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Clindamycin fungal biotransformation aimed analogues with pharmacologic potential

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Microbial biotransformations are low cost, rapid and an efficient alternative that uses the enzymatic machinery of a microorganism to catalyze stereo and region-selective reactions for structural changes, aiming new molecules for therapeutic uses [1]. Despite recent medicinal chemistry advances, few antimicrobials were found, while new drug-resistant strains have emerged. Clindamycin (**1**), belongs to the lincosamide class. This drug inhibits the protein synthesis of gram-positive bacteria that express *mef* gene, however shows low efficacy on pathogens where *erm* gene is over-expressed (e.g. *S. pneumoniae*). Therefore, biotransformations of this drug might be used to obtain new clindamycin analogues, and thus new compounds for chronic infections treatment. For the biosynthetic process, we used the filamentous fungi *Rhinocladiella similis* initially incubated in three flasks filled with 250 mL of sterile Potato Dextrose Agar (PDB), at 35ºC under 120 rpm, one week. After filtering the mycelium was re-incubated with a poor sucrose source solution with a phosphate buffer medium (pH 7), during 144 hrs. and 50mg of clindamycin were added to the solution. After the incubation period, the broth was filtered and extracted with ethyl acetate, dried at low pressure, furnishing a crude extract. This extract was analyzed by HPLC-DAD and then by semi-preparative HPLC for isolation of the biotransformation products. We discovered six clindamycin analogues: clindamycin sulfoxide (**2**) and five diastereoisomers (**3**-**7**) whose structure was elucidated by means of one and two-dimensional NMR and HR-ESI-MS. The antimicrobial-test using resistant and sensitive strains is being currently evaluated as well as for cytotoxicity, using HCT-116 (colon-rectal carcinoma) and MCF-7 (breast adenocarcinoma).

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