10th Brazilian Conference on Natural Products
XXXVI RESEM
4-7 November 2025, Belo Horizonte, MG, Brazil
Section: 05

BIOACTIVE NATURAL PRODUCTS FROM A *Melipona quadrifasciata* ASSOCIATED *Streptomyces* sp.

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Microorganisms associated with social insects are valuable sources of bioactive natural products, particularly actinobacteria engaged in defensive mutualistic symbioses. Despite their ecological importance as pollinators, the microbiomes and symbiotic interactions of stingless bees remain underexplored, especially in *Melipona quadrifasciata*. This study aimed to characterize the metabolites produced by *Streptomyces* sp. MQFBRP26, isolated from forager bees, and assess its bioactive potential. The strain was cultivated on solid ISP2 medium and subjected to overlay soft-agar antagonism assays against entomopathogens (*Beauveria bassiana*, *Metarhizium anisopliae*, *Paenibacillus larvae*) and human pathogens (*Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Candida albicans*), showing activity against *S. aureus* and *P. larvae*. For large-scale cultivation (350 Petri dishes, 90 mm), the culture was extracted with ethyl acetate and fractionated using C18 SPE cartridges with a solvent gradient of H_2O, MeOH/H_2O mixtures (25%, 50%, 75%, 100%), and acetone. The fractions were evaluated for antimicrobial activity and cytotoxicity against tumor cell lines. Active fractions were chemically profiled using HPLC-DAD-ELSD and HPLC-MS/MS, and dereplication employed GNPS and the Dictionary of Natural Products and Natural Products Atlas databases. The fractions showed significant cytotoxicity against HCT-116, SK-MEL-28, and MCF-7 cell lines (IC_{50} 0.014–0.045 µg/mL) and antimicrobial activity against seven bacterial strains, including *Staphylococcus epidermidis, Staphylococcus aureus* (two strains)*, Enterococcus faecalis, Enterococcus faecium, Escherichia coli,* and *Acinetobacter baumannii* (MICs 8–512 µg/mL). Dereplication of the MeOH 75% and 100% fractions revealed quinoxalines, including annotations of quinomycins A, B, C, E, G, triostin C, and depsipechinoserin, as well as ions consistent with putative novel analogs. The MeOH 100% fraction was selected for isolation, yielding six compounds, two identified as quinomycins A and C, supporting the dereplication data. Additional chromatographic bands exhibited UV-Vis spectra similar to quinomycins A and C, but at low concentrations. The OSMAC strategy will be applied to modulate culture conditions and optimize metabolite production. These results highlight *Streptomyces* sp. MQFBRP26 as a promising source of bioactive quinoxalines with potential antimicrobial and anticancer applications, while improving understanding of defensive symbioses in *M. quadrifasciata*. The authors thank their institutions and acknowledge financial support from CNPq (grant 141619/2023-6), CAPES (Finance code 001) and FAPESP (grants 2013/07600-3; 2025/10223-4).

Keywords: *Streptomyces, Melipona quadrifasciata, quinoxalines, natural products, symbiosis, cytotoxicity*