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Lanostane-type C_{31} triterpenoid derivatives from the fruiting bodies of cultivated *Fomitopsis palustris*

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ABSTRACT

Fifteen undescribed and five known lanostane-type C_{31} triterpenoid derivatives were isolated from the aqueous EtOH extract of the fruiting bodies of cultivated *Fomitopsis palustris*. Their structures were identified from the spectroscopic data and chemical degradation studies. The structures of palustrisoic acids A and H were confirmed by X-ray crystallography. Polyporenic acid B showed strong cytotoxicity against the HCT116, A549, and HepG2 cell lines with IC_{50} values of 8.4, 12.1, and 12.2 μM, respectively. Palustrisolides A, C, and G displayed weak cytotoxicity.

1. Introduction

The species of *Fomitopsis* (family Fomitopsidaceae) have been used for centuries as popular medicines to prevent and/or treat different diseases in Asia. Chemical studies on the fungi of this genus led to the identification of several classes of natural products such as chlorinated coumarins, steroids, lanostane-type triterpenoids, polyphenols, and polyketides (Chiba et al., 2014; De Silva et al., 2013; Hwang et al., 2013; Keller et al., 1996; Pleszczyńska et al., 2017; Quang et al., 2005; Rösecke and König, 1999; Shi et al., 2017; Yoshikawa et al., 2005). Some of them showed cholesterol reduction (Chiba et al., 2014), antiviral and antibacterial (Keller et al., 1996; Pleszczyńska et al., 2017), antitumor (Shi et al., 2017), and anti-inflammatory activities (Yoshikawa et al., 2005; Pleszczyńska et al., 2017). *F. palustris* was reported to cause wood brown rot, a disease resulting from the enzymatic breakdown of cellulose, the major wood component (Konuma et al., 2015). The extracts of the fruiting bodies of cultivated *F. palustris* showed cytotoxicity against different cancer cell lines (Yu et al., 2014). The preliminary results revealed that the aforementioned extracts inhibited the growth of tumor cells and promoted the apoptosis of tumor cells (Yu et al., 2014). In the course of the chemical investigations on the cytotoxic extract of the fruiting bodies of cultivated fungus *F. palustris*, 20 lanostane-type C_{31} triterpenoid derivatives were obtained and identified from the spectroscopic data and alkaline hydrolysis experiments. Lanostane-type triterpenoids are well-known tetracyclic triterpene derivatives (Hill and Connolly, 2017; Nes, 2011). Most of them showed very interesting biological activities, such as anti-AIDS (Li et al., 1993), anti-inflammatory (Kamo et al., 2003), and cytotoxicity (Lai et al., 2016; Tohtahon et al., 2017). Herein we report the isolation, structure elucidation, and cytotoxicity of these lanostane-type C_{31} triterpenoid derivatives.

2. Results and discussion

The 95% EtOH extract of the fruiting bodies of cultivated *F. palustris* was partitioned between H_2O and EtOAc to afford the

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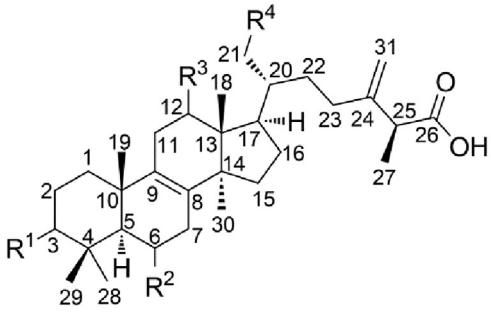
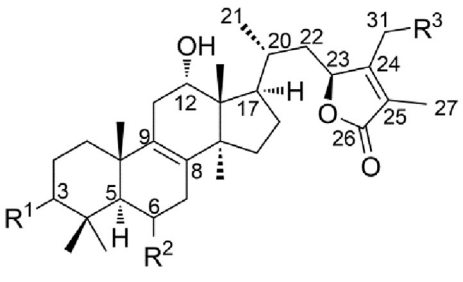
crude cytotoxic residue. The residue was separated and purified by column chromatography and semi-preparative HPLC to give 15 undescribed and 5 known lanostane-type C_{31} triterpenoid derivatives (Fig. 1).

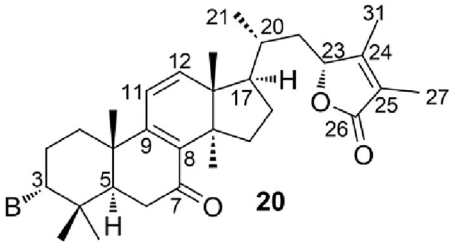
Compound **1** was isolated as a white powder. Its molecular formula $C_{37}H_{58}O_9$ was determined from the ^{13}C NMR (Table 1) and HRESIMS [*m/z* 669.3964 ([M+Na]$^+$)] data. The IR spectrum indicated the presence of hydroxy (3441 cm^{-1}) and carbonyl (1732, 1705 cm^{-1}) groups in **1**. Eight methyls, three oxygenated methines, a 1,1-di-substituted double bond, a tetra-substituted double bond, and three carbonyls were recognized from the NMR spectroscopic data of **1** (Table 1), together with ten aliphatic methylenes, four aliphatic methines, and five quaternary carbons. A 3-hydroxy-3-methylglutaryloxy moiety [$HOOCCH_2C(CH_3)(OH)CH_2C(O)O$-, moiety A, Fig. 2A] was established from the following HMBC correlations: H-2′/C-1′, C-3′, C-6′; H-4′/C-3′, C-5′, C-6′; and H-6′/C-2′, C-3′, C-4' (Fig. 2A). The remaining NMR spectroscopic data were similar to those of 3α-acetylpolyporenic acid A (**10**, Fig. 1), an acetylated lanostane-type C_{31} tetracyclic triterpenoid acid (Wangun et al., 2004). Comparison of the NMR spectroscopic data of **1** (Table 1) with those of **10** suggested that another oxygenated methine rather than a methylene group presented in **1** (Fig. 1). The HMBC correlations of H-6/C-5, C-7, C-8, C-10 and H-12/C-9, C-11, C-13, C-14, C-18 suggested that two hydroxy groups were located at C-6 and C-12, respectively (Fig. 2A). The moiety A was located at C-3 according to the key HMBC correlation of H-3/C-1′ (Fig. 2A). Comparing the coupling constants of H-3 and H-2 with those from the similar structures (Jiang et al., 1977; Kamo et al., 2003; Lai et al., 2016; Li et al., 1993; Tohtahon et al., 2017; Wang et al., 2003), the double doublets of H-3 (δ_H 4.45, 1 H, dd, J = 11.6, 4.3 Hz) in **1** suggested a β-orientation of moiety A, which was confirmed by the NOESY correlation of H-3 and the α-orientated H-5 in all lanostane-type triterpenoids (Jiang et al., 1977; Kamo et al., 2003; Lai et al., 2016; Li et al., 1993; Tohtahon et al., 2017). The relative configurations of **1**



	R^1	R^2	R^3	R^4
1	β-A	β-OH	α-OH	H
2	β-A	H	α-OH	H
3	β-A	H	β-OH	H
3a	β-OH	H	β-OH	H
4	β-A	H	H	OH
5	α-A	H	H	OH
6	α-B	H	= O	H
7	β-OH	H	α-OH	H
8	α-A	H	α-OH	H
9	α-B	H	α-OH	H
10	α-OAc	H	α-OH	H



	R^1	R^2	R^3
14	α-B	H	H
15	α-A	H	H
16	α-B	H	OH
17	α-C	H	H
18	β-A	H	H
19	β-A	β-OH	H



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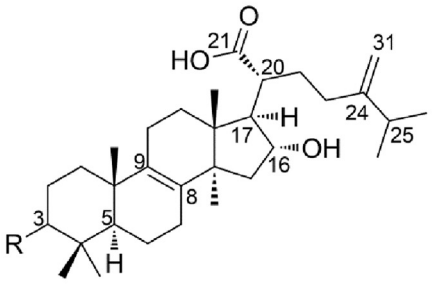

	R
11	α-B
12	β-OH
13	β-OAc

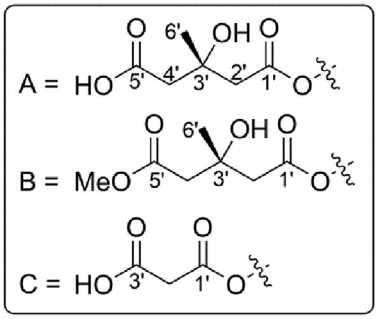

Fig. 1. Structures of the lanostane-type C_{31} triterpenoid derivatives from *Fomitopsis palustris*.