RESEARCH
O&G Forum 2024; 34 – 2s: 526 - 530

OSTEOGENIC EVALUATION OF METAL NANOPARTICLES COATED TITANIUM IMPLANTS FOR BONE REGENERATION

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Abstract
Introduction : Infection and inflammation play a role in healing and soft tissue integration, which can lead to some dental implant therapy failures. When dental implants are surgically placed into the jawbones, a process known as osseointegration, which is the biological fixation of the implants, takes place. The long-term success of implant-supported prostheses is thought to depend on such a fixation. Nanotechnology advancements have given us solutions for bone tissue engineering. This study's objective is to assess the osseointegration capacity of titanium implants covered with CuO and ZnO for bone regeneration.
Materials and methods : CuO & ZnO NPs, Ti implant, osteogenic medium, RT-PCR for Run x2, ALP & Col-I expression
Results : The PCR results show that the expression of Run x2 and ALP were high in coated implant whereas they were low and equal in non coated implant and normal cells.
Conclusion : Run x2 has increased in coated implants and it also enhanced the proliferation of alkaline phosphatase (ALP) activity of osteoblast. Hence, metal coated implants are better over non coated implants to promote osseointegration.
Keywords : CuO & ZnO NPs, Gene expression, Osseointegration, RT-PCR, Ti implants

Introduction

Osseointegration was defined as a direct structural and functional connection between organized, live bone and the surface of a load-bearing implant. A process called as "biological fixation" occurs as soon as a dental implant is surgically inserted into the jawbones; this is when the implant permanently fuses to the jawbones. On such fixation, it is thought that implant-supported prostheses will succeed in the long run. (Elias 2011) Osseointegration, or the direct attachment of such implants to the surrounding host bone, is a reliable sign of titanium implant clinical success. Although endosseous dental implants frequently succeed, they do occasionally fail. Lack of primary stability, surgical stress, and infection seem to be the three main causes of early implant failure. (Wilson and Harrel 2020) Large bone lesions remain challenging to rebuild, necessitating creative strategies that integrate expertise from the domains of material science, biology, and tissue engineering in order to outperform the few existing methods. (Ahmed and Tomer 2021) Aseptic loosening and infections connected to the prosthesis can play a significant role in implant failure. Therefore, there is a pressing need to enhance the osseointegration and antimicrobial properties of orthopedic implants.

The engineering of bone tissue offers a crucial frontier in the domains of nanotechnology, materials science, and bone tissue given the complex architecture of this tissue. The development of artificial bone-like nanomaterials with customizable mineral concentrations, nanostructures, bone-specific chemistry, and substitutes for cartilage tissue has drawn increasing interest. (Piotto et al. 2017)

The focus of nanotechnology is on the physical, chemical, and biological properties of structures and their component pieces. Titanium dental implants have been successfully implanted in patients for many years, but they still have issues because of perfect osseointegration and the fact that they don't have the same mechanical properties as bone. Developments in the synthesis of nanoparticles for coating implant surfaces are enabling improvements in implant physiologic functions and osseointegration. (Chaughule 2018)

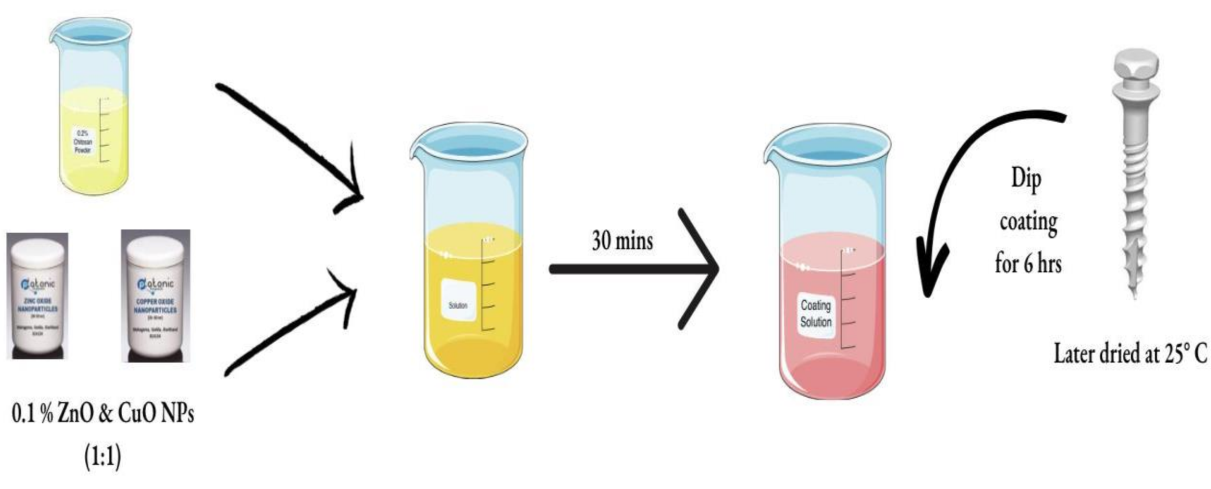
Numerous dental materials have been altered using metal nanoparticles (NPs) such as gold, silver, platinum, palladium, nickel, copper, zirconium, aluminum, titanium, chromium, beryllium, boron, and zinc. Among other metals, zinc and copper have attracted a lot of attention in medicine due to their biological effects. Zinc oxide nanoparticles (ZnO NPS) have been the subject of numerous studies to better understand their outstanding antibacterial, antifungal, electrical, chemical, and optical properties. Recent studies have demonstrated that ZnO nanoparticles are non-toxic to human cells at the same concentration at which they are fatal to bactericidal cells. (Kishen 2015)

The biocompatibility, corrosion resistance, and antibacterial properties of CuO NPs are well documented. Both ZnO and CuO NPs are easily manufactured using a variety of methods, and they are also claimed to be potentially more biocompatible than many other metal oxides. (Sadasivuni et al. 2019) In this research, we evaluate the osseointegration potential of CuO & ZnO Nanoparticles coated Ti implants for bone regeneration.

Materials & Methods

Study set up - The current study was carried out in Department ofForensic Odentology, Saveetha Dental College & Hospitals, Chennai.

Duration of the study - 3 months



1. Dip coating of CuO & ZnO nanoparticles on Ti implant
2. Assessment of osteogenic property of coated implants under osteogenic medium.
3. RT-PCR for RunX2, ALP & Col-I expression

Results

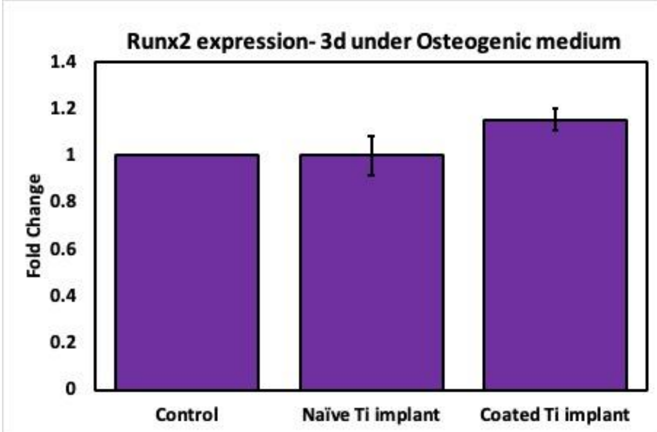


Fig.1. RunX2 Expression - 3D under Osteogenic Medium

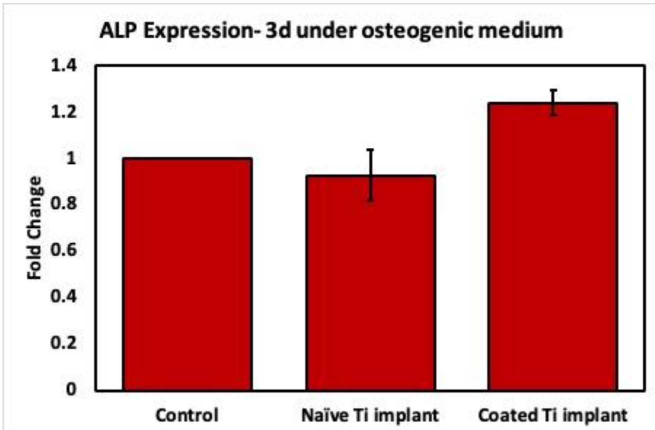


Fig.2. ALP Expression - 3D under Osteogenic Medium

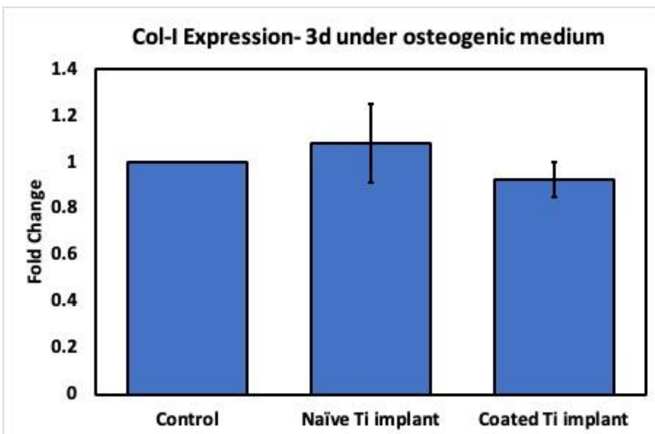


Fig.3. Col-I Expression - 3D under Osteogenic Medium

Discussion

Even without the assistance of additional composite materials, the adoption of a nZnO coating for future dental and orthopedic implants may promote better bone formation and create a device that is more biocompatible, osteoconductive, and antibacterial. In turn, this may contribute to the prevention of joint replacement failure brought on by aseptic loosening and infection and may significantly affect patient quality of life and expenses associated with revision treatments. This cutting-edge, multifunctional implant coating technique is probably about to start a crucial step of clinical testing. (Chaughule and Dashaputra 2020)

The appropriate substitutes that have been suggested as potential agents in preventing bio-film formation in the oral cavity are copper oxide (CuO) nanoparticles. The important elements that cause cell death, according to researchers, are the passage of Cu nanoparticles through the bacterial cell membrane and subsequent harm to the essential enzymes of bacteria. Additionally, it has been discovered that CuO nanoparticles limit bacterial development by passing through tiny pores found on the cellular membranes of the majority of bacteria. According to research findings, these nanoparticles are not harmful to the HeLa cell line. A literature review states that the size, stability, and concentration of Cu nanoparticles introduced to the growing media determines how bactericidal they are. (Taylor & Francis Group 2021)

CuO nanoparticles can be effective as a dental coating to prevent infections in the mouth. Using the zone of inhibition, they determined the antibacterial medicines' diffusibility from the CuO nanoparticles coated titanium dental implants to slow the development of test bacteria sown on plates. The zone of inhibition measurements (in millimeters) showed that copper oxide nanoparticles coated titanium dental implants had antibacterial activity against all of the test pathogens. For uncoated materials, the results showed no inhibitory zones, while titanium dental implants coated with CuO nanoparticles demonstrated large inhibitory zones. (Parnia et al. 2017)

Earth has a lot of chitin, a form of polycarbohydrate that is utilized to deacetylate and create chitosan. It is also possible to employ chitosan as a paper coating material and benefit from its advantages. Once more, it is viewed as a substitute polymer for synthetic materials in various industries. When used as a film material, its mechanical characteristics and selective permeability are advantageous against gases, however its low resistance to moisture is a drawback. (Tang et al. 2016)

SiC sheets were used to grind Ti implants one at a time. After cleaning the Ti substrates with ethanol for 10 minutes, they were sonicated for 10 minutes to deionize them. The Ti substrates underwent an alkali treatment by being submerged in a 5 M NaOH solution at 70 °C for 12 hours, and then were cleaned with ethanol and distilled water (the resulting specimens were dubbed Ti/OH). The chitosan employed in this study had an average molecular weight of 115 KD and a degree of deacetylation of 91.2% (Charming&Beauty CO.). The solution's pH was then raised to 5.5 by adding 0.1% NaOH solution after 2 mL of acetic acid and 2 g of chitosan powder were first dissolved in 100 mL of deionized water.

To get rid of any contaminants, the fluid was filtered. We bought ZnO and CuO powder from Platonic Nanotec Pvt. Ltd. that was almost spherical and had a diameter under 130 nm.

The aforementioned solution was combined with the ZnO and CuO powder in an equal ratio (1:1) using sonication for 0.5 hours and magnetic stirring for 5 hours at 25 °C. (Song TY et al)

Dip coating is a straightforward, traditional method of applying a homogeneous thin film of liquid for coating solidification to a substrate, particularly tiny slabs and cylinders. The basic flow is steady, and the rivalry between the forces of gravity, capillary (surface tension), and viscous flow determines the film's thickness. The characteristics of flow in the liquid bath and gas above can affect thickness and homogeneity. The film is deposited thicker the quicker the substrate is removed. Using volatile solutes and coupling rapid enough drying with the fundamental liquid flow helps combat this. (Scriven LE et al)

The chitosan or chitosan/ZnO-CuO solution was dip-coated onto the alkali-treated Ti implants for 6 hours before allowing them to dry at 25 °C.

For three days, osteogenic media was allowed to develop uncoated, coated, and normal cells without implants. In order to perform PCR to check for Run x2, ALP, and COL-I, mRNA and cDNA from the samples were taken.

Runx2 (AKA Cbf1), is a crucial regulator of osteoblast differentiation, which encourages preosteoblasts to develop into mature osteoblasts. Osteoblasts that have specifically lost Runx2 exhibit poor intramembranous ossification and postnatal bone formation. In the early stage of osteogenesis, when preosteoblasts commit to becoming osteoblasts by secreting alkaline phosphatase (ALP) and type I collagen (Col-I) and expressing the differentiation marker osteopontin (OPN), Runx2 regulates the expression of genes. In the later stage, when the mature osteoblast markers osteocalcin (OC), a calcium binding protein, bone sialo protein (BSP), and matrix metalloproteinase-13 (M The dynamic equilibrium between cartilage and cortical bone development is the fundamental requirement for bone growth. (Chou LY et al)

The PCR results show that Run x2 and ALP were high in coated implant whereas they were low and equal in non coated implant and normal cells. But there was no change at all in collagen.

Conclusion

The primary transcription factor for the expression of the bone mineralization gene is run x2. According to the findings, Run x2 did increase coated implants and it also increased osteoblast alkaline phosphatase (ALP) activity. Therefore, metal-coated implants are preferable to non-coated implants for osseointegration promotion.

Recommendations

It is yet uncommon to find clinical and in vivo information about these nano-size coatings and their advantageous applications. Future research should look into the long-term antibacterial effects of nanoparticles on dental and medical biomaterials, as well as their physical and clinical impacts.

These cutting-edge materials and production techniques offer better osseointegration as well as integrity, which makes them desirable for orthopedic applications.

Conflicts of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

Author contributions

All authors have equally contributed.

Acknowledgement

The authors would like to thank Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University for providing research laboratory facilities and the required equipment to carry out the study successfully.

Source of Funding

Kumaran Department Store
Saveetha Dental College and Hospitals
Saveetha Institute of Medical and Technical Sciences
Saveetha University

Ethical Clearance Number : Since it is an in vitro study, ethical clearance is not needed.

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