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Original article

Cytotoxic and protective DNA damage of three new diterpenoids from the brown alga *Dictyota dichotoma*

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ABSTRACT

Three new diterpenes Amijiol acetate (**3**), dolabellane, Dolabellatrienol (**4**), and dolastane, Amijiol-7, 10-diacetate **(9)** were isolated together with the previously described Pachydictyol A (**1**), Isopachydictyol A (**2**), 8β-hydroxypachydictyol A (**5**), Amijiol (**6**), Isodictyohemiacetal (**7**) and Dictyol C (**8**) from the Red Sea brown alga *Dictyota dichotoma* var. *implexa*. The structures and relative stereochemistry of the new diterpenoids were proposed on the basis of their spectral data. Compounds **3** and **9** have potent activity against DNA damage, cytotoxicity against WI-38, HepG2, and MCF-7 cell lines, and antioxidant using ABTS and erythrocytes hemolysis.

1. Introduction

Brown algae (Phaeophyceae) belonging to order Dictyotales, have emerged as an exceptionally rich source of terpenoids, which form part of a defensive strategy against herbivores in the marine environment [1,2]. Phytochemical studies have been undertaken on the family Dictyotaceae resulting in the isolation of more than 300 diterpenoids from at least 35 species collected all over the world. These Dictyotaceae produce a significant number of secondary metabolites, especially diterpenes. Generally, these diterpenes have three types of carbon skeletons: xenicanes; dolabellanes and extended sesquiterpenes. Many members of the family though, produce cyclic diterpenoids, unique in the structural variety of marine natural products. Biological studies have shown a significant number of dictyota secondary metabolites to possess cytotoxic, anti-bacterial, ichthyotoxic and anti-feedant activities [3–5].

In continuation of our search program for the isolation of bioactive natural products from marine organisms of the Red Sea [6–14], we collected *Dictyota dichotoma* at El-shuaiba 80 km south of Jeddah. Fractionation of the pet. ether:ether extract afforded three new diterpenoids as well as six known compounds. The chemotaxonomic implication of these findings is also discussed.

2. Results and discussion

2.1. Chemistry

The pet. ether–ether extract of the brown alga *Dictyota dichotoma* was fractionated on neutral aluminum oxide using a gradient of pet. ether–ether as eluant. The fractions were monitored by TLC using 50%-sulfuric acid in methanol as spray reagent, to afford, in order of elution nine compounds (Fig. 1). Structures of the known isolated compounds Pachydictyol A (**1**) [15], Isopachydictyol A (**2**) [4], 8β-Hydroxypachydictyol A (**5**) [16], Amijiol (**6**) [17], Isodictyohemiacetal (**7**) [18] and dictyol C (**8**) [19] were established by comparing their physical and spectral data with those in the literature.

Compound **3** was found by mass spectrometry and ^{13}C NMR spectroscopy to have the molecular formula $C_{22}H_{34}O_3$. The IR spectrum of **3** contained hydroxyl (3437 cm^{-1}) and carbonyl (1736 cm^{-1}) absorption bands. A three-proton singlet at δ 2.15 in

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