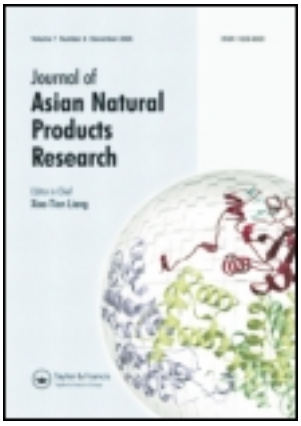

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Paniculacin, a new coumarin derivative from *Murraya paniculata*

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Paniculacin, a new coumarin derivative from *Murraya paniculata*

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Paniculacin (**1**), a new coumarin derivative, has been isolated from the ethyl acetate soluble fraction of the ethanolic extract of *Murraya paniculata* along with umbelliferone, scopoletin, 4-hydroxybenzoic acid, *trans*-cinnamic acid, and β-sitosterol. Their structures were elucidated on the basis of spectral data.

Keywords: *Murraya paniculata*; Rutaceae; coumarin; paniculacin

1. Introduction

The genus *Murraya* (Rutaceae) comprises 12 species that are distributed in tropical and subtropical regions of Southeast Asia, Mediterranean countries, N. America, Australia, and S. Africa. In Pakistan, this genus is represented by two species, one of which is *Murraya paniculata*. It is an evergreen shrub growing commonly in Sindh and Punjab provinces of Pakistan [1]. It is used by the local people to treat different ailments including diarrhea, chronic dysentery, gastralgia, toothache, skin irritation, swelling, bruises, and as a stimulant for menstrual flow [2]. Previously, alkaloids [3,4], coumarins [5,6], and flavones [7,8] were reported from this species. The chemotaxonomic and ethnopharmacological importance of the genus *Murraya* prompted us to carry out further phytochemical studies on *M. paniculata*. As a result, a new coumarin derivative named as paniculacin (**1**), along with umbelliferone (**2**), scopoletin (**3**), 4-hydroxybenzoic acid (**4**), *trans*-cinnamic acid (**5**), and β-sitosterol (**6**), was isolated from the title plant, and compounds **5** and **6** were reported for the first time from this species. Herein, we report on their isolation and the structure elucidation of compound **1**.

2. Results and discussion

The ethanolic extract of *M. paniculata* was suspended in water and successively partitioned with *n*-hexane, ethyl acetate, and *n*-butanol. The column chromatographic techniques applied to the ethyl acetate soluble fraction resulted in the isolation of paniculacin (**1**) along with known compounds **2**–**6**, respectively (Figure 1).

Paniculacin (**1**) was obtained as a colorless oil with $[\alpha]_D^{25}$ −60.5. The IR spectrum showed the presence of hydroxyl group (3419 cm^{-1}), carbonyl (1767 and 1730 cm^{-1}), olefinic bond (1607 cm^{-1}), and an aromatic moiety (1605–1400 cm^{-1}). The UV spectrum exhibited the absorption maxima at 322, 258, and 240 nm, which are characteristics of coumarins. No bathochromic shift was observed on the addition of NaOH or $AlCl_3$ showing the absence of phenolic group at C-7 [9]. The negative mode

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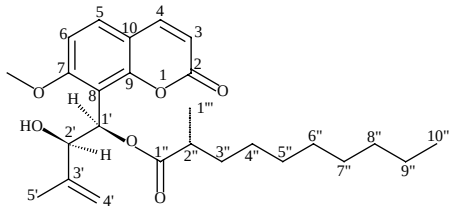

Figure 1. Structure of paniculacin (**1**).

HR-FAB-MS gave the pseudomolecular $[M - H]^-$ peak at *m/z* 443.2425, which is consistent with the molecular formula $C_{26}H_{35}O_6$. It was further confirmed by broad band and DEPT ^{13}C NMR spectra, which showed 26 well-resolved signals comprising four methyl, eight methylene, seven methine, and seven quaternary carbons. The signals at δ 162.8, 113.3, and 146.2 were characteristics of a coumarin nucleus. It further showed an ester carbonyl at δ 175.1 and oxygenated aromatic carbon at δ 162.2. The olefinic carbons were observed at δ 113.7 and 146.3, whereas the oxymethine carbons resonated at δ 79.1 and 69.9. It also showed signals of 2-methyldecanoyloxy moiety as illustrated in Table 1.

The ^1H NMR spectrum of **1** showed characteristic conjugated olefinic protons of the coumarin nucleus at δ 7.86 and 6.34 (1H each, d, $J = 9.6$ Hz). The presence of *ortho*-coupled protons at δ 7.53 and 7.03 (1H each, d, $J = 8.8$ Hz) suggested the presence of substituents at C-7 and C-8 [9]. The methoxyl protons were shown as a singlet at δ 3.94. The spectrum further showed a doublet for the oxymethine proton at δ 5.33 (1H, d, $J = 8.8$ Hz), which showed the COSY correlation with another oxymethine proton at δ 4.83 (1H, d, $J = 8.8$ Hz). The signals for disubstituted olefinic protons were observed as broad singlets at δ 4.63 and 4.53, while the methyl group attached to the olefinic carbon resonated as a singlet at δ 1.63. The signals of a 2-methyldecanoyloxy moiety are shown in Table 1.

The ^1H–^1H COSY, HMQC, and HMBC spectra were used to assign various functionalities. The methoxyl protons at δ 3.94 showed ^3J correlation with C-7 (δ 162.2), while the oxymethine proton at δ 5.33 showed ^2J correlations with C-8 (δ 117.9) and C-2′ (δ 79.1) as well as ^3J correlations with C-3′ (δ 146.3), C-7 (δ 162.2), C-9 (δ 154.2), and C-1″ (δ 175.1), allowing us to assign it to C-1′. Its downfield shift was due to the presence of 2-methyldecanoyloxy moiety confirmed by the methine proton at C-2″ showing ^2J correlations with C-1″ (δ 175.1) and C-1‴ (δ 11.4). The other oxymethine proton at δ 4.83 showed ^2J correlations with C-1′ (δ 69.9) and C-3′ (δ 146.3) as well as ^3J correlations with C-4′ (δ 113.7), C-5′ (δ 17.5), and C-8 (δ 117.9) allowing us to assign it to C-2′ (Figure 2).

The relative stereochemistry at C-1′ and C-2′ was assigned *threo* based on split

Table 1. ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectral data of compound **1** ($CDCl_3$).

Position	δ_C	δ_H (mult., *J*, Hz)
2	162.8	–
3	113.3	6.34 (1H, d, $J = 9.6$ Hz)
4	146.2	7.86 (1H, d, $J = 9.6$ Hz)
5	130.3	7.53 (1H, d, $J = 8.8$ Hz)
6	109.6	7.03 (1H, d, $J = 8.8$ Hz)
7	162.2	–
8	117.9	–
9	154.2	–
10	114.9	–
1′	69.9	5.33 (1H, d, $J = 8.8$ Hz)
2′	79.1	4.83 (1H, d, $J = 8.8$ Hz)
3′	146.3	–
4′	113.7	4.63 (1H, br s)
		4.53 (1H, br s)
5′	17.5	1.63 (3H, s)
1″	175.1	–
2″	40.2	2.31 (1H, m)
3″	30.1	1.28 (2H, br s)
4″	25.0	1.28 (2H, br s)
5″	30.7	1.28 (2H, br s)
6″	30.5	1.28 (2H, br s)
7″	30.6	1.28 (2H, br s)
8″	31.6	1.28 (2H, br s)
9″	24.1	1.28 (2H, br s)
10″	14.4	0.87 (3H, t, $J = 7.2$ Hz)
1‴	11.4	0.94 (3H, d, $J = 6.8$ Hz)
OMe	56.7	3.94 (3H, s)

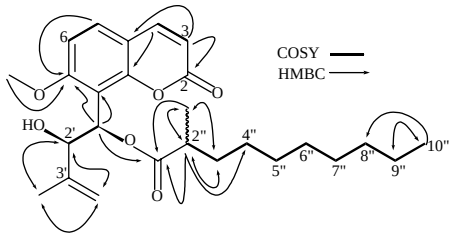

Figure 2. $^{1}H-^{1}H$ COSY and HMBC correlations of paniculacin (**1**).

signals of olefinic protons at C-4′ [6,10] and confirmed by NOESY correlation between H-1′ and H-2′. On the basis of these evidences, the structure of paniculacin (**1**) could be assigned as 1′-[*O*-(2-methyldecanoyl)] murrangatin (Figure 1).

Known compounds were identified as umbelliferone (**2**) [11], scopoletin (**3**) [5], 4-hydroxybenzoic acid (**4**) [12], *trans*-cinnamic acid (**5**) [13], and β-sitosterol (**6**) [14] by comparing their physical and spectral data with those reported in the literature.

3. Experimental

3.1 General experimental procedures

Optical rotation was measured using JASCO DIP-360. IR spectra were recorded on Shimadzu FTIR-8900 spectrometer. UV spectra were recorded on Thermoelectron Visionpro Software V4.10. NMR spectra were recorded on Bruker AM-300, -400, and AMX-500 spectrometers with tetramethysilane as an internal standard. Mass spectra (El and HR-EI) were obtained in an electron impact mode on Finnigan MAT-112 and MAT-113 spectrometers and ions were given in *m/z* (%). FAB mass spectra were carried out on Jeol JMS HX 110 spectrometer. Column chromatography (CC) was performed on silica gel (70–230 mesh, E. Merck, Darmstadt, Germany), and TLC was performed on pre-coated silica gel G-25 UV_{254} plates (E. Merck).

3.2 Plant material

The aerial part of *M. paniculata* was collected from Karachi University and identified by Dr Rubina Dawar, Plant Taxonomist, Department of Botany, University of Karachi, where a voucher specimen has been deposited in the herbarium (voucher No. 67974).

3.3 Extraction and isolation

The freshly collected plant material of *M. paniculata* was shade dried (1.5 kg), ground, and extracted with ethanol (3 × 15 L, 10 days each). The combined extract was evaporated under reduced pressure at a room temperature to produce a residue (276 g), which was suspended in water (1.0 L) and successively extracted with *n*-hexane (35 g), ethyl acetate (60 g), and *n*-butanol (120 g). The ethyl acetate fraction (60 g) was subjected to CC over silica gel and eluted with *n*-hexane, *n*-hexane–ethyl acetate, and ethyl acetate–methanol in an increasing order of polarity to collect 14 fractions (A–K). The fraction obtained with *n*-hexane–EtOAc (8.0:2.0) (1.2 g) was a mixture and re-chromatographed over silica gel eluting with *n*-hexane–EtOAc (9.0:1.0) to afford β-sitosterol (**6**) (30 mg). The fraction eluted with *n*-hexane–EtOAc (7.5:2.5) (2.4 g) was a mixture of binary compounds, which was re-chromatographed over silica gel and eluted with *n*-hexane–EtOAc (9.0:1.0 and 8.5:1.5) to afford 4-hydroxybenzoic acid (**4**) (14 mg) and *trans*-cinnamic acid (**5**) (17 mg), respectively. The fraction obtained with *n*-hexane–EtOAc (6.5:3.5) (1.8 g) was re-chromatographed over silica gel eluting with *n*-hexane–EtOAc in an increasing order of polarity to collect six sub-fractions. The sub-fraction obtained with *n*-hexane–EtOAc (2.5:7.5) (17 mg) was a semi-pure compound, which was further purified through preparative TLC with $CHCl_3$–MeOH (9.6:0.4) to afford scopoletin (**3**) (13 mg). The sub-fraction obtained with

n-hexane–EtOAc (3.5:6.5) (15 mg) was also a semi-pure compound and was purified through preparative TLC eluting with $CHCl_3$–MeOH (9.4:0.6) to afford umbelliferone (**2**) (12 mg). The fraction obtained with *n*-hexane–EtOAc (5.0:5.0) (2.6 g) from the main column was re-chromatographed over silica gel and eluted with mixtures of *n*-hexane–EtOAc to furnish six sub-fractions. The sub-fraction obtained with *n*-hexane–EtOAc (0.5:9.5) (33 mg) was a semi-pure compound and was purified through preparative TLC with $CHCl_3$–MeOH (9.5:0.5) to afford paniculacin (**1**, 30 mg).

3.4 Paniculacin (1)

Colorless oil; $[\alpha]_D^{25}$ −60.5; UV λ_{max} ($CHCl_3$) nm (log ε): 322 (2.4), 258 (3.1), 240 (2.2); IR ν_{max} (KBr) cm^{-1}: 3419 (OH), 1767, and 1730 (O—C═O), 1607 (C═C), 1605–1400 (aromatic moiety); ^1H ($CDCl_3$, 400 MHz) and ^{13}C ($CDCl_3$, 100 MHz) NMR spectral data, see Table 1; EI-MS *m/z* (rel. int. %): 219 (2), 205 (100), 190 (11), 175 (39), 161 (16), 147 (13), 105 (7); HR-FAB-MS (−ve): *m/z* 443.2425 $[M - H]^-$ (calcd for $C_{26}H_{35}O_6$, 443.2434).

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References

[1] E. Nasir and S.I. Ali, *Flora of Pakistan* (PanGraphics, Islamabad, 1980), No. 132, pp. 1–29.
[2] S.R. Baquar, *Medicinal and Poisonous Plants of Pakistan* (Printase, Karachi, 1989), p. 230.
[3] M.T. Fauvel, J. Gleye, C. Moulis, and I. Fouraste, *Plant Med. Phytother.* **12**, 207 (1978).
[4] Y.C. Kong, K.H. Ng, K.H. Wat, A. Wong, I.F. Saxena, K.F. Cheng, P.P.H. But, and H.T. Chang, *Planta Med.* **4**, 304 (1985).
[5] F. Imai, K. Itoh, N. Kishibuchi, T. Kinoshita, and U. Sankawa, *Chem. Pharm. Bull.* **37**, 119 (1989).
[6] C. Ito, H. Furukawa, H. Ishii, T. Ishikawa, and J. Haginiwa, *J. Chem. Soc. Perkin Trans. 1* **7**, 2047 (1990).
[7] T. Kinoshita and K. Firman, *Phytochemistry* **42**, 1207 (1996).
[8] M.A. Sukari, S.A. Azziz, M. Rahmani, A.M. Ali, N. Aimi, and M. Kitajima, *Nat. Prod. Sci.* **9**, 56 (2003).
[9] R.D.H. Murray, J. Mendez, and S.A. Brown, *The Natural Coumarins: Occurrence, Chemistry and Biochemistry* (Wiley, New York, 1982), p. 27.
[10] N. Negi, A. Ochi, M. Kurosawa, K. Ushijima, Y. Kitaguchi, E. Kusakabe, F. Kasho, T. Kimachi, N. Teshima, M. Ju-Ichi, A.M. Abou-Douh, C. Ito, and H. Furukawa, *Chem. Pharm. Bull.* **53**, 1180 (2005).
[11] The Committee of Chinese Herb Information, *Zhiwuyao Youxiao Chengfen Shouce* (Renmin Weisheng Publisher, Beijing, China, 1986), p. 1097.
[12] R.L. Khosa, *J. Res. Indian Med.* **10**, 75 (1975).
[13] T.A. Wittstruck and E.N. Trachtenberg, *J. Am. Chem. Soc.* **89**, 3803 (1967).
[14] S. Arata, H. Kurosu, and I. Ando, *J. Mol. Struct.* **513**, 133 (1999).