

 <p>UniSR Università Vita-Salute San Raffaele</p>	<p>APPLICATION TO ACT AS SUPERVISOR AND RESEARCH PROJECT PROPOSAL</p>	<p>MO 20-5 ed. 01 del 21/02/2025 PO 20 Page 4 of 10</p>
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PROJECT

Supervisor: ROTUNDO ROBERTO

Title: DENTAL BIOCHEMISTRY

Curriculum: CLINICAL AND EXPERIMENTAL MEDICINE

Link to the personal page of the University or relevant hospital site website: <https://www.unisr.it/docenti/r/rotundo-roberto>

Description of the Project (max 3,000 characters including spaces)

Background/gap of knowledge

Dental biochemistry is aimed to study the biochemical processes and molecular interactions that occur within the oral cavity and impact dental health. It combines principles from biochemistry, molecular biology, and dentistry to understand the chemical composition of saliva, enamel, dentin, oral soft tissues and their behavior in contact with other external agents. Within these agents, particular attention has been shown toward oral antiseptics. Chlorhexidine (CHX) is a broad-spectrum antimicrobial biguanide used as a topical antiseptic (mouthwash) in dentistry. Its bacteriostatic effect is induced by the adsorption and prolonged release of CHX from oral surfaces. It carries activity against a broad range of pathogens including bacteria, yeasts, and viruses. CHX destroys the integrity of the cell membrane and can penetrate into the cell, causing leakage of intracellular components and cell death. However, some recent studies reported that CHX exerts potent cytotoxic effects on human gingival/periodontal tissues, such as gingival fibroblasts, gingival epithelial cells, periodontal ligament cells, and on osteoblastic cells. It also reduces gingival fibroblast adhesion to fibronectin and prevents fibroblast attachment to root surfaces, interfering with periodontal treatment and regeneration procedures.

Rationale and hypothesis

Different CHX concentrations have shown varying degrees of clinical efficacy. However, to date, there is a paucity of information defining the effects of non-lethal doses on the phenotype of human gingival fibroblasts, considering also its dilution in the saliva. The hypothesis is that there is a cut-off concentration value able to inhibit or reduce cellular proliferation and protein production.

Objectives and specific aims



The aim of the present PhD project is to investigate the characteristics of CHX as oral antiseptic in vitro and in vivo. Its combination with other agents, such as N-acetyl cysteine (NAC) and Hyaluronic Acid (HA), may represent a promising alternative to avoid or reduce the negative impact on wound healing process, but maintaining its antimicrobial characteristics. The in vitro investigation will allow us to better identify a threshold value of concentration between its negative and positive effect tested on human gingival fibroblasts. For this purpose, different dilutions will be tested. The in vivo investigation, set as a randomized clinical trial, will focus on wound healing processes analyzed after a routine dental surgery.

Expected outcomes

The use of CHX+NAC+HA, diluted at a defined concentration, would represent the most suitable combination of chemical agents used as mouthrinse product. To ensure the clinical relevance of this project and to effectively evaluate the biocompatibility and potential cytotoxicity of CHX, the average concentration of CHX in the oral cavity of a patient undergoing mouthwash therapy will be considered. To guarantee biological validity and eliminate stochastic effects on the results, a dose-response curve will be generated to monitor the effects of CHX on fibroblasts based on the dose.

Skills that the student should acquire (max. 600 characters including spaces):

A PhD student in dental biochemistry should acquire the following set of skills to succeed in both research and clinical applications:

- **Apply advanced Laboratory Techniques** to analyze biomolecules in oral tissues and fluids
- **Develop concepts of Molecular Biology** such as gene expression, protein function, and cellular pathways that influence oral health, enabling the design of experiments to investigate oral diseases at a molecular level.
- **Develop critical thinking and problem solving in clinical trials:** Ability to analyze complex biological problems, design clinical experiments, and interpret data to address issues in oral health and disease mechanisms.



References (max. 15)

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