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Research Article

CHITOSAN: INTRODUCTION AND ITS ROLE AS A DRUG DELIVERY VEHICLE

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A R T I C L E I N F O

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A B S T R A C T

Nowadays, nanoparticles has revolutionized the concept of drug targeting system and there are various nanoparticle available around us and from that one of them is Chitosan. Chitosan is a mucopolysacharide and it is the biproduct of exoskeletons in crustaceans. The chitosan nanoparticles is considered as a safe material due to its biocompatibility, better stability, low toxicity, simple preparation methods and it act as a very good adjuvant for the process of drug delivery and thusact as a valuablevehicle for the delivery of drugs in the present era. The present review highlights about various aspects of chitosan and how it holds promise as a suitable material for biomedical applications. The predicted aspects of chitosan's targeting area in human has been discussed here for the first time.

INTRODUCTION

The field of 'Nanomedicine' specifically relates to the development of all nano-sized tools for the diagnosis, prevention and treatment of disease. As the name indicate 'Nano' means 'very small' 'particles' means 'a tiny piece of anything are solid colloidal natural, synthetic or semi-synthetic polymers which act as a drug carriers and lies in the ranges of 10-1000 nm in diameter attached or enveloped with the drug molecule and also act as an adjuvent. Due to its biocompatibility, low toxicity it is easier to formulate techniques and offers various advantages over others polymeric carriers for nanoparticulate drug delivery. Due to the variation in targeting tissues, accessing drug release with the help of nanoparticle has become the sensation among the pharmaceutical scientist that will be applied in aquaculture as well as for the future prospective and need of human.

Today's scinerio is totally based on technology and as a result of that various branches of biology like Bioinformatics, Nanotechnology, Biotechnology, etc has been came into existence. After various discoveries it has been clear that Nanoparticle has lots of advantages like in medical field, cosmetics industries, ceramic industries, glasses, polymers, zeolithes, biomolecules, and various other field for the betterment of Environment and Human life. Impact of Nanoparticle has an important issue for the environmental aspects and visualizing the effect in fishes may be an important point for sustainable development.

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Till date various nano particle are present in the market and various new nano particle are developing day by day such as Silver, Gold, Titanium, Cerium,etc.

Titanium NP has an important property to affect fish survival in diseased condition by modulating immune responses and interfering with resistance to bacterial pathogens, manufactured TiO_2 nanoparticle has the potential to affect fish survival in a disease outbreak (*Boris Jovanovi et al ., 2015*). ZnO NPs induces genotoxicity, in real case it mediate oxidative stress and can be further linked to different pathways (*Schins and Knaapen, 2007*). ZnO NP have a capability to prove useful it as nanomedicine based antimicrobial agents at selective therapeutic dosing regimes (*Reddy et al 2007*).Ceria NPs with show various catalytic and physiochemical properties that could contribute to antioxidant or prooxidant properties (*Dowding JM et al 2013*). Au-supported CeO_2NPs may act as a potent nanomaterial for in vivo application having biocompatible and antibacterial properties (*Babu et al 2014*). Chitosan with its biocompatibility and biodegradability has various application and it is extensively applied in various aspects like gene delivery, immunoadjuvent for vaccine, chemotherapeutic delivery (*Anish Babu and Rajagopal Ramesh 2017*).

Present study will emphasise on treatment of disease by using properties of Chitosan in Nanopharmaceuticals. Chitosan act as a carrier for the various drugs discovery and development procedure which suffers from various problems like elevated cost, solubility, flexibility, viability, relation to toxicity, contrasting effect on different individual and organ etc. Several survey paper indicated that, in the USA, a new lead compound takes 10–15 years on average to reach the market, with an associated cost of approximately US$1.8 billion and an

average success rate of only 8% (*Saifur R. Khan et al., 2014*) and with the help of this type of data we came to know about the loss .To cope up from this type of problem ,the application of unique toxicogenomic has given the platforms for the production of safer and cheaper drugs and decrease research and development costs.

What is Chitosan

The term Chitosan itself describe a huge group of natural or artificial polymer having different molecular weight varies from 50kDa-2000kDa, viscosity (1% chitosan in 1% acetic acid < 2000 mPaS), degree of deacetylation (40%-98%) with positive charge and it is a biproduct of chitin.Chitin comes as a second most ubiquitous natural polysaccharide after cellulose on earth (*Dutta et al 2004*) . Chitosan is an aliphatic heterocyclic compounds and act as Chelates in many transitional metal ions andconsist of reactive amino groups and hydroxyl groups .They can be easily converted into various forms such as membranes, sponges, gels, scaffolds, microparticles, nanoparticles and nanofibers for a variety of applications like cosmetics industry, drug targeting, gene therapy, tissue engineering and wound healing.

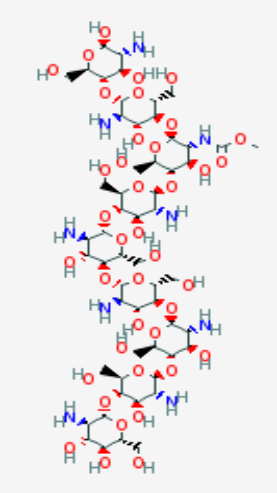
Structure of Chitosan

Chitosan is a modified natural polymer of carbohydrate and formed by the deacetylation of Chitin and closely related to cellulose.

The structure of chitosan has been retrieved from PubChem database with PubChem CID - 71853.Computer-aided properties of Chitosan (has been adopted from https://pubchem.ncbi.nlm.nih.gov/compound/71853#section=Chemical-and-Physical-Properties and http://www.hmdb.ca/metabolites/HMDB03404) are as-

Table 1 Computed Properties of Chitosan from PubChem

Property	Value
Molecular Formula	$C_{56}H_{103}N_9O_{39}$
Molecular Weight	1526.464 g/mol
Water Solubility	69.3 mg/mL
XLogP3-AA	-21.4
LogP	-2.6
LogS	-1.3
pKa (Strongest Basic)	9.32
Physiological Charge	8
Formal Charge	0
Hydrogen Acceptor Count	46
Hydrogen Donor Count	29
Polar Surface Area	808 Å^2
Rotatable Bond Count	27
Complexity	2630
Refractivity	321.21 m^3·mol^{-1}
Polarizability	144.58 Å^3
Number of Rings	9
Bioavailability	0
Heavy atom count	104
Rule of Five	Yes
Ghose Filter	Yes
Veber's Rule	Yes
Compound is Canonicalised	Yes
MDDR-like Rule	Yes



Aoccording to KEGG(http://www.genome.jp/kegg/pathway.html) its Compound ID is C00734 and from there we came to know about ;

-It mainly involve in two type of pathway-

- Amino sugar and nucleotide sugar metabolism
- Metabolic pathways

-Mainly there are 3 enzyme associated-

- chitosanase
- exo-1,4-beta-D-glucosaminidase
- chitin deacetylase

-The main reaction envolve are as-

1. Chitin amidohydrolase;
   Chitin + n H2O <=> Chitosan + n Acetate
2. Chitosan N-acetylglucosaminohydrolase;
   Chitosan + H2O <=> D-Glucosaminide + Chitosan
3. chitosan exo-1,4-beta-D-glucosaminidase;
   chitosanglucosaminohydrolase; Chitosan(n+1) + H2O <=> Chitosan

-There are 254 genes which are associated with Chitosan.

2D NMR

Spectra Property in the form of image with peak assignments-

Solvent:	Water
Sample Assessment:	Poor
Spectrum Assessment:	Poor
Instrument Type:	Bruker
Nucleus X:	1H
Sample Temperature:	25.0 C
Chemical Shift:	DSS

Chitosan as a Nanoparticle

Chitosan nanoparticle is emerging as a new drug carrier because of its properties like biocompatibility , improvement of intracellular penetration and easy to modify.

Charecteristics of Chitosan

Solubility

Chitosan is soluble in water but due to its low water solubility it has a major limitation for the gene and drug targeting applications and there solubility depends on deacetylation degree (DD) ,ionic strength, molecular weight, structure and pH.The low solubility of chitosan in neutral and alkaline medium limits its application for various targeting system.

Flexibility

The linear structure of chitosan molecule reflect chain flexibility, its conformation is highly dependent on the ionic strength of the solubilizing vehicle. These properties are considered as an essential property for mucoadhesion.The importance of the mucoadhesiveproperties of chitosan as well as the importance of the absorption enhancing properties has been demonstrated earlier.

Toxicity

Chitosan is famous for its various properties and from that one of them is low toxicity which distinguish it from other nanoparticle and due to this property it can be easily

encorporate with different biological components and also with drugs for its paramedical use.

Derivatives of Chitosan

Chitosan's structure consist of OH and NH_2 groups that can give rise to hydrogen bonding which later on result in the production of various derivatives of chitosan and from that some of the very usefull chitosan derivatives has been reported and they are:- *N*-phthaloylation of Chitosan**,** Dendronized Chitosan-sialic Acid Hybrid **,** Methylthiocarbamoyl and PhenylthiocarbamoylChitosans **,** Lactic/glycolic Acid-chitosan Hydrogels **,** CdS Quantum dots (QDs) Chitosan Biocomposite**,** Chitosan-gadopentetic Acid Complex Nanoparticles for Cancer Therapy **,** Nanocomposite from Chitosan , etc.

Carboxymethylated chitosans (CMCs) are most commonly derived derivative of Chitosan. By exploring amino or hydroxyl groups we can extends the water solubility of chitosan to basic pH values and provides the polymer with amphotericcharacteristics. N-CMC is usually prepared using glyoxylic acid while O-CMC is prepared by using monochloroacetic acid.CMCs have been studied for their applicability in biomedical use, tissue engineering (hydrogels, scaffolds and nerve regeneration), pharmaceutical (drug delivery) and cosmetic fields.

Trimethylated chitosans (TMCs) are water soluble with pH that lies in the range of 1.0–9.0 (*Kotze etal 1997*)and has been shown to maintain the absorption enhancing properties of chitosan both in vitro and in vivo(*Snymanetal2000*)even though large decreases of molecular weight duringthe derivatization reactions have been observed under allconditions tested (*Rinaudo et al 2006*) TMC has been investigated as amucosal absorption enhancer.

PEGylated chitosans are another derivative of chitosan which is well studied and explored. PEG is nontoxic and with additional features PEG and Chitosan complex become more safer and stable , as a result of that it has advantage of being water soluble and it lies in the pH range of 1.0 to 11.0.PEGylated chitosan derivatives has potential for the delivery of drugs, genes and siRNA.PEGylated particles showed comparatively higher uptake of drug by brain and spleen than conventional non-PEGylated nanoparticles (*Calvo, et al2001*).The grafting is more often carried out on the NH_2 group with different approaches available. Various reports have been published related to the water solubility and bioactivity of PEGylated chitosans and there is evidence that shows that PEGylated chitosan not only enhances water solubility and biocompatibility of chitosan, but also providesfurther improved biological functionality to improve the drug bioavailability in vivo.

Method of Synthesis of Chitosan

According to *Dutta et al 2004* there are major following four stepswhich are needed for the production of Chitosan from the residue of crustacean shells on the basis of which we can arranged them in thesequential order of the process which:-

(i) Deproteinization,
(ii) Demineralization
(iii) Decolouration, and
(iv) Deacetylation. In general they are describe as-

Crustacean shells → Size reduction → Protein separation → (NaOH) → Washing Demineralization(HCl) → Washing and Dewatering → Decolouration → Chitin → Deacetylation (NaOH) → Washing and Dewatering → Chitosan

Application of Chitosan

It is biocompatible to normal body constituents, safe, less toxic and binds to mammalian and microbial cells very frecuently, it has regenerative effect on connective gum tissue with additional properties like Immuno adjuvant, dipressent, antimicrobial,etc. There are multifarious applications of chitosan like Water Engineering, Paper Industry, Textile Industry, Food Processing, Cosmetics, Chromatographic Seperations, Photography, Agriculture, Chitosan Gel for LED, Wound Healing/Wound Dressing, Burn Treatment, Opthalmology, Artificial Skin, et .

Chitosan in Drug Delivery and its impact

Despite of the numerous applications of chitosanwhich has beenmentioned above, they are still utilized in the pharmaceutical field and play a vital role in Drug Targeting Systems. Due to the less toxicity of chitosan it does not cause any biological hazard and are inexpensive, these polymers might be suitable for use in the preparation of dosage forms of commercial drugs and they are very good vehicle for drug targeting system and there are various ways according to which they are delivered and some of them has been described in the table which is given below-

Role of Chitosan in Research area in Small teleost

Dietry intake of Chitosan enhance lipid metabolism, immune competence and protect from pathogen invasion in case of teleost (i.e; gibel carp). Along with that it also result in the increased number ofof intestine microbiota in fishes and that may be beneficial to fish immune responses(*Y. Chen et al 2014*).

Aquaculture is very much susceptible to viral diseases and for the improvement of aquaculture new way of drug delivery route has been created i.e; Chitosan encapsulating DNA vaccine (CP-pNNV) were used to reduce the mortality rate of European sea bass (*Dicentrarchuslabrax*) affected due to the exposure of nodavirus (NNV) by neutralizing specific antibody (Ig M) .Vaccine will up-regulate the expression of gene associated with cell-mediatedcytotoxicity (CMC; *tcrb* and *cd8a*) and interferon pathway (IFN; *ifn*, *mx* and *ifng*) in the posterior gut but also inhibit the production of specific antibody as a result of that after 90 days of exposure mortality rate gets lower upto 45% (Yulema Valero et al 2016).With the advancement of these we can improve the anti-NNV vaccine and to understand the related mechanisms in other cases also which is elaborated in the figure mentioned.

S.No.	Route of Administration	Special Feature of the study
1	Parentral Drug Delivery	The susceptibility of chitosan to lysozyme makes itbiodegradable and act as an ideal drug vehicle (*Nordtveit et al 1994*). Low solubility of Chitosan limits its use as absorption enhancer innasal or preoral delivery systems.To overcome from this type of problem, a number of cationic or anionic chitosan derivatives have been synthesized and tested (*Thanou et al 2010*).
2	Per-oral and Nasal or Mucosal Drug DeliveryAdministration	
3	Non-viral Gene Delivery	

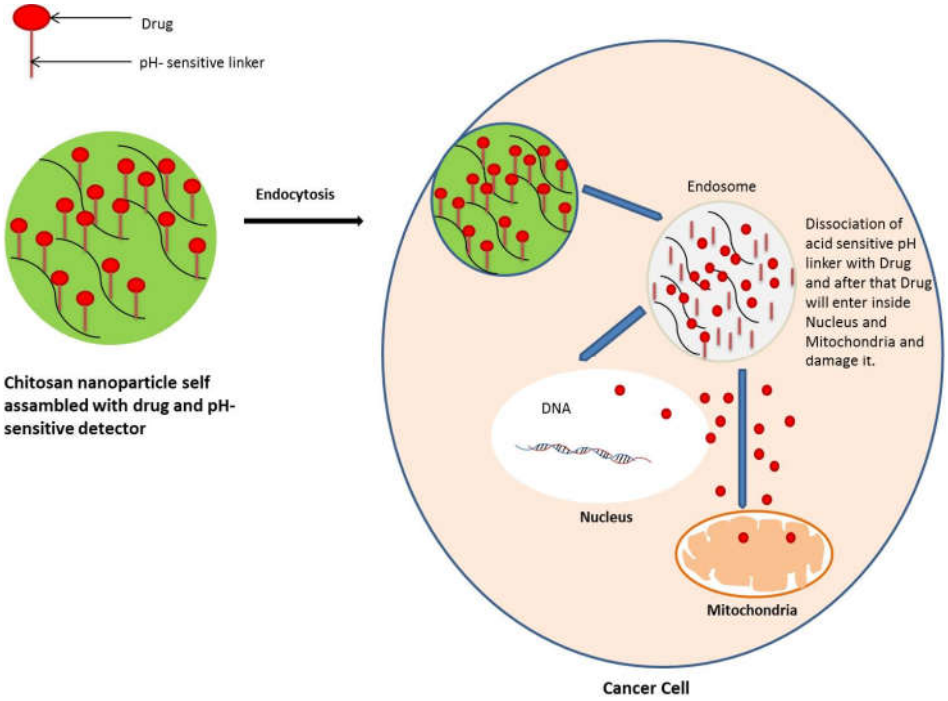


Fig.4 Acid sensitive drug delivery with the help ofchitosan nanoparticles. Chitosan has been linked to drug molecules with a pH-sensitive linker (*Anish et al 2017*).

Due to high binding capacity of Chitosan and its loading efficiency, it has a capacity to form complex of chitosan–TPP nanoparticles with entrapped siRNA .Chitosan–TPP nanoparticles show much potential as viable vector candidates for safer and cost-effective siRNA delivery. The chitosan nanoparticles have also been used as non-viral vectors for gene delivery or as delivery carriers for protein molecules.

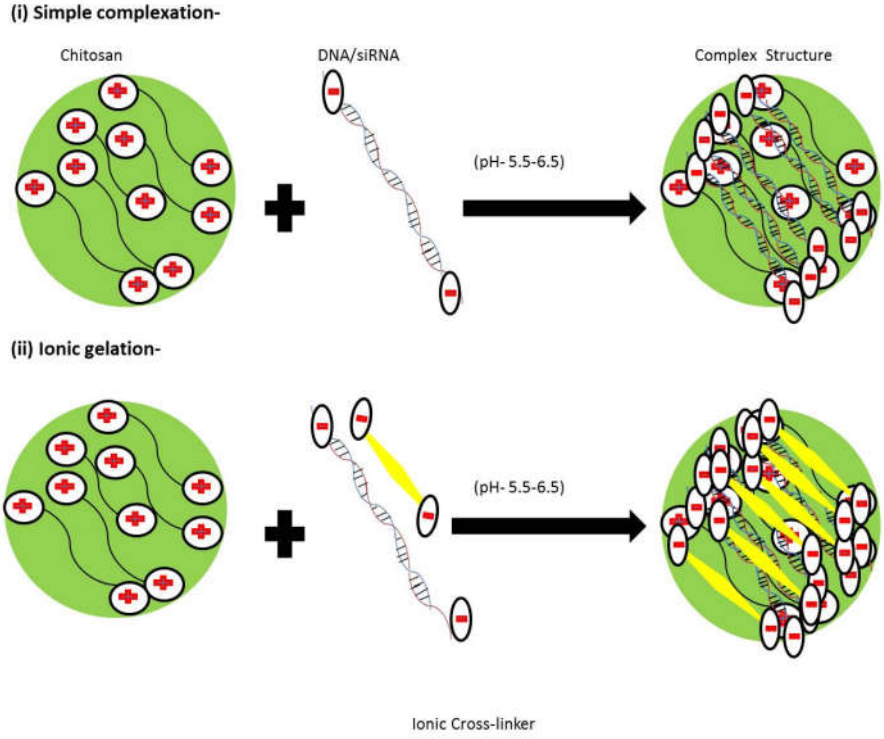


Fig 5 Common way of preparation methods of chitosan nanocarrier for DNA/siRNA delivery. (i) simple complexation; (ii) ionic gelation.(*Anish et al. 2017*)

First evidence for a successful delivery of nasal immunization against Bordetella pertussis in mice combining different antigens with chitosanwas given by *Jabbal-Gill et al 1998*. Various chitosan-based carriers have been designed and that has been evaluated for nasal delivery of antigens showing valid levels of both systemic and local immune response. Chitosan is also known for its humoral and cellular immune responses and enhance the immune-stimulatory activity of cancer vaccines.

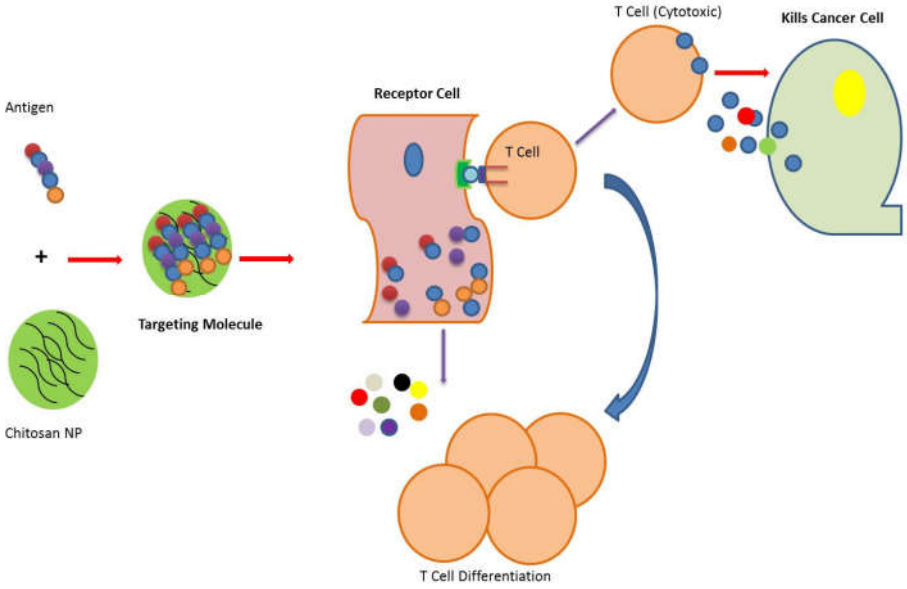
4	Vaccine Delivery	

Fig.6Role of Chitosan in case of Vaccine Delivery and its role as a vehicle(*Anish et al. 2017*).

5	Ocular Drug Delivery	Chitosan colloidal suspensions *in vivo* studies showed a significant increase in ocular drug bioavailability (*Calvoet al 1997*).It acts as agood ocular tolerance as bioadhesion- and permeability-enhancing properties, and also interesting physico-chemical characteristics.Thus it acts as an unique material for designing of ocular drug delivery vehicles.
6	Gene Delivery	Chitosan has comparable efficacy with less toxicity of other synthetic vectors and can,therefore, be an effective gene-delivery vehicle *in vivo* (*Valerie et al 1998*).
7	Topical delivery	Chitosan has good bioadhesiveproperty ,ability to sustain the release of theactive constituents and thus used intopical delivery systems. Microparticles composed of Chitosan and designed aspowders for topicalwound-healing properties (*Conti et al 2000*).
8	Brain Targeting	Chitosan-polysorbate complex is used for brain targeting of the drugs. Chitosan is used to enhance the efficiency for brain targetingby the direct nose to brain pathway especially for drugs for treatment of central nervous system (CNS) disorders. Furtherit also combined with the active drug for targeting to the olfactory region with controlled release due to its bioadhesiveproperty for maintaining the drug on the absorption site.Besides this, the estradiol chitosan have higher estradiol concentration in CSF at each sampling time following intranasal delivery. This proves a better quality ofchitosan as a suitable formulation for estradiol delivery to CNS. It has also been reported that both chitosan structural features and molecular weight play a key role in promoting the intranasal absorption of 2,3,5,6-tetramethylpyrazine phosphate (TMPP)(*Mei D. et al 2008*).
9	Stability Improvement	The chitosan–TPP nanogels containing drugs, genes, or proteins is used as drug delivery systems successfully in human fluids.When the particles are loaded with macromolecules or drugs,the gel network effectively make particles much more stable due to the interaction between them. The different properties with different conditions maymodify foods to novel textures, novel optical properties, or increased stabilities(*Kalpana et al 2010*).Chitosan–caseinate complexes is also used for the improvement of stability.
10	Controlled Drug Delivery	Chitosan are involved inchemical crosslinking, ionic crosslinking and ionic complexation and due to that it forms colloidal particles and entraps bioactive molecules and alsoit has high affinity for cell membranes, and thus it is used as a coating agent for liposome formulations andact asvehicle for controlled drug delivery system (*Kalpana et al 2010*).
11	Vaginal drug delivery	Chitosan-based vaginal tablets containing metronidazole are being used by direct compressing the polymer,loosely cross-linked with glutaraldehyde, together with sodium alginate with or without microcrystalline cellulose (*El-Kamel et al 2002*).
12	Intravesical drug delivery	Mucoadhesive properties of chitosanplay a vital role on the intravesical mucosa in order to prolong the residence time of instilled drugs in urinary bladders. It was shown that thiolated chitosan might be a useful tool for local intravesical drug delivery,which act as an adjuvant as it increases the residence time of the drug and enables sustainabledelivery for an extended period of time (*Barthelmes et al 2011*).
13	Tissue Engineering	Chitosan-thioglycolic acid (chitosan-TGA) complexis a promising candidate as scaffolding substance in tissue engineering (Kast *et al 2003*).This is used for healing purpose and also for various other experimental needs.
14	Insulin Delivery	Chitosan - dextran sulphate and chitosan - Alg nanoparticles have been employed as a promising insulin and other polypeptides' carriers as itenhances the systemic absorption of insulin following nasal instillment and the insulin-loaded chitosan is alsousedas an effective complex to reduce the blood glucose level in case of diabetic rat model.The chitosan improve the absorption enhancing effect in an aqueous solution as compare to powder form . The amount and molecular weight of chitosan did not have a significant effect on the insulin response(*Kalpana et al 2010*).Thus it is beneficial for the insulin delivery purpose.

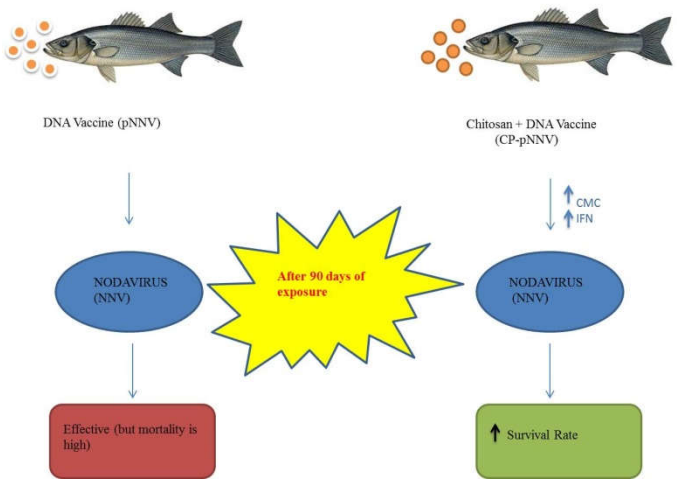
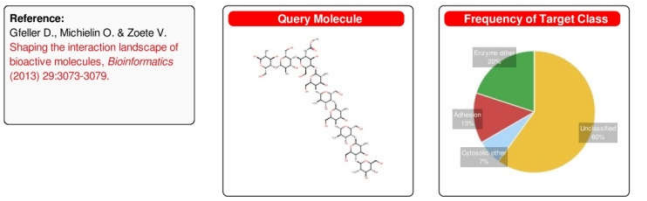


Fig.7 Experimentl layout of the treatment

In silico prediction of target site of Chitosan in Human

Chemical Structure of Chitosan was extracted from PubChem CID 71853 and that was used for predicting target site in Human by using online server i.e.; Swiss Target Prediction and as a result of that we came on the conclusion that most prominent class for Chitosan is Enzymes, Adhesion, Cytosolic and rest are unclassified respectively.

SwissTargetPrediction report:



Target	Uniprot ID	Gene code	ChEMBL ID	Probability	# sim. cmpds (3D / 2D)	Target Class
Galectin-8	O00214	LGALS8	CHEMBL5475		0 / 2	Unclassified
Galectin-3	P17931	LGALS3	CHEMBL4531		0 / 7	Cytosolic other
Galectin-4	P56470	LGALS4	CHEMBL1671608		0 / 2	Unclassified
P-selectin	P16109	SELP	CHEMBL5378		0 / 18	Adhesion
E-selectin *(by homology)*	P16581	SELE	CHEMBL3890		0 / 18	Adhesion
Beta-galactosidase	P16278	GLB1	CHEMBL2522		0 / 1	Enzyme
Beta-galactosidase-1-like protein *(by homology)*	Q6UWU2	GLB1L			0 / 1	Enzyme
Galectin-7	P47929	LGALS7	CHEMBL5008		0 / 1	Unclassified
Galectin-9 *(by homology)*	O00182	LGALS9	CHEMBL5474		0 / 1	Unclassified
Galectin-9B *(by homology)*	Q3B8N2	LGALS9B			0 / 1	Unclassified
Galectin-9C *(by homology)*	Q6DKI2	LGALS9C			0 / 1	Unclassified
Tyrosyl-DNA phosphodiesterase 1	Q9NUW8	TDP1	CHEMBL1075138		0 / 1	Enzyme
Myelin-associated glycoprotein	P20916	MAG	CHEMBL5807		0 / 23	Unclassified
Muscleblind-like protein 1	Q9NR56	MBNL1	CHEMBL1293317		0 / 4	Unclassified
Muscleblind-like protein 2 *(by homology)*	Q5VZF2	MBNL2			0 / 4	Unclassified

Fig 8 Analysed Report obtained by using online server i.e; SwissTargetPrediction

CONCLUSION

Nanoparticulate drug delivery systems is very reliable and promising strategy for the biopharmaceutical industry. They have advantages over conventional drug delivery systems. They can increase the bioavailability, solubility and permeability of many potent drugs which are otherwise difficult to deliver orally. This type of drug delivery systems will also reduce the amount of drug dosage and will result in the increase in patient compliance. In near future this type of drug delivery systems can be used for changing many biological drugs which have poor aqueous solubility, less permeability and less bioavailability. Nanoparticles can minimize some of these drugs unique properties by safeguarding stability by preserving their structure. In addition, nanoparticles provide ingenious treatment by enabling targeted delivery and controlled release.

The structural analysis and effects of Chitosan in the field of medicine and other related areas has been reviewed in this paper. As a result ofrecent advancementin studies, a bigger compassion of drug targeting and developmental aspects will appear in the near future .In this review, an attempt has also been made to enhance the knowledge for chitosan by visualising the structure and describing the various important aspectsincludingcharecterisation, analysis, processing, properties and applications. In view, this study will attract the attention of various fields like industrialists, academicians, and mainly pharmaceutical industries.

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References

1. A. Babu and R. Ramesh.Multifaceted Applications of Chitosan in Cancer Drug Delivery and Therapy.*Marine Drugs*2017;15(96):1-19.
2. A. E. Kamel, M. Sokar, V. Naggar and S. A. Gamal.Chitosan and sodium alginatebasedbioadhesive vaginal tablets. *AAPS J*. 2002;4: 224–230.
3. A.V. Pogozheva, E.K. Baigarin, S.A. Derbeneva S, E.A. Varsanovich and M.A. Miagkova.The study of influence of chitosan on clinical, metabolic and immune parameters in patients with cardiovascular diseases. *VoprPitan*. 2005;74(4):27-30.
4. B. Conti, P. Giunchedi, I. Genta and U. Conte.The preparation and in vivo evaluation of the wound-healing properties of chitosan microspheres. *STP Pharma. Sci*. 2000; 10: 101–104.
5. B. Z. Markiewicz, M. Krotkiewski, M. O. Glinianowiczand A. Zurakowski.Effect of chitosan in complex management of obesity. *Pol MerkurLekarski* 2002;13(74):129-32.
6. C.A. Stone, H.Wright, T. Clarke, R. Powell and V.S. Devaraj.Healing at skin graft donor sites dressed with chitosan. *Br J PlastSurg* 2000;53(7):601-6.
7. C. E. Kast, W. Frick, U. Losert and A. B. Schnurch. Chitosanthioglycolic acid conjugate: a new scaffold material for tissue engineering. *Int J Pharmaceutics* 2003; 256 : 183.
8. C.M. Springate, J.K. Jackson, M.E. Gleaveand H.M. Burt. Efficacy of an intratumoral controlled release formulation of clusterin antisense oligonucleotide complexed with chitosan containing paclitaxel or docetaxel in prostate cancer xenograft models. *Cancer ChemotherPharmacol* 2005;56(3):239-47.
9. C.W. Lin and J.C. Lin.Characterization and blood coagulation evaluation of the water-soluble chitooligosaccharides prepared by a facile fractionation method. *Biomacromolecules*.2003;4(6):1691-7.
10. D.Mei, S. Mao,W. Sun ,Y. Wang and T. Kissel.Effect of chitosan structure properties and molecular weight on the intranasal absorption of tetramethylpyrazine phosphate in rats . *European Journal of Pharmaceutics and Biopharmaceutics*2008;70: 874—881.

11. F. Croisierand C. JeromeChitosan-based biomaterials for tissue engineering. *European Polymer Journal* 2013;49(4): 780-792.
12. G.I. Howling, P.W. Dettmar, P.A. Goddard, F.C. Hampson, M. Dornishand E.J. WoodThe effect of chitin and chitosan on the proliferation of human skin fibroblasts and keratinocytes in vitro. *Biomaterials* 2001;22(22):2959-66.
13. G. Saintigny, M. Bonnard,O. Damour and C.Collombel. Reconstruction of epidermis on a chitosan cross-linked collagen-GAG lattice: effect of fibroblasts. *ActaDermVenereol.*1993;73(3):175-80.
14. Lisbeth Illum.Chitosan and its use in Pharmaceutical Excipient.*Pharmaceutical Research*1998;15:9
15. I. Jabbal-Gill, A.N. Fisher, R. Rappuoli, S.S. Davis and L. Illum.Stimulation of mucosal and systemic antibody responses against Bordetella pertussis filamentous haemagglutinin and recombinant pertussis toxin after nasal administration with chitosan in mice.*Vaccine* 1998;16:2039–2046.
16. I.M. van der Lubben, J.C. Verhoef, G. Borchardand H.E. Junginger.Chitosan for mucosal vaccination . *Adv Drug Deliv Rev*2001;52(2):139-44.
17. J. Barthelmes, G. Perera, J. Hombach, S. DünnhauptandA. B. Schnürch.Development of a mucoadhesivenanoparticulate drug delivery system for a targeted drug release in the bladder. *Int. J. Pharm.*2011;416:339–345.
18. J.X. Guo, Q.N. Ping, J.Dong, Z.R. Li and C.J. Li.Mechanisms of action of transportation of liposomes and chitosan-coated liposomes containing leuprolide across intestine and Caco-2 cell, *Yao XueXueBao.*2005;40(1):65-70.
19. K. Nagpal, S. K. Singh, and D. N. Mishra .Chitosan Nanoparticles: A Promising System in Novel Drug Delivery. *Chem. Pharm. Bull.* 2010;58(11):1423-1430.
20. M.Gingras, I. Paradisand F.Berthod. Nerve regeneration in a collagen-chitosan tissue-engineered skin transplanted on nude mice. Biomaterials 2003;24(9):1653-61.
21. M.Lekka, P. Laidler , J. Ignacak , M. Labedz , J. Lekki, H.Struszczyk, Z. StachuraandHrynkiewiczAZ .The effect of chitosan on stiffness and glycolytic activity of human bladder cells. *Biochim Biophys Acta*.2001;1540(2):127-36.
22. M.R. Cortes, J.P. Sandoval, J. B. Pineda, E.E.C.Martinez, U.A.G. Pinedo UA and E.A. RodriguezRegeneration of the axotomised sciatic nerve in dogs using the tubulisation technique with Chitosan biomaterial preloaded with progesterone .*Rev Neurol.*2003;36(12):1137-41.
23. Nordtveit, R.J., Varum, K.M. and Smidsrod.O. .Degradation of fully water-soluble, partially *N*-acetylated chitosans with lysozyme.*Carbohydrate Polymers*1994; 23(4):253–260.
24. N.Majeti and V. R. Kumar.A review of chitin and chitosan applications.*Reactive and Functional Polymers*2000;46(1): 1-27.
25. P. Calvo, J.L. Vila-Jato, and M.J. Alonso. Evaluation of cationic polymer-coated nanocapsules as ocular drug carriers. Int. *J. Pharm.* 1997;153: 41–50.
26. P. K. Dutta, J.Dutta and V. S. Tripathi.Chitin and chitosan: Chemistry, properties and applications. *Journal of Scientific & Industrial Research* 2004;63:20-31.
27. S. R. Khan, A. Baghdasarian, R. P. Fahlman, K. Michail and A. G. Siraki.Current status and future prospects of toxicogenomics in drug discovery. *Drug Discovery Today*2014;19:562-578.
28. T.Kean and M.ThanouBiodegradation, biodistribution and toxicity of chitosan. *Advanced Drug Delivery Reviews*2010;62(1):3-11.
29. T. Suzuki, Y. Mizushima,T. Umedaand R.Ohashi. Further biocompatibility testing of silica-chitosan complex membrane in the production of tissue plasminogen activator by epithelial and fibroblast cells. *J BiosciBioeng1999;88(2):194-9.*
30. V. Dodane and V. D. Vilivalam. Pharmaceutical applications of chitosan .*Research Focus*1998;1: 246-253.
31. V. Rana, K. Babita, D. Goyal and A.Tiwary.Sodium citrate cross-linked chitosan films: optimization as substitute for human/rat/rabbit epidermal sheets. *J Pharm Pharm Sci.*2004;8(1):10-7.
32. L.Casettari, D.Vllasaliu, E.Castagnino, S.Stolnik, S.Howdle and L.Illum.PEGylated chitosan derivatives: Synthesis, characterizations and pharmaceutical applications. *Progress in Polymer Science*2012;37:659–685.
33. P. Calvo, *et al.* PEGyl ated polycyanoacrylate nanoparticles as vector for drug delivery in prion diseases. *J. Neurosci. Methods*2001;111 (2):151–155.
34. Kotze AR, Lue_en HL, de Leeuw BJ, de Boer BG, Verhoef JC, JungingerHE. N-Trimethyl chitosan chloride as a potential absorption enhancer across mucosal surfaces: in vitro evaluation in intestinal epithelial cells (Caco-2). *Pharm Res*1997;14:1197–202.
35. Snyman D, Hamman JH, Kotze JS, Rollings JE, Kotze AF.The relationship between the absolute molecular weight and the degree of quaternization of N-trimethyl chitosan chloride.*CarbohydrPolym*2002;50:145–50.
36. Rinaudo M..Chitin and chitosan—properties and applications.*ProgPolymSci* 2006;31:603–32.
37. Y. Chen, X. Zhu, Y. Yang, D. Han , J. Jin ,S. Xie.Effect of dietary chitosan on growth performance, haematology, immune response, intestine morphology, intestine microbiota and disease resistance in gibel carp (Carassiusauratusgibelio). *Aquaculture Nutrition* 2014;20:532-546.
38. Yulema Valero, ElhamAwad, Francesco Buonocore, Marta Arizcun, M. Angeles Esteban, Jos_eMeseguer , Elena Chaves-Pozo, Alberto Cuesta.An oral chitosan DNA vaccine against nodavirus improves transcription of cell-mediated cytotoxicity and interferon genes in the European sea bass juveniles gut and survival upon infection. *Developmental and Comparative Immunology* 2016;65: 64-72.
39. Boris Jovanovi, Elizabeth M. Whitley, Kayoko Kimura, Adam Crumpton, DusanPali. Titanium dioxide nanoparticles enhance mortality of fish exposed to bacterial pathogens, *Environmental Pollution*2015;203 :153-164.
40. Schins, R.P.F., Knaapen, A.M..Genotoxicity of poorly soluble particles. *Inhal.Toxicol*.2007; 19, 189–198.
41. K. M. Reddy, Kevin Feris, Jason Bell, Denise G. Wingett, Cory Hanley, Alex Punnoose. Selective

toxicity of zinc oxide nanoparticles to prokaryotic and eukaryotic systems. *Applied Physics Letters*2007;90, 213902.

42. Dowding JM, Seal S, Self WT. Cerium oxide nanoparticles accelerate the decay of peroxynitrite. *Drug DelivTransl Res*. 2013;3(4):375–379.
43. K.Suresh Babu, M Anandkumar, T Y Tsai, T H Kao, B Stephen Inbaraj, B.H.Chen. Cytotoxicity and antibacterial activity of gold-supported cerium oxide nanoparticles. *International Journal of Nanomedicine* 2014 ;9: 5515–5531.

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