Comparatives Antimicrobial Activity of Clove and Ginger Formulation and its Mediated Titanium Oxide Nano Particles Against Oral Pathogens

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**Abstract:** The emergence of antibiotic resistance among oral pathogens necessitates the exploration of natural antimicrobial agents and nanotechnology-based solutions. This study evaluates the comparative antimicrobial efficacy of clove and ginger formulations and their mediated titanium oxide (TiO₂) nanoparticles against common oral pathogens. Clove and ginger extracts were prepared and synthesized with TiO₂ nanoparticles using a green synthesis approach. The antimicrobial activity was assessed against *Streptococcus mutans*, *Candida albicans*, and *Porphyromonas gingivalis* using the agar well diffusion and minimum inhibitory concentration (MIC) methods. Results demonstrated that both clove and ginger exhibited potent antimicrobial activity, with clove showing a higher inhibition zone. TiO₂ nanoparticles enhanced the efficacy of the formulations, indicating their potential as effective antimicrobial agents in oral healthcare. This study suggests that herbal-nanocomposite formulations could serve as promising alternatives to conventional antimicrobial agents for managing oral infections. These have gained ground recently, and research has shown that they are useful in a variety of technical and biological contexts. In the field of science known as nanotechnology, objects smaller than one nanometer (or "nanoparticles") are studied (NPs). Between one and one hundred nanometers in size, nanomaterials are little solid particles. The positive to incendiary effects of leukotrienes are thwarted by ginger because it also inhibits 5-lipoxygenase and reduces leukotriene production. According to studies, ginger concentrate from the Zingiberaceae family suppresses a few properties required for explosive reactions. 300,000 people worldwide die each year from wound infection, a common and deadly condition. In vitro study was conducted with bacteria which were inoculated in the presence of suitable environment for the culture with a suitable medium, the microorganism species that were tested in this study are Streptococcus mutans, Staphylococcus aureus and Enterococcus faecalis and C, albicans. The culture specimens were inoculated in Agar wells by diffusion method, this method is implemented in order to measure the antibacterial effectiveness of the nanoparticles at 25 L, 50 L, 100 L, and control groups. At 100 L, the Zone of Inhibition has been identified to be highest against Streptococcus mutans, Enterococcus faecalis, and Staphylococcus aureus at14 mm, 14 mm, and 12 mm, respectively. The current in vitro study suggests that the incorporation of titanium oxide nanoparticles in a few medicinal plants, such as ginger and clove extracts, may have the comparable capacity to act as a an inhibiting agent against the oral bacteria and may be used as a substitute for commercially available **antimicrobials.**

**Keywords:** Titanium oxide, ginger, clove, antimicrobial, wound pathogens

# INTRODUCTION

The ultrafine sized elements which are known as Nanoparticles were widely used in the day to day research fields for manufacturing processes and a wide variety of coatings where the size ranges from 1 to 100 nanometers [(Aparna et al., 2021; Poornima et al., 2021; Verma & Muthuswamy Pandian, 2021)](https://paperpile.com/c/4l3ln0/yTpgo+Ej6QV+Z4yTe). These have grown in prominence recently and it has been demonstrated that they have a wide range of technological and biological applications [(R. Kumar et al., 2021)](https://paperpile.com/c/4l3ln0/dxPSq). The research scholars are particularly interested in many nanoparticles and one among them is silver nanoparticles. These are the elements among the metals that have properties like chemical stableness, anti-inflammatory properties, antiseptic and antioxidant in nature, antibacterial, antiviral and antifungal action. [(Michael Conn, 2008)](https://paperpile.com/c/4l3ln0/FiFbL) These particles can frequently be generated through physical or chemical processes that are not only toxic to the environment but also impart a number of biologically potential hazards. [(Rajeshkumar et al., 2020)](https://paperpile.com/c/4l3ln0/Tl2TV) In order to minimize the damage causing to the natural environment, it is crucial to adopt alternative approaches that includes the the green production of nanoparticles using a variety of naturally occurring agents, consisting of organisms to plants such as fungi and bacteria, herbal extracts, or biological material from plants. [(Shukla & Iravani, 2018)](https://paperpile.com/c/4l3ln0/cx1OE)

Nanotechnology is a discipline of research centered around nanoparticles, or objects reduced than a nanometer (NPs) and nanomaterials are substances which constitute nanoscale solid particles with diameters ranging from one to one hundred nanometers in size [(Merchant et al., 2022; Pandiyan et al., 2022)](https://paperpile.com/c/4l3ln0/Bp8xI+OSsSp), [(Ganapathy 2021; Merchant et al., 2022; Pandiyan et al., 2022)](https://paperpile.com/c/4l3ln0/Bp8xI+OSsSp+hvied), [(Chokkattu et al., 2022; Ramamurthy et al., 2022)](https://paperpile.com/c/4l3ln0/kYdXe+LLB8Q). Nanomaterials are substances that offer enhanced, along with unique chemical and physical characteristics with notably very small dimensions but a substantial surface area to mass ratio, with better reactivity, making them suitable for therapy with antibacterial agents. [(Baniasad & Ghorbani, 2016; Emam & Ahmed, 2018)](https://paperpile.com/c/4l3ln0/BGeF9+FYXDS) The quality of the final products can be raised by including many functional groups into the nanoparticle. As a result, a variety of industrial, medicinal, and dental fields use nanoproducts extensively [(P. S. M. Kumar et al., 2017; Pugazhendhi et al., 2018)](https://paperpile.com/c/4l3ln0/44hdh+7YRo6). A novel technique called nanobiotechnology has stimulated the creation of numerous nanobiomaterials with uses in biology and medicine [(Emmanuel et al., 2015, 2017; Saravanan et al., 2018)](https://paperpile.com/c/4l3ln0/TRpq7+gZ7l2+SBPPP) .

Ginger is fundamentally known as Zingiber officinale, it has a place with the group of Zingiberaceae [(Chokkattu et al., 2022; Ramamurthy et al., 2022)](https://paperpile.com/c/4l3ln0/kYdXe+LLB8Q), [(Marya et al., 2022)](https://paperpile.com/c/4l3ln0/RLJhN), [(Jain & Verma, 2022; Marya et al., 2022)](https://paperpile.com/c/4l3ln0/RLJhN+TTOPs). The readiness is finished by dissolvable extraction of dried rhizomes. It contains an unstable oil in a structure of around 30 - 35 ml/100 g. Ginger has been known to make mitigating impacts. Ginger represses cyclooxygenase and smothers prostaglandin discharge, consequently achieving calming impacts [(Grzanna et al., 2005)](https://paperpile.com/c/4l3ln0/p1hxX). Ginger additionally restrains 5-lipoxygenase, stifles leukotriene creation, consequently hinders the favorable to incendiary impacts of leukotrienes. Ginger concentrate from the Zingiberaceaehas been displayed to repress a few qualities that are obligated for incendiary reactions [(R. Kumar et al., 2021)](https://paperpile.com/c/4l3ln0/dxPSq) . Ginger's active ingredients, 6-gingerol and shogaol which have been recognized for their soothing properties as well as anticancer and cell reinforcing properties. The oleoresin's has a composition that may vary depending on the solubles that were used in the extraction of the ingredients. [(MacFaddin, 1983)](https://paperpile.com/c/4l3ln0/FnFCB). Syzygium aromaticum, a member of the Mirtaceae family and a native of the islands of Maluku, which are in east Indonesia, is most well known by the common name "clove." It is a medium in size (8–12 m) tree with a confined habitat. The trade in cloves has long been a factor in this area's economic growth [(Shukla & Iravani, 2018)](https://paperpile.com/c/4l3ln0/cx1OE) Eugenol, a physiologically active chemical and organic solvent, is extracted from cloves and found in around 14.650 ml of oil per 100 Grams [(Wadhwani et al., 2022)](https://paperpile.com/c/4l3ln0/JOawv), [(Sreevarun et al., 2023)](https://paperpile.com/c/4l3ln0/ZOxdF), [(Adel et al., 2023)](https://paperpile.com/c/4l3ln0/WozPs). The antibacterial properties have been demonstrated against a number of bacterial and fungi species. investigated the antibacterial properties of many Indian spice plants, including clove, ginger, garlic, mustard, and mint. [(Liu, n.d.; Wei et al., 2022)](https://paperpile.com/c/4l3ln0/KrW3P+eCmVz)

These elements lengthen the hospital stay of patients and speed up the spread of infection to nearby tissue. Different bacteria can infect wounds in different ways.Among all photocatalytic substances, titanium oxide (TiO2) NPs have been employed extensively as photocatalysts. TiO2 NPs have the ability to operate as a broad-spectrum antibiotic, are non-toxic, chemically stable, and self-cleaning. [(Chabanyuk, n.d.; Lal et al., 2021)](https://paperpile.com/c/4l3ln0/v40d3+KNvuh) Previous investigations has been carried out on the effects of extracts such as ginger oleoresin a and for the assessment of its specific characteristics such as its anticancer potential against liver tumor cell lines, Titanium Oxide nanoparticles for treatment of oral infections, Zinc Oxide Nanoparticles which are prepared from Clove and Cinnamon which acts against oral pathogens, Spices such as cloves, cardamom, and cinnamon possess antimicrobial properties towards bacillus and pseudomonas. [(R. Kumar et al., 2021)](https://paperpile.com/c/4l3ln0/dxPSq), [(Alhadrami & Shoudri, 2021)](https://paperpile.com/c/4l3ln0/413d2), [(Shukla & Iravani, 2018)](https://paperpile.com/c/4l3ln0/cx1OE), [(“Colloquies on the Simples and Drugs of India: Cinnamon, Cloves, Mace and Nutmeg, Pepper,” 2017)](https://paperpile.com/c/4l3ln0/N9rXD)

The basis for the present study is that no previous research has been done to evaluate the antibacterial effects of titanium oxide nanoparticles supplemented with ginger and clove.

# MATERIALS AND METHODS

## Study Setting

This is an In vitro Cell line Research which was conducted. This research was performed in the laboratory for 1 month where the samples were obtained from Nanomedicine laboratory, the experiment was conducted in the same lab followed by the microbial testing in Microbiology lab. The study research procedures were evaluated, the comprehensive evaluation of the study protocols was discussed.

## Study Design

This cell line research typically entails the collection of tissue samples, which are then cultured in a controlled environment in a laboratory. This type of study, known as an in vitro investigation, is extremely valuable for appreciating the behaviors of cells, the course of disease, and the advantages and disadvantages of therapeutic interventions.

## Test Specimens and Organisms

The test organisms includes S.mutans, S.aureus, E.faecalis which are gram positive bacteria and yeast C. albicans, which were sourced from culture collections.

## Extraction of plant material and synthesis of the extract

Using a food processor, the ginger and clove were first powdered. Distilled water measuring 100 mL is mixed with 1 mg ginger powder and 1 mg clove powder. The mixed preparation was bring to boil for 10 minutes in a heating mantle at 600C as boiling aids in the extraction of active chemicals from plant material, the filtering was done using funnel and Whatman cellulose filtrate paper to eliminate any contaminants left over from the extraction procedure. This filtered solution collected and stored in turbinate flask, which was refrigerated overnight in an airtight container. Refrigeration aids in the preservation of the extract by decreasing its growth.

## Nano particle Preparation and Synthesis of Titanium oxide Nanoparticle pellets

Using 60 milliliters of distilled water, 0.35 grams of titanium oxide were extracted in order to produce the particles in powder form and everything was harmoniously blended. The solution was subsequently augmented with 40 mL of the plant extract, which contained clove and ginger. Following that, the resultant mixture was put into a shaker with an orbital mechanism. The color of the solution was checked and recorded every two hours for a duration of thirty-six hours. Under a UV Spectrophotometer, these observations were documented. The solution needs to be put through centrifugation for 10 minutes at 7000 rpm after the 36-hour period, this process of centrifugation will produce the particles by moving the denser sized particles towards the bottom of the centrifuge to form pellets. zinc oxide nanoparticles supplemented with ginger and cloves were produced. This process allowed for the synthesis of these unique nanoparticles of zinc oxide supplemented with ginger and clove with the desired properties.[Figure 1 ]

## Methods of evaluation of the Antimicrobial Activity

The Agar in the petri dishes were formed into wells called Well Diffusion Method, where the microbes were inoculated in the presence of an zinc oxide nano particle antimicrobial agent which was previously synthesized, the antimicrobial agent decreases the activity of the microbes by inhibiting the formation of the microbial colonies.

## Media Preparation for the inoculation of test specimen

To prepare cell culture medium, 100 milliliters of Mueller Hinton agar was used which is frequently used to cultivate microscopic test specimen organisms, the medium was prepared for the test organisms, which was sterilized before being poured into petri dishes and allowed to solidify before being used for the inoculation procedure.

## Microbial Inoculation Procedure

The culture medium which has been solidified in the petri dishes were labeled as per microbe to be tested was inoculated with the test specimens by swabbing method where a sterile swab was used for each petri dish inoculation. [ Figure 2 ]

## Procedure for Well Formation in Perti Dishes

Using a gel puncher, four wells were created on each plate following swabbing. Titanium Oxide nanoparticle solution containing ginger and cloves was added to those four wells in the following concentration ranges: 25 µL, 50 µL, and 100 µL, along with a control group. Following a 24-hour incubation period at 37 degree Centigrade which is optimal for the growth of the microorganisms.

## Interpretation of the microbial Zone of Inhibition

A zone of inhibition is a clear area around the formed colonies by the microorganisms which was previously inoculated in the agar medium, the petri dishes were held in front of a lamp to accurately observe and measure the clear inhibition zone. A measuring devise will be used which was held against the petri dishes on its back, where the clear inhibited zones were measured in milli meters.



Figure 1: Materials for titanium dioxide synthesis were taken at a weight of 0.35 gm, which is 50 mM, and dissolved in 50 ml of distilled water, to which 50 ml of clove ginger formulation was added and kept on magnetic stirrer for 42 to 72 hours. Following the pellet collection

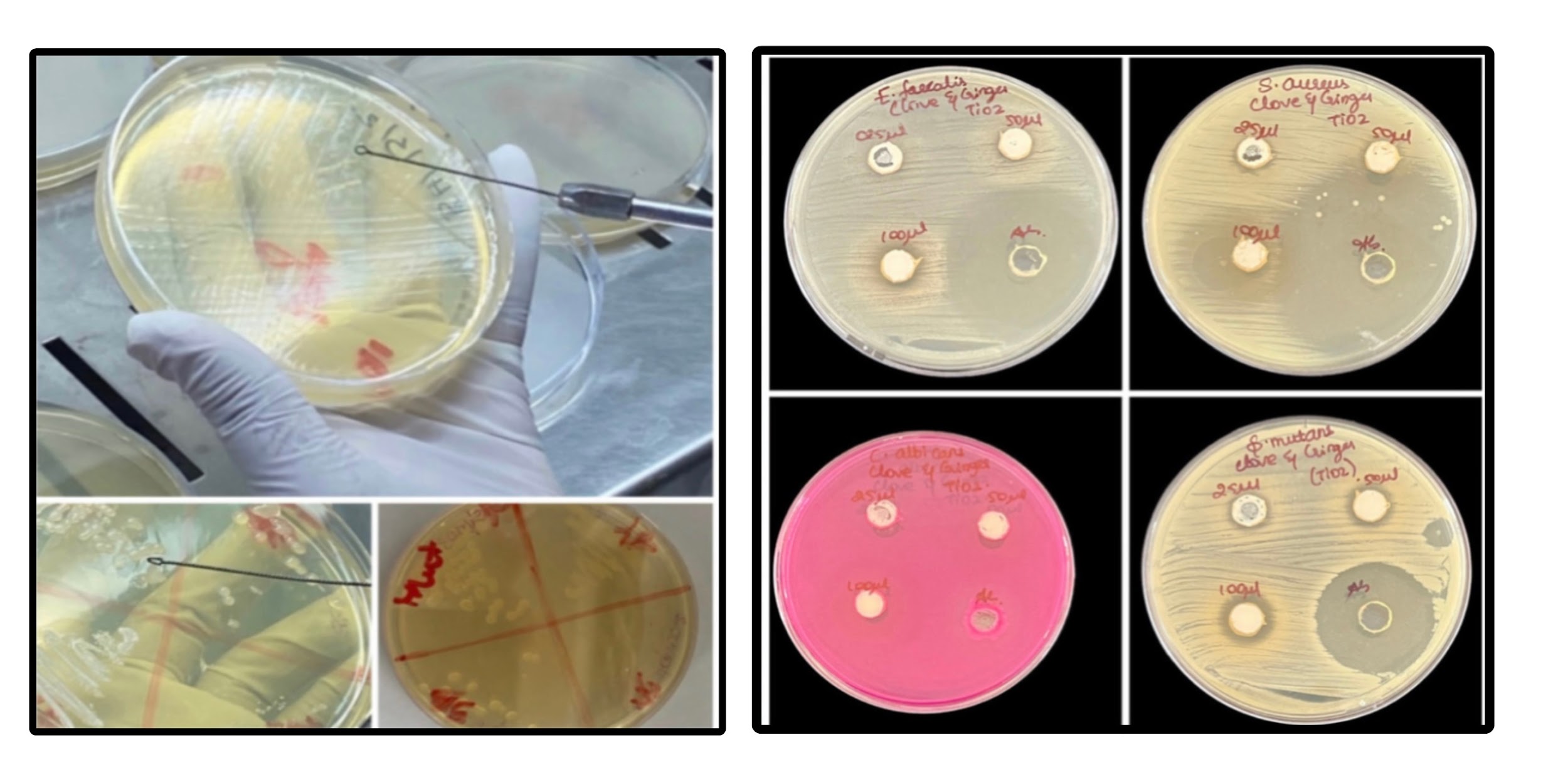


Figure 2: The above image shows inoculation and zone of inhibition in the petri dishes

# RESULTS

Figure 3 illustrates how titanium oxide nanoparticles enhanced with ginger and clove extract have antibacterial impacts on the mutans strain of Streptococcus. The study results showed that the extent of inhibition was largest at concentrations of 100 μL (14 mm) and 50 μL (11 mm), which is a satisfactory. The antibacterial activity against S.aureus appears to be maximum at concentrations of 100 L (12 mm) and 50 L (10 mm). The antibacterial activity against E.faecalis appears to be maximum at concentrations of 100 L (14 mm) followed by 50 μL (9 mm). S.mutans shows higher zone of inhibition which shows sensitivity to clove and ginger titanium qnanoparticles.

Table 1:The above table depicts the test specimens diluted at 25 µL, 50 µL and 100 µL which are all susceptible to the action of the antimicrobial preparation.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Specimens** | **25 µL** | **50 µL** | **100 µL** | **Antibiotic** |
| C Albicans | 9 | 9 | 9 | 11 |
| E.faecalis | 9 | 9 | 14 | 35 |
| S.Mutans | 10 | 11 | 14 | 40 |
| S. aureus | 10 | 10 | 12 | 28 |

The table is divided into four columns: "Specimens," "25 L," "50 L," "100 L," and "Antibiotic." The first column lists the bacterial species tested: Candida albicans, E. faecalis, Staphylococcus Mutans, and Staphylococcus aureus. The next three columns show the number of bacteria that survived antibiotic treatments of 25, 50, and 100 µLL, respectively. The final column displays the total number of microorganisms that survived antibiotic treatment.

According to the table, the efficiency of antibiotics varies depending on the bacterial species and the drug concentration. The data, for example, reveals that the antibiotic was most efficient against C. Albicans, with the fewest number of germs surviving after 100 L of treatment. In contrast, the antibiotic was least efficient against S. aureus, with the greatest number of bacteria surviving after 100 L of antibiotic treatment.

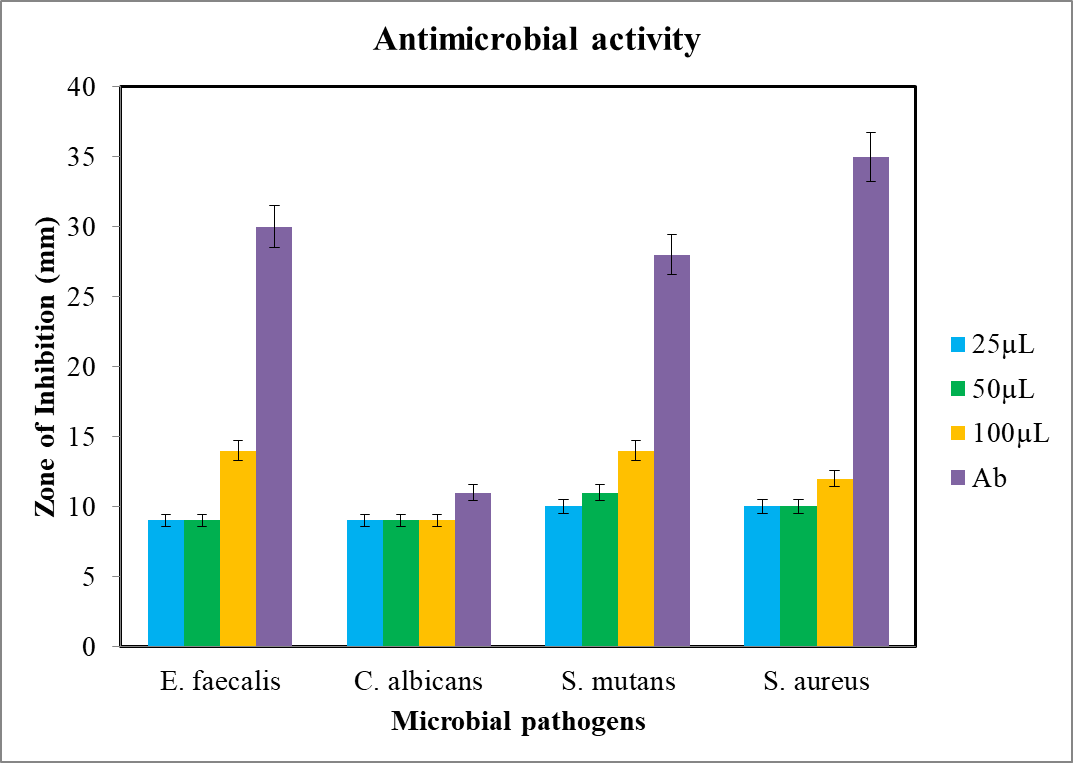
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Figure 3: This is a bar graph that depicts the antibacterial activity of various concentrations of a drug against various microbiological infections. The x-axis depicts the many microbial pathogens: E. faecalis, Candida albicans, Staphylococcus mutans, and Staphylococcus aureus. The y-axis represents the inhibition zone in millimeters. Different hues depict different concentrations of the µLmicrobial specimens of the study: 25µL (yellow), 50µL (green), 100µL (blue), and Ab (purple). With 100L of the compound, the highest antibacterial activity is shown against S. aureus. The more the antibacterial activity, the higher the bar.

# DISCUSSION

In contemporary research, there is a greater tendency to use compounds or extracts derived from plants, these Natural compounds are gaining popularity because these extracts have good tolerance profiles. A notable feature of these natural chemicals is its potential against antibacterial agents, which offers a practical methods in controlling different microbes [(Benelli, 2019)](https://paperpile.com/c/4l3ln0/BmzKL).

A significantly expected objective is antimicrobial improvement, which stops the growth of harmful bacteria [(Subramanian & Harikrishnan, 2023)](https://paperpile.com/c/4l3ln0/pcDz9),[(Solanki et al., 2023)](https://paperpile.com/c/4l3ln0/YSoXI), [(Ganapathy 2021)](https://paperpile.com/c/4l3ln0/6e2pP). The formation of a dense bio-film matrix as a result of microbial cell colonization and growth can shield the underlying germs from host defense mechanisms and drugs. Significant infection can result from microbial infestation. [(Jones et al., 2006)](https://paperpile.com/c/4l3ln0/lBIjM) Food deterioration, the development of food-borne illnesses, and material biofouling are all associated with these infections [(Chokkattu et al., 2023)](https://paperpile.com/c/4l3ln0/0cIAa),[(Laghari et al., 2023; Ramakrishnan et al., 2023)](https://paperpile.com/c/4l3ln0/kMC0+LonX6), [(Muthuswamy Pandian et al., 2022)](https://paperpile.com/c/4l3ln0/vgeB) . The development of antimicrobial surfaces and materials for use in the food, biomedical, health, and personal hygiene areas is therefore of great interest. [(Nazarpour, 2013)](https://paperpile.com/c/4l3ln0/Sc92C) The metal-ion-based nanomaterials are biocidal against a wide range of bacteria, fungi, and viruses. Nanomaterials have the ability to coordinate with electron-donating groups like amides, imidazoles, carboxylates, thiols, and others to deactivate DNA and biological enzymes. [(Grumezescu, 2016)](https://paperpile.com/c/4l3ln0/4QYFA) With viable drug usage the micro organisms evolved with increased drug resistance against commonly used anti microbial drugs. This made a necessity to develop newer drugs which can effectively work on these microbes(Chehelgerdi et al., 2023). Every area of science has undergone a fresh revolution as a result of nanotechnology, a rising subject of study. [(Shukla & Iravani, 2018)](https://paperpile.com/c/4l3ln0/cx1OE) In comparison to other inorganic nanoparticles, titanium oxide is affordable, easy to manufacture, and safe. It also offers a wide range of dental applications. These characteristics make titanium oxide a specific topic of interest for researchers [(Rico et al., 2011)](https://paperpile.com/c/4l3ln0/QTTLB) [(Muthuswamy Pandian et al., 2022; Ramakrishnan et al., 2023)](https://paperpile.com/c/4l3ln0/vgeB+kMC0)[(Rico et al., 2011)](https://paperpile.com/c/4l3ln0/QTTLB).

One of the most investigated materials in the field of microbiological applications is titanium dioxide nanoparticles (TiO2 NPs) because of its special properties, which include bactericidal photocatalytic properties, safety, and self-cleaning capabilities. [(Dicastillo et al., 2021)](https://paperpile.com/c/4l3ln0/pUqCx) S.mutans shows higher zone of inhibition which shows sensitivity to clove and ginger titanium nanoparticles as compare to other studies shows that S.mutans shows that good result when it is incorporated with ginger and cinnamon [(Mohapatra et al., 2020)](https://paperpile.com/c/4l3ln0/Pv3tD). Another article from 2023 mentions the usage of TiO2 nanoparticles that have been combined with ginger and clove as an antibacterial agent to fight Lactobacillus species. The TiO2 NPs are a potentially strong candidate to be used as a lactobacillus-specific antibacterial agent, according to this. When combined with ginger and cinnamon, S.mutans exhibits positive results when compared to other studies [(Ansari & Rehman, 2021)](https://paperpile.com/c/4l3ln0/vMaUg). The antimicrobial evaluation of a study by Senapati et al. using gold and silver Nanoparticles (NPs)made provision of evidence about the structural properties and its biological applications during the origin of Nano particle synthesis for the purpose of research, such research evaluations are used to study the potential of TiO2 NP’s and its antibacterial behaviors [(Saquib et al., 2020; Shukla & Iravani, 2018)](https://paperpile.com/c/4l3ln0/Ctqnb+cx1OE),[(Emmanuel et al., 2015; Lal et al., 2021)](https://paperpile.com/c/4l3ln0/v40d3+SBPPP)

Any research which involves the animal models and are reliable and similar to human participants or volunteers for the research is critical for a complete understanding of the behavior of the nano particles within the bio-systems. Such studies will give most accurate interactions and the systemic pathways of interactions that happen between the micro organisms and the Nano particles (Saadh et al., 2024).

# CONCLUSION

The aspects of the present research that have been investigated are the effects of the natural plant extract on the study specimens. The following are outcomes of this in vitro experiment.

1. The Nano particles used in the invitro analysis are effective against the test specimens which means that they may be used in place of antimicrobials that are currently on the market.
2. The study interprets under different concentrations of the microbial specimens used in the study as: 25µL , 50µL, 100µL, and Ab a commercial antimicrobial compound and with 100µL of the specimen, the highest antibacterial activity is shown against S. aureus.
3. The data reveals that the antibiotic was most efficient against C. Albicans, with the fewest number of germs surviving after 100µL of treatment. In contrast, the antibiotic was least efficient against S. aureus, with the greatest number of bacteria surviving after 100µL of antibiotic treatment.

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