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Constituents of *Chrysothamnus viscidiflorus*

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Abstract

A phytochemical investigation of the aerial parts of *Chrysothamnus viscidiflorus* var. *viscidiflorus* afforded three new [chrysothol (**1**), **2** and **4**] and seven known compounds, including five sesquiterpenes, two cinnamic acid derivatives, two ketoalcohol derivatives and one coumarin glucoside. The structures of two previously reported compounds, **1b** and **1c**, were revised on the basis of chemical reaction. Structures of the compounds were determined by extensive NMR studies, including DEPT, COSY, NOE, HMQC, HMBC and X-ray analysis. The unpublished X-ray data of the known compounds **6** and **7** are reported. Compounds chrysothol (**1**), and **8**–**10** showed anti-cancer activity against human breast cancer cells.

Keywords: *Chrysothamnus viscidiflorus* var. *viscidiflorus*; Asteraceae; Guaiane sesquiterepene; *p*-Coumaric acid derivatives; Sesquiterpenoid glucoside; Coumarin glucoside; Anti-cancer activity

1. Introduction

Green rabbitbrush (*Chrysothamnus viscidiflorus*, Asteraceae) is a common and widespread ecologically important shrub in the dry interior habitats of western North America. Previous chemical research on the genus has shown a long history of interest in using these plants, and in particular *C. nauseosus* (gray rabbitbrush) as an alternative source of rubber (Hall and Goodspeed, 1918; Hegerhorst et al., 1988). *C. nauseosus* has also been shown to exhibit antifeedant effects on the Colorado potato beetle (Rose et al., 1980). Previous investigations of *C. viscidiflorus* have focused on flavonoids (Urbatsch et al., 1975; Stevens et al., 1999), diterpene acids (Le-Van and Pham, 1980) a hydroxyacetophenone and chromanone derivatives (Le-Van and Pharm, 1981). In the present study, we wish to report on the isolation of three new compounds [chrysothol (**1**), **2**, **4**] and seven known compounds (**3**, **5**–**10**), reported for the first time in this species. Compounds chrysothol (**1**) and **8**–**10** were shown to have anti-cancer activity against human breast cancer cells.

2. Results and discussion

Compound **1** was isolated as a colorless oil, $[\alpha]_D^{25} + 13.0°$ ($CHCl_3$, $c = 0.2$) and the absorption band at 3500 cm^{-1} in the IR spectrum indicated the presence of a hydroxyl group. The molecular formula of **1**, $C_{15}H_{26}O_2$, was established by HRCI-MS (*m/z* 239.201105, $[M+H]^+$) and ^{13}C NMR data. The ^1H and ^{13}C NMR spectra (Tables 1 and 2) in $CDCl_3$ showed signals of a guaiane sesquiterpene skeleton. The ^1H NMR spectrum of **1** displayed a broad doublet at δ 4.01 (1H, $J = 4.0$ Hz, H-6), a multiplet at δ 2.32, for two protons (H-1 and H-5), a doublet triplet at δ 2.17

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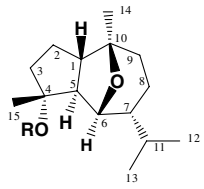

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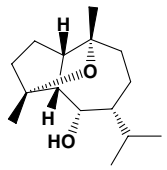

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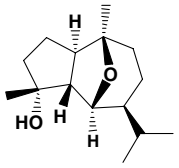

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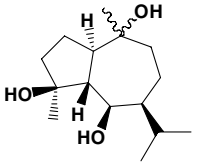
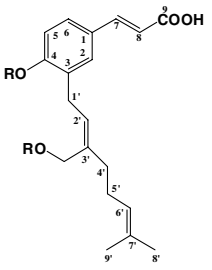


1d αOH, βMe
1e βOH, αMe



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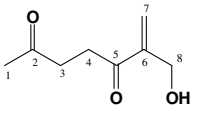

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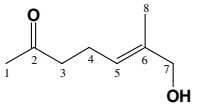

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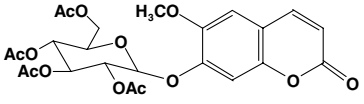

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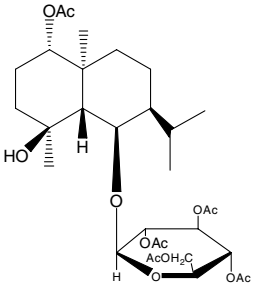

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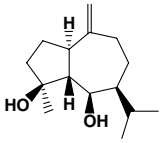

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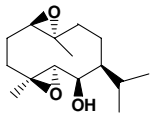

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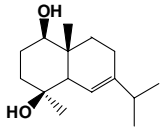

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Table 1
^{1}H NMR of **1** and **1a** (500 MHz, δ-values)

Position	**1**[a]	**1**[b]	**1a**[a,c]
1	2.32 *m*	2.25	2.35 *ddd* ($J = 14.0, 11, 5$)
2a	1.56 *m*	1.38	1.52
2b	1.54 *m*	1.38	1.54 *dt* ($J = 11.0, 9.5, 9.5$)
3a	2.17 *dt* ($J = 14.3, 9.5, 9.5$)	2.01	2.10
3b	2.80 *dd* ($J = 14.3$)	1.90	2.44
5	2.32 *m*	2.13	2.29 *dd* ($J = 14.0, 4.5$)
6	4.01 *brd* ($J = 4.0$)	3.77	4.08
7	1.39 *m*	1.61	1.53
8a	1.80 *m*	1.74	1.81
8b	1.78 *m*	1.35	1.59
9a	1.76 *m*	1.56	1.71
9b	1.74 *m*	1.35	1.39
11	1.72 *m*	1.61	1.79
12	0.97 *d* ($J = 7.0$)	0.87	0.96
13	0.97 *d* ($J = 7.0$)	0.87	0.97
14	1.19 *s*	1.05	1.17
15	1.42 *s*	1.10	1.55

[a] In $CDCl_3$.
[b] In DMSO-d_6.
[c] AcO, δ 1.98 (*s*).

Table 2
^{13}C NMR of **1**–**1$_e$** (125 MHz, δ-values)

Position	**1**[a]	**1**[b]	**1a**[a]	**1b**[c]	**1c**[a]	**1d**[a]	**1e**[a]
C-1	53.3 *s*	52.2 *s*	52.3 *s*	53.3 *s*	45.8 *s*	51.6 *s*	52.1 *s*
C-2	23.9 *t*	23.5 *t*	23.4 *t*	23.8 *t*	23.1 *t*	23.6 *t*	23.2 *t*
C-3	48.2 *d*	47.6 *d*	46.4 *d*	37.5 *d*	40.6 *d*	41.0 *d*	41.2 *d*
C-4	74.5 *s*	73.5 *s*	82.2 *s*	74.4 *s*	79.9 *s*	81.2 *s*	81.1 *s*
C-5	68.2 *d*	67.7 *d*	66.5 *d*	68.2 *d*	55.8 *d*	53.9 *d*	55.4 *d*
C-6	75.9 *d*	75.1 *d*	77.9 *d*	75.9 *d*	69.8 *d*	71.3 *d*	71.4 *d*
C-7	38.5 *d*	37.6 *d*	37.8 *d*	38.5 *d*	51.3 *d*	45.7 *d*	45.6 *d*
C-8	20.3 *d*	19.8 *d*	19.9 *d*	20.2 *d*	20.6 *d*	19.9 *d*	20.5 *d*
C-9	37.5 *d*	37.1 *d*	37.2 *d*	48.2 *d*	47.7 *d*	47.1 *d*	48.1 *d*
C-10	74.4 *s*	72.3 *s*	73.9 *s*	74.4 *s*	73.4 *s*	73.0 *s*	75.5 *s*
C-11	32.6 *s*	32.4 *d*	32.3 *d*	32.7 *s*	29.7 *s*	29.7 *s*	29.6 *s*
C-12	21.1 *q*	20.8 *q*	20.1 *q*	21.1 *q*	21.5 *q*	21.2 *q*	21.1 *q*
C-13	21.1 *q*	20.1 *q*	21.1 *q*	21.1 *q*	21.1 *q*	21.3 *q*	21.5 *q*
C-14	21.9 *q*	21.9 *q*	21.9 *q*	21.9 *q*	22.9 *q*	29.9 *q*	22.2 *q*
C-15	25.8 *q*	25.7 *q*	21.6 *q*	25.8 *q*	21.8 *q*	23.9 *q*	23.1 *q*

[a] In $CDCl_3$.
[b] In DMSO-d_6.
[c] AcO, δ 22.0 (*q*), 170.6 (*s*).