Optimizing Implant Safety: a Novel Approach With Antibiotic-Infused Hydroxyapatite/Porous Silica for Combating Infections and its Clinical Applications

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**Abstract:** In recent years, there has been a notable rise in implant infections among patients, primarily due to bacterial growth in the vicinity of bone tissue. In this study, composite ceramic materials were utilized to incorporate antibiotic drugs, aiming to combat bacterial infections. The presence of drug molecules was confirmed with and without loaded particles through UV-Visible spectrum analysis at 320 nm. The surface morphology of the drug-loaded particles revealed a matrix phase characterized by a porous granular structure. Analysis also confirmed the presence of silica and hydroxyapatite functional groups. The antibacterial efficacy was assessed using the zone of inhibition method, where the control group consisted of antibiotics. The composite material was tested at two different concentrations: 100 mg and 50 mg of sample. Both concentrations exhibited significant activity against S. aureus. Thus, the composite drug-loaded material demonstrates effective potential for treating infections at implantation sites.

**Keywords:** Drug, silica, Hydroxypatite, Dental infections

# Introduction

The demand for dental implants has surged in recent years due to advancements in dental technology, increasing aesthetic and functional expectations, and a growing elderly population [(Harsha & Subramanian, 2022)](https://paperpile.com/c/mMncsm/riak8)[(Deepika et al., 2022)](https://paperpile.com/c/mMncsm/C6beP)[(Solanki et al., 2022)](https://paperpile.com/c/mMncsm/VT9Hu). In India, the prevalence of edentulism is particularly high among older adults, largely due to factors such as poor oral hygiene, periodontal disease, and limited access to regular dental care[(Chidambaram et al., 2022)](https://paperpile.com/c/mMncsm/J1Eik).[(Ajay, Sasikala, et al., 2022)](https://paperpile.com/c/mMncsm/Ccclt). As people live longer and the importance of oral health becomes more widely recognized, dental implants have emerged as a preferred solution for restoring missing teeth, offering superior durability and function compared to traditional dentures[(Ajay, Rakshagan, et al., 2022)](https://paperpile.com/c/mMncsm/ldmPd). This has led to a significant rise in the number of dental implant procedures across the country, improving the quality of life for many patients by restoring their smiles and oral function[(Jabin et al., 2021)](https://paperpile.com/c/mMncsm/pzdcy)[(Balaji Ganesh S & Sugumar, 2021)](https://paperpile.com/c/mMncsm/ww1IA) [(Govindaraj & Dinesh, 2021)](https://paperpile.com/c/mMncsm/qWIvL).

However, with the increasing use of implants, there is also a corresponding rise in complications like post-surgical infections which remain a persistent concern [(Ajay, Suma, et al., 2022)](https://paperpile.com/c/mMncsm/YZ7Pi) [(Katyal et al., 2021)](https://paperpile.com/c/mMncsm/2V7YX). Peri-implantitis, in particular, a condition marked by inflammation and infection around the implant site has become a major concern. It can lead to bone loss, implant failure, and in severe cases, systemic infection [(Tiwari & Jain, 2023)](https://paperpile.com/c/mMncsm/j6lFp)[(Graf et al., 2023)](https://paperpile.com/c/mMncsm/fWJSB). The prevalence of implant-related infections has grown as more people receive implants, and bacterial biofilms on the implant surface can often be difficult to manage with conventional treatments[(Sabarathinam & Madhulaxmi, 2021)](https://paperpile.com/c/mMncsm/XzayR)[(Sushanthi et al., 2021)](https://paperpile.com/c/mMncsm/C6kkZ)[(Harsha et al., 2022)](https://paperpile.com/c/mMncsm/8xsYF). This highlights the urgent need for advanced solutions, such as antibiotic-loaded materials and bioactive surfaces, to prevent and combat bacterial infections at the implant site [(Neha et al., 2021)](https://paperpile.com/c/mMncsm/1Qy2m)[(Maliael et al., 2021)](https://paperpile.com/c/mMncsm/Iak7O)[(Lakshmi, 2021)](https://paperpile.com/c/mMncsm/Ma3vD). By incorporating antibacterial properties directly into the implant materials, the risk of infection can be minimized, thus ensuring the long-term success and safety of dental implants in the growing population of edentulous patients.Conventional methods to prevent implant infections primarily include stringent sterilization protocols, systemic antibiotic administration, and the use of antimicrobial mouthwashes or rinses [(Dharman et al, 2021)](https://paperpile.com/c/mMncsm/msaAk). Preoperative and postoperative antibiotics are commonly prescribed to reduce the risk of bacterial contamination at the implant site. While these measures can help lower the incidence of infections, they are not without limitations. Systemic antibiotics may contribute to antibiotic resistance, and their effectiveness is often limited to the early stages of healing. Additionally, these approaches do not address bacterial biofilm formation on the implant surface, a leading cause of peri-implantitis. Other drawbacks include the potential for adverse side effects from prolonged antibiotic use and incomplete bacterial eradication. As a result, there is an ongoing search for alternative solutions, such as antibiotic-loaded implant materials, bioactive coatings, and local drug delivery systems, which aim to provide more targeted and effective infection control while minimizing systemic complications.In an effort to address this issue, researchers have been exploring innovative solutions, one of the most promising being the use of antibiotic-loaded hydroxyapatite (Hap) and porous silica to reduce infections [(Anggraini & Wijaya, 2014; Arcos & Vallet-Regí, 2010)](https://paperpile.com/c/mMncsm/pKef+AH1E). This cutting-edge technique seeks to achieve a dual purpose: preventing bacterial colonization on the implant surface and promoting osseointegration, the crucial process that ensures the implant bonds effectively with the surrounding bone tissue [(Avcu et al., 2018, 2019)](https://paperpile.com/c/mMncsm/facC+xbH1). The composite material, consisting of hydroxyapatite—a calcium phosphate compound that closely mimics the natural mineral structure of bone—and porous silica, is designed to optimize antibiotic release while offering an ideal matrix for drug incorporation. This combination enhances both the sustained release of antibiotics and the overall effectiveness of the material in combating infections [(Baino et al., 2016; Balagna et al., 2012)](https://paperpile.com/c/mMncsm/RQf6+yjKX).Research and development in this field represent a significant leap forward in dental implantology. Clinical studies and ongoing research efforts aim to refine and optimize this technology continually. The ultimate objective is to improve the long-term success and safety of dental implant procedures by effectively preventing and treating infections. By employing antibiotic-loaded Hap/porous silica, this innovative approach holds the potential to revolutionize the field [(Avcu et al., 2019; Balagna et al., 2012; Cakir‐Omur et al., 2019)](https://paperpile.com/c/mMncsm/yjKX+xbH1+Iq2t). Patients who choose dental implants as their preferred tooth replacement method can look forward to a future where infections are less of a concern, ensuring both their continued comfort and good overall oral health [(Duraisamy et al., 2021)](https://paperpile.com/c/mMncsm/FlX5). Dental professionals, too, stand to benefit from this advancement, as it simplifies the management of post-implant surgical complications, ultimately leading to better outcomes and patient satisfaction [(Berendjchi et al., 2011; Besra & Liu, 2007)](https://paperpile.com/c/mMncsm/nCdw+AWSz). The aim of this study was to use composite ceramic materials for incorporating antibiotic drugs, with the goal of effectively combating bacterial infections in dental implants.

# Materials and Methods

## Preparation of Hydroxyapatite and silica composite drug

Using previously described protocols, orthophosphoric acid (H3PO4) solution and calcium hydroxide (Ca(OH)2) were combined to create synthetic hydroxyapatite (HA) via a standard aqueous precipitation reaction. To attain the required Ca/P molar ratio of 1.67, which corresponds to a phase-pure stoichiometric HA, the reactant concentrations were modified.To prepare samples of silicon-substituted hydroxyapatite (SiHA), a procedure similar to that described by Gibson et al. for hydroxyapatite (HA) was followed. In this method, silicon tetraacetate (SiAc; Si(CH3CO2)4) was introduced into the hydroxyapatite along with calcium hydroxide and an orthophosphoric acid solution, providing silicate ions. After incorporating Flagyl (100 mg) into the SiHA, the mixture was dried at 100 degrees Celsius. Subsequently, the sample was subjected to characterization studies.

## UV-Visible Spectrum

The UV-Vis spectra for drug and drug-loaded Hap with silica were obtained using a Shimadzu UV-2400 PC series spectrophotometer equipped with a 1 cm quartz glass cell and an opening width of 2.0 nm. The analysis was conducted within a wavelength range of 200-800 nm.

## Surface characterization studies

## Surface morphological analysis

The morphological structure of drug-loaded Hap /silica was examined using a Field Emission Scanning Electron Microscope, coupled with a JEOL Energy Dispersive X-ray Spectrometer (EDS) model (JSM-IT800 NANO SEM).

## FT-IR spectra

FT-IR studies were conducted to identify the functional groups in the gelatin film incorporating metal oxide. The analysis was performed using an Alpha II Bruker model spectrometer within the wave number range of 4000 to 5000 cm-1.

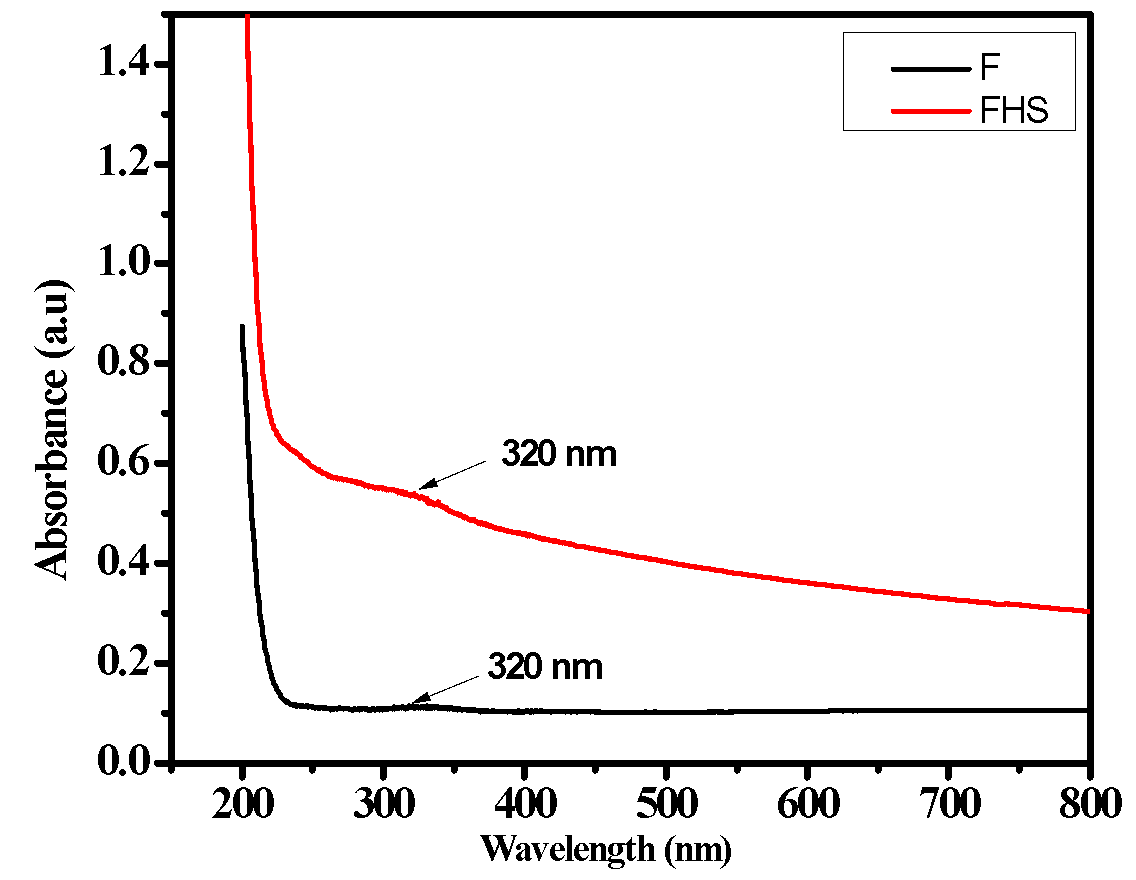
## Antibacterial activity

This study employed two types of bacteria: Gram-negative *Escherichia coli* and Gram-positive *Staphylococcus aureus*. The bacteria were sourced from frozen stock cultures and were shifted to Trypcase Soy Agar (TSA). Following this, the plates were incubated at 37 °C for 18–24 hours. Subsequently, the bacteria were transported to 50 mL of sterile Tryptic Soy Broth (TSB) solution and allowed to grow at 37 °C, 80 rpm for 18–24 hours. Before inoculation, the bacterial straining was subcultured into fresh TSB at a 1:50 ratio and incubated for 2 hours at 37 °C, 80 rpm

# Results

## UV-Visibile studies

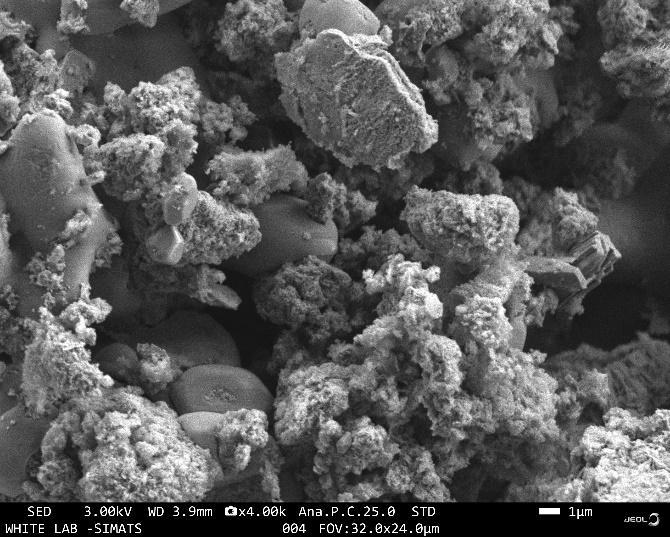
The UV-visible spectra analysis depicted in Fig. 1 reveals the presence of both the drug and the coated composite materials. The drug spectra were obtained by dissolving 200 mg of the drug in distilled water and examining it using UV-visible absorbance spectroscopy. A peak absorption at λmax of 320 nm confirmed the presence of the drug. The composite material, after being coated with the drug, exhibited no significant alteration in the λmax value (320 nm), indicating successful drug incorporation. Thus, the presence of the drug-loaded composite material was confirmed through UV-visible spectra analysis. In this study, the drug-loaded material demonstrated its potential as an antibiotic for biomedical applications. Further characterization studies focused on analyzing the drug-loaded composite materials.



**Figure 1.** UV-visible spectra of HAP/Silica with and without dopant Flagyl

## Surface topography analysis

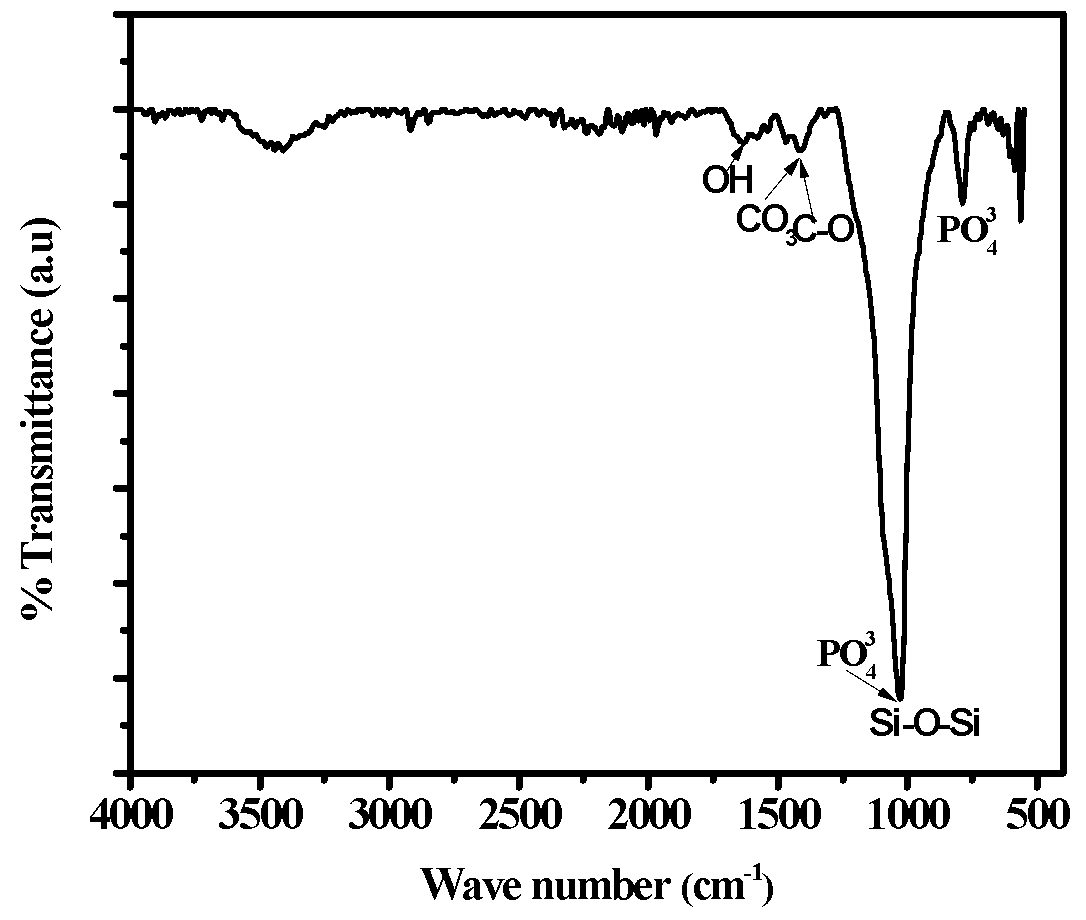
Figure 2 illustrates the surface morphology analysis of mesoporous silica with hydroxyapatite/flagyl composition. The analysis reveals the presence of a matrix phase characterized by porous granular features on the surface. The combination of hydroxyapatite and silica shows an interconnected surface with agglomerate platelets and porous granular structures. The formation of agglomerate-like structures is attributed to the drug coating process on the prepared surface. The porous nature of the surface also supports the nucleation of the tissue engineering osseointegration process.



**Figure 2.** SEM image of HAP/Silica with Flagyl

## FT-IR spectroscopic analysis

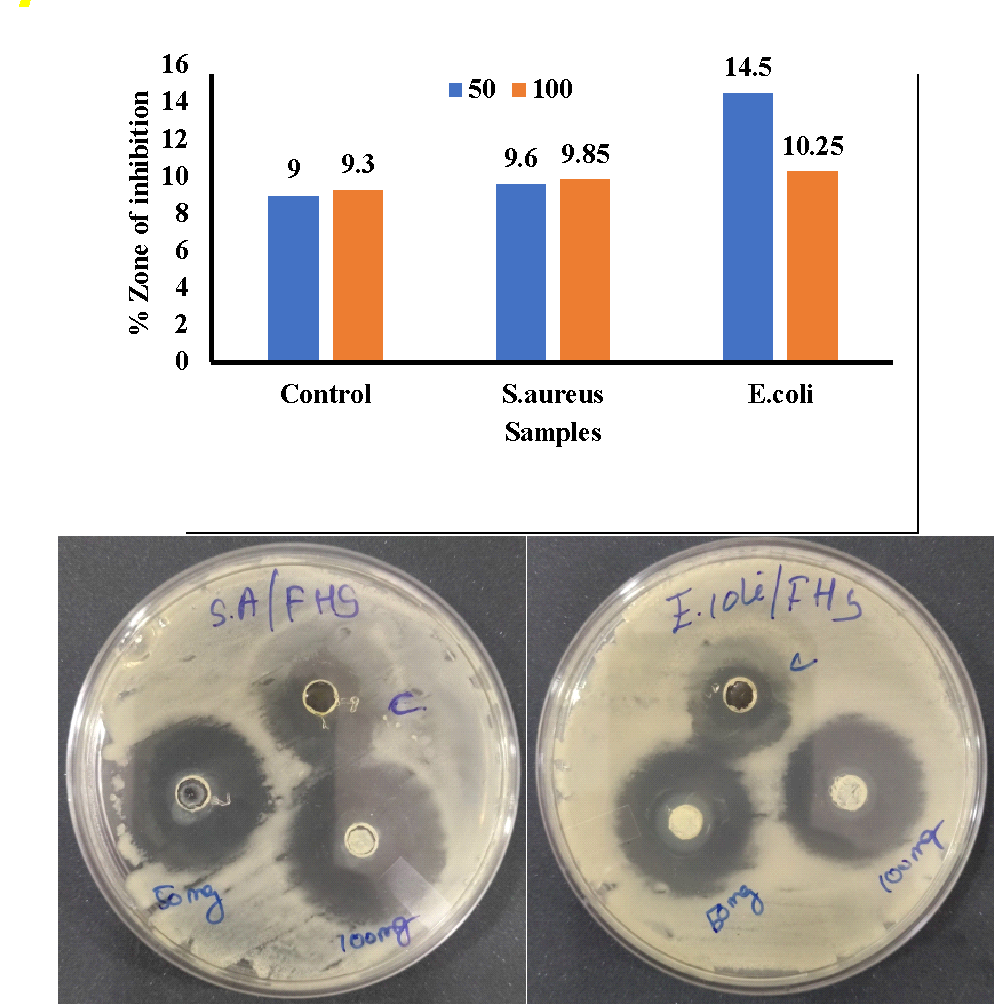
Figure 3 presents the FT-IR spectra analysis, displaying functional groups and chemical compounds within the range of 4000 to 400 cm-1. The spectra of the composite material show a peak around 3500 cm-1, indicating the presence of hydroxyl groups (OH). A stretching vibration band at 1022 cm-1 corresponds to Si-O-Si and phosphate (PO4) groups, overlapping with the silica network. Additionally, a ν3 vibration peak at 730 cm-1 signifies the presence of the phosphate group in hydroxyapatite, confirming the composite coating. The carbonate peak at 1430 cm-1 overlaps with drug molecules and is attributed to the C-O carboxyl group. A small intensity peak at 1645 cm-1 is assigned to water molecules. These findings confirm the presence of silica/hydroxyapatite-coated, Flagyl drug-loaded molecules in the composite coating.



**Figure 3.** FT-IR spectra of HAP/Silica dopant Flagyl

# Antibacterial studies

The antibacterial activity of the composite material was evaluated against Gram-positive (S. aureus) and Gram-negative (E. coli) bacteria, as shown in Fig. 4. The antibiotic served as a control, while test materials at two concentrations (50 mg and 100 mg) were incubated for 24 hours. The zones of inhibition were measured in millimeters (mm). Fig. 4a displays the zone of inhibition percentages compared to the control. For Gram-positive bacteria, the 50 mg and 100 mg concentrations produced inhibition zones of 9.6 mm and 9.85 mm, respectively. For Gram-negative bacteria, the inhibition zones were 14.5 mm and 10.25 mm for the 50 mg and 100 mg concentrations, respectively. These results indicate that S. aureus had lower activity compared to E. coli, likely due to the bacteriostatic interaction of the drug-loaded material, which disrupts the bacterial cell wall, leading to cell death. The significant value was calculated using the ANOVA two-way method, with a p-value of <0.05. This indicates that the drug-loaded material is effective for use in implant applications.



**Figure 4**. Antibacterial activity of a) zone of inhibition percentage bar graph b) S.aureus c) E.coli HAP/Silica dopant Flagyl for the zone of inhibition

# Discussion

Infections are a common issue with implants and can lead to implant failure. To mitigate this, bioactive and antibacterial coatings have been proposed to reduce inflammation and infection. This study examines the use of silica and its composites for dental implants. Silica is effective for drug delivery due to its high surface area and biocompatibility.Tasnuva T. et al. demonstrated that mesoporous silica loaded with antibiotics can control drug release at implant infection sites. They created antibiotic-loaded silica films stable for up to three months to protect against bacterial infections. The study showed that amine-functionalized, drug-loaded silica nanoparticles were highly effective, reducing E. coli and S. aureus populations by about 80% in bacterial models. These findings suggest that mesoporous silica composites could significantly enhance the safety and effectiveness of dental implants by providing sustained antibacterial protection [(Tamanna et al., 2015; Yilmaz & Ozay, 2022)](https://paperpile.com/c/mMncsm/ycCF+OX6n).Carinci et al. observed that bacterial biofilm formation in the oral cavity and microbial activity around implant tissue can affect the interface between bone and implant, potentially causing inflammation and increasing the risk of mucositis and peri-implantitis. Their clinical trial aimed to investigate the bacterial quality of a new antibacterial coating on the internal chamber of implants over six months. The PIXIT implant (Edierre srl, Genova Italy) uses a coating made from an alcoholic solution containing polysiloxane oligomers and 1% chlorhexidine gluconate [(Carinci et al., 2019)](https://paperpile.com/c/mMncsm/xVHx).

The study involved 15 healthy patients (nine women and six men, aged 45–61, mean age 53), all non-smokers with no significant medical history, who received 60 implants for bilateral fixed prostheses or crown restorations. No adverse effects or implant failures were reported after four months. Soft tissue healing was satisfactory, and there was no local inflammation.Real-Time Polymerase Chain Reaction (PCR) analysis compared bacterial counts on coated versus uncoated implants. The coated implants had significantly fewer bacteria in the internal chamber (81,038 units/reaction) compared to uncoated implants (90,057 units/reaction) (p < 0.01). The chlorhexidine coating effectively controlled bacterial loading in the peri-implant tissue and influenced the quality of the microbiota, particularly targeting species associated with peri-implantitis and long-term implant failure.The silica incorporated hydroxyapatite influences modification of the phase structure properties and it enhances the bioactive molecules which can encapsulate drug molecules. Therefore, it is used for a better drug delivery system for implant infections (Rafi et al., 2024). In the earlier stage, the hydroxyapatite to mimic the osteoblast activity of the bone cells (17), which has incorporated the silica will act as a drug carrier molecule and function of bond bonding interface of composite material and host tissue (Tuluwengjiang et al., 2024). Our present work is compared with the above results which have observed the bacterial infection and treated it as an infection of dental implants.

The primary advantage of this approach lies in its ability to provide controlled and sustained antibiotic release directly at the implant site. This controlled release is essential for combating bacterial infections, especially during the critical early postoperative period when the risk of infection is at its highest. Additionally, the composite material possesses intrinsic properties that support bone regeneration and implant stability while acting as a physical barrier against bacterial adhesion. Furthermore, the composition can be tailored to the specific needs of individual patients, allowing for a personalized approach to implant infection prevention and treatment [(Balagna et al., 2012; Banga et al., 1995)](https://paperpile.com/c/mMncsm/55Qw+yjKX).

# Conclusion

In conclusion, antibiotic-loaded hydroxyapatite and porous silica were successfully fabricated and the results were summarized. The ceramic composite materials are loaded with antibiotic drugs to treat bacterial infections. The drug molecules were examined with and without loaded particles using UV-visible spectrum analysis at 320 nm. The presence of silica and hydroxyapatite was confirmed by the functional groups identified. The results indicated that S. aureus exhibited higher activity at both concentrations. Consequently, the composite drug-loaded material demonstrated effective utility in infection sites resulting in implantation. This technology offers a promising solution for treating and preventing infections, enhancing the overall success and safety of dental implant procedures, and improving the quality of life for patients seeking durable and natural-looking tooth replacements.

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