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Mini Review

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Chitosan based nanoparticles towards biomedical applications

Abstract

This review outlines the bioapplications of newly developed chitosan based nanoparticles. Over the last decade, much interest has been developed in biopolymer based materials due to their biocompatible, biodegradable, non-toxic and non-allergenic nature. Here, we review the recent scientific advances in chitosan based nanoparticles not only for cancer therapy but also for various biomedical applications. An overview of chitosan, its derivatives and the formation of chitosan nanoparticles is provided along with the inherent and specific therapeutic efficacy. Major progresses in drug delivery approaches and gene delivery as well as tissue engineering applications have been summarized.

Keywords: Chitosan nanoparticles, Anti-microbial, Anti-cancer, Biomedical engineering

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Introduction

Over last few decades, the advancement in the field of nanotechnology revolutionized by its application in the biological, pharmaceutical, and health sciences, leading to noteworthy improvements in life expectancies worldwide.[1] Nanoparticles offer many advantages such as small particle size, greater drug efficacy, lower toxicity, enhanced drug solubility and stability also accumulation into tumor site through enhanced permeability and retention (EPR) effect.[2] Chitosan, (poly-β (1→4)-2-amino-2-deoxy-D-glucose), a natural linear amino-polysaccharide derived from chitin, has been widely accepted as a material of self-assembled polymeric nanoparticles and also been investigated as a potential biomaterial in biomedical fields for its biocompatibility, non-toxicity, biodegradability and bacteriostatic properties.[3]

The advantages of using chitosan are

i. The polymer can be obtained from waste products (i.e., shells) of the seafood industry and

ii. The polymer is renewable, non-toxic, and biodegradable.

The amino contents are the main factors contributing to the differences in their structures and physico-chemical properties. Moreover, their random distribution makes them easy to generate intra- and inter-molecular hydrogen bonds. Despite many advantages, generally chitin and chitosan are insoluble in water which is the major limiting factor for their utilization in living systems and restrict successful application in drug delivery in vivo. However, enzymatic or chemical functionalization of chitosan, chitosan oligosaccharides (CS) (Figures 1 & 2) have been proposed to overcome these drawbacks.[4] CS has many properties particularly suitable for developing self-assembled polymeric nanoparticles, including the availability for cross-linking with free amino groups and the cationic nature which allows ionic cross-linking with multivalent anions.[5] Chitosan and its derivatives have attracted considerable attention as biomedical materials, owing to their unique biological effects such as antioxidant, anti-allergic, anti-inflammatory, anticoagulant, anti-bacterial, anti-HIV, anti-hypertensive, anti-Alzheimer's, anti-diabetic, anti-obesity, and anti-cancer properties.[6] The reason for the extensive use of chitosan for the design of polysaccharide-based targeted nanocarriers is partially due to the presence of naturally-occurring primary amino groups on the chitosan backbone that can be reacted with ester-activated or aldehyde-containing compounds such as, ligands, linkers for further coupling, polymer chains (e.g. polyethylene glycol), or octreotide-modified N-octyl-O, N-carboxymethyl chitosan to finely tune its solubility.[7]

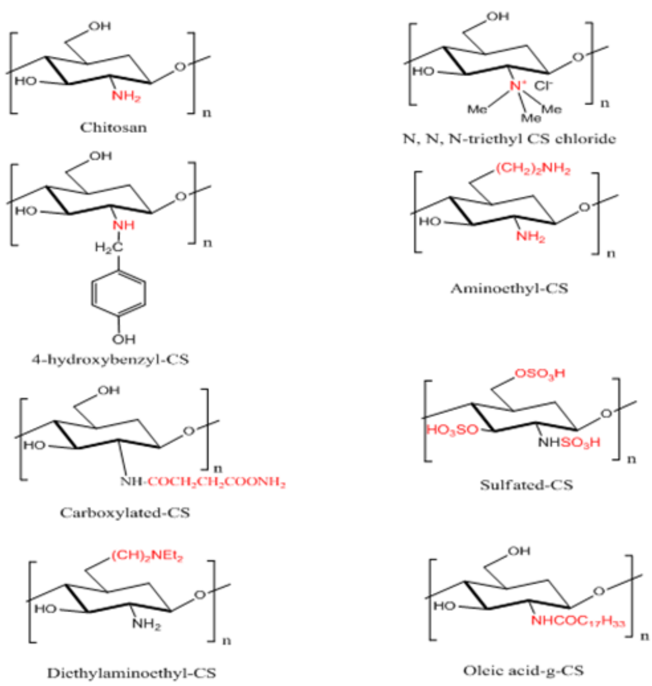

Figure 1 Structure of chitosan and its derivatives.

Formation of chitosan nanoparticles (NPs)

Chitosan-based NPs have recently drawn much attention in nanomedicine due to their stability and ease of surface modification. Chitosan-based NPs have been prepared using a variety of methods including solvent evaporation, emulsion, diffusion, ionic gelation, coacervation or precipitation, spray drying, self assembled and cross linked.[8]

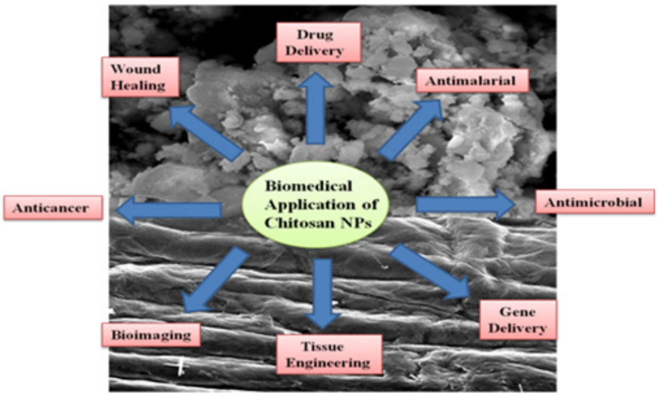

Figure 2 Various biomedical applications of chitosan based nanoparticles.

Biomedical applications of chitosan based nanoparticles

In general, chitosan offers several advantages, and these include its ability to control the release of active agents and to avoid the use of hazardous organic solvents while fabricating particles. Chitosan has some advantages due to its nontoxicity and biodegradability without damaging the environment. In various disciplines of health care and hygienic applications, chitosan is used for contact disinfectants in many biomedical applications.

Chitosan based nano as an antimicrobial agent

Despite the great progress in antimicrobial agents development, many infectious diseases remain difficult to treat, due to a lot of reasons such as the emergence and spread of resistant clones, the lack of the antimicrobial structures and suboptimal pharmacological properties of the existent antimicrobial substances, which sometimes are difficult to reach active concentrations inside bacterial strains or in some body sites. Chitosan, a promising biocompatible and biodegradable biopolymer shows potential antimicrobial activity.[9] Unlike, chitosan the nanocomposites of chitosan have been found to exhibit a broad spectrum of antimicrobial activity against various pathogens (both Gram-positive and Gram-negative bacteria).[10]

Chitosan nano in anti-cancer drug

Although, there is considerable progress in medical research, cancer is still one of the high-ranking causes of death in the world. Successful cancer management depends on accurate diagnostics along with specific treatment protocols. Among various anticancer agents reported, chitosan and its derivatives can be used as an excellent candidate for cancer diagnosis as their chemical properties allow them to be easily processed into gels, sponges, membranes, beads, and scaffold forms too.

Chitosan oligosaccharide-arachidic acid conjugate have been successfully synthesized and used for the development of self-assembled nanoparticles for doxorubicin delivery.[11] Targeting function can also be grafted onto chitosan to achieve specific targeting. For example, RGD (arginine-glycine-aspartic acid) peptide has been conjugated with chitosan using a thiolation reaction. RGD enhances selective intratumoral delivery of siRNA loaded in RGD-chitosan nanoparticles (RGD-CH-NPs) and induces significant antitumoral activity.[12]

Recently, a biodegradable polymer-drug conjugate of doxorubicin conjugated with a stearic acid-grafted chitosan nanosized oligosaccharide showed high efficiency for cellular uptake and found efficient on suppression of tumor growth.[13]

Chitosan based nano towards drug delivery system

The implementation of novel delivery approaches is less expensive than finding new drugs. Chitosn based nano compounds were found to be well adapted towards antimalarial drug delivery as a nanocarrier,[14] as a promising drug delivery system to improve antiviral potency of drugs to the viral reservoirs for the treatment of HIV infection,[15] modified by folic acid towards targeted drug delivery,[16] development of responsive hybrid nanogels by poly(methacrylic acid) for pH responsive drug release,[17] and magnetic chitosan nanoparticles, as multifunctional nanocarriers, were loaded with bleomycin as a functional nanocarrier have been proved to be effective towards targeting system.[18]

Chitosan nano towards tissue engineering applications

Tissue engineering comprises the basic principles and methods of utilization of structural and functional relationships in normal and infected tissue to develop biological substitutes to restore, and improve biofunction. Polysaccharides like chitosan based materials are known for biocompatible, and promote cell adhesion, proliferation, and differentiation has been used extensively for orthopaedic tissue engineering.[19] Chitosan based hybrid nanocomposites have been reported as bone tissue engineering materials,[20] cartilage regeneration,[21] and liver and nerve tissue engineering.[22]

Chitosan nano in wound-healing applications

Wound healing is a complex pathway of biologically regulated reactions allied to the general phenomenon of growth and tissue regeneration. It progresses through a series of stages in which several cellular and matrix components act together to reestablish the damaged and replacement of lost tissues.[23] Chitosan-based nanomaterials, produced in varying formulations like composite scaffolds, chitosan based sponges, immobilized scaffolds and drug loaded scaffolds etc, have been used in a number of wound-healing applications.[24]

Chitosan nano in gene therapy and bioimaging applications

The cellular delivery of nucleic acids is the foundation of gene therapy and has the potential to treat many currently incurable diseases. Chitosan possesses many characteristics of an ideal gene delivery system. Chitosan–DNA nanoparticles formulation readily done by coacervation between the positively charged amine groups on the chitosan and negatively charged phosphate groups on the DNA resulting higher stability and enhancing gene transfer properties.[25] Bioimaging applications of chitosan nano are also gaining rapid attention due to its biocompatible properties. The incorporation of imaging agents such as Fe3O4 for Magnetic Resonance Imaging (MRI) into the self-assembled nanoparticles could enhance targeted tumor imaging.[26]

Conclusion

In this review, the various properties such as anti-microbial, anti-cancer and biomedical applications of chitosan based nano-materials have been covered. Chitosan, with its exciting properties, is one of the most promising bio-based polymers for drug delivery, tissue engineering, gene therapy and bioimaging applications. Most of the studies revealed that chitosan is a non-toxic, slowly biodegradable and biocompatible material and it is almost the only cationic polysaccharide in nature with such great innate medical properties.

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Overall, in understanding the application of chitosan, herein we represented structure, chemistry and formation of different chitosan nano-derivatives in the creation of high-value-added biomaterials with opening up new application towards the biomedical field.

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Conflicts of interest

None.

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