Fitoterapia 142 (2020) 104512

Contents lists available at ScienceDirect

Fitoterapia

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

Subnudatones A and B, new *trans*-decalin polyketides from the cultured lichen mycobionts of *Pseudopyrenula subnudata*

Thuc-Huy Duong[a,b], Hung-Huy Nguyen[c], Thanh-Trung Le[d], Thanh-Nha Tran[e], Jirapast Sichaem[f,*], Thanh-Trung Nguyen[g], Thi-Phuong Nguyen[h], Dinh-Tri Mai[i,j], Huu-Hung Nguyen[k], Hoang-Duy Le[l,*]

[a] Department for Management of Science and Technology Development, Ton Duc Thang University, Ho Chi Minh City, Viet Nam
[b] Faculty of Applied Sciences, Ton Duc Thang University, Ho Chi Minh City, Viet Nam
[c] Department of Inorganic Chemistry, University of Science, Ha Noi National University, 19 Le Thanh Tong Street, Hoan Kiem District, Ha Noi City, Viet Nam
[d] Hue University of Science, Hue City, Viet Nam
[e] Faculty of Chemistry, University of Education, 280 An Duong Vuong Street, District 5, Ho Chi Minh City, Viet Nam
[f] Faculty of Science and Technology, Thammasat University Lampang Campus, Lampang 52190, Thailand
[g] Institute of Research and Development, Duy Tan University, Da Nang 550000, Viet Nam
[h] Faculty of Biotechnology, Nguyen Tat Thanh University, 300A Nguyen Tat Thanh, District 4, Ho Chi Minh City, Viet Nam
[i] Graduate University of Science and Technology, Vietnam Academy of Science and Technology, 18 Hoang Quoc Viet, Cau Giay, Ha Noi, Viet Nam
[j] Institute of Chemical Technology, Vietnam Academy of Science and Technology, 01 Mac Dinh Chi, Ho Chi Minh City, Viet Nam
[k] Faculty of Environment and Biotechnology, Van Lang University, 45 Nguyen Khac Nhu, District 1, Ho Chi Minh City, Viet Nam
[l] Pham Van Dong University, Quang Ngai Province, Viet Nam

ARTICLE INFO

Keywords:
Pseudopyrenula subnudata
Subnadatones A and B
trans-decalin polyketide
Cytotoxicity

ABSTRACT

Chemical investigation of the cultured polyspore-derived mycobionts of a *Pseudopyrenula subnudata* lichen led to the isolation of two new compounds, subnudatones A and B (**1** and **2**), together with four known compounds, 1-(2-hydroxy-1,2,6-trimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl)ethanone (**3**), libertalide C (**4**), aspermytin A (**5**), and 6,7-dimethoxy-4-hydroxymellin (**6**). Their chemical structures were elucidated by extensive 1D and 2D NMR analysis and high resolution mass spectroscopy, and comparisons were made with the literature. The absolute configuration of **1** was defined unambiguously using single crystal X-ray crystallography. Compound **1** represents the first dimeric decalin polyketide to be found in nature. The *in vitro* cytotoxicity of **1** against two cancer cell lines (K562 and MCF-7) was evaluated. Compound **1** showed moderate cytotoxic activity with IC_{50} values of 23.5 ± 1.0 and 51.9 ± 1.4 μM, respectively.

1. Introduction

Lichens are symbiotic associations of an algal or cyanobacterial photobiont and a fungal mycobiont, and produce a range of bioactive metabolites. However, the metabolites that are extracted from cultured lichen mycobionts are not detectable in natural lichens under stressed conditions. Phytochemical investigation of mycobionts cultured from Vietnamese lichens identified bioactive compounds with unique scaffolds [1–3]. In our search for metabolites of crustose lichen mycobionts, the mycobionts of *Pseudopyrenula subnudata* lichen were isolated and cultivated on MY10 at 18oC in the dark over several months. The colonies were then harvested and extracted with EtOAc. The extract was separated by a combination of chromatographic procedures to afford two new compounds, subnadatones A and B (**1** and **2**), along with four known compounds, 1-(2-hydroxy-1,2,6-trimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl)ethanone (**3**) [4], libertalide C (**4**) [5], aspermytin A (**5**) [6], and 6,7-dimethoxy-4-hydroxymellin (**6**) [7]. The structures of these compounds were determined by extensive spectroscopic analysis (1D, 2D-NMR, and HRESIMS) and single-crystal X-ray crystallography. Compound **1** was assessed for its *in vitro* cytotoxicity against the MCF-7 (breast cancer) and K562 (chronic myelogenous leukemia) cell lines.

2. Experimental

2.1. General experimental procedures

NMR spectra were measured on Bruker Avance II (500 MHz for ^{1}H

* Corresponding authors.
E-mail addresses: duongthuchuy@tdtu.edu.vn (T.-H. Duong), Jirapast@tu.ac.th (J. Sichaem), lhduy@pdu.edu.vn (H.-D. Le).

https://doi.org/10.1016/j.fitote.2020.104512
Received 20 December 2019; Received in revised form 12 February 2020; Accepted 12 February 2020
Available online 13 February 2020
0367-326X/