Inhibition of WHO Critical Priority Multidrug-Resistant Pathogens by Cutaneous Bacteria of *Phyllomedusa distincta* (Anura: Phyllomedusidae)

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The worldwide dissemination of WHO critical priority pathogens exhibiting a multidrug-resistan (MDR) profile to clinically relevant antibiotics is a serious public health problem that deserves the investigation of new antimicrobials agents. In this regard, the potential of cutaneous microbiota to inhibit pathogenic bacteria have been shown for many vertebrate species. Therefore, microbial symbionts of the amphibian skin could be a source of antimicrobial metabolites against WHO critical priority pathogens. In this study, we isolated skin bacteria from *Phyllomedusa distincta*, an endemic Brazilian amphibian, and evaluated their inhibitory activities by using a modified double-layer method, against international clones of extended-spectrum beta-lactamase (CTX-M)- and/or carbapenemase (KPC-2 and NDM-1)-producing Enterobacterales, and metallo-beta-lactamase (SPM-1)-producing *Pseudomonas aeruginosa*, isolated from hospital infections. Strikingly, seven skin bacterial strains identified as *Pseudomonas* spp., *Enterobacter* spp., and *Serratia* spp. showed inhibitory activity against *P. aeruginosa* SPM-1 (clone ST277), *P. aeruginosa* VIM-2 (clone ST233), *Klebsiella pneumoniae* IMP-1 (clone ST442), *K. pneumoniae* KPC-2 (clone CC258), *Escherichia coli* NDM-1 (ST155), and *E. coli* CTX-M (ST4012). Interestingly, *P. distincta* used in this study were not colonized by *Batrachochytrium dendrobatidis*, the main fungal species causing fatal infection in amphibian hosts, supporting that skin colonization represent an unspecific host defense against fungal and bacterial pathogens. In summary, we report for the first time the inhibitory potential of metabolites produced by skin bacteria from *P. distincta* against WHO critical priority MDR pathogens, highlighting a clinical potential that deserves further investigation.

Keywords: *Phyllomedusa distincta*, bacteriocins, multidrug-resistant bacteria, critical priority pathogens,

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