Elyns Publishing Group
Explore and Exploit

http://elynsgroup.com

Review Article | Journal of Biomedical Technology and Research | Open Access

Chitosan in the Light of Nanobiotechnology: A Mini Review

Tanvi Jain[1,2], Sushil Kumar[1] and PK Dutta[2,3]*

[1]*Department of Chemical Engineering, Motilal Nehru National Institute of Technology, Allahabad 211004, U.P., India*
[2]*Department of Chemistry, Motilal Nehru National Institute of Technology, Allahabad 211004, U.P., India*
[3]*Centre for Medical Diagnostic & Research, Motilal Nehru National Institute of Technology, Allahabad 211004, U.P., India*

Received Date: March 23, 2015, **Accepted Date:** April 17, 2015, **Published Date:** April 30, 2015.

***Corresponding author:** *PK Dutta, Centre for Medical Diagnostic & Research, Motilal Nehru National Institute of Technology, Allahabad 211004, U.P., India, Tel: 91-993-674-0953; Fax: 91-0532-254-5341; E-mail: pkd_437@yahoo.com, pkd@mnnit.ac.in*

Abstract

The field of biotechnology emerged in the fast pace of biology with the interface of science, engineering and technology and mostly known for its multidisciplinary nature. As we progress successively in this domain, the refinement of the field is quite obvious. Looking into an era of nanoscience and technology, now a days , we are using the broader term "nanobiotechnology" which includes all basic scientific research currently studying the fundamental, biologically related physicochemical properties of nanomaterials and cellular nanoscale phenomena like biopolymer-protein assemblies, molecular motors, cellular electrochemical behavior and so on. Such fantastic nature based research understanding has guided us to utilize the natural polymer obtained from crustacean shells, fungi etc.: chitin the second most naturally occurring polysaccharide just after cellulose. Chitosan, the principle derivative of chitin is much more versatile and finds curiosity-driven research in nanobiotechnology. This mini review focuses on various formulation based on chitosan utilized in clinical as well as biomedical field with special emphasis on quantum dots, nanoparticles, carbon dots and also about some of the application such biosensors and biomarkers detection in the light of biopolymer, chitosan.

Keywords: Nanobiotechnology; Quantum dots; Biosensors; Carbon dots; Chitosan

Introduction

In recent years, the interface between biological sciences, engineering and nanotechnology has given rise to a term called as nanobiotechnology. This new area helps to indicate the merger of biological research with various fields of nanotechnology. Nanobiotechnology**,** which refers to those methods that nanotechnology, can used to create devices to study biological systems. Nanobiotechnology aims to exploit advances in nanotechnology for improving biotechnology, whereas the other term bionanotechnology takes benefit of natural or biomimetic systems to fabricate exclusive nanoscale structures. Hence, both the technologies are interrelated but complementary to each other. The interface between nanobiotechnology and bionanotechnology is shown in Figure 1.

Nanobiotechnology has already established its presence in the eyes of the researchers and has various applications like cell structure and physiology, virus detection (viral & non-viral vectors), radiation/chemotherapy drug delivery, siRNA/DNA delivery, biosensors, utilization of imaging devices like quantum dots etc. apart from the above mentioned areas, enormous nanomaterials such as polymers like chitosan, alginate, chitin, PLGA etc., and silica have also been significantly investigated for theranostics applications as well [1]. The various applications of nanobiotechnology are shown in Figure 2.

Currently, nanobiotechnology is a need for various clinical diagnosis and biomedical applications. For example, detection of

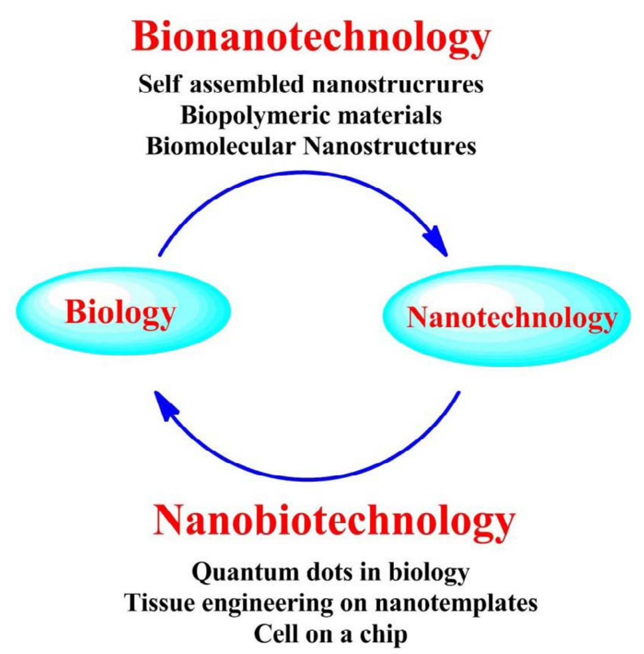

Figure 1: Relation between nanobiotechnology and bionanotechnology.

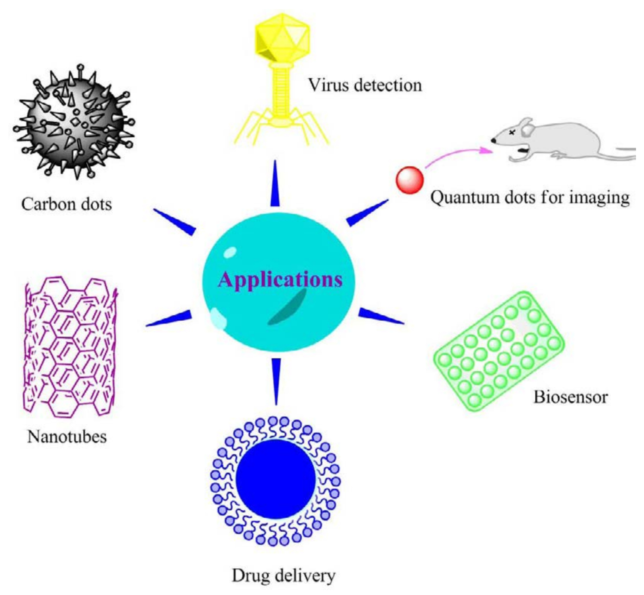

Figure 2: Diagram of various applications of nanobiotechnology.

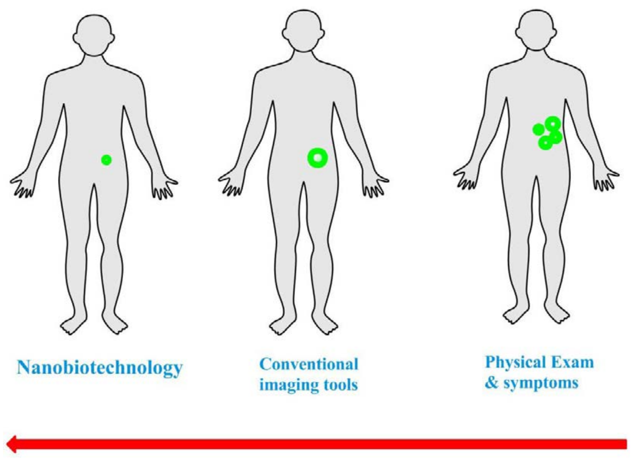

Figure 3: Diagrammatic representation on how nanodevices can enhance cancer detection and diagnosis.

cancer at primary stages is a very crucial process in improving and developing cancer treatment. At present, detection and diagnosis of cancer normally depend on variations in cells and tissue size and behavior that are only detected by a doctor's imaging expertise. Now a days, some scientists are trying to make it feasible to detect the cancer at earliest molecular changes, long before a physical exam or imaging technology is effective. To do this, they need a new set of modalities like biosenors, biomarkers, nanovehicles etc. Figure 3 is showing how these nanodevices can enhance cancer detection and diagnosis of cancer. Chitosan being the second most abundant polysaccharide can be used extensively in many fields such as nanobiotechnology, theranostics and other biomedical applications like drug delivery, tissue engineering and wound healing etc. The advantages of chitosan includes excellent biodegradability, biocompatibility and also having low toxicity with various biological activities such as antimicrobial activity and low immunogenicity which provides generous opportunities for numerous applications in the field of tissue engineering, drug delivery, wound healing and other uses [2–8].

The present mini review will describe in brief the role of chitosan for the development of various formulations used in the field of nanobiotechnology with reference to quantum dots, and nanoparticles, carbon dots and its applications like chitosan based biosensors and chitosan based formulations for the detection of biomarkers especially for the detection of cancer.

Different Formulations of Chitosan in Nanobiotechnology

Chitosan with carbon dots

Carbon dots (CDs) defined as a division of 'zero-dimensional' carbon based nanomaterials that have recently received considerable attention by researchers due to its profitable characteristics, like outstanding water solubility, biocompatibility and better photostability which make CDs effectively suitable for fluorescent biosensing or imaging [9,10]. Lot of researchers has shown their interest for various applications of chitosan based carbon dots to enhance the characteristics features of synthesized nanocomposite. In one study, Konwar, et al. [11] developed chitosan–carbon dots nanocomposite film by taking "tea" as a green source for the synthesis of carbon dots. They observed that chitosan–carbon dots nanocomposties are smooth & soft in nature but become robust with superior UV–visible blocking, swelling, thermal and mechanical properties in comparison to conventional chitosan film which offers various uses in biomedical applications. Yang, et al. [12] fabricated chitosan derived carbon dots by hydrothermal reactions and the process is called as carbonization at a mild temperature. The results showed that the fabricated particles showed low cytotoxicity and excellent biocompatibility. Xiao, et al. [13] synthesized greatly amino functionalized fluorescent carbon nitride dots (CNDs) using dehydration process of chitosan. The study revealed that the prepared CNDs have effective water solubility and demonstrate strong fluorescence which can be beneficial for medical diagnosis and treatment of cancer. Chowdhury, et al. [14] reported the synthesis of fluorescent CDs using chitosan gel and also prepared CDs using chitosan/Ag and chitosan/Au nanocomposites. The analysis was done by photoluminescent (PL) using CDs prepared in different pH conditions. The above study showed the enhancement of PL emission for the CDs prepared from above mentioned nanocomposites. Sachdev, et al. [15] synthesize multicolour passivated carbon dots (CPs) utilizing chitosan through microwave aided pyrolysis process. This study showed the biolabeling potential of CPs against two 45 different bacterial model methods which evidently proves that the above prepared CPs can be used as biolabeling agents for biomedical applications. The authors' laboratory has also verified the hydrothermal and solvothermal synthesis of CDs from chitosan-ethanol system and the result depicted in visible range dark brown and UV-short wave 254 nm light blue colour [16]. Very recently, Titirici, et al. [17] synthesized, characterized, and used for the first time to build solid-state nanostructured solar cells from three different biomass, namely chitin, chitosan and glucose –derived functional carbon quantum dot sensitizers new hybrid materials consisting of ZnO nanorods with the highest efficiency of a layer-by-layer coating of two different types of CDs.

Chitosan with quantum dots as an imaging agent

Fluorescent semiconductor nanocrystals called as quantum dots (QDs), are a breakthrough technique in the field of nanobiotechnology and acts as an excellent imaging agent for the detection of diseases. The optical characteristics can be altered by varying the size of the particle and its arrangement. These inorganic fluorescent nanocrystals comprise groups of III–V (i.e InP and InAs); II–VI (i.e. CdSe and CdTe) semiconductor entities**.** The main drawback of QD's as an imaging agent is its toxicity and indiscretion [18,19]. Mansur et al. [20] developed a novel facile route for synthesising ZnS QDs capped by chitosan performed using a single-step aqueous colloidal process at room temperature with optical properties tuned by pH. The nanobioconjugates of ZnS nanocrystals showed fluorescent properties as influenced by the pH during the synthesis with exhibited luminescent activity for possible applications like probes in biology, medicine and pharmacy.

The author's laboratory has already synthesised a highly luminescent chitosan-l-cysteine functionalized CdTe QDs film with the good result of antibacterial study which tells that the fabricated QDs based chitosan composite is an excellent candidate for broad range of biomedical applications [21].

Dilag et al. [22] had developed biopolymeric matrix using chitosan in which cadmium sulfide (CdS) quantum dots (QDs) has been further encapsulated for latent fingermark detection. The results showed that fresh latent fingermarks deposited on aluminium foil were clearly indicated and can be examined under a rofin polilight at 450 nm by scattering with a freeze-dried solution of the CdS/chitosan nanocomposite giving a quantum dot surfactant powder proves to be a very beneficial for forensic sciences. In another study, Sharma et al. [23] studied about electrophoretic layering of nanocomposite synthesized from chitosan(CS)–cadmium-telluride quantum dots (CdTe-QDs) on to indium-tin-oxide coated glass. The researcher also fabricated an electrochemical DNA biosensor for the detection of chronic myelogenous leukemia (CML) by immobilizing the amine terminated oligonucleotide probe sequence which contained 22 base pairs, taken from BCR–ABL fusion gene. The results showed that the prepared bio sensor can detect as low as 2.56 pM concentration of corresponding target DNA with a response time of 60s. Also, Wee et al. synthesized chitosan encapsulated QDs to deliver human epidermal growth factor receptor 2 (HER2) si-RNA to MCF-7 (human breast adenocarcinoma-7) and SKBR3 - human breast cancer cell line cells, where, the surface of the QD–chitosan composite was altered with the help of HER2 antibodies to attain targeted delivery of si-RNA to HER2 receptors. SKBR3 cells presented a larger number of HER2 receptors and as a consequence, more internalization was found in SKBR3 cells when distinguished with MCF-7 cells. After comparison with the control, HER2 gene expression levels were reduced to 80% when QD–chitosan composite was used to deliver HER2 si-RNA [24]. Jie et al. [25] synthesized CdS quantum dots (QDs) - carbon nanotubes (CNTs) and gold nanoparticles-chitosan (GNPs-CHIT) was presented. Then, these GNPs-CHIT nanocomposites were used to fabricate a valuable antibody immobilization matrix with exceptional steadiness and bioactivity. This study showed that the prepared nanocomposite was faster and steady when compared with earlier prepared immunosensors, which retains superior capability for the detection of protein in clinical research laboratory and Kang et al. [26] successfully fabricated chitosan-coated CdSe quantum dots (CdSe/CS QDs) in liquid medium through γ-radiation route under ambient pressure. The results showed that the diameter of the prepared QDs composite was about 4 nm and also exhibited an absorption peak at 460 nm and its emission peak at 535 nm.

Chitosan based nanoparticle formation for DNA/siRNA

In past few decades, many researchers has grown rapid interest in gene delivery because of its enormous potential as a future strategy for nanobiotechnology which can be used in various therapeutical applications to cure various categories of diseases by treating silencing unwanted gene expression , defective genes, substituting missing genes [27]. Therefore, it is important to develop safe and effectual gene carriers for the benefit of gene therapy [28].In recent years, many researchers are using chitosan-based nanocarriers that have gained increasing interest as a safe delivery technique for gene materials including plasmid DNA (pDNA), oligonucleotides and siRNA due to the excellent features of chitosan [29,30] as well as a high positive charge density. Proper mechanism of chitosan based DNA nanocarriers are shown in Figure 4.

Mumper et al. [31] were the first to report about the promising feature of chitosan which can be used for *in vitro* pDNA delivery. Zhao et al. [32] prepared chitosan-pEGFP nanoparticles by complex coacervation method with pEGFP, to study the capability of chitosan as a gene delivery vector to deliver an exogenous gene into primary chondrocytes which can be used to treat joint diseases. The study included transfection process of primary chondrocytes in various conditions by altering pH of the medium, molecular weight of chitosan and different plasmid dosage. The results proved that the synthesized nanoparticles have the good potential to deliver therapeutic genes directly into joint to treat various types of joint diseases.

To improve transfection efficiency, a lot of studies had been done by modifying chitosan. Malmo J et al. [33] studied about the self-branching mechanism of chitosans to develop its gene transfer characteristics without negotiating its biocompatibilty. Here, both Self-branched (SB) as well as self-branched trisaccharide-substituted (SBTCO) chitosans were prepared, characterized, and compared with their linear counterparts for evaluating transfection efficiency, cellular uptake, formulation stability, and cytotoxicity.

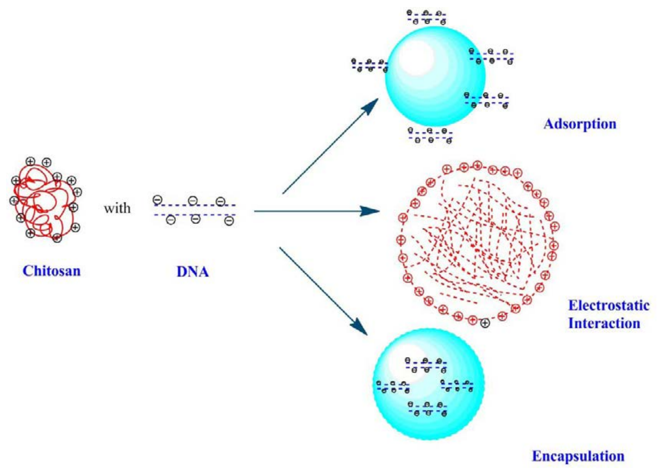

Figure 4: Synthesis of chitosan-based DNA/siRNA nanoparticles using different methods.

Varkouhi et al. [34] studied whether the thiol groups in (N,N,N-trimethylated chitosan) TMC improves the extracellular efficiency of the nanocomplexes and promotes the intracellular release of siRNA. The results showed that TMC-SH had improved extracellular activity and also good silencing activity and thus concluded that TMC-SH are more appealing systems for other *in vivo* evaluations. In another related studies, PEGylated chitosan and chitosan/cyclodextrin nanoparticles were identified as promising tools for DNA-based drug delivery [35,36].

Likewise, Yoon et al. [37] prepared glycol chitosan (GC)-based nanoparticles (CNPs) serve as useful nanocarriers that can effectively entrap both chemotherapy drugs and si-RNA to attain maximum efficacy by overcoming resistance. Doxorubicin, DOX-encapsulated CNPs (DOX-CNPs) or Bcl-2 si-RNA-encapsulated CNPs (si-RNA-CNPs) was evaluated and their physiochemical properties, including size, surface properties and pH sensitive behaviour were studied, regardless of the different physical features of DOX and Bcl-2 si-RNA and the researcher confirms that CNP platform applied to two different types of drugs results in similar in vivo bio distribution and chemical kinetics, embellishing treatment in a dose-dependent manner. Tahara et al. [38] have synthesized chitosan-modified poly(d,l-lactide-co-glycolide) nanocomposites. In this study, degree of binding of the plasmid with the nanocomposite was determined. The results showed that the prepared nanocomposite would be an effective and beneficial nonviral device used for gene delivery. Here, Nielsen et al. [39] have recently synthesized an aerosolised form of chitosan nanoparticles for enhanced pulmonary siRNA delivery and also gene silencing in mice in which *in vitro* silencing of various formulations was analysed in an (enhanced green fluorescent protein) EGFP transgenic mice, endogenous-expressing H1299 cell line using flow cytometry. The results demonstrated that minimal alteration in gene silencing efficiency before (68%) and after (62%) aerosolisation in EGFP-expressing H1299 cells which was very beneficial for the delivery of a gene.

Application of Chitosan Based Formulations

Biosensor

Many researchers have developed interests in the field of biosensors have increased curiosity for their beneficial characteristics as analytical tools, specially the potential miniaturization, portability, low cost and friendly use comparison to other well established lab based methods [40]. A sensor is a type of a device that receives and responds to a signal and thus converts it into magnetic or in electrical form, which can be further used in an electronic device. The sensor utilized for the biological entities is called biosensor. It is a diagnostic tool that utilized specific biochemical reactions arbitrated by a biological entity like DNA, enzymes, antibody cells or any tissues immobilized onto a signal transducer. The major analytical merits of any biosensor are adaptability, portability, high sensitivity, intrinsic selectivity and simplicity to use in moderately complex environments due to their quick response [41-43].

Chitin or chitosan has been also used as a framework element for the immobilization of recognition elements in various sensor gadgets. The excellent biological properties of chitosan have made these elements as attractive matrixes for synthesis of enzyme sensors. Due to above mentioned characteristics of chitosan; its nanocomposite-based biosensors are examined for various types of detection [44 -46]. Likewise, Wang et al. developed a novel tyrosinase biosensor based on Fe_3O_4 nanoparticles/chitosan nanocomposites for the detection of catechol. Porous morphology of chitosan and large surface area due to the iron oxide provided the surface for high loading of tyrosinase enzyme. This tyrosinase biosensor amperometrically determine phenolic compounds [47]. In another study, Kang et al. [48] utilized biocompatible chitosan to diffuse graphene and fabricate glucose measuring biosensors. It was found that chitosan supported a well-dispersed graphene solution and also helps in immobilizing the enzyme molecules, and at last graphene-based enzyme sensor exhibited excellent sensitivity which results in long-term stability for estimating glucose. In another related study, Hong et al. [49] developed glucose oxidase-Platinum-graphene-chitosan biocomposite film for sensing of glucose. A highly sensitive sensor with a detection limit of 0.6 μM was formed by using graphene with platinum nanoparticles. Thus, the large surface area and effective electrical conductivity of graphene recommended that it has a potential to become an effective sensor. Ying et al. [50] developed chitosan- carbon nanotubes composite biosensing matrix in which facilely fabricated amperometric biosensor by encapsulating laccase into the CS- CNTs composite has been synthesized which can be effectively utilized in the development of not only in biosensors but also includes biofuel cells, and other bioelectrochemical tools. Also, Tiwari et al. [51] synthesized chitosan-graft-polyaniline nanocomposite having creatinine amidinohydrolase (CAH) which was then immobilized onto the electrochemically active composites. The Michaelis–Menten study showed that the above matrix had a extraordinary affinity for immobilization of CAH enzyme. Thus, the use of chitosan in biosensor frameworks assists in maintaining the stability and durability of the biosensor system.

Biomarkers

A characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention [52]. Biomarkers are also used to manage cancers and for other kind of diseases [53]. The practice of biomarkers in clinical research as well as in clinical practice has become so commonplace that their presence as primary endpoints in clinical trials is now accepted almost without question [54]. A recent application of various formulations of chitosan also includes detection of biomarkers for various diseases. Currently, biomarkers have expanded immense technical and clinical as well as medicinal importance. There are three important roles of biomarkers, firstly; biomarkers can be easily utilized for screening and risk assessment before diagnosis of any disease. Secondly, they can diagnose staging, grading, and selection of initial therapy. Thirdly, they can be used to monitor the therapy, modify or select additional therapy if required during treatment [55,56]. The main features of any ideal biomarker are shown in Figure 5.

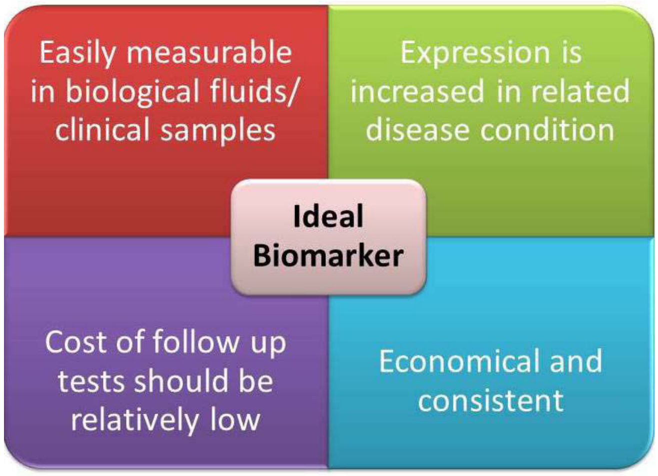

Figure 5: Features of an ideal biomarker.

Chitosan helps in detecting various types of biomarkers for treating number of diseases. Domnanich et al. [57] fabricated gold chips coated with polyelectrolyte multilayers (PEMs) for signal improvement for melanoma-related biomarkers in which PEMs composed of xanthan and chitosan. The results showed that the above prepared substrate can be valuable tool in a various biosensing & bioimaging applications. Dan et al. [58] fabricated electrochemical immunosensor by graphene based sensor modified with chitosan with carbon nanospheres (CNSs) marked with horseradish peroxidase-secondary antibodies (HRP-Ab2) used for the detection of cancer biomarker α -fetoprotein (AFP). The results explained that the dual signal amplification strategy of graphene sheets along with multi enzymes, the synthesized immunosensor displayed a 7-fold increament in the detection signal when it was compared to the immunosensor without graphene modification and CNSs labeling. In another related study, Chen et al. [59] developed an electrochemical based sensor for the detection of biomarkers, alpha-fetoprotein (AFP) and carcinoembryonic antigen (CEA) by using chitosan nanocomposites. The results clearly signifies that assay analysis of the used samples with the proposed techniques had given more satisfying conclusion than from standard ELISA technique which can be utilized further in the field of clinical diagnosis. Therefore, integration of biomarkers into medical field will be of utmost importance to accomplish 'personalization' of treatment and disease prevention.

Drug Delivery

There has already been immense number of researches to elucidate polymer-based (like PEG, PLGA, Hyaluronic acid (HA) etc., drug delivery carriers which are having advantageous encapsulation properties of polymers. Presently, variety of chitosan based nanoparticles is extensively used for drug delivery applications. Chitosan has been widely utilized as drug delivery systems for low molecular drugs, peptides and genes [60-62]. Qu et al. [63] studied the effect of PEG conjugation on PTX-loaded N-octyl-sulfate chitosan nanoparticles. Also, Varshosaz et al. [64] investigated chitosan microspheres which was coated with cellulose acetate butyrate using emulsion-solvent evaporation method, for delivery of 5-ASA into the colon. A lot of studies have been earlier done on chitosan based nanocarriers for targeted drug delivery into the kidney [65-67]. In another related study, Janes et al. [68] effectively encapsulate DOX into the chitosan nanoparticles synthesized by ionotropic gelation technique. The results showed that the cytotoxicity of DOX-loaded nanoparticles in human melanoma cells (A375) and (C26) murine colorectal carcinoma cells indicated that the synthesized formulations were able to sustain cytostatic activity relative to free DOX. Also, the confocal microscopy studies revealed that DOX-loaded chitosan nanoparticles are adopted by these cells and thus also degraded to release the drug intracellularly.

Recently, Yongling D et al. [69] synthesized chitosan (CS) based carboxymethyl-β-cyclodextrin (CM-β-CD) polymer modified by using Fe_3O_4 magnetic nanoparticles for delivery of anticancer drug 5-fluorouracil. The results indicated that results indicated that the quantity of cross linking agent and bonding times played a vital role in analyzing the morphological characteristics of the prepared hybrid nanocarriers. Therefore, chitosan based nanocarriers for drug delivery plays a vital role in the treatment of various diseases

Conclusion

Nanobiotechnology, one of the relatively recent, promising and yet, largely untapped field of science, has its origins in the nanotechnological advances made in the last four decades. It is a marriage between the fields of technical and biological sciences and combines the complementary strengths of biological molecules and nanoelectronics for biomedical based devices. There are three specific areas of application where chitosan based formulations like quantum dots, carbon dots, biosensors, nanoparticles is being utilized in nanobiotechnology with excellent outcome. In this mini review, recent effort in the evolving field of nanobiotechnology, we have mentioned chitosan based formulations like nanovehicles for DNA/SiRNA delivery, quantum dots and nanocomposites. Due to the excellent biological properties of chitosan, a lot of work can be done in the field of medical diagnosis for various disease treatments as well as in biomedical research like in drug delivery, tissue engineering etc. Last five years this area has been witnessed a proliferation of high-resolution devices (biosensors) for in-vivo imaging of diseases in animal models using quantum dots; and the detection of biomarkers for generating new diagnostic and therapeutic techniques and also for utilized for drug delivery treatment of diseases like cancer. Apart from this nanobiotechnology raises many issues as with any introduction of new modality, including concerns about the toxicity and environmental impact of nanomaterials, and their capability on the world economy. Therefore, chitosan based nanobiotechnology is capable of creating several novel nanomaterials and devices with an infinite range of applications, such as in medicine, theranostics, biomedical and clinical applications for the benefit of mankind.

References

1. Jain T, Kumar S, Dutta PK. Theranostics: A way of modern medical diagnostics and the role of chitosan. J Mol Genet Med. 2015; 9:1-5.
2. Archana D, Singh BK, Dutta J, Dutta PK. Chitosan-PVP- nano silver oxide wound dressing: In vitro and in vivo evaluation. Int J Biol Macromol. 2015; 73: 49-57. doi: 10.1016/j.ijbiomac.2014.10.055.
3. 3.Dutta J, Chattopadhyaya MC, Tripathi VS, Dutta P K (2004) Chitin & Chitosan: Novel biomaterials waiting for future developments. J Polym Mater 21: 321-332.
4. Rinaudo M. Main properties and current applications of some polysaccharides as biomaterials. Polym Int. 2008; 57(3):397–430.
5. Jain T, Dutta PK (2011) Chitin nanoparticles for drug delivery: Preparation, characterization and evaluation. Asian Chitin J 7: 13-18.
6. Dutta PK, Tripathi S, Mehrotra GK, Dutta J. Perspectives for chitosan based antimicrobial films in food applications. Food Chem. 2009; 114(4): 1173–1182.
7. Dutta PK, Srivastava Rohit, Dutta Joydeep. Functional nanoparticles and chitosan-based functional nanomaterials. Multifaceted development and applications of biopolymers towards biology, biomedicine and nanotechnology. In: P.K. Dutta, Joydeep Dutta. Advances in Polymer Science, Vol. 254, Springer-Verlag Berlin Heidelberg; 2013.
8. Yi H, Wu LQ, Bentley WE, Ghodssi R, Rubloff GW, Culver JN, et al. Biofabrication with chitosan. Biomacromolecules. 2005; 6(6): 2881–2894.
9. Zhu H, Wang X, Li Y, Wang Z, Yang F , Yang X. Microwave synthesis of fluorescent carbon nanoparticles with electro chemiluminescence properties. Chem Commun. 2009; 34: 5118–5120.
10. Liu JM, Lin LP, Wang XX, Lin SQ, Cai WL, Zhang LH, et al. Highly selective and sensitive detection of $Cu2^+$ with lysine enhancing bovine serum albumin modified-carbon dots fluorescent probe. Analyst. 2012; 137(11): 2637–2642. doi: 10.1039/c2an35130g.
11. Konwar A, Gogoi N, Majumdar G, Chowdhury D. Green chitosan–carbon dots nanocomposite hydrogel film with superior properties. Carbohydr Polym. 2015; 115: 238–245. doi: 10.1016/j.carbpol.2014.08.021.
12. Yang Y, Cui J, Zheng M, Hu C, Tan S , Xiao Y, et al. One-step synthesis of amino-functionalized fluorescent carbon nanoparticles by hydrothermal carbonization of chitosan. Chem Commun (Camb). 2012; 48(3): 380–382. doi: 10.1039/c1cc15678k.
13. Xiao D, Yuan D, Hea H, Lu J. Microwave-assisted one-step green synthesis of amino-functionalized fluorescent carbon nitride dots from chitosan. Luminescence. 2013; 28(4):612-615. doi: 10.1002/bio.2486.
14. Chowdhury D, Gogoi N, Majumdar G. Fluorescent carbon dots obtained from chitosan gel. RSC Advances. 2012; 32: 12156–12159. DOI: 10.1039/C2RA21705H.
15. Sachdev A, Matai I, Kumar U, Bhushan B, Dubey P, Gopinath P. A novel one-step synthesis of PEG passivated multicolour fluorescent carbon dots for potential biolabeling application. RSC Adv. 2013; 38: 16958–16961. DOI: 10.1039/C3RA42415D
16. Dutta PK, Ghosh T, Kumar H and Jain T. (2015) Hydrothermal and solvothermal synthesis of carbon dots from chitosan-ethanol system. Asian Chitin J 11: 1-4.
17. Briscoe J, Marinovic A, Sevilla M, Dunn S, Titirici M. Biomass-derived carbon quantum dot sensitizers for solid-state nanostructured solar cells . Angew Chem Int Ed Engl. 2015; 54(15): 4463-8. doi: 10.1002/anie.201409290.
18. Zhu ZJ, Yeh YC, Tang R, Yan B, Tamayo J, Vachet RW, et al. Stability of quantum dots in live cells. Nat Chem. 2011; 3(12):963–968. doi: 10.1038/nchem.1177.
19. Medintz IL, Uyeda HT, Goldman ER, Mattoussi H. Quantum dot bioconjugates for imaging, labelling and sensing. Nat Mater. 2005; 4(6): 435-446.
20. Ramanery FP, Mansur AP, Mansur HS. One-step colloidal synthesis of biocompatible water-soluble ZnS quantum dot/chitosan nanoconjugates. Nanoscale Res Lett. 2013; 8(1):512. doi: 10.1186/1556-276X-8-512.
21. Kumar H, Srivastava R, Dutta PK. Highly luminescent chitosan-l-cysteine functionalized CdTe quantum dots film: Synthesis and characterization. Carbohydr Polym. 2013; 97(2): 327– 334. doi: 10.1016/j.carbpol.2013.04.056.
22. Dilag J, Kobus H, Ellis VA. Cadmium sulfide quantum dot/chitosan nanocomposites for latent fingermark Detection. Forensic Sci Int. 2009; 187(1-3): 97-102. doi: 10.1016/j.forsciint.2009.03.006.
23. Sharma A, Pandey CM ,Sumana G, Soni U, Sapra S, Srivastava AK, et al. Chitosan encapsulated quantum dots platform for leukemia detection. Biosens Bioelectron. 2012; 38(1): 107-13. doi: 10.1016/j.bios.2012.05.010.

24. Tan WB, Jiang S, Zhang Y. Quantum-dot based nanoparticles for targeted silencing of HER2/neu gene via RNA interference. Biomaterials. 2007; 28(8):1565–1571.

25. Jie G, Liu P, Wang L, Zhang S. Electrochemiluminescence immunosensor based on nanocomposite film of CdS quantum dots-carbon nanotubes combined with gold nanoparticles-chitosan. Electrochem commun. 2010; 12(1): 22–26. doi:10.1016/j.elecom.2009.10.027.

26. Kang B, Chang SQ, Dai DY, Chen D. Synthesis of green CdSe/chitosan quantum dots using a polymer-assisted γ-radiation route. Radiat Phys Chem. 2008; 77(7): 859–863. doi:10.1016/j.radphyschem.2007.11.008

27. Kim T, Jiang H, Jere D, Park I, Cho MH, Nah JW, et al. Chemical modification of chitosan as a gene carrier in vitro and in vivo. Prog Polym Sci. 2007; 32(7): 726–753. doi:10.1016/j.progpolymsci.2007.05.001.

28. Rolland A. Gene medicines: the end of the beginning? Adv Drug Deliv Rev. 2005; 57(5): 669–673.

29. Shu XZ, Zhu KJ. The influence of multivalent phosphate structure on the properties of ionically cross-linked chitosan films for controlled drug release. Eur J Pharm Biopharm. 2002; 54(2): 235–243.

30. Lee MK, Chun SK, Choi WJ, Kim JK, Choi SH, Kim A, et al. The use of chitosan as a condensing agent to enhance emulsion mediated gene transfer. Biomaterials. 2005; 26(14): 2147–2156.

31. RJ Mumper, JJ Wang, JM Claspell, AP Rolland (1995) Novel polymeric condensing carriers for gene delivery. Proceedings of the International Symposium. Controlled Release Bioactive Materials.

32. Zhao X, Yu SB, Wu FL, Mao ZB, Yu CL. Transfection of primary chondrocytes using chitosan–pEGFP nanoparticles. J Control Release. 2006; 112(2) :223–228.

33. Malmo J, Vrum KM, Strand SP. Effect of chitosan chain architecture on gene delivery: comparison of self-branched and linear chitosans. Biomacromolecules. 2011; 12(3): 721–729. doi: 10.1021/bm1013525.

34. Varkouhi AK, Verheul RJ, Schiffelers RM, Lammers T, Storm G, Hennink WE. Gene silencing activity of siRNA polyplexes based on thiolated N,N,N-trimethylated chitosan. Bioconjug Chem. 2010; 21(12): 2339-46. doi: 10.1021/bc1003789.

35. Osorio DT, Lopez CP, Alonso MJ. Chitosan/cyclodextrin nanoparticles can efficiently transfect the airway epithelium in vitro. Eur J Pharm Biopharm. 71(2): 257–263. doi: 10.1016/j.ejpb.2008.09.020.

36. 36.Malhotra M, Lane C, Duchesneau CT, Saha S, Prakash S. A novel method for synthesizing PEGylated chitosan nanoparticles: strategy, preparation, and in vitro analysis. Int J Nanomedicine. 2011; 6: 485-94. doi: 10.2147/IJN.S17190.

37. Yoon HY, Son S, Lee SJ, You DG, Yhee JY, Park JH. Glycol chitosan nanoparticles as specialized cancer therapeutic vehicles: Sequential delivery of doxorubicin and Bcl-2 siRNA. Sci Rep. 2014; 4: 6878. doi: 10.1038/srep06878.

38. Cosco D, Federico C, Maiuolo J, Bulotta S, Molinaro R, Paolino D, et al. Physicochemical features and transfection properties of chitosan/ poloxamer 188/poly(D,L-lactide-co-glycolide) nanoplexes. Int J Nanomedicine. 2014; 9: 2359-72. doi: 10.2147/IJN.S58362. eCollection 2014.

39. Nielsen EJ, Nielsen JM, Becker D, Karlas A, Prakash H, Glud SZ, et al. Pulmonary gene silencing in transgenic EGFP mice using aerosolised chitosan/siRNA nanoparticles. Pharm Res. 2010; 27(12):2520-2527. doi: 10.1007/s11095-010-0255-y.

40. Shukla SK, Mishra AK, Arotiba OA, Mamba B. Chitosan-based nanomaterials: A state-of-the-art review. Int J Biol Macromol. 2013; 59: 46-58. doi: 10.1016/j.ijbiomac.2013.04.043.

41. Zou Y, Xiang C, Sun LX, Xu F. Glucose biosensor based on electrodeposition of platinum nanoparticles onto carbon nanotubes and immobilizing enzyme with chitosan-SiO_2 sol–gel. Biosens Bioelectron. 2008; 23(7): 1010-6.

42. Li J, Wang J, Bachas LG. Biosensor for Asparagine Using a Thermostable Recombinant Asparaginase from *Archaeoglobus fulgidus.* Anal Chem. 2002;74(14):3336-41.

43. Alaejos MS, García Montelongo FJ. Application of amperometric biosensors to the determination of vitamins and α-amino acids. Chem Rev. 2004; 104(7): 3239–3266.

44. Ohashi E, Karube. Development of an enzyme sensor using multienzyme system immobilized in beta-chitin membrane. I Fish Sci. 1995; 61(5): 856-859.

45. Reiss M, Heibges A, Metzger J, Hartmeier W. Determination of BOD-values of starch-containing waste water by a BOD-biosensor. Biosens Bioelectron. 1998; 13(10):1083-1090.

46. Ohashi E, Karube. Development of a thin membrane glucose sensor using beta-type crystalline chitin for implantable biosensor. J Biotechnol. 1995; 40(1):13-9.

47. Wang S, Tana Y, Zhaoa D, Liu G. Amperometric tyrosinase biosensor based on Fe3O4 nanoparticles–chitosan nanocomposite. Biosens Bioelectron. 2009; 23(12): 1781–1787. doi: 10.1016/j.bios.2008.02.014.

48. Kang XH, Wang J, Wu H, Aksay AI, Liu J, et al. (2010) Graphene based electrochemical sensors and biosensors: a review. Electroanalysis 22:1027 – 1036.

49. Wu H, Wang J, Kang X, Wang C, Wang D, Liu J, et al. Glucose biosensor based on immobilization of glucose oxidase in platinum nanoparticles/ graphene/chitosan nanocomposite film. Talanta. 2009; 80(1): 403-6. doi: 10.1016/j.talanta.2009.06.054.

50. Liu Y, Qu X, Guo H, Chen H, Liu B, Dong S. Facile preparation of amperometric laccase biosensor with multifunction based on the matrix of carbon nanotubes–chitosan composite. Biosens Bioelectron. 2006; 21(12): 2195-201.

51. Tiwari A, Shukla SK. Chitosan-g-polyaniline: a creatine amidinohydrolase immobilization matrix for creatine biosensor. Express Polym Lett. 2009; 3: 553-559. doi: 10.3144/expresspolymlett.2009.69.

52. Atkinson AJ, Colburn WA, De Gruttola VG. Biomarkers Definitions Working Group. Biomarkers and surrogate end points: preferred definitions and conceptual framework. Clin Pharmacol Ther. 2001; 69(3):89-95.

53. Karley D, Gupta D, Tiwari A. Biomarkers: The Future of Medical Science to Detect Cancer. J Mol Biomark Diagn. 2011; 2:5-11. doi: 10.4172/2155-9929.1000118.

54. Strimbu K, Tavel JA. What are biomarkers? Curr Opin HIV AIDS. 2010; 5(6): 463–466. doi: 10.1097/COH.0b013e32833ed177.

55. Atkinson AJ, Colburn WA, DeGruttola VG. Biomarkers and surrogate endpoints: preferred definitions and conceptual framework. Clin Pharmaco Ther. 2001; 69(3):89–95.

56. Kumar M , Sarin SK. Biomarkers of diseases in medicine. Current trends in Science. 2009; 403-416.

57. Domnanich P, Pena DP, Preininger C. Xanthan/chitosan gold chip for metal enhanced protein biomarker detection. Biosens Bioelectron. 2011; 26(5): 2559-65. doi: 10.1016/j.bios.2010.11.006.

58. Du D, Zou Z, Shin Y, Wang J, Wu H, Engelhard MH, et al. Sensitive immunosensor for cancer biomarker based on dual signal amplification strategy of graphene sheets and multienzyme functionalized carbon nanospheres. Anal Chem. 2010; 82(7): 2989–2995. doi: 10.1021/ ac100036p.

59. Chen X, Ma Z. Multiplexed electrochemical immunoassay of biomarkers using Chitosan nanocomposites. Biosens Bioelectron. 2014; 55: 343-9. doi: 10.1016/j.bios.2013.12.037.

60. Amidi M, Romeijn SG, Borchard G, Junginger HE, Hennink WE, Jiskoot W. Preparation and characterization of protein-loaded N-trimethyl chitosan nanoparticles as nasal delivery system. J Control Release. 2006; 111(1-2):107–116.

61. Kim JH, Kim YS, Park K, Lee S, Nam HY, Min KH, et al. Antitumor efficacy of cisplatin-loaded glycol chitosan nanoparticles in tumor-bearing mice. J Control Release. 2008; 127(1): 41-49. doi: 10.1016/j. jconrel.2007.12.014.

62. Yoo HS, Lee JE, Chung H, Kwon IC, Jeong SY. Self-assembled nanoparticles containing hydrophobically modified glycol chitosan for gene delivery. J Control Release. 2005; 103(1): 235–243.

63. Qu G, Yao Z, Zhang C, Wu X, Ping Q. PEG conjugated N-octyl-O-sulfate chitosan micelles for delivery of paclitaxel: in vitro characterization and in vivo evaluation. Eur J Pharm Sci. 2009; 37(2): 98-105. doi: 10.1016/j.ejps.2009.01.004.

64. Varshosaz J, Dehkordi AJ, Golafshan S. Colon-specific delivery of mesalazine chitosan microspheres. J Microencapsul. 2006; 23(3): 329–339.

65. Suzuki K, Susaki H, Okuno S, Sugiyama Y. Renal drug targeting using a vector "alkylglycoside". J Pharmacol Exp Ther. 1999; 288(1): 57-64.

66. Wilk S, Mizoguchi H, Orlowski M. Gamma-glutamyl dopa: a kidney-specific dopamine precursor. J Pharmacol Exp Ther. 1978; 206(1): 227–232.

67. Haas M, Kluppel AC, Wartna ES, Moolenaar F, Meijer DK, de Jong PE, et al. Drug-targeting to the kidney: renal delivery and degradation of a naproxen–lysozyme conjugate in vivo. Kidney Int. 1997; 52(6):1693–1699.

68. Janes KA, Fresneau MP, Marazuela A, Fabra A, Alonso MJ. Chitosan nanoparticles as delivery systems for doxorubicin. J Control Release. 2001; 73(2-3): 255–267.

69. Ding Y, Shen SZ, Sun H, Sun K, Liu F, Qi Y, et al. Design and construction of polymerized-chitosan coated Fe3O4 magnetic nanoparticles and its application for hydrophobic drug delivery. Mater Sci Eng C Mater Biol Appl. 2015; 48: 487-98. doi: 10.1016/j.msec.2014.12.036.

***Corresponding author:** PK Dutta, Centre for Medical Diagnostic & Research, Motilal Nehru National Institute of Technology, Allahabad 211004, U.P., India, Tel: 91-993-674-0953; Fax: 91-0532-254-5341; E-mail: pkd_437@yahoo.com, pkd@mnnit.ac.in

Received Date: March 23, 2015, **Accepted Date:** April 17, 2015, **Published Date:** April 30, 2015.

Citation: Jain T, Kumar S, Dutta PK (2015) Chitosan in the Light of Nanobiotechnology: A Mini Review. J Biomed Tech Res 1(1): 101.