Unlocking New Antibacterial Agents: Rare Actinobacteria from the Caatinga as Bioactive Hotspots

MATHEUS LUCAS SANTOS ROCHA[1], GABRIELA BRITO DUARTE[1], RAYSSA RODRIGUES DOS SANTOS[1], ARIANE FERNANDES FERREIRA SILVA[1], LUIZ GUSTAVO VIEIRA OLIVEIRA [1], DINO ADLER QUEIROZ SILVA[1], FELICE SOARES ROCHA[1], AMANDA OLÍMPIA DA SILVA[1], **LAÍS OLIVEIRA LEITE**[1], JOÃO MOREIRA DE MATOS NETO[1], JOSÉ LUCAS SOUSA DE ANDRADE[1], ARIEL DE FIGUEIREDO NOGUEIRA MESQUITA[1], LEONARDO LIMA BANDEIRA[1], CLAUDIA MIRANDA MARTINS[1], SUZANA CLAUDIA SILVEIRA MARTINS[1]

[1.] UNIVERSIDADE FEDERAL DO CEARÁ, FORTALEZA / CE, BRASIL

Antibacterial resistance remains one of the most critical challenges to global public health, intensifying the search for novel bioactive compounds capable of combating multidrug-resistant microorganisms. Actinobacteria have gained attention due to their remarkable biosynthetic capacity, producing a wide array of secondary metabolites with significant pharmaceutical and biotechnological potential. The phylum represents one of the largest phyla in the Bacteria domain, with the *Streptomyces* genus being the largest among them and standing out for its ability to synthesize diverse bioactive molecules, including antibacterial, antifungal, antiviral, immunosuppressive, and antitumor agents. At the same time, the exploration of new phylogenetic groups of bacteria and new ecological niches is becoming a powerful trend in the natural product discovery field. Although the genus *Streptomyces* is more prominent in the general literature, the so-called rare actinobacteria, which comprise morphologically and phylogenetically distinct genera, emerge as promising sources for the discovery of new bioactive compounds, as they are less explored and possess possible unknown mechanisms, such as pathways for the production of metabolites with antimicrobial activity. In this context, the present work aimed to isolate and characterize the antimicrobial potential of 16 strains of rare actinobacteria, designated as AU, from soil samples of the Caatinga biome in the semi-arid Northeast of Brazil. Initial screening of antimicrobial activity using the cross-streak technique with the pathogens *Staphylococcus aureus* (ATCC 25923), *Salmonella enterica* (ATCC 14028), and *Klebsiella pneumoniae* (ATCC 10031) revealed that four of these strains (AU-1, AU-2, AU-8, and AU-11), corresponding to 25% of the total, exhibited a promising inhibitory profile. These strains were then subjected to a fermentation assay under standard conditions and in co-culture, with subsequent collection of their cell-free supernatants (CFSs), obtained by centrifugation of the fermented broths. The collected CFSs were re-evaluated for their antimicrobial potential using the well diffusion method – a more specific step, where only strains AU-2 and AU-8 maintained their antimicrobial activity, with AU-2 demonstrating a notable broadening of its spectrum of action against the tested pathogens. The findings of this study confirm that the Caatinga biome is a promising hotspot for the discovery of rare actinobacteria with significant biosynthetic capacity. The selection of the AU-2 and AU-8 strains, after rigorous screening, highlights the feasibility of isolating bioactive compounds from less explored genera of the order Actinomycetales. In particular, the robustness of the AU-2 strain against different pathogens positions it as a high-value biological model for future biotechnological investigations. This work therefore contributes to strengthening the pharmacognosy of natural products, pointing the way to the isolation of new chemical entities capable of mitigating the global impact of bacterial resistance.

Agradecimentos: