WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 13, Issue 17, 271-281. Review Article ISSN 2277–7105

APPLICATION OF CHITOSAN NANOPARTICLES: A REVIEW

Khushvant Joshi* and Dr. Rajendra Pal Singh Rathore

Bhupal Nobles' Institute of Pharmaceutical Sciences, Udaipur Rajasthan, India.

Article Received on
16 July 2024,
Revised on 06 August 2024,
Accepted on 27 August 2024
DOI: 10.20959/wjpr202417-33718

***Corresponding Author**
Khushvant Joshi
Bhupal Nobles' Institute of Pharmaceutical Sciences,
Udaipur Rajasthan, India.

ABSTRACT

The processing of shellfish is a widespread industry in coastal regions. Only the meat is removed during processing; the head and shells are thrown away as waste. The sea food industry generates 80,000 tonnes of waste annually on average. Recycling shell waste into commercially viable products like chitin is a very easy and effective way to mitigate this environmental hazard. The N-acetyl derivative of chitin that results from N-deacetylation is called chitosan. Chitosan finds extensive application in the food and bioengineering sectors for the encapsulation of potent food ingredients, enzyme immobilisation, controlled drug delivery, and plant growth promotion in agriculture. Nanotechnology has garnered interest recently in a number of domains due to its numerous emerging and innovative applications. Chitosan is an antimicrobial agent as well as a defence elicitor. Interesting characteristics of chitosan include its polycationic nature, biocompatibility, biodegradability, bioactivity, encapsulation, antimicrobial agent, plant growth-promoting agent and plant protector. The use of chitosan nanoparticles as drug delivery vehicles has increased due to their increased stability, low toxicity, ease of preparation, and ability to be administered through a variety of routes.

KEYWORDS: Chitosan, Chitosan nanoparticles;, Drug Delivery, Anti-bacterial.

1. INTRODUCTION

The pharmaceutical industry has developed appropriate noninjectable drug carriers to address these limitations. Since they have a higher surface-to-volume ratio and can interact intimately with epithelial surfaces, nanoparticles have become one of the most exciting tools in this context. Stability and/or penetration problems commonly impede the use of macromolecules in therapy. The encapsulated molecules' ability to maintain biological activity throughout the production process and subsequent release is further facilitated by nanoparticles. Nanotechnology, in spite of its name, has completely changed business operations worldwide.

All around the world, nanotechnology has had a subtle yet significant impact on a number of industries. The industrialised world is one place where the rapid rise of nano-scale markets over the past ten years is a clear example of how quickly technology is developing. Being a general-purpose technology, nanotechnology is not a novel idea. The size of nanoparticles varies from 1 to 100 nm. Their properties are different from those of their bulk counterparts because of the reduction in dimension to the atomic level. Materials undergo changes in their properties at the nanoscale. This is because, while the percentage of surface atoms relative to bulk material increases as size decreases, bulk materials have generally constant properties regardless of size. This results in unexpected nanoparticle characteristics.

The ability of many medications to reach the site of therapeutic action frequently limits their efficacy. Conventional dosage forms typically result in only a small portion of the administered dose reaching the target site; the remainder of the drug is distributed throughout the body based on its physicochemical and biochemical properties. Therefore, creating a drug delivery system that minimises a drug's harmful in vivo side effects while optimising its pharmaceutical action is a difficult task. Because they have a higher surface-to-volume ratio and can interact intimately with epithelial surfaces, nanoparticles have become one of the most exciting tools. The encapsulated molecules' ability to maintain biological activity throughout the production process and subsequent release is further facilitated by nanoparticles. Chitosan nanoparticles, may have antibacterial properties as a unique feature. Because it can be used in a variety of ways to create nanoparticles, chitosan has gained prominence as a carrier-forming material.

Nanoparticles are classified into organic and inorganic types. Inorganic nanoparticles have grown in importance due to their ability to withstand harsh processing conditions. Osan is a modified biopolymer derived from partial deacetylation of chitin. The structure consists of alternating ($1 \rightarrow 4$) linked N-acetyl glucosamine and glucosamine units. It's a white, hard, inelastic, nitrogenous polysaccharide. Chitosan's nontoxic, biodegradable, and antimicrobial properties make it useful in a variety of applications. It has various applications, including biomedical, agricultural, genetic engineering, food, environmental pollution control, water treatment, paper manufacturing, and photography.[1]

Chitosan nanoparticles (ChNP) have the characteristics of chitosan and the properties of nanoparticles such as surface and interface effect, small size and quantum size effects.[2] Peptides, proteins, vaccines, DNA, and medications for parenteral and non-parenteral administration are just a few examples of the therapeutic agents for which natural polymers, in particular polysaccharides, have been employed as drug delivery vehicles. The production of nanoparticles (NPs) frequently uses chitosan, the second most prevalent naturally occurring polysaccharide after cellulose. Chitosan is a mucoadhesive polymer that is both biocompatible and biodegradable. It was discovered that drug-loaded chitosan nanoparticles were bioactive, stable, and permeable.[3]

The use of chitosan nanoparticles (CNPs) in agriculture has shown promise. Because of these innate qualities as well as their antimicrobial, antioxidant, and eliciting activities, CNPs can significantly boost nutrient absorption, improve pest management techniques, and increase agricultural productivity. With the ability to encapsulate different agricultural amendments, the chitosan nano-formulation offers precise and targeted delivery mechanisms for increased efficiency. This allows for the controlled release of pesticides, fertilisers, plant growth promoters, and biocontrol agents.[4] Chitosan nanoparticles (CNPs) are widely used in biomedical applications, particularly as contrast agents for medical imaging and as vehicles for drug and gene delivery into tumours. Their small size, which provides a large surface-to-volume ratio, and their physicochemical properties that may differ from those of their bulk counterparts make them particularly useful. Since CNPs originate from a naturally occurring biopolymer, it is easy to functionalise them with medications, RNA, DNA, and other molecules to achieve a specific goal in vivo. Crustaceans, such as crabs, prawns and lobsters, produce chitin, the second most abundant natural polysaccharide, from which chitosan, a fibrous compound, is derived. Chitosan is comparatively inexpensive and possesses all of the necessary therapeutic qualities, such as hydrophilicity, biodegradability, and biocompatibility.[5]

1.1 Discovery of Chitosan

Rouget's work from 1859 is the first documented instance of chitosan, the primary derivative of chitin. Nonetheless, Hoppe-Seyler coined the term "chitosan" in 1894. The first chitin derivative, glykosamin, was found in 1876 by Ledderhose through hydrolysing arthropod chitin.

Over the past 20 years, chitosan has also drawn significant interest from a wide range of other fields, including biotechnology, ophthalmology, dentistry, veterinary medicine, hygiene and personal care, packaging, agrochemistry, aquaculture, functional textiles and cosmetotextiles, catalysis, chromatography, wastewater treatment and sludge dewatering, and photography. A biopolymer called chitosan is made from chitin, which is one of the most plentiful and renewable materials on the planet. Chitin is a major component of fungal cell walls, the exoskeletons of arthropods (including crabs, lobsters, and prawns), insects, mollusc radulae, cephalopod beaks, fish scales, and lissamphibian scales. Henri Braconnot is credited with discovering chitin in 1811, while Charles Rouget's work on chitosan is credited with its invention in 1859. Felix Hoppe-Seyler did, however, coin the term "chitosan" in 1894. Commencing in the late 1970s, chitosan has garnered significant interest from the scientific and industrial community due to its unique macromolecular structure, biocompatibility, biodegradability, and other inherent functional attributes. There are useful uses for chitosan and its derivatives in pharmacy, medicine, food industry, agriculture, cosmetology, textile and paper industries, and chemistry.[6]

Since it can bind to a wide range of materials, including minerals, acids, and lipophilic substances, chitosan has been used for water purification for more than 30 years (Jing et al., 1997). For the past 20 years, chitosan has been marketed as an over-the-counter medication to prevent the absorption of fat in Europe and Japan (Au Natural Herbals, 2001). In the late 1990s, chitosan was first sold as a dietary supplement in the US.[7]

1.2 Application of Chitosan nanoparticles

Chitosan nanoparticles can improve drug absorption and shield pharmaceuticals from deterioration in the gastrointestinal system. They are especially helpful for orally administering vaccines, peptides, and proteins. Its nanoparticles can be specifically delivered to the lungs by being made into inhalable aerosols. This helps with the treatment of respiratory conditions. In order to lessen systemic toxicity and improve the therapeutic effect, it can also be utilised to deliver chemotherapeutic agents straight to tumour cells. Chitosan nanoparticles are helpful for gene therapy applications because they can encapsulate genetic material (DNA, RNA, etc.) and make it easier for cells to receive it. Chitosan nanoparticles (CSNPs) have garnered significant interest in the field of drug delivery due to their unique properties and potential to improve the efficacy and safety of therapeutics. Technology related to encapsulation and immobilisation is crucial for the bioengineering and food processing sectors. Chitosan is a naturally occurring polysaccharide that is produced when chitin is N-deacetylated. Thanks to its important biological and chemical properties, including biodegradability, biocompatibility, bioactivity, and polycationicity, it has been widely used in the food and bioengineering industries, including the encapsulation of active food ingredients, in enzyme immobilisation, and as a carrier for controlled drug delivery.[8] Polymeric nanoparticles are commonly used for drug delivery due to their biodegradability. Among the various polymers, chitosan has gained popularity among researchers. It was widely used in polymeric nanoparticles to target drugs. In pharmaceutical applications, ChNP was used as an antimicrobial coating to promote wound healing, prevent infections, and combat the spread of infectious disease. Furthermore, ChNP demonstrated significant inhibitory activities against foodborne microorganisms, particularly on fruits and vegetables. It is worth noting that ChNP can also be used to deliver antimicrobial drugs, increasing the efficacy and stability of the antimicrobial agent.[9] Tea polyphenols have a wide range of applications in the food, medical, and pharmaceutical industries due to their multi-health benefits, which include antioxidant and antibacterial properties, cancer prevention, anti-radiation, and immune enhancement. However, the low absorption rate of tea polyphenols reduces their bioactivity in vivo. Low absorption and bioavailability have been attributed to poor stability, passive diffusion, and active efflux in the gastrointestinal tract. The pharmaceutical industry has widely used nanoparticle delivery systems based on chitosan (CS), a natural biomaterial, to improve bioactive compound absorption. A few studies have shown that using chitosan nanoparticles improves the absorption and bioavailability of tea polyphenols.[10]

Chitosan and chitosan nanoparticles have several unique biological properties that make them promising materials for a variety of applications, including biosafety, biocompatibility, increased solubility, and biodegradability. The aforementioned properties allowed them to be used in a variety of fish aquaculture applications, including improving growth performance and immune function. Furthermore, they serve as safe feed additives, drug carriers, and are commonly used in water treatment.[11] Fusarium head blight (FHB), caused by Fusarium graminearum, is one of the most common wheat diseases in humid and warm climates. This disease significantly reduces yield and seed quality. In vitro, CS and CS/NPs (chitosan nanoparticles (CS/NPs)) at varying concentrations significantly inhibited both radial mycelial growth and the number of colonies formed against F. graminearum. The application of 1000 and 5000 ppm concentrations of CS and CS/NPs resulted in the greatest inhibition of radial mycelial growth in comparison to the control. Microscopic examination of treated F. graminearum with CS and CS/NPs revealed dehydration and deformation in mycelial growth, as well as the collapse of some hyphae.[12]

Recent years have seen the effective rise of nanomedicine as a means of addressing many of the drawbacks of traditional medicine, including its poor pharmacokinetics, lack of selectivity, and unfavourable side effects. Because of their special physicochemical qualities, nanoparticle (NP) technology has drawn increased attention in nanomedicine-based approaches for cancer therapy. Despite extensive research on NPs for tumour targeting, which has yielded some encouraging results, little is known about the pharmacokinetic (PK) and pharmacodynamic (PD) characteristics of NPs or their effectiveness in targeting tumours. Therefore, more chances to convert nanomedicine techniques into better clinical outcomes may arise from growing understanding of these problems in NPs technology.[13] One of the most difficult orthopaedic issues to solve is orthopaedic infection. Antibiotic-resistant bacteria also progressively evolve. Because of its high levels of biocompatibility, biodegradability, and antibacterial activity, chitosan is used extensively in the biomedical industry. Drug delivery systems based on chitosan are widely used to achieve controlled drug release. Antibiotics and other substances together can have synergistic antibacterial effects. One of the most popular uses of chitosan-based nanoparticles in medication delivery systems is in drug delivery.[14]

The most effective way to deliver the medication is to load it into chitosan nanoparticles (CSNPs), which are medicated drug carriers. The Ionic gelation method was used for preparation, and it involved a reaction between the binding material sodium tripolyphosphate (STPP) and the chitosan (CS), which was extracted from prawn shells. Chitosan nanoparticles were used to load the drug, and various techniques were used to verify this, including FT-IR and X-ray diffraction spectrum analysis, particle size analysers to determine particle size before and after loading, and emission electron scanning microscopes (FE-SEM).[15] In addition to their potential as drug delivery vehicles, nanoparticles have demonstrated efficacy as an adjuvant for vaccines and provide non-invasive administration routes, including oral, nasal, and ocular. Notwithstanding these benefits, the perfect nanoparticle system does not yet exist. The majority of nanoparticles made from polymers that aren't soluble in water involve high shear forces, heat, or organic solvents that may be detrimental to the stability of the drug. Chitosan is one of the water-soluble polymers that has been researched the most.

This is because chitosan has several characteristics that make it an excellent polymeric carrier for nanoparticles, including being affordable, nontoxic, biocompatible, and biodegradable. Moreover, it has a positively charged state and demonstrates an enhancement of absorption. Chitosan is a very appealing material as a drug delivery carrier because of these qualities. Chitosan nanoparticles, or chitosan NP, have been thoroughly developed and investigated for use in pharmaceuticals over the past 20 years.[16]

Chitosan is a polymer with a vast array of potential uses since its chemical functional groups can be changed to accomplish particular objectives. When made with chitosan and its derivatives, nanoparticles (NP) have a positive surface charge and mucoadhesive qualities that allow them to stick to mucous membranes and release the drug payload gradually. Applications for chitosan-based nanoparticles (NP) in non-parenteral drug delivery include the treatment of ocular infections, gastrointestinal disorders, lung disorders, cancer, and drug delivery to the brain.[17] One of the most common malignant diseases in the world is cancer. Because of their severe side effects to healthy tissues, cytotoxicity, poor solubility in aqueous media, and multidrug resistance, current antitumor agents are restricted during chemotherapy. The creation of targeted drug nanocarriers would both selectively transport anticancer medications to cancerous tissues and intensify their side effects. Anticancer agents have been delivered specifically using a range of nanocarriers, including carbon nanotubes, liposomes, polymeric nanoparticles, dendrimers, and nanogels. These nanocarriers use either passive or active efficacy mechanisms to deliver loaded drugs to the desired locations. Because of its special qualities—hydrophilicity, biocompatibility, and biodegradability, for example—chitosan and its derivatives have gained interest for use in nanocarrier technology. Active targeting involving the grafting of cancer-specific ligands onto Chitosan nanoparticles that result in ligand-receptor interactions has been developed successfully.[18]

Chitosan nanoparticles have the potential to be employed as a vehicle for the delivery of medications and vaccine antigens due to their superior adhesion, biodegradability, and low toxicity. The foundation for using chitosan nanoparticles as a drug or vaccine delivery vehicle was established by these encouraging studies. Functional groups are necessary for the conjugation of particular ligands, which aids in delivering loaded medications to the site of inflammation or infection. Chitosan's slow biodegradation lowers dosage frequency, allows for controlled and sustained release of loaded moieties, and enhances patient compliance with antimicrobial medication therapy. Because of its muco-adhesion, chitosan is a desirable option for the delivery of anti-inflammatory drugs, where the main issue is the active moiety's quick clearance owing to increased tissue permeability. A method of passively targeting active drug moieties to inflammatory sites is provided by the pH-dependent swelling and drug release characteristics of chitosan.[19] Numerous biological domains, such as drug and gene delivery, tissue engineering antiviral therapies, and immunological adjuvant techniques, have explored the potential of chitosan. It is a cationic copolymer of N-acetyl and D-glucosamine that differs from the former and latter in terms of molecular chain lengths, compositions, and sequences. It is recyclable and bioresorbable in addition to being cyto- and biocompatible. Chitosan nanoparticles are fashioned into a variety of pathways, making them efficient drug delivery vehicles. This article aims to give a general overview of its antiviral application as a nanocarrier for antiviral drugs, emphasising the advantages, restrictions, and drawbacks.[20]

The use of viral or lipid carriers for conventional gene delivery is fraught with drawbacks, including poor transfection efficiency, cytotoxicity, and immunogenicity. The creation of biodegradable polymers with lower toxicity, the addition of cell-targeting moieties, enhanced chemistry for the synthesis of polymers with uniform size and topology, and other methods are just a few of the approaches being investigated to help increase efficiency. Chitosan, a cationic polysaccharide that occurs naturally, is becoming more and more of a viable option for gene delivery applications because of its low cytotoxicity and respectable transfection efficiency. The potential for chitosan and its nanoparticles to bind to DNA in a polyelectrolyte complex makes them valuable as non-viral vectors for gene therapy applications.[21] In a high shear cell, chitosans are drained collectively with marine organisms to create a film that subsequently confines those exfoliated with other biomolecules. Consequently, one of the long-standing problems in the development of biopolymer nanofilms has been resolved as the water-vapor permeability of the nanoencapsulated chitosan film has been significantly reduced. Moreover, it has been demonstrated that adding dispersed chitosan to protein greatly increases the mechanical strength of the nanofilm, making the application of these films in food production feasible.[22]

1.3 Future Trends of Chitosan

Chitosan is a promising material for targeted drug delivery, especially in cancer therapy because of its capacity to form hydrogels and nanoparticles. Subsequent studies might concentrate on enhancing the effectiveness of medication encapsulation and controlled release. By using its antimicrobial qualities, new antibacterial coatings for implants and medical equipment can be created, lowering the chance of infection. It is anticipated that the use of chitosan-based biopesticides and fertilisers will rise as a natural and eco-friendly substitute, encouraging sustainable farming methods. Chitosan is helpful in the treatment of wastewater because of its capacity to adsorb dyes and heavy metals. Potential directions for future research could include increasing its regenerability and adsorption capacity. Chitosan-based biodegradable plastics are becoming more popular as worries about plastic pollution grow. Technological advancements in processing could result in more useful and economical production. At the nanoscale, hitosan can be blended with other materials to produce composites that have improved mechanical and functional qualities. These have numerous potential uses, ranging from electronics to packaging. The development of sensitive and selective biosensors for environmental monitoring and medical diagnostics is being investigated using nanomaterials based on chitosan. Chitosan is a possible carrier for gene therapy applications because of its capacity to form complexes with both DNA and RNA. Enhancing these complexes' stability and delivery effectiveness may be the main focus of future research. Research is being done on the potential applications of chitosan-based materials in renewable energy, like the creation of biofuel cells. Chitosan appears to have a bright future in a variety of industries overall, and further research and development should help to expand its uses while also enhancing current ones.

2 CONCLUSION

The Uses of chitosan nanoparticles were outlined in this review. This review concludes that nanostructured chitosan have potential applications as carriers of bioactive ingredients. They could function as carriers of immobilisation or encapsulation. Their favourable biological properties, including their nontoxicity, biocompatibility, biodegradability, and antibacterial capacity, make them intriguing candidates for use as drug delivery vehicles and as boosters of cell proliferation. Because of its natural origin, useful qualities, and advantages for the environment, chitosan is a valuable material in a variety of industries. Its uses are expected to grow with further research and development, meeting new requirements in the fields of environmental protection, food safety, healthcare, and agriculture.

REFERENCES

1. Divya, K., & Jisha, M. S. Chitosan nanoparticles preparation and applications. Environmental chemistry letters, 2018; 16: 101-112.

2. Ingle, A., Gade, A., Pierrat, S., Sonnichsen, C., & Rai, M. Mycosynthesis of silver nanoparticles using the fungus Fusarium acuminatum and its activity against some human pathogenic bacteria. *Current nanoscience*, 2008; *4*(2): 141-144.
3. Matalqah, S. M., Aiedeh, K., Mhaidat, N. M., Alzoubi, K. H., Bustanji, Y., & Hamad, I. Chitosan nanoparticles as a novel drug delivery system: a review article. *Current drug targets*, 2020; *21*(15): 1613-1624.
4. Riseh, R. S., Vatankhah, M., Hassanisaadi, M., & Varma, R. S. A review of chitosan nanoparticles: Nature's gift for transforming agriculture through smart and effective delivery mechanisms. *International Journal of Biological Macromolecules*, 2024; 129522.
5. Jha, R., &Mayanovic, R. A. A review of the preparation, characterization, and applications of chitosan nanoparticles in nanomedicine. *Nanomaterials*, 2023; *13*(8): 1302.
6. Morin-Crini, N., Lichtfouse, E., Torri, G., & Crini, G. Fundamentals and applications of chitosan. *Sustainable agriculture reviews 35: chitin and chitosan: history, fundamentals and innovations*, 2019; 49-123.
7. Novak, K., Cupp, M. J., & Tracy, T. S. Chitosan. In *Dietary supplements: toxicology and clinical pharmacology*, 2003; 33-39. Totowa, NJ: Humana Press.
8. Zhao, L. M., Shi, L. E., Zhang, Z. L., Chen, J. M., Shi, D. D., Yang, J., & Tang, Z. X. Preparation and application of chitosan nanoparticles and nanofibers. *Brazilian Journal of Chemical Engineering*, 2011; *28:* 353-362.
9. Rozman, N. A. S., Yenn, T. W., Ring, L. C., Nee, T. W., Hasanolbasori, M. A., & Abdullah, S. Z. Potential antimicrobial applications of chitosan nanoparticles (ChNP). *Journal of microbiology and biotechnology*, 2019; *29*(7): 1009-1013.
10. Liang, J., Yan, H., Puligundla, P., Gao, X., Zhou, Y., & Wan, X. Applications of chitosan nanoparticles to enhance absorption and bioavailability of tea polyphenols: A review. *Food Hydrocolloids*, 2017; *69:* 286-292.
11. El-Naggar, M., Medhat, F., & Taha, A. Applications of chitosan and chitosan nanoparticles in fish aquaculture. *Egyptian Journal of Aquatic Biology & Fisheries*, 2022; *26*(1).
12. Kheiri, A., Jorf, S. M., Malihipour, A., Saremi, H., & Nikkhah, M. Application of chitosan and chitosan nanoparticles for the control of Fusarium head blight of wheat (Fusarium graminearum) in vitro and greenhouse. *International Journal of Biological Macromolecules*, 2016; *93:* 1261-1272.

13. Jee, J. P., Na, J. H., Lee, S., Kim, S. H., Choi, K., Yeo, Y., & Kwon, I. C. Cancer targeting strategies in nanomedicine: design and application of chitosan nanoparticles. *Current Opinion in Solid State and Materials Science*, 2012; *16*(6): 333-342.
14. Shi, S., Shi, W., Zhou, B., & Qiu, S. Research and Application of Chitosan Nanoparticles in Orthopedic Infections. *International Journal of Nanomedicine*, 2024; 6589-6602.
15. Almukhtar, J. G. J., & Karam, F. F. Preparation characterization and application of Chitosan nanoparticles as drug carrier. In *Journal of Physics: Conference Series*, November 2020; 1664(1): 012071. IOP Publishing.
16. Tiyaboonchai, W. Chitosan nanoparticles: a promising system for drug delivery. *Naresuan University Journal: Science and Technology (NUJST)*, 2003; *11*(3): 51-66.
17. Mohammed, M. A., Syeda, J. T., Wasan, K. M., & Wasan, E. K. An overview of chitosan nanoparticles and its application in non-parenteral drug delivery. *Pharmaceutics*, 2017; *9*(4): 53.
18. Ghaz-Jahanian, M. A., Abbaspour-Aghdam, F., Anarjan, N., Berenjian, A., & Jafarizadeh-Malmiri, H. Application of chitosan-based nanocarriers in tumor-targeted drug delivery. *Molecular biotechnology*, 2015; *57:* 201-218.
19. Rajitha, P., Gopinath, D., Biswas, R., Sabitha, M., & Jayakumar, R. Chitosan nanoparticles in drug therapy of infectious and inflammatory diseases. *Expert opinion on drug delivery*, 2016; *13*(8): 1177-1194.
20. Safer, A. M., & Leporatti, S. Chitosan nanoparticles for antiviral drug delivery: A novel route for COVID-19 treatment. *International Journal of Nanomedicine*, 2021; 8141-8158.
21. Jayakumar, R., Chennazhi, K. P., Muzzarelli, R. A. A., Tamura, H., Nair, S. V., & Selvamurugan, N. Chitosan conjugated DNA nanoparticles in gene therapy. Carbohydrate Polymers, 2010; 79(1): 1-8.
22. Manigandan, V., Karthik, R., Ramachandran, S., & Rajagopal, S. Chitosan applications in food industry. In *Biopolymers for food design*, 2018; 469-491. Academic Press.