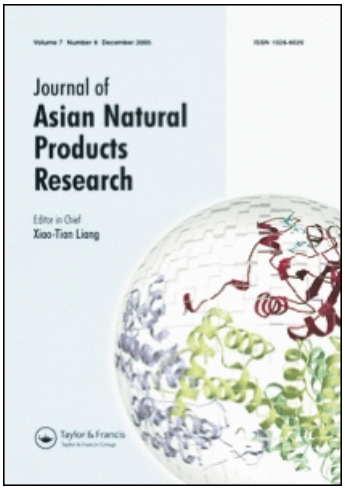

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One new triterpene ester from *Nepeta suavis*

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One new tetracyclic triterpene ester (**1**) has been isolated from the chloroform-soluble portion of the whole plant of *Nepeta suavis* along with two known compounds, namely artemetin (**2**) and jaceidin (**3**). The structures of the isolated compounds were assigned on the basis of their ^{1}H and ^{13}C NMR spectra including two-dimensional NMR techniques such as COSY, HMQC, and HMBC experiments and comparison with the literature data.

Keywords: Labiatae; *Nepeta suavis*; triterpene ester

1. Introduction

Nepeta is a multiregional genus of the family Lamiaceae (Labiatae), comprising about 250 species distributed mainly in Southwest and Central Asia, Europe, North Africa, and North America [1,2]. Several species of the genus *Nepeta* are rich in interesting biological activities and, for this reason only, many members of *Nepeta* have been investigated for bioactive constituents [3]. Among the various medicinal properties, *Nepeta* species are famous for treating cardiovascular complaints, such as angina pectoris, cardiac thrombosis, tachycardia, and weakness of the heart [4]. Several Iranian *Nepeta* species have been of great interest for use in Iranian folk and traditional medicines, and are used in the treatment of various diseases [5] including *Nepeta hindostana* for sore throat [6] and its decoction for fever and pain, such as ear and toothaches [7]. *Nepeta glomerulosa* is used to treat digestive disorders, pneumonia, and itching [8]. Most *Nepeta* plants are rich in essential oils and, among their constituents, triterpenes are the most common [9–12].

These medicinal properties prompted us to carry out phytochemical investigation on *Nepeta suavis*. Our current study has led to the isolation of one new triterpene ester (**1**), together with known compounds artemetin (**2**) and jaceidin (**3**), which have been isolated for the first time from the title species (Figure 1).

2. Results and discussion

Compound **1** was isolated as a colorless powder from the chloroform-soluble part of the aqueous methanolic extract of *N. suavis*. The HR-EI-MS of **1** showed a

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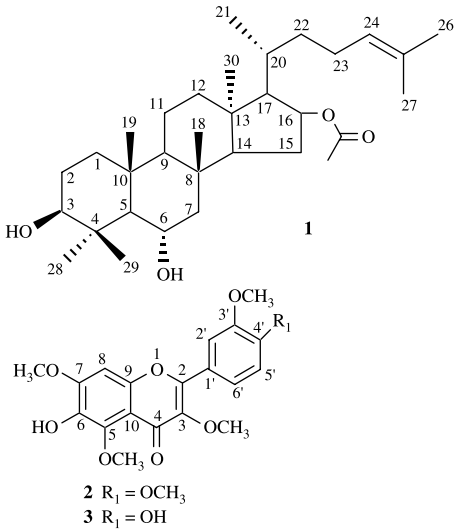

Figure 1. Structures of compounds **1**–**3**.

molecular ion peak $[M]^+$ at *m/z* 502.4022 in agreement with the molecular formula $C_{32}H_{54}O_4$ indicating five degrees of unsaturation, while its IR spectrum showed absorption peaks at 3422 (OH) and 1624 (C=C) cm^{-1}.

The ^1H NMR spectrum (Table 1) exhibited nine methyl signals at δ 0.92 (3H, s, H-19), 0.92 (3H, s, H-29), 1.01 (3H, s, H-18), 1.13 (3H, d, $J = 6.5$ Hz, H-21), 1.29 (3H, s, H-28), 1.14 (3H, s, H-30), 1.73 (3H, s, H-26), 1.63 (3H, s, H-32), and 1.73 (3H, s, H-27), an olefinic proton at δ 5.26 (1H, t, $J = 7.0$ Hz, H-24) and three oxygenated methines at δ 3.13 (1H, dd, $J = 4.9$, 11.9 Hz, H-3), 4.03 (1H, ddd, $J = 3.2$, 10.4, 13.7 Hz, H-6), and 4.24 (1H, m, H-16), suggesting that the molecule is a tetracyclic triterpenoid.

The ^{13}C NMR spectrum (Table 1) showed 32 signals and identified as nine methyls, eight methylenes, nine methines, and six quaternary carbons on the basis of the DEPT experiment. The detailed analysis of the ^1H–^1H COSY, HMQC, and HMBC experiments allowed us to determine the structure. The olefinic proton (1H, H-24) was correlated with the carbon at δ 129.3 (C-24) in the HMQC spectrum and showed long-range correlations with the vinylic methyl carbon at δ 21.6 (C-26) and another methyl carbon at δ 20.3 (C-27) in the HMBC spectrum, as shown in Figure 2.

This showed that both methyls are attached to the olefinic carbon and are located at the terminal of the side chain. Further, more interactions were also observed in the NOESY experiment

Table 1. ^1H and ^{13}C NMR spectral data of compound **1**.

Position	δ_C	δ_H
1	40.1	–
2	27.8	–
3	79.6	3.13 (1H, dd, $J = 4.9$, 11.9 Hz, H-3)
4	40.5	–
5	62.8	–
6	68.9	4.03 (1H, ddd, $J = 3.2$, 10.4, 13.7 Hz, H-6)
7	47.8	–
8	42.4	–
9	50.8	–
10	40.3	–
11	22.4	–
12	27.7	–
13	50.0	–
14	42.9	–
15	42.3	–
16	74.8	4.24 (1H, m, H-16)
17	59.7	1.32 (1H, dd, $J = 7.5$, 11.3 Hz, H-17)
18	17.8	1.01 (3H, s, H-18)
19	17.6	0.92 (3H, s, H-19)
20	37.2	0.98 (1H, m, H-20)
21	25.3	1.13 (3H, d, $J = 6.5$ Hz, H-21)
22	43.0	–
23	22.9	–
24	129.3	5.26 (1H, t, $J = 7$ Hz, H-24)
25	135.5	–
26	21.6	1.73 (3H, s, H-26)
27	20.3	1.73 (3H, s, H-27)
28	31.4	1.29 (3H, s, H-28)
29	16.1	0.92 (3H, s, H-29)
30	18.1	1.14 (3H, s, H-30)
31	180.1	–
32	22.3	1.63 (3H, s, H-32)

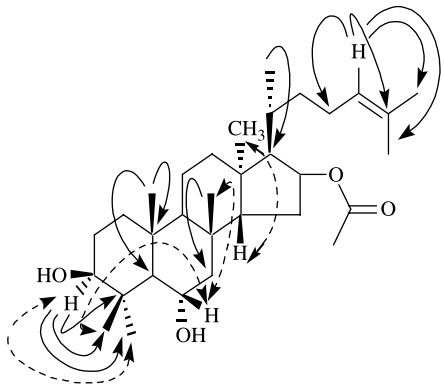

Figure 2. Significant correlation observed in the HMBC (➔) and NOESY (⟷) spectra of **1**.

between the vinylic proton at C-24 and the terminal methyl protons at C-26 of compound **1**.

The chemical shift at δ 79.6 (CH) was due to the hydroxyl group present at C-3 of compound **1**. The β-orientation of the hydroxyl group was inferred from the chemical shift and coupling pattern of the C-3 proton. The downfield signal at δ 68.9 (CH) was assigned to C-6 bearing an α-hydroxyl group [13]. The latter also caused a downfield shift of the C-28 methyl group (δ 31.4). On the other hand, the signal at δ 74.8 was due to C-16 bearing an ester group, and the corresponding H-16 was absorbed at δ 4.24, which is in agreement with the reported compound having the hydroxyl group at C-16 [14]. This assignment was based on the multiplicity of the signals at H-15 and H-17, as well as the pronounced downfield shift of the C-17 signal at δ 59.7 as compared to the usual shifts of C-17 in the compound, which do not have the ester group [15,16].

The complete stereochemistry was established by NOESY. The cross-peaks observed between H_3-29/H-6, H_3-18/H-6, and between H_3-18/H-16 confirm the α-position of the hydroxyl group at C-6 and the ester group at C-16 (Figure 2). From these observations and from the comparison of spectral data with those reported in the literature, compound **1** was determined to be a lanostane-type triterpene ester [16]. Artemetin and jaceidin were also isolated from the chloroform fraction of the crude extract and identified by comparison with the literature data [17,18].

3. Experimental

3.1 General experimental procedures

Optical rotation $[\alpha]_D$ was determined using a Jasco-DIP-360 digital polarimeter. UV and IR spectra were recorded on Hitachi-UV-3200 and Jasco-320-A spectrophotometers, respectively. The ^1H and ^{13}C NMR, COSY, HMQC, and HMBC spectra were recorded on Bruker spectrometers operating at 400 and 100 MHz, respectively, in CD_3OD using TMS as the internal standard. The chemical shift values are reported in ppm (δ) units and the coupling constants (J) are in Hz. EI- and CI-MS were recorded using JMS-HX-110 with a data acquisition system and on JMS-DA 500 mass spectrometers. The sample was subjected to column chromatography using silica gel (E. Merck, Darmstadt, Germany) having a 70–230 mesh size, followed by flash column chromatography using silica gel having a 230–400 mesh size. Thin layer chromatography was performed using pre-coated silica gel G-25-UV_{254} plates while its detection was observed at 254 nm, and by the ceric sulfate reagent followed by heating.

3.2 Plant material

The whole parts of *N. suavis* (Labiatae) were collected in July 2006, at the Parachinar Kurram Agency NWFP, and were identified by Botanist Mr Siraj Ahmad at the Department of Botany Post Graduate College, Jehanzeb Swat. A voucher specimen (No. GPGC. 507) has been deposited at the herbarium of the department.

3.3 Extraction and isolation

The air-dried, ground whole parts of *N. suavis* (4.0 kg) were initially extracted with (4.0 liters) MeOH at room temperature three times. The solvent was evaporated under reduced pressure to give a dark residue (120.0 g), which was partitioned between hexane (30.0 g), chloroform (60.0 g), and butanol (20.0 g) and water (10.0 g). The chloroform extract was subjected to silica gel chromatography using hexane with a gradient on chloroform up to 100% and followed by methanol. Twelve fractions were collected. Fraction 4 (5.6 g) of the first column was loaded on silica gel and eluted with ethyl acetate–hexane (7:3) to give compound **1** (11 mg). Fraction 6 (6.3 g) of the first column was also subjected to column chromatography and eluted with ethyl acetate–hexane (6:4) to give compound **2** (23 mg). Fraction 9 of the first column, which contained compound **3**, was loaded on a silica gel column using hexane–ethyl acetate (50:50) to purify compound **3** (38.0 mg).

3.3.1 Triterpene ester (*1*)

Colorless powder (11 mg), $[\alpha]_D^{25} + 23.73$ ($c = 0.163$ MeOH). UV (MeOH) λ_{max} ($\log \varepsilon$): 254 nm; IR (KBr, $CHCl_3$) ν_{max} (cm^{-1}): 3422, 1725, 1624; ^1H and ^{13}C NMR spectral data, see Table 1; EI-MS *m/z* (rel. int.): 502 [M^+], 55 (35), 59 (38), 111(42), 248 (100). HR-EI-MS *m/z*: 502.4017 $[M]^+$ (calcd for $C_{32}H_{54}O_4$, 502.4022).

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