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SHORT COMMUNICATION

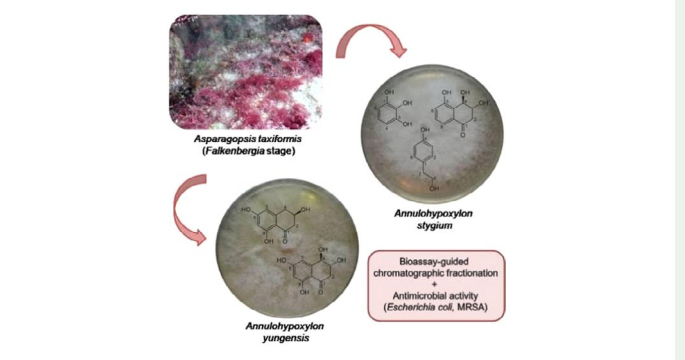
Aromatic compounds produced by endophytic fungi isolated from red alga *Asparagopsis taxiformis - Falkenbergia* stage

Rebeca P. Medina[a], Angela R. Araujo[a], Raymond J. Andersen[b], Marcos A. Soares[c], Fabio de A. Silva[c] and Dulce H. S. Silva[a]

[a]Núcleo de Bioensaios, Biossíntese e Ecofisiologia de Produtos Naturais (NuBBE), Departamento de Química Orgânica, Instituto de Química, UNESP - Univ. Estadual Paulista, Araraquara, Brazil; [b]Department of Chemistry and Department of Earth, Ocean and Atmospheric Sciences, University of British Columbia, Vancouver, Canada; [c]Instituto de Biociências, Universidade Federal de Mato Grosso, Cuiabá, Brazil

ABSTRACT

Endophytic fungi were isolated from red alga *Asparagopsis taxiformis - Falkenbergia* stage, collected from the Brazilian coast, and were identified as *Annulohypoxylon stygium* (AT-03) and *A. yungensis* (AT-06) based on their macro/micromorphological and molecular features. Bioassay-guided fractionation of the EtOAc extract from laboratory cultures of both strains yielded known compounds pyrogallol from *A. stygium*, (3*R*)-scytalone and (3*R*,4*R*)-4-hydroxy-scytalone from *A. yungensis*. Pyrogallol was active against methicillin-resistant *Staphylococcus aureus* (MRSA) and *Escherichia coli* strains. An inactive fraction from *A. stygium* afforded two additional compounds, (3*R*,4*R*)-3,4,5-trihydroxy-1-tetralone and tyrosol. Optically active compounds had their stereochemistry determined by circular dichroism (CD) spectroscopy.



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CONTACT Dulce H. S. Silva dhsilva1@gmail.com

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1. Introduction

Recent studies on marine-derived endophytic microorganisms existing in distinct habitats have demonstrated their potential as a source of new pharmacologically active substances with a marked chemodiversity (Flewelling et al. 2015).

Endophytic fungi from red algae have shown a diversity of bioactive compounds such as antimicrobial curvularin-type macrolides (Dai et al. 2010) and cytotoxic polyketides (Gao et al. 2011). In this context, our work describes the isolation and identification of metabolites from fungal strains isolated from red alga *Asparagopsis taxiformis* (diploid phase), guided by antimicrobial assays.

2. Results and discussion

After fractionation of crude extracts from each strain (AT-03 - *A. stygium* and AT-06 - *A. yungensis*), the fractions and crude extracts were tested for antimicrobial activity. The samples tested were inactive against *Pseudomonas aeruginosa*, *Bacillus subtilis* and *Candida albicans*. However, fractions AT-03-F8, AT-06-F8 and AT-06-F9 were active against *E. coli* with inhibition zone diameters (Φ_i) of 2, 2 and 6 mm at 40 µg/disk, respectively. Fractions AT-03-F8 and AT-06-F9 were also active against MRSA (Φ_i 2 and 3 mm at 40 µg/disk, respectively). The positive controls polymyxin B (30 µg/disk for *E. coli*) and rifamycin (10 µg/disk for MRSA) presented Φ_i 15 and 3 mm, respectively.

Purification of fractions with antimicrobial activity using reversed-phase HPLC led to isolation of compounds **1**–**3** (Figure 1). Their structures were elucidated from NMR, MS and CD experiments and comparison with data in the literature. Compound **1** was identified as pyrogallol. Its ^{1}H NMR spectrum (Figure S2) showed a double doublet at δ 6.40 (J_{5-4} 7.8; J_{5-6} 7.8 Hz; 1H; H-5) and a doublet at δ 6.23 (J_{4-5} 7.8; 2H; H-4/H-6).

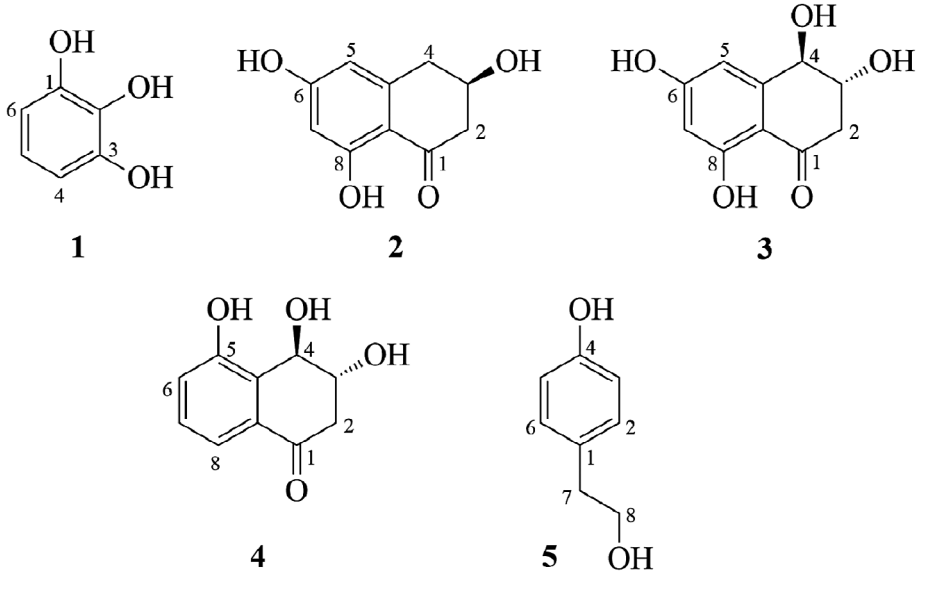

Figure 1. Isolated compounds from *A. stygium* (**1**, **4** and **5**) and *A. yungensis* (**2** and **3**).

Compounds **2** and **3** were identified as scytalone (Li et al. 2012) and 4-hydroxy-scytalone (Gremaud and Tabacchi 1996), respectively. Their absolute configurations were established by CD spectroscopy. The CD spectrum of scytalone (**2**) (Figure S4) indicated a (3*R*)-configuration (λ_{ext} 311 nm, $\Delta\varepsilon$ + 0.65) (Husain et al. 2014). The CD spectrum of compound **3** showed positive and negative Cotton effects at 279 and 214 nm, respectively (Figure S7), indicating a (4*R*)- configuration. A positive Cotton effect at 321 nm and the coupling constant (J_{3-4} 7.2 Hz) in the ^{1}H NMR spectrum (Figure S8), indicated a *trans* relative configuration for H-3/H-4 (Bringmann et al. 2001).

Compounds **1**–**3** were also tested for antimicrobial activity. Pyrogallol was active against MRSA and *E. coli* (Φ_i 4 and 3 mm at 40 µg/disk, respectively), whereas compounds **2** and **3** were inactive against both strains.

The inactive fraction AT-03-F5 was purified using reversed-phase HPLC and afforded 3,4,5-trihydroxy-1-tetralone (**4**) (Fujimoto et al. 1986) and tyrosol (**5**) (Chu et al. 2014) (Figure 1). The CD spectrum of compound **4** (Figure S10) was similar to that of compound **3** and evidenced (3*R*)- and (4*R*)- configurations (Bringmann et al. 2001).

Tetralone derivatives **2**–**4** could be regarded as chemotaxonomic markers as they have been considered intermediates or side products in 1,8-dihydroxynaphthalene (DHN) type melanin biosynthesis in fungal sources (Wheeler et al. 2008). In addition, chemotaxonomy has been a key tool in delimiting species within *Annulohypoxylon*, especially in recently identified *A. yugensis* (Kuhnert et al. 2016). Thus the isolation of these compounds from the studied strains indicates the DHN melanin-type biosynthetic pathway is active in such microorganisms.

3. Conclusion

This is the first report on endophytic fungi from the red alga *A. taxiformis*, and the identification of *A. stygium* and *A. yungensis* as its endophytes. The isolation of compounds **1**–**5** contributes to the chemotaxonomy of the *Annulohypoxylon* genus and expands knowledge on the chemodiversity of marine natural products from Brazilian biomes.

Supplementary material

Experimental details and spectroscopic data are available online.

Disclosure statement

No potential conflict of interest was reported by the authors.

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ORCID

Dulce H. S. Silva http://orcid.org/0000-0002-1516-7765

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