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Antileishmanial activity of compounds from *Cystoseira baccata*

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Palavras Chave: Cystoseira baccata, *antileishmanial*, *bioactivity*.

Introduction

Several bioactivities have already been described for marine macroalge from genus *Cystoseira*, mainly acetylcholinesterase[1] α-glucosidase[1] and butyrylcholinesterase[1] inhibition, antiproliferative, anti-inflamatory[2], scavenging, antioxidant[3], antibacterial[4], antifungal[4], antiviral[5], mycotoxins inhibition[6], and antiprotozoal[7]. Despite this biological approach, there are no previous studies reporting the chemical compounds responsible to the antiprotozoal effect. Due this, this work aimed the identification of chemical compounds responsible to the antileishmanial activity against *Leishmania (L.) infantum* promastigotes from crude extract of *C. baccata*, using a bioactivity guided fractionation.

Results and Discussion

As part of a continuous study aiming the evaluation of *in vitro* antileishmanial activity of marine macroalgae from Iberian Coast, the hexane extract from *C. baccata* displayed activity against *L. (L.) infantum* promastigotes (IC_{50} 94.1 ± 1.5 µg/mL) and selectivity against and human monocytic THP1 cells (CC_{50} > 125.0 µg/mL). Thus, this crude extract was subjected to successive purification procedures using SiO_2 and Sephadex LH-20 to afford a fraction that displayed an IC_{50} value of 29.0 ± 0.5 µg/mL and an CC_{50} value of 47.0 ± 1.5 µg/mL for *L. (L.) infantum* promastigotes and THP-1 human monocyte cells, respectively.

The bioactive fraction was thus analyzed by ^{1}H NMR which showed two peaks assigned to aromatic ring at δ_H 6.45/6.46 (d, *J* = 3.0 Hz) and 6.59/6.60 (d, *J* = 3.0 Hz), one methoxyl group at δ_H 3.73/3.74 (s) as well as six singlets assigned to methyl groups at δ_H 2.17/2.16, 1.28, 1.24/1.19, 1.14/1.12, 1.09/1.03, 0.91/0.83. ^{13}C and DEPT 135° NMR spectra confirmed the presence of aromatic ring due the peaks at range δ_C 152.6 – 111.1, methoxyl group at δ_C 55.6, carbinolic carbons at δ_C 76.4/76.2 and 71.1/70.8 as well as an α,β-unsaturated carbonyl carbon at δ_C 154.5/153.7, 133.3/132.9 and 208.9/208.5. Finally, LRESIMS showed the $[M+H]^+$ and $[M + Na]^+$ peaks at *m/z* 441 and 463, respectively, indicating the molecular formula $C_{28}H_{40}O_4$. Based in these results and those reported in the literature[8], was possible the identification of the inseparable epimeric mixture of (3R)- (**1**) and (3S)- (**2**) tetraprenyltoluquinol, as showed in figure 1.

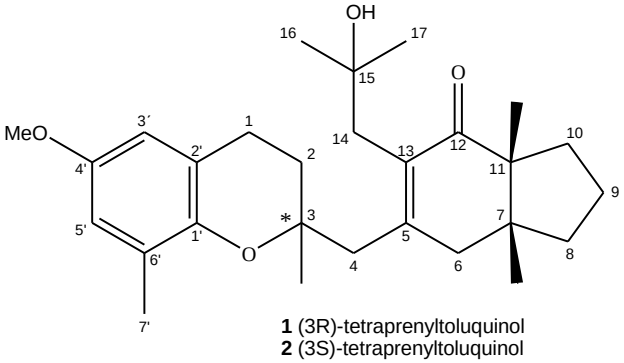

Figure 1. Structures of tetraprenyltoluquinol derivatives isolated from *C. baccata*.

When tested against promastigote forms of *L. (L.) infantum*, these compounds displayed an IC_{50} = 9.2 ± 0.8 µg/mL, suggesting to be responsible for the antileishmanial activity of the studied algae. Compounds **1** and **2** were previously reported as main constituents from non-polar extracts of *C. baccata*,[8] but this first report which describes the antileishmanial activity of tetraprenyltoluquinol derivatives.

Conclusion

This work described the bioactivity guided fractionation of hexane extract from *C. baccata* against *L. (L.) infantum* promastigotes. The obtained results suggest that epimeric mixture at C-3 of tetraprenyltoluquinol derivatives **1** and **2** could be, at least in part, responsible for the antiplasmodial activity observed on crude extract.

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