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Phytochemical Study of the Aerial Parts of *Conyza discoridis* Growing in Saudi Arabia

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Abstract – Phytochemical investigation of the aerial parts of *Conyza discoridis* (L.) Desf. resulted in the isolation of the new sesquiterpene dilactone ester vernomenin-6-(2-hydroxymethyl)-acrylate (**4**) and two known sesquiterpene dilactones vernolepin (**1**) and vernomenin (**3**). Two known flavonols, 3-*O*-methylquercetin (**2**) and transilin (3-*O*-methylquercetin 7-*O*-β-D-glucopyranoside) (**5**), were also identified. The structures were determined utilizing physical, chemical and spectral methods.
Keywords – *Conyza discoridis*, Astraceae, Sesquiterpene dilactones, Vernomenin-6-(2-hydroxymethyl)-acrylate, Flavonols

Introduction

Six members of the genus *Conyza* Less. (Asteraceae) are present in the flora of Saudi Arabia (Migahid, 1996). *Conyza incana* is used in Saudi folk medicine as sedative, tranqulizier, and analegisic for muscle and joint pain (Al-Yahya, *et al*., 1990; Ghazanfar, 1994; El-Shanawany, 1996). *C. linifolius* is commonly used as antispasmodic herb in Egypt (Mossa, *et al*., 1987). Study of the volatile components of *C. discoridis* (*Pluchea discoridis*) revealed that sesquiterpene hydrocarbons and oxygenated sesquiterpenes are the major components. The volatile fraction showed a marked mosquito larvicidal activity against *Culex pipiens* (Grace, 2002). Study of Egyptian collections of *C. discoridis* resulted in the isolation of several eudesmane derivatives such as eudesmanolides I, II, pluchecin and 2α-hydroxyeudesma-4,11(13)-dien-12,8β-olide 2-*O*-β-D-xylopyranoside. 9β-Hydroxycostunolide, 15-hydroxyisocostic acid and eudesmanoic acids were also reported (Omar *et al*., 1983; Bohlmann *et al*., 1984; Dawidar and Metwally, 1985; Abdallah *et al*., 1995; Mahmoud, 1997). Both location and time of collection have significant influence on the secondary metabolites present in the plant (Dawidar and Metwally, 1985).

In the present study, phytochemical investigation of the aerial parts of *C. discoridis* growing in Saudi Arabia was conducted aiming to identify the secondary metabolites. Three elemanolide dilactone sesquiterpenes and two flavonols were identified. Elemanolide dilactone sesquiterpenes were not previously reported from genus *Conyza*.

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Experimental

General – Melting points were determined in open capillary tubes using Thermosystem FP800 Mettler FP80 central processor supplied with FP81 MBC cell apparatus, and were uncorrected. UV absorption spectra were obtained in methanol and with different shift reagents on a Unicum Heyios α UV-Visible spectrophotometer. Optical rotations were recorded on a JASCO P-2000 Polarimeter. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX-500 (Central Lab at the College of Pharmacy, King Saud University) spectrometer operating at 500 MHz for proton and 125 MHz for carbon, respectively. The chemical shift values are reported in δ (ppm) relative to the internal standard TMS or residual solvent peak, the coupling constants (*J*) are reported in Hertz (Hz). 2D-NMR experiments (COSY, HSQC, HMBC and NOESY) were obtained using standard Bruker program. ESIMS were obtained using Liquid Chromatography/Mass Spectrometer (Quattro micro API) equipped with a Z-spray electrospray ion source (Micromass®, Quattro micro™, WATERS). HRFABMS of **4** were measured using a JEOL JMS-HX-110 instrument. Silica gel 60/230 - 400 mesh (EM Science) and RP C-18 silica gel were used for column chromatography, while silica gel 60

F254 (Merck) was used for TLC. Centrifugal preparative TLC (CPTLC; using Chromatotron (Harrison Research Inc. model 7924): 1 - 4 mm silica gel P254 disc.

Plant material – The plants of *Conyza discoridis* (L.) Desf. (Synonymous *Pluchea discoridis* (L.) DC.) were collected in 2004 from Aqubat Al-Abnaa Baljorashi, southern region of Saudi Arabia. The plant was identified by Dr. M. Atiqur Rahman, Prof. of Taxonomy, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia. A voucher specimen (#14038) was deposited at the herbarium of the Research Center for Medicinal, Aromatic and Poisonous Plants of the same College.

Extraction and Isolation – The air dried aerial parts of *C. discoridis* (1.9 kg) were exhaustedly extracted with 90% ethanol (15 L) at room temperature. The ethanol extract was evaporated under vacuum to yield 120 g of dark green residue. The residue was dissolved in acetone/$CHCl_3$ (1 : 1) to yield 45 g soluble extract and 70 g insoluble residues. Part of the residue (50 g) was chromatographed on a silica gel column (600 g, 4.0 cm). Elution started with $CHCl_3$ and polarity was increased by MeOH in a gradient elution technique. Fifty one fractions, 300 ml each were collected, screened by TLC and similar fractions were pooled. Fraction 6 (0.46 g) eluted with 10% MeOH in $CHCl_3$ was subjected to CPTLC (2 mm silica gel disc) using 3% MeOH in $CHCl_3$ to give 135 mg of **1**. Fractions 7 - 24 (320 mg) eluted with 10% MeOH in $CHCl_3$ were subjected to CPTLC (2 mm silica gel disc) using 8% MeOH in $CHCl_3$ to give 35 mg of **2**. Fractions 36 - 41 (470 mg) eluted with 15% MeOH in $CHCl_3$ were repeatedly subjected to CPTLC (2 mm silica gel disc) using 8% MeOH in $CHCl_3$ to give 63 mg of **3** and 33 mg of **4**. Fractions 45 - 50 (135 mg) eluted with 20% MeOH in $CHCl_3$ were subjected to CPTLC (2 mm silica gel disc) using 8% MeOH in EtOAc to give 12 mg of **5**.

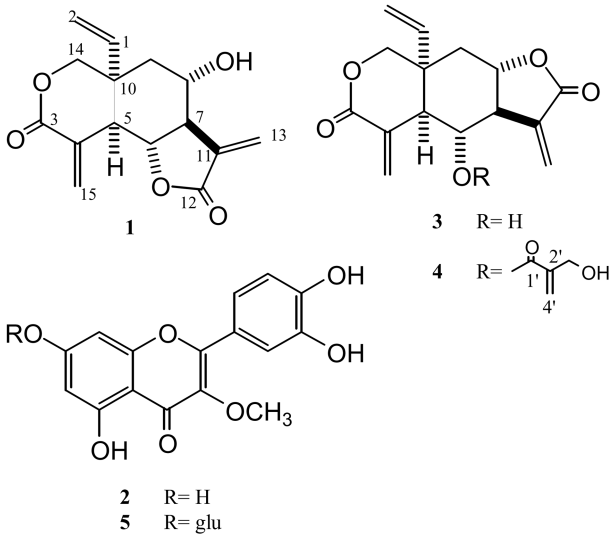
Vernolepin (1) – Colorless crystals, m.p. 163 - 164 °C (MeOH), $[\alpha]_D$ + 120.8° (c = 0.5, MeOH), ^{1}H- and ^{13}C-NMR: Table 1, ESIMS (rel. abund. %): 299 (M^++Na, 100), 277 (M^++H, 7).

3-*O*-Methylquercetin (2) – Yellow crystals, m.p. 262 -

Table 1. ^{1}H and ^{13}C NMR data (δ) of **1**, **3** and **4** in CD_3OD[a]

Pos.	1		3		4	
	^{1}H[b]	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C
1	5.82 (dd, *J* = 11, 11)	142.5	5.73 (dd, *J* = 17.5, 17.5)	142.1	5.83 (dd, *J* = 11 , 15.5)	141.9
2	5.27 (d, *J* = 8) 5.30 (d, *J* = 14.8)	116.3	5.13 (d, *J* = 17.5) 5.17 (d, *J* = 17.5)	116.1	5.32 (m)	116.9
3	–	166.1	–	166.4	–	166.4
4	–	133.0	–	133.0	–	132.8
5	3.17 (d, *J* = 11)	47.4	2.54 (d, *J* = 10)	54.5	3.27 (d, *J* = 11)	47.4
6	4.22 (t, *J* = 11)	80.0	3.82 (t, *J* = 10)	69.8	5.32 (m)	70.1
7	2.75 (m)	54.4	2.60 (m)	54.2	3.18 (m)	51.37
8	4.03 (ddd, *J* = 4.5, 4.5, 4.5)	67.2	4.05 (ddd, *J* = 4, 4, 4)	77.2	4.40 (m)	79.4
9	1.60 (dd, *J* = 10,10.5) 1.95 (dd, *J* = 4.5, 14)	44.5	1.78 (t, *J* = 13) 2.04 (dd, *J* = 4, 13)	38.0	1.74 (dd, *J* = 13, 14) 2.04 (dd, *J* = 4.5, 14)	39.9
10	–	42.4	–	42.2	–	42.4
11	–	139.3	–	139.1	–	138.3
12	–	171.5	–	171.9	–	170.7
13	6.02 (d, *J* = 3) 6.13 (d, *J* = 3)	120.9	5.90 (d, *J* = 3) 6.00 (d, *J* = 3)	120.6	5.68 (d, *J* = 2.5) 6.12 (d, *J* = 2.5)	120.8
14	4.31 (dd, *J* = 1.5, 12) 4.65 (d, *J* = 12)	72.2	4.22 (dd, *J* = 2, 12) 4.54 (d, *J* = 12)	72.2	4.40 (m) 4.76 (d, *J* = 12)	71.9
15	5.93 (d, *J* = 1) 6.64 (d, *J* = 1)	135.3	5.75 (d, *J* = 1) 6.51 (d, *J* = 1)	135.1	5.96 (bs) 6.66 (bs)	135.4
1'					–	165.9
2'					–	141.6
3'					4.29 (d, *J* = 10), 4.40(m)	61.66
4'					5.97 (bs), 6.31 (bs)	126.3

[a] Assignments based on 2D-NMR and comparison with literature.
[b] *J* values in parenthesis in Hz.



265 °C (MeOH), $UV_{\lambda max}^{MeOH}$: 256, 268 (sh), 295, 356; NaOMe: 271, 328, 404; $AlCl_3$: 275, 305 (sh), 419; $AlCl_3$/HCl: 268, 300, 364, 403; NaOAc: 274, 325, 388. ^{1}H-NMR (500 MHz, CD_3OD): δ 3.79 (3H, s, OCH_3), 6.20 (1H, d, J = 2Hz, H-8), 6.39 (1H, d, J = 2Hz, H-6), 6.91 (1H, d, J = 8 Hz, H- 6'), 7.53 (1H, dd, J = 2, 8 Hz, H-5'), 7.64 (1H, d, J = 2 Hz, H- 2'). ^{13}C- NMR (125 MHz, CD_3OD): δ 60.5 (OCH_3), 94.7 (C-8), 99.8 (C-6), 105.9 (C-10), 116.4 (C-2'), 116.5 (C-5'), 122.4 (C-6'), 123.0 (C-1'), 139.5 (C-3), 146.5 (C-3'), 149.9 (C-4'), 158.0 (C-2), 158.4 (C-9), 163.1 (C-5), 165.9 (C-7), 180.0 (C-4). ESIMS (rel. abund. %): 339 (M^++Na, 100), 317 (M^++H, 14).

Vernomenin (3) – Colorless crystals, m.p. 85 - 87 °C (MeOH), $[\alpha]_D$ + 389° (c = 0.5, MeOH), ^{1}H- and ^{13}C-NMR: Table 1, ESIMS (rel. abund. %): 315 (M^++K, 19), 299 (M^++Na, 100), 277 (M^++H, 6).

Vernomenin-6-(2-hydroxymethyl)-acrylate (4) – Colorless crystals, m.p. 79 - 80 °C (MeOH), $[\alpha]_D$ + 458° (c = 0.5, MeOH), ^{1}H- and ^{13}C- NMR: Table 1, ESIMS (rel. abund. %): 383 (M^++ Na, 100), HRESIMS (rel. abund. %): 743.2323 ($2M^+$+Na, 65), (calc. for [$C_{38}H_{40}O_{14}$+Na] 743.2315); 383.1104 (M^++Na, 35), (calc. for [$C_{19}H_{20}O_7$+Na] 383.1104); 361.1284 (M^++H, 43), (calc. for [$C_{19}H_{20}O_7$+H] 361.1284).

Transilin (3-*O*-methylquercetin 7-*O*-β-D-glucopyranoside) (5) – Yellow crystals, m.p. 221 - 223 °C (MeOH), $UV_{\lambda max}^{MeOH}$: 256, 268 (sh), 293, 354; NaOMe: 265, 400; $AlCl_3$: 275, 300 (sh), 339, 436; $AlCl_3$/HCl: 269, 298, 362, 400; NaOAc: 262, 392, ^{1}H-NMR (500 MHz, CD_3OD): δ 3.39 (6H, m, H-2"-H-6"), 3.79 (3H, S, OCH_3), 5.08 (1H, d, J = 7.5Hz, H-1"), 6.20 (1H, d, J = 2Hz, H-8), 6.39 (1H, d, J = 2Hz, H-6), 6.91 (1H, d, J = 8 Hz, H- 6'), 7.53 (1H, dd, J = 2, 8 Hz, H-5'), 7.64 (1H, d, J = 2 Hz, H- 2'), ^{13}C-NMR (125 MHz, CD_3OD): d59.7 (OCH_3), 60.5 (C-6"), 69.5 (C-4"), 73.1 (C-2"), 76.3 (C-3"), 77.1(C-5"), 94.4 (C-8), 99.1 (C-6), 99.8 (C-1"), 105.8 (C-10), 115.6 (C-2'), 115.7 (C-5'), 120.5 (C-6'), 120.6 (C-1'), 137.9 (C-3), 145.2 (C-3'), 148.9 (C-4'), 156.2 (C-2), 155.9 (C-9), 160.8 (C-5), 162.8 (C-7), 178.1 (C-4), ESIMS (rel. abund. %): 501 (M^++Na, 100).

Results and Discussion

The plants of *C. discoridis* were extracted with ethanol. The residue left after evaporation of the solvent was extracted with acetone/$CHCl_3$ (1 : 1). Purification of the resulted fraction by chromatography afforded three sesquiterpenes and two flavonoid derivatives.

Compound **1** was isolated as colorless crystals. The ESIMS of **1** indicated a molecular weight of 276 consistent with the molecular formula $C_{15}H_{16}O_5$. The 15 carbons were clear in the ^{13}C-NMR (Table 1) and were sorted by DEPT experiments into 5 x CH_2 including 2 terminal methylenes, 5 x CH and 5 quaternary carbons including 2 carbonyl groups. The data of **1** were identical with those reported for vernolepin previously isolated from *Vernonia* species. Vernolepin showed antitumor, antimicrobial and antiplatelet aggregation (Kupchan *et al*, 1968; Kupchan *et al*, 1969; Toubiana *et al*., 1975; Laekeman *et al*., 1983; Jakupovic *et al*., 1985; Laekeman *et al*., 1985; Chagonda *et al*., 1989; Jisaka *et al*., 1993; Abegaz *et al*., 1994; Magboul *et al*., 1997).

The MS and NMR data of **3** indicated that it is isomeric to **1** (experimental and Table 1). Significant differences were the chemical shifts of positions 5 - 9. ^{1}H- and ^{13}C-NMR (Table 1) explained that the difference excite in the site of cyclization of the 5-memberd lactone ring from C-6 hydroxyl group in **1** to C-8 hydroxyl in **3**. The data of **3** was consistent with those reported for vernomenin (Kupchan *et al*., 1968; Kupchan *et al*., 1969). Vernomenin is less active as antitumor agent than vernolepin and also less common in nature (Kupchan *et al*., 1968). This is the first isolation of **1** and **3** from source other than *Vernonia* species.

The HRESIMS of **4** (experimental) showed $2M^+$+Na at 743.2323 m/z, M^++Na at 383.1104 m/z and M^++H at 361.1284 m/z for the molecular formula $C_{19}H_{20}O_7$. The 19 carbons were clear in ^{13}C-NMR and were sorted by DEPT experiments into 7 x CH_2, 5 x CH and 7 fully substituted carbons. Both ^{1}H- and ^{13}C-NMR (Table 1) were closely related to those of **3**. The only significant difference was the downfield shift of H-6 from δ_H 3.82 in **3** to δ_H 5.32 in **4** indicating that the C-6 hydroxyl group is acylated. In the ^{13}C-NMR the four extra carbons (2 x CH_2

including one terminal methylene and two quaternary carbons including one carbonyl carbon) were assigned to a 2-hydroxymethyl-acrylate (Bohlmann and Zdero, 1988). The position of the 2-hydroxymethyl-acrylate at C-6 was confirmed by HMBC experiment where H-6 at δ_H 5.32 showed 3-bonds correlation with C-1' carbonyl at δ_C 165.9 and 4-bonds correlation with C-2' at δ_C 141.6. Compound **4** is isolated for the first time from natural source.

The UV data of **2** indicated a substituted flavonol with 5, 7, 3', 4' free hydroxyl groups (Harborne *et al*., 1975). ^{1}H- and ^{13}C-NMR were in complete agreement with the proposed structure. Both ^{1}H- and ^{13}C-NMR showed a methyl signal at δ_H 3.79 and δ_C 60.5 respectively that must be located at C-3. HMBC experiment supported the position of the methyl group at C-3. The data of **2** enable its identification as 3-*O*-methylquercetin. Previously isolated from *Opuntia* (Chen *et al*., 2003), *Achillea nobilis* (Krenn *et al*., 2003), *Achyroclin alata* (Bauer *et al*., 1989), *Astragalus* species (Imomnazarov *et al*., 1988), Neoporteria (Iwashina *et al*., 1984), *Inula graveolens* (Souleles *et al*., 1979) and *Artemisia cina* (Klyshev and Baltabaeva, 1978).

Comparing the UV data of **5** with **2** indicated that C-7 hydroxyl is substituted where NaOAc failed to produce any shift in band II (Harborne *et al*., 1975). The MS and NMR data of **5** were diagnostic for the presence of glucosyl substations. In an HMBC experiment the methyl group at δ_H 3.79 showed a correlation with C-3 at δ_C 137.9 while H-1" at δ_H 5.08 of glucose showed correlation with C-7 at δ_C 162.8. Acid hydrolyses of **5** produced **2** and glucose. From the above discussion **5** was identified as transilin (3-*O*-methylquercetin 7-*O*-β-D-glucopyranoside). Compound **5** was isolated from *Opuntia* (Chen *et al*., 2003), *Achyroclin alata* (Bauer *et al*., 1989), *Parodia sanguiniflora* (Iwashina *et al*., 1984), *Trifolium pratense* (Jain *et al*., 1986), *Nicotiana* species (Jurzysta *et al*., 1983), *Carthamus glaucus* (Khafagy *et al*., 1978) and *Inula viscose* (Oksuz *et al*., 1977).

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