

TITLE: CYTOTOXICITY AND ANTIMICROBIAL EFFECT OF ANALOGUES OF CATIONIC PEPTIDES

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ABSTRACT

Short peptides or analogues of peptides based in original cationic antimicrobial peptides have attracted attention because of their potentially low cost of production and optimization of their antimicrobial and immunological properties. The objectives of the study were to evaluate the cytotoxicity and inhibitory activity of analogues of cationic peptides on planktonic growth and biofilm of microorganisms associated with endodontic infections. L-929 fibroblast cells were exposed to serial dilutions of peptides LL-37, hBD-3-1C^V and KR-12-a5 and cell metabolism was evaluated using MTT assays. Minimal inhibitory concentration (MIC) and minimal lethal concentration (MLC) of peptides and controls (Chlorhexidine – CHX) were determined for *Streptococcus mutans*, *Actinomyces israelii*, *Enterococcus faecalis*, *Candida albicans*, *Fusobacterium nucleatum* and *Porphyromonas gingivalis*, using the microdilution method, after 4, 24, 48, or 72h. *E. faecalis* and *F. nucleatum* biofilms were exposed to 5X and 10X MLC of the best antimicrobial peptide analogue and analyzed using CFU/mL counts and Confocal Laser Scanning Microscopy (CLSM). LL-37 and hBD-3-1C^V affected cell metabolism at concentrations above 500µg/mL and KR-12-a5 above 250µg/mL. KR-12-a5 had the best MIC/MLC values against all microorganisms and both periods of exposure. *E. faecalis* and *C. albicans* growth was affected only for KR-12-a5 and CHX. hBD-3-1C^V and LL-37 had similar inhibitory effect against *S. mutans* and *A. israelii*. KR-12-a5 reduced *E. faecalis* growth in biofilm assays, with results similar to CHX. KR-12-a5 and CHX killed 100% of *F. nucleatum* biofilm. Considering CLSM analysis, KR-12-a5 significantly reduced viable cells inside dentin tubules similar to CHX. KR-12-a5 had superior inhibitory activity when compared to another peptides and showed anti-biofilm activity similar to CHX, causing minimal toxicity to fibroblast cells. KR-12-a5 is a potential antimicrobial agent and could be used for endodontic applications.

Keywords: Biofilms; Cationic Antimicrobial Peptides; Cell Culture; Confocal Microscopy; Microbial Sensitivity Tests.

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