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Short communication

Cytotoxic cytochalasins from the endophytic fungus Eutypella scoparia **PSU-H267**



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1. Introduction

The fungus Eutypella scoparia produced bioactive secondary metabolites such as the antibacterial diaporthein B and scoparasin B (Pongcharoen et al., 2006), cytotoxic phenochalasin B (Sun et al., 2011a) as well as antitumor diaporthein B (Li et al., 2011). Chemical investigation of this fungus has resulted in the discovery of various types of metabolites, including chromenes (Pongcharoen et al., 2006; Sun et al., 2013), cytochalasins (Pongcharoen et al., 2006; Ciavatta et al., 2008; Sun et al., 2011a, 2013), cytosporin-related compounds (Ciavatta et al., 2008), pimarane diterpenes (Pongcharoen et al., 2006; Sun et al., 2011b, 2012a), sesquiterpenes (Sun et al., 2011a, 2012b) and steroids (Sun et al., 2011b). In this study, we chemically investigated secondary metabolites produced by E. scoparia PSU-H267 isolated from a leaf of Hevea brasiliensis collected in Songkhla Province, Thailand. The broth EtOAc extract of E. scoparia PSU-H267 showed interesting cytotoxic activity against KB-cells with an IC₅₀ value of 1.63 μ g/mL. Purification of the broth EtOAc extract led to the isolation of 11 compounds including one new cytochalasin derivative, scoparasin C (1), four

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ABSTRACT

Eleven compounds including one new cytochalasin derivative, scoparasin C(1), four cytochalasins (2–5), four pimarane diterpenes (6-9) and two chromene derivatives (10 and 11) were obtained from a culture broth of Eutypella scoparia PSU-H267 which was isolated from a leaf of Hevea brasiliensis. Their structures were determined by spectroscopic evidence. For compounds **2**. **3** and **5**, the structures were confirmed by single-crystal X-ray diffraction crystallography. Compounds 1, 3, 4 and 7 were strongly active against Vero cell lines with IC₅₀ values of 1.19, 0.04, 1.01 and 2.50 μM, respectively. Only compound **3** displayed potent cytotoxic activity towards KB-oral cavity cancer cell lines with the IC₅₀ value of 2.46 µM.

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known cytochalasin derivatives: scoparasin A (2) (Pongcharoen et al., 2006), phenochalasin B (3) (Tomoda et al., 1999), $\Delta^{6,12}$ isomer of 5,6-dehydro-7-hydroxy-29-methoxycytochalasin E (4) and [12]-cytochalasin (5) (Sharma et al., 2005), four known pimarane diterpene derivatives: diaportheins A (6) and B (7) (Dettrakul et al., 2003), 11-deoxydiaporthien A (8) (Yoshida et al., 2007) and scopararane A (9) (Pongcharoen et al., 2006), and two known chromene derivatives: cytosporin D (10) (Ciavatta et al., 2008) and (R)-3,4-dihydro-4,8-dihydroxy-6-methoxy-4,5-dimethyl-3-methyleneisochromen-1-one (11) (Tayone et al., 2011). The isolated compounds 1-8 were evaluated for antimicrobial, antimycobacterial, antimalarial and cytotoxic activities.

2. Results and discussion

The broth ethyl acetate extract of E. scoparia PSU-H267 was subjected to chromatographic techniques leading to the isolation of one new (1) and 10 known compounds (2-11). The structures of all metabolites (Fig. 1) were elucidated by analysis of spectroscopic data. For known compounds, their structures were confirmed by comparison of the ¹H and ¹³C NMR data as well as specific rotations with those previously reported in the literature. The X-ray data of 2, 3 and 5 (Fig. 2) are reported for the first time.



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Fig. 1. Structures of compounds 1-11 isolated from Eutypella scoparia PSU-H267.



Fig. 2. ORTEP drawings of 2, 3 and 5.

Scoparasin C (1) was obtained as a colorless solid, melting at 140–142 °C, and had the molecular formula $C_{28}H_{32}NO_8$ by HRESIMS. The UV spectrum showed maximum absorption bands at 225, 277 and 285 nm, indicating the presence of a conjugated aromatic chromophore (Tomoda et al., 1999). The IR spectrum exhibited absorption bands at 3278 cm⁻¹ for a hydroxy group, 1769 cm⁻¹ for a vinyl carbonate carbonyl moiety and 1715 cm⁻¹ for ketone and lactam carbonyl functional groups (Pongcharoen et al.,

2006). The ¹H NMR spectrum (Table 1) displayed the characteristic signals for four *ortho*-coupled aromatic protons of a *para*disubstituted benzene ($\delta_{\rm H}$ 6.99 and 6.80, each d, *J*=8.7 Hz, 2H), one amino proton ($\delta_{\rm H}$ 6.65, br s, 1H), one hydroxy proton ($\delta_{\rm H}$ 4.70, br s, 1H), *trans*-olefinic protons of the unsaturated carbonate moiety ($\delta_{\rm H}$ 6.45 and 5.59, each d, *J*=11.7 Hz, 1H) (Pongcharoen et al., 2006), *trans*-olefinic protons of a nonconjugated alkene [$\delta_{\rm H}$ 5.85 (m, 1H) and 5.20 (ddd, *J*=14.7, 10.5 and 3.6 Hz, 1H)], six Download English Version:

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