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Short communication

# Two new cytochalasins from an endophytic fungus, KL-1.1 isolated from *Psidium guajava* leaves

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ABSTRACT

Chemical investigation of the endophytic fungus, KL-1.1, isolated from the leaves of *Psidium guajava* (Linn) led to the isolation of two new cytochalasin derivatives, 18-desoxy-19,20-epoxycytochalasin C and 18-desoxycytochalasin C, together with five other known derivatives. The structures of the isolated compounds were elucidated by one and two dimensional nuclear magnetic resonance spectroscopy as well as by mass spectrometry. These compounds represent novel chemical scaffold with potential for development into anticancer agents.



## 1. Introduction

Natural products have contributed greatly to the development of novel therapeutic molecules. Many drugs currently in clinical use were either derived from natural products or developed from natural products scaffolds. At some point in time, investigation into natural products as sources of novel therapeutic molecules suffered a huge decline. This was occasioned by the perceived low hit rates associated with compounds derived from whole plants or plant parts. Over the last two decades, however, there has been a renaissance and renewed interest in natural products, particularly those of microbial origin. Endophytic fungi, a very diverse polyphyletic group of microorganisms, which can thrive asymptomatically in the tissues of plants, including stems, leaves and/or roots have shown great promise in this regards. Metabolites of endophytic fungi have been a source of inspiration for development of novel therapeutic agents (Aly et al., 2010; Strobel and Daisy, 2003; Strobel et al., 2004).

Nigeria is endowed with several rainforest zones and vegetation belts. Despite the huge biodiversity, bioprospecting for active molecules have relied heavily on plant tissues, with little attention on the potentialities of fungal endophytes as veritable sources of novel bioactive compounds. Our recent report on the isolation of novel anti-inflammatory and immuno-modulatory secondary metabolites from an endophyte of a Nigerian medicinal plant, *Gongronema latifolium* (Okoye et al., 2013a,b) could lend credence to the speculated enormous potentials which abound in endophytes of Nigerian medicinal plants. This has stimulated our interest to further explore Nigerian medicinal plants for novel fungal endophytes with potentials of generating unique bioactive molecules.

In our recent investigation, we isolated some cytochalasins from an endophytic fungus, KL-1.1, obtained from the leaves of *Psidium guajava*. Cytochalasins are a group of cytotoxic phenyl isoindolyl derivatives, which have shown great promise as anticancer agents (Trendowski, 2015; Trendowski et al., 2015). This class of compounds possess unique chemical scaffold which will obviously make their laboratory synthesis cumbersome and expensive. Before now, several reports on the occurrence of cytochalasins were limited to macroscopic terrestrial fungi of the

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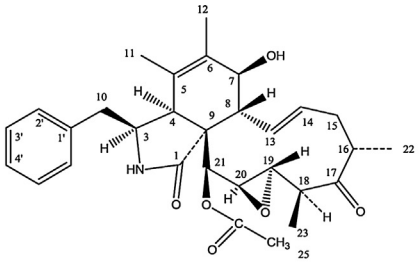
genus *Xylaria* (Abate et al., 1997; Espada et al., 1997; Buchanam et al., 1995; Dague et al., 1994). There are, however, few recent reports of occurrence of cytochalasins in endophytic fungi (Pongcharoen et al., 2006; Kongprapan et al., 2015; Chen et al., 2015). It is therefore interesting to report the isolation of new cytochalasins from an endophytic fungus obtained from the leaves of *P. guajava*, a Nigerian rain forest medicinal plant.

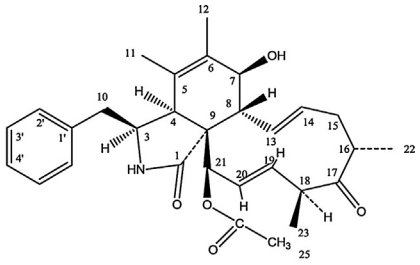
## 2. Results and discussion

The pure strain of the endophytic fungus, KL-1.1, isolated from the leaves of *P. guajava*, was cultured on solid rice media for 2 weeks and the metabolites exhaustively extracted with ethyl acetate. The crude ethyl acetate extract, which completely inhibited the growth of mouse lymphoma cell line (L5178Y) at 10 μg/mL was chromatographed over silica gel and Sephadex LH-20. Final purification of the Sephadex fractions by semipreparative HPLC afforded two new cytochalasins **1** and **2**, including five known cytochalasins **3–7** (Fig. 1).

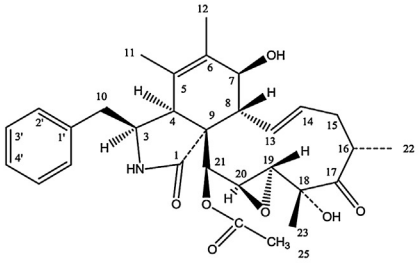
Compound **1** was isolated as white micro-crystals. The molecular formula was deduced as $C_{30}H_{37}NO_6$ based on ESI-MS molecular ion peak at $m/z$ 508.1 $[M+H]^+$ in the positive mode and $^{13}C$ NMR analysis. The proton NMR data of **1** showed features very similar to the previously reported 19, 20-epoxycytochalasin C (Abate et al., 1997). These signals include the presence of amide functionality (NH) at $\delta_H$ 6.04 br s, the presence of acetate functionality at $\delta_H$ 2.17 s and the presence benzyl group, which occurred as 5 aromatic protons signals of the AA′BB′C system at $\delta_H$



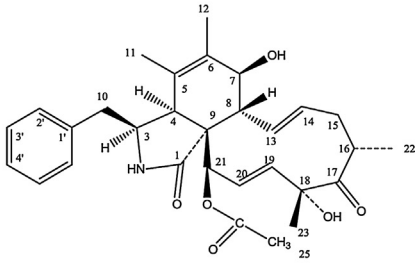
**1** (18-Desoxy-19, 20-epoxycytochalasin C)



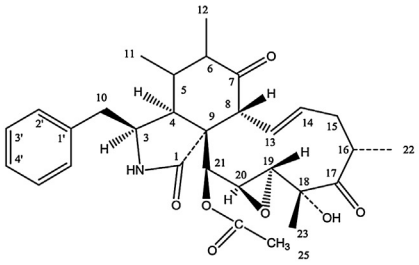
**2** (18-Desoxycytochalasin C)



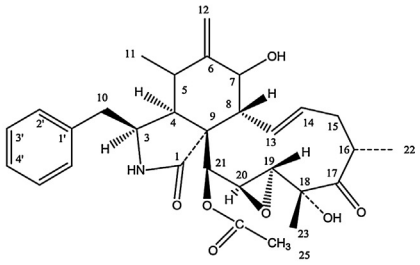
**3** (19, 20-Epoxycytochalasin C)



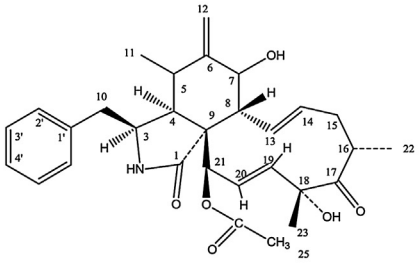
**4** (Cytochalasin C)



**5** (5,6-dihydro-7-oxo-19, 20-Epoxycytochalasin C)



**6** (19, 20-epoxycytochalasin D)



**7** (Cytochalasin D)

**Fig. 1.** Chemical structures of the isolated cytochalasins.