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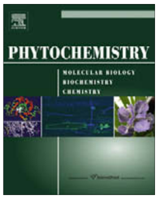

Diterpenoids from *Jatropha multifida* ☆

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ABSTRACT

Chemical investigation on the stems of *Jatropha multifida* yielded two diterpenoids, multifolone and (4*E*)-jatrogrossidentadione acetate along with five known diterpenoids, a flavone and a coumarino-lignan. The structures of the compounds were settled by detailed analysis of their 1D and 2D NMR spectra. The X-ray crystallographic analysis of (4*E*)-jatrogrossidentadione acetate was also accomplished.

1. Introduction

Jatropha multifida Linn (Euphorbiaceae), a shrub of 2–3 m in height, is naturalized in different regions of India (Chopra et al., 1965). The plant exhibits antibacterial properties (Aiylaagbe, 2001). Previously from the latex of the plant some cyclic peptides, phenolics and glucosides were isolated (Kosasi et al., 1989a,b; Van der Berg et al., 1995). However, the chemical constituents of the other parts of the plant have not yet been reported.

During our investigation (Ravindranath et al., 2003a,b, 2004; Das et al., 2005) on the constituents of various *Jatropha* species we have recently examined the stems of *J. multifida* and isolated two new diterpenoids, multifolone (**1**) and (4*E*)-jatrogrossidentadione acetate (**2**) along with the known diterpenoids, jatrophone (Kupchan et al., 1970), citlalitrione (Villarreal et al., 1988), 3β-acetoxy-12-methoxy-13-methyl-podocarpa-8,11,13-trien-7-one (Ravindranath et al., 2004), (4*E*)-jatrogrossidentadione (Schmeda-Hirschmann et al., 1992) and 15-*epi*-(4*E*)-jatrogrossidentadione (Schmeda-Hirschmann et al., 1992), a flavone, pictonarigenin (Vedantham et al., 1977) and a coumarino-lignan, cleomiscosin A (Das et al., 2003). Here we report the structure elucidation of the new compounds **1** and **2** (Fig. 1).

2. Results and discussion

Multifolone (**1**) was isolated as a white semi-solid. Its molecular formula was deduced to be $C_{20}H_{30}O_4$ from its mass spectrum (m/z: 357 $[M+Na]^+$ in ESIMS), elemental analysis and ^{13}C NMR spectrum. The IR spectrum indicated the presence of hydroxyl and carbonyl groups in the molecule. The ^1H and ^{13}C NMR spectra (Table 1) of the compound suggested it to be a lathyrane diterpenoid (Schmeda-Hirschmann et al., 1992). All the signals for the protons and carbons in the ^1H and ^{13}C NMR spectra respectively were assigned from 2D NMR (^1H–^1H COSY, HSQC, HMBC and NOESY) and DEPT experiments. A comparison of these spectral data of **1** with those of the known constituent, (4*E*)-jatrogrossidentadione (**3**) (Schmeda-Hirschmann et al., 1992) clearly suggested that the structures of both the compounds are closely related. However, the latter contains two hydroxyl (at C-6 and C-15) and two carbonyl groups (at C-3 and C-14) while **1** contains only one carbonyl and three hydroxyl groups. The carbonyl group in **1** has reasonably been placed at C-3 and the hydroxyls at C-6, C-14 and C-15 by observation of the correlations in ^1H–^1H COSY and HMBC experiments. The ^1H–^1H COSY experiment showed the sequence: H-7–H-8–H-9–H-11–H-12–H-13–H-14. The HMBC experiment indicated that H-14 (δ 3.82) was correlated with C-1 (δ 155.7), C-4 (δ 137.4) and C-20 (δ 21.3) suggesting the presence of a hydroxyl group at C-14. Thus the structure of **1** is similar to that of **3** but having a hydroxyl group at C-14 instead of a carbonyl group present at this position in the latter.

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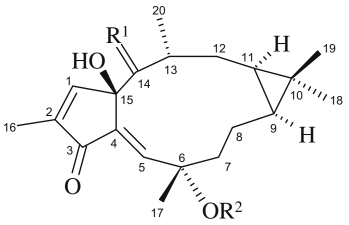

1 $R^1 = H, \beta\text{-OH}; R^2 = H$
2 $R^1 = O; R^2 = Ac$
3 $R^1 = O; R^2 = H$

Fig. 1. Structures of compounds **1**–**3**.

The relative stereochemistry of **1** was settled by NOESY correlations and was found to be similar to that of **3**. In the NOESY experiment H-9 was correlated to H-11 and Me-20 (δ 1.21) which in turn was correlated to H-14 (δ 3.82) suggesting that H-9, H-11, H-14 and Me-20 are all alpha. The protons of two hydroxyl groups (δ 5.44, brs, 2H) also showed correlations with H-13 (δ 1.64, 1H, m) but any of them did not show any correlation with Me-20. The structure and stereochemistry of multifolone (**1**) were thus clearly derived and the compound was characterized as 14-deoxy-14β-hydroxy-(4*E*)-jatrogrossidentadione.

(4*E*)-Jatrogrossidentadione acetate (**2**), the other new diterpenoid, was obtained as white crystals. Its molecular formula was deduced to be $C_{22}H_{30}O_5$ from its mass spectrum (*m*/*z*: 397 $[M+Na]^+$ in ESIMS), elemental analysis and ^{13}C NMR spectrum. The IR spectrum showed the presence of hydroxyl and carbonyl groups in the molecule. The ^{1}H and ^{13}C NMR spectra (Table 1) suggested **2** to be also a lathyrane diterpenoid (Schmeda-Hirschmann et al., 1992). These spectral data in conjunction with ^{1}H–^{1}H COSY, HSQC, HMBC, NOESY and DEPT experiments clearly indicated the structure of **2** to be closely related to that of the known constituent (4*E*)-jatrogrossidentadione (**3**) (Schmeda-Hirschmann et al., 1992) and the former is a monoacetyl derivative of the latter which possesses two hydroxyl groups at C-6 and C-15. The acetoxy group in **2** was reasonably placed at C-6 because in the ^{1}H NMR spectrum Me-17 (δ 1.75) showed a downfield shift compared to the position (δ 1.48) of the corresponding proton of **3**. In the ^{13}C NMR spectrum C-6 (δ 84.4) also shifted downfield compared to the position (δ 73.5) of the same carbon of the latter (Schmeda-Hirschmann et al., 1992).

The NOESY experiment revealed that **2** and **3** had the same relative stereochemistry. Correlations were observed from H-9 and H-11 to the acetate methyl and from Me-17 to H-13 and Me-19. The structure of **2** was thus clearly established as 6-*O*-acetyl-(4*E*)-jatrogrossidentadione. Finally the structure of **2** was confirmed by X-ray crystallographic analysis (Fig. 2).

Along with the compounds **1** and **2** seven other constituents including five diterpenoids, jatrophone, citlalitrione, 3β-acetoxy-12-methoxy podocarpa-8,11,13-trien-7-one, (4*E*)-jatrogrossidentadione and 15-*epi*-(4*E*)-jatrogrossidentadione, a flavone, pictolinarigenin and a coumarino-lignan, cleomiscosin A were also isolated. The structures of the known compounds were established by comparison of their physical and spectral properties with those reported in the literature. The occurrence of these compounds in *J. multifida* is observed here for the first time.

3. Experimental

3.1. General

Melting points were measured in a Buchi-510 instrument and are uncorrected. Optical rotations were determined with a Jasco DIP-360 digital polarimeter. Spectra were recorded with the

Table 1
NMR spectral data of compounds **1** and **2**[a]

Position	Compound **1**			Compound **2**		
	^{1}H NMR	Multiplicity (*J* in Hz)	^{13}C NMR	^{1}H NMR	Multiplicity (*J* in Hz)	^{13}C NMR
1	6.85	*s*	155.7	6.82	*s*	151.0
2	–	–	143.6	–		145.3
3	–	–	195.5	–		195.4
4	–	–	137.4	–		132.0
5	6.53	*s*	141.9	7.04	*s*	145.8
6	–	–	74.9	–		84.4
7	2.15(a)	*m*	42.9	2.26(a)	*m*	36.9
	1.82(b)	*m*		1.78(b)	*m*	
8	1.74(a)	*m*	20.5	1.63(a)	*m*	18.1
	0.96(b)	*m*		1.14(b)	*m*	
9	0.41	*br t* (9.0)	26.0	0.34	*m*	27.1
10	–	–	17.3	–		17.5
11	1.14	*m*	21.5	0.41	*m*	20.1
12	1.49(a)	*m*	24.9	1.85(a)	*m*	29.5
	1.15(b)	*m*		1.69(b)	*m*	
13	1.64	*m*	30.5	3.35	*m*	43.6
14	3.82	*m*	81.5	–		212.0
15	–	–	79.3	–		85.3
16	1.86	*s*	10.5	1.90	*s*	10.7
17	1.39	*s*	29.5	1.75	*s*	23.7
18	0.99	*s*	28.7	0.95	*s*	29.0
19	0.69	*s*	14.5	0.82	*s*	14.9
20	1.21	*d* (6.7)	21.3	1.10	*d* (7.0)	16.5
–OH	5.44(×2)	*br s*	–	4.22	*br s*	–
	5.36	*br s*	–			
–OAc	–	–	–	2.05	*s*	170.1
						22.1

(a) and (b) indicate the δ-values of two protons attached to a carbon.

[a] The spectra were run in $CDCl_3$ at 500 MHz (^{1}H NMR) and 100 MHz (^{13}C NMR).

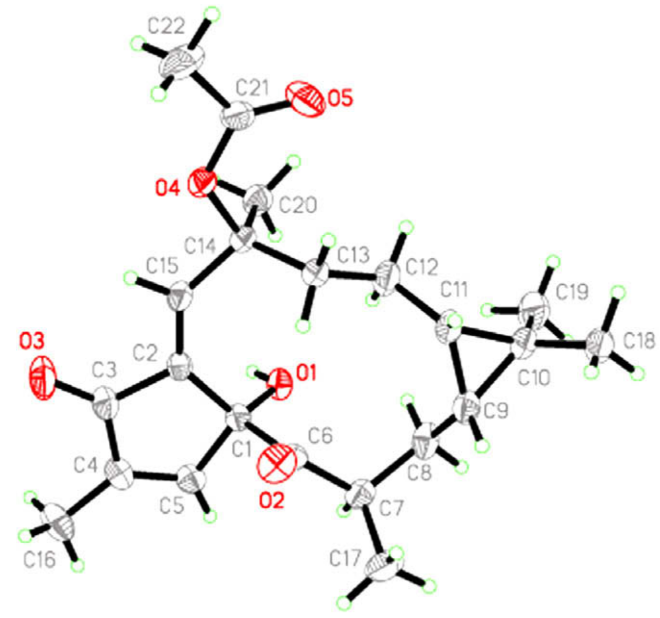

Fig. 2. Crystal structure of compound **2**.

following instruments: IR, Perkin–Elmer RX 1 FT-IR spectrometer, NMR, Varian Gemini 200 MHz, Bruker Avance 300 MHz, Inova 400 MHz and 500 MHz; EIMS: VG Micromass 7070 H (70 eV) and ESIMS: LC-MSD-Trap-SL. X-ray analysis was carried out with Bruker Smart Apex CCD difractometer with graphite monochromated Mo Kα radiation. Column chromatography was performed over silica gel (BDH 100–200 mesh) and TLC with silica gel GF 254.

3.2. Plant material

The stems of *J. multifida* were collected from Botanical Garden, Osmania University, Hyderabad, in August, 2006 and botanically identified. A voucher specimen (No. 56112) is preserved in IICT herbarium.

3.3. Extraction and isolation

The shade dried plant material (4 kg) was powdered and extracted three times (72 h in each case) with a mixture of $CHCl_3$ and MeOH (1:1, 4 L) at room temperature. The total extract was concentrated to afford a thick brown mass (102.5 g). The residue (102 g) was subjected to column chromatography and the column was eluted with solvents of increasing polarity using hexane and EtOAc. The following compounds were obtained in sequence: jatrophone (21 mg), citlalitrione (13 mg), (4*E*)-jatrogrossidentadione (18 mg) (eluted with hexane–EtOAc, 9:1); 3β-acetoxy-12-methoxy-13-methyl-podocarpa-8,11,13-trien-7-one (25 mg), 15-*epi*-(4*E*)-jatrogrossidentadione (30 mg), (4*E*)-jatrogrossidentadione acetate (17 mg), multifolone (14 mg) and pictolinarigenin (21 mg) (eluted with hexane–EtOAc, 8:2) and cleomiscosin A (16 mg) (eluted with hexane–EtOAc, 6:4).

*3.4. Multifolone (**1**)*

White semi-solid, $[\alpha]_D^{25}$–132.5 (c 0.004, $CHCl_3$); IR (KBr): υ_{max} 3425, 1703, 1653, 1455, 1375 cm^{-1}; ^1H and ^{13}C NMR: Table 1; ESIMS: *m*/*z* 357 $(M+Na)^+$, Anal Calcd. for $C_{20}H_{30}O_4$: C, 71.85; H, 8.98%. Found: C, 71.12; H, 9.05%.

*3.5. (4E)-Jatrogrossidentadione acetate (**2**)*

White crystals, m.p. 204 °C ($CHCl_3$), $[\alpha]_D^{25}$ + 273.7 (c 0.007, $CHCl_3$); IR (KBr): υ_{max} 3553, 1705, 1659, 1286 cm^{-1}; ^1H and ^{13}C NMR: Table 1; ESIMS: *m*/*z* 397 $(M+Na)^+$, Anal Calcd. for $C_{22}H_{30}O_5$: C, 70.59; H, 8.02%. Found: C, 70.84; H, 8.15%.

*3.6. X-ray crystallographic analysis of **2***

Compound **2** crystallized in chloroform. The crystal system was orthorhombic and space group was $P2_12_12_1$ with $a = 12.1456(10)$ Å, $b = 12.6177(11)$ Å, $c = 13.8605(12)$ Å, $\alpha = \beta = \gamma = 90°$, $V = 2124.1(3)$ Å^3, $\rho_{calc} = 1.171$ mg m^{-3}, $\lambda = 0.71073$ Å, (Mo Kα) = 0.082 mm^{-1}, $F_{000} = 808$, $T = 294(2)$ K. The crystal size was $0.22 \times 0.18 \times 0.12$ mm^3. Data collection yielded 15341 reflections resulting in 2131 unique, averaged reflections, 2000 with $I > 2\sigma(I)$, θ range: 2.18–25.00°. The structure was solved by direct methods using SHELXS-97 (Sheldrick, 1997) and refined by full-matrix least-squares refinement using SHELXL-97 (Sheldrick, 1997) leading to a final $R = 0.0313$, $w_R = 0.0862$ and GOF = 1.054. Intensity data were measured on Bruker Smart Apex with CCD area detector. The CCDC No. 690604 contains supplementary crystallographic data for the structure **2**.

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