Tailored Synthesis of Alginate Based Nanoparticles doped with mangrove extract for Targeted Antioxidant and Antibacterial Therapy

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**Abstract:** The development of biopolymer-based nanoparticles has garnered considerable attention due to their potential in targeted therapeutic applications. This study investigates the tailored synthesis of alginate-based nanoparticles (ABNs) doped with mangrove extract for antioxidant and antibacterial therapy. Sodium alginate, a biocompatible and biodegradable polymer, was employed for the fabrication of nanoparticles through ionic gelation, thereby ensuring efficient encapsulation and controlled release of bioactive compounds. The incorporation of mangrove extract, recognized for its rich phenolic and flavonoid content, aimed to enhance the antioxidant and antimicrobial efficacy of the nanoparticles. The antibacterial activity, evaluated using the agar well diffusion method, exhibited significant inhibition against pathogenic bacteria such as E. coli and E. faecalis. Furthermore, the DPPH assay confirmed a strong antioxidant potential, indicating the capacity of the nanoparticles to mitigate oxidative stress. Fourier-transform infrared spectroscopy (FTIR) and X-ray diffraction (XRD) analyses substantiated the successful integration of functional groups and affirmed the structural integrity of the nanoparticles. These findings underscore the therapeutic potential of alginate-based nanoparticles as a novel biomaterial for wound healing, infection control, and antioxidant defense, thereby paving the way for advanced drug delivery systems in biomedical applications.

**Keywords**: Alginate Nanoparticles; Mangrove Extract; Antioxidant Therapy; Antibacterial Activity; Targeted Drug Delivery.

# Introduction

The field of creating nanotechnology through the use of nanoparticles as carriers of both tiny and large molecules has attracted a lot of research interest in recent decades. Nanoparticles have been formulated using a variety of polymers. The best works in the subject of nanotechnology are highlighted in this review [(Harsha & Subramanian, 2022)](https://paperpile.com/c/B6WGSK/iSPR7)[(Deepika et al., 2022)](https://paperpile.com/c/B6WGSK/dXQsf)[(Solanki et al., 2022)](https://paperpile.com/c/B6WGSK/DZsnQ). The Latin root of the term "Nano" implies midget. Nanometers are one thousand millionth of a meter (1n=109m). Nano size is defined as one thousand millionth of a certain unit [(Chidambaram et al., 2022)](https://paperpile.com/c/B6WGSK/Ut7yr)[(Ajay, Sasikala, et al., 2022)](https://paperpile.com/c/B6WGSK/sOHXQ). For many years, the scientific disciplines of electronics, physics, and engineering have been the ones to most frequently utilize the word "nanotechnology."[(Ajay, Rakshagan, et al., 2022)](https://paperpile.com/c/B6WGSK/20QIq) The biomedical and pharmacological disciplines, however, have not yet been fully investigated. The multidisciplinary field of nanotechnology involves the convergence of fundamental sciences [(Ajay, Suma, et al., 2022)](https://paperpile.com/c/B6WGSK/gUjkH) [(Katyal et al., 2021)](https://paperpile.com/c/B6WGSK/EJmXZ).Nanoparticles are incredibly small particles or structures that are typically between one and one hundred nanometers in size, having dimensions in the nanometer scale. In order to generate innovative or superior physicochemical features that are not achievable in their bulk solid equivalents, they are engineered at the atomic or molecular level. This is because, according to all compounds usually have a specific size threshold range or value beyond which their properties drastically change [(Jabin et al., 2021)](https://paperpile.com/c/B6WGSK/GPU7J)[(Balaji Ganesh S & Sugumar, 2021)](https://paperpile.com/c/B6WGSK/0cpN5) [(Govindaraj & Dinesh, 2021)](https://paperpile.com/c/B6WGSK/TzeVa). The characteristics of these nanoparticles differ from those of their ordinary solid counterparts. They are essentially between the characteristics and traits of conventional solids and atomic or molecular formations.

Alginate is a marine-derived biopolymer with special biological qualities that has a lot of potential applications in a variety of industries, such as the production of innovative products for the food, pharmaceutical, biomedical, and environmental sectors [(Tiwari & Jain, 2023)](https://paperpile.com/c/B6WGSK/4xNqm)[(Graf et al., 2023)](https://paperpile.com/c/B6WGSK/MJBRm). As one of the most prevalent substances in nature, alginate is seen as a very promising material from the perspective of the circular economy and as a potential replacement for petroleum-derived polymers, along with other polysaccharides (such as chitosan, celluloses, etc.)[(Sabarathinam & Madhulaxmi, 2021)](https://paperpile.com/c/B6WGSK/s2kZb)[(Sushanthi et al., 2021)](https://paperpile.com/c/B6WGSK/T6ZlK)[(Harsha et al., 2022)](https://paperpile.com/c/B6WGSK/WHOAZ).Among others, one of the reasons for alginate success is its unique capability to bind different cations leading to stable and tailor-made hydrogels.[(Bibi et al., 2023)](https://paperpile.com/c/B6WGSK/K5ts5).

Although less so for nanoparticles, alginate is a versatile polymer that is often utilized in the formation of microparticles. Applications for it can be found in many different industries, including as the food and beverage industry (for example, as stabilizers in ice cream, drinks, and jellies), pharmaceuticals, ethanol manufacturing, cell culture, dental materials, tablets, and wound dressings[(Neha et al., 2021)](https://paperpile.com/c/B6WGSK/IfcKd)[(Maliael et al., 2021)](https://paperpile.com/c/B6WGSK/mTGfJ)[(Lakshmi, 2021)](https://paperpile.com/c/B6WGSK/4r0gq). Since the 1940s, alginate has been used in medicine for encapsulating islet cells, delivering cells, delivering peptides and proteins orally, releasing drugs gradually, and immobilizing cells and enzymes[(Dharman et al., 2021)](https://paperpile.com/c/B6WGSK/SPnIB). Its main functions are stabilizing, gel-forming, and thickening.Alginates are noteworthy for applications involving controlled release in medication delivery. When incorporated into nanoparticles, they lessen toxicity and enhance drug bioavailability. These nanoparticles are being investigated for use in medication formulations, along with beads, foams, fibers, and sponges. Alginic acid is used as an alginate and sodium alginate tablet binding agent.helps break down tablets so they can be released right away. Alginate-based delivery systems are appropriate for pH-responsive or magnetically triggered delivery systems because they can modify drug release based on physiological requirements. This highlights the significance of alginate-based systems for future pharmaceutical research [(Singh et al., 2022)](https://paperpile.com/c/B6WGSK/Sdox).

One of the polymers, sodium alginate (SA), is obtained from brown algae and is made up of a-L-guluronic acid (G-block) and b-D-mannuronic acid (M block) residues arranged randomly. It is widely utilized in culinary and pharmaceutical applications due to its excellent biocompatibility, ease of processing, and mild gelling capabilities. Alginate is also a great matrix for the extended release of many different pharmacological substances. Because SA matrices are quickly absorbed and degraded by the body both during and after drug molecule release, they are widely used in the production of controlled and sustained release formulations [(Reddy Obireddy et al., 2023)](https://paperpile.com/c/B6WGSK/RGgky).

Mangroves provide a variety of environmental functions, including as capturing and recycling organic debris, giving aquatic and terrestrial species surfaces and shelter, and enhancing the general health of coastal habitats. The mangrove ecosystem, which receives freshwater, sediments, nutrients, and silt deposits from upland rivers, as well as daily tides from the ocean, symbolizes an intermediate state between terrestrial and marine life. Mangroves can grow as shrubs or trees depending on the edaphic characteristics, terrain, salt of the water, and climate of the place in which they are found. In 124 tropical and subtropical nations and regions, mangroves are salt-tolerant evergreen trees that are located along protected coastlines, shallow-water lagoons, estuaries, rivers, or deltas.([(Syahidah & Subekti, 2019; Website, n.d.)](https://paperpile.com/c/B6WGSK/d1seW+0HTL8).

Mangroves are known to contain 81 different species globally. Several physiologically active chemicals, including those with anticancer, antiulcer, antioxidant, antidiabetic, and antibacterial properties, have been identified from mangroves and have been shown to have varying degrees of medicinal potential.The Avicennia marina is one of Indonesia's most prevalent and accessible mangrove species. Indigenous peoples have long used this species extensively for a variety of reasons, such as building materials and traditional medicine for treating skin conditions, rheumatism, ulcers, and smallpox. The plant is widely used in traditional medicine, and its extracts are thought to contain a variety of bioactive chemicals that could have advantages for the pharmaceutical sector.[(Azis et al., 2022)](https://paperpile.com/c/B6WGSK/COgvq)

# Materials and methods

## Sample collection

The mangrove was collected from Tamil Nadu, India. The sample was cleaned in 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 mangrove Extract

The mangrove 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.

## Antioxidant Activity

## DPPH Assay

The radical scavenging activity of a sample was measured by the DPPH (2.2-diphenyl-1-pricrylhydrazyl) assay method. The lyophilized sample (10 mg/mL) of varying concentrations (50µl, 100µl, 150µl, 200µl) is added to makeup 3 mL with DPPH and incubated for 30 mins in the dark room. After 30 minutes of incubation, the absorbance of the DPPH solution was determined, and the optical density was measured at 510 nm.The percentage of scavenging activity inhibition was calculated.DPPH scavenging effect (%) = [(𝐴0 − 𝐴1) × 100] / 𝐴0

where, A0 is the absorbance of control and A1 is the absorbance of sample.

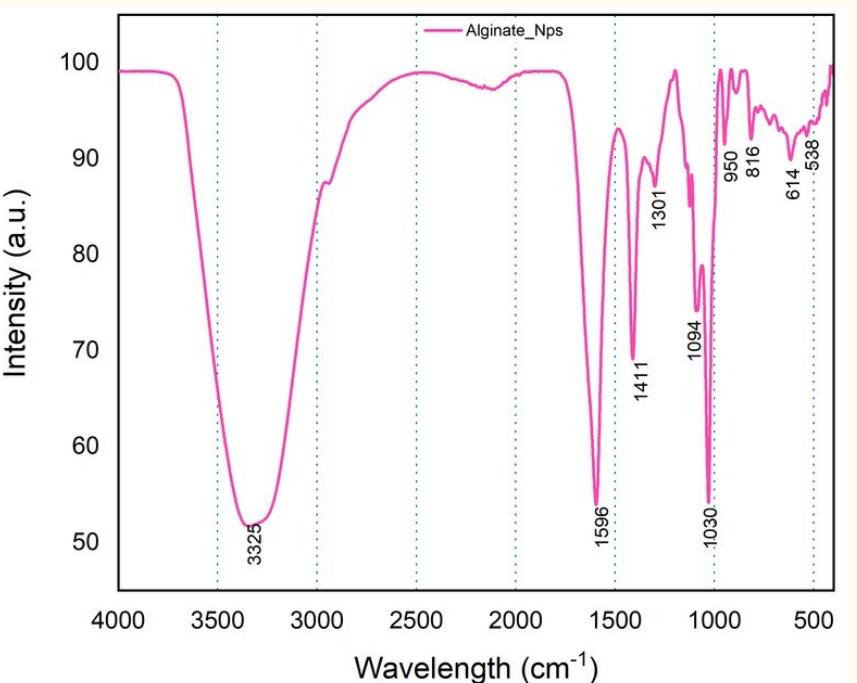
## Antibacterial activity

## 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 in the plates. Four wells with a diameter of 10 mm and a depth of 4 mm was 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.

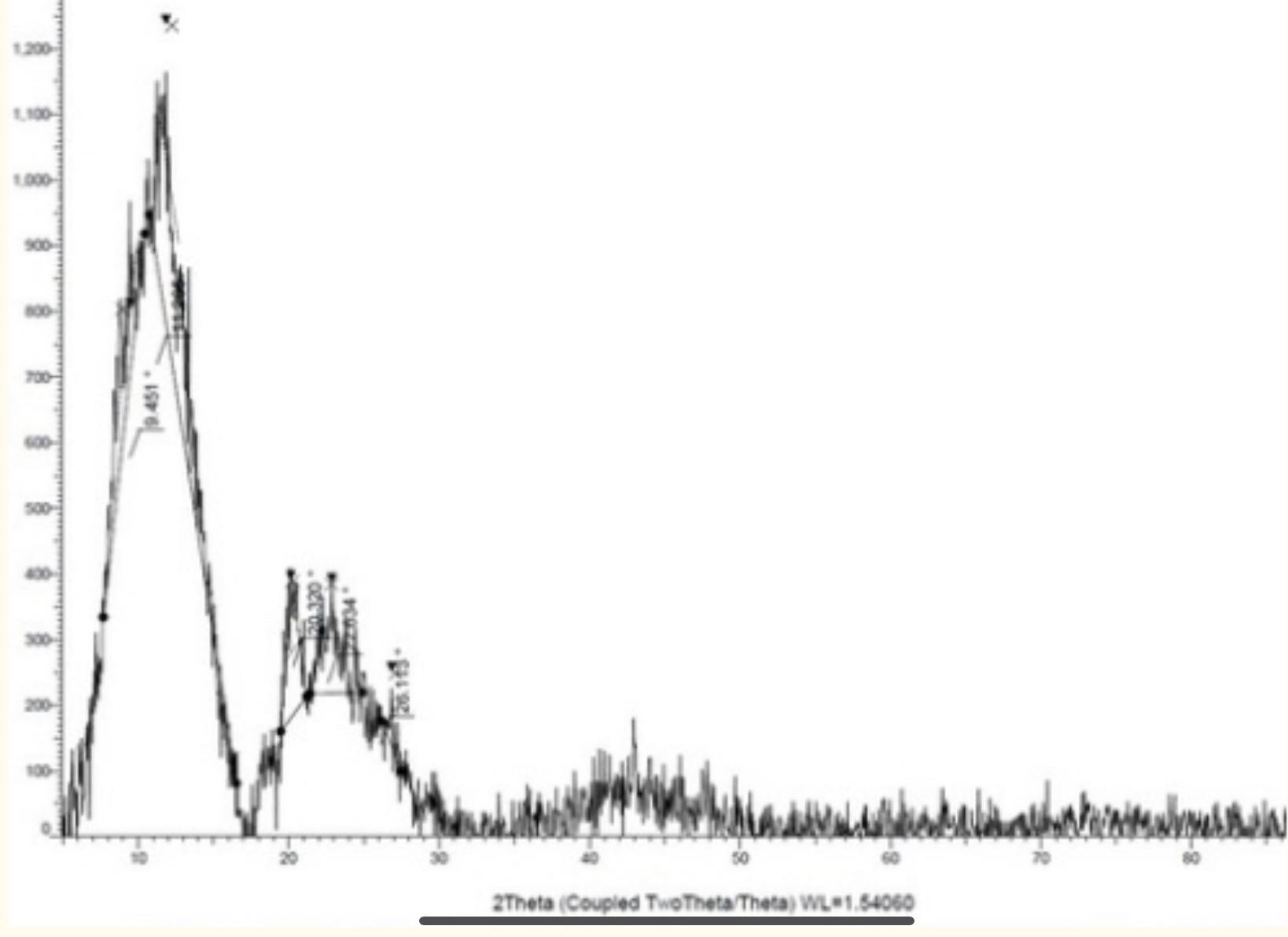
# Results and Discussion

The FTIR Analysis of synthesised alginate nanoparticles revealed several significant peaks indicative of chemical structure and molecular int within the nanoparticle. The peak absorbance at 3325cm-1 is attributed to the stretching vibration of O-H groups resulting in hydrogen bonding. It indicates the presence of hydroxyl group in alginate. The peak at 1596cm-1 and 1411cm-1 is assigned to the stretching vibration of C=O in the carboxylate group. This aligns with the known chemistry of alginate, a biopolymer derived from brown algae, composed of mannuronic acid and guluronic acid units, both of which contain carboxyl groups. A absorption peak at 1307cm-1 which is associated with the C-H stretching vibration of the aliphatic or possibly aromatic component with polysaccharide structure, these peaks may be less prominent compared to C=O and O-H stretches. A peak at 1094cm-1 and 1030cm-1 is attributed to C-O stretching vibration of ether or alcohol group. It indicates the pre of hydroxyl and ether functionalities within alginate structure. Strong and broad peaks show more indicative of alginate and mangrove extract due to abundance of carboxyl group and hydroxyl groups and weaker and sharp peaks indicate the presence of aliphatic C-H bonds , presence of ether and alcohol group. The peak at 538cm-1 is associated with bending vibrations in polysaccharide structure of alginate and some organic or inorganic components in the mangrove extract.



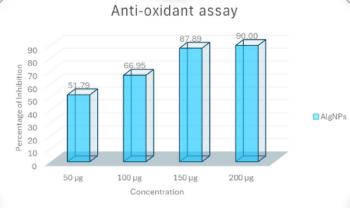
**Figure 1:** Ftir of sodium alginate nanoparticles

The image's X-ray diffraction (XRD) pattern shows the crystalline structure of the sample under study through different diffraction peaks. The y-axis shows the intensity of the diffracted X-rays, expressed in counts, and the x-axis depicts the 2-theta angle, which is equivalent to the diffraction angle. A prominent peak at approximately 8 degrees 2-theta, exhibiting an intensity near 1300 counts, suggests the presence of a substantial crystalline component in the sample. This peak indicates that the crystalline structure in question has a certain d-spacing property. Around 18 degrees 2-theta, a second noticeable peak with an intensity of around 800 counts is noticed. This peak may indicate a different crystallographic phase or a different orientation within the same phase.Between 20 and 40 degrees 2-theta, a number of minor peaks can be seen in addition to these larger ones. The presence of additional crystalline phases or distinct orientations of the same phase is indicated by these tiny peaks, which add to the overall complexity of the sample's structure. The wide background signal that was seen from 10 to 80 degrees 2-theta indicates that there may be some amorphous material or phase disturbance in the sample. Particularly at lower 2-theta angles, the peaks' crispness suggests clearly defined crystalline areas. Through a comparison of these detected peaks with conventional reference patterns found in XRD databases, the precise crystalline structures found in the sample can be determined. Overall, the XRD examination shows that the material includes several phases and is mostly crystalline.The diffraction profile of all alginate nanoparticles were similar having XRD peaks in range of 13o,220,330,450 indicate the presence of crystalline phase. (Joint Committe of Powder Diffraction Society) JCPDS file number 00-001-0628.



**Figure 2:** Xrd of sodium alginate nanoparticles

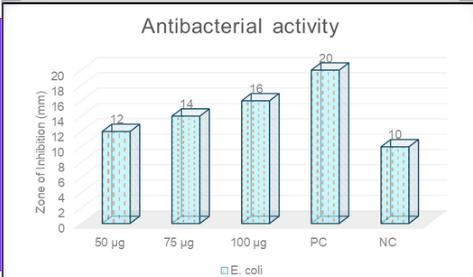
The antioxidant activity of alginate nanoparticles encapsulating the mangrove extract was determined based on DPPH radical scavenging assay. DPPH solution (20mg/ml) was prepared to dissolve in methanol. Different series of mangrove extract and its alginate nanoparticles (1-20 mg/ml) were prepared. Methanol (80 microliters), prepared mangrove extract and its encapsulated nanoparticles(50 microliters)and the DPPH solution (60 μL) were added to the microplate. The resultant solution was incubated at 37 °C for 10 min. The absorbance values were measured at a wavelength of 510 nm. The antioxidant activity of alginate nanoparticles encapsulating the mangrove extract was calculated and expressed, in terms of IC50 (concentration of alginate nanoparticles encapsulating the mangrove extract at 50% inhibition). The IC50 value of the alginate nanoparticles encapsulating the mangrove extract was compared with the standard compound Trolox.



**Figure 3:** Antioxidant assay

## Antibacterial activity

The pictures offer a thorough examination of a substance's antibacterial effectiveness against E. coli. The zones of inhibition at various concentrations are quantified by the bar graph, which measures 12 mm for 50 µg, 14 mm for 75 µg, and 16 mm for 100 µg. The negative control has a low inhibition zone of 10 mm, most likely because antibacterial agents are not present, whereas the positive control, which is probably a conventional antibiotic, displays the maximum inhibition zone of 20 mm, demonstrating its better antibacterial efficacy. Visual verification of these findings is provided by the petri dish, which has distinct zones surrounding the discs for each concentration and control. The positive control has a noticeable clean zone, highlighting its antibacterial qualities, whereas the negative control shows minimal inhibition, proving itsstrong antibacterial action. Higher concentrations of the tested chemical appear to enhance its inhibitory action against E. coli, as seen by its concentration-dependent rise in antibacterial efficiency. Although the substance's efficacy does not match that of the positive control, it exhibits considerable potential as an antibacterial agent. To completely determine its potential applications and maximize its antibacterial characteristics, more study is required. This research should include testing against various bacterial strains, stability assessments, and cytotoxicity evaluations. These results open the door for the substance's research and implementation in industrial or medicinal settings by highlighting its potential usefulness in situations requiring powerful antibacterial action.



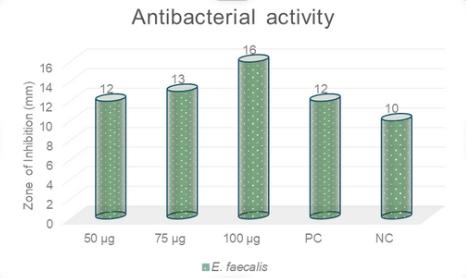
**Figure 4:** Antibacterial activity



**Figure 5:** Antibacterial activity of E.coli

An antibacterial agent's antibacterial activity against Enterococcus faecalis (E. faecalis) at three distinct concentrations (50 µg, 75 µg, and 100 µg) is shown in the first image along with positive (PC) and negative (NC) controls. The zone of inhibition, which shows how well the antibacterial drug inhibits bacterial growth, is measured on the y-axis in millimeters (mm). The zone of inhibition is 12 mm at 50 µg, which suggests moderate antibacterial activity. A somewhat bigger zone of inhibition of 13 mm is obtained at 75 µg, indicating a minor increase in activity. With a notable 16 mm zone of inhibition and the maximum antibacterial activity at 100 µg, these data point to a dose-dependent rise in efficacy. The advantageous control (PC) also shows a zone of inhibition of 12 mm, indicating its efficacy as a known antibacterial agent. In contrast, the negative control (NC) displays a lower zone of inhibition at 10 mm, confirming the baseline measurement without any antibacterial agents.

The second image shows a petri dish with antibacterial activity assays for different sample volumes (50 µl, 75 µl, and 100 µl) and positive (+ve) and negative (-ve) controls. The clear zones around the samples indicate the inhibition of bacterial growth, correlating with the bar graph result



**Figure 6:** Antibacterial activity



**Figure 7:** Antibacterial activity of E. faecalis

The FTIR analysis of the mangrove extract and alginate in this study reveals distinctive peaks that both support and contradict the results of other studies in the same field. The FTIR spectra of alginate in this study shows prominent peaks at 3325 cm-1 (O-H stretching), 1596 cm-1 (C=O stretching), and 1030 cm-1 (C-O stretching). These peaks match the hydroxyl, carboxylate, and ether linkages that are recognized as functional groups in alginate(Chehelgerdi et al., 2023). [(Pereira et al., 2011)](https://paperpile.com/c/B6WGSK/9Le6O) discovered similar articles of ftir analysis, with alginate nanoparticles exhibiting a wider peak, measuring from 3543 to 3135 cm^1, is shown in SA footage, along with further distinctive peaks at 1616, 1414, and 1036 cm^1. The hydroxyl group (3410 to 3543–3135 cm^1) in the unprocessed alginate powder that was converted into films changed the band and displaced the peaks at 1635, 1419, and 1050 cm^1 to 1616, 1414, and 1036 cm~1, respectively. [(Murillo-Álvarez & Hernández-Carmona, 2007)](https://paperpile.com/c/B6WGSK/SVcWa)studied alginate nanoparticles and found identical FTIR peaks the sodium alginate spectrum revealed significant bands of absorption related to carboxylic, ether, and hydroxyl functional groups. In the region of 3000–3600 cm−1, stretching vibrations of alginate's O–H bonds were seen. At 2920–2850 cm−1, aliphatic C–H stretching vibrations were detected. The carboxylate salt ion's asymmetric and symmetric stretching vibrations were identified as the cause of the bands observed at 1649 and 1460 cm−1, respectively. Similar corroborations are found in the work of [(Dalal et al., 2021)](https://paperpile.com/c/B6WGSK/7TBXd) the broad band of absorption at 3465 cm−1 in the FTIR spectra of alginate is indicative of a hydroxyl group (–OH stretching). In contrast, acids and alcohol could be associated with spectral peaks positioned between 4000 and 3400 cm−1. Significant peaks between 1628 and 1428 cm−1 were identified as symmetric and asymmetric stretching vibrations, which were linked to carboxylate anions (COO−).[(Deniz et al., 2022)](https://paperpile.com/c/B6WGSK/11oqC) in their investigation of alginate-chitosan nanoparticles, noted similar FTIR peaks of isolated sodium alginate and standard showed mannuronic acid functional group at wavenumber 884 cm-1 and the uronic acid at wavenumber 939 cm-1, OH functional group at wavenumber 3200-3400 cm-1, and CH2 stretching at wavenumber 2928 cm-1. Similar peaks observed in [(Shalaby, 2017)](https://paperpile.com/c/B6WGSK/Yca5u)typical peaks in the sodium alginate spectra were seen at 1,411 cm-1 and 1,600 cm-1, corresponding to the vibrations of the symmetric group COO and the asymmetrical -COO- group, respectively. In the formulated particle, all of the key diclofenac sodium peaks were found to be nearly unchanged.

Alginate and mangrove extract nanoparticles exhibit different crystalline properties according to XRD measurements. The large diffraction peaks at 2θ

values at 13° and 22° in the XRD pattern of alginate nanoparticles in this work indicate that the material is semi-crystalline.is usually crystalline due to strong interaction between the alginate chains through intermolecular hydrogen bonding. This analysis is[(Sundarrajan et al., 2012)](https://paperpile.com/c/B6WGSK/Fvxwn) because of the strong intermolecular hydrogen bonding between the alginate chains, sodium alginate is typically crystalline (Saadh et al., 2024). Because of the reflection of their plane from the poly guluronate unit, plane from the polymannuronate unit, and the other from the amorphous halo, three diffraction peaks were found at 20 values: 13.5°, 22°, and 39° for sodium alginate.The crystalline form of sodium alginate was impacted by the nucleation and development of semiconductor nanoparticles, as seen by the significant decrease in the strength of alginate diffraction peaks in the Alg-MS experiment.

The images offer a thorough analysis of how well a material fights bacteria when it comes to E. coli. With a negative control at 10 mm and a positive control at 20 mm, the inhibition zones as indicated by a bar graph are 12 mm for 50 µg, 14 mm for 75 µg, and 16 mm for 100 µg. These results are visibly confirmed in Petri dishes, where the negative control exhibits little inhibition while the positive control shows a distinct zone reflecting high antibacterial qualities. Though it is still less effective than the positive control, the substance's antibacterial activity is enhanced at higher doses. To fully realize its antibacterial potential and investigate industrial or medicinal applications, more study is required. This research should include stability assessments, cytotoxicity evaluations, and tests on a variety of bacterial strains. [(Irianto et al., 2021)](https://paperpile.com/c/B6WGSK/9aa1E)discovered similar articles with an increase in lemongrass essential oil concentration from 2.5% to 7.5% and an inhibitory zone diameter of 6.00 mm to 8.70 mm, an alginate-based antibacterial edible coating solution utilizing lemongrass essential oil demonstrated antibacterial activity against E. coli. At an increased concentration of lemongrass essential oil of 5% to 7.5%, the rate of antibacterial activity considerably decreased. Because of this, adding up to 5% of lemongrass essential oil to the edible coating made of alginate will provide the best antibacterial activity if the goal is to inhibit the development of Escherichia coli.Propolis and chitosan as irrigants demonstrated comparable antibacterial activity against E. faecalis, according to [(Shamma et al., 2023)](https://paperpile.com/c/B6WGSK/MUPVE).Therefore, whether they were employed as an irrigant material or as an intracanal medication in between endodontic treatment sessions, chitosan and propolis are both reliable in eliminating bacteria.

The antioxidant activity of alginate nanoparticles encapsulating mangrove extract was assessed using the DPPH radical scavenging assay. A 20 mg/ml DPPH solution was prepared in methanol. Various concentrations of the mangrove extract and encapsulated nanoparticles (1-20 mg/ml) were mixed with methanol and DPPH solution, then incubated at 37°C for 10 minutes. Absorbance at 510 nm was measured, and the IC50 value, representing the concentration at 50% inhibition, was calculated. This value was compared to the standard antioxidant Trolox. Similar observation seen in [(Hassani et al., 2020)](https://paperpile.com/c/B6WGSK/Z5zGg) with doses of 100 µg/mL and 200 µg/mL, respectively, the antioxidant activity of empty nanoparticles (ALG-GA) and nanoparticles containing curcumin were 12.35% and 7.6%, respectively. In all concentrations, the curcumin-loaded nanoparticles' antioxidant activity were marginally greater than those of ALG-GA nanoparticles, although they were most notable between 100 µg/mL and 200 µg/mL. Consequently, at concentrations of 100 µg/mL and 200 µg/mL, respectively, the significant differences in scavenging activity between Trolox and nanoparticles were 33.1% and 23.76%. Therefore, in a dose-dependent manner, gum arabic and sodium alginate both enhance curcumin's antioxidant qualities.

# Conclusion

A major breakthrough in targeted antioxidant and antibacterial therapy has been made with the tailored manufacture of alginate-based nanoparticles doped with mangrove extract. These nanoparticles have improved therapeutic efficacy and specificity by utilizing the inherent qualities of mangrove extracts and the biocompatibility of alginate. In addition to enhancing the antioxidant and antibacterial qualities, the use of mangrove extract guarantees targeted distribution to the affected areas and regulated release. With less negative effects, this novel technique should lead to better treatment outcomes. Subsequent studies can concentrate on synthesis parameter optimization and wider therapeutic use exploration. Taken together, this approach shows how sophisticated nanotechnology and natural ingredients can be used to solve a variety of challenging health issues.

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