Sesquiterpene Coumarins from *Ferula gumosa*

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A new sesquiterpene coumarin, gumosin (**1**), two new sesquiterpene coumarin glycosides, gumosides A (**2**) and B (**3**), and 10 known compounds, namely, cauferoside (**4**), feselol (**5**), conferoside, ferilin, ferocaulidin, ligupersin A, conferol, and daucosterol, and the phenolic compounds acantrifoside E and 4-hydroxybenzoic acid 4-(6-*O*-sulfo)glucopyranoside, were isolated from a methanolic extract of *Ferula gumosa* roots. The structures of **1**−**3** were elucidated by spectroscopic data interpretation. The cytotoxic activity of the sesquiterpene coumarin derivatives was evaluated against a small panel of cancer cell lines.

The genus *Ferula* (Apiaceae) comprises about 180 species, with most of these growing in Central Asia, the Middle East, and Central Europe.[1] Various plant parts of *Ferula* species such as the oleogum resin of *F. assafetida,* the roots of *F. gumosa*, and the leaves of *F. latisecta* have been used traditionally to treat stomachache, hysteria, infant colitis, and asthma.[2,3]

The chemistry of the genus *Ferula* has been studied by many researchers, and it is well documented as being a good source of biologically active compounds such as sesquiterpene derivatives,[4−8] sulfur-containing compounds,[9,10] and coumarins.[6,11−14] There are also a few reports on polar secondary metabolites such as sesquiterpene coumarin glycosides from *Ferula* species.[15,16]

Ferula gumosa Boiss. is an Iranian medicinal plant (the oleoresin of the plant called "Barijeh" in Persian) and has been used traditionally as a tonic, anticonvulsant, and emmenagogue herb.[2] Recent studies demonstrated some biological activities including anticonvulsant,[17] spasmolytic,[18] and antibacterial[19] effects from different parts of the plant. In addition, it has been reported that an extract of this plant could be useful for the alleviation of morphine-withdrawal syndrome.[20]

In the present study, the methanolic extract of *F. gumosa* roots was investigated, which afforded a new sesquiterpene coumarin glycoside, gumosin (**1**), two new sesquiterpene coumarin glycosides, gumosides A and B (**2**, **3**), along with cauferoside (**4**),[21] feselol (**5**),[13] conferoside,[21] ferilin,[22] ferocaulidin,[13] ligupersin A,[13] conferol,[12] and daucosterol,[23] and the phenolic compounds acantrifoside E[24] and 4-hydroxybenzoic acid 4-(6-*O*-sulfo)glucopyranoside.[25] The structures of these known compounds were elucidated by spectroscopic data comparison to literature values.

Sesquiterpene coumarin ethers (7-hydroxycoumarin derivatives) have been reported to possess various biological activies, including squalene-hopene cyclase inhibition, human rhinovirus coat protein inhibition, antibacterial activity, and NF-κB inhibition. A potential cancer chemopreventive effect and cytotoxic activity are documented for farnesiferol C and for conferol, respectively.[26]

Recently, the potential anticancer activity of the alcohol-soluble extract of Resina Ferulae, which is the dried resinous exudate obtained from the root and rhizomes of plants such as *Ferula asafoedida* L., *F. conocaula* Korovin, *F. narthex* Boiss., *F. fetida* Regel, *F. fukanensis* K.M. Shen, *F. sinkiangensis* K.M. Shen, and *F. rigida* Ten., has been reported.[27] Moreover, galbanic acid and other sesquiterpene coumarins isolated from Resina Ferulae have been reported to exert inhibitory activities against human cancer cell line proliferation such as A549 (human lung cancer), SK-OV-3 (ovary cancer), SK-HEL-2 (melanoma), and HCT-15 (colon cancer).[27] On the basis of the above reports, the cytotoxic activities of sesquiterpene coumarins isolated from *F. gumosa* were evaluated against a small panel of cancer cell lines.

The roots of *F. gumosa* were extracted with MeOH. The methanolic extract was subjected to column chromatography and purified by different chromatographic steps to yield three new compounds (**1**−**3**).

Gumosin (**1**) was obtained as an amorphous, white solid, and its molecular formula, $C_{24}H_{30}O_5$, was deduced by HRMALDITOFMS analysis (*m/z* 399.2168 $[M + H]^+$, calcd for $C_{24}H_{31}O_5$, 399.2172). Compound **1** was determined to be a sesquiterpene coumarin by the presence of diagnostic peaks in the ^{1}H NMR and ^{13}C NMR spectra (Table 1). The ^{13}C NMR spectrum of **1** displayed 24 carbon signals, with nine being typical of an umbelliferone skeleton[14] and 15 ascribable to a sesquiterpene moiety.[28] The ^{1}H NMR spectrum of **1** showed signals due to five aromatic protons at δ 6.27 (d, J = 9.6 Hz), 6.92 (d, J = 2.3 Hz), 6.97 (dd, J = 8.2, 2.3 Hz), 7.56 (d, J = 8.2 Hz), and 7.90 (d, J = 9.6 Hz), typical of an umbelliferone moiety. For the sesquiterpene portion, signals corresponding to two olefinic protons at δ 5.73 (dd, J = 10.8, 2.7 Hz) and 5.78 (dd, J = 10.8, 1.3 Hz), a primary alcoholic function at δ 4.44 (dd, J = 10.6, 3.7 Hz) and 4.21 (dd, J = 10.6, 5.7 Hz), a secondary alcoholic function at δ 3.28 (dd, J = 11.5, 4.4 Hz), and four tertiary methyl groups at δ 0.87, 1.04, 1.08, and 1.37, were evident. The HSQC experiment allowed the identification of 10 methines, of which five, at δ_C 112.9 (C-3), 145.4 (C-4), 130.1 (C-5), 113.8 (C-6), and 101.7 (C-8), were characteristic for the umbelliferone unit, and five, at δ_C 54.8, 58.3, 79.2, 127.9, and 136.2, were attributable to the sesquiterpene moiety. Further HSQC correlations were indicative of two aliphatic methylenes at δ_C 27.3 and 37.0, an oxygenated methylene at δ_C 67.3, characteristic for C-11′ usually involved in the linkage with the coumarin moiety, and four methyls at δ_C 15.7, 16.3, 28.3, and 30.4. HMBC correlations between the proton signal at δ 1.37 (Me-12′) and the carbon resonance at δ 58.3 (C-9′) and between the protons at δ 4.44 and 4.21 attributable to C$\underline{H_2}$-11′ with the same carbon C-9′ revealed the location of a tertiary methyl group (Me-12′) at C-8′. The correlation of Me-12′ with the quaternary carbon at δ 70.6 allowed the occurrence of a tertiary alcoholic function to be deduced at C-8′. A further HMBC correlation between the singlet methyl at δ 1.04 (Me-15′) and the carbon resonances at δ 37.0 (C-1′), 37.8 (C-10′), and 58.3 (C-9′)

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Chart 1

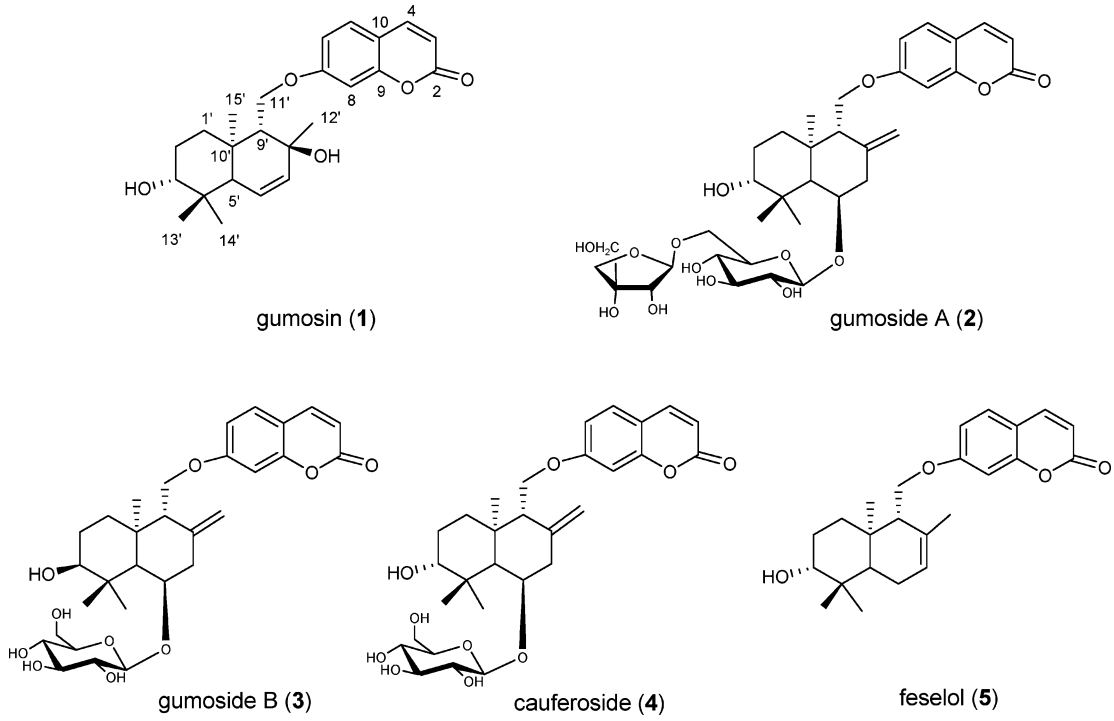

Table 1. NMR Spectroscopic Data (600 MHz, CD_3OD) for Compound **1** and the Aglycon Moieties of Compounds **2**−**4**[a]

	1		2		3		4	
	δ_C	δ_H (J in Hz)	δ_C	δ_H (J in Hz)	δ_C	δ_H (J in Hz)	δ_C	δ_H (J in Hz)
2	163.4, C		163.5, C		163.5, C		163.5, C	
3	112.9, CH	6.27, d (9.6)	112.7, CH	6.27, d (9.6)	113.1, CH	6.29, d (9.6)	112.7, CH	6.27, d (9.6)
4	145.4, CH	7.90, d (9.6)	145.2, CH	7.91, d (9.6)	145.3, CH	7.92, d (9.6)	145.5, CH	7.91, d (9.6)
5	130.1, CH	7.56, d (8.2)	130.0, CH	7.55, d (8.2)	130.0, CH	7.56, d (8.2)	130.0, CH	7.56, d (8.2)
6	113.8, CH	6.97, dd (8.2, 2.3)	113.7, CH	6.94, dd (8.2, 2.3)	112.8, CH	6.96, dd (8.2, 2.3)	113.9, CH	6.94, dd (8.2, 2.3)
7	157.3, C		157.4, C		157.2, C		157.2, C	
8	101.7, CH	6.92, d (2.3)	101.8, CH	6.95, d (2.3)	101.8, CH	6.95, d (2.3)	101.8, CH	6.95, d (2.3)
9	163.5, C		163.7, C		163.9, C		163.7, C	
10	113.8, C		113.8, C		113.6, C		113.8, C	
1′	37.0, CH_2	1.72, m α 1.44, brd (10.6) β	38.4, CH_2	1.84, m α 1.52, brd (10.6) β	33.2, CH_2	1.94, m β 1.51, brd (12.2) α	38.2, CH_2	1.83, m α 1.50, brd (10.6) β
2′	27.3, CH_2	1.74, m 1.67, m	27.7, CH_2	1.70, m 1.70, m	26.3, CH_2	2.00, m 1.63, dd (12.9, 2.6)	27.6, CH_2	1.70, m 1.70, m
3′	79.2, CH	3.28, dd (11.5, 4.4)	79.6, CH	3.21, t (8.2)	78.4, CH	3.31, t (2.7)	79.6, CH	3.22, t (8.2)
4′	39.4, C		40.5, C		39.2, C		40.8, C	
5′	54.8, CH	1.74, m	59.1, CH	1.49, d (10.9)	53.4, CH	1.87, d (10.9)	59.4, CH	1.50, d (10.8)
6′	127.9, CH	5.78, dd (10.8, 1.3)	76.2, CH	4.13, ddd (11.0, 11.0, 4.5)	75.9, CH	4.14, td (10.9, 5.2)	76.2, CH	4.08, td (10.8, 3.7)
7′	136.2, CH	5.73, dd (10.8, 2.7)	44.7, CH_2	2.96, dd (4.5, 12.8) α 2.20, t (11.3) β	44.1, CH_2	2.96, dd (5.2, 12.8) α 2.20, t (11.6) β	44.2, CH_2	2.96, dd (3.7, 12.8) α 2.20, t (11.5) β
8′	70.6, C		145.5, C		145.1, C		145.2, C	
9′	58.3, CH	1.78, t (4.2)	55.5, CH	2.32, brs	55.3, CH	2.41, brs	55.4, CH	2.32, brs
10′	37.8, C		40.1, C		39.6, C		40.5, C	
11′	67.3, CH_2	4.44, dd (10.6, 3.7) 4.21, dd (10.6, 5.7)	66.8 CH_2	4.33, dd (10.0, 3.5) 4.25, dd (10.0, 5.7)	66.9, CH_2	4.35, dd (10.0, 3.2) 4.26, dd (10.0, 5.4)	67.2, CH_2	4.33, dd (10.0, 3.2) 4.26, dd (10.0, 5.4)
12′	30.4, CH_3	1.37, s	109.7, CH_2	5.02, brs 4.67, brs	109.9, CH_2	4.99, brs 4.67, brs	109.3, CH_2	5.00, brs 4.67, brs
13′	28.3, CH_3	1.08, s	31.2, CH_3	1.34, s	32.2, CH_3	1.29, s	31.8, CH_3	1.34, s
14′	16.3, CH_3	0.87, s	15.6, CH_3	1.09, s	22.2, CH_3	1.13, s	15.4, CH_3	1.08, s
15′	15.7, CH_3	1.04, s	17.2, CH_3	0.95, s	17.5, CH_3	0.95, s	17.1, CH_3	0.94, s

[a] Assignments were confirmed by HSQC and HMBC experiments.

revealed that the singlet methyl should be placed at C-10′. The remaining methyl groups were determined to be at C-4′ from the HMBC correlations between the proton signals at δ 0.87 (Me-14′) and 1.08 (Me-13′) and the carbon resonances at δ 39.4 (C-4′), 54.8 (C-5′), and 79.2 (C-3′). The locations of the olefinic protons at C-6′ and C-7′ were deduced from the COSY spectrum, which showed a correlation between the proton at δ 1.74 (H-5′) and the proton at δ 5.78 (H-6′), which, in turn, was coupled to the olefinic proton at δ 5.73 (H-7′). In the HMBC spectrum, correlations between the proton signal at δ 5.73 and the carbon resonances at δ 30.4 (Me-12) and 70.6 (C-8′) and between the proton at δ 5.78 (H-6′) and carbons at δ 54.8 (C-5′), 70.6 (C-8′), 39.4 (C-4′), and 37.8 (C-10′) confirmed the occurrence of a C-6 double bond. The relative configurations at C-3′, C-5′, C-8′, C-9′, and C-10′ were deduced from a ROESY experiment. In particular, ROE cross-peaks between $C\underline{H_2}$-11′ and Me-12′, Me-15′, and H-1′α (δ 1.72) showed α-orientations for Me-12′, Me-15′, and H_2-11′. The β-orientation for H-3′ and Me-13′ was confirmed by the ROEs between H-3′/Me-13′ and H-3′/H1′β (δ 1.44). Accordingly, the structure of gumosin was established as **1**.

Table 2. NMR Spectroscopic Data (600 MHz, CD_3OD) for the Sugar Moieties of Compounds **2**−**4**[a]

	2		**3**		**4**	
	δ_C	δ_H (J in Hz)	δ_C	δ_H (J in Hz)	δ_C	δ_H (J in Hz)
		β-D-Glc		β-D-Glc		β-D-Glc
1″	100.9, CH	4.42, d (7.8)	100.7, CH	4.45, d (7.8)	100.7, CH	4.47, d (7.8)
2″	74.9, CH	3.20, dd (7.8, 9.0)	75.0, CH	3.20, dd (7.8, 9.0)	75.1, CH	3.21, dd (7.8, 9.0)
3″	77.7, CH	3.39, dd (9.0, 9.0)	77.9, CH	3.41, dd (9.0, 9.0)	77.8, CH	3.40, dd (9.0, 9.0)
4″	71.5, CH	3.33, dd (9.0, 9.0)	71.9, CH	3.30, dd (9.0, 9.0)	71.5, CH	3.31, dd (9.0, 9.0)
5″	79.3, CH	3.21, m	77.5, CH	3.32, m	77.4, CH	3.32, m
6″	68.4, CH_2	4.00, dd (2.5, 12.0)	62.8, CH_2	3.93, dd (2.5, 12.0)	62.4, CH_2	3.82, dd (2.5, 12.0)
		3.61, dd (4.5, 12.0)		3.70, dd (4.5, 12.0)		3.70, dd (4.5, 12.0)
		β-D-Api				
1‴	110.6, CH	5.00, d (1.8)				
2‴	77.7, CH	3.91, d (1.8)				
3‴	80.4, C					
4‴	74.9, CH_2	3.96, d (9.6)				
		3.79, d (9.6)				
5‴	65.6, CH_2	3.62, (2H) brs				

[a] Assignments were confirmed by HSQC and HMBC experiments.

Gumoside A (**2**) was obtained as an amorphous, white solid, and its molecular formula, $C_{35}H_{49}O_{14}$, was deduced by HRMALDITOFMS analysis (*m/z* 693.3120 $[M + H]^+$, calcd for $C_{35}H_{49}O_{14}$, 693.3122). The NMR data of **2** (Table 1) were similar to those of **1** for the coumarin moiety but differed for the sesquiterpene signals and because of the occurrence of signals indicative of sugar units. The ^{1}H NMR spectrum of **2** displayed for the sesquiterpene unit signals due to an exomethylene function at δ 5.02 (brs) and 4.67 (brs), a primary alcoholic function at δ 4.33 (dd, J = 10.0, 3.5 Hz) and 4.25 (dd, J = 10.0, 5.7 Hz), two secondary alcoholic functions at δ 4.13 (ddd, J = 11.0, 11.0, 4.5 Hz) and δ 3.21 (t, J = 8.2 Hz), and three tertiary methyl groups at δ 0.95, 1.09, and 1.34. In the HMBC spectrum, correlations between the exomethylene signals at δ 5.02 and 4.67 (CH_2-12′) and the carbon resonance at δ 55.5 (C-9′) and between $C\underline{H}_2$-11 at δ 4.33 and 4.25 and C-9′ revealed the location of an exomethylene function at C-8′. COSY correlations between the proton signal at δ 1.49 (H-5′) and the proton at δ 4.13, which, in turn, was coupled with the protons at δ 2.96 (H-7′α) and 2.20 (H-7′β), allowed a secondary alcoholic function in **2** to be located at C-6′. The ROESY experiment supported the relative configurations of the stereogenic centers at C-3′, C-5′, C-6′, C-9′, and C-10′. In particular, ROE correlations between $C\underline{H}_2$-11′/Me-15′, Me-15′/H-6′, and H-6′/Me-14′ helped to establish an α-orientation for CH_2-11′, Me-14′, Me-15′, and H-6′. Further ROE correlations between H-3′/Me-13′ and H-3′/H-5′ were used to determine a β-orientation for Me-13′, H-3′, and H-5′.

The ^{1}H NMR spectrum of **2** showed signals corresponding to two anomeric protons at δ 5.00 (d, J = 1.8 Hz) and 4.42 (d, J = 7.8 Hz). 1D-TOCSY, HSQC, HMBC, and DQF-COSY correlations demonstrated the presence of a β-apiofuranosyl and a β-glucopyranosyl unit (Table 2). The configuration of the sugar units was assigned after hydrolysis of **2** with 1 N HCl, and the sugar units were determined to be D-apiose and D-glucose. The glycoside structure of **2** and its linkage sites were confirmed from the HMBC spectrum, which showed long-range correlations between the anomeric proton at δ 4.42 (H-1_{glc}) and the carbon resonance at δ 76.2 (C-6′) and between the anomeric proton at δ 5.00 (H-1_{api}) and the carbon resonance at δ 68.4 (C-6_{glc}). Therefore, the structure of gumoside A was determined as **2**.

Gumoside B (**3**), obtained as an amorphous, white solid, showed a pseudomolecolar ion peak in the HRMALDITOFMS at *m/z* 561.2697 $[M + H]^+$, consistent with the molecular formula $C_{30}H_{41}O_{10}$ (calcd for $C_{30}H_{41}O_{10}$ 561.2700). The ^{1}H NMR spectrum of **3** displayed for the sesquiterpene unit signals due to an olefinic exomethylene group at δ 4.99 (brs) and 4.67 (brs), a primary alcoholic function at δ 4.35 (dd, J = 10.0, 3.2 Hz) and 4.26 (dd, J = 10.0, 5.4 Hz), two secondary alcoholic functions at δ 4.14 (dd, J = 10.9, 5.2 Hz) and 3.31 (t, J = 2.7 Hz), and three tertiary methyl groups at δ 0.95, 1.13, and 1.29 (Table 1). For the sesquiterpene moiety, the ^{13}C NMR spectrum of **3** was closely related to that of **2**, showing only some differences in the carbon resonances of C-3′, C-5′, and Me-14′ (Table 1). The upfield chemical shifts of C-3′ (δ 78.4) and C-5′ (δ 53.4) and the downfield chemical shift of Me-14′ (δ 22.2) suggested for gumoside B (**3**) the same sesquiterpene moiety of gumoside A (**2**) but a different orientation for the secondary alcoholic function at C-3′. The small coupling costant of H-3′ (δ 3.31, t, J = 2.7 Hz) and the occurrence of a ROE correlation between Me-14′ and H-3′ allowed an α-orientation to be assigned to H-3′.

The ^{1}H NMR spectrum of **3** showed only one anomeric proton signal at δ 4.45 (d, J = 7.8 Hz), ascribable to a β-glucopyranosyl unit on the basis of NMR data (Table 2). The configuration of the sugar unit was assigned after hydrolysis of **3** with 1 N HCl and was determined as D. The linkage of the glucose unit at C-6′ was suggested by the HMBC correlation between the anomeric proton at δ 4.45 (H-1_{glc}) and the carbon resonance at δ 75.9 (C-6′). The structure of gumoside B was, therefore, assigned as **3**.

The MeOH extract of *F. gumosa* roots afforded also cauferoside (**4**), a sesquiterpene coumarin glycoside differing from gumoside B only in the stereochemistry at C-3′, previously isolated from *Ferula concaula*.[21] NMR data of **4** are reported in Table 1.

Antiproliferative activities of the compounds isolated from *F. gumosa* were tested against M14 (human melanoma), MCF-7 (breast carcinoma), T98G (glioblastoma), A549 (lung carcinoma), Saos-2 (osteosarcoma), FRO (thyroid carcinoma), and U937 (leukemic monocyte lymphoma) cell lines using the MTT assay. Of all compounds tested, only feselol (**5**) was active (IC_{50} < 10 μM) for a cancer cell line, and this exhibited an IC_{50} value of 8 μM against the U937 cell line.

Experimental Section

General Experimental Procedures. Optical rotations were measured on a JASCO DIP 1000 polarimeter. IR measurements were obtained on a Bruker IFS-48 spectrometer. UV spectra were obtained on a Beckman DU 670 spectrometer. NMR experiments were performed on a Bruker DRX-600 spectrometer at 300 K. All 2D-NMR spectra were acquired in CD_3OD (99.95%, Sigma-Aldrich), and standard pulse sequences and phase cycling were used for DQF-COSY, HSQC, HMBC, ROESY, and TOCSY spectra. The ROESY spectra were acquired with t_{mix} = 400 ms. ESIMS analyses were performed using a ThermoFinnigan LCQ Deca XP Max ion-trap mass spectrometer equipped with Xcalibur software. Exact masses were measured by a Voyager DE mass spectrometer. Samples were analyzed by matrix-assisted laser desorption ionization time-of-flight

(MALDITOF) mass spectrometry. A mixture of analyte solution and α-cyano-4-hydroxycinnamic acid (Sigma) was applied to the metallic sample plate and dried. Mass calibration was performed with the ions from ACTH (fragment 18−39) at 2465.1989 Da and α-cyano-4-hydroxycinnamic acid at 190.0504 Da as internal standards. HPLC was performed on a Knauer system with a Smartline pump including a 50 mL pump (EA4301 V4) and UV detector, using a Eurospher 100−10 C_{18} column (250 × 16 mm) at 2 mL/min and monitored at 254 nm.

Plant Material. The roots of *F. gumosa* were collected in the Alibolagh Valley, Hezarmasjed Mountains, Khorasan-Razavi Province, Iran, in May 2009, and identified by Mohammadreza Joharchi, Ferdowsi, University of Mashhad Herbarium (FUMH). A voucher specimen has been deposited at the herbarium of the School of Pharmacy, Mashhad University of Medical Sciences (accession no. 1015).

Extraction and Isolation. The milled plant material (600 g) was extracted by maceration with dichloromethane (2 L × 3). The dichloromethane extract was discarded, and the remaining plant powder was extracted again as above with methanol (2 L × 3). The resultant extract was filtered and evaporated under reduced pressure to afford 54.21 g of a brown residue. A part of this residue (12 g) was subjected to silica gel column chromatography (56 × 5 cm) by elution with EtOAc−MeOH−H_2O (100:0:0, 24:1:1, 12:1.5:0.5, 8:1.5:0.5, 6:1.5:0.5, 3:1.5:0.5, respectively) to give nine fractions (F1−F9). Reversed-phase (C_{18}) preparative thin-layer chromatography (TLC) of F1 and F2, using the solvent system MeOH−H_2O, gave ferocaulidin (8 mg), conferol (44 mg), and feselol (**5**) (7 mg). Fraction 3 was purified by reversed-phase preparative TLC (MeOH−H_2O, 90:10) to give ligupersin A (1 mg). Fractions 5 and 6 were similarly fractioned by reversed-phase preparative TLC (MeOH−H_2O, 75:25) to afford compound **3** (56 mg), cauferoside (**4**) (94 mg), and conferoside (4 mg). Fractions 4 and 7 were further purified by reversed-phase HPLC (Eurospher 100−10 C_{18} column, MeOH−H_2O, 70:30, flow rate 2.0 mL/min) to give daucosterol (7 mg) and acantrifoside E (230 mg), respectively. Fraction 8 was similarly fractioned by reversed-phase HPLC using the same conditions as for fractions 4 and 7 to yield ferilin (14 mg) and compounds **1** (17 mg) and **2** (68 mg). 4-Hydroxybenzoic acid 4-(6-*O*-sulfo)glucopyranoside (6 mg) was purified from fraction 9 by reversed-phase HPLC (Eurospher 100-10, C_{18} column, MeOH−H_2O, 55:45, flow rate 2.0 mL/min).

Gumosin (1): white, amorphous powder; $[\alpha]^{25}_D$ −24.6 (*c* 0.11, MeOH); UV (MeOH) λ_{max} (log ε) 325 (4.05), 235 (3.50) nm; IR (KBr) ν_{max} 3468, 2960, 1750, 1685, 1610 cm^{-1}; ^1H NMR (CD_3OD, 600 MHz) and ^{13}C NMR (CD_3OD, 150 MHz), see Table 1; ESIMS *m/z* 399 $[M + H]^+$; HRMALDITOFMS *m/z* $[M + H]^+$ calcd for $C_{24}H_{31}O_5$, 399.2172, found 399.2168.

Gumoside A (2): white, amorphous powder; $[\alpha]^{25}_D$ −38.5 (*c* 0.17, MeOH); UV (MeOH) λ_{max} (log ε) 325 (4.00), 225 (3.40) nm; IR (KBr) ν_{max} 3466, 2960, 1748, 1685, 1617 cm^{-1}; ^1H NMR (CD_3OD, 600 MHz) and ^{13}C NMR (CD_3OD, 150 MHz), see Table 1; ^1H NMR (CD_3OD, 600 MHz) and ^{13}C NMR (CD_3OD, 150 MHz) data of the sugar portion, see Table 2; ESIMS *m/z* 693 $[M + H]^+$; HRMALDITOFMS *m/z* $[M + H]^+$ calcd for $C_{35}H_{49}O_{14}$ 693.3122, found 693.3120.

Gumoside B (3): white, amorphous powder; $[\alpha]^{25}_D$ −55.0 (*c* 0.17, MeOH); UV (MeOH) λ_{max} (log ε) 324 (4.00), 225 (3.40) nm; IR (KBr) ν_{max} 3470, 2964, 1756, 1685, 1610 cm^{-1}; ^1H NMR (CD_3OD, 600 MHz) and ^{13}C NMR (CD_3OD, 150 MHz), see Table 1; ^1H NMR (CD_3OD, 600 MHz) and ^{13}C NMR (CD_3OD, 150 MHz) data of the sugar portion, see Table 2; ESIMS *m/z* 561 $[M + H]^+$; HRMALDITOFMS *m/z* $[M + H]^+$ calcd for $C_{30}H_{41}O_{10}$ 561.2700, found 561.2697.

Acid Hydrolysis. A solution (0.8 mg each) of **2** and **3** in 1 N HCl (0.25 mL) was stirred at 80 °C for 4 h. After cooling, the solution was concentrated under N_2. The residue was dissolved in 1-(trimethylsilyl)imidazole and pyridine (0.1 mL), and the solution was stirred at 60 °C for 5 min. After drying the solution with a stream of N_2, the residue was partitioned between H_2O and CH_2Cl_2 (1 mL, 1:1 v/v). The CH_2Cl_2 layer was analyzed by GC using an L-Chirasil-Val column (0.32 mm ×25 m). Temperatures of the injector and detector were 200 °C for both. A temperature gradient system was used for the oven, starting at 100 °C for 1 min and increasing up to 180 °C at a rate of 5 °C/min. Peaks of the hydrolysate of **2** were detected at 14.72 min (D-glucose) and 11.90 (D-apiose). Peak of the hydrolysate of **3** was detected at 14.72 min (D-glucose). Retention times for authentic samples after being treated simultaneously with 1-(trimethylsilyl)imidazole in pyridine were detected at 14.70 min (D-glucose) and 11.88 (D-apiose).

Cancer Cell Lines. Human melanoma (M14), breast (MCF-7), glioblastoma (T98G), lung (A549), osteosarcoma (Saos-2), and thyroid (FRO) cancer cells, obtained from ATCC (Manassas, VA), were cultured in DMEM medium supplemented with 2 mM L-glutamine, 10% heat-inactivated fetal bovine serum (FBS), 1% penicillin/streptomycin (all from Cambrex Bioscience, Verviers, Belgium), and human leukemic monocyte lymphoma (U937) cells were cultured in RPMI medium (Cambrex Bioscience) supplemented with 2 mM L-glutamine, 10% FBS, and 1% penicillin/streptomycin at 37 °C in an atmosphere of 95% O_2 and 5% CO_2. The cells were used up to a maximum of 10 passages.

MTT Bioassay. Human cancer cells (3×10^3) were plated in 96-well culture plates in 90 μL of culture medium and incubated at 37 °C in humidified 5% CO_2. The next day, 10 μL aliquots of serial dilutions of each test compound (1−50 μM) were added to the cells and incubated for 48 h. Cell viability was assessed through the MTT assay. Briefly, 25 μL of MTT (5 mg/mL) was added, and the cells were incubated for an additional 3 h. Thereafter, cells were lysed and the dark blue crystals solubilized with 100 μL of a solution containing 50% *N*,*N*-dimethylformamide and 20% SDS (sodium dodecyl sulfate) with an adjusted pH of 4.5. The optical density (OD) of each well was measured with a microplate spectrophotometer (Titertek Multiskan MCC/340) equipped with a 620 nm filter. Cell viability in response to treatment was calculated as percentage of control cells treated with DMSO solvent at the final concentration 0.1%: % viable cells = (100 × OD treated cells)/OD control cells.

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Supporting Information Available: ^1H, HSQC, HMBC, and ROESY NMR spectra for compounds **1**−**3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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