Potential therapeutic role of antimicrobial peptides against SARS-CoV-2 evidenced by computational analyses of peptide-protein interactions

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ABSTRACT

Introduction: The pandemic of coronavirus disease 2019 (COVID-19) poses critical challenges for the public health, research, and medical communities worldwide. While vaccines were made available at record speed, there remains the need to develop effective therapeutic agents. Therefore, we evaluated the potential pharmaceutical role of naturally occurring antimicrobial peptides (AMPs) against SARS-CoV-2 by studying their peptide-protein interactions through computational analyses. **Materials and methods:** Antimicrobial peptides from the antimicrobial peptide database (APD3) were considered and shortlisted based on stringent physicochemical properties. Promising AMPs were subjected to 3D structure predictions by ab initio modeling, and the peptide best models were selected based on their higher confidence score (C-score). Schrödinger Maestro's protein preparation wizard was used to prepare and optimize the modelled peptides' structure. The spike protein of SARS-CoV-2 and peptide-protein docking were evaluated using the Piper module. Additionally, protein-protein non-bonding interactions were assessed. Furthermore, the stability of the top complex was subjected to explicit molecular dynamics. The study was funded by Malaysian Fundamental Research Grant Scheme [[ref no. FRGS/1/2020/SKK0/UNIKL/02/1]. **Results and conclusion:** Of the shortlisted thirty AMPs, five potential peptides that efficiently bound to the spike protein were identified based on the lowest Piper energy scores – HD-5, Rat NP-4, Kalata B8, HFIAP-3, and Circulin D. These potential AMPs were further analysed by molecular dynamic simulations to verify the stability of the docked complexes, and HD-5 was observed to have robust interaction with the spike protein. Thus, the findings of the computational analyses highlight the antiviral potential of AMPs in inhibiting host cell entry of SARS-CoV-2 and could serve as anti-SARS-CoV-2 therapeutic candidates, and further future *in vitro* and *in vivo* experimental studies are warranted.