166.6
5′	6.45 d (9.5)	107.6	6.43 d (9.3)	107.3	6.54 dd (9.0, 2.1)	108.8	6.56 dd (9.0, 2.1)	108.7
6′	7.66 d (9.5)	132.8	7.62 d (9.3)	132.5	7.71 d (9.0)	133.9	7.71 d (9.0)	133.4
7′						196.3		196.3
Me-3	1.21 s	23.8	1.14 s	23.1				
Me-4					1.10 d (6.6)	13.8	1.10 d (6.9)	13.1
Me-5					1.39 s	20.9	1.55 s	24.2
Me-7	1.64 s	16.7	1.84 s	25.0				
Me-9					1.70 s	16.9	1.70 s	17.0
Me-11	2.17 s	21.0	0.9 d (6.6)	22.6				
Me-13					2.19 s	21.1	2.21	21.1
OCH_3	3.86 s	55.6	3.83 s	55.5	3.90 s	56.1	3.90	56.1
OH	13.07 s		13.09 s		12.52 s		12.52 s	

[a] *J* values are in parentheses and reported in Hz; chemical shifts are given in ppm; assignments were confirmed by ^{1}H−^{1}H COSY, HMQC, HMBC, and ROESY experiments. [b]Resonance partially obscured.

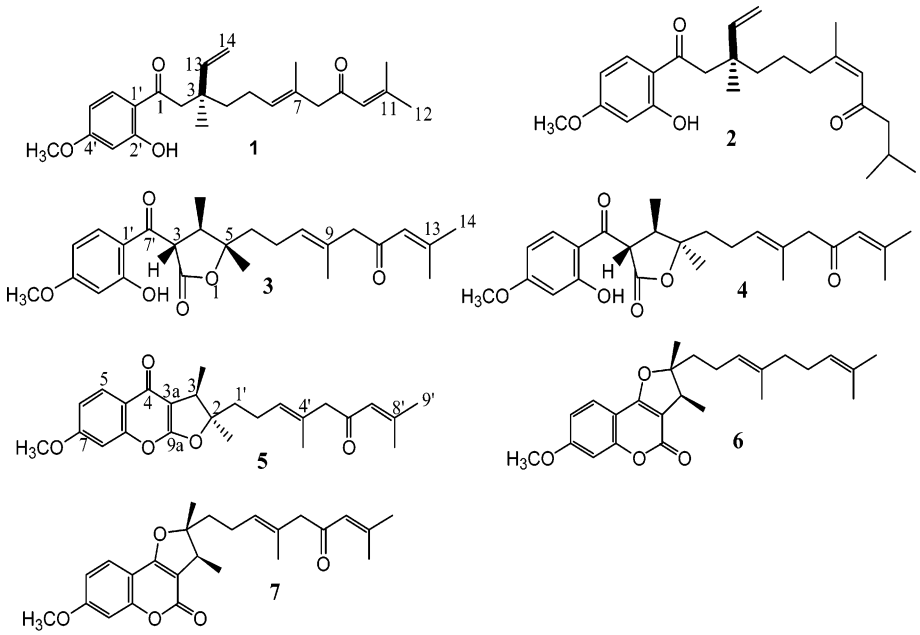

Figure 1. Compounds **1**−**7** isolated from *Dorema kopetdaghense.*

(Figure 2). The proposed structure was further supported by ^{1}H−^{1}H COSY data. The configuration of the C-7 double bond was determined as *Z* on the basis of a ROESY experiment, in which a cross-peak was observed between Me-7 and H-8. In addition, no ROE was detected between H-6 and H-8, confirming the *Z* configuration in **2**. Other ROESY correlations were identical to those of **1**. Therefore, the structure of compound **2** was elucidated as 1-(2-hydroxy-4-methoxyphenyl)-3,7,-11-trimethyl-3-ethenyl-7(*Z*)-dodecene-1,9-dione and was named kopetdaghin B.

Compound **3** was obtained as a yellow oil and showed an absorption band for a lactone carbonyl (1772 cm $^{-1}$) in its IR spectrum. The ^{1}H NMR spectrum of the sesquiterpene portion of **3** displayed resonances for five methyl singlets (δ 1.39, 1.70, 1.92, 2.19, and 3.90), the typical Me-4 resonance at δ 1.10 (d, J = 6.6 Hz), two characteristic olefinic protons at δ 5.28 (t, J = 6.6 Hz) and 6.15 (s), and the typical H-3 resonance at δ 4.27 (d, J = 11.8 Hz). The ^{1}H NMR and COSY spectra also indicated that the methine at δ 4.27, methine at δ 3.18 (dq, J = 11.8 and 6.6 Hz), and one methyl group at δ 1.10 (d, J = 6.6 Hz) were connected as a CH−CH−CH_3 unit. These data were corroborated by the ^{13}C NMR spectrum, which showed five methyl (δ 13.8, 16.9, 20.9, 21.1, and 28.1), three methylene (δ 22.9, 39.8, and 55.6), two methine (δ 41.6 and 54.9), and six quaternary carbons (δ 88.4, 131.3, 156.4,

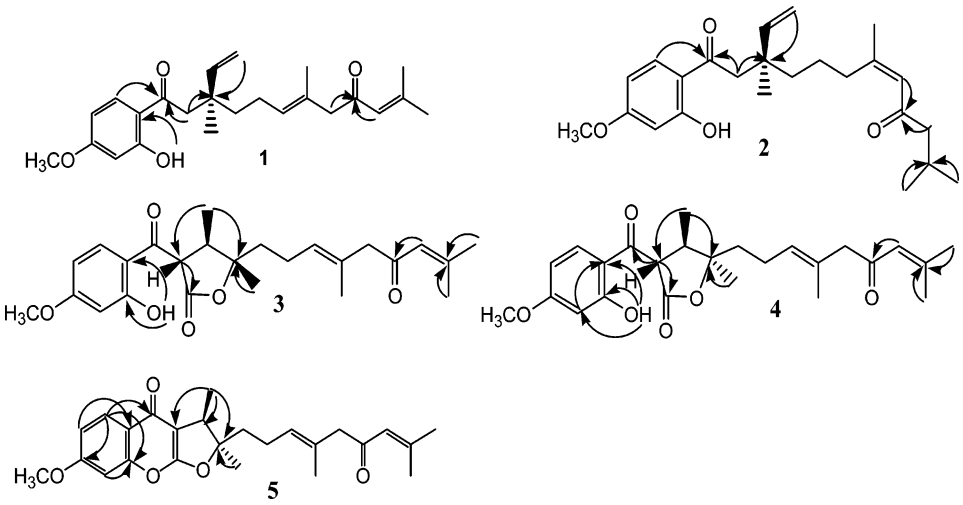

Figure 2. Selected HMBC correlations for compounds **1**−**5**.

171.4, 196.3, and 199.5) (Table 1). The C-2, C-5, C-10, and C-7′ carbons were assigned through HMQC and HMBC experiments. H-3 (δ 4.27) showed $^2J_{H,C}$ correlations with C-2 (δ 171.4) and C-4 (δ 41.6). Me-4 and Me-5 also showed $^3J_{H,C}$ and $^2J_{H,C}$ correlations with C-5 (δ 88.4), respectively. Other HMBC correlations were similar to those of **1** (Figure 2). The configurations of C-3, C-4, and C-5 were determined by comparison of the chemical shifts of adjacent protons with those in previous studies for similar structures[8] and by a ROESY experiment. In particular ROEs H-3/Me-4/Me-5 established an α-orientation for H-4 and a β-orientation for H-3, Me-4, and Me-5. The configuration of the C-8 double bond was determined as *E* on the basis of the ROESY experiment, in which a cross-peak was observed between H-8 and H-10.

From the foregoing spectroscopic data, kopetdaghin C was determined as 3*S**-(2-hydroxy-4-methoxybenzoyl)-4*R**,5*S**-dimethyl-5-[3(*E*),7(*E*)-nonadien-11-one-6-yl] dihydrofuran-2(3*H*)-one.

The ^{1}H NMR and ^{13}C NMR data for **4** were comparable to those of **3** (see Table 1) and exhibited either overlapping or distinct resonances with relatively small differences in chemical shifts. The most discernible differences between the two diastereoisomers were the chemical shifts of H-6 at δ_H 1.67 and Me-5 at δ_H 1.55 in **4** and at δ_H 1.83 and 1.39 in **3**, respectively. These differences in chemical shifts were in accordance with those of similar diastereoisomers[8] and by a ROESY experiment. In particular ROEs H-3/Me-4 and H-4/Me-5 established an α-orientation for H-4 and Me-5 and a β-orientation for H-3 and Me-4. The configuration of the C-8 double bond was determined as *E* on the basis of the ROESY experiment, in which a cross-peak was observed between H-8 and H-10.

Therefore, the structure of compound **4** was elucidated as 3*S**-(2-hydroxy-4-methoxybenzoyl)-4*R**,5*R**-dimethyl-5-[3(*E*),7(*E*)-nonadien-11-one-6-yl]dihydrofuran-2(3*H*)-one and was named kopetdaghin D.

Compound **5** was obtained as an optically active yellow oil. The ^{1}H NMR data of this compound suggested the presence of a 1,2,4-trisubstituted benzene ring at δ_H 8.14 (1H, d, J = 8.8 Hz, H-5), 6.99 (1H, dd, J = 8.8, 2.3 Hz, H-6), and 6.87 (1H, d, J = 2.3 Hz, H-5). The remaining ^{1}H and ^{13}C NMR data of **5**, except for those of the sesquiterpene unit, indicated a 7-oxygenated chromone compound (Table 2). In the HMBC spectrum of **5**, the correlations of δ_H 1.55 (Me-2) with δ_C 95.6 (C-2), 43.7 (C-3), and 35.1 (C-1′) and δ_H 1.35 (Me-3) with δ_C 43.7 (C-3), 95.6 (C-2), and 99.4 (C-3a) suggested that C-1′ is connected to C-2. That C-2 is connected to C-9a by an ether bond was deduced according to the unsaturation value and the chemical shifts of C-2 (δ_C 95.6) and C-9a (δ_C 167.2). The configuration of C-2 and C-3 was determined with respect to the chemical shifts of the stereogenic carbons and the chemical shifts of adjacent protons and with those reported.[9] In similar compounds, the orientations of Me-2 and Me-3 are α and β, respectively, and the ^{13}C NMR chemical shifts of C-2 and C-3 are typically at δ 95−96 and 43−44, respectively. When the orientation of the methyl groups at these two positions is β (C-3) and α (C-2), the shifts of C-2 and C-3 are, on average, 2−3 ppm further upfield.[9] In addition, no ROE interaction was observed between Me-2 and Me-3. Therefore, compound **5** was established as 2,3-dihydro-7-methoxy-2*R**,3*R**-dimethyl-2[4,8-dimethyl-3(*E*),7-nonadienyl-6-one]-furo[2,3-*b*]chromone and was named kopetdaghin E.

Table 2. ^{1}H NMR and ^{13}C NMR Data for Compound **5** ($CDCl_3$, 500 MHz)[a]

position	δ_H	δ_C
2		95.6
3	3.32 q (7)	43.7
3a		99.4
4		175.5
4a		118.3
5	8.14 d (8.8)	127.3
6	6.99 dd (8.8, 2.3)	113.6
7		163.4
8	6.87 d (2.3)	101.3
8a		155.3
9a		167.2
1′	1.94 m[b]	35.1
2′	2.23 m	23.3
3′	5.24 t (6.0)	128.4
4′		131.1
5′	3.11 s	55.5
6′		199.4
7′	6.15 s	123.3
8′		156.3
9′	1.92 s	28.1
Me-2	1.55 s	25.7
Me-3	1.35 d (7.0)	14.4
Me-4′	1.71 s	16.9
Me-8′	2.21 s	21.1
OCH_3	3.86 s	55.6

[a] J values are in parentheses and reported in Hz; chemical shifts are given in ppm; assignments were confirmed by ^{1}H−^{1}H COSY, HMQC, HMBC, and ROESY experiments. [b] Resonance partially obscured.

Compounds **6** and **7** are known compounds, whose structures were elucidated by comparison with literature data.[9−11]

Experimental Section

General Experimental Procedures. The optical rotation was measured on a Polax-2L ATAGO polarimeter. UV spectra were obtained in CH_2Cl_2 on a Shimadzu UV-1650 PC spectrophotometer, and IR spectra were recorded on a Unicam SP1100 infrared spectrophotometer and a Thermo Nicolet 5700 FT-IR spectrometer. ^{1}H and ^{13}C NMR, DEPT, ^{1}H−^{1}H COSY, HMQC, and HMBC spectra were recorded on a Bruker Avance DRX 500 spectrometer. The high-resolution electrospray (ESI) mass spectra were obtained on a Bruker Apex III 70e Fourier transform ion cyclotron resonance mass spectrometer (Bruker Daltonics, Billerica, MA) equipped with an Infinity cell, a 7.0 T superconducting magnet (Bruker, Karlsruhe, Germany), an rf-only hexapole ion guide, and an external APOLLO electrospray ion source (Agilent, off-axis spray). Nitrogen was used as drying gas at 150 °C. The sample solutions were introduced continuously via a syringe pump with a flow rate of 120 μL h^{-1}. All data were acquired with 256K data points and zero filled to 1024K by averaging 32 scans.

Column chromatography was conducted with silica gel 230−400 mesh, Merck. Preparative TLC was performed on silica gel 60 GF_{254} plates (Merck), and observation of plates was carried out under a UV CAMAG spectrometer (254 nm).

Plant Material. The plant material (*D. kopetdaghense* M.Pimen.) was collected from Khor Valley, Khorasan Razavi Province, Iran, in May 2005. The plant material was identified by Mohammad Reza Joharchi, Ferdowsi University of Mashhad Herbarium (FUMH). A voucher specimen (no. 1001) has been deposited at the herbarium of the Faculty of Pharmacy, Mashhad University of Medical Sciences.

Extraction and Isolation. The air-dried aerial parts (350 g) were ground into a powder and extracted exhaustively by maceration at room temperature with acetone. After filtration, the extract was concentrated under vacuum to yield 15 g of a dark residue. The extract (15 g) was subjected to column chromatography on Si gel (5 × 50 cm, 342 g) using petroleum ether with increasing volumes of acetone [petroleum ether−acetone (100:0, 1.5 L), (90:10, 2.5 L), (80:20, 3 L), (70:30, 2 L), (60:40, 1 L), (50:50, 1 L), (0:100, 2 L), and MeOH (1 L)]. The fractions (200 mL each) were compared by TLC (silica gel using petroleum ether−EtOAc, 4:1), and those giving similar spots were combined. Nineteen fractions were finally obtained. Fraction 1 was subjected to silica gel PTLC (petroleum ether−acetone, 4:1) to give **1** (42.7 mg) and **2** (3.5 mg). Fraction 4 was chromatographed on Si gel PTLC, eluting with petroleum ether−acetone (4:1), to give **3** (9 mg) and **7** (21.5 mg). Fraction 14 afforded 89 mg of white crystals: a mixture of β-sitosterol 3-*O*-glucoside and stigmasterol 3-*O*-glucoside.

The air-dried roots (500 g) were ground into a powder and extracted exhaustively by a Soxhlet apparatus with $CHCl_3$. After filtration, the extract was concentrated under vacuum to yield 184 g of a brown residue. Part of the extract (17 g) was subjected to column chromatography on Si gel (400 g) using petroleum ether with increasing volumes of acetone [petroleum ether−acetone (20:1, 3 L), (15:1, 8 L), (10:1, 9.2 L), and (5:1, 3 L)]. The fractions (200 mL each) were compared by TLC (Si gel using petroleum ether−EtOAc, with proportions of 10:1 for fractions 1−15 and 4:1 for fractions 16−24), and those giving similar spots were combined. Twenty-four fractions were finally obtained. Fraction 1 was subjected to Si gel PTLC (petroleum ether−acetone, 10:1) to give **2** (6.8 mg). Fraction 2 was chromatographed on Si gel PTLC, eluting with petroleum ether−acetone (10:1), to give **1** (66.6 mg). Compound **6** (29.9 mg) was obtained from fraction 5 by chromatography on Si gel PTLC (petroleum ether−acetone, 10:1). Fraction 16 was subjected to Si gel PTLC (petroleum ether−acetone, 5:1) to give **4** (17 mg). Fraction 20 was also chromatographed on Si gel PTLC (petroleum ether−acetone, 4:1) to give **3** (10.5 mg). Fraction 22 was chromatographed on silica gel PTLC using petroleum ether−acetone (3:1) as solvent to obtain 17.2 mg of **5**. It should be pointed out that only a part of each column fraction was used for further purification by PTLC.

Kopetdaghin A (1): yellow oil; $[\alpha]^{25}_D$ ±0 (*c* 0.27, CH_2Cl_2); UV (CH_2Cl_2) λ_{max} (log ϵ) 237 (4.04), 277 (3.95), 318 (3.63) nm; IR ν_{max} ($CHCl_3$) 3375 (br OH), 2897, 1683, 1625, 1375, 1213.

Kopetdaghin B (2): yellow oil; $[\alpha]^{23}_D$ +4.8 (*c* 0.22, MeOH); UV (MeOH) λ_{max} 231 (4.00), 277 (3.92), 313 (3.58) nm. IR ν_{max} ($CHCl_3$) 3420 (br OH), 2924, 1731, 1681, 1614, 1236, 1128.

Kopetdaghin C (3): yellow oil; $[\alpha]^{25}_D$ +166 (*c* 0.12, CH_2Cl_2); UV (CH_2Cl_2) λ_{max} (log ϵ) 238 (4.14), 282 (4.10), 321 (3.84) nm; IR ν_{max} ($CHCl_3$) 3433 (br OH), 2933, 1772 (lactone), 1639, 1375, 1213; HREIMS $[M + Na]^+$, *m*/*z* 451.20930, calcd 451.20963.

Kopetdaghin D (4): yellow oil; $[\alpha]^{25}_D$ +80.2 (*c* 0.18, CH_2Cl_2); UV (CH_2Cl_2) λ_{max} (log ϵ) 237 (4.14), 282 (4.12), 318 (3.83) nm; IR ν_{max} ($CHCl_3$) 3433 (br OH), 2931, 1766 (lactone), 1622, 1375, 1226; HREIMS $[M + Na]^+$, *m*/*z* 451.20811, calcd 451.20963.

Kopetdaghin E (5): yellow oil; $[\alpha]^{25}_D$ +153.8 (*c* 0.13, CH_2Cl_2); UV (CH_2Cl_2) λ_{max} (log ϵ) 242 (4.17), 282 (4.04) nm; IR ν_{max} ($CHCl_3$) 2931, 1622, 1492, 1242, 1098; HREIMS $[M + Na]^+$, *m*/*z* 433.19892, calcd 433.19907.

Acknowledgment. The authors are very grateful to M. R. Joharchi of the Ferdowsi University of Mashhad Herbarium, for help with the identification of the plant. This research was supported by grants from the Mashhad University of Medical Sciences Research Council and Iran National Science Foundation.

References and Notes

(1) Rechinger, K. H. *Flora Iranica*; Akademische Druck-u. Verlagsanstalt: Graz, 1987; Vol. 28, p 384.
(2) *Iranian Herbal Pharmacopoeia*; Ministry of Health and Medical Education: Tehran, 2002; Vol. 2, pp 766−771.
(3) Rajani, M.; Saxena, N.; Ravishankara, M. N.; Desai, N.; Padh, H. *Pharm. Biol.* **2002**, *40*, 534−541.
(4) Appendino, G.; Nano, G. M.; Viterbo, D.; Demunno, G.; Cisero, M.; Palmisano, G.; Aragno, M. *Helv. Chim. Acta* **1991**, *74*, 495−500.
(5) Arnone, A.; Nasini, G.; Depava, O. V.; Camarda, L. *Gazz. Chim. Ital.* **1991**, *121*, 383−386.
(6) Wollenweber, E.; Dorr, M.; Rustiyan, A. *Phytochemistry* **1995**, *38*, 1417.
(7) Bukreeva, T. V.; Pimenov, M. G. *Khim. Prir. Soedin.* **1992**, *27*, 722−723.
(8) Kojima, K.; Isaka, K.; Ondognii, P.; Zevgeegiin, O.; Davgiin, K.; Mizukami, H.; Ogihara, Y. *Chem. Pharm. Bull.* **1999**, *47*, 1145−1147.
(9) Nagatsu, A.; Isaka, K.; Kojima, K.; Ondognii, P.; Zevgeegiin, O.; Gombosurengyin, P.; Davgiin, K.; Irfan, B.; Iqubal, C. M.; Ogihara, Y. *Chem. Pharm. Bull.* **2002**, *50*, 675−677.
(10) Isaka, K.; Nagatsu, A.; Ondognii, P.; Zevgeegiin, O.; Gombosurengyin, P.; Davgiin, K.; Kojima, K.; Ogihara, Y. *Chem. Pharm. Bull.* **2001**, *49*, 1072−1076.
(11) Kojima, K.; Isaka, K.; Ondognii, P.; Zevgeegiin, O.; Gombosurengyin, P.; Davgiin, K.; Mizukami, H.; Ogihara, Y. *Chem. Pharm. Bull.* **2000**, *48*, 353−356.

NP070043U