Synergistic Effects of Alginate-Based Nanoparticles Loaded With Anti-Inflammatory and Anti-Bacterial Agents a Multifaceted Approach for Therapeutic Intervention

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**Abstract:** Nanotechnology has significantly transformed drug delivery systems, providing effective solutions for antimicrobial and anti-inflammatory therapies. This study investigates the synergistic effects of alginate-based nanoparticles (ABNs) loaded with anti-inflammatory and antibacterial agents for therapeutic intervention. Alginate, a biocompatible and biodegradable biopolymer, was utilized to synthesize nanoparticles through controlled ionic crosslinking, which ensured effective encapsulation of bioactive compounds. The antibacterial efficacy of ABNs was evaluated using the agar well diffusion method, demonstrating enhanced bacterial inhibition against E. coli and S. aureus, with larger inhibition zones corresponding to higher nanoparticle concentrations. Furthermore, the anti-inflammatory potential was assessed through the protein denaturation assay, where ABNs exhibited a dose-dependent increase in inhibition, confirming their effectiveness in reducing inflammatory responses. Fourier-transform infrared spectroscopy (FTIR) analysis validated the successful integration of functional groups necessary for nanoparticle stability, while structural integrity was examined through X-ray diffraction (XRD). These findings position ABNs as a multifunctional platform for targeted drug delivery, wound healing, and infection control, providing a sustainable alternative to conventional antibiotics. By combining antibacterial and anti-inflammatory properties, this approach enhances therapeutic efficacy, bioavailability, and controlled drug release, establishing alginate nanoparticles as a promising solution for biomedical applications and regenerative medicine.

**Keywords:** Alginate Nanoparticles; Antibacterial Activity; Anti-inflammatory Agents; Drug Delivery System; Biomedical Applications.

# Introduction

Nanoparticles, referred to as particles with nanoscale dimension, are considered to be the fundamental units of nanotechnology. The ability of these materials to synthesize and manipulate have caused a recent resurgence in the use of these particles in these size ranges,which have been utilized by various industries and humanity for thousands of years.[(Biswas & Wu, 2005)](https://paperpile.com/c/S6ODwI/uczM)*.* Nanoparticles can be generally classified into 4 types: inorganic based nanoparticles, carbon based nanoparticles, organic/bio based nanoparticles and composite based nanoparticles. Inorganic based nanoparticles include metal based nanoparticles such as silver lined,(Ag) zinc oxide(ZnO), silica(siO2), iron oxide (Fe3O4), cadmium (Cd). Carbon based nanoparticles include fullerene, graphene and carbon black. Biopolymers include alginate, chitosan, cyclodextrin, liposome. Composite based nanoparticles are a combination of organic, carbon and inorganic nanoparticles [(Deepika et al., 2022; Harsha & Subramanian, 2022; Solanki et al., 2022)](https://paperpile.com/c/S6ODwI/ubZGW+lczPD+NyJ4P).

Alginate is a biopolymer that is commonly acknowledged as a substance that is both biocompatible and biodegradable. It is one of the most beneficial marine [biopolymers](https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/biopolymer) and it can join with several other compounds to build biopolymers [(Ajay, Rakshagan, et al., 2022; Ajay, Sasikala, et al., 2022; Chidambaram et al., 2022)](https://paperpile.com/c/S6ODwI/rd378+jVCs2+atCmZ). The primary source of alginate is isolation from the cell walls and the intracellular spaces of several brown seaweeds around the world, such as *Laminaria hyperborea*, *Macrocystis pyrifera*, and *Ascophyllum nodosum*. Alginate has shown the most promising potential for building a drug delivery system for anti cancer drugs [(He et al., 2020)](https://paperpile.com/c/S6ODwI/nvSD).Nano hydrogels , nanofibres, nanoemulsions, and nanocomplexes are examples of alginate based nanoparticles. Recent research investigations have not included metal based nanoparticles due to their increased toxicity and of metal deposits in the body[(Sánchez-López et al., 2020)](https://paperpile.com/c/S6ODwI/yLk0). Alginate based [nanoparticles](https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/nanoparticle) (ABNs) are extensively used in the field of medicine for various [therapeutic uses](https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/therapeutic-use) such as wound healing, and biomedical applications where it has the ability to encapsulate bio active molecules such as drugs and proteins. Alginate is water soluble and exhibits mucoadhesive properties in contrast to chitosan [(Merchant et al. 2025; Shenoy et al. 2022; Shenoy et al. 2023)](https://paperpile.com/c/wr9Yj3/Yk3B+ZF2O+LZna). These [nanoparticles](https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/nanoparticle) work on the principle of immobilization. A high water content hydrophilic polymer matrix forms the basis of three-dimensionally cross-linked networks known as hydrogels [(Ajay, Suma, et al., 2022; Katyal et al., 2021; Maiti, 2021)](https://paperpile.com/c/S6ODwI/Q026F+4X5Gs+k7mCu). When cells are incorporated into hydrogels, they move into a highly swollen state that facilitates transport of nutrients and cellular waste products in and out of them[(Sun & Tan, 2013)](https://paperpile.com/c/S6ODwI/snjj). Alginate is composed of *α*-L-guluronic acid and *β*-D-mannuronic acid that is prevalent in nature and easily turns into hydrogel in the presence of divalent or trivalent metal ions. The metal ions and the carboxylic acid groups on the polymer framework form an organized structure through ionic interaction and intramolecular bonding, and the resulting cavities are well suited for the entrapment of bioactive compounds and drugs [(Saadatidizaji et al., 2024; Sun & Tan, 2013)](https://paperpile.com/c/S6ODwI/snjj+PJhs). One of the most effective ways to deal with the problem of low drug solubility in water is using nanotechnology. Bio Polymeric nanoparticles are unique among the diversity of nano-delivery technologies available because they offer extra benefits. It not only improves drug solubility but also offers superior stability in storage and bloodstream dispersion. The polymer matrix's optimum drug absorption capacity allows for the drug's sustained release[(Maghsoudi et al., 2020)](https://paperpile.com/c/S6ODwI/5TA8)*.* While alginate exhibits remarkable stability in physiological circumstances; they gradually implement cleavage of glycosidic linkages that may occur in acidic and basic environments. Nevertheless, there is no indication that human enzymes are able to degrade this polymer [(“Polymer-Based Biomaterials for Pharmaceutical and Biomedical Applications: A Focus on Topical Drug Administration,” 2023)](https://paperpile.com/c/S6ODwI/iu2Z). It was demonstrated by several studies that intravenously administered alginate can be excreted by the renal system only for a molecular weight lower than the renal clearance threshold.

Pathogenic bacteria infection is a major public health problem due to the high morbidity and mortality rates, as well as the increased expenditure on patient management. Bacterial infection typically coexists with wound healing. Drug resistance is caused by the overuse of synthetic antibiotics, which poses a threat to human health. Nanoparticles based wound dressings have become a popular and efficient way to heal wounds by reducing bacterial infections [(Zhong et al., 2020)](https://paperpile.com/c/S6ODwI/L5In). Although there are several options for antimicrobial therapy, their efficacy is limited because of the occurrence of drug-resistant bacteria. In the past decade, a great advance in nanomedicine holds promise for bacterial infection treatment. The nanoparticles can act as antibacterial agents or the carriers for loading antibacterial drugs to promote the bioavailability and effectiveness of antibiotics[(Yeh et al., 2020)](https://paperpile.com/c/S6ODwI/2VdB). Alginate-based nanoparticles can often increase and improve antibacterial activity through four major pathways in their role as a medication delivery vehicle. First off, drug absorptivity is enhanced when drug particles are smaller since this increases drug solubility. Second, excellent bioavailability is ensured by protecting medications as they are delivered to the site of action, in this example, bacterial cells. Thirdly, drug selectivity is improved by the ionic interaction between the positive charge on alginate and the negative charge on the surface of bacterial cells. Finally, medications are released sustainably and have long-lasting antibacterial effects[(Eleraky et al., 2020)](https://paperpile.com/c/S6ODwI/0btU)*.* Biopolymers are currently blooming under the field of recent research on how their use can be precise and increase their use in the field of medicine in the future.

# MATERIALS AND METHODS

Collection of plant sample:

The seagrass clary was collected from the Palk Bay coast, Tamil Nadu, India. The sample was hand-picked and cleaned in salt water to remove the debris. The sample was transported to the laboratory in an icebox, properly rinsed with tap water to eliminate any leftover salt, and then blotted on paper to absorb moisture.

Preparation of extract:

The seagrass clary was thoroughly washed, dried, and powdered. The powdered material was subjected to extraction using 80% methanol with the help of mortar and pestle to obtain the extract rich in bioactive compounds.

Synthesis of nanoparticles

To prepare the sodium alginate solution, 5 grams of sodium alginate were dissolved in 40 mL of distilled water and mixed at 70°C and 990 rpm for 2.5 hours. Subsequently, 3 drops of glacial acetic acid were added to the preparation. The mixture was then stirred for an additional 30 minutes, totaling 3 hours of stirring.Finally, the prepared solution underwent lyophilization to complete the process.

Antibacterial activity:

Agar well diffusion method:

Nutrient broth was prepared and inoculated with bacteria strains respectively. Incubated at 37 degree Celsius for 2-3 hrs hours. After incubation turbidity was adjusted using the 0.5 McFarland Standard. Mueller Hinton agar was prepared aseptically and poured into sterile petri plates. Then the bacterial lawn culture was performed on the plates. Four wells with a diameter of 10 mm and a depth of 4 mm were made using sterile gel puncture. For negative control dimethyl sulfoxide (DMSO) was added into the well and positive control antibiotic disc was placed in the media. The plates were then incubated at 37°C for 24 hours. after the incubation diameter of the zone was measured.

Anti-inflammatory Activity:

Protein Denaturation assay:

The Prepared Phosphate buffer of 4.780 μl and 0.2 μl of BSA were added along with the lyophilized sample (10 mg/mL) of varying concentrations ( 50μl, 100 μl, 150μl , 200μl ) and vortex before being allowed to incubate in a water bath for 20 minutes, and the OD was taken at 660nm. The inhibition percentage was calculated.

Anti-inflammatory activity (%) = [(Control - Sample) / Control] × 100 (1)

# RESULTS

## Antibacterial Activity

Antibacterial activity of alginate nanoparticles against E.coli and S.aureus was observed. In well diffusion technique, a zone of inhibition of 11mm was observed in a 50µL concentration. A slightly bigger zone of inhibition of 12mm was seen in a 75µL sample indicating stronger antibacterial action at higher concentrations. At 100µL, the zone of inhibition of 15mm was even greater indicating that the antibacterial efficacy was substantially increased at this dose. The Negative control (NC) showed a zone of inhibition measuring 10mm, showing limited antibacterial activity whereas the positive control (PC) produced a zone of inhibition of 25mm demonstrating significant antibacterial activity against E.coli.The diameter of inhibition zone of E.coli bacteria in correlation to concentration of extracts is listed in figure 2 and demonstrated in Fig. 1.

The results also showed various antimicrobial agent concentrations have antibacterial action against Staphylococcus aureus. The clear zone surrounding the discs in the petri dish during agar well diffusion methods indicated the inhibition zones of different measurements as shown in fig.2. These inhibition zones are quantified in a bar chart as depicted in graph 2, which shows that the zone of inhibition is 11mm at 50µg, 12mm at 75µg and 15mm at 100µg. While the negative control (NC) has a 10mm zone that indicates minimal or no antimicrobial activity, the positive control (PC) exhibits a substantially higher zone of inhibition of 20mm suggesting a sturdy antimicrobial action(Chehelgerdi et al., 2023). These findings imply that antimicrobial agents efficacy against S.aureus is a concentration- dependent increase.

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Figure 1: the agar diffusion test results that demonstrate the zone of inhibition of alginate based nanoparticles loaded with antibacterial agents at various concentrations which show effective inhibition of the growth of the bacteria; Escherichia coli.

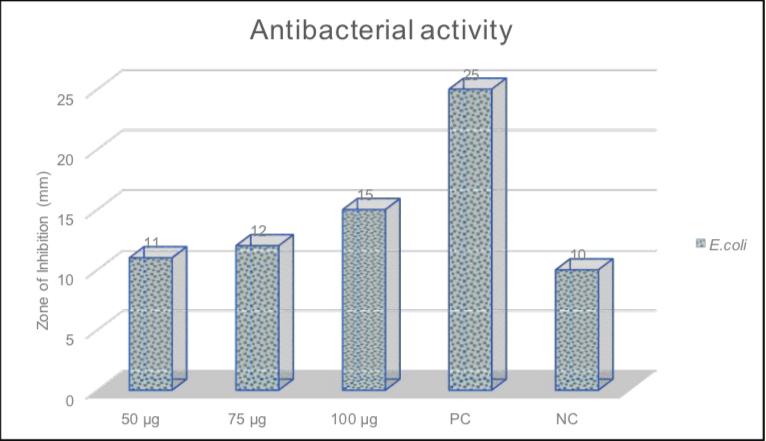
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Figure 2: Antibacterial activity against E.coli showing the diameter of zone of inhibition (mm) in correlation to various concentrations of alginate nanoparticles.



Figure 3: The agar diffusion test results demonstrate the zone of inhibition of alginate based nanoparticles loaded with antibacterial agents at various concentrations which show effective inhibition of the growth of the bacteria; Staphylococcus aureus.

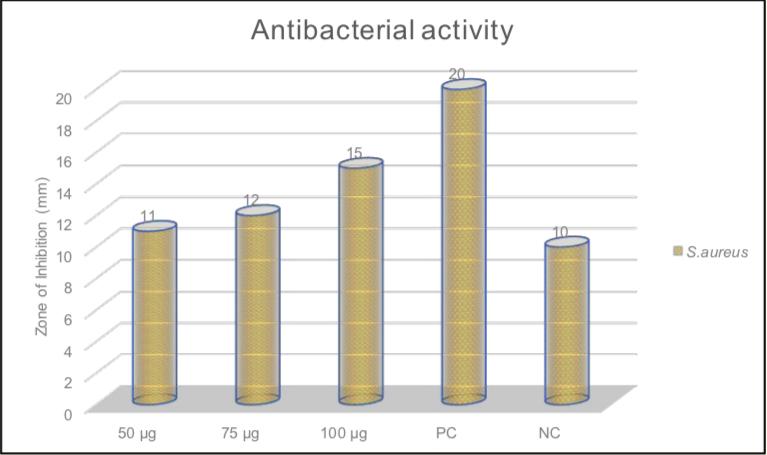
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Figure 4: Antibacterial activity against S.aureus showing the diameter of zone of inhibition (mm) in correlation to various concentrations of alginate nanoparticles.

# Anti-Inflammatory Activity

The anti-inflammatory activity of AlgCnNPs at various concentrations were observed.Approximately 45% inhibition is shown by AlgCnNPs at the lowest concentration of 50µg. This suggests that the compound has a considerable anti-inflammatory effect even at a low concentration. The inhibition% increases to 54.5% when the concentration is 100µg. This implies that the anti-inflammatory action is enhanced when the concentration is doubled. A substantial increase is observed on raising the concentration to 150µg, where the percentage of inhibition is 69.5%. And at 200µg, the percentage inhibition is at 81.5%. This shows that the drug’s efficacy increases with increase in dosages. Therefore data depicted in fig.4. reveals a clear dose-dependent relationship, where higher concentrations of AlgCnSNPs correspond to greater anti-inflammatory effects.

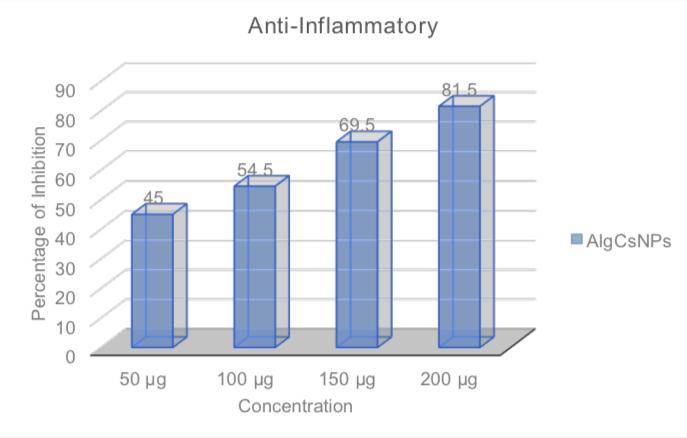


Figure 5: Bar graph showing the % of inflammatory inhibition against different concentrations of AlgCnNPs (50 µg, 100 µg, 150 µg, and 200 µg).

## FT-IR Analysis

The FTIR analysis of the synthesized alginate nanoparticles revealed several significant peaks indicative of the chemical structure and the molecular interactions within the nanoparticle (Saadh et al., 2024). The peak absorbance at 3329 cm^-1 represents the O-H functional group, suggesting that it reacts with hydrogen atoms thus generating a water molecule. The absorption peak at 2937 cm^-1 is due to the alkaline medium stretching vibrations of C-H bonds. The peak at 1596 cm^-1 is assigned to C=C stretching, indicating the presence of a cyclic alkene group. The strong absorption peak at 1412 cm^-1 is assigned to S=O stretching, indicating the presence of a sulfate group. The strong peak at 1299 cm ^-1 is assigned to C-O stretching indicating an aromatic ester group. The peak at 1086 cm^-1 indicates a strong C-O stretching showing the presence of an aliphatic ether group. The medium absorption peak at 1029 cm^-1 is assigned to a C-N stretching, indicating an amine group. The absorption peak at 940 cm^-1 is assigned to C=C bending, indicating a strong alkene group. The absorption peak at 812 cm^-1 represents a strong C-H bending indicating 1,2,3,4-tetra substituted compound. The peak at 624 cm^-1 represents a strong C-Br stretching indicating the presence of an halocompound. The absorption peak at 534cm^-1 represents a strong C-l stretching indicating the presence of halocompound. These FTIR results as depicted in fig.4. confirm the successful incorporation of alginate into the nanoparticles, thus maintaining the functional groups essential for the structural integrity and biocompatibility of the nanoparticle. This integrity is vital for the application of these compounds in biomedicine and targeted drug delivery providing a sustained release of the drug onto the targeted tissue.

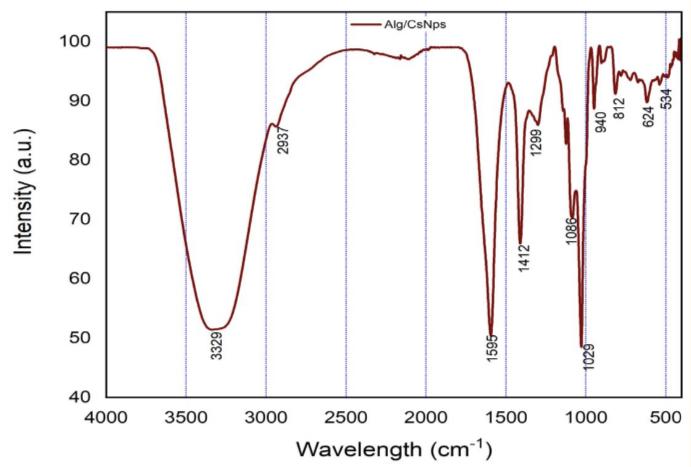


Figure 6: FT-IR spectrum

# DISCUSSION

In recent times under the field of research and biomedical applications, naturally occurring extracts are in great demand due to their minimal side effects. AlgNPs have emerged as a promising material in this field due to their biocompatibility, enhanced therapeutic efficacy, large surface area and nano size. This research compares the results with previous findings on the antibacterial activity of AlgNPs loaded with anti-inflammatory and antibacterial drugs.

The study's FTIR spectra of the alginate nanoparticles (AlgNPs) shows distinctive peaks that indicate the existence of functional groups connected to both the alginate and the loaded medicinal medicines. There are prominent peaks in the spectra at approximately 3329cm⁻¹ (O-H stretching), 2937cm⁻¹ (C-H stretching), 1596 cm⁻¹ (C=C stretching), 1412 cm⁻¹ (S=O bending), and 1029 cm⁻¹ (C-N stretching). These peaks show good nanoparticle production since they match the typical alginate absorption bands. Similar findings were reported by [(Belattmania et al., 2020)](https://paperpile.com/c/S6ODwI/0fcq), where the FTIR spectra of alginate nanoparticles showed peaks at 1710 cm⁻¹ (C=O), 1610 cm⁻¹ (C=C stretching), and 1025 cm⁻¹ (S=O stretching), which are compatible with the findings of the current investigation.

Furthermore,[(Ahmad et al., 2022)](https://paperpile.com/c/S6ODwI/nHR4) in their investigation of nerolidol-loaded chitosan-alginate nanoparticles, noted similar FTIR peaks, exhibiting strong absorption bands at 3373 cm⁻¹(O-H stretching), 1099cm⁻¹(C-N stretching), 1637 cm⁻¹(C=C bend), confirming the distinct functional groups of alginate and its effective encapsulation of chitosan. Additionally, FTIR spectra of alginate polymeric nanoparticle- loaded α-Mangostin were reported by[(Muchtaridi et al., 2023)](https://paperpile.com/c/S6ODwI/b1B6) , showing peaks at 1029.24 cm⁻¹, 2948.21cm⁻¹, 3358 cm⁻¹, and 1400 cm⁻¹. [(Zaineb et al., 2022)](https://paperpile.com/c/S6ODwI/quk9) observed similar characteristic peaks. They showed absorption bands at 3416cm⁻¹ (O-H stretching), 1610cm⁻¹ (C=Cstretching), and 1017 cm⁻¹ (S=O stretching), thus confirming the successful formulation of calcium alginate based microspheres encapsulated with TiO2 nanoparticles. The study conducted by [(Babić Radić et al., 2024)](https://paperpile.com/c/S6ODwI/QYiL) analyzed the FTIR spectra of Gelatin-/alginate based hydrogels scaffolds reinforced with TiO2 nanoparticles [(Balaji Ganesh S & Sugumar, 2021; Jabin et al., 2021)](https://paperpile.com/c/S6ODwI/PI2Ij+R3FYv). Their results revealed peaks at 3281 cm⁻¹ (O-H stretching), 1160 cm⁻¹ (C-C stretching), 1290 cm⁻¹(C-O bend), 1028 cm⁻¹ (S=O stretching), thus validating the presence of similar functional groups as obtained in this study. These spectra confirmed the effective synthesis of AlgNPs and provided additional evidence for the presence of comparable functional groups [(Govindaraj & Dinesh, 2021; Rajeshkumar et al., 2021; Sushanthi , 2021)](https://paperpile.com/c/S6ODwI/vWspF+vW29b+0MCZZ).

Utilizing a protein denaturation assay, the anti-inflammatory properties of alginate nanoparticles (AlgNPs) loaded with anti-inflammatory drugs were determined in this study. At various concentrations, the results demonstrated a considerable reduction of protein denaturation. In particular, the AlgNPs showed inhibitory percentages of 81.5% at a concentration of 200 µg/mL which were similar to those seen in prior research findings using other nanoparticles for anti-inflammatory effects [(Graf et al., 2023; Ramamurthy & Jaiganesh, 2021; Tiwari & Jain, 2023)](https://paperpile.com/c/S6ODwI/z2yo0+WyF0t+RJ2TR). According to the study done by [(Aslam et al., 2023)](https://paperpile.com/c/S6ODwI/tu6b) , a unique bioactive substance that was isolated from plants had strong anti-inflammatory properties. On performing the in vitro tests, the substance decreased IL-6 and TNF-α levels by around 45% and 50%, respectively. It also reduced COX-2 activity by around 60%. In comparison to controls, the chemical in animal models reduced tissue damage caused by inflammation by around 78%. According to the study done by [(Eltahir et al., 2024)](https://paperpile.com/c/S6ODwI/XjGE), The extracts of Hibiscus rosa-sinensis, Aloe vera, and Coriandrum sativum produced less nitric oxide (63%, 47%, and 52%, respectively), and TNF-α. The study conducted by [(Tyavambiza et al., 2021)](https://paperpile.com/c/S6ODwI/YSA2) indicated that at a concentration of 200 µg/mL, silver nanoparticles (AgNPs) derived from Azadirachta indica extract exhibited a 60% inhibition of nitric oxide generation. Moreover, they caused a 50% and 55% decrease in the levels of pro-inflammatory cytokines IL-6 and TNF-α. The results suggested that these AgNPs have the potential to be useful tools for controlling inflammation.

According to this study, AlgNPs have a substantial antibacterial effect against E.coli and S.aureus that are dose-dependent, with increase in concentrations the zone of inhibition increases. The ZOI measured 11mm in the 50µL sample, 12mm in the 75µL sample and 15mm in the 100µL sample was observed. The effectiveness of these results shown are consistent with the previous findings showing that nanoparticles have the potential to be strong antibacterial agents. According to a research by [(Martínez-García et al., 2024)](https://paperpile.com/c/S6ODwI/VEOl), inhibitory zones measuring between 10 and 20 mm were observed by alginate-based nanoparticles containing silver ions against a variety of bacterial species, such as S. aureus and E. coli. In particular, the inhibition zone for S. aureus was around 17 mm and that of E. coli was about 15 mm at a concentration of 100 µg/mL. The findings show a potent antibacterial action, with greater inhibition zones correlating to increased nanoparticle concentrations of silver ions.

Similar study conducted by [(Abd El-Hady & Saeed, 2020)](https://paperpile.com/c/S6ODwI/6BEc) reported that an inhibitory zone of 18 mm was obtained against E. Coli and 16 mm against S. aureus in the formulation that included curcumin and silver nanoparticles. These findings show that the antibacterial efficiency of chitosan nanoparticles containing silver and curcumin is increased, with a notable effect against E. coli. According to a study by [(Almeleebia et al., 2024)](https://paperpile.com/c/S6ODwI/LCVA) inhibition zones of ciprofloxacin-loaded alginate nanoparticles against different bacterial strains ranged from 15 mm to 22 mm, with the greatest zone of 22 mm seen against E. coli. Furthermore, these nanoparticles demonstrated antifungal efficacy against Candida albicans, with inhibition zones of up to 18 mm. These findings highlight the possibility of using silver nanoparticles in conjunction with ciprofloxacin-loaded alginate nanoparticles to effectively treat bacteria and fungi.

The therapeutic value of AlgNPs with further optimization is promising when compared to conventional antibiotics. According to an “In Vitro Study" done by[(Chandran et al., 2024)](https://paperpile.com/c/S6ODwI/GSkP) the biosynthesized silver nanoparticles (AgNPs) exhibited significantly higher antimicrobial activity compared to chemically synthesized AgNPs. The biosynthesized AgNPs showed zones of inhibition (ZOI) of 20mm against Enterococcus faecalis, whereas the chemically synthesized AgNPs had ZOIs of 15mm. Additionally, the biosynthesized AgNPs demonstrated lower cytotoxicity, suggesting their safer profile for potential clinical applications​. According to study done by [(Al-Otibi et al., 2020)](https://paperpile.com/c/S6ODwI/gpW0)biosynthesized silver nanoparticles exhibited good antifungal efficacy against Fusarium solani, limiting fungal growth to 1.5 mm, and inhibitory zones of 19.00 ± 2.94 mm against Staphylococcus aureus. These findings demonstrated the silver nanoparticles produced by biosynthesis as strong antibacterial agents, providing a substitute for conventional chemical synthesis techniques.This shows that although AlgNPs are useful, more optimization and formulational refinement is required to make these particles more efficient as or even more so than traditional antibiotics.

# CONCLUSION

This study successfully synthesized and characterized alginate nanoparticles highlighting the promising antibacterial and anti-inflammatory potential against S.aureus and E.coli. The FT-IR analysis validated the successful incorporation of therapeutic agents due to presence of functional groups. The protein denaturation assay showcased AlgNPs as a promising material for multifaceted therapeutic interventions. The antibacterial activity against E.coli and S.aureus highlighted the nanoparticles ability to combat common pathogens. AlgNPs showed superior activity when compared to other nanoparticles in antibacterial and anti inflammatory activity. Further in vivo and clinical trials are needed to ensure safety and effectiveness in clinical healthcare practices.

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