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Egyptian Soil Isolate Shows Promise as a Source of a New Broad-spectrum Antimicrobial Agent Against Multidrug-resistant Pathogens

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Abstract : Multidrug-resistant (MDR) pathogens pose a global threat to healthcare settings. The exhaustion of the current antibiotic arsenal and the scarcity of new antimicrobials in the pipeline aggravate this threat and necessitate a prompt and effective response. This study focused on two major pathogens that can cause serious infections: carbapenem-resistant Acinetobacter baumannii (CRAB) and methicillin-resistant Staphylococcus aureus (MRSA). Multiple soil isolates were collected from several locations throughout Egypt and screened for their conventional and non-conventional antimicrobial activities against MDR pathogens. One isolate exhibited potent antimicrobial activity and was subjected to multiple rounds of fractionation. After fermentation and bio-guided fractionation, we identified pure microbial secondary metabolites with two scaffolds that exhibited promising effects against CRAB and MRSA. Scaling up and chemical synthesis of derivatives of the identified metabolite resulted in obtaining a more potent derivative, which we designated as 2HP. Cytotoxicity studies indicated that 2HP is well-tolerated by human cells. Ongoing work is focusing on formulating the new compound into a nano-formulation to enhance its delivery. Also, to have a better idea about how this compound works, a proteomic approach is currently underway. Our findings suggest that 2HP is a potential new broad-spectrum antimicrobial agent. Further studies are needed to confirm these findings and to develop 2HP into a safe and effective treatment for MDR infections.

Keywords : broad-spectrum antimicrobials, carbapenem-resistant acinetobacter baumannii, drug discovery, methicillin-resistant staphylococcus aureus, multidrug-resistant, natural products
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