10th Brazilian Conference on Natural Products
XXXVI RESEM
4-7 November 2025, Belo Horizonte, MG, Brazil
Section: 07

SEMISYNTHESIS AND BIOLOGICAL ACTIVITIES OF PALITANTIN DERIVATIVES

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Palitantin is a secondary metabolite first isolated in 1936 from cultures of *Penicillium palitans*. It exhibits moderate antiparasitic and antifungal activities, and it is a potent inhibitor of acetylcholinesterase. However, synthetic derivatives of this compound have never been described, mainly due to the low overall yield (≤25%) obtained by multistep total syntheses. In this study, we aimed to produce (+)-palitantin by a fermentative approach using the fungal strain *Penicillium* sp. (AMF1a), which provided a yield of approximately 160 mg/L, and to explore, through semisynthesis, the generation of new bioactive derivatives by reactions of palitantin with nitrogen nucleophiles, as well as to develop an efficient methodology for the reduction of imine derivatives of palitantin. A total of 2.5 g of (+)-palitantin was isolated from 10 L of 2% malt medium produced by *Penicillium* sp AMF1a. Five imine derivatives of palitantin were obtained: three hydrazones, one sulfonyl hydrazide, and one oxime in yields of 73.1%, 83.4%, 88.3%, 75.7% and 90.4%, respectively. Several reductive conditions were evaluated. Purification methodologies are currently under optimization prior to assessing the biological activities of these derivatives, including antiplasmodial, anti-*Leishmania* spp., anti-*Trypanosoma cruzi*, antibacterial, and cytotoxic assays. All these results will be presented and discussed.

Financial support: FAPESP, CAPES and CNPq.

Keywords: *Semisynthesis, (+)-palitantin derivatives, selective reduction of imine derivatives, fungal metabolite.*