Kaempferol Biofunctionalized Gold Nanoparticles as an Effective Drug to Treat Dental Pathogen Streptococcus Mutans

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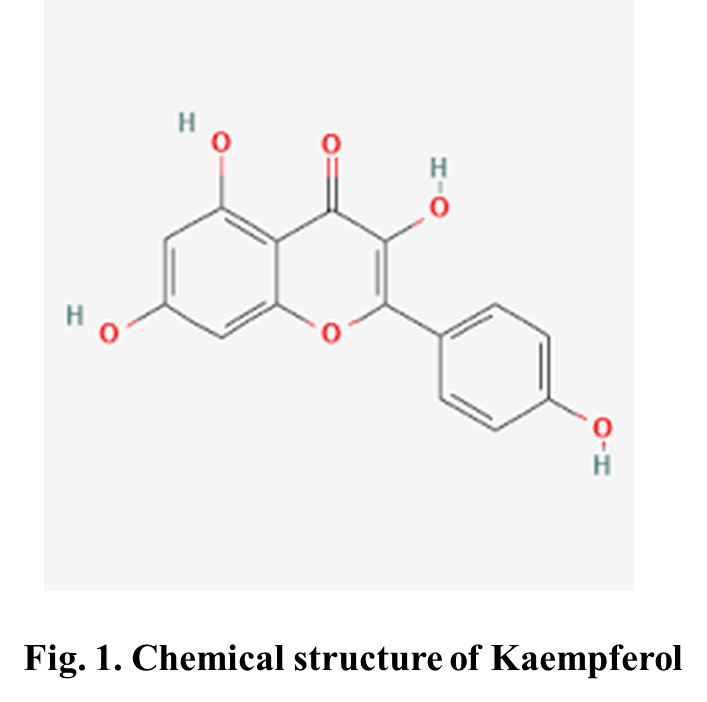
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**Abstract:** Dental infections, like dental caries and periodontal disease, are the most prevalent bacterial infections in humans, primarily caused by *Streptococcus mutans.* Conventional antimicrobial agents used in oral healthcare are often associated with resistance development, cytotoxicity, and limited efficacy. To overcome this issue, Kaempferol, a flavonoid found in many naturalplants, has been categorized to assess the antibacterial activity against dental pathogen *S. mutans*. So, we have developed kaempferol biofunctionalized gold nanoparticles (K-AuNPs) to enhance the antibacterial efficacy of kaempferol. In this study, kaempferol biofunctionalized gold nanoparticles (K-AuNPs) were successfully synthesized and tested for antibacterial activity against dental pathogen *S. mutans*. The synthesized K-AuNPs appeared spherical in shape with an average size of 100 nm. K-AuNPs were found to exhibit antibacterial activity against *S. mutans* with a zone of inhibition of around 13 ± 0.9 mm and Minimum Inhibitory Concentration (MIC) range of about 10µg/mL. Overall, the present study reveals that kaempferol and K-AuNPs hold as promising novel solutions for treating dental pathogen *S. mutans*,thus expanding the therapeutic options in antibacterial strategies.

***Keywords***: Dental infection, *Streptococcus mutans*, Kaempferol, Gold nanoparticles, Antibacterial activity assessment

# Introduction

Dental infections such as tooth decay and periodontal disease are the most common bacterial infections in humans [(Bartsch et al., 2025)](https://paperpile.com/c/L1ryym/3uCf) which can be caused by multiple risk factors including consumption of dietary sugars, inadequate fluoride exposure, reduced saliva flow, poor oral hygiene, and harmful presence of oral microbiota [(Desai & Nair, 2023)](https://paperpile.com/c/L1ryym/5IPS). In the human dental flora, almost 780 bacterial species are present, and the dominant bacteria are *Streptococcus mutans* which play an important discriminatory role in disease establishment and progression of dental infections [(Selvaraj et al., 2024)](https://paperpile.com/c/L1ryym/PNkb). *S. mutans* is a gram-positive bacterium that progresses dental infections by exhibiting strong biofilm-forming ability [(Desai & Nair, 2023; Gao et al., 2023)](https://paperpile.com/c/L1ryym/5IPS+Iesr), synthesizing glucans for adhesion, and interacting with other bacteria species, resulting in the formation of dental infections [(Zhang et al., 2022)](https://paperpile.com/c/L1ryym/A1ts).Currently, number of antimicrobial agents are used in oral healthcare sectors (Chlorhexidine [(Rath et al., 2021)](https://paperpile.com/c/L1ryym/vO8x), antimicrobial peptides [(Luong et al., 2022)](https://paperpile.com/c/L1ryym/tYdO), non-thermal plasma therapies, targeted antimicrobial therapy [(Elashiry et al., 2021)](https://paperpile.com/c/L1ryym/HKJU), and mechanical removal [(Oh et al., 2022)](https://paperpile.com/c/L1ryym/3A5T), having broad-spectrum activity that are often associated with side effects and limitations, such as the risk of resistance development, cellular toxicity, and stability of the compound. In recent years, flavonoids have gained increased attention as alternative agents based on their broad availability, low toxicity, and prominent antibacterial capacity [(Donadio et al., 2021)](https://paperpile.com/c/L1ryym/2vqv).Flavonoids are polyphenols found in the major human diet. Among them kaempferol, a flavonoid commonly found in various food substances such as beans, tea, broccoli, tomatoes, strawberries, etc [(Garde-Cerdán & Gonzalo-Diago, 2016; Venkatesan & Palanivel, 2024)](https://paperpile.com/c/L1ryym/uBEF+Jun2). The pharmacological property of this flavonoid is vast, including anti-inflammatory, antioxidant, antibiotic, anticancer, anti-allergic, anti-osteoporotic, cardioprotective, and neuroprotective actions [(Rajeshkumar & Lakshmi, 2021; Sivakumar et al., 2021)](https://paperpile.com/c/L1ryym/GFjX+i2mG). Kaempferol has excellent biological activities compared to other molecules because of a specific arrangement of free hydroxyl groups. **Fig 1** determines the chemical structure of kaempferol. However, the insoluble nature of kaempferol prevents it from penetrating the skin. Nanoparticles have greater efficiency in enhancing the penetration of drugs into the skin due to their large surface area [(Gunasekaran et al., 2024; Khodami et al., 2024)](https://paperpile.com/c/L1ryym/oUte+ifCq). Therefore, the development of novel kaempferol biofunctionalized gold nanoparticles that are capable of transporting kaempferol across the skin is of great significance [(Gandhi et al., 2021; Katyal et al., 2023; Priyadharshini et al., 2023)](https://paperpile.com/c/L1ryym/DGYHg+ZMySg+PCNcJ).



In this study, the kaempferol biofunctionalized gold nanoparticles (K-AuNPs) were synthesized and the synthesized particles were characterized using UV-Vis spectrophotometry, High Resolution Scanning Electron Microscopy (HR-SEM), Energy dispersive X-ray (EDX) analysis, and Fourier Transform Infrared Spectroscopy (FTIR). Further, the antibacterial activity was assessed against *S. mutans* [*(Chokkattu et al., 2023; Dharman et al., 2023; Govindaraj & Shanmugam, 2023)*](https://paperpile.com/c/L1ryym/agmTd+B2YyF+LQkK0).

## Materials and Methods

## Chemicals and reagents

Kaempferol was purchased from Tokyo Chemical Industry, Japan. Gold precursor chloroauric acid (HAuCl4) was obtained from Aladdin (Shanghai, China). Nutrient agar, Nutrient broth, Muller Hinton agar, Muller Hinton broth, and antibiotic (Amikacin) were purchased from HiMedia Laboratories (Mumbai, India). Dimethyl sulfoxide (DMSO) was purchased from Merck Life Science (Mumbai, India). Deionized water was obtained from Indion® Lab-Q Water Maker. All other chemicals and reagents utilized in this study were of analytical grade. Kaempferol stock solution of 100 mM was prepared by dissolving 28.62 mg/mL of DMSO

## Synthesis of Kaempferol biofunctionalized gold nanoparticles (K-AuNPs)

Synthesis K-AuNPs is performed according to the protocol of [(Selvaraj et al., 2024)](https://paperpile.com/c/L1ryym/PNkb). In this method, K-AuNPs were synthesized by mixing a 1:2.5 M ratio of kaempferol with chloroauric acid and pH was adjusted to 8 under 30 ˚C. The synthesized K-AuNPs were confirmed by the red color formation, followed by characterization such as UV-Vis spectrophotometry, HR-SEM (JEOL, JSM-IT-800, Japan), EDX analysis (Bruker D8 Advance, Germany, and FTIR analysis (ATR-FTIR; Bruker Alpha II, Germany). The K-AuNPs were centrifuged at 8000 rpm for 5 min at 4 ˚C. Finally, the obtained pellet was dried and stored in an airtight container at 25 ˚C for further studies.

## Physicochemical characterization of synthesized nanoparticles

The physicochemical properties of the synthesized K-AuNPs were analyzed using HR-SEM to obtain high-resolution images of the sample’s surface, composition, and texture and the size of nanoparticles was calculated using ImageJ software. EDX characterization was performed to confirm the composition and elemental distribution of gold and its purity. FTIR analysis identifies and characterizes the functional groups that are involved in their reduction and stabilization during the synthesis of gold nanoparticles.

## Antibacterial activity assessment

An antibacterial susceptibility test was conducted according to the protocol established by the Clinical and Laboratory Standards Institute (CLSI) for kaempferol and K-AuNPs using the Kirby-Bauer disc diffusion method [(Lilly et al., 2025)](https://paperpile.com/c/L1ryym/55Bj). Using sterile cotton swabs, *S. mutans* strains were evenly spread onto the surface of an agar plate and wells were created using a well cutter of size 9 mm, 25 mcg of kaempferol and 100 mcg of K-AuNPs were loaded into the wells of MHA plates, and a standard antibiotic (Amikacin) is used as a positive control. The plates were kept at room temperature for 2 hours until the drugs were diffused into the media and incubated at 37° C for 24 hours. After incubation, the plates were visualized for the zone of inhibition, and the zones were calculated using the HiAntibiotic Zone scale.

## Minimum Inhibitory Concentration Assessment

The standard broth microdilution method was used to study the MIC of kaempferol and K-AuNPs by evaluating the visible growth of microorganisms in the agar broth according to the protocol of [(Lilly et al., 2025)](https://paperpile.com/c/L1ryym/55Bj). Serially two-fold dilutions of kaempferol and K-AuNPs in the concentrations ranging from 0.01 µg/mL to 100 µg/mL with a bacterial concentration of 0.5 McFarland standard were used to determine MIC in a 96-well plate. After the addition of antibacterial agents, the plates were incubated at 37 °C for 24 h. Then, the optical density of the sample was read at 600 nm wavelength in a microplate reader (BioTeK SYNERGY H1). The MIC level is the lowest concentration of kaempferol and K-AuNPs that inhibits 90 % of the visible growth of *S. mutans* after overnight incubation.

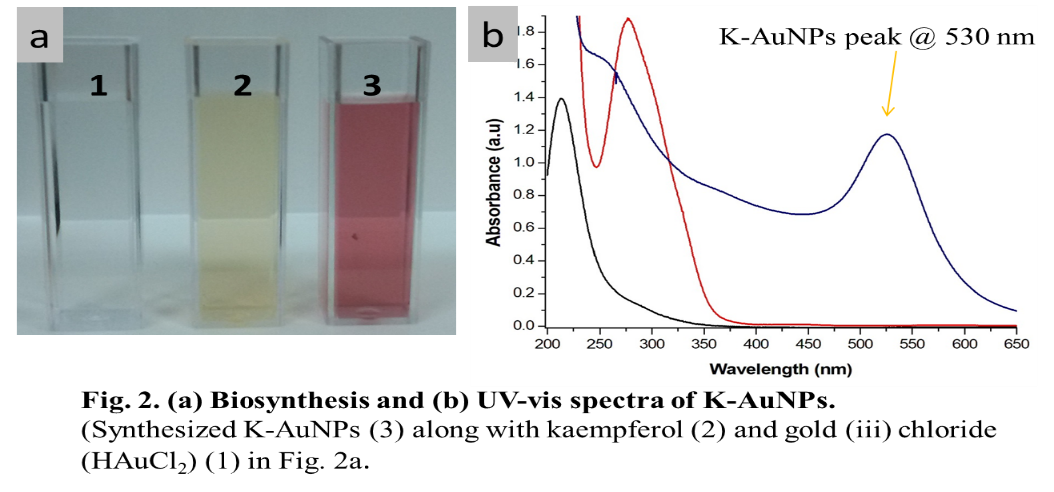
# Statistical analysis

All experiments were conducted in triplicate, and the results were presented as the mean along with standard deviation values. Data analysis and graphical representation were carried out using Origin software.

# Results and discussion

## Synthesis of K-AuNPs

The synthesis of nanoparticles biologically can be achieved by using plant extracts according to our previous protocol [(Selvaraj et al., 2024)](https://paperpile.com/c/L1ryym/PNkb). This plant-based green synthesis provides several advantages over the direct use of medicinal plants globally. (**Fig. 2a)** represents the biological synthesis of K-AuNPs by observing the color formation after mixing aqueous gold chloride and kaempferol, which changed from pale yellow to red which is an indication of nano-particle synthesis. This color indicates the oscillations of electron transmission in the surface plasmon resonance (SPR) band. A prominent SPR peak was obtained at a wavelength of 530 nm, which confirmed the formation of gold nanoparticles of K-AuNPs **(Fig. 2b)**.

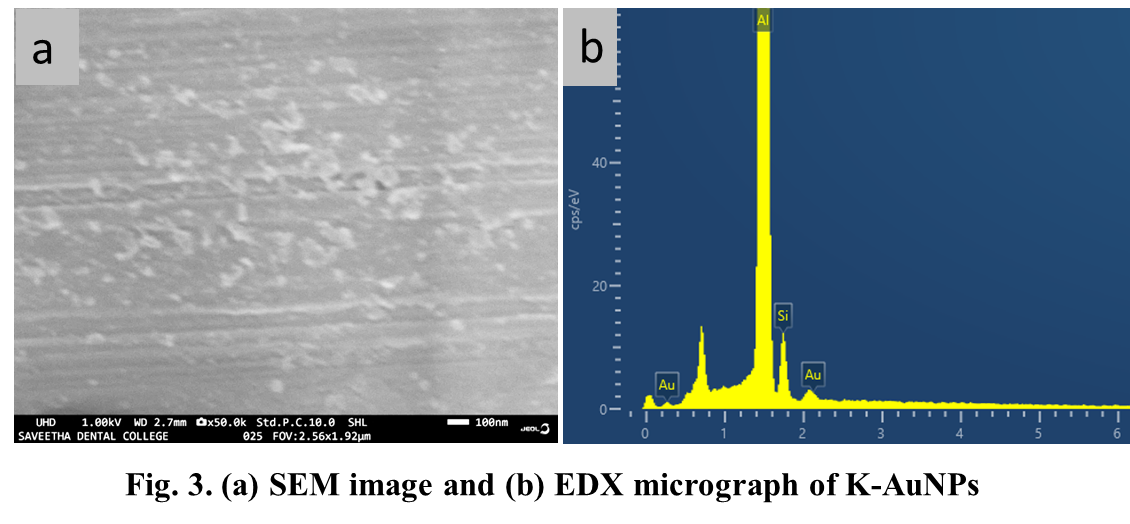


1. (b)

Fig 2: (a) biosynthesis (b) UV-sis

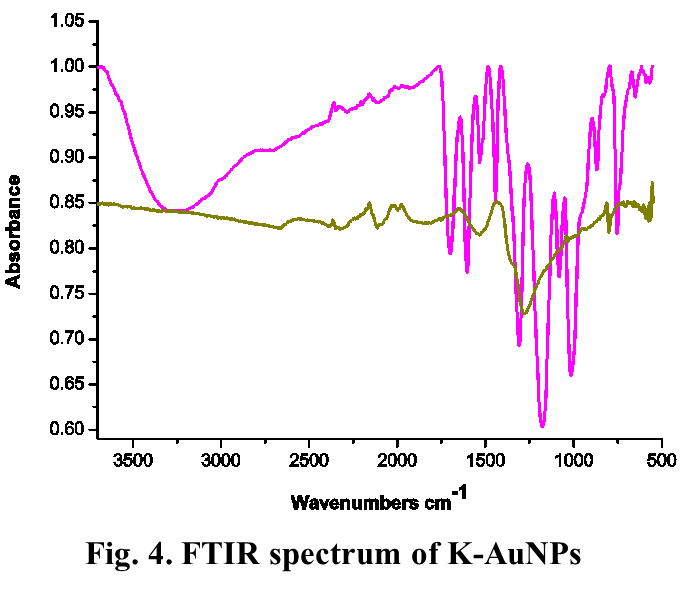
## Characterization of synthesized K-AuNPs

The synthesized K-AuNPs nanoparticle's size was confirmed by HR-SEM. The K-AuNPs have a spherical shape and range in size from 100 nm. **(Fig. 3a)**. The EDX profile of K-AuNPs exhibited prominent signals at energy levels of 2 and 10 keV **(Fig. 3b)**, indicating the presence of gold nanoparticles(Rafi et al., 2024). This result supports the phenomenon according to which kaempferol extract acts as a capping and reducing agent for synthesized nanoparticles.



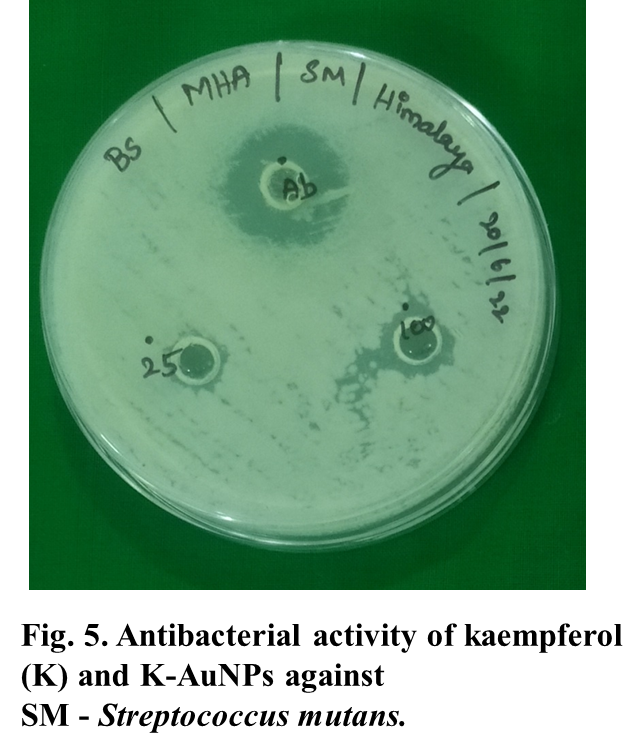
## Fourier transform infrared spectroscopy

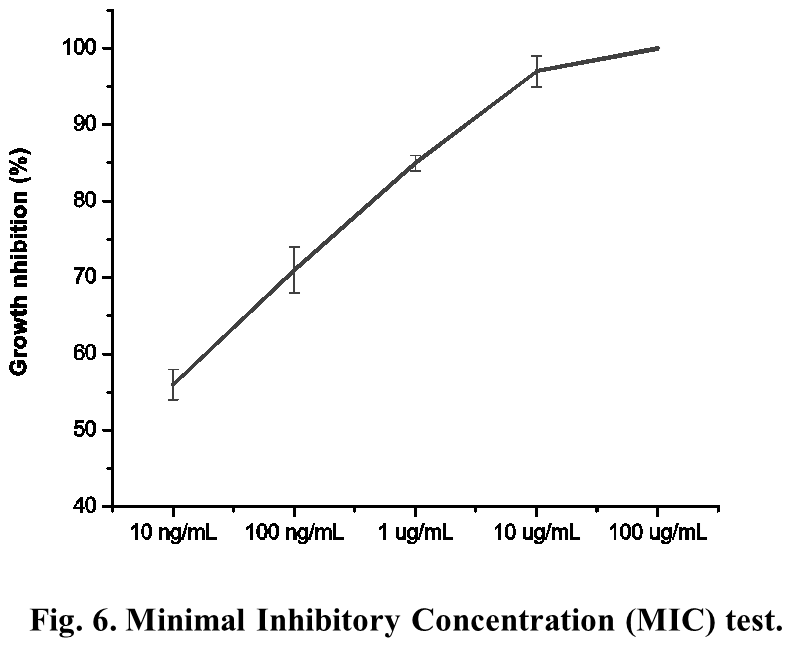
The FTIR spectra of kaempferol (pink) and K-AuNPs (green). **(Fig. 4)** reflects separate peaks at approximately 3332 cm−1, 2972 cm−1, 1739 cm−1, 1639 cm−1, 1439 cm−1, 1367 cm−1, corresponding to the-OH group, Csingle bondH stretch, C=O stretch, C=C stretch, respectively.



## Antibacterial activity assessment

AuNPs effectively kill bacteria because they are safe for human cells and the bacteria cannot easily develop resistance to them (Tuluwengjiang et al., 2024).Recent research has shown that AuNPs synthesized in an environmentally friendly manner possess potent antimicrobial properties against a variety of microorganisms [(Dykman & Khlebtsov, 2017)](https://paperpile.com/c/L1ryym/Ngzr). Following a 24-hour incubation period, it was observed that K-AuNPs exhibited excellent antibacterial activity against *S. mutans* that are shown in **Fig. 5**, representing the zone of inhibition values of the standard antibiotic amikacin (30mcg), kaempferol and K-AuNPs, against *S. mutans* on MHI plate as 22 ± 0.5 mm, 11 ± 0.8 mm, and 13 ± 0.9 mm in diameter respectively. It indicates that K-AuNPs exhibit high antibacterial activity compared to kaempferol. In a previous study comparing the antibacterial effects of Au, Zinc and silver nanoparticles against *S. mutans*, AuNPs were highly effective [(Kesharwani, 2023)](https://paperpile.com/c/L1ryym/VqiR). The MIC values of K-AuNPs against *S. mutans* have significant differences in effectiveness. In contrast, the MIC values for the kaempferol were higher (100 μg/mL) than the K-AuNPs (10 μg/mL). According to the results of **Fig. 6,** it is clear that K-AuNPs have a lower MIC range than kaempferol.





# Discussion

There is an urgent need for new treatments as traditional antibiotics are becoming less effective due to widespread antimicrobial resistance. This study aimed to determine the antibacterial activity of gold nanoparticles against *S. mutans*, a dental bacterium using the disk diffusion method. The advantage of direct contact tests over the agar diffusion method is that they are independent of the diffusion properties of the tested material and media [(Lilly et al., 2025)](https://paperpile.com/c/L1ryym/55Bj)**.** Serial dilutions of a solution are used for MIC to determine the lowest concentration of compound that would still show antibacterial properties [(Kowalska-Krochmal & Dudek-Wicher, 2021)](https://paperpile.com/c/L1ryym/unlG)**.** The antibacterial effects of gold are mostly attributed to gold ions. Because of the bigger surface area of gold nanoparticles, they show a stronger and better bactericidal effect. The main reason for the bactericidal properties of gold nanoparticles is interfering with the integrity of the bacterial cell by binding to essential cellular structure[(Janani et al., 2021; Kachhara et al., 2021; Subramanian et al., 2023)](https://paperpile.com/c/L1ryym/1hMfj+24a8S+oXeyK). In contrast**,** nanoparticles were used as an alternative approach due to their effectiveness in controlling microbial infections[(Doshi et al., 2023; Lampl et al., 2023; Pandiyan et al., 2023)](https://paperpile.com/c/L1ryym/PFC7U+RkAzv+cIjxC). To follow a green synthesis approach, kaempferol, a naturally derived compound, was used to synthesize gold nanoparticles. In the reaction, kaempferol reduced gold trichloride ions, leading to the formation of K-AuNPs [(Pavithra et al., 2023; Shenoy et al., 2023; Thomas & Jain, 2023)](https://paperpile.com/c/L1ryym/iluYp+LPqqr+kTrEc). The color change from yellow to red confirmed the initial synthesis, as reported in our previous studies [(Selvaraj et al., 2024)](https://paperpile.com/c/L1ryym/PNkb)Further confirmation came from UV-Vis spectroscopy, where an absorption peak at 530 nm indicated the presence of K-AuNPs, aligning with absorption patterns of AuNPs synthesized from other natural sources [(Ramsundar et al., 2023; Rieshy et al., 2023; Singh et al., 2023)](https://paperpile.com/c/L1ryym/NJjtF+Sb6uS+dCs65). The morphology analysis confirmed that K-AuNPs had a spherical structure with a 100 nm size. FTIR results showed that flavonoid kaempferol played a key role in their synthesis, as well as in providing antibacterial properties. The green synthesized gold nanoparticles of K-AuNPs have strong antibacterial activity with a MIC value of 10 μg/mL, due to the presence of bioactive molecules on the surface of gold nanoparticles. Moreover, the biological synthesis of K-AuNPs was simple, fast, cost-effective, and environmentally friendly. Compared to previous methods, this approach using flavonoid kaempferol under different pH and temperature conditions proved to be more reliable and reproducible. K-AuNPs have potential applications in medicine and pharmaceuticals, particularly in drug delivery and molecular diagnostics. The obtained experimental and theoretical results clearly demonstrate that K-AuNPs could be useful in oral management in the future. Following clinical experiments, it could be incorporated into dental treatment procedures. Various studies have concluded that gold nanoparticles possess antimicrobial effects against many bacteria and fungi, including *S. mutans, Candida albicans, Pseudomonas aeruginosa, Enterococcus faecalis,* and *Staphylococcus aureus*, which could decrease the occurrence of secondary caries, fungicidal infection, endodontic failure, and dental implant losses. For example, Ghoreish et al. (2025) reported the synthesis of gold nanoparticles using *tangerine* peel extract, exhibiting strong antibacterial against *S. mutans* [*(Ghoreishi & Mortazavi-Derazkola, 2025)*](https://paperpile.com/c/L1ryym/LodQ).Alsamhary et al. (2020) reported the flavonoid triacetin as a reducing agent for the synthesis of gold nanoparticles effectively inhibited opportunistic bacterial pathogens like *Acinetobacter pittii, Escherichia fergusonii, Bacillus licheniformis, Staphylococcus aureus,* that cause respiratory infections [(Alsamhary et al., 2020)](https://paperpile.com/c/L1ryym/zYez). Selvaraj et al. (2024) demonstrated the synthesis of gold nanoparticles by tannic acid for the treatment of antibiofilm forming *S. mutans* . He concluded that MIC values of 4 μg/mL and the antibiofilm range of 4xMIC (16 μg/mL) completely inhibited *S. mutans* growth [(Selvaraj et al., 2024)](https://paperpile.com/c/L1ryym/PNkb).

# Conclusion

Overall, this study suggests that the kaempferol biofunctionalized gold nanoparticles (K-AuNPs) could be used as an effective nano-drug to treat *S. mutans*. In the future, we recommend that the synthesized K-AuNPs be utilized as nanomedicine for treating various other dental pathogens after clinical trials.

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