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EREMURUS PERSICUS, A NEW SOURCE OF MEDICINALLY IMPORTANT COMPOUNDS

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Abstract

Phytochemical investigation of *Eremurus persicus* collected from the Kirbi Kuch Ziarat, Pakistan led to the isolation of an antimalarial compound 2-acetyl-1-hydroxy-8-methoxy-3-methylnaphthalene, (compound 1,) and helminthosporin (Compound 2), a derivative of anticancer agents, from ethyl acetate fraction. Their structures were established by a combination of spectral methods (UV, IR, 1D and 2D NMR and MS) and comparison with literature data. In the present study, occurrence of these compounds is being reported for the first time as metabolites of *Eremurus persicus.*

Introduction

Plants, microorganisms, echinoderms and insects are capable of producing a huge variety of structurally diverse secondary metabolites. Some of these metabolites have been considered as potential source for medicines, herbicides as weed controller (Copping & Duke, 2007; Peter & Towers, 1995; Saxena & Pandey, 2001; Strange, 2007). Some of the anthraquinone derivatives isolated from natural sources exhibited significant cytotoxicity against cancer cell lines (El-Gamal *et al.*, 1996; Fujitake *et al.*, 1998; Solis *et al.*, 1995; Todorova *et al.*, 2010). Both the anthraquinones and naphtalene derivatives have been found to coexist in nature, indicating the biogenetic relationship among them (Chong *et al.*, 2000; Gill & Gimenez, 1992).

The genus *Eremurus* is known as foxtail lilies or desert candles**.** It is a genus of forty species found in the western and central Asia. Ten species of this genus are found in Baluchistan and Khyber Pakhtunkhwa provinces of Pakistan. The phytochemical investigation of different plants of the genus *Eremurus* showed the presence of anthraquinones, bianthraquinones, chrysophanols, naphthalene derivatives and polysaccharides. *Eremurus chinensis* Fedtsch has been used in Chinese folk medicine for the treatment of rheumatism and physical weakness (Berdikeev *et al.*, 1982; Chong *et al.*, 2000; Igamberdieva *et al.*, 1974, 1976; Rakhimov *et al.*, 1973; Ali & Qaiser, 2009).

The plant *Eremurus persicus* was least explored and no chemical investigation has been reported in the literature. Our chemical investigations resulted in the isolation of naphthalene and anthraquinone derivatives.

Material and Methods

Plant material: The plants, *Eremurus persicus* (Asphodelaceae*),* were collected from Kirbi Kuch Ziarat, Pakistan in April 2006 and identified by Dr. Rasool Bakhsh Tareen. A voucher specimen number (ES-RBT-M06) was deposited at the Herbarium of the Faculty of Botany, Baluchistan University, Quetta, Pakistan.

Extraction and isolation: The air dried whole plant of *Eremurus persicus* (6 kg) was extracted in methanol and evaporated under vacuum. The residue (450 g) was dissolved in water and partitioned between hexane and water. The aqueous layer was further partitioned between ethyl acetate and water. The ethyl acetate extract (78 g) was subjected to column chromatography over silica gel. The fraction obtained by ethyl acetate: hexane, 1:1, was again subjected to repeated column chromatography and flash chromatography with hexane/ ethyl acetate as eluting solvents in a gradient manner and finally 2-acetyl-1-hydroxy-8-methoxy-3-methylnaphthalene, compound 1, was isolated as pale yellow crystals and the compounds 2, (1, 5, 8-trihydroxy-3-methylanthraquinone) was isolated.

This is the first report of the occurrence of both the antimalarial compound 2-acetyl-1-hydroxy-8-methoxy-3-methylnaphthalene, (compound 1,) and the anticancer derivative 1, 5, 8- trihydroxy-3-methylanthraquinone, (compound 2), as metabolites in *Eremurus persicus.*

General experimental conditions: Column and flash chromatography were performed on silica gel 60 (230-400 μm mesh).TLC was developed on the E. Merck Silica gel aluminum plates (0.25 mm) and detected by cerium sulphate reagent followed by heating. Melting points of the isolated compounds were recorded on a YANACO apparatus. The infrared spectra were obtained on a *JASCO A*-100 spectrophotometer. Ultra- violet spectra were recorded in methanol on Shimadzu UV 254 spectrophotometer. The Proton and carbon nuclear magnetic resonance (^{1}H and ^{13}C - NMR) spectra were scanned at 500 and 125 MHz respectively on *Bruker Av* (Avance) instruments. Low resolution electron impact mass spectra were recorded on *a Finnigan* MAT *312* and *MAT 312* spectrometers, coupled with *PDP11/34* computer system. High resolution mass spectrum and FAB Positive-MS were recorded on *Jeol JMS HX 110* mass spectrometer.

Results and Discussions

The structures of the two compounds were established by a comprehensive study of the combination

of spectral data (UV, IR, 1D and 2D NMR and MS) and their comparison with literature data (Eijk & Roeymans, 1981; Chong *et al.*, 2000).

The ^{1}H-NMR (500 MHz) spectrum of 1 displayed resonances for the two methyls, Me-12 and Me-13 at δ_H 2.65 and 2.34 respectively, methoxy group, OMe-8 at δ 4.04 singlet, one phenolic proton at δ 9.77 Hz and the four aromatic protons [δ_H 7.08 (br s, H-4), 6.74 (br *d*, H-7), 7.32 (overlap, H-6) and 7.29 (overlap, H-5). The locations of the functional groups were confirmed by COSY, HMQC, and HMBC spectra and were found in agreement with the reported compound 2-acetyl-1-hydroxy-8-methoxy-3-methylnaphthalene (Eijk & Roeymans, 1981; Chong *et al.*, 2000). Its structure was also confirmed by the comparison of ^{13}C-NMR spectra given in the Table 1. Hence the compound 1, a tetrasubstituted naphthalene, was 2-acetyl-1-hydroxy-8-methoxy-3-methylnaphthalene.

Table 1. ^{13}C and ^{1}H-NMR ($CDCl_3$, 125 MHz and 500 MHz) spectral data of compounds 1 & 2 isolated from *Eremurus persicus*.

Position of carbons of 1	^{13}C (δ = ppm) of 1	^{1}H (δ = ppm) of 1	Position of carbons of 2	^{13}C (δ = ppm) of 2	^{1}H (δ = ppm) of 2
1	152.4s		1	162.8 s	
2	124.6 s		2	124.6 d	7.10, br. s
3	134.2 s		3	149.1 s	
4	119.7 d	7.08, br. s	4	120.8 d	7.69, br. s
5	121.0 d	7.29, overlap	4a	136.5s	
6	127.0 d	7.32, overlap	5	157.6 s	
7	104.0 d	6.74, br. d	6	136.7d	7.28, d, *J* =7.4Hz
8	156.5 s		7	129.6 d	7.28, d, *J* =7.4Hz
9	113.2 s		8	158.2 s	
10	136.6 s		8a	113.9 s	
11	205.4 s		9	190.6 s	
12	31.9 q	2.65, s	9a	119.4 s	
13	19.7 q	2.34, s	10	186.6 s	
8-OMe	56.2	4.04, s	10a	119.9s	
1-OH		9.77, s	11	22.3 q	2.46, s
			1-OH		13.00, s
			5-OH		12.30, s
			8-OH		12.13, s

Characterization of compound 1 , (2-acetyl-1-hydroxy-8-methoxy-3- methylnaphthalene): Pale yellow needles; mp 107-108 ^{o}C; UV ($CHCl_3$); λ_{max} 235-335 nm; IR (KBr) ν_{max} ; 3310, 2917, 2847, 1672, 1628, 1580, 1467, 1438, 1254, 1166, 1089 and 759 cm^{-1}; EIMS *m/z* 230 $[M]^+$ (47), 215 (100), 200 (49), 115 (32); HREIMS *m/z* 230.0942 (calculated for $C_{14}H_{14}O_3$ 230.0939); ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 2.34 (3H, s, H-13), 2.65 (3H, s, H-12), 4.04 (3H, s, OMe-8), 6.74 (br d, H-7), 7.08 (1H, br s, H-4),7.29 (overlap, H-5), 7.32 (overlap, H-6) and 9.77 (1H, s, OH-1); ^{13}C-NMR ($CDCl_3$, 125 MHz), see Table 1. Fig. 1.

The ^{1}H-NMR ($CDCl_3$, 500 MHz) spectrum of 2 displayed resonances for one methyl, (Me-11) at δ 2.46 (3H, *s*, H-11), three hydroxyl group at δ 13.0 (1H, s, OH-1), 12.3 (1H, s, OH-5), 12.1 (1H, s, OH-8) and the four aromatic protons displayed their signals between δ 7.1-7.7. The doublet at δ 7.28 integrated for two protons demonstrated the same chemical environment. These protons also showed coupling interaction with the carbons which resonated at δ 136.7 (C-6) and 129.6 (C-7). The other two signals at δ 7.1 appeared at (1H, s, H-2) and δ 7.69 for (1H, s, H-4).The signals of the two adjacent aromatic protons appeared at δ 7.28 (2H, s, H-6 and H-7). All the functional groups were confirmed by COSY, HMQC, and HMBC spectra and were found in agreement with the reported compound (Chong *et al.*, 2000; Eijk *et al.*, 1981). Hence the structure of 2 was finally established as 1, 5, 8- trihydroxy- 3- methyl anthraquinone or helminthosporin (Fig. 2).

Characterization of compound 2 , (1, 5, 8- trihydroxy-3- methylanthraquinone (Helminthosporin): Orange needles; mp 227-228 ^{o}C; UV ($CHCl_3$); λ_{max} 250-442 nm; IR (KBr) ν_{max} ; 3433 (OH), 1635, and 1625 cm^{-1} (quinone carbonyl), 1457, 1296, 1181, and 805 cm^{-1}; FAB Positive-MS *m/z*, 271$[M+H]^+$; HREIMS *m/z* 271.06008 (calculated for $C_{15}H_{10}O_5$);^{1}H-NMR ($CDCl_3$, 500 MHz): δ 7.10 (1H, s, H-2), 7.69 (1H, s, H-4), 7.28 (2H, m, one each, H-6, H-7), 2.46 (3 H, s, H-11), 13.0 (1H, s, OH-1), 12.3 (1H, s, OH-5), 12.1 (1H, s, OH-8); ^{13}C-NMR ($CDCl_3$, 125 MHz), see Table 1.

The compound 1 was reported by Abraham *et al.*, (2005) to have antimalarial activity, with an ED_{50} value of 15.4 µg/ml inhibition of the growth of the *Plasmodium falciparum.* The derivatives of compound 2 (helminthosporin), 1, 5, 8- trihydroxy- 3-methylanthraquinone,were found by El-Gamal *et al.*, (1996) and Solis *et al.*, (1995) to have significant cytotoxicity against cancer cell lines.

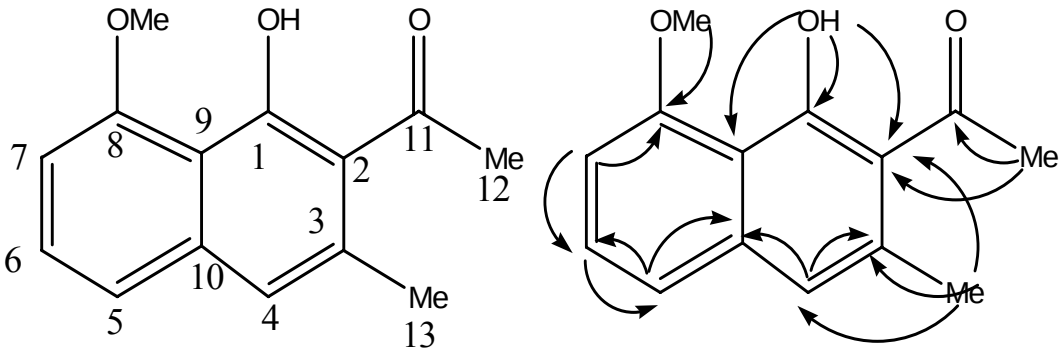

Fig. 1. Positions of carbons and key HMBC correlations of compound **1**. H→C.

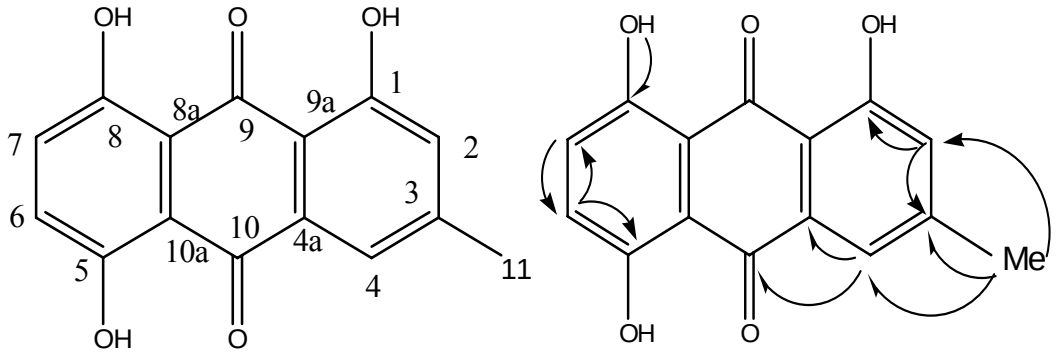

Fig. 2. Positions of carbons and key HMBC correlations of compound **2**. H→C.

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