Chapter 13
Modifications and Applications of Chitosan-Based Nanocomposites in Orthopaedics and Dentistry

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Abstract Chitosan has been studied extensively and widely used in the applications of biopharmaceutical and biomedical fields. Further, chitosan can be modified into nanocomposites. The possible applications of chitosan are quite vast, and fascinating properties of chitosan-based nanocomposites like biocompatibility, antimicrobial, antioxidant, anti-inflammatory, good mechanical strength, etc., make chitosan very promising in the sector of orthopaedics and dentistry in tissue engineering and regenerative medicine. This chapter focusses on the different strategies adopted for the modification of chitosan as chitosan nanocomposites in the field of dentistry and orthopaedics. Biomedical applications of chitosan-based nanocomposites in orthopaedics and dentistry have also been covered in the chapter. Lastly, the advantages of chitosan nanocomposites in the fields are also highlighted.

Keywords Chitosan-based nanocomposites · Orthopaedics · Dentistry

Abbreviations

3D	Three dimensional
ABC	Acrylic bone cements
CNT	Carbon nanotubes
CTS	Chitosan
GO	Graphene oxide
GTR	Guided tissue regeneration
HAp	Hydroxyapatite
MMT	Montmorillonite
ZnO	Zinc oxide

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1 Introduction

Chitosan is a naturally occurring biomaterial that is extracted mainly from chitin, which is derived from the exoskeleton of crabs and shrimps. Chitosan is obtained by deacetylation of chitin, the second most abundant natural biopolymer (Fig. 1) [1].

The need for biocompatible, antimicrobial, antibacterial, and non-toxic derivatives is being fulfilled by nanocomposites obtained from different biopolymers in biomedical and pharmaceutical fields. Since, chitosan has proved itself to be helpful

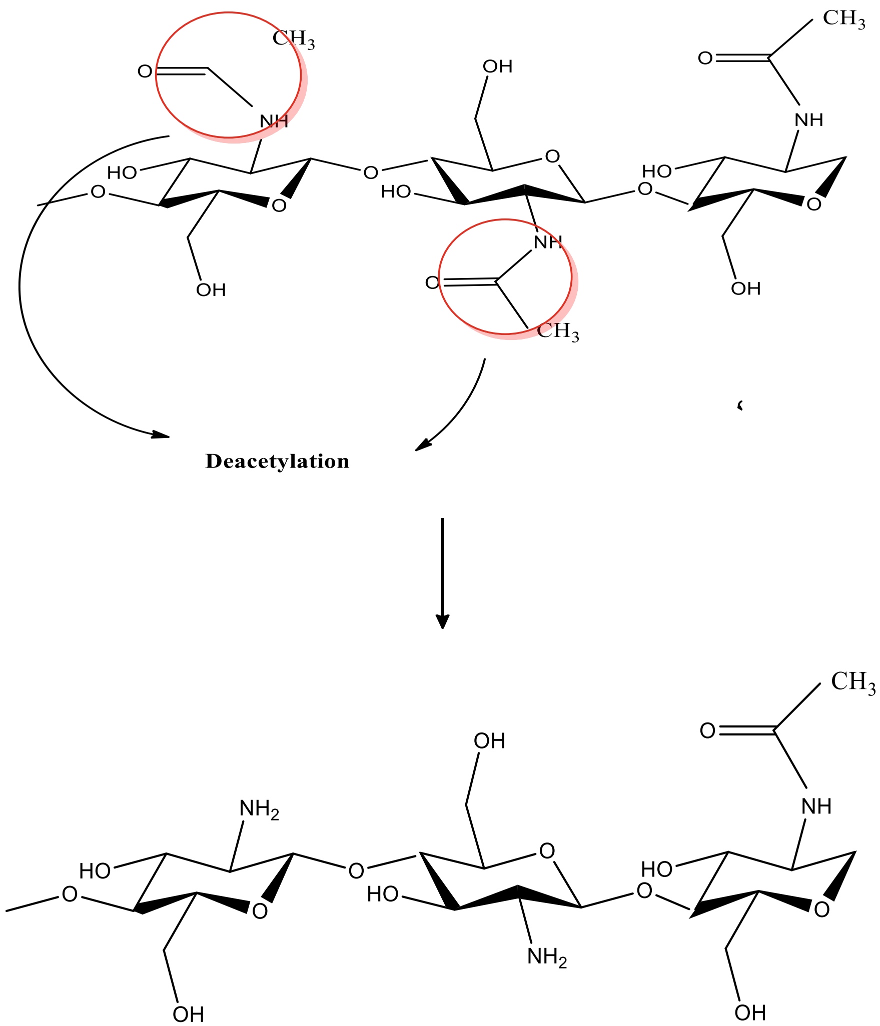

Fig. 1 Preparation of chitosan from deacetylation of chitin

in the fields of biopharmaceuticals and biomedicine having a large number of applications due to its properties, (i.e. antiviral, antibacterial, and antifungal) its nanocomposites have also been showing evident results in the field of biopharmaceuticals and biomedical applications. The synthesis of nanocomposites of chitosan can be achieved using different chemical methods depending upon the field of application [1]. High bioactivity being a prominent property of chitosan and its nanocomposites make it appropriate to be used in the fields of orthopaedics and dentistry [2]. These nanocomposites can be moulded or modified into different formulations for their potential applications in the field of tissue engineering or in the studies of bone regeneration in the field of orthopaedics [3]. It also serves well in enamel repair, oral drug delivery, implants for dental complications, etc., in the field of dentistry.

Presently, the demand for chitosan and its nanocomposites in these fields is high, as ongoing research in the field of nano-scale biomedical applications is growing at an enormous rate. The study of modifications and bio-application of chitosan-based nanocomposites have shown tremendous outcomes.

2 Modifications of Chitosan-Based Nanocomposites

Chitosan-based nanocomposites play a vital role in the fields of biomedicine and biopharmaceuticals. However, the biocompatibility and drug delivery of nanocomposites based on chitosan only are up to a lower extent in the fields of orthopaedics and dentistry. To uplift the bioactivity and compatibility of chitosan-based nanocomposites for increasing the properties like mechanical strength, antibacterial characteristics, thermal stability, etc., these nanocomposites have been modified using different nano-scaled or layered (in the form of thin films) chemical reagents to enhance these properties in orthopaedics and dentistry.

3 Modification of Chitosan-Based Nanocomposites in the Field of Orthopaedics

Various chemical modifications have been done to enhance the ability of chitosan nanocomposites in the orthopaedics sector. These nanocomposites have been modified with hydroxyapatite(HAp), carbon nanotubes (CNT), and acrylic bone cements (ABC) with graphene oxide (GO), etc.

3.1 Hydroxyapatite (HAp)

Chitosan (CTS)-based nanocomposites alone cannot mimic all the needed properties of a natural bone in a human body, but along with modifications in their chemical parts, it shows many similar properties of a natural bone.

Many studies have shown that calcium and phosphate-based materials show osteoconduction (i.e. growing of a bone on a surface), imitating the best properties of a natural bone, becoming materials of great interest in the studies of bone tissue engineering. Therefore, hydroxyapatite (HAp) with the molecular formula $[Ca_{10}(PO_4)_6(OH)_2]$ is used in CTS-based nanocomposites, with HAp being one of the most stable calcium phosphate forms with the abundance of its occurrence (approx. 60–67%) in the natural bone making it a major component. With the variety of applications of Hap in the field of orthopaedics, it also serves its purpose as an essential compound in the sector of preparation of artificial bones in the human body. With CTS-based nanocomposites alone, the cell growth of osteoblast cells (cells responsible for the synthesis of bone) has been found to be slightly increased in orthopaedic treatment, whilst CTS/HAp (chitosan and hydroxyapatite)-based nanocomposites with a quite stable chemical interaction (Fig. 2) significantly increased the osteoblastic cell growth in a natural bone giving its skeletal structure good stability and greater molecular density along with antibacterial properties. Also, CTS/HAp-based nanocomposites fulfil the role of the inorganic as well as the organic portion of a natural bone [4].

3.2 Carbon Nanotubes (CNT)

Studies have shown that the modification of chitosan (CTS) combined with CNT (carbon nanotubes) results in a significant increase in the mechanical strength and structural properties of the nanocomposite serving its role in the natural bone. CNT is also associated with the study of biomaterials, mainly those materials which are used to position the bone in the human body, like—materials used in prosthetics, plates, and screws in case of fractures, drug delivery systems, preparation of scaffolds for regeneration of bone, etc. According to reports the interaction of CNT with CTS, where CNT is uniformly distributed along with the CTS matrix (Fig. 3).

The observable change in properties like tensile strength and mechanical structural integrity is significantly enhanced with the addition of even small amounts of CNT in the CTS matrix. Numerically, with the introduction of about 0.8% of CNT in the CTS matrix improves the tensile properties of nanocomposites by about 93%.

Also, the use of CNT with CTS nanocomposites in bone treatment as an alternative material has been reported, with a possibility of natural bone regrowth. Hence, cells with similar properties to osteoblastic cells were grown on CNT (electrically neutral in nature) to produce a natural bone [4].

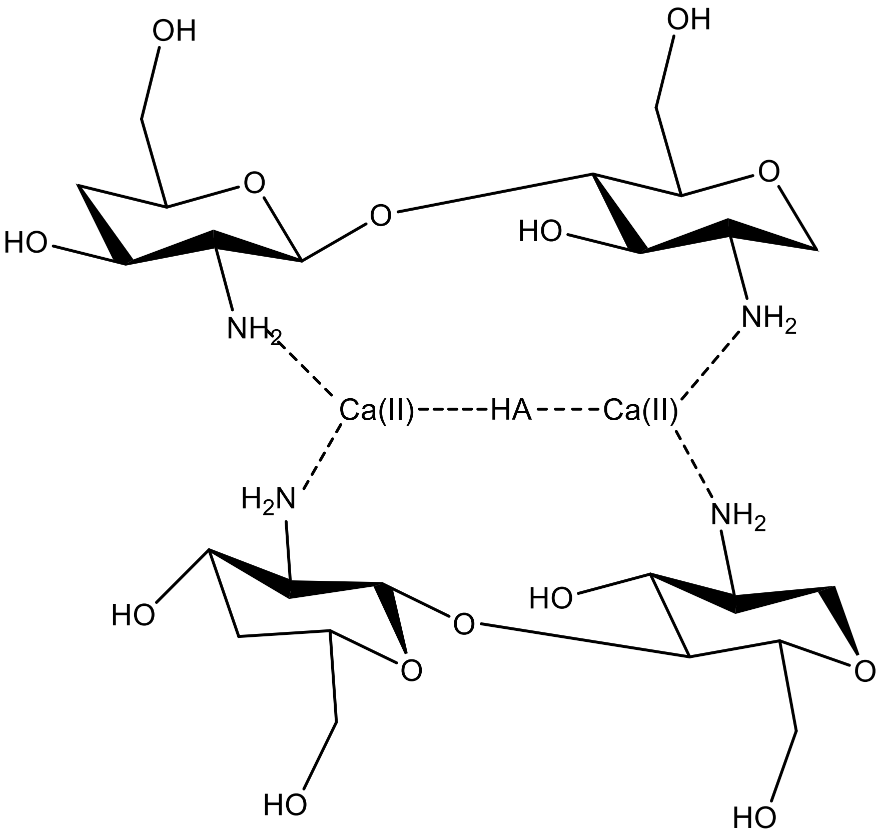

Fig. 2 Chemical interaction of CTS with HAp

3.3 Acrylic Bone Cements (ABC) with Graphene Oxide (GO)

The role of acrylic bone cements (ABC) in orthopaedic surgeries is quite significant, but an increase in their use in other applications has been recorded, such as cancer-causing bone remodelling, cranioplasty (the surgical repair of a bone defect in the skull), and vertebroplasty (for stabilizing compression fractures in the spine), etc. The introduction of ABC along with graphene oxide (GO) in chitosan (CTS)-based nanocomposites leads to changes in mechanical, biological, thermal, and physicochemical properties of the nanocomposites acting upon the bones.

It is observed that using the modification with the formulation of CTS/ABC/GO, i.e. CTS containing ABCs and GO simultaneously, results in the enhancement of thermal stability, osteogenic activities (i.e. the ability of the material to induce bone formation in non-bone-forming sites) and antibacterial properties, making it an essential modification in orthopaedic applications. Moreover, this formulation resulted in enhanced biocompatibility showing potential use in biomedical applications, and GO

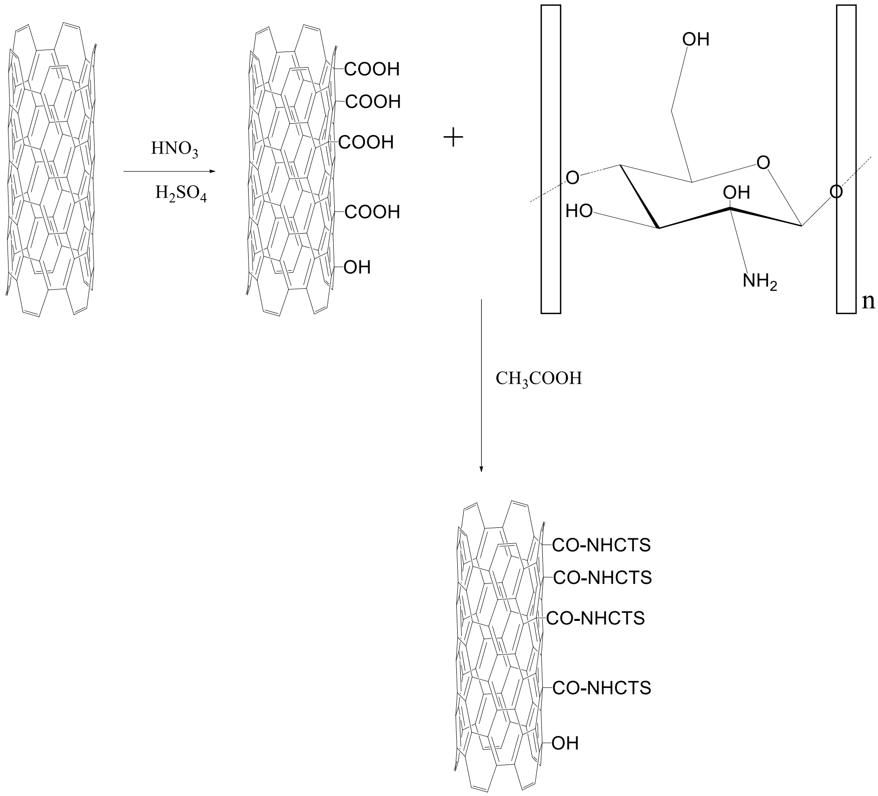

Fig. 3 Chemical interaction between CTS and CNT

present in the formulation was mainly responsible for the mechanical augmentation and antibacterial characteristics [5].

4 Modification of Chitosan-Based Nanocomposites in the Field of Dentistry

In the dentistry sector, these nanocomposites have been modified with montmorillonite, zinc oxide (Table 1).

Table 1 Modifications of chitosan-based nanocomposites, their inferences, and applications

S. No.	Modification of chitosan-based nanocomposites	Inferences and applications	Reference
1	Hap-CTS (modification of chitosan-based nanocomposites with hydroxyapatite in orthopaedics)	Stable chemical interaction between CTS and Hap results in increased osteoblastic cell growth, stable skeletal structure, greater molecular density, and antibacterial properties Also, fulfilling the role of organic and inorganic part of a natural bone	[4]
2	CNT-CTS (modification of chitosan-based nanocomposites with carbon nanotubes in orthopaedics)	Interaction of CNT and CTS results in enhancing tensile strength and structural integrity, possibility of natural bone regrowth	[4]
3	ABC with GO-CTS (modification of chitosan-based nanocomposites with acrylic bone cements and graphene oxide in orthopaedics)	The formulation of CTS/ABC/GO enhances thermal stability, osteogenic activities, and antibacterial properties Also, enhanced biocompatibility for the use of biomedical applications	[5]
4	MMT-CTS (modification of chitosan-based nanocomposites with montmorillonite clay in dentistry)	Increase in tensile properties, material strength, and elasticity (depends upon the concentration of the clay particles) were observed Enhanced antimicrobial properties with the addition of $AGNO_3$ Also, electrostatic interaction between CTS and silicate layers increases the thermal stability	[6]
5	ZnO-CTS (modification of chitosan-based nanocomposites with size-controlled ZnO nanoparticles in dentistry)	This formulation results in antibacterial, antidiabetic, antioxidant, and aytotoxic agents Also, ZnO-CTS interaction results in increased bond strength and mechanical properties	[7]

4.1 *MMT-CLAY (Montmorillonite)*

The preparation of chitosan-based nanocomposites loaded with clay (montmorillonite) (CS/MMT) is done by mixing chitosan biopolymer and sodium montmorillonite particles physically. The process of physical mixing is done to get thin transparent films that serve as a dental material in dental applications and dental surgeries. Different concentration of clay particles is used to prepare these thin films, and the measurement of antibacterial and mechanical properties takes place. The studies have shown a significant amount of increase in tensile properties, material strength, and elasticity as per the increase in the concentration of clay particles. Also, it was observed that the addition of $AgNO_3$ (silver nitrate) nanoparticles

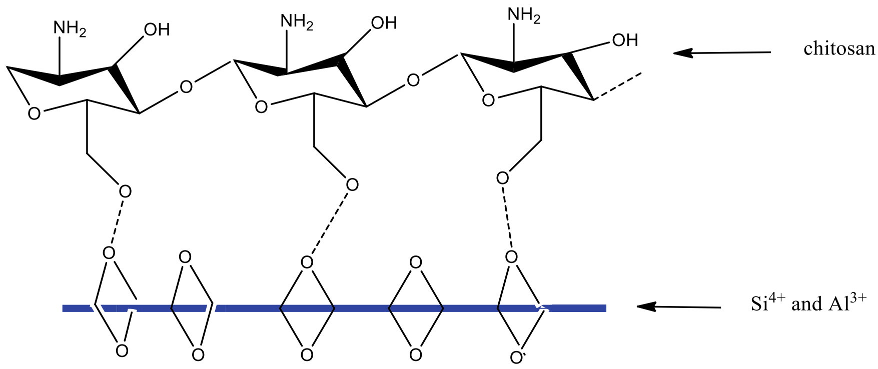

Fig. 4 Depiction of the interaction between chitosan and silicate layers

resulted in enhanced antimicrobial properties as compared to pure chitosan-based nanocomposite films. A strong electrostatic interaction was found between chitosan and silicate layers which is responsible for the significant increase in thermal stability, whereas the layer-layer stacking structure of chitosan nanocomposites enhances the antimicrobial activities (Fig. 4) [6].

4.2 Zinc Oxide (ZnO)

In dental fields, the use of metal-oxide nanoparticles used in dental restoration surgeries is a new and highly used process with its high-antibacterial activities against bacteria growing pathogenic species.

The preparation of ZnO infused chitosan (CTS)-based nanocomposites with size-controlled ZnO nanoparticles is achieved via chemical routes, resulting in stable nanostructures. These chemically extracted ZnO nanoparticles infused CTS nanocomposites proved to be antibacterial, antidiabetic, antioxidant, and cytotoxic agents. These CTS nanocomposite encapsulated ZnO nanoparticles are highly used in restorative dental applications as an antibacterial dental adhesive used during dental surgeries with increased mechanical characteristics and increase in bond strength due to CTS/ZnO interaction Fig. 5 [7].

5 Applications of Chitosan-Based Nanocomposites

As discussed above, chitosan (CTS)-based nanocomposites have proven to be helpful in the field of biopharmaceuticals and biomedicine, adding to that when they get modified with different nano-scaled chemical compounds and chemical films, their bioactivity, biocompatibility, drug delivery, etc., enhance up to significant results,

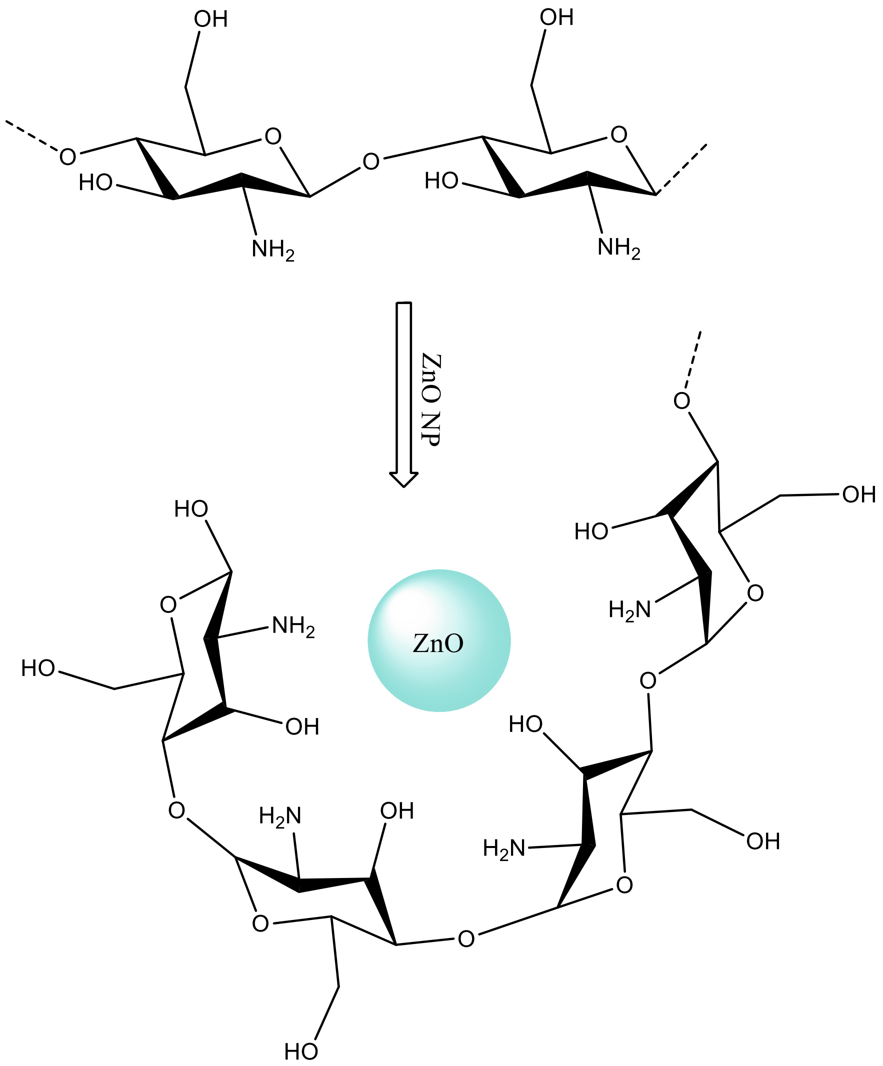

Fig. 5 Interaction of CTS-based nanocomposites and ZnO nanoparticles

this makes these nanocomposites to deliver several biomedical applications. These biomedical applications of chitosan-based nanocomposites (both with CTS alone or modified) have acquired a prominent place in the sectors of orthopaedics and dentistry, in different regions like drug delivery, enamel repair, bone, and dental tissue regeneration.

6 Biomedical Applications of Chitosan-Based Nanocomposites in Orthopaedics

The natural bone comprises of three-dimensional nanocomposite structured matrix. The study of bone structure and matrix comes under the bio-application of bone tissue engineering in the field of orthopaedics.

The field of bone tissue regeneration is comparatively new (started about three decades ago), its applications mainly include the study and modification of 3D (three-dimensional) structures, which serve their part in giving support, reinforcement to the bone material and in certain cases organizing bone replacements and tissue regeneration in a natural way. Bone tissue engineering encourages a full-fledged regeneration of the tissue of a new bone in the human body with the combinations and modifications of different biomolecules, biosynthetic materials, drugs for delivery, growth-enhancing factors, etc. Along with the significant advancement in the field, the selection of material for bone tissue engineering applications becomes crucial to making these applications become a proper clinical practice in the field of orthopaedics. To fulfil the needs of bone tissue engineering as a biomedical application in orthopaedics, researchers have developed biomaterial composites (nano-scaled) that promote osteogenesis (the formation of bone with the help of osteoblast cells) in the bone, and also various research groups have been showing their interest in the significance and advancements in bone tissue engineering resulting in expanding their work associated with the application of modified chitosan-based nanocomposites for orthopaedic procedures regarding bone tissue regeneration, due to the properties of chitosan being biocompatible, provides structural strength, etc.

Also, chitosan-based nanocomposites have been developed under several kinds of research and have been found suitable for the applications of bone tissue engineering because of the non-toxic properties of chitosan along with the ease of getting moulded or modified to give different suitable biomaterials (as discussed in the above section) [8] (Table 2). This makes the function of chitosan-based nanocomposites easier to add side groups to it in order to optimize itself for bone tissue engineering. In recent times, the use of CTS-based nanocomposites at defective bone sites in bone tissue regeneration has been increased [9]. The main focus of these applications is to overcome the problems that occur very often in the field of orthopaedics, like low availability, transfer of different pathogens, donor-site morbidity, immune response causing destruction to the bone, etc., by substituting the treatment methods with suitable ones [8].

7 Biomedical Applications of Chitosan-Based Nanocomposites in Dentistry

Chitosan-based nanocomposites have proved their non-toxicity towards cells in mammals along with different properties like being compatible with the tooth colour

Table 2 Biomedical applications of chitosan-based nanocomposites in orthopaedics

S. No.	Area of study	Biomedical applications of chitosan-based nanocomposites in orthopaedics	References
1	Modification of 3D structure matrix of bone	Giving structure and support to the bone, reinforcement to the bone material, natural tissue regeneration	[8]
2	Bone tissue engineering	Promotes osteogenesis, enhances growth, highly biocompatible, provides structural strength, non-toxic in nature, and increased tissue regeneration at defective bone sites	[8, 9]
3	Orthopaedic surgeries	Easily available, economically favourable, enhanced drug delivery, and enhanced wound healing	[8]

and being economically inexpensive. Their easy availability and wide range of possibilities for modifications make CTS nanocomposites which make them a clear winner for their potential uses. Chitosan-based nanocomposites compatibility and availability for a large range of bio-dental applications are depicted as follows, Fig. 6 [1].

7.1 Oral Drug Delivery

Chitosan-based nanocomposites can be utilized to develop a systematic arrangement of direct drug delivery with the required properties like mechanical strength, enough contact time with a good release profile being in close contact with the mucosa (oral), they also increase the bioavailability for the treatment in different oral pathologies. For the delivery of antibiotics (e.g. nystatin, chlorhexidine, and metronidazole) to periodontal (the structures surrounding and supporting the teeth) tissues, CTS-based nanocomposites in the form of nano-films can be used against fungal infections and mucositis (oral). CTS-based nanocomposites are also useful in the inhibition of plaque pathogens causing dental issues being an effective plaque controller [1].

7.2 Guided Tissue Regeneration

Guided tissue regeneration (GTR) is a developing strategy that involves the regeneration of periodontal cells. The main principle lies in the isolation of the given periodontal defect using a physical membrane that enhances the rate of bone regeneration. Chitosan and its nanocomposites fill this spot with ease, and they prove

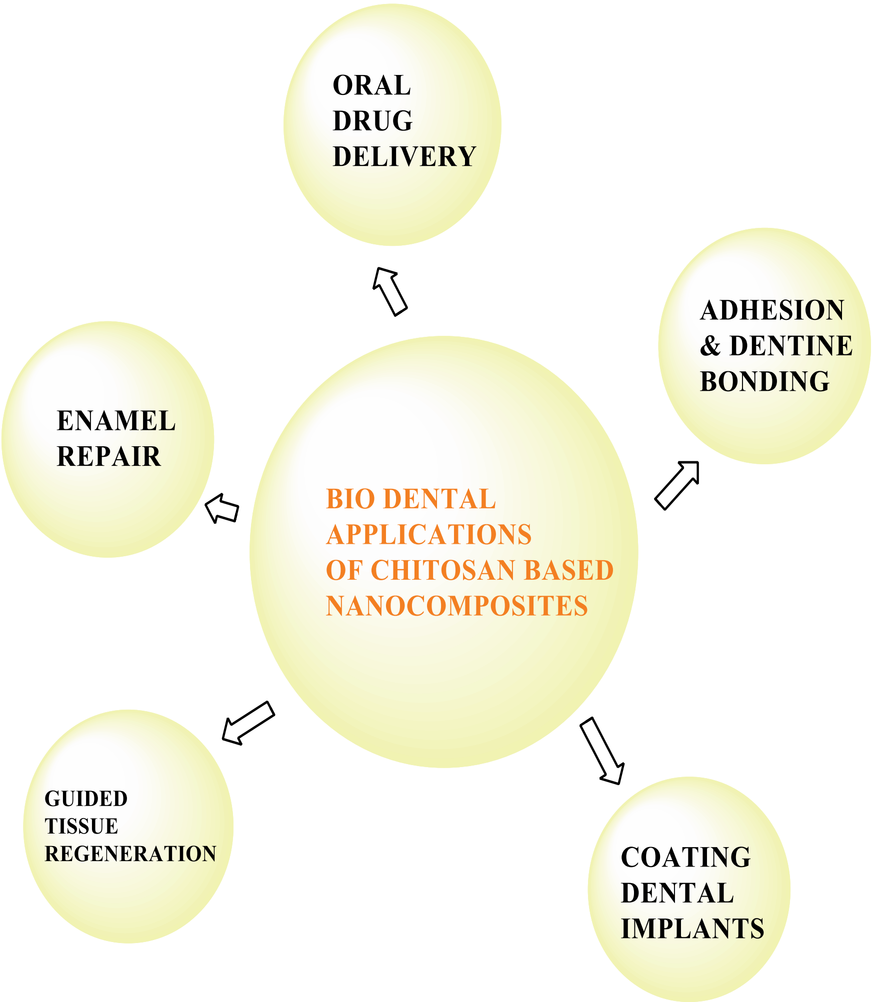

Fig. 6 Bio-dental applications of chitosan-based nanocomposites

to be a favourable substance for GTR because of their optimal size and good biocompatibility (biological behaviour) [1].

7.3 *Enamel Repair*

Studies have shown that tooth enamel is the hardest non-vascular tissue present in the human body, which makes it difficult to repair or regenerate. An abundant amount of chemical techniques have been developed with the use of chitosan-based nanocomposites to achieve the regeneration of human teeth enamel through the successful delivery of drug agents like organic amelogenin at defect sites. Along with nanocomposites, chitosan-based hydrogels as delivery agents are also being used nowadays for enamel regeneration [1].

7.4 For Coating Dental Implants

The coating of dental implant material in the process depends upon the osseointegration (direct structural and functional connection between ordered, living bone and the surface of a load-carrying implant) value of the material. Several studies have given positive results of chitosan-based nanocomposites being a good coating material in dental implants affecting the surface of the teeth with a change of mechanical, biological, and surface properties [1].

7.5 Adhesion and Dentine Bonding

Research has been conducted to study the durability of dentine bonding and dentine-restoration techniques. This comes under the area of use of bio-adhesive polymers in dental complications, which is fulfilled by chitosan-based nanocomposites resulting in better dentine bonding and a significant increase in shear strength of the bond [1] (Table 3).

8 Conclusion

Chitosan has been studied extensively due to the significant properties of the biopolymer being economically friendly, with excellent biodegradability and biocompatibility, along with non-toxic traits, antimicrobial, and antibacterial properties making the biopolymer a good candidate in the fields of biomedicine and biopharmaceuticals [10]. When chitosan nanocomposites get modified with different nano-scaled materials and films, they show significant properties increase in the rate of bone regeneration, better-targeted drug delivery, enhanced wound healing, and increased osteogenesis. Therefore, research shows a great potential for chitosan-based nanocomposites (both modified and only CTS-based) for biomedical applications in the orthopaedic and dentistry sectors [11].

Chitosan and its nanocomposites offer significantly to the future of biomedicine and biopharmaceutics, and it has also been studied that chitosan-based medical material will be of great use in upcoming times [2].

Table 3 Biomedical applications of chitosan-based nanocomposites in dentistry

S. No.	Area of study	Biomedical applications of chitosan-based nanocomposites in dentistry	Reference
1	Oral drug delivery	Develops a systematic arrangement for drug delivery with mechanical strength, good contact time, and increased bioavailability	[1]
2	Guided tissue regeneration (GTR)	Increased rate of GTR (due to optimal size and good biocompatibility of CTS-based nanocomposites)	[1]
3	Enamel repair	CTS-based nanocomposites works on regenerating human teeth enamel through successful drug delivery	[1]
4	Coating dental implants	Good coating material in dental implants with enhancing mechanical, biological, and surface properties	[1]
5	Adhesion and dentine bonding	Results in better dentine bonding and increase in the bond strength	[1]

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