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Note

Two new eudesmanolides from *Sphaeranthus indicus* (Linn)

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Two new eudesmanolides have been isolated from the aerial part of *Sphaeranthus indicus* and their structures have been established as 11α,13-dihydro-3α,7α-dihydroxyeudesm-4-en 6α, 12-olide **1**, 4-en-6β,7α-eudesmanolide **3**, on the basis of spectral data and comparison of spectral data with those of reported data of compounds **2**, **4** and **5**.

Keywords: Eudesmanolides, *Sphaeranthus indicus,* olide

IPC Code: Int Cl.^{8} A61K

Sphaeranthus indicus, is a medicinally important plant has long been used in indigenous medicine in the treatment of styptic gastric disorders, skin diseases and as antihelmintic. It is also used for the treatment of glandular swelling, bronchitis, jaundice and nervous depression[1-5]. So far from this plants fifteen 7-hydroxyeudesmanolides have been reported by different groups[6-10], Rahman Atta-Ur and co-workers[11], have reported the antimicrobial activity for compound 7-hydroxyfrullanolide and Shekhani *et al.*[12], have reported the immunostimulatory activity for compound 7-hydroxyfrullanolide glycoside, isolated from *S. indicus*. Further chemical investigation has led to the isolation of compound **1** having *trans* lactone ring in 7-hydroxyeudesmanolide for the first time in this plant extracts and a another compound **3** is very rare compound having 6β, 7α lactone ring junction in the eudesmanolide skeleton.

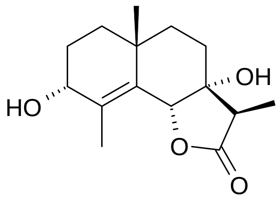
Results and Discussion

Compound 1: Crystalline solid, m.p. 123-24ºC, $[\alpha]_D^{25} = +11.6$ ($CHCl_3$, *c* 0.3), molecular formula, $C_{15}H_{22}O_4(M^+)$, *m/z* 266. It showed characteristic bands in the IR spectrum (3608, 3397, 1771, 1655 and 1215 cm^{-1}). Its ^1H NMR (**Table I**) spectrum showed the presence of an angular methyl and a methyl on olefinic bond was evident from the two-singlets at δ 1.03 and 1.94, respectively. As the ^1H NMR spectrum did not exhibit a signal assignable to olefinic proton, it was inferred that the double bond is tetra substituted. Furthermore the lactonic proton H-6 appeared as a singlet at δ 4.88, revealing the quaternary nature of C-5 and C-7. From these spectral data, it became evident that the compound was a eudesmanolide with an olefinic linkage at C-4 to C-5 and a tertiary hydroxyl group at C-7.

The ^1H NMR spectrum showed further a quartet at δ 2.76 (J = 7.5 Hz) and a doublet at δ 1.22 (J = 7.5 Hz), which was assigned to H-11 and the 13-methyl group, respectively. The broad doublet of one proton resonating at δ 4.0 (J = 2.0, $W_{1/2}$ = 10 Hz) was assigned to H-3. The position and stereochemistry of secondary hydroxyl group was confirmed by critical comparison of the ^1H NMR spectrum with those of 11α, 13-dihydro-3α, 7α-dihydroxyfrullanolide **2** (ref. 13).

The ^{13}C NMR spectrum (**Table II**) of compound **1** showed 15 carbon atoms, multiplication of carbon signals was determined by the DEPT pulse sequence. Compound **1** has three CH, four CH_2, three CH_3, and five quaternary carbon atoms. Assignment of the ^1H NMR signals at H-3 and H-11 was achieved-using homonuclear decoupling (**Figure 1**). Comparison of ^1H NMR spectral data of compound **1** with those of compound **2** showed it to be similar except for the chemical shift of H-6 which appeared as a singlet at 4.88 where as in compound **2**, the H-6 proton signal appeared as a doublet at δ 4.99 (J = 1.2 Hz). The main differences in the physical properties like melting point and specific rotation between compound **1** and **2**. Compound **1,** m.p. 123-24ºC, $[\alpha]_D^{25} = +11.6$ ($CHCl_3$, *c* 0.3), Compound **2**, mp 63.0ºC, $[\alpha]_D^{26} = -7.1$ ($CHCl_3$, *c* 0.112)[13]. Since compound **2** showed negative optical rotation $[\alpha]_D^{26} = -7.1$ ($CHCl_3$, *c* 0.112)[13] while compound **1** under discussion showed positive specific rotation $[\alpha]_D^{25} = +11.6$ ($CHCl_3$, *c* 0.3).

From the above spectral and physical data, it was clear that compound **1** was a C-15 carbons possessing three methyls, a secondary and a tertiary hydroxyl



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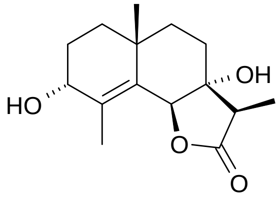

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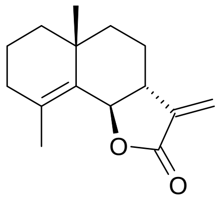

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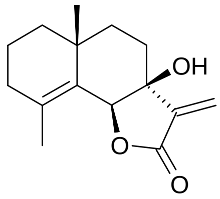

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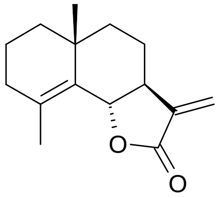

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group. Based on these data the structure of **1** was characterized as 11α 13-dihydro-3α,7α-dihydroxy-eudesm-4-en-6α,12-olide. This is the first reported isolation of a *trans* lactone ring in 7-hydroxyl eudesmanolide in the extract of *S.indicus*.

Compound **3** was obtained as a viscous oil, molecular formula $C_{15}H_{20}O_2$, *m/z* 232 (M^+). It showed characteristic bands in its IR spectrum (1753, 1640 and 1216 cm^{-1}) and signals in its ^1H NMR spectrum (**Table I**) δ 5.56 and 6.14, which revealed the presence of an α-methylene-γ-lactone. The presence of an angular methyl group and a methyl on the double bond was evident from the two-singlets at 1.05 and 1.79 respectively. As its ^1H NMR spectrum did not exhibit any signal assignable to an olefinic proton it was inferred that the double bond is tetra substituted, which was supported by the signals at δ C 145.86 and 138.80 in the ^{13}C NMR of compound **3.**

In addition, the lactonic proton (H-6) appeared as a doublet at δ 5.25 (*J* = 7.0Hz) and a one-proton multiplate at δ 2.95 revealed the presence of a proton at C-7 (**Table I**).

The ^{13}C NMR spectrum of compound **3** showed 15 carbon atoms. Multiplication of carbon signals was determined by the DEPT pulse sequence. Compound **3** has two CH, six CH_2, two CH_3 and five quaternary carbon atoms. The position and stereochemistry of H-6 and H-7 position was confirmed by critical comparison of the ^1H NMR spectrum and specific rotation of compound **3** with those of reported compound **4** (ref. 6), and **5** (ref. 14).

Based on these data the structure of **3** was characterized as 4-en-6β, 7α-eudesmanolide. This is a very rare compound, which is having α-7,11 bond, and very few molecules were reported in the literature[6].

Table I — ^1H NMR spectral data of compounds **1 - 5** ($CDCl_3$, 200 and 500 MHz)

H	Compound **1**	Compound **2**	Compound **3**	Compound **4**	Compound **5**
H-3α	4.0 d, (2.0Hz; W1/2= 10.0Hz)	3.99 d, (2.0Hz;)	----	----	----
H-6α	----	4.99 d, (1.2Hz)	5.25 d, (7.0Hz)	5.10 s	----
H-6β	4.88 s	----	----	----	4.52 d, (11.5, 1.5Hz)
H-7α	----	----	----	----	2.53 m
H-7β	----	----	2.95 m	----	----
H-11α	2.76 q, (7.5Hz)	2.75 q, (7.2Hz)	----	----	----
H-13a	1.22 d, (7.5Hz)	1.15 d, (7.2Hz)	5.56 br.s	5.84 s	5.52 d (3.0Hz)
H-13b	----	----	6.14 br.s	6.24 s	6.09 d (3.2Hz)
H-14	1.94 s	1.92 s	1.79 s	1.78 s	1.86 br.s
H-15	1.03 s	1.00 s	1.05 s	1.08 s	1.11s

Experimental Section

IR spectra in $CHCl_3$ were recorded on a Research Series 847-FTIR and ^1H and ^{13}C NMR spectra on 500 MHz and 200 MHz in $CDCl_3$ with TMS as an internal standard. Optical rotations were performed on a JASCO-DIP-181 digital polarimeter; and mass spectrum was recorded on a Finningan Mat-1020, automated GC-MS. A voucher specimen is deposited in our laboratory.

Table II — ^{13}C NMR spectral data of compounds **1, 2** and **3** ($CDCl_3$, 50 and 125.75 MHz)

C	Compound **1**	Compound **2**	Compound **3**
C-1	34.8 t	38.8 t	39.61 t
C-2	25.0 t	24.9 t	25.57 t
C-3	69.6 d	69.8 d	38.30 t
C-4	139.7 s	139.0 s	142.86 s
C-5	131.3 s	131.3 s	138.80 s
C-6	79.9 d	80.1 d	76.30 d
C-7	77.2 s	77.3 s	41.69 d
C-8	27.4 t	35.7 t	33.57 t
C-9	33.9 t	33.8 t	18.65 t
C-10	33.8 s	34.8 s	33.14 s
C-11	47.8 d	47.7 d	129.13 s
C-12	176.3 s	176.6 s	171.24 s
C-13	7.1 q	7.8 q	120.37 t
C-14	24.0 q	24.2 q	26.28 q
C-15	17.7 q	18.0 q	19.75 q

The whole plant, collected near Mulshi, Maharashtra, India during Jan. 2001 was shade dried and powdered. The powder (850 g) was extracted with Me_2CO to give an extract (27.1 g), a portion (20 g) of which was fractionated over silica gel (200 g, 60-120 mesh) using mixture of Me_2CO-petrol with increasing proportions of Me_2CO as the elution gradient to provide seven broad fractions: A (3.2 g); B (2.8 g); C (2.5 g); D (4.2 g); E (1.78 g); F (1.98 g) and G (2.18 g).

Isolation of Compound 1

Fraction F (1.90 g) on repeated column chromatography yielded compound **1** as a crystalline solid (22 mg), m.p. 123-24ºC, $[\alpha]_D^{25}$ = +11.6 ($CHCl_3$, *c* 0.3), IR spectrum (3608, 3397, 1771, 1655 and 1215 cm^{-1}), ^{1}H NMR (500 MHz, $CDCl_3$): See **Table I**; ^{13}C NMR (125 MHz, $CDCl_3$): See **Table II**; EIMS: *m/z* (rel.int.): 266 (M$^+$ 22%), 248 (23), 233 (11), 215 (23), 205 (10), 187 (26), 164(52), 147 (54), 135 (30), 123 (70), 105 (47), 91 (62), and 55(92),

Compound 3: Fraction B (1.5 g) after repeated column chromatography followed by preparative TLC gave compound **3** as a viscous liquid (12 mg), $[\alpha]_D^{26}$ =-24.32 ($CHCl_3$, *c* 0.7), IR spectrum: 1753, 1640 and 1216 cm^{-1}, ^{1}H NMR (200 MHz, $CDCl_3$): See **Table I**; ^{13}C NMR (50 MHz, $CDCl_3$): See **Table II**; EIMS: *m/z* (rel.int.): 232 (M$^+$ 16%), 217 (100), 204 (5), 189 (6), 171(22), 161 (23), 145 (18), 119 (7), 105 (32), 91 (36), 79 (42), 67 (22) and 59(27),

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