ANTIMICROBIAL PEPTIDE COATING METHODS FOR TITANIUM DENTAL IMPLANTS

A Live Brief Project in Cooperation with TestLabs

Created & Presented by: Valentine Aneke, Monika Diglyte, Mohammad Awan & Sozyar Jamil.

Anglia Ruskin University

1 INTRODUCTION

Here we discuss the application methods of Antimicrobial Peptides (AMP's) to titanium dental implants and their limitations. Peri-implantitis is a common issue faced by dentists, which is an infectious disease caused by bacteria, the most common one know as *Staphylococcus aureus* (Sahrmann *et al.*, 2020). Peri-implantitis causes inflammation of soft tissues around the tooth, that results in bone loss around the osseointegrated implant (Prathapachandran and Suresh, 2012).

Antimicrobial peptides (AMP's) are minute proteins that are naturally generated by a variety of organisms, including humans, to combat microbial infections. These peptides interact with the negatively charged bacteria cell membrane which results in the death of bacteria and the growth of an extensive range of microorganisms (Lei *et al.*, 2019). AMP's inhibit bacterial cell division by inhibiting DNA replication and DNA damage response mechanisms, this blocks the cell cycle and causes potential loss of chromosomes (Huan *et al.*, 2020).

In comparison to conventional antibiotics, AMP's have a more comprehensive range of activity, which makes them a hopeful substitute. Additionally, they are less prone to inducing the emergence of antibiotic-resistant bacterial strains, which makes them a viable and effective long-term solution for microbial infections (Lei *et al.*, 2019).

2 APPLICATION

Dental implant AMP coating techniques vary in their goals of improving osseointegration and surface resistance to bacterial colonization (Angelo Michele Inchingolo *et al.*, 2023).

Application methods for titanium dental implants:

- **Metal peptide binding sequences:**
  - A peptide is modified to be able to attach to a substrate (Drexelius and Neundorf, 2021).
  - A bifunctional peptide that contains a titanium-binding domain that has a function to recognize and bind with a high affinity to the titanium implant surface, fused through a rigid spacer domain with an antimicrobial domain (Wisdom *et al.*, 2020).
  - Modified AMP is applied onto titanium surface by incubation (Drexelius and Neundorf, 2021).
- **Covalent peptide linker layers:**
  - This method introduces chemical linkers that are coated onto the titanium and acts like an anchor to the AMP by covalently linking (Sun *et al.*, 2023).
- **AMP's infused hydrogels:**
  - Antimicrobial Peptides are inserted into matrix from which AMP's are released over time.

3 LIMITATIONS

Overall disadvantages of antimicrobial peptide coatings:

- AMP's have a complex structure, making them expensive to fabricate. (Esteves *et al.*, 2022).
- Few studies have been performed to evaluate the safety of their use (Singha *et al*, 2017).
- AMP's are known to lead to hemolytic activity (Lei *et al.*, 2019).
- Tendency to be non-stable with a short half-life (Lei *et al.*, 2019).
- A more complex mode of testing may need to be developed as the current testing for AMP's involves testing on simple cell organisms rather than complex ones (Drexelius and Neundorf, 2021).
- AMP's are susceptible to protease hydrolysis, this means that proteases inhibit the effects of AMP's (Drexelius and Neundorf, 2021).
- Metal ions can have a negative effect on AMP's as interactions with them can lead to the destruction of their alpha helix structure (Drexelius and Neundorf, 2021).

Disadvantages of the 3 application methods for titanium dental implants:

- Metal peptide binding sequences:
  - The modified AMP is less stable in biological surroundings and could potentially cause side effects due to cytotoxicity (Drexelius and Neundorf, 2021).
- Co-electrospinning AMP with Polymers:
  - Two step approach and therefore more time consuming (Drexelius and Neundorf, 2021).
  - The peptides must be modified with groups that allow covalent binding to the surface of titanium (Drexelius and Neundorf, 2021).
- AMP infused hydrogels:
  - Long preparation and application time (Copling *et al.*, 2023).

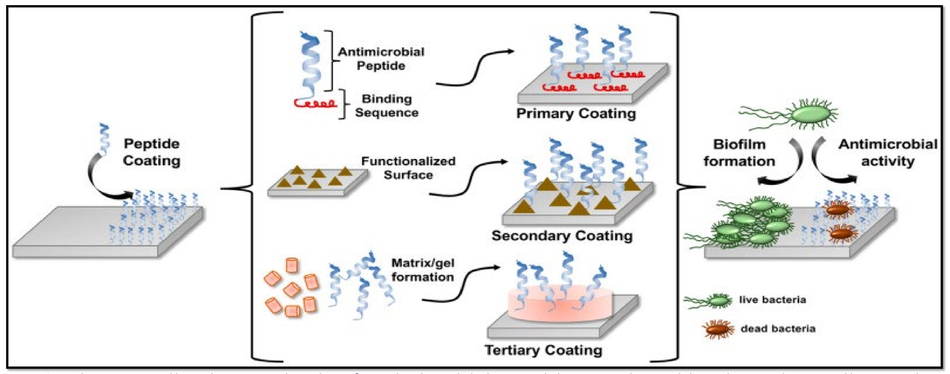

Figure 1: Three application methods of antimicrobial peptides on dental implants (Drexelius and Neundorf, 2021).

4 BENEFITS

- **Overall benefits of using Antimicrobial peptides for coating dental implants:**
  - AMPs are perfect for use as implant coating materials due to their wide-ranging antibacterial action and lack of potential to cause bacterial resistance (Sun *et al.*, 2023).
  - Help with osseointegration, meaning the bone growth will grow into the implant creating a functional connection between the surface of a dental implant and the living bone in the jaw (Parithimarkalaignan and Padmanabhan, 2013).
- **Metal peptide binding method of application complements the compatibility with the coating technique and its use:**
  - Almost a 100% binding to the surface of titanium even if the area is already contaminated (Wisdom et al., 2020).
  - Ability to withstand regular teeth brushing with a widely available electric toothbrushes (Wisdom et al., 2020).
  - Antimicrobial properties on the surface of the implant if bacterial colonization occurs (Wisdom et al., 2020).
  - The ability of the bifunctional peptide application to new and existing previously placed implants, to minimize bacterial colonization against peri-implantitis (Wisdom et al., 2020).
- **Covalent peptide linker layers:**
  - This method is low cost and effective in killing bacteria longevity (Drexelius and Neundorf, 2021).
- **AMP's infused hydrogels:**
  - The antimicrobial activity is provided to the surface but also within the surrounding tissue (Drexelius and Neundorf, 2021).
  - The antimicrobial peptides are controllable over time, so the concentration of AMP's is monitored and less likely to cause cytotoxicity (Drexelius and Neundorf, 2021).
  - Effectively killing gram-positive and gram-negative bacteria (Copling *et al.*, 2023).
  - Enhances wound healing (Copling *et al.*, 2023).

5 CONCLUSION

The purpose of this research was to investigate methods of application for antimicrobial peptides onto titanium dental implants, and how their advantages and disadvantages outweigh each other to limit the likelihood of peri-implantitis and increase the success rates of dental implant procedures.

All three application coating methods researched have great antimicrobial properties for all types of bacterial. However, antimicrobial peptides have a short life therefore, other infections could still occur at later stages after dental implantation. AMP infused hydrogels are less likely cause cytotoxicity and cause the patient harm unlike the other two methods, because the Antimicrobial peptide release is controlled. AMP infused hydrogels also enhance would healing, which could aid the patient's recovery time.

There is still further research pending into improving these methods in the long run. Primarily, investigating cytotoxicity and how that can be avoided and the possibility of improving antimicrobial peptide life span.

6 REFERENCES