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Evaluation of Naturally Derived Peptides for Selective Anticancer Therapy

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Antimicrobial peptides (AMPs) are small, sequenced peptides that are abundant in nature and, act as an inhibitor against bacteria. Recently AMPs have been employed as cancer therapeutic agents and are called anticancer peptides (ACP), due to the biocompatibility and high specificity and selectivity between cancerous and non-cancerous cells. Nevertheless, pre-clinical screenings for such drugs are often costly and time-consuming to report such peptide drugs. To address these challenges, more efficient techniques have been developed, such as in silico methods, which are considered promising alternatives. The Gomesin and XLasp-P2 peptides were selected for further studies as an ACP. A naturally occurring peptide called XLasp-P2 was extracted from *Xenopus laevis* skin tissues, while Gomesin is a natural AMP derived from the *Acanthoscurria gomesiana* Brazilian spider. The Akt1 protein, known to play a pivotal role in cancer cell growth signaling, was identified as the target protein using the PharmMapper server. The Gomesin peptide's homology structure was retrieved from the Protein Data Bank (PDB) on the RCSB server, and XLasp-P2 was modelled with PEP-FOLD. The homology modeling of the Akt1 protein was conducted via the CHARMM-Gui web server using data from the UniProt database. Studies incorporating molecular docking were conducted using HADDOCK to determine the interaction between peptide inhibitors and Akt1. The results indicated that the binding regions of the peptide-protein complex are probably inhibited through allosteric inhibition. The dynamic motion behavior of the peptide-Akt1 complex was analyzed over 100 nanoseconds employing the NAMD web server. The findings demonstrated that the XLasp-P2 exhibited strong affinity and stability, suggesting its potential to effectively disrupt cancer growth signaling pathways. In parallel, wound healing remains a complex biological process involving a series

of intricate molecular and cellular events. This study focuses on the incorporation of electrospun cellulose acetate (CA) nanofibers loaded with XLasp-P2 that hold great potential as a therapeutic agent for enhanced wound healing. The XLasp-P2-loaded CA nanofibers were synthesized with three different loading percentages: 0.1 %, 0.2 %, and 0.3 % w/w. The nanofibers were characterized with Scanning electron microscopy (SEM) and Fourier-transform infrared spectroscopy (FT-IR) and evaluated for their antimicrobial potential using MTT assay and Agar overlay methods. In the in vitro release study during the 24 hrs, 87 % of the peptide was released which was approximately 5.2 mg; which more precisely matched the Higuchi square root model, according to the in vitro release research. The Agar overlay method exhibited, where *Escherichia coli* (ATCC 25922) and *Pseudomonas aeruginosa* (ATCC 27853) had moderate susceptibility with inhibition zones of 17.66 ± 0.38 mm and 17.44 ± 0.38 mm, respectively. In contrast, *Staphylococcus aureus* (ATCC 25923) and *Bacillus cereus* (ATCC 11778) showed promising responses with inhibition zones of 19.89 ± 0.69 mm and 23.00 ± 0.33 mm, respectively. Graphene oxide (GO) incorporated with XLasp-P2 was conducted for MTS assay as anticancer analysis for preliminary understanding. Meanwhile, peptide incorporated CA mat and GO holds great promise as an effective platform for delivering therapeutic peptides, offering a novel approach to both cancer therapy and wound healing.

Keywords:

Anticancer peptide, AKT1, Molecular docking, MD simulation, wound healing