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Sedative and antinociceptive activities of two new sesquiterpenes isolated from *Ricinus communis*

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[ABSTRACT] Two new sesquiterpenes, trivially named ricinusoids A (**1**) and ricinusoids B (**2**), were isolated from ethyl acetate fraction of *Ricinus communis*. The structures of new compounds were elucidated by detailed spectroscopic techniques, including 1D- and 2D-NMR, UV, IR spectroscopy, and mass spectrometry. The compounds (**1**–**2**) were also assessed for *in-vivo* sedative and analgesic like effects in open field and acetic acid induced writhing tests respectively at 5, 10, and 20 $mg \cdot kg^{-1}$ i.p. Pretreatment of both test compounds caused significant ($P \leq 0.05$) reduction in locomotive activity like sedative agents and abdominal constrictions like analgesics. Both compounds (**1**–**2**) possessed marked sedative and antinociceptive effects in animal models.

[KEY WORDS] *Ricinus communis*; Sesquiterpenoids; Euphorbiaceae; Spectroscopic techniques; Antinociceptive activity

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Introduction

Ricinus communis, known as castor bean, is a tropical plant of family Euphorbiaceae distributed throughout the world. It grows as annual herb in temperate regions and is also cultivated for ornamental purposes [1-2]. *R. communis* is reported to have anticancer, antidiabetic, and antiprotozoal activities [3]. Similarly, leaf, root and seed oil of *R. communis* have been used by local practitioners for cure of inflammation, hypoglycemic, and liver disorders [3-4]. The ethanolic extract of *R. communis* is reported to have antidiabetic and antiasthmatic activities and is also effective to prevent infections when used in combination with immunosuppressant drugs [5-6]. *R. communis* has been used as insecticidal agent against termites to prevent damage of wood [7]. *R. communis* also possesses antioxidant, anti-inflammatory, free radical scavenging, antifertility, and antitumor activities [8-11].

Various chemical constituents isolated from leaves of *Ricinus communis* are kaemferol-3-*O*-*β*-drutinoside, kaemferol-3-*O*-*β*-d-xylo pyranoid, tannins, gallic acid, and quercetin [12-13]. Phytochemicals like Ricin A, Ricin B, ricinus agglutinin, and indole-3-acetic acid have been isolated from seeds of *Ricinus communis,* while ricinine and diterpenoid hydrocarbons are reported from fruits and seedlings of castor bean [14-18].

The isolated new sesquiterpenoids provisionally called ricinusoids A (**1**) and ricinusoids B (**2**) have been isolated first ever time from genus *Ricinus*. Keeping in view the medicinal importance of *Ricinus communis,* two new sesquiterpenes ricinusoids A (**1**) and ricinusoids B (**2**) were isolated from *Ricinus communis* and investigated for *in vivo* sedative and analgesic activities.

Results

The ethyl acetate fraction of *Ricinus communis* was subjected to column chromatography, which resulted the isolation of two new sesquiterpenoids (**1**–**2**) and structure elucidation were carried out by different spectroscopic techniques, with

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comparison of literature as well.

Compound **1** was isolated as gummy solid and assigned a molecular formula ($C_{16}H_{20}O_3$) on the basis of highest peak at *m/z* 260 $[M]^+$ in HR-EI-MS. The IR spectrum showed absorption bands at 2 960, 1 680, 1 402, and 906 cm^{-1}, indicating the presence of alkenyl group, carbonyl group, and ether moiety, while UV spectrum showed bands at λ_{max} 230 and 290 nm.

The ^1H NMR spectrum (Table 1) of compound **1** revealed the presence of three methyl groups at δ_H 1.40 (3H, s), 1.62 (3H, s), and 1.80 (3H, s) and a methoxy group appeared at δ_H 3.56 (3H, s), while two olefinic protons centered at δ_H 4.92 (2H, s). Similarly, ^1H NMR also revealed the presence of two methylene groups at δ_H 2.14 (2H, s), 2.52 (1H, m), and 2.87 (1H, m) and two methine groups at 6.50 (1H, s) and 2.20 (1H, dd, J = 11.6, 6.1 Hz). The ^{13}C NMR DEPT experiment suggested the presence of sixteen carbon atoms comprising of three methyl groups, one methoxy group, three methylenes, two methines, and seven quaternary carbons (Table 1). The ^{13}C NMR spectrum showed quaternary carbons at δ_C 138.4, 120.3, 40.1, 167.1, and 142.7, while two carbonyl carbons at δ_C 199.6 and 185.4. Three methyl groups centered at δ_C 14.7, 24.4, and 23.1 and a signal for methoxy group at 57.4 were displayed in ^{13}C NMR spectrum (Fig. 1).

The accurate placement of substituent in compound **1** was supported by HMBC (Heteronuclear multiple bond correlation) and COSY (Correlation spectroscopy) experiments. The COSY spectrum showed strong correlations between H-8/H-8a. In HMBC spectrum H-2 (δ_H 6.50) with C-1 (δ_C 199.6) and C-3 (δ_C 167.1), C-9 (δ_C 142.7), C-4 (δ_C 36.9), and C-8a (δ_C 44.7), while H-8 (δ_H 2.52 & 2.87) showed correlation with C-8a (δ_C 44.7) and C-7 (δ_C 185.4), C-6 (δ_C 138.4) and C-1 (δ_C 199.6). Similarly CH_3-12 showed HMBC cross peaks with C-4a (δ_C 40.1), C-4 (δ_C 36.9) and C-5 (δ_C 120.3). Finally, correlations of CH_3-11 with C-9 (δ_C 142.7), C-3 (δ_C 167.1) and C-10 (δ_C 114.7) confirmed the position of alkenyl moiety. In the same way, the placement of side chain alkenyl moiety was further supported by the HMBC correlations of CH_2 (δ_H 4.92) with that of C-9 (δ_C 142.7), C-11 (δ_C 23.1), and C-3 (δ_C 167.1). OCH_3 was positioned at C-6 (δ_C 138.4) as depicted in Fig. 2. Compound **1** had two steriogenic centers and the relative stereochemistry was suggested by Nuclear over Hauser Effect (NOE) experiment. The observed NOE interactions were that of CH_3-12 to H-8a, and hence these groups were disposed *cis* to each other as shown in Fig. 3. On the basis of all these facts and comparison with literature [18] the structure of ricinusoid A was established as **1**.

Ricinusoid B (**2**) was isolated as yellow gummy solid from ethyl acetate fraction of *Ricinus communis*. Compound **2** was quite similar to compound **1**, except for few additional signals in NMR. This was also evident from TLC as there was a slight difference in R_f values. Compound **2** was slightly polar. The molecular formula of compound **2** was suggested to be $C_{17}H_{20}O_4$ by HR-EI-MS at *m/z* 288 $[M]^+$ (calculated for $C_{17}H_{20}O_4$. Mass was quite informative in the structure determination of compound **2**, because there was an extra fragment of *m/z* 28 to compound **1**. The UV spectrum showed bands at λ_{max} 218 and 284 nm while IR spectrum showed the presence of alkenyl group, ester moiety and carbonyl group from the absorption bands at 2 940, 1 685, 1 412, 898 cm^{-1} respectively.

Table 1 ^1H NMR and ^{13}C NMR (500 MHz) of compounds 1 and 2 in $CDCl_3$ (*J* in Hz)

Carbon No.	Compound **1**		Compound **2**	
	δ_H	δ_C	δ_H	δ_C
1	–	199.6	–	197.6
2	6.50 (1H, s)	141.7	6.60 (1H, s)	140.1
3	–	167.1	–	162.6
4	2.14 (2H, s)	36.9	2.20 (2H, s)	35.1
4a	–	40.1	–	39.1
5	–	120.3	–	130.6
6	–	138.4	–	146.8
7	–	185.4	–	187.6
8	2.52 (1H, m) 2.87 (1H, m)	38.7	2.60 (1H, m) 3.01 (1H, m)	41.2
8a	2.20 (1H, dd, *J* = 11.6, 6.1)	44.7	2.30 (1H, dd, *J* = 12.7, 5.6)	45.2
9	–	142.7	–	144.1
10	4.92 (2H, s)	114.7	4.86 (2H, s)	112.1
11	1.80 (3H, s)	23.1	2.01 (3H, s)	21.6
12	1.40 (3H, s)	24.4	1.46 (3H, s)	26.1
13	1.62 (3H, s)	14.7	1.70 (3H, s)	16.1
14	3.56 (3H, s)	57.4	–	172.6
15	–	–	2.22 (3H, s)	24.6