

An Endophyte of *Amphipterygium adstringens* as Producer of Cytotoxic Compounds

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Abstract : A bioassay-guided study for anti-cancer compounds from endophytes of the Mexican medicinal plant *Amphipterygium adstringens* resulted in the isolation of a streptomycete capable of producing a group of compounds with high cytotoxic activity. Microorganisms from surface sterilized samples of various sections of the plant were isolated and all the actinomycetes found were evaluated for their potential to produce compounds with cytotoxic activity against cancer cell lines MCF7 (breast cancer) and HeLa (cervical cancer) as well as the non-tumoural cell line HaCaT (keratinocyte). The most active microorganism was picked for further evaluation. The identification of the microorganism was carried out by 16S rDNA gene sequencing, finding the closest proximity to *Streptomyces scabrissporus*, but with the additional characteristic that the strain isolated in this study was capable of producing colorful compounds never described for this species. Crude extracts of dichloromethane and ethyl acetate showed IC₅₀ values of 0.29 and 0.96 µg/mL for MCF7, 0.51 and 1.98 µg/mL for HeLa and 0.96 and 2.7 µg/mL for HaCaT. Scaling the fermentation to 10 L in a bioreactor generated 1 g of total crude extract, which was fractionated by silica gel open column to yield 14 fractions. Nine of the fractions showed cytotoxic activity. Fraction 4 was chosen for subsequent purification because of its high activity against cancerous cell lines, lower activity against keratinocytes. HPLC-UV-MS/ESI was used for the evaluation of this fraction, finding at least 10 different compounds with high values of m/z (≈588). Purification of the compounds was carried out by preparative thin-layer chromatography. The prevalent compound was Steffimycin B, a molecule known for its antibiotic and cytotoxic activities and also for its low solubility in aqueous solutions. Along with steffimycin B, another five compounds belonging to the steffimycin family were isolated and at this moment their structures are being elucidated, some of which display better solubility in water: an attractive property for the pharmaceutical industry. As a conclusion to this study, the isolation of endophytes resulted in the discovery of a strain capable of producing compounds with high cytotoxic activity that need to be studied for their possible utilization.

Keywords : amphipterygium adstringens, cytotoxicity, streptomyces scabrissporus, steffimycin

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