New α-Glucosidase Inhibitors from the Mongolian Medicinal Plant Ferula mongolica

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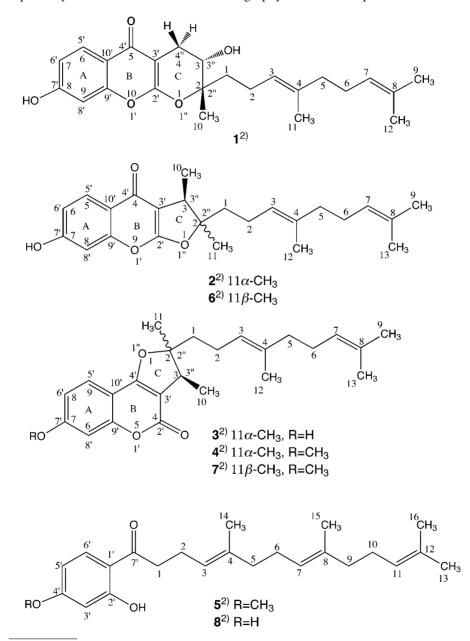
The four new and four known sesquiterpenoid derivatives 1-4 and 5-8, respectively, were isolated from the air-dried roots of *Ferula mongolica*. The structures of these compounds were determined by spectroscopic methods and found to be *rel*-(2*R*,3*R*)-2-[(3*E*)-4,8-dimethylnona-3,7-dienyl]-3,4-dihydro-3,8-dihydroxy-2-meth-yl-2*H*,5*H*-pyrano[2,3-*b*][1]benzopyran-5-one (1), *rel*-(2*R*,3*R*)-2-[(3*E*)-4,8-dimethylnona-3,7-dienyl]-2,3-dihydro-7-hydroxy-2,3-dimethyl-4*H*-furo[2,3-*b*][1]benzopyran-4-one (2), *rel*-(2*R*,3*R*)-2-[(3*E*)-4,8-dimethylnona-3,7-dienyl]-2,3-dihydro-7-hydroxy-2,3-dimethyl-4*H*-furo[3,2-*c*][1]benzopyran-4-one (3), *rel*-(2*R*,3*R*)-2-[(3*E*)-4,8-dimethylnona-3,7-dienyl]-2,3-dihydro-7-methoxy-2,3-dimethyl-4*H*-furo[3,2-*c*][1]benzopyran-4-one (4), (4*E*,8*E*)-1-(2-hydroxy-4-methoxyphenyl)-5,9,13-trimethyltetradeca-4,8,12-trien-1-one (5), the *rel*-(2*R*,3*S*) diastereoisomer **7** of **4**, and (4*E*,8*E*)-1-(2,4-dihydroxyphenyl)-5,9,13-trimethyltetradeca-4,8,12-trien-1-one (8). These compounds were tested as inhibitors against the enzyme α -glucosidase. The compounds **1**-**6** and **8** exhibited significant inhibitory activity and, therefore, represent a new class of α -glucosidase inhibitors.

1. Introduction. – *Ferula mongolica* SEUD. (Umbelliferae), an important species of the genus *Ferula*, grows in Bulgan Somone of Hovd district of Mongolia. Ancient texts recorded its usage for abortive purposes, and the crude MeOH extracts of the plant were found to inhibit implantation of fertilized eggs in rats [1]. *F. communis* is used in the treatment of various diseases as antinociceptive, antipyretic, anti-inflammatory, and antibacterial agent [2][3]. In this paper, we report the α -glucosidase inhibitory activity of compounds isolated from this plant for the very first time. The enzyme α -glucosidase is involved in the hydrolytic cleavage of glucose from disaccharides and oligosaccharides. Inhibition of this enzyme prolongs the overall carbohydrate digestion time and thus reduces the rate of glucose absorption. It is effective in controlling postprandial hyperglycaemia and avoids the late complications associated with type-II diabetes like retinopathy, neuropathy, and microangiopathy [4].

Our present study on the MeOH extracts of the roots of *Ferula mongolica* resulted in the isolation and characterization of the four new compounds 1-4 along with the four known compounds 5-8 which are all reported for the first time from this species. Ketone 5 has not been reported as yet from any natural source. The compounds 1-8were evaluated as inhibitors of α -glucosidase from yeast.

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2. Results and Discussion. – The MeOH extract obtained from the roots of *Ferula* mongolica was dissolved in distilled H_2O and defatted with hexane. The defatted aq. extract was further fractionated with AcOEt. The residue of the AcOEt extract was repeatedly submitted to column chromatography to afford compounds 1-8.



²) Arbitrary numbering of 1-8 is used in the *General Part*; systematic names are given in the *Exper. Part*.

Baigene A (1) was isolated as a colorless gum. The HR-EI-MS showed the M^+ at m/z 398.2091 (C₂₄H₃₀O₅⁺; calc. 398.2093) indicating ten degrees of unsaturation. The IR spectrum exhibited the typical absorptions for OH (3250 cm⁻¹), conjugated C=O (1707 cm⁻¹), and aromatic moieties (1610 and 1470 cm⁻¹), while the characteristic UV absorptions at 289, 260, 248, and 243 nm indicated the presence of a benzopyran skeleton for 1 [5]. The ¹H- and ¹³C-NMR (*Tables 1* and 2), HMBC, HMQC, and NOESY data established that baigene A (1) is *rel-*(2*R*,3*R*)-2-[(3*E*)-4,8-dimethylnona-3,7-dienyl]-3,4-dihydro-3,8-dihydroxy 2-methyl-2*H*,5*H*-pyrano[2,3-*b*][1]benzopyran-5-one.

In the ¹H-NMR spectrum of **1**, the aromatic $H-C(5')^2$) resonated at δ 7.91 (d, J(6',5') = 8.7 Hz), H-C(6') at δ 6.88 (dd, J(6',8') = 2.2 Hz, J(6',5') = 8.7 Hz), and H-C(8') at δ 6.76 (d, J(6',8') = 2.2 Hz) [6]. Two *m* at δ 5.15 – 5.11 and 5.06 – 5.02 were assigned to the olefinic H-C(3) and H-C(7), respectively. The 4 CH₂ groups of the side chain at C(2'') appeared as *m* at δ 1.75 – 1.70 (CH₂(1)), 2.22 – 2.15 (CH₂(2)), 1.97 – 1.93 (CH₂(5)), and 2.06 – 2.01 (CH₂(6)) [7]. The (CH₂(4'') group gave rise to 2 '*dd*' (*ABX*) at δ 2.82 (H_a – C(4''), J(4''a,3'') = 5.1 and J(4''a,4''b) = 16.4 Hz) and 2.55 (H_b – C(4''), J(4''b,3'') = 6.1 and J(4''a,4''b) = 16.4 Hz) [5], and H – C(3'') appeared at δ 3.92 (dd, J(3'',4''a) = 5.3 and J(3'',4''b) = 5.9 Hz), typical for a methine proton geminal to an O-atom. The 4 Me groups gave rise to *s* at δ 1.62 (Me(9)), 1.41 (Me(10)), 1.60 (Me(11)), and 1.54 (Me(12)) [5].

The broad-band decoupled ¹³C-NMR spectrum of **1** showed resonances for all 24 C-atoms in the molecule. DEPT Spectra revealed the presence of 4 CH₃, 5 CH₂, 6 CH, and hence 9 quaternary C-atoms. The HMQC experiment established ¹H, ¹³C connectivities for H-C(3") (δ 3.92) and C(3") (δ 67.6), CH₂(4") (δ 2.82 and 2.55) and C(4'') (δ 25.4), and $CH_3(10)$ (δ 1.41) and C(10) (δ 19.0). The presence of a benzopyran (rings A and B) and pyran moiety (ring C) was deduced from the HMBC experiment which showed long-range interactions of the aromatic H-C(5') (δ 7.91) with C(4') (δ 179.9) and C(9') (δ 156.5), and interactions of CH₂(4") (δ 2.82 and 2.55) with C(4') (δ 179.9), C(2') (δ 164.1), and C(3') (δ 93.6), establishing the attachment of ring C (pyran ring) to ring B [5]. $CH_3(10)$ (δ 1.41) showed couplings with C(2") (δ 87.5), C(3") (δ 67.6), and C(1) (δ 38.2), further confirming the above mentioned assignment. The relative configuration at the chiral centers C(2'') and C(3'')was suggested by a 10% NOE at δ 3.92 (H-C(3'') on irradiation at δ 1.41 CH₃(10), indicating the cis relationship of H-C(3'') and $CH_3(10)$ and suggesting their β orientation as previously reported in similar cases [5]. The HMBC plot established the coupling of the olefinic H–C(3) (δ 5.15–5.11) with C(2) (δ 22.5), C(1) $(\delta 38.2), C(11) (\delta 16.0), and C(5) (\delta 40.7) and of H-C(7) (\delta 5.06-5.02) with C(6) (\delta 27.7), C(9), (\delta 25.8), and C(5) (\delta 55.8)$ C(12) (δ 17.7), indicating the terminal position of the C(7)=C(8) bond. The CH₂(2) protons (δ 2.22–2.15) coupled with C(3) (δ 124.7), C(4) (δ 136.7) and C(1) (δ 38.2), and the CH₂(6) protons (δ 2.06–2.01) with C(5) (\$\delta 40.7), C(4) (\$\delta 136.7), C(7) (\$\delta 125.3), and C(8) (\$\delta 132.1) [7]. The (E) configuration of the C(3)=C(4) bond in the side chain as reported previously for similar structures [7], was determined by an NOESY experiment which revealed cross peaks for H-C(3)/H-C(5) and $H-C(7)/CH_3(9)$.

The ¹H- and ¹³C-NMR spectrum of baigene B (**2**) resembled closely that of baigene A (**1**). Some spectral differences allowed to assign to **2** the structure of rel-(2R,3R)-2-[(3E)-4,8-dimethylnona-3,7-dienyl-2,3-dihydro-7-hydroxy-2,3-dimethyl-4H-furo[2,3-b]-[1]benzopyran-4-one.

The major spectral differences between **1** and **2** were that the ¹H-NMR signals of CH₂(4") and H–C(3") of **1** were replaced by a *q*- for H–C(3") (δ (H) 3.25, *J*(3",10) = 6.9 Hz; δ (C) 44.2), exhibiting geminal coupling with Me(10) (δ (H) 1.28, *d*, *J*(3",10) = 6.9 Hz; δ (C) 14.4) in **2** (see *Tables 1* and 2), indicative of a MeCH moiety sandwiched between two quaternary C-atoms. This difference was in accordance with a five-membered ring C [8] and with cross peaks in the COSY-45° plot for interactions between H–C(3") (δ 3.25) and CH₃(10) (δ 1.28) [8]. This fact was also suggested by the HMBC experiment in which H–C(3") showed long-range couplings with C(3') (δ 100.2), C(2') (δ 169.2), C(11) (δ 25.4), and C(10) (δ 14.4). Similarly, CH₃(11) (δ 1.51) was coupled with C(2") (δ 97.2), C(3") (δ 44.2), and C(1) (δ 35.9), which was consistent with a five-membered ring C [8]. The coupling of CH₃(10) (δ 1.28) with C(3") (δ 44.2), C(3") (δ 44.2), C(3") (δ 40.2), C(3") (δ 44.2), C(3") (δ 44.2), C(3") (δ 100.2), and C(2") (δ 97.2) further confirmed the furan moiety [8][9]. The relative configuration was established as *rel*-(2*R*,3*R*) by comparing the ¹H-chemical shifts of CH₃(11) and CH₂(1) with reference data [8][9] and confirmed by the absence of an NOE between CH₃(10) (δ 1.28) ind CH₃(11) (δ 1.51), indicating their *trans* relationship [8][9].

					1			
	δ(H)							
	1	2	3	4	5	6	7	8
$CH_2(1)$	1.75-1.70 (m)	1.79-1.71 (m)	$1.80 - 1.73 \ (m)$	$1.79 - 1.71 \ (m)$	2.97 $(t, J = 7.1)$	1.85-1.81 (m)	1.85 - 1.80 (m)	2.97 $(t, J = 7.2)$
$CH_2(2)$	2.22-2.15 (m)	2.25 - 2.19 (m)	2.29-2.21 (m)	2.28–2.25 (m)	2.39 $(q, J = 7.1)$	2.18-2.12 (m)	2.19-2.12 (<i>m</i>)	2.39 $(q, J = 7.1)$
H-C(3)	5.15-5.11 (m)	5.21-5.17 (<i>m</i>)	5.20-5.17 (m)	5.22-5.18 (m)	5.20-5.16 (m)	5.15-5.11 (m)	5.15-5.12 (m)	5.21-5.15 (<i>m</i>)
$CH_2(5)$	$1.97 - 1.93 \ (m)$	1.95 - 1.87 (m)	$1.99 - 1.92 \ (m)$	$1.93 - 1.85 \ (m)$	$1.99 - 1.90 \ (m)$	$1.96 - 1.92 \ (m)$	$1.93 - 1.90 \ (m)$	$1.97 - 1.90 \ (m)$
$CH_2(6)$	$2.06 - 2.01 \ (m)$	2.08 - 2.02 (m)	2.09-2.03 (m)	2.09-2.01 (m)	2.08-2.02 (<i>m</i>)	_	2.07-2.0 (m)	2.07-2.0 (<i>m</i>)
H-C(7)		5.12-5.07 (m)	5.08-5.05 (m)	5.10-5.06 (m)	5.08-5.04 (m)	5.08-5.04 (m)	5.07-5.02 (m)	5.07-5.04 (m)
Me(9) or $CH_2(9)$	-	1.64(s)	1.64(s)	1.64(s)	$1.99 - 1.90 \ (m)$	1.64(s)	1.63(s)	$1.97 - 1.90 \ (m)$
Me(10) or $CH_2(10)$	1.41	1.28 $(d, J = 6.9)$	1.23 $(d, J = 7.0)$	$1.27 \ (d, J = 7.0)$	2.08-2.02 (m)	1.33 $(d, J = 7.0)$	$1.29 \ (d, J = 7.0)$	2.07-2.0 (<i>m</i>)
Me(11) or H–C(11)	1.60	1.51(s)	1.48(s)	1.50(s)	5.08-5.04 (<i>m</i>)	1.48(s)	1.48(s)	5.07-5.04 (m)
Me(12)	1.54(s)	1.66(s)	1.62(s)	1.65(s)	I	1.57(s)	1.64(s)	I
Me(13)	I	1.57(s)	1.57(s)	1.58(s)	1.65(s)	1.57(s)	1.56(s)	1.64(s)
Me(14)	I	I	I	I	1.57(s)	I	I	1.56(s)
Me(15)	I	I	I	I	1.56(s)	I	I	1.55(s)
Me(16)	I	1	1	1	1.61(s)	1	I	1.60(s)
H-C(3'')	3.92 (dd,	3.25 (q, J = 6.9)	3.15 (q, J = 7.0)	3.18 (q, J = 7.0)	I	3.37 (q, J=7.0)	3.27 (q, J = 7.0)	I
	J = 5.3, 5.9							
$CH_{2}(4'')$	2.82 (dd,	I	I	I	I	I	I	I
	J = 5.1, 16.4)							
	J = 6.1, 16.4							
MeO		I	I	3.89(s)	3.83(s)	I	3.89(s)	I
H-C(3')	I	I	I	Ì	6.41 $(d, J = 2.5)$	I	ļ	$6.41 \ (d,$
								J = 2.5)
H-C(5')	$7.91 \ (d, J = 8.7)$	7.94(d, J = 8.5)	7.50 (d, J = 8.5)	7.58(d, J = 9.4)	$(6.49 \ (dd, I) = 2.5, 8.5)$	7.93 (d, J = 8.7)	7.57 (d, J = 9.3)	$(6.49 \ (dd, I = 2.5, 8.5))$
H-C(6')	6.88 (dd,		$6.80 \ (dd,$	6.96 (<i>dd</i> ,	7.79 (d, J = 8.9)	(40, 60, 60, 60, 60, 60, 60, 60, 60, 60, 6	6.95 (dd,	7.79 (d, J = 8.9)
11 - 2787	J = 2.2, 8.7		J = 2.0, 8.5	J = 2.2, 9.4			J = 2.3, 9.4)	
$H-C(\delta)$	0.00 (a, J = 2.2)	0.81 $(a, J = 2.0)$	(0.7 = r, a) c/0	(2.5, a, b) = 2.2	I	0.81 (a, J = 2.2)	(c.7 = t, a) cc.0	I

Table 1. ¹H-NMR (CD₃OD) Chemical Shifts of Compounds **1–8**. δ in ppm, J in Hz. Arbitrary numbering

Helvetica Chimica Acta – Vol. 84 (2001)

	$\delta(H)$							
	1	2	3	4	5	6	7	8
C(1)	38.2	35.9	36.2	36.2	40.7	42.6	42.7	40.8
C(2)	22.5	23.7	23.8	23.8	24.4	23.0	23.1	24.5
C(3)	124.7	124.5	125.0	124.8	124.7	124.5	124.9	125.5
C(4)	136.7	136.8	136.6	136.6	137.4	136.8	136.6	137.3
C(5)	40.7	40.7	40.7	40.7	40.6	40.7	40.7	40.9
C(6)	27.7	27.6	27.7	27.7	27.4	27.6	27.6	27.6
C(7)	125.3	125.3	125.1	125.0	125.3	125.3	124.7	125.3
C(8)	132.1	131.0	132.1	132.1	136.0	131.0	132.1	135.9
C(9)	25.8	25.8	25.9	25.8	38.9	25.8	25.8	38.9
C(10)	19.0	14.4	13.9	13.8	27.8	14.9	14.4	27.9
C(11)	16.0	25.4	25.6	25.5	124.1	20.6	20.8	124.0
C(12)	17.7	16.6	16.1	16.0	132.0	16.0	16.0	132.0
C(13)	_	17.7	17.8	17.7	25.8	17.7	17.7	26.2
C(14)	-	-	-	-	16.1	_	-	16.5
C(15)	_	_	_	_	16.0	_	-	16.4
C(16)	-	-	-	-	17.7	-	-	18.1
C(2'')	87.5	97.2	97.8	98.0	-	97.6	98.5	-
C(3'')	67.6	44.2	45.3	45.4	_	42.0	43.1	_
C(4'')	25.4	-	-	-	-	_	-	-
MeO	_	_	_	56.4	56.11	_	56.4	_
C(1')		-	-	-	114.8	_	-	114.1
C(2')	164.1	169.2	163.6	163.4	166.4	169.8	163.3	166.2
C(3')	93.6	100.2	104.1	104.8	101.9	100.0	104.5	103.9
C(4')	179.9	177.7	167.2	166.9	167.6	177.7	167.1	166.3
C(5')	127.6	127.4	125.3	125.3	108.3	127.4	125.3	109.2
C(6')	115.5	115.5	114.3	113.8	133.4	115.5	113.8	133.6
C(7')	164.0	163.6	163.6	165.1	206.4	163.6	165.1	205.7
C(8')	103.0	103.2	103.5	101.7	_	103.7	101.7	_
C(9')	156.5	156.5	158.2	158.1	_	156.6	158.1	_
C(10')	115.7	117.0	106.2	107.1	_	117.0	107.1	_

Table 2. ¹³C-NMR (CD₃OD) Chemical Shifts [ppm] of Compounds 1-8. Arbitrary numbering

Baigene C (**3**) exhibited the characteristic absorptions at 316, 292, and 261 nm in the UV spectrum, suggesting the presence of a coumarin (=2*H*-1-benzopyran-2-one) skeleton which was also supported by the typical IR absorption bands for OH (3200 cm⁻¹) and coumarin (1610 and 1630 cm⁻¹) [10][11]. The structure of **3** was deduced from its spectral data as *rel*-(2*R*,3*R*)-2-[(*E*)-4,8-dimethylnona-3,7-dienyl]-2,3-dihydro-7-hydroxy-2,3-dimethyl-4*H*-[3,2-*c*][1]benzopyran-4-one.

The ¹³C-NMR spectrum of **3** showed signals at δ 163.6 (C(2')), 104.1 (C(3')), and 167.2 (C(4')) characteristic of a furanocoumarin skeleton [9][12]. The HMBC spectrum established correlations of H–C(5') (δ 7.50) of ring A with C(9') (δ 158.2) and C(4') (167.2) and also of H–C(8') (δ 6.73) of ring A with C(10') (δ 106.2) and C(4') (δ 167.2), further confirming the presence of a coumarin moiety [10][12][13]. The absence of typical pairs of *d* for H–C(3') and H–C(4') indicated that C(3') and C(4') were substituted in **3** [14]. Comparison of its ¹H- and ¹³C-NMR data with those reported for similar structures allowed to determine the fusion site of the furan ring C [5][9]. This was confirmed by HMBC showing the coupling of H–C(3'') (δ 3.15) with C(3') (δ 104.1), C(4') (δ 3.62). The coupling of CH₃(10) (δ 1.23) with C(3'') (δ 45.3), C(3'') (δ 104.1), and C(2'') (δ 3.15) with CH₃(10) (δ 1.23). The comparatively similar ¹H- and ¹³C-NMR

spectral values of the vicinal chiral centers C(2'') and C(3'') of **3** and **2** suggested identical relative configurations at these centers. This was confirmed by a 34.6% NOE at δ 1.48 (CH₃(11)) when H–C(3'') (δ 3.15) was irradiated, indicating the *trans* position of CH₃(10) and CH₃(11), and suggesting CH₃(11) to be α oriented [9].

O-Methylbaigene C (**4**) was found to be the 7'-*O*-methyl derivative of **3** (MeO at δ 3.89 (*s*) and δ (C) 56.4), *i.e.*, *rel-*(2*R*,3*R*)-2-[(*E*)-4,8-dimethylnona-3,7-dienyl]-2,3-dihydro-7-methoxy-2,3-dimethyl-4*H*-furo[3,2-*c*][1]benzopyran-4-one.

The 4'-O-methyldshamirone (5) was also isolated from *F. mongolica*; earlier, **5** was only reported as a synthetic derivative of a natural compound isolated from *F. communis* [15]. The parent dshamirone (8) was also shown to be present in *F. mongolica*, as a new source; previously, **8** was reported to occur in *F. dshaudshamyr* [16][17]. The ¹H-NMR spectra of **5** and **8** exhibited an *ABX* system typical of the 2,4-dihydroxybenzoyl moiety (4-methoxy in case of **5**) and other signals similar to reported data.

Compounds **6** and **7** were isolated for the first time from *F. mongolia* and were shown to be the 11β -methyl diastereoisomers of baigene B (**2**) and 7'-O-methyl-baigene C (**4**), respectively. Compounds **6** and **7** have been recently reported from *Ferula ferulioides* [18]. Their structures were confirmed by the NMR data (¹H-NMR: typical *ABX* system for aromatic protons, all the signals for the sesquiterpene portion present, MeO signal for **7**; *cf.* [8][18]; ¹³C-NMR: δ 177.7 (C(4') of **6**) and 167.1 (C(4') of **7**), typical for the presence of the chromone and furo-coumarin moiety, resp. (*cf.* [9][18]).

Compounds 1-6 and 8, isolated from the MeOH extract of *F. mongolia*, were found to be inhibitors of the enzyme α -glucosidase (*Table 3*). Apparently, the olefinic side chain and the phenol moieties are responsible of the observed activity. Decrease in the activity was observed when a MeO group was present at the aromatic ring system instead of OH function. On the other hand, the relatively low activity of compound **7** indicates the importance of the configuration at $C(2'')^2$ of the furo-coumarin moiety.

	1	2	3	4	5	6	8
IC ₅₀ (±s.e.m.)	56.06	32.21	$63.68 (\pm 2.68)$	79.87	82.41	20.50	9.31
[µм] ^a)	(±2.56)	(±1.38)		(± 2.97)	(± 3.21)	(±1.62)	(±0.15)

Table 3. α -Glucosidase Inhibition by Compounds 1–6 and 8

Experimental Part

General. Column chromatography (CC): silica gel, 70–230 mesh. TLC: precoated silica gel 60 F_{254} aluminium foils (*E. Merck*); detection at 254 and 366 nm, and by ceric sulfate reagent. Optical rotations: *Schmidt & Haensch Polartronic D*. UV and IR spectra: *Hitachi UV-3200* and *Jasco 302-A* spectrophotometers, resp.; λ_{max} (log ε) in nm and \overline{v} in cm⁻¹, resp. ¹H- and ¹³C-NMR, COSY, HMQC, and HMBC Spectra: *Bruker AM-*400 and AMX-500 spectrometers, resp.; chemical shift δ in ppm rel. to SiMe₄ as internal standard and coupling constants *J* in Hz. *Varian MAT-311A* and *Jeol HX-110* mass spectrometers; *m/z* (rel. int.).

Enzyme Assay. Inhibitory activities of compounds 1-8 against α -glucosidase of type VI (from brewer yeast, *Sigma G6136*) were observed spectrophotometrically at pH 6.8 and at 37°, with 0.7 mM 4-nitrophenyl α -D-glucopyranoside (PNP-G) as a substrate and 0.017 units/ml of enzyme, in 50 mM sodium phosphate buffer containing 100 mM NaCl. As a positive control 0.3 mM 1-deoxynojirimycin was used; IC_{50} of 1-deoxynojirimycin

was reproduced as reported by *Asano et al.* [19]. The absorption increase at 400 nm due to the hydrolysis of PNP-G by α -glucosidase was monitored continuously spectrophotometrically with a microtitre-plate reader (*Molecular Devices*, USA) [3].

Plant Material. Roots of *F. mongolica* SEUD. were collected from Bulgon Somone of district Hovd of Mongolia in August 1997, and the voucher specimen (No. 00-309) was deposited at the Botanical Institute of the Mongolian Academy of Sciences, Ulaanbaatar, Mongolia.

Extraction and Isolation. Air-dried roots of *F. mongolica* (500 g) were extracted with MeOH. After evaporation, the MeOH extract (32 g) was dissolved in distilled H₂O and defatted with hexane. The defatted aq. extract was further fractionated with AcOEt (51). Evaporation gave 9 g of extract. The AcOEt extract was subjected to CC (pure hexane, then gradient of AcOEt and MeOH): *Fractions* 1-5. *Fr.* 1, on CC (5% AcOEt/hexane) afforded **5** (18.25 mg). *Fr.* 2, on CC (5% AcOEt/hexane) gave **4** (15.23 mg) and **7** (20.25 mg). *Fr.* 3, after CC (5% acetone/hexane), yielded **8** (100.25 mg). *Fr.* 4, after CC, gave *Frs.* 4a and 4b. *Fr.* 4a, on CC (15% acetone/hexane) afforded **3** (40.60 mg) and *Fr.* 4b, on CC (20% AcOEt/hexane), yielded **2** (25.25 mg) and **6** (30.26 mg). *Fr.* 5, on CC (1% MeOH/CHCl₃) gave **1** (45.42 mg).

Baigene A (= rel-(2R,3R)-2-[(3E)-4,8-Dimethylnona-3,7-dienyl]-3,4-dihydro-3,8-dihydroxy-2-methyl-2H,5H-[2,3-b][1]benzopyran-5-one; **1**). White gum (45.42 mg, 4.54 \cdot 10⁻²% yield). R_f 0.27 (1% MeOH/CHCl₃). [α]_D²⁷ = -38.46 (c = 0.02, MeOH). UV (MeOH): 289 (3.03), 260 (2.44), 248 (2.81), 243 (2.81). IR (CHCl₃): 3250, 1707, 1610, 1470, 1150. ¹H-NMR. *Table 1.* ¹³C-NMR: *Table 2.* HR-EI-MS: 398.2091 (C₂₄H₃₀O₅⁺; calc. 398.2093). EI-MS: 69 (100), 81 (74), 248 (30), 191 (84), 398 (16).

Baigene B (=rel-(2R,3R)-2-[(3E)-4,8-Dimethylnona-3,7-dienyl]-2,3-dihydro-7-hydroxy-2,3-dimethyl-4H-furo[2,3-b][1]benzopyran-4-one; **2**): White gum (25.25 mg, 2.52 \cdot 10^{-2%} yield). $R_{\rm f}$ 0.37 (20% AcOEt/hexane). [α]_D²⁷ = -33.3 (c = 0.02, MeOH). UV (MeOH): 291 (3.39), 194 (2.93), 202 (3.86). IR (CHCl₃): 3200, 1707, 1611, 1150. ¹H-NMR: *Table 1.* ¹³C-NMR: *Table 2.* HR-EI-MS: 382.2145 ($C_{24}H_{30}O_{4}^{+}$; calc. 382.2144). EI-MS: 69 (100), 205 (96.2), 137 (78), 231 (40), 382 (17).

Baigene C (=rel-(2R,3R)-2-[(3E)-4,8-Dimethylnona-3,7-dienyl]-2,3-dihydro-7-hydroxy-2,3-dimethyl-4H-furo[3,2-c][1]benzopyran-4-one; **3**): White gum (40.60 mg, 4.06 $\cdot 10^{-2}$ % yield). $R_{\rm f}$ 0.44 (15% acetone/hexane). $[\alpha]_{\rm D}^{27}$ = 33.33 (c = 0.01, MeOH). UV (MeOH): 316 (3.14), 292 (2.72), 261 (3.21). IR (CHCl₃): 3200, 1705, 1630, 1610, 1150. ¹H-NMR: *Table 1.* ¹³C-NMR: *Table 2.* HR-EI-MS: 382.2142 ($C_{24}H_{30}O_{4}^{+}$; calc. 382.2144). EI-MS: 69 (100), 382 (79), 205 (75), 231 (63), 313 (19).

O-Methylbaigene C (=rel-(2R,3R)-2-[(3E)-4,8-Dimethylnona-3,7-dienyl]-2,3-dihydro-7-methoxy-2,3-dimethyl-4H-furo[3,2-c][1]benzopyran-4-one; 4): White gum (15.23 mg, 1.52 $\cdot 10^{-2}\%$ yield). $R_{\rm f}$ 0.37 (8% AcOEt/hexane). $[a]_{27}^{27}$ =45.5 (c = 0.02, MeOH). UV (MeOH): 316 (2.81), 294 (2.52), 260 (2.36), 201 (3.40). IR (CHCl₃): 2850, 1705, 1637, 1610, 1150. ¹H-NMR: *Table 1.* ¹³C-NMR: *Table 2.* HR-EI-MS: 396.2296 ($C_{25}H_{32}O_{4}^+$; calc. 396.2301). EI-MS: 69 (100), 151 (93), 245 (72), 327 (39), 396 (19).

4'-O-Methyldshamirone (=(4E,8E)-1-(2-Hydroxy-4-methoxyphenyl)-5,9,13-trimethyltetradeca-4,8,12-trien-1-one; **5**): Yellow gum (18.25 mg, $1.82 \cdot 10^{-2}$ % yield). $R_{\rm f}$ 0.57 (1.5% AcOEt/hexane). $[\alpha]_{27}^{27} = \pm 0$ (c = 0.01, MeOH). UV (MeOH): 312 (3.85), 275 (4.16), 230 (3.90). IR (CHCl₃): 3350, 1700, 1610, 1150. ¹H-NMR: Table 1. ¹³C-NMR: Table 2. HR-EI-MS: 370.2503 ($C_{24}H_{34}O_3^+$; calc. 370.2508). EI-MS: 151 (100), 69 (72), 135 (57), 233 (26), 370 (18).

rel-(2R,3S)-2-[(3E)-4,8-Dimethylnona-3,7-dienyl]-2,3-dihydro-7-hydroxy-2,3-dimethyl-4H-furo[2,3-b][1]benzopyran-4'-one (6): White gum (30.26 mg, $3.02 \cdot 10^{-2\%}$ yield). $R_{\rm f}$ 0.42 (20% AcOEt/hexane). $[a]_{\rm D}^{27} = -11.9$ (c = 0.08, MeOH). UV (MeOH): 292 (3.33), 243 (3.18), 235 (3.17), 207 (3.53). IR (CHCl₃): 3200, 1707, 1610, 1150. ¹H-NMR: *Table 1.* ¹³C-NMR: *Table 2.* HR-EI-MS: 382.2141 ($C_{24}H_{30}O_{4}^{+}$; calc. 382.2144). EI-MS: 69 (100), 137 (76), 205 (62), 231 (31), 382 (11).

rel-(2R,3S)-2-[(3E)-4,8-Dimethylnona-3,7-dienyl]-2,3-dihydro-7-methoxy-2,3-dimethyl-4H-furo[3,2c][1]benzopyran-4-one (7): White gum (20.25 mg, $2.02 \cdot 10^{-2\%}$ yield). R_f 0.41 (8% AcOEt/hexane). $[\alpha]_{D}^{27} = 41.6$ (c = 0.02, MeOH). UV (MeOH): 316 (3.57), 292 (3.20), 261 (3.62), 206 (4.04). IR (CHCl₃): 2850, 1705, 1635, 1612, 1150. ¹H-NMR: *Table 1.* ¹³C-NMR: *Table 2.* HR-EI-MS: 396.2298 ($C_{25}H_{32}O_{4}^{+}$; calc. 396.2301). EI-MS: 135 (100), 69 (84), 219 (77), 245 (31).

Dshamirone (= (4E,8E)-1-(2,4-Dihydroxyphenyl)-5,9,13-trimethyltetradeca-4,8,12-trien-1-one; **8**): Yellow gum (100.25 mg, $1.00 \cdot 10^{-20}$ yield). $R_{\rm f}$ 0.32 (5% acetone/hexane). $[a]_{27}^{27} = \pm 0$ (c = 0.02, MeOH). UV (MeOH): 317 (3.94), 279 (4.18), 248 (3.89). IR (CHCl₃): 3350, 1700, 1610, 1150. ¹H-NMR: *Table 1.* ¹³C-NMR: *Table 2.* HR-EI-MS: 356.2348 ($C_{23}H_{32}O_{3}^{+}$; calc. 356.2351). EI-MS: 135 (100), 152 (20.8), 219 (11.7), 287 (7.9).

We gratefully acknowledge the financial assistance of *Macter Pharmaceutical (Pvt.) Ltd.* to *I. B.* One of us (*P. Ö.*) is thankful to the *Third World Academy of Sciences*, Italy, for the travel support.

Helvetica Chimica Acta - Vol. 84 (2001)

REFERENCES

- [1] N. Farnsworth, Pharmaceutical Sciences 1975, 64, 535.
- [2] T. Marsui, C. Yoshimoro, K. Osajima, T. Oki, Y. Osajima, Biosci. Biotech. Biochem. 1996, 60, 2019.
- [3] E. Valencia, M. Feria, J. G. Diaz, A. Gonzalez, J. Bermejo, Planta Med. 1994, 60, 395.
- [4] H. Bischoff, Eur. Journal Clin. Investigation 1994, 24, 3.
- [5] M. Miski, J. Jahupovic, Phytochemistry 1990, 29, 1995.
- [6] K. Kojima, K. Ishaka, O. Purev, O. Zevgeeiin, H. Mizukami, G. Jaragalsaikhan, Chem. Pharm. Bull. 1999, 47, 690.
- [7] K. Kojima, K. Ishaka, O. Purev, O. Zevgeeiin, H. Mizukami, Chem. Pharm. Bull. 1999, 47, 1145.
- [8] B. N. Su, Y. Takaishi, G. Honda, M. Itoh, Y. Takeda, J. Nat. Prod. 2000, 255.
- [9] K. Kojima, K. Ishaka, O. Purev, O. Zevgeeiin, H. Mizukami, Chem. Pharm. Bull. 2000, 48, 690.
- [10] M. G. Valle, G. Appendino, G. M. Nano, V. Picci, Phytochemistry 1987, 26, 253.
- [11] C. Zdero, F. Bohlmann, R. M. King, H. Robinson, Phytochemistry 1986, 25, 509.
- [12] D. Lamnaouer, B. Bodo, M. T. Martin, D. Molho, Phytochemistry 1987, 26, 1613.
- [13] G. Appendino, S. Taglipietra, P. Gariboldi, G. M. Nano, V. Picci, Phytochemistry 1987, 27, 3619.
- [14] A. Banargi, B. Mallick, A. Chatterjee, Tetrahedron Lett. 1988, 29, 1557.
- [15] G. Appendino, S. Taglipietra, G. Cravotto, G. M. Nano, Gazz. Chim. Ital. 1989, 119, 385.
- [16] K. M. Kmilov, G. K. Nikonov, Phytochemistry 1976, 7, 2157.
- [17] K. Kojima, K. Ishaka, O. Purev, G. Jaragalsaikhan, D. Suran, H. Mizukami, Y. Ogihara, *Chem. Pharm. Bull.* 1998, 46, 1781.
- [18] K. Kojima, K. Ishaka, H. Mizukami, Y. Oghara, O. Purev, Tennen Yuki Kagobutsu Toronkai Koen Yoshishu 1999, 41, 211.
- [19] N. Asano, Koseki, E. Kaneko, K. Matsui, Carbohydr. Res. 1994, 258, 255.

Received December 13, 2000