Chapter 2

Chitosan-Derived Synthetic Ion Exchangers: Characteristics and Applications

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Additional information is available at the end of the chapter

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Abstract

Today growing science and technological needs explored various biopolymers to procure novel utilities in its modern developments. Consequently, polysaccharides embraced huge prospective and vastly caters such desired growing needs. Amid, chitin the second most ubiquitous after cellulose comprise of β-[1,4]-2-acetamido-2-deoxy-d-glucose flexible skeleton undergo alteration for requisite physico-chemical features and its highly sophisticated utility superseded counterpart cellulose. Chitosan have unique parameters namely bio-compatibility, non-toxicity, hemeostaticity, anti-microbials which offer competent solutions of many challenging problems. Thus, many products namely biomarkers, biosensors, quantum dots are fabricated via adoptable productive chitosan matrixes. Advancement in chitosan chemistry proffers unambiguous industrial utility in cosmetics, pharmaceuticals, nanobiotechnology, water purifications etc. Chitosan composites own enhanced muco-adhesivity that aids pharmacological safe and successful DNA/SiRNA/tissue releases with bioavailability at target specific carriers. ZnO, ZnS, TiO2 filled/imposed in chitosan and resultant hybrids, quantum dots, surface active microcapsules and nanoparticles are used as biosensors, bio-markers, adsorbents that proffers revolutionary medical usage. Nanointegrated chitosan own complementary strengths and possess assorted utility namely nano-electronic high-resolution devices, for in-vivo imaging, diseases diagnosis, generating new therapeutic and smart tissue engineering scaffolds. Novel modalities with innovative formulations are skillfully designed via chitosan matrix for myriad benefit in biology, chemistry, polymer, and pharmaceutics are displayed in this chapter.

Keywords: chitosan, chitin, biopolymers, biomarker, biosensor, drug delivery, water, membrane, nanotechnology, pharmaceuticals

1. Introduction

Bioactive molecules and natural polymers obtained from animals, plants, fungi and bacteria have ever fascinated the global scientists due to their survival profile for our environment and life [1]. Amid these bio-polymers, polysaccharides namely cellulose, chitin and starch pertaining functions in genetics as cell wall architecture, in biology as energy storage, in material science for bio-composite designing/discovery and for physic-chemical adsorption in chemistry respectively. Today S&T indispensably practices biopolymers for inclusive development in perspective of connectivity, communicative transactions and economic progression in medical sciences besides to cope up advanced biotechnology demands. Twenty-first century scientific innovations and technological throughput ingeniously boosts myriad fields like pharmaceutics, environment and nanotechnology besides uplift our living by enabling reachable services and numerous reliable products in health care. Nevertheless, the requisite new innovative materials are being fabricated from both, chitin and chitosan matrixes due to inherent characteristics uniqueness as futuristic, multi-functional; novel, versatile and peculiar diversity which is devoid in conventional/counterparts.

Chitin is the second most abundant biopolymers after cellulose as explored for R&D besides numerous remarkable papers/patents catering futuristic demands in S&T besides utility in biochemistry, organic/polymer chemistry, pharmacology and medicines. In fact chitin polysaccharide comprise of β-[1,4]-2-acetamido-2-deoxy-ᴅ-glucose repetitive units i.e., *N*-acetylglucosamine linked via glucosidic bonds that are facile for physico-chemical adaption to yield into new bio-composites, hybrids and blends owing superior capabilities widespread over cellulose. Deacetylated chitin called chitosan can be categorized by means of purity/quality found to possess exclusive features namely bio-compatibility, bio-degradable, non-toxicity, antimicrobials and hemeostatic. Advance nano-technology exploited superior, productive and widely derived matrixes from flexible chitin/chitosan, thus signifies their chemistry in science and technology [1]. About 1500 tons/year of chitin is usually produced throughout the world. In past decades, progressive bendable chitin/chitosan makes it an ideal model matrix for desired physic-chemical and/or enzymatic alterations/modulations as advantageous in modern S&T [1, 2]. Incredibly practical impact of chitosan in modern S&T is attributed to its liberal super-active $—NH_2$/$—OH$ groups with subsequently performed diverse chemical modifications namely *N*-acylation/alkylation, *N*-quaternization and C-6 carboxylation. Literature reported that such substantial adaptation onto chitin/chitosan matrix persuades inclusive cationic charge via amine protonation to ammonium ion/NH_3^+ further improve its pH dependency (acid to alkaline) and resultant solubility [2]. Thus certain chitosan based materials owing wide putative applications are portrayed as below.

Chitosan matrixes extensively provides generous opportunities in biotechnology, theranostic and pharmaceuticals for drug/gene release, tissue engineering and wound healing respectively due to exceptional features like biodegradability, biocompatibility, antimicrobial profile, besides low toxicity, and immunogenicity [2–8]. This mini review signifies chitosan for advanced formulations in nano-science/biotechnology with reference to quantum dots, and nanoparticles, carbon dots, biosensors and biomarkers.

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2. Advances in chitosan chemistry: unambiguous myriad applications in modern S&T

Chitosan own adaptable promising applications de-acetylated chitin derivative, despite its limited mechanical strength and solubility. The proactive functionalities of native chitosan like primary amino and hydroxy groups are facile to undergo many possible physical/chemical modifications/alternations through grafting and ionic interactions so as to yield assorted derivatives which can offer specific and requisite commercially utilities. The following sections comprise contemporary research in chitin/chitosan matrix towards applications in numerous industrial and clinical fields.

2.1. Chitin/chitosan processing

Chitin/chitosan are commercial natural resources, as well 150,000 metric tons as a sea-food industry wastes generate via processing from crab, shrimp, shell-fish, krill, clam, oyster and squid processing beside extracted from certain fungi. Compared to synthetics/counterparts, chitin/chitosan own exclusive nitrogen content and high concentrations of proteins along with calcium carbonate as procured via physic-chemical/biological extractions/treatments. Further chitin undergoes de-acetylation by means of alkali refluxing yields 85% product called chitosan. Chronological step-wise treatments like deproteinization, demineralization, decolouration and de-acetylations performed to produce chitosan from sea-food shown below:

Crustacean shell-size reduction—protein separation by NaOH/alkali reflux—washing—demineralization by HCl/mineral acid—dewatering—chitin decolouration—deacetylation by NaOH—washing/dewatering yield 85% chitosan.

2.2. Solubility of chitin/chitosan

Chitin/chitosan owes anhydro-glucoside link akin to cellulose, yet characteristics are vastly different as being strong hydrophobic insoluble in water/aqueous state. Many organic solvents, too cannot dissolve chitin/chitosan instead solvent mixtures are employed for its dissolution namely hexa-fluoroisopropanol, hexa-fluoroacetone, chloro-alcohol, 5% LiCl added dimethylacetamide, 30% aqueous acetic acid, aqueous *N*-methyl morpholine-*N*-oxide and aqueous mineral acids. Chitin and chitosan being highly basic (pH > 7) are soluble in various aqueous-organic/mineral-acid mixtures to form invariably poly-electrolytic jelly that's easily transformed into myriad compositions including salt, film, hybrid, chelate/complex and gels [2].

2.3. Chitin/chitosan salient treatments

Concentrated acid hydrolysis and drastic treatment onto chitin/chitosan produces serviceable β-ᴅ-glucosamine: amino sugar functional unit. Chitin/chitosan, based on deacetylation degree owns 6–8% w/v nitrogen/free —NH_2 being facile for varied chemical transformations/modifications namely *N*-acylation and Schiff-base reactions. Chitosan on treatment with keto-acids followed by sodium borohydride reduction yields proteic/non-proteic amino acid (1,3/1,6)-β-ᴅ-glucan and melanin linkage pertaining effective immuno-stimulant behaviour to boost immunity in human/animals. Chitosan undergoes many chemical reactions like forms *N*-acylation with acid anhydrides/acyl halides aldimine and ketimine with aldehyde and ketone respectively at NTP. Hydrogenation and *N*-alkylation with more bulky substituent weakens hydrogen bonding in chitosan skeleton; so *gets* swelled in water and retains film forming tendency in spite of hydrophobic alkyl chains. Further chitosan is quite versatile than chitin due to the presence of amino groups at the C-2 skeleton.

2.4. Chemical and biological properties of chitosan

Chitosan is linear polyamine skeleton owing free-active functionalities like primary amino and hydroxyl both can chelate transitional metals to form complexes. Biological chitosan is biocompatible natural polymer which is biodegradable to normal body constituents, hence safe and non-toxic to environment upon disposal. Chitosan binds to mammalian and microbial cells assertively own connective gum tissue regeneration and accelerate osteoblast formation as vital for bone regeneration, Moreover, chitosan possess board microbiological profile namely as hemostatic, fungistatic, spermicidal, antitumor, anticholesteremic besides acts as central nervous system depressant and immune adjuvant.

2.5. Chitosan derivatives

Chitin/chitosan is readily derivatized at primary amine, primary and secondary hydroxyl functionalities [3]. These derivatives own potential significance via further bi/poly-functional chemical reaction yields polymeric composites, blends, gels and industrially applied polyampholytes effective in remediation of pollution. Chitosan chelated complexes with transition metals acts as matrix for enzyme immobilizations [12]. Reactions with pure chitin have been carried out mostly in the solid state owing to the lack of solubility in ordinary solvents. Chitin/chitosan of about 50% degree of de-acetylation found to be water soluble [17] and used as feedstock for smooth modifications, through various solution phase transformation as enumerated below:

A. *N-phthaloylation of chitosan*: phthalic anhydride-DMF reacts with chitosan to yield *N*-phthaloylated chitosan which found to enhance solubility and affixed bulkiness due to breaking hydrogen of primary amine and averts hydrogen bonding to firm backbone/skeleton.

B. *Chitosan-sialic acid dendrond hybrid*: the water-solubility of chitosan matrix gets improved effectively via gallic acid and tri-ethylene glycol dendronized chitosan-sialic acid hybrid synthesis. Residual amine functionality can be further *N*-succinylated to impart great water solubility of such novel chitosan derivatives.

C. *Alkyl/aryl-thiocarbamoyl chitosan*: methyl/phenyl-thiocarbamoyl chitosan derivatives are prepared for selective metal ionic sorptions from aqueous solution/contaminated waters.

D. *Chitosan hydrogels*: chitosan hydrogels can be straight grafted by treatment with ᴅ,ʟ-lactic and/or glycolic acid owing great interfacial water-chitosan interaction due to grafting with such acids. Chitosan side chains can physically cross-linked/aggregated to yield pH-sensitive hydrogels that owe potential biomedical functions namely wound dressing/healing, gene and drug delivery.

E. *Chitosan composite base quantum dots*: nano-cadmium sulphide doped chitosan improved thermal and mechanical besides aqueous solubility in parent bio-polymeric matrix. Efficient chitosan based CdS-QD/film/composite can be easily obtained by mixing chitosan, $Cd(Ac)_2$ and CdS in 1% aqueous acetic acid solution.

F. *Chitosan based nano-particals/composites*: gadolinium neutran capture therapy (Gd-NCT) induced chitosan-gadopentetic acid nanoparticles used for cancer therapy appropriate for intra-tumoral treatment. Flexible chitosan skeleton endure facile blends with synthetic polymers via mechano-chemical routes yields novel composites/nano-particles. Thermal performance and molecular signaling of synthetic polymeric matrix/composites are exclusively dissimilar from each/both components. These blends impart strong integrated chitosan cascades owing talented compatibility under mild conditions as utilized in smart and advanced drug-gene delivery.

2.6. Biological profile of chitin/chitosan

Human body fluids enzyme, lysozyme can dissolve some bacteria via cell-wall material cleaving, also facile to assemble in chitin/chitosan matrixes and impose myriad therapeutic usages in past decade. Certain vital medical usages of such chitosan matrixes including fibroplasias inhibition resulted wound healing/dressing, as absorbable sutures and supports in tissue/cell growth or differentiating tissues. Such chitosan based sutures found to resist attack in urine, bile and pancreatic juice while hasten to enhance wound healings dressings/textures that's hardly achieved by absorbable counterparts.

2.7. Industrial utility of chitin/chitosan matrixes

Apart from this chitin/chitosan apparel industrial usages and impending functions are exploited in wastewater/water purifications especially heavy metal and organic pollutant removal via chelation with wide scope and possibility. Chitosan base derivatives impart range of pharmaceutical and cosmetic products way from water treatment to plant/food protections.

2.7.1. Cosmetics

Unlike to other polyanionic hydrocolloids, this natural amino-polysaccharide chitosan encompassed hydrocolloids are exclusively cationic that gets viscous/semi-solid upon neutralization with aqueous organic acid solutions. Such viscous/semisolid chitosan facilitates intervene common integuments like skin covers and hairs. Chitin/chitosan both are fungicidal and fungi-static and thus compatible with other highly integrated biological counterparts used in such beauty products. Chitosan-alginate (1–10 μ size) microcapsules embodied various hydrophobic materials are utilized in range of cosmetic/beauty products. Substances absorbing harmful UV light and assorted dyes get linked to amino functionality of chitosan via covalent bonding. Consequently, chitosan enclosed compositions were developed by *Sonat* Company USA that can insert anti-oxidants, anti-allergic, and anti-inflammatory agents as novel depilatory designed in many areas of cosmetics like skin care, hair care, and curling hairs besides oral care. Chitin/chitosan and human hairs can harmonize mutually owing to opposite electrical charges as chitosan is cationic and hairs are anionic. Chitosan containing solution forms clear, elastic film or foam and create emulsifying action on hairs so, boots softness, smoothness, and mechanical strength. Chitosan based compositions also forms hydro-gel in aqueous alcohol thus used in shampoo, rinse, permanent wave agent and styling lotion besides hair spray/colorant and tonic. Several chitosan based compounds namely glyceryl chitosan, *n*-hydroxypropyl chitosan, quaternary hydroxypropyl chitosan, polyoxyalkylene chitosan, chitin sulphate and carboxymethyl chitosan own potential in hair care products. Chitosan derivatives are good candidate for skin care as they impart positive electrical charge, and due to high molecular weights it cannot infiltrate human skin, so act as a moisturizer and might compete with hyaluronic acid in this perspective. Chitin/chitosan both own wide utilities in formulation like creams, pack material, lotions, foundation, eye shadow, lipstick, cleansing, bath agents and nail enamel/lacquers. Rather diacid anhydride treated chitosan derivatives are best employed in many skin care products besides usage in paste, mouthwash and chew gum. Chitosan based salts are supplemented in toothpaste for mask silicon oxide unpleasant taste besides acts as powder binder to uphold granular shapes. Chitin materials are used as dental fillers that vitally absorb candida/thican, teeth sticking fungi, so recover cleaning false teeth.

2.7.2. Chitosan based scaffolds in medical/clinical/pharmaceuticals

Chitosan based skeletons are well-known in biomedical utility namely drug/gene release, wound dressing and advanced nanotechnology [1]. Chitosan based 2D/3D scaffolds like sponge, foam, gels fibers/film are more developed for modern tissue and bone engineering [2]. Notable *N*-trimethyl-*N*-octyl-chitosan scaffolds have established its potential utility as controlled drug delivery of hydroxyl-camptothecin anticancer agent [3]. Antitumor drug delivery is also reported with specially fabricated magnetic nano-iron doped maltosyl chitosan hybrids [2, 3]. Several clinical reports endorse impact chitosan matrixes in cancer chemo-prevention due to precise nutrients encapsulation which imparts enhanced drug delivery in blood with fewer side effects on healthy cells [1, 2].

2.7.3. Chitosan based matrixes in science and technology

Synthetic plastic are produced @ 300 million tons/year with only 3% recyclability, rather 97% plastic wastes break down in oceans or in landfills and harms the green environment. But, polysaccharide derived 3D bio-plastics offered predictable hardiness e.g., Wyss Institute, USA, has derived chitin based bio-degradable plastic "*Shrilk*" silk protein substitute. Shrilk's hardness and peculiarity offered myriad utilities namely implantable medical devices, bone-tissue gallows, laminated silk fibroin, bio-composts/fertilizer (release nitrogen nutrients), implantable foams, films, surgical closure scaffolds, wound healing, and FDA-approved devices.

2.7.4. Fabricated chitosan matrix via nano-biotechnology

Biotechnology can interfaces between science, engineering and technology. Amid, nano-biotechnology is complementary yet untapped science field that can exploits/improves biotechnology and aids to fabricate natural/bio-mimetic nano-structures. Nano-science technology covers and merges biological R&D with various fields as it alters material's parameters including biological, physicochemical and cellular electrochemical responses along with molecular motions. Advanced nano-biotechnology fantastically utilizes natural polysaccharides like chitin/chitosan in such perspectives [1, 2]. Thus, varied matrixes are formulated through chitin/chitosan skeleton owing clinical, biomedical and industrial applicable bio-polymeric prominence like quantum/carbon dots, nano-particle/composite and biomarkers usages in cancer detection. Nano-biotechnology exploited unique and admirable features of chitosan namely biodegradability, biocompatibility, low/no toxicity, antimicrobial activity and low immunogenicity in drug delivery, siRNA/DNA delivery, tissue engineering, and wound healing, biosensors besides theranostics utilities **Figure 1**. Chitosan based many novel nano-materials/devices owns vast beneficial applications to mankind. Strategic chitosan nano-matrixes carriers vital impact on global pharmaceutical use to control drug release due to enhance drugs solubility, superior protein bioavailability, and better uptake of hydrophilic substances across epithelial layers besides great intracellular drug delivery [2–5].

2.7.4.1. Chitosan-carbon dots

Quantum dot are 'nanometer scale' i.e., zero-dimensional particles own semiconducting, optical and electronic characteristics emitted at specific frequency of light that can be adjusted via matter utilized and size, shape and arrangements of dot/particle. Nano-chitonous based carbon quantum dot empowered fluorescent benefits for bio-sensing or imaging due to prominent features namely extremely tune-ability, brilliant water solubility, biocompatibility and better photo-stability [1–4]. Certain chitosan-carbon dots [2–3] yield as smooth, soft films which are robust to UV-visible blockage exploited in biomedical usages imparting low cytotoxicity and excellent biocompatibility with enhanced swelling, better thermal/mechanical properties over pure chitosan film. Amino functionalized fluorescent carbon nitride dots own improved water

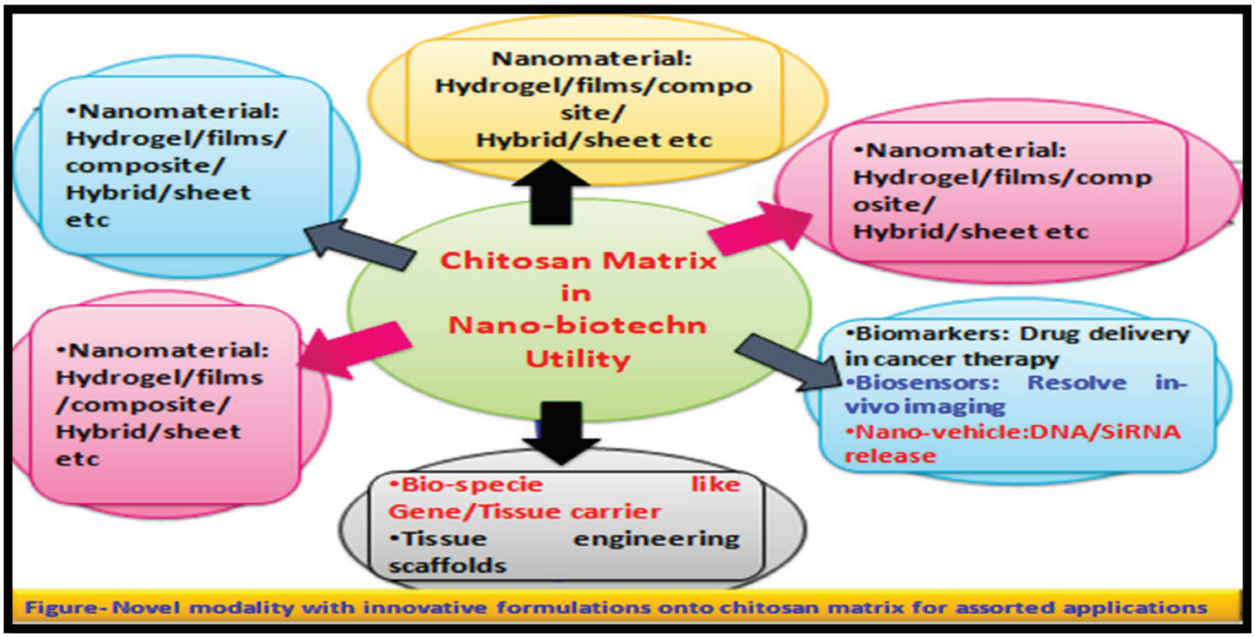

Figure 1. Chitosan matrix in nano-biotechnology.

solubility and strong fluorescent effect as advantageous in medical diagnosis and cancer treatments. Multi-color chitosan-carbon dots exhibited bio-labelling potential with varied bacterial model methods for biomedical usages [2–4]. Solid nano-solar cells are designed via chitin, chitosan and glucose based carbon quantum dot, hybrids as competence of mixed utmost with layer-by-layer sensitizer nanozinc-oxide coating. Such fluorescent nano-crystals/quantum dots can acts as an imaging agent for diseases detection with significant utility. Thus, novel chitosan-zinc sulphide based quantum dots obtained with pH dependent/tuneable optical/electrical properties as probed in pharmaceutical usages [2]. Luminescent chitosan-L-cysteine impregnated cadmium-tellurium films/dots showed antibacterial profile for broad range of biomedical utility. Chitosan-cadmium-telluride quantum dots generated onto indium-tin-oxide coated glass acts as electrochemical biosensor for culprit DNA in chronic myelogenous leukemia treatment or cancer detection. CdS- and/or nano-gold doped chitosan quantum dots are used to formulate antibody immobilization that own brilliant control and bioactive profile compared to other immune-sensors for protein detection studies [2–4]. Such nano-chitosan formations are frequently developed for delivery of safe, effectual plasmid DNA, siRNA, and oligo-nucleotides as gets rapid noticed by genetic materials so as to treat silencing unwanted gene's expression, defects and substituted missing in diseases curing therapeutics [1–5].

Nano-particles can be easily deposited on porous chitosan surfaces to offer homogeneous QDs for multiple active sites adsorption and desorption of hydrogen gas. Certain nano-metallic particles gets integrated into flexible chitosan to exploit for many purpose like catalytic activity, manipulated electronic and chemical characteristics in modern S&T [5]. Polyaniline-chitosan-platinum films are designed on pencil graphite electrode showed brilliant synergic performance in water electrolysis for electro-catalytic hydrogen generation. Thus, chitosan based cheap well-designed gels, films and composites yields via immobilizing desired quantum dots for facilitated hydrogen evolution reaction (HER) and practically skillful hydrogen production with long-term durable electro-catalyst. Flexible organic matrixes of chitosan can be altered for its superior fluorescent, semiconductor behaviour by hyper-branched ligand stabilizer own gelated quantum dots. These fabricated QDs offers solution to multi-responsive novel applications in nano-science for imaging, bio-sensing and drug delivery actions.

2.7.4.2. Chitosan based surface active microcapsules

Chitosan based surface active microcapsule resembles quantum dots as being nano-scale size pertains optical and electronic properties rather intermediate between bulk and discrete. Surface active microcapsules compactly detain electrons/electron-holes varied with size/shape and nature of raw/feedstock to own tuneable features like specific opticity, huge quantum yield, longer fluorescence, enhance photo-stability as advantageous over traditional organic fluorophores in recognition, tagging and imaging in biology and clinical sciences [1–5]. The surface active integrated chitosan skeletons are non-toxic, biodegradable and biocompatible owing liquid-core microcapsule, micro-particle, and macromolecule matrixes own myriad utilities in advanced nanotechnology [6]. Laminar cationic chitosan skeleton owns $-NH_2-OH$ linkages that found to assist microcapsule formations via anionic interlocks to implant better biocompatibility and stability in resultant hybrids [6, 7]. Sodium alginate and/or nano-ZnS can micro-capsule chitosan to yield nano-hybrid/nano-gel responsible for many pharmaceutical applications including bio-imaging, bio-labelling and gene/drug release purpose. Flexible chitosan skeleton can catatonically interacts with anionic surface-active surfactants via apparent loss of positive charge to yield insoluble composites or complexes. Such, rational design chitosan based homogenized microcapsule acquired via co-acervation, emulsification, solvent-evaporation, gas-liquid micro-fluidic and layer-by-layer assembly techniques impart improved bioavailability, reproducibility and repeatable drug release/delivery in today's advanced nano-biotechnology [7]. Host-guest interactive and responsive external stimuli sensibility imparts hydrophobic tails/cavities in resultant microcapsules that crucially control its inherent functions as induced via intrusion or doping with surfactants like cyclodextrins and sodium dodecyl sulphate. Strategically controlled/uniform size nano-cadmium sulphide entrapped chitosan quantum dots or microcapsules with stimuli-accountable α-hydrophobic cavities are developed for detection of toxic/hazardous chemicals as beneficial in remediation of ever increasing environmental pollution. Requisite chemical's stimuli-response gets formulated as in rationally controlled chitosan-CdS and/or ZnS quantum dots as liquid-core microcapsules encapsulated with poly(DL-lactide-co-glycolide) showed good fluorescent stability in aqueous condition. Rather usage of surfactants like α-cyclodextrin induces changes/slight influence on shape and fluorescent color in rationally designed chitosan-bends with CdS/ZnS in resulted mono-disperse micro-capsulation. These surfactant induced chitosan stimuli-responsive micro-capsules are cost effective micro-detectors for assorted chemicals than traditional counterparts.

2.7.4.3. Chitosan based nanoparticle

Chitosan based nano-particle performs efficient exogenous gene release into primary chondrocytes and imparts immense potential for requisite delivery of therapeutic drugs used in treatment of various diseases. Chitosan skeletal alteration found to enhance transfect ion efficiency by virtue of enhanced self-branching achieved in resultant composites/matrixes/hybrids. Tri-saccharide substitution linear chitosan counterparts compel better gene transfer with intact biocompatibility for cellular uptake with superior stability [3–7]. *N*,*N*,*N*-trimethylated chitosan scaffolds encourages *in-vivo* intracellular si-RNA delivery with improved extracellular competence and fine silencing profile along with effective DNA-drug release [1, 8]. Glycol-chitosan scaffolds that can entrap chemo-theraptic like doxorubicin and DOX drugs attenuated utmost si-RNA delivery via surmounts resistance observed in adorn dose-dependent *in-vivo* analysis [8, 9]. Chitosan-poly-D,L-lactide-co-glycolide matrix acts as precise non-viral devices for lot of uses like pulmonary si-RNA release, *in-vitro* H1299 gene silencing and fluorescent protein cell expression [9].

2.7.4.4. Biosensors & bio-markers

Sensor receives and responds to signals by converting into magnetic/electrical fields that further detected by an electronic device. Biosensor for biological entities comprises bio-polymeric coalesce and utilizes for physicochemical detection of assorted sensitive natural species like; tissues, cells microorganisms, organelles, enzymes, antibodies and nucleic acids [9]. Biosensor interacts with these analytes and performs recognition/diagnosis based on corresponding interactive evaluation as employed for DNA/RNA, enzymes, antibodies and signal transduced/immobilized tissues [9]. Bio-engineered analytical gizmo aids to offer myriad chitosan based bio-sensores which are beneficial due to uniqueness namely cheap, bio-compatible, eco-friendly, adaptable, portable, high sensitive, intrinsic selective and benign to use in moderately complex environments by virtue of quick responses compared to traditional sensors [10]. Flexible chitosan skeleton recognizes the sample species via immobilization in fabricated matrixes to be exploited for complicated enzyme sensing [11]. Tyrosinase-Fe_3O_4 dope chitosan used to bio-sense/detects certain organic pollutants like catechol onto specifically designed porous nano-iron oxide proactive surfaces [12]. Chitosan diffusion into graphene skeleton induces huge surface area and electrical conductivity in resultant matrix which is used for effectual bio-sensing or immobilization of enzymes and glucose estimation with splendid sensitivity besides durable stability [13]. Nanocarbon dope chitosan yields amperometric matrix to be used for assorted purpose like biosensors, biomarkers, to encapsulate lactase and bio-fuel cells besides as bio-electrochemical devices [14]. Polyaniline-nano-chitosan entrapped creatinine amidino-hydrolase shown good immobilization of CAH enzyme with better stability and durability.

Biomarker is biological indicator use to perform characteristic objective measurements, detections and/or indications for validity of certain phenomenon namely biological state, living organism existence, pathogenic processes and therapeutic intervening pharmacologic responses besides manage cancers and other diseases [15]. Biomarker established doubt in advanced pharmaceutical for facile screening and risk assessment before its diagnosis besides detect diseases with staging, grading and preliminary treatment options for monitoring supplementary therapy [16]. Gold coated chitosan-xanthan biosensor is used for bio-imaging in numerous diseases diagnosis [17] and signal improvement for melanoma. Chitosan-graphene nano sphere marked horseradish peroxidase in α-fetoprotein induce cancer diagnosis with enhanced signal augmentation than electrochemical immuno-sensors [18]. Nano-chitosan biomarkers are preferred detect alpha-fetoprotein and carcino-embryonic antigen with more precision and accuracy over ELISA test. Thus, chitosan integrated biomarkers own stupendous including haemostatic, fungi-static, bacteriostatic, spermicidal, anti-cholestermic and

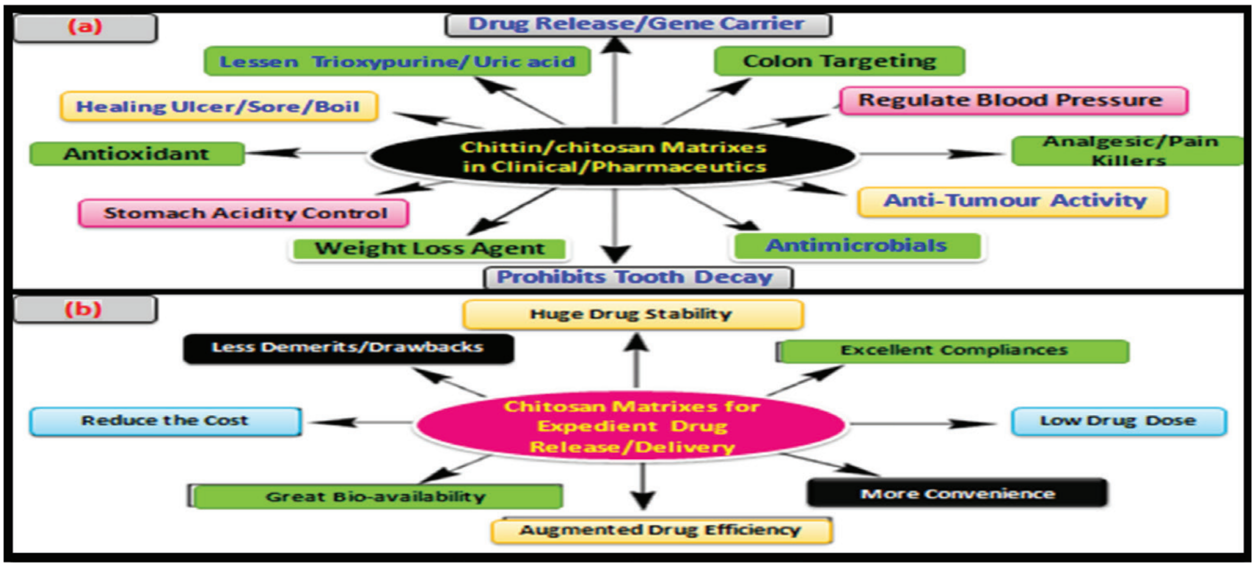

Figure 2. Chitosan base matrixes for pharmaceutical/clinical and expedient drug delivery.

anti-carcinogenic features fascinated for skillful healings, disease prevention/diagnosis, drug delivery and tissue engineering. Primary —NH_2 link of chitosan smartly offers surface active cationic charge variations (below pH 5.5) achieved via H-bonding imparts adhesion for tissues and subsequent fabricated matrixes offers novel clinically applied products. Some pharmaceutical/clinical expedient utilities of chitosan matrix includes dentistry, orthopedic, ophthalmology, surgical measures, optical and wave guiding utilities as shown in **Figure 2**.

2.7.4.5. Chitosan-doped $Ca(OH)_2$ microcapsules

Liberal —NH_2 groups of chitosan gets protonated in acidic conditions, thus chitosan based microcapsules, micelles and hydrogels can be synthesized to favor varied biomedical/clinical applications. Certain pH-triggered calcium hydroxide coated chitosan hybrids are used for endodontic treatment with long-lasting antibacterial activity against *Enterococcus faecalis* refractory strains. Ethylcellulose-calcium hydroxide coated onto chitosan yields [CS-EC@$Ca(OH)_2$] microcapsule found to have unique features namely non-toxic, biocompatible, possess superior host immunity, tender controlled drug/gene release besides usage for apical periodontitis in confronted customary root canal therapy. Such CS-EC@$Ca(OH)_2$ microcapsule recuperates innate calcium hydroxide properties which approved osteogenesis effect along with lessening inflammation as beneficial for apical periodontitis in bone defects healing.

Vitapex, calcium hydroxide coated chitosan paste/gels is clinically used to accomplish prominent apical periodontitis effect via stagnant release $Ca(OH)_2$ than other aqueous counterparts. Thus, amid gel vehicles chitosan based microcapsules like Ca (OH)2 loaded propylene glycol-chitosan/agar formulation releases calcium hydroxide via altering gel bases in chronic inflammatory lesion around apex of tooth treatment, besides offered controlled drug delivery with decrease cytotoxicity. Chitosan EC@$Ca(OH)_2$ scaffolds/pH-triggered microcapsule release $Ca(OH)_2$ rapidly in acidic conditions own many significances like inhibits bacterial infections, endorses AP repairs/periapical periodontitis, wide antibacterial activity against *Enterococcus faecalis* refractory strains, great anti-inflammatory profiles and evade bone resorptions. Such, facile and sustainable pH-triggered calcium EC@calcium hydroxide-CS-matrixes own significantly extended antibacterial profile and showed amazingly diminish inflammation to persuade osteogenesis capable in endodontic diseases therapy.

3. Drawbacks and remedies

Amid, all above meritorious usages of chitosan chemistry, it also own certain drawbacks namely as weak basicity at low physiological pH (pka = 6.2) besides, only soluble in aqueous organic acid solution due to protonated —$NH_3^+X^-$ salt formation. Chitosan shows elevated swelling in aqueous medium and carry out unavoidable quick/instant drug delivery, needs to modify/alter chitosan inherent framework. Certain above mentioned demerits in chitosan utility can be trounced by —NH_2 and/or —OH glucosamine derivative formation which solve few complications to cater wide utility. The imperative and characteristics applications of chitosan based bio-polymeric adsorbents established in the environmental pollution remediation is [19] summarized in **Table 1**.

SN	Material types	Practical characteristics		Applications
		Useful property	Adverse property	
1	Nano-filtrations (RO/FO)	Reliable, automated, charge based repulsion, high selectivity, low pressure, costly	High energy, costly, membrane chock, intense polarized, nano-pore dimension	Lessen hardness, color, odor, remove heavy metals, sea water desalination and wastewater treatments
2	Nano-composite membranes	Viable hydrophilic/hydrophobic, huge porosity, more water flux/permeability, thermal stable, mechanically robust, foul resistant, stay at high pressure	Nano-particle leakage, bulk nano-materials needed for oxidation, and composite dependent	Reverse osmosis; eliminate pollutants, composites in ultra-filtration, cartridges nano-fiber composites
3	Self-assemble membrane	Uniform, nano-porous, tuneable size/shape, facile design	Applied on lab/small scales	Ultra-filtrations and process scale up
4	Dendrimer/dendrons (arborol cascade)	Inner hydrophobicity, outer hydrophilicity, water soluble, bio-mimics, easy encapsulation, handy, non-toxic and reusable	Dendrimer/dendron formations are complex multistage processes	Organic/heavy metal removals, biodegradable, biocompatible dendrite
5	Metals magnetic nano-particles	Biocompatible, tuneable colloidal nano-particle, super-paramagnetic, highly recyclable, facile residual separation and huge surface: volume ratio	Stabilization (surface modification needed to enhance its potential	Remediation of hazardous/toxic pollutants, cation/magnetic sensors, nano-beads used for sorption

Table 1. Characteristics of chitosan base membranes in water treatments/purification.

4. Futuristic prospective applications of chitosan matrixes in water purifications

Certain rationally engineered chitosan based adsorbents are vulnerable and flexibly adjustable for facile elimination of contaminants from water/wastewater [14, 20] than compatibly integrated traditional treatments. Bio-materials are beneficially benign to integrate into diversified multifunctional membranes to facilitate both particle retention and contaminant mitigations than conventional materials based water treatments [20]. Further, such chitosan based materials usage own superior process efficiency and high adsorption profile besides adaptable mass scale utility in point-of-use devices [12, 14, 15].

Membrane-based water purifications or treatment processes can address the global challenges of water scarcity and aquatic environmental pollutions [14, 18]. Conservative water purification membranes owe constrained due to inherent limits of conventional materials used in their fabrications [18]. Advanced nano-technology has developed sophisticated methods to control the structural and chemical functionality in chitosan based film, sheet, hydrogel, microcapsule and dots to new classes of materials for water purification [12]. Technologically manufactured chitosan based materials caters the need for futuristic advanced water purification/treatments. Such molecularly designed well selective and focus materials are highlighted by surface modification to minimize interfacial interactions, inherent limitations and enhance efficiency over customarily used materials as in **Table 2**.

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Utility	Nature of work	Features
Energy	Sunlight conversion (like DSSCs, PBs)	• Efficient light-harvesting, especially in biomaterials replica or biocomposites examples; • fast charge separation, high current density; • high gas permeability; • high storage density; • fast electron and ion transport; • small resistance
Life sciences	Engineered/designed Biomaterials/films/composites	• Biocompatibility; • promoting cell adhesion; • good mechanical property; • controlled shapes/sizes
Chemical sciences	Pre-concentration device Bioreactors For separation and adsorption	• High permeability; • homogeneous flow-through pore structure; • control pore structures and surface properties; • used monolithic column

Table 2. Applications of chitosan matrixes.

5. Conclusion

Chitosan biopolymer is preferred for biomedical and pharmacological promising purposes as its safe/harmless besides impart successful drug delivery/releases. Muco-adhesive chitosan improved abode span and consequently provide drug's bioavailability in target specific carriers. Certain fillers like ZnO, ZnS and TiO_2 chosen to intrude into chitosan skeleton to yield resultant matrixes/hybrids/composites with widen utilities in clinical/pharmaceuticals. Systematically performed R&D in chitosan based scaffolds/matrixes owing interactive filler/dopant added to improve its applicability which opens subsistence revolutionary and advanced medical usages.

Nanobiotechnology integrated technology and complementary strengths of bio-molecule chitosan with the nano-electronics to own assorted applications/outcomes as biosensor and biomarker proliferation as high-resolution devices (for *in-vivo* imaging) and drug delivery treatment in cancer respectively. Further advance biotechnology exploited excellent biological characters of chitosan so as to introduce novel modality with innovative formulations namely nanovehicles for gene/DNA/SiRNA delivery and quantum dots/nanobio-composites for various diseases diagnosis, generating new therapeutic techniques besides development of tissue engineering scaffolds. Thus, nano-biotechnology skillfully explored chitosan matrix to design and device never-ending clinical and scientific applications for the benefit of human besides environment/nature.

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References

[1] Dongre RS. Biological Activities & Application of Marine Polysaccharides. Vol. 1. Croatia: In-Tech Open; 2017. pp. 181-206. DOI: 10.5772/65786

[2] Jain1 T, Kumar S, Dutta PK. Chitosan in the light of nano-biotechnology: A mini review. Journal of Biomedical Technology and Research. 2015;**1**(1):101-107

[3] Bănică F-G. Chemical Sensors & Biosensors: Fundamentals & Applications. Vol. 176. UK: John Wiley Sons; 2012. ISBN: 978-0-470-71067-8

[4] Jianc H, Su W, Caracci S, Bunninc TJ, et al. Optical wave guiding and morphology of chitosan thin films. Journal of Applied Polymer Science. 1996;**61**:1163-1171

[5] Burkatovskaya M, Tegos GP, Swietlik E, Demidova TN, P Castano A. Use of chitosan bandage to prevent fatal infections developing from highly contaminated wounds in mice. Biomaterials. 2006;**27**:4157-4164

[6] Kurita K. Chitin & chitosan: Functional biopolymers from marine crustaceans. Marine Biotechnology. 2006;**8**(3):203-226

[7] Mourya VK, Inamdar NN. Chitosan-modifications and applications: Opportunities galore. Reactive and Functional Polymers. 2008;**68**(6):1013-1051

[8] Sashiwa H, Shigemasa Y. Chemical modification of chitin & chitosan 2: Preparation & water soluble property of N-acylated or N-alkylated partially deacetylated chitins. Carbohydrate Polymers. 1999;**39**(2):127-138

[9] Dutta PK, Dutta J, Tripathi VS. Chitin and chitosan: Chemistry, properties & applications. Journal of Scientific and Industrial Research. 2004;**63**:20-31

[10] Peter MG, Domard A, Muzzarelli RAA. Advances in Chitin Science. Vol. IV. Potsdam, Germany: Universität Potsdam; 2000. p. 395. ISBN: 3-9806494-5-8

[11] Hudson SM, Jenkins DW. Chitin & Chitosan. Encyclopedia of Polymer Science and Technology-1. 3rd ed. New York: Wiley Interscience. DOI: 10.1002/0471440264.pst052

[12] Dutta PK, Ravikumar MNV, Dutta J. Chitin and chitosan for versatile applications. Journal of Macromolecular Science-C, Polymer Review. 2002;**42**(3):307-354

[13] Noipa T, Ngamdee K, Tuntulani T, Ngeontae W. Cysteamine CdS quantum dots decorated with Fe^{3+} as a fluorescence sensor for the detection of PPi. Spectrochimica Acta—Part A: Molecular and Biomolecular Spectroscopy. 2014;**118**:17-23

[14] Yan J-J, Wang H, Zhou Q-H, You Y-Z. Reversible and multisensitive quantum dot gels. Macromolecules. 2011;**44**(11):4306-4312

[15] Hardison D, Deepthike HU, Pathirathne T, Wells MJ. Temperature-sensitive microcapsules with variable optical signatures based on incorporation of quantum dots into highly biocompatible hydrogel. Materials Chemistry. 2008;**18**(44):5368-5375

[16] Sá-Lima H, Caridade SG, Mano JF, Reis RL. Stimuli-responsive chitosan-starch injectable hydrogels combined with encapsulated adipose-derived stromal cells for articular cartilage regeneration. Soft Matter. 2010;**6**(20):5184-5195

[17] Thongngam M, McClements DJ. Influence of pH, ionic strength & temperature on self-association & interactions of sodium dodecyl sulfate in the absence & presence of chitosan. Langmuir. 2005;**21**(1):79-86

[18] Chen Y, Yao R, Wang Y, Chen M, Qiu T, Zhang C. CdS QDs-chitosan microcapsules with stimuli-responsive property generated by gas–liquid microfluidic technique. Colloids and Surfaces. B, Biointerfaces. 2015;**125**:21-27

[19] Li X, Yang Z. Chitosan-decorated calcium hydroxide microcapsules with pH-trigger release for endodontic application. Journal of Materials Chemistry B. 2015;**3**:8884-8891

[20] Kayan DB, Koçak D, İlhan M. The activity of PAni-Chitosan composite film decorated with Pt nanoparticles for electrocatalytic hydrogen generation. International Journal of Hydrogen Energy. 2016;**41**(25):10522-10529