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Terpenoids from the Deep-Sea-Derived Fungus *Penicillium thomii* YPGA3 and Their Bioactivities

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Abstract: A chemical study of the ethyl acetate (EtOAc) extract from the deep-sea-derived fungus *Penicillium thomii* YPGA3 led to the isolation of a new austalide meroterpenoid (**1**) and seven known analogues (**2**–**8**), two new labdane-type diterpenoids (**9** and **10**) and a known derivative (**11**). The structures of new compounds **1**, **9**, and **10** were determined by comprehensive analyses via nuclear magnetic resonance (NMR) and mass spectroscopy (MS) data. The absolute configurations of **1**, **9**, and **10** were determined by comparisons of experimental electronic circular dichroism (ECD) with the calculated ECD spectra. Compound **1** represented the third example of austalides bearing a hydroxyl group at C-5 instead of the conserved methoxy in other known analogues. To our knowledge, diterpenoids belonging to the labdane-type were discovered from species of *Penicillium* for the first time. Compound **1** showed cytotoxicity toward MDA-MB-468 cells with an IC_{50} value of 38.9 μM. Compounds **2** and **11** exhibited inhibition against α-glucosidase with IC_{50} values of 910 and 525 μM, respectively, being more active than the positive control acarbose (1.33 mM).

Keywords: *Penicillium thomii* YPGA3; deep-sea-derived fungus; austalide meroterpenoid; labdane-type diterpenoid; bioactivities

1. Introduction

Austalides are a class of natural meroterpenoids with attractive scaffolds. Previous biosynthetic studies revealed that they are biosynthesized by cyclization and oxidative modification of 6-[(2*E*, 6*E*)farnesyl]-5,7-dihydroxy-4-methylphthalide [1]. These meroterpenoids were mainly produced by the species of the fungal genera *Aspergillus* and *Penicillium*, especially those from marine environments. Since austalides A–E were first reported in 1981, a total of 36 analogues have been identified [2–11]. The structural variations of austalides are attributed to oxidation occurring at C-13, C-14, C-17, and the isopropyl (C-15, C-25, C-26) to generate alcohol, isopropenyl, lactone, ester, or