Phytochemistry Letters 24 (2018) 51–55

Contents lists available at ScienceDirect

Phytochemistry Letters

journal homepage: www.elsevier.com/locate/phytol

Cytotoxic lactam and naphthoquinone alkaloids from roots of *Goniothalamus lanceolatus* Miq.

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ARTICLE INFO

Keywords:
Goniothalamus lanceolatus
Annonaceae
Lactam alkaloid
Naphthoquinone alkaloids
Cytotoxic activity

ABSTRACT

Two new alkaloids, (−)-goniolanceolactam (**1**) and 2-acetyl-3-amino-1,4-naphthoquinone (**2**), along with two known naphthoquinone alkaloids, 2-acetyl-3-amino-5-hydroxy-1,4-naphthoquinone (**3**) and cleistopholine (**4**) were isolated from the cytotoxic, dichloromethane root extract of *Goniothalamus lanceolatus* (Annonaceae). The structures were elucidated by spectroscopic techniques and the absolute configuration of **1** was established by single-crystal X-ray diffraction. Alkaloid **1** showed cytotoxic activity on human colon and lung cancer cell lines with IC_{50} values ranging from 5.32 to 9.91 μM.

1. Introduction

In Malaysia, *Goniothalamus* species are widely used as a traditional remedy for abortion and postpartum treatment, as well as for fever and skin infections (Wiart, 2007). *Goniothalmus lanceolatus* is an ethomedicinal plant indigenous to Sarawak, Malaysia. Among other uses, this plant is used by the indigenous people as a treatment for cancer. Several lactam and naphthoquinone alkaloids isolated from species of this genus were reported to possess cytotoxic activity (Cao et al., 1998; Soonthornchareonnon et al., 1999; Macabeo et al., 2013; Tran et al., 2013; Nordin et al., 2016). In this study, the dichloromethane root extract of *G. lanceolatus* (100 μg/mL) exhibited promising cytotoxic activity against a panel of human colon and lung cancer cell lines with percent cell viability of less than 15%. Herein the isolation of two new alkaloids; (−)-goniolanceolactam (**1**) and 2-acetyl-3-amino-1,4-naphthoquinone (**2**), along with two known alkaloids, 2-acetyl-3-amino-5-hydroxy-1,4-naphthoquinone (**3**) and cleistopholine (**4**) are reported from the dichloromethane root extract of *G. lanceolatus* (Fig. 1). Alkaloid **1** demonstrated cytotoxicity with IC_{50} values of less than 10 μM against a panel of eight human colon and lung cancer cell lines.

2. Results and discussion

Alkaloid **1** was obtained as white crystals, $[\alpha]_D^{25}$ −31.0 (c 0.52, MeOH) with a melting point of 165–167 °C. Its molecular formula was determined to be $C_{17}H_{14}O_4N$ by LC-ESI-OBITRAP-MS (*m/z* 296.0919, $[M+H]^+$; calculated 296.0917). The IR spectrum displayed an adsorption band at 1733 cm^{-1} for the lactam carbonyl functionality, and the UV spectrum showed absorption bands at λ_{max} 211, 264, and 326 nm. The ^{13}C NMR spectrum (Table 1) showed presence of 17 carbons. Carbon signals for the methylenedioxy, methoxy, and lactam carbonyl were observed at δ_C 102.5, 65.0, and 169.6, respectively. In addition, the DEPT spectrum revealed methylene and methine carbons at δ_C 34.7 and 58.0, respectively. The ^1H NMR spectrum (Table 1) showed two doublets at δ_H 6.09 and 6.18 for the methylenedioxy protons, a methoxy group at δ_H 4.00, and five aromatic protons, one of which is an isolated proton (δ_H 7.08). The proton and carbon NMR spectra of **1** have strong resemblance to those of tapisoidin, a 9,10-dihydroarisolactam alkaloid isolated from *G. tapisoides* (Kim et al., 2013). The presence of a methylenedioxy group between C-3 and C-4 in **1** was confirmed through HMBC correlations of its protons to C-3 (δ_C 150.2) and C-4 (δ_C 147.6). The isolated aromatic proton at δ_H 7.08 (s) was assigned to H-2 of ring A, while the four adjacent aromatic protons at δ_H 7.90 (H-5, *d*, 7.4), 7.35 (H-6 and H-7, *m*), and 7.29 (H-8, *m*) were assigned to ring C (Fig. 2). Assignment of H-10 (δ_H 4.52) and H-9 (δ_H 2.77 and 3.39) were confirmed through a COSY experiment. The remaining quaternary carbons at C-1, C-4a, C-5a, C-8a, and C-11 were established through their HMBC correlations, as listed in Table 1. The

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https://doi.org/10.1016/j.phytol.2018.01.009
Received 27 October 2017; Received in revised form 10 January 2018; Accepted 19 January 2018