# Chapter 5
# Marine Polysaccharides Based Nano-Materials and Its Applications

**Abstract** Marine polysaccharides and its associated nano-materials are currently considered as an excellent source for nano-technological applications. These applications are broadly categorized in the field of cancer therapy, wound dressing, drug delivery, gene delivery, tissue engineering, water treatment and biosensor. Promising biological functions are due to their structure and physicochemical characteristics, which certainly depend on the source of the organism. Production of marine polysaccharides based nano-materials is simple, economical, biodegradable, and well suggested to be used in the large-scale production of bio-nanomaterials. These polysaccharides are highly biocompatible, biodegradable, nontoxic, low cost, stable, safe, and abundant. Nevertheless the majority of the commercial applications are still at the laboratory level. Moreover in vivo investigations and clinical applications are required to develop industrial nanoproducts. In addition to these applications marine polysaccharide-based nano-materials have various applications biomedical sciences, fabric and food industries, and pharmaceutical industries.

**Keywords** Marine • Nanomaterial • Nanoparticle • Polysaccharide • Polymer • Alga

## 5.1 Introduction

Marine polysaccharides especially derived from algal sources offers various potential applications in modern medicine and nanobiotechnology field. These polysaccharides have several applications in drug delivery, gene delivery, wound dressing and tissue engineering [1]. Algae especially seaweeds present an array of therapeutic compounds with diverse structures and remarkable biological activities. These bioactive compounds contain rich source of sulfated polysaccharides such as porphyran, agarose, alginate, fucoidan, carrageenan, and ulvan. Sulfated polysaccharides are derived from various sources as mentioned in Fig. 5.1. In addition to algal sources exoskeleton of marine crustaceans offer some bioactive polysaccharides



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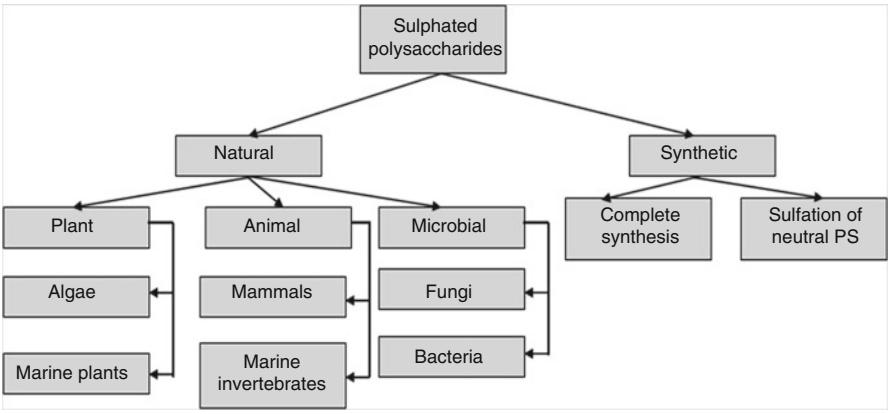



**Fig. 5.1** Various sources of sulphated polysaccharides

such as chitosan (CS), chitin, and oligosaccharides [2]. Various marine organisms produce exopolysaccharides (EPS) as an approach for growth adhering to solid surfaces and to survive in adverse conditions. These marine microorganisms producing EPS are a complex mixture of biopolymers chiefly comprised of polysaccharides as well as lipids, proteins, nucleic acids and humic substances [3]. Owing to the various advantages such as nanotoxicity, biocompatibility, low cost, biodegradability, and abundance offered by marine polysaccharide-based nanomaterials they endow significant applications in biomedical and chemical research [4]. Currently pharmaceuticals based on marine bionanoparticles of polymers such as nanomaterials, liposomes, dendrimers, metals or metaloxides or micelles are mainly investigated for fighting against different diseases, including cancer and bacterial infections and for drug delivery, gene delivery, wound healing and tissue engineering [5]. Sulfated polysaccharides and EPS are easily developed in to various nano and micro (nanoparticles, nanofibers, microparticles) membranes, gels, scaffolds, beads, and sponge forms. There pharmaceuticals have been used for variety of biomedical applications in drug delivery, tissue engineering, cancer therapy, wound dressing, biosensors, and water treatment in the area of nanobiotechnology (Table 5.1) [7]. This chapter highlights marine polysaccharide-based nanomaterials for nanotechnological and biomedical applications.

## 5.2 Polysaccharides Derived from Marine Sources

Among all living organisms marine polysaccharides derived from various resources such as marine algae, crustaceans, and microorganisms [4] forms one of the major components and considered as the most abundant source of

**Table 5.1** Description of various sulphated polysaccharides highlighting their own biological activity and applications [6]

| Polysacchari-des | Marine organisms (source) | Class | Biological properties | Applications |
|---|---|---|---|---|
| Heterofucans | *Canistrocarpus cervicornis*<br>a.k.a. *Dictyota cervicornis*<br>*Dictyopteris delicatula* | Chromophyta<br>Dictyotales | Anticoagulant, antioxidant; anti-proliferative, anti-thrombotic, antiviral | Vaccines for immunotherapy<br>Production of nanofibers<br>Gluing and soft tissue closure after surgery<br>Lubricants for bone joints<br>Nanotechnology |
| S-fucans | *Canistrocarpus cervicornis*<br>a.k.a. *Dictyota cervicornis*<br>*Dictyopteris delicatula*<br>*P. tetrastromatica*<br>*Cladosiphon okamuranus*<br>a.k.a. *Okinawa mozuku*<br>*Spatoglossum schröederi*<br>*Ascophyllum nodosum*<br>Fucus spp.<br>F. vesiculosus<br>Hizikia fusiforme<br>a.k.a. Sargassum fusiforme<br>Sargassum spp. | Chromophyta<br>Dictyotales<br>Ectocarpales<br>Fucales | Anti-proliferative, antiviral, anti-inflammatory, antiadhesive, Antitumor, immunomodulator, angiogenic, gastroprotective, Cardioprotective, restenosis preventive | |
| S-galactofucans | *D. menstrualis*<br>*Lobophora variegate*<br>*Spatoglossum schröederi*<br>*Adenocystis utricularis*<br>*Costaria costata*<br>*L. japonica*<br>*a.k.a. Saccharina japonica*<br>*Undaria pinnatifida* | Chromophyta<br>Dictyotales<br>Ectocarpales<br>Laminariales | Anti-thrombotic; Peripheral anti-nociceptive; Anti-proliferative, anti-adhesive, antioxidant | |
| LMW-S-fucans | *Nemacystus decipiens*<br>*P. canaliculata* | Fucales<br>Ectocarpales | Anticoagulant | |
| S-fucoidan | *C. novae-caledoniae*<br>*Saccharina cichorioides*<br>*a.k.a. Laminaria cichorioides*<br>*Laminaria spp.*<br>*S. horneri*<br>*S. henslowianum* | Fucales<br>Ectocarpales | Antitumor | |
| Fucoidans | *Eisenia bicyclis*<br>*Lessonia vadosa* | Fucales | Anticoagulant | |
| S-galactofucans Fucoidan | *Undaria pinnatifida* | Fucales | Antiviral, anticoagulant, antitumor, anti-proliferative, immunomodulatory, anti-inflammatory induced osteoblastic differentiation | |
| LMW-fucoidan | *S. patens* | Fucales | Antiviral | |
| S-laminaran | *Laminaria sp. (or Saccharina)* | Fucales | Antitumor, anticoagulant, decreases liver triglyceride, cholesterol and phospholipid levels; serum hypocholesterolaemic, hypotensive, antibacterial, immunomodulator | |

(continued)

**Table 5.1** (continued)

| Polysacchari-des | Marine organisms (source) | Class | Biological properties | Applications |
|---|---|---|---|---|
| Laminarans | *Eisenia bicyclis* | Fucales | Anti-proliferative, antitumor, anticoagulant; Antitumor, serum hypocholesterolaemic, hypotensive, antibacterial, immunomodulator | Wound healing<br>Burn-wound dressings<br>Tissue regeneration |
| S-galactan porphyran | *Porphyra spp.* | | Antitumor, hypotensive, regulates blood cholesterol | Cell encapsulation<br>Scaffolds for tissue engineering<br>Wound healing and dressings<br>Revascularization |
| Porphyran | *P. yezoensis*<br>*P. haitanensis* | Rhodophyta<br>Bangiales | Antitumor, immunomodulatory, hypolipidaemic | |
| S-agarans | *Bostrychia montagnei*<br>*Cryptopleura ramose*<br>*Digenea simplex*<br>*Gloiopeltis complanata*<br>*Aghardiella tenera G. corticata* | Rhodophyta<br>Bangiales<br>Ceramiales<br>Cryptonemiales | Antiviral | |
| LMW-PS | *Corallina sp.*<br>*C. ocellatus*<br>*Furcellaria lumbricalis*<br>*Hypnea charoides*<br>*Soliera chordalis* | Corallinales<br>Gigartinales | Antiviral;<br>Antitumor | |
| Agaroid-carrageenan | *G. furcata* | Cryptonemiales | | |
| di-S-galactan | *Gelidium crinale* | Gelidiales | | |
| Hybrid DL-galactans | *Pterocladia capillacea*<br>*Gymnogongrus torulosus* | Gigartinales | | |
| S-λ-carrageenan | *Chondrus crispus*<br>*E. spinosa*<br>*G. skottsbergii*<br>*Phyllophora brodiei*<br>*Stenogramme interrupta* | Gigartinales | Anticoagulant, antithrombotic | |
| LMW-PS | *Hypnea charoides* | | Immunostimulant | |
| LMW-S-carrageenans | *Kappaphycus striatus* | | Antitumor, immunomodulator | |
| sPS | *Gracilaria caudate*<br>*G. verrucosa*<br>*U. conglobata*<br>*U. fasciata*<br>*U. lactuca*<br>*U. rigida*<br>*C. cupressoides* | Gracilariales<br>Chlorophyta<br>Bryopsidales<br>Ulvales<br>Diatoms<br>Chlorophytes<br>Prasinophyte<br>Prymnesiophyte/ haptophyte | Antiviral, anti-inflammatory, immunomodulator, anti-proliferative, prevention of tumour cell growth | |
| S-galactans | *G.corticata*<br>*Grateloupia indica*<br>*Schizymenia dubyi*<br>*S. binderi*<br>*U. lactuca*<br>*Caulerpa spp.*<br>*Aghardiella tenera*<br>*Euchema cottonii*<br>*Pterocladia capillacea* | Ulvales<br>Rhodymeniales<br>Nematomatales<br>Halymeniales<br>Gracilariales<br>Gigartinales | Anticoagulant, antithrombotic | |

(continued)

**Table 5.1** (continued)

| Polysacchari-des | Marine organisms (source) | Class | Biological properties | Applications |
|---|---|---|---|---|
| S-mannans | *Nemalion helminthoides*<br>*Capsosiphon fulvescens* | Ulotrichales<br>Nemaliales | Antiviral<br>Immunomodulator | Drugs carriers<br>Encapsulation,<br>Scaffolds for ligaments and tissue engineering<br>Regeneration of tissues<br>Moulding in dentistry<br>Wound healing and dressings |
| Xylogalactans<br>S-xylomannans | *Nothogenia fastigiata* | Nemaliales | Antiviral, anticoagulant | |
| di-S-galactan<br>LMW-sPS | *Botryocladia occidentalis*<br>*Champia feldmannii* | Rhodymeniales | Anticoagulant,<br>anti-venom | |
| S-xylomannans | *Sebdenia polydactyla* | Nemaliales | Antiviral | |
| S-arabinogalactans | *Codium spp.* | Chlorophyta<br>Bryopsidales | Anticoagulant,<br>antithrombotic, antiviral | |
| S-pyrulylated-galactans | *C. isthmocladum* | Chlorophyta<br>Bryopsidales | Antioxidant,<br>anticoagulant,<br>anti-proliferative | |
| S-rhamnans and LMW-S-rhamnans<br>Rhamnans | *Monostroma latissimum*<br>*M. nitidum*<br>*Enteromorpha intestinalis* | Ulotrichales | Anticoagulant,<br>antithrombotic,<br>hepatoprotective,<br>antitumor,<br>immnunomodulator | |
| S-ulvans and Derivatives, LMW-S-ulvan or otherwise modified | *E. prolifera*<br>*U. pertusa* | Ulvales | Antioxidant,<br>anti-proliferative,<br>Hypocholesterolaemic | |
| EPS | *Haslea ostrearia*<br>*Nitzschia closterium*<br>*Skeletonema costatum*<br>*Chaetoceros spp.*<br>*Amphora sp.*<br>*Dunaliella salina*<br>*Ankistrodesmus angustus*<br>*Botryococcus braunii* | Diatoms<br>Chlorophytes<br>Cyanobacteria | Antiviral, antibacterial,<br>prevention of tumour<br>Cell growth | |
| s-Spirulan | *Arthrospira platensis* | Cyanobacteria | Anti-proliferative,<br>anti-adhesive,<br>Anti-metastatic | |

polysaccharides (Table 5.2) (Figs. 5.2 and 5.3). These polysaccharides exhibit various biological and biomedical applications, namely [8], antiangiogenic [9], antimetastatic [10], and anticoagulant [11], antioxidant [11], anti-inflammatory, immunomodulating [8], antiproliferative [11], antitumor [12], antiparasitic antiviral [8] properties. Among all class sulphated polysaccharides have been of great interest because of the presence of sulphur group and their potential to generate new bioactive compounds [10].

**Table 5.2** Chief sources of polysaccharides and its description

| Sources | Description | Name | Bio-prop. | Biopolymer | Application |
|---|---|---|---|---|---|
| Green algae sulfated polysaccharides | (1-3(6))-Linked galactose,(1-3 (4))-linked arabinose,(1-4)- linked glucose and terminal,(1-4)-linked xylose residues. Sulfation soccuron O6 of galactose and O3 of arabinose. Sulfate ester content: 9 % | Green algae, Caulerpa racemosa | Antiviral activity (herpes simplex virus type 1 and 2) | Ulvan | Tissue engineering |
| | (1-2)-Linked L-rhamnose residues with sulfate groups substitute dat positions of C3 and/or C4. Sulfate ester content: 23 %/25 % | Green algae, Monostroma latissimum | Anticoagulant activity | | |
| Brown algae sulfated polysaccharides | Fucan: (1-3)-linked α-L-fucopyranosyl backbone, mostly sulfated atC4, and branched at C2 with non-sulfated fucofuranosyl and fucopyranosyl units, and 2-sulfated fucopyranosyl units. Galactan: D-galactopyranose units linked on C3 and C6, and sulfation mostly on C4. Sulfate ester content: 30–34 %/21–24 % | Brown algae, Adenocystis utricularis | Antiviral activity (herpes simplex virus type 1 and 2), Antiretroviral activity (HIV-1) | Alginate | Drug delivery, Anti-tubercular and antifungal, Antitumor |
| | Mainly composed of fucose (82 %), galactose (14 %), and small amounts of xylose and mannose Sulfate ester content: 92 % | Brown algae, Ecklonia cava | Antiproliferative activity, anticancer activity | | |
| | Fucose, galactose. Sulfations occur on position-2 and-3. Sulfate ester content: 41–92 % | Brown algae, Ecklonia cava | Anti-inflammatory activity | Algal fucoidan | Cytotoxic activity, anticancer |

| | | | | | |
|---|---|---|---|---|---|
| Red algae sulfated polysaccharides (porphyran) | Backbone of alternating β-(1-3)- linked D-galactosyl units and α- (1-4)-linked L-galactosyl,(1-6)- sulfate or3,6-anhydro-α-L-galactosyl units. Sulfate ester content: 17 % | Red algae, Porphyra haitanensis | Antioxidant activities, anticoagulant activities | Agarose & porphyran | Cytotoxic activity Antibacterial activity Drug delivery |
| Shrimp and crab | Biopolymer family of lin-ear polysaccharide that is composed of glucosamine and N-acetyl glucosamine units via ˇ-(1 → 4) linkages randomly or block-spread throughout the polymer chain, depending on the extraction pro-cedures to derive CS from chitin | Shrimp and crab | Gene delivery, Antimicrobial activity, Tissue engineering, Anticancer activity, Wound dressing | Chitosan | Drug delivery |
| | Water-soluble anionic derivative of chitin containing carboxyl groups | | Wound dressing, Antibacterial activity, Drug delivery | Chitin (Carboxymethyl chitin) | Drug delivery |
| | COS, a low molecular weight depolymerization product of CS, | | Anticancer | Chitooligosaccharide | Drug delivery |

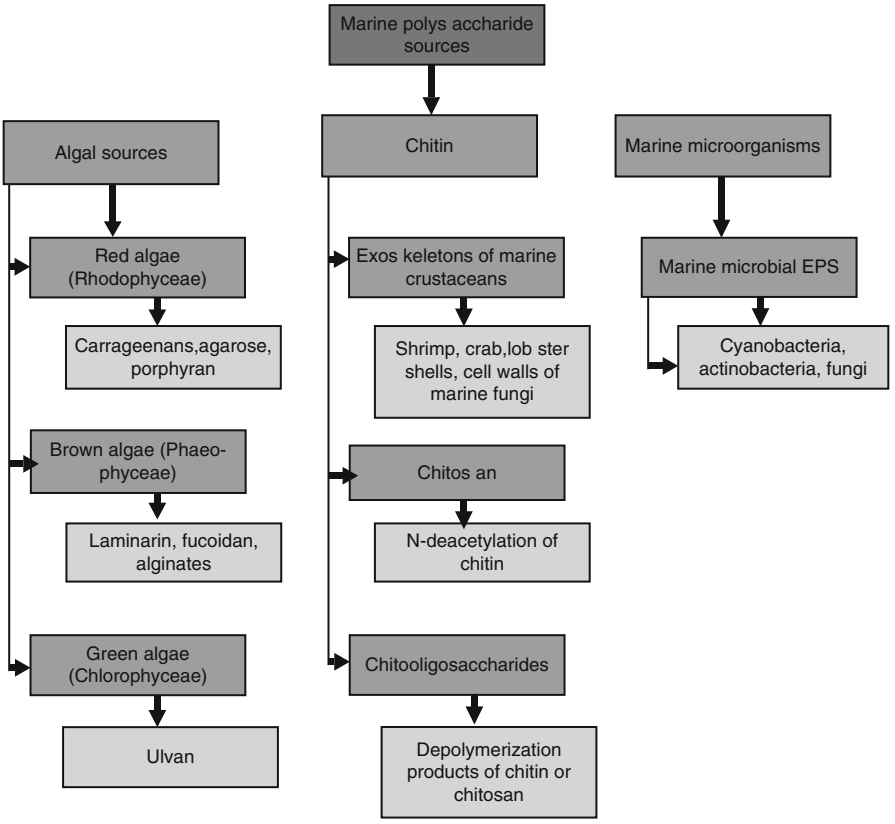



**Fig. 5.2** Marine based polysaccharides and its sources

### *5.2.1 Marine Algae Based Polysaccharides*

Marine algae polysaccharides especially sulfated polysaccharides received a greater importance as natural resources of marine natural products. Owing to the potential properties of seaweed and other marine sources derived polysaccharides they have received considerable attention in the cosmeceutical, nutraceutical, and pharmaceutical fields [13]. Marine algae chiefly classified in to three: green algae (Chlorophyceae), brown algae (Phaeo-phyceae) and red algae (Rhodophyceae) (Fig. 5.2).

From the research and commercial point of view there are some prominent sources (such as carrageenans, agarose, and porphyran) of sulfated polysaccharides extracted from red seaweeds [14], ulvan is a natural polysaccharide isolated from green algae [15] and laminarin, fucoidan, and alginates are chiefly derived from marine brown algae.

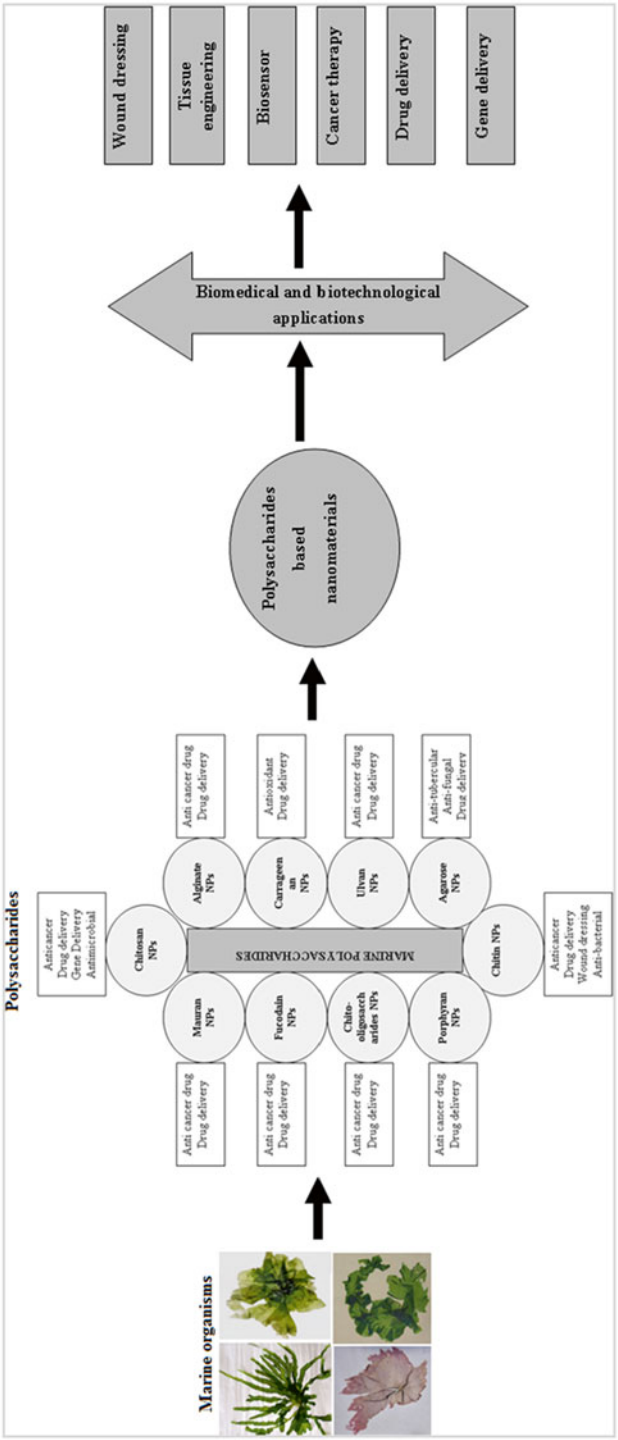



**Fig. 5.3** Various types of sulfated polysaccharides and their applications in nanobiotechnology

## *5.2.2 Marine Crustaceans Derived Polysaccharides*

### 5.2.2.1 Chitin

Among all the polysaccharides chitin is reported as one of the most abundant natural polymers and chiefly found in the exoskeletons of marine crustaceans and cell walls of marine fungi [5]. Shrimp, crab, and lobster shells are the major sources chitin and form the existing waste products of the seafood industry. According to present research this polymers can be easily modified in to chitosan and other forms whereas both unmodified as well as modified forms can be easily processed into microparticles, nanoparticles, nanofibers, scaffolds, sponge forms, beads, gels, and membranes. There maximum utilization in biomedical field is based on excellent low toxicity, high biodegradability and biocompatibility [16]. Such properties endow various biomedical applications such as wound dressing, targeted drug delivery, tissue engineering and gene delivery, and offer significant applications in nanotechnology [17].

### 5.2.2.2 Chitosan and Chitooligosaccharides

Modification of chitin helps in improving its various properties such as improvement in molecular weight, biocompatibility and toxicity profile. Chitosan, a naturally occurring polysaccharides isolated by the N-deacetylation of chitin has now become the most highlighted polymer in chemical, nutraceutical and pharmaceutical industries [18]. One more modification which has been now highlighted for its excellent properties is chitooligosaccharides obtained by the depolymerization products of chitin or chitosan by enzymatic and acidic hydrolysis methods. These methods significantly affect the molecular weight and ease of control and safety. Additionally such modification methods impart excellent properties such as high water solubility nonotoxicty, good biocompatibility, excellent biodegradability and low cost [19]. Chitosan and chitooligosaccharides are now recently considered for its great promising application in biomedical science, such as hypocholesterolemic effects [20], wound healing [21], drug delivery [22], tissue engineering [23], antitumor effects [24], and antimicrobial activity [25].

### 5.2.2.3 Marine Microorganisms

Among the potential class of marine based polysaccharides microbial polysaccharides especially

EPS are abundantly present in various marine sources such as fungi [26], bacteria [27], actinobacteria [28], and cyanobacteria [29]. Currently, EPS presents various interesting applications in cosmeceutical, nutraceutical and pharmaceutical industries. Additionally EPS also plays an important role in wastewater treatment and detergent applications [30]. All marine based microbial polysaccharide offers an increasing attention for biological activities such as antitumor, antiviral, anti-

inflammatory properties [31]. According to previous reports extremophilic bacterial polysaccharide, mauran (MR), explored as novel biocompatible and stable biomaterial and therefore becomes more favorable for its utilization in nanotechnology, pharmaceutics and biomedical field [1]. Previous findings also suggested the role of Streptomyces sp. based polysaccharides in the production of polysaccharide-based bioflocculant for the green synthesis of silver nanoparticles [32]. These NPs can be treated as choice for the advancement in novel bactericidal bio-nanomaterials especially for several biotechnological applications and wastewater treatment.

## 5.3 Nanomaterials Derived from Marine Sources

Owing to high biodegradability, good biocompatibility, nontoxic nature, low cost and other features, marine polysaccharide-based nanomaterials are considered as most suitable novel carriers in nanotechnology science [33]. Because of their unique physicochemical properties these polysaccharides have attracted considerable attention for imaging and therapeutic agents. Some special features such as its abundance, hydrophilic, biocompatible, biodegradable, inexpensive, nontoxic, safe, hydrophilic and biocompatible nature they are of particular importance in the area of nanotechnology and have a promising future as biomaterials. Recent research on polysaccharides based nanomaterials offers various biomedical application such as drug delivery, antimicrobial activity, tissue engineering, gene delivery, cancer therapy, and wound dressing [34–36].

### *5.3.1 Nano Scaffolds Derived from Fucoidan*

Brown seaweeds derived sulfated polysaccharide known as Fucoidan (1) is an excellent drug candidate for pharmaceutical applications. Similarly fucan sulfates were obtained from marine invertebrates are having excellent pharmaceutical applications [37]. Fucoidan in the presence of formamide, pyridine and acetic anhydride yields acetylated nanoparticles. Whole process is conducted at room temperature for 24 h (Fig. 5.4, Table 5.3). Fucoidan is considered as an excellent candidate for various biological applications such antiproliferative properties, immunomodulating properties [47], anticoagulant [48], antiviral [47], antiangiogenic, antitumor, anti-inflammatory, [49], antioxidant [50]. Previous findings suggested that compounds such as fucoidans are now considered as the novel bioactive agents especially for nanotechnology and biomedical applications [38]. Recent research has investigated the role of fucoidans in the biosynthesis of metalnanoparticles, cancer treatment and drug delivery. Synthesis and characterization of fucoidan-coated poly (isobutylcyanoacrylate) nanoparticles was reported by Lia et al. [51]. Polymerization and redox radical emulsion polymerization were used to prepare of isobutylcyanoacrylate using fucoidan as a novel coating biomaterial. These nanoparticles exhibit potential in vitro cytotoxic effect against different fibroblast cell lines. Nanoparticles

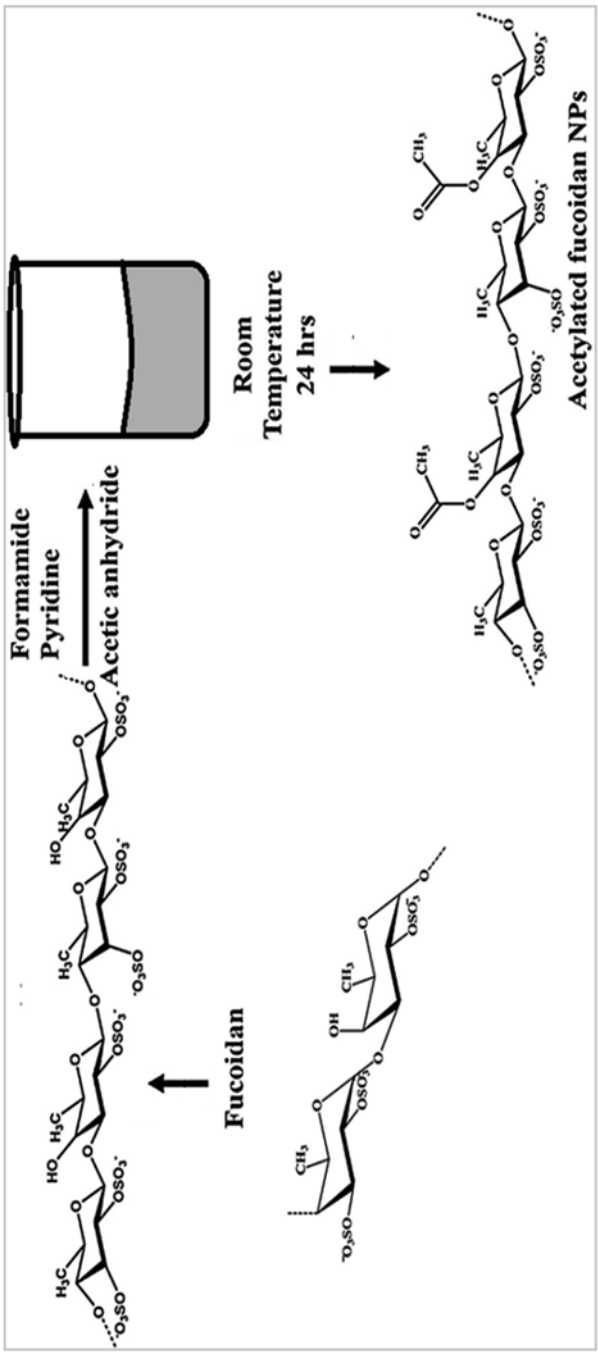



**Fig. 5.4** Synthesis of acetylated fucoidan NPs from natural fucoidan

**Table 5.3** Various advancement and applications of fucodain in nanoparicle drug delivery [38–46]

| Polysaccharides | Modifications | Nanoaprticles | Drug delivery applications |
|---|---|---|---|
| Fucodain | Oversulphated, acetylated and benzoylated fucoidan<br>Phosphorylated and aminated derivatives offucoidan<br>Radical degradation<br>Polyethylene terephthalate (PET) polymer surface attachment<br>Fucosidase,enzyme degradation and microvate associated degradation<br>Degraded fucoidans were coupled with several hydrophobic groups (oligofucose-dodecylaniline combination) | Cytotoxicity and fucoidan-coated nanoparticles<br>Stromal cell-derived factor-1 released from chitosan/ tripolyphosphate/ fucoidan nanoparticles<br>Carboxymethylated-curdlan and fucoidan<br>Green synthesis of silver nanoparticles<br>Chitosan/Fucoidan pH Sensitive Nanoparticles<br>Fucoidan-Stabilized Gold Nanoparticles | Suppressive effect of fucoidan on an attachment of Cryptosporidium parvum<br>Fucoidan cures infection with both antimony-susceptible and -resistant strains of Leishmania donovani<br>Growth-inhibitory effect of a fucoidan<br>On Plasmodium parasites<br>Asexual growth inhibiton of Babesia bovis |

prepared by anionic emulsion polymerization nanoparticles showed $IC_{50}$ at 2 g/mL. As far as the sources are concerned fucoidans are derived from various sources two of marine algae such as *Cladosiphon okamuranus* and Kjellamaniellacrassifolia. Recent research showed its potential application in green synthesis of gold nanoparticles [52]. Previous findings on production of silver nanoparticles using carboxymethylated curdlan or fucoidan as reducing and stabilizing agents has opened gateway for the synthesis of metallic nanoparticles [39]. C. okamuranus derived fucoidan encapsulated in nanoparticles using liposomes as nanocarriers showed potential in vitro anticancer activity against osteosarcoma [53]. It was observed that hydrophobically modified fucoidan (synthesized by the acetylation of fucoidan) was required to prepare the chemotherapeutic agent loaded nanoparticles e.g. acetylated fucoidan nanoparticles was used to encapsulate Doxorubicin.

### *5.3.2 Alginate Nanoparticles*

Owing to excellent properties such as low cost, low toxicity, biocompatibility and mild gelation, alginate 'a natural polysaccharide' derived from brown seaweeds has been widely investigated and used for biomedical applications [54]. Previous findings have explored various functionalization and modification steps for alginate to yield modified alginate with improved physic-chemical and biological properties (Fig. 5.5). Current research on alginate-based nanoparticles offers various

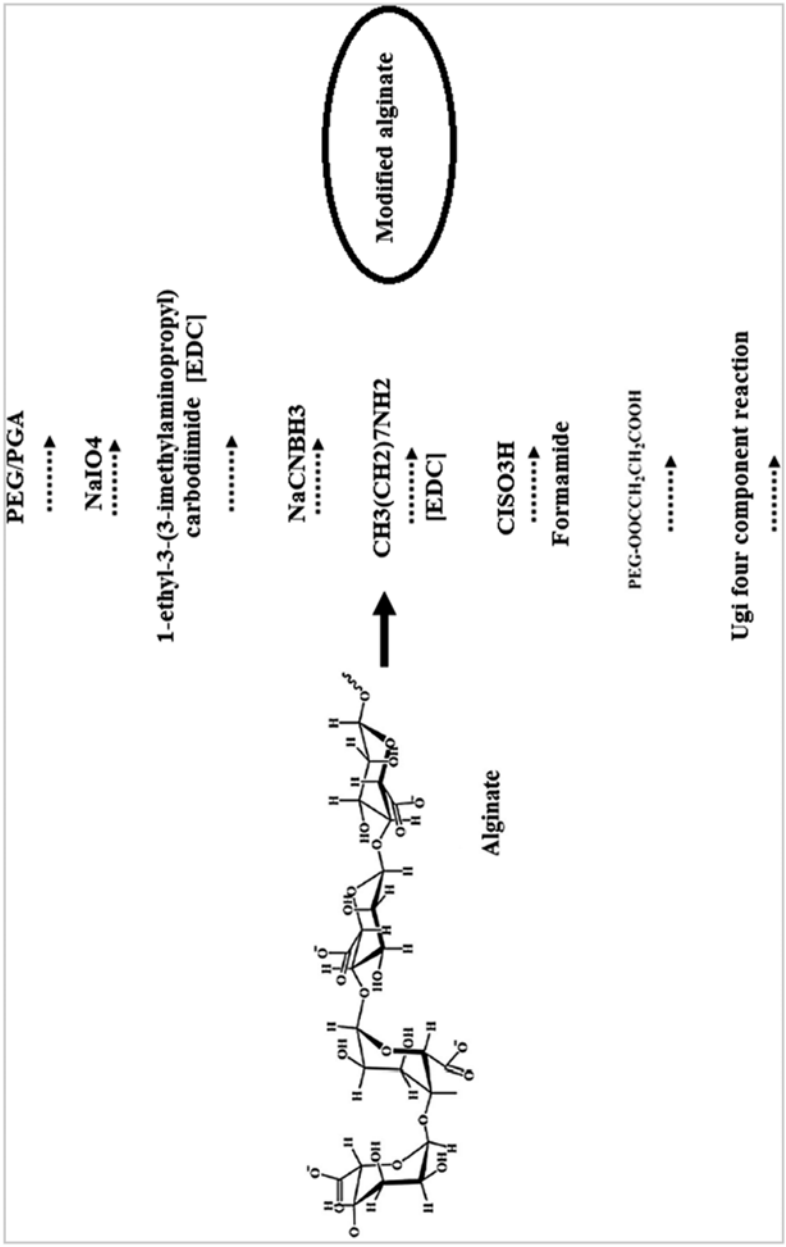



**Fig. 5.5** Various functionalization and modification steps recently explored to yield modified alginate

applications in insulin delivery [55] and antifungal and antitubercular drugs [56]. Alginate based nanoparticles have raised greater interest in the medical field e.g. [55] insulin-loaded nanoparticles using alginate ionotropic pre-gelation followed by CS polyelectrolyte complexation. This has proven the elastic nature of alginate to hold and shield drug by polyelectrolyte complexation with chitosan. During this study it was observed that insulin-loaded nanoparticles using alginate showed loading capacity of 14.3 %. Similarly loading of insulin in alginate–dextran nanospheres through nanoemulsion dispersion resulted in increase in encapsulation efficiency up to 82.5 %. Various methods like irradiation method was also reported for the preparation of gold nanoparticles using alginate as a stabilizer. Utilization of effective methods such as irradiation method for the preparation of gold nanoparticles using alginate as astabilizer was also reported. During this study it was observed that irradiation technique is suitable for the production of alginate-stabilized gold nanoparticles with controllable size and high purity. This technique yields alginate-stabilized gold nanoparticles which are spherical in nature having particle size ranging from 5 to 40 nm [57]. Recently hydrothermal synthesis of silver nanoparticles using sodium alginate as a reducing and stabilizing agent was studied by Yang and Pan [58]. During this study it was observed that incubation time and temperature of the reaction played an important role under suitable effective sodium alginate concentrations and $Ag^{+}$ precursor in the development of silver nanoparticles with desirable shapes. So generally triggering the temperature and incubation time of reaction were favorable for the formation of nanoplates whereas low temperature and short incubation time of reaction were shown to result in the formation of nanospheres. In one report the role of alginate in DOX-loaded glycyrrhetinic acid-modified alginate nanoparticles was suggested by determining liver-targeting efficiency, and antitumor activity. It was observed that nanoparticles showed strong liver-targeting efficiency, reduced cardiac toxicity and improved antitumor activity of DOX against liver tumors [59, 60]. One of the major causes of therapeutic failure of antituberculosis medicines is patient non-compliance. This happens due to the multidrug administration for at least 6 months. Delivery systems such as nano formulations are more suitable for co-bacterial infections (such as tuberculosis) [61]. An alginate-encapsulated anti-tubercular drugs such as isoniazid, rifampicin, pyrazinamide, and ethambutol was studied by Ahmad et al. [62]. During their oral administered to mice it was observed that all the encapsulated drugs in nano forms showed better antitubercular effects. Additionally these nanoparticles showed high encapsulation efficiency with average particle size. Various nanoparticle applications and its recent modification/functionalization of alginate are mentioned in Table 5.4.

### *5.3.3 Carrageenan Based Nanoparticles*

Red algae such as Kappaphycus sp. and Eucheuma sp are the chief source of carrageenan. This natural polymer is having D-galactose and anhydro-galactose units joined by glycosidic linkages and ester sulfate groups. Carrageenan on the basis of

**Table 5.4** Alginate modifications and its recent nanparticulate forms [57, 63–124]

| Polymer | Modification | Nano applications | Drug delivery applications |
|---|---|---|---|
| Aliginate | • Modification of hydroxyl groups of alginate include oxidation, reductive-amination, sulfation, copolymerization and coupling of cyclodextrin units<br>• Methods used for modification of carboxyl groups include esterification, use of the Ugi reaction, and amidation.<br>• Surface modification of sphalerite with sodium alginate<br>• Degradation by epimerases<br>• Ionotropic gelation of sodium alginate using N,N′-methylenebisacrylamide and carboxy-methylcellulose<br>• Covalent modification of alginate with polyethylene glycol–conjugated anthracene molecules has the potential to both stabilize the alginate and act as a photosensitive crosslinker<br>• Chemoselective cross-linking of alginate with thiol-terminated peptides for tissue engineering applications<br>• Modification of alginate through partial crosslinking with a matrix metalloproteinase (MMP)<br>• By simple covalent modifications<br>• Novel crosslinking reagent (alginate dialdehyde) for biological tissue fixation<br>• Thermo-sensitive alginate-based injectable hydrogel for tissue engineering<br>• Alginate dialdehyde for biological tissue fixation<br>• Modification of alginate by grafting of N-vinyl-2-pyrrolidone<br>• The effects of peptide-based modification of alginate<br>• Modification of alginate through the grafting of 2-acrylamidoglycolic acid<br>• Effect of gamma radiation on the physico-chemical properties of alginate<br>• Hydrophobically modified alginate<br>• Modification of alginate degradation properties using orthosilicic acid<br>• Calcium alginate<br>• Sodium alginate sulfates<br>• Modification of PVA–alginate as a suitable immobilization matrix | • Alginate/Chitosan nanoparticles<br>• Insulin-loaded alginate nanoparticles<br>• Chitosan/alginate nanoparticles encapsulating antisense oligonucleotides<br>• Alginate–AgNPs composite sponge<br>• Paraquat-loaded alginate/chitosan nanoparticles<br>• Chitosan or N-trimethyl chitosan and a cisplatin–alginate complex NPs<br>• Superparamagnetic iron oxide nanoparticles stabilized by alginate<br>• Thiolated alginate-albumin nanoparticles<br>• Silica/alginate nanoparticles as Hybrid Magnetic Carriers<br>• Magnetite nanoparticles,<br>• Alginate–quaternary ammonium NPs<br>• Alginate stabilized gold nanoparticles,<br>• Silica/alginate nanoparticles as Hybrid Magnetic Carriers<br>• Lipid nanoparticles into calcium alginate beads<br>• Chitosan–sodium alginate microcapsules containing ZnS nanoparticles<br>• Maghemite nanoparticles for Pb(II) removal in aqueous solution<br>• Inhalable alginate nanoparticles<br>• Superparamagnetic iron oxide nanoparticles stabilized by alginate<br>• Layer by layer chitosan/alginate coatings on poly(lactide-co-glycolide) nanoparticles<br>• Barium alginate caged Fe3O4@C18 magnetic nanoparticles<br>• Alginate/Fe@Fe3O4 core/shell structured nanoparticles<br>• Multifunctional alginate microspheres<br>• Curcumin in alginate-chitosan-pluronic composite nanoparticles | Aliginate based leishmani vaccine<br>Alginate-Capped Amphotericin B Lipid Nanoconstructs Against Visceral Leishmaniasis<br>Acyclovir-loaded alginate mucoadhesive microspheres |

extraction procedures and resources is further classified in to three types kappa, iota, and lambda (Fig. 5.6). Major difference between these types is that they all having sulphur group which is differing in the substitution degree. From gelling point of view, kappa and iota show high gelling efficiency whereas delta carrageenan is a non gelling polysaccharide [125]. Among these kappa carrageenan is rigid and firm whereas iota carrageenan elastic and soft in nature [126]. Using these all types Daniel-da-Silva et al. [127] studied the biosynthesis of magnetite nanoparticles and examined for their particle size morphology and chemical stability. Carrageenan has various applications in nanotechnological, biological and pharmaceutical field (Table 5.5). Additionally carrageenan also exhibit various food and non-food applications. Six types of sulfated polysaccharides from marine brown and red seaweeds was isolated and investigated for their respective antioxidant activities by DeSouza et al. [128]. It was observed that carrageenan and fucoidan exhibit strong antioxidant activity. In an another study inhibitory effects of delta carrageenan and a mixture of sulfated polysaccharides derived from red seaweeds against feline herpesvirus-1 under in-vitro was investigated [129]. Delta-carrageenan showed $IC_{50}$ 5 μg/mL against feline herpes virus -1. Carrageenan and chitosan nanoparticles were investigated by Grenha et al. [130]. These nanoparticles were produced by hydrophilic conditions using very mild protocol and preventing the use of organic solvents and other intensive chemical conditions. This protocol yields suitable nanoparticles that can present sustained and controlled form of drug delivery system and can be treated as excellent candidates for biomedical applications. Additionally it has been studied that these nanoparticles were proved for their low toxicity against fibroblast cell lines as well as superior biocompatibility and high

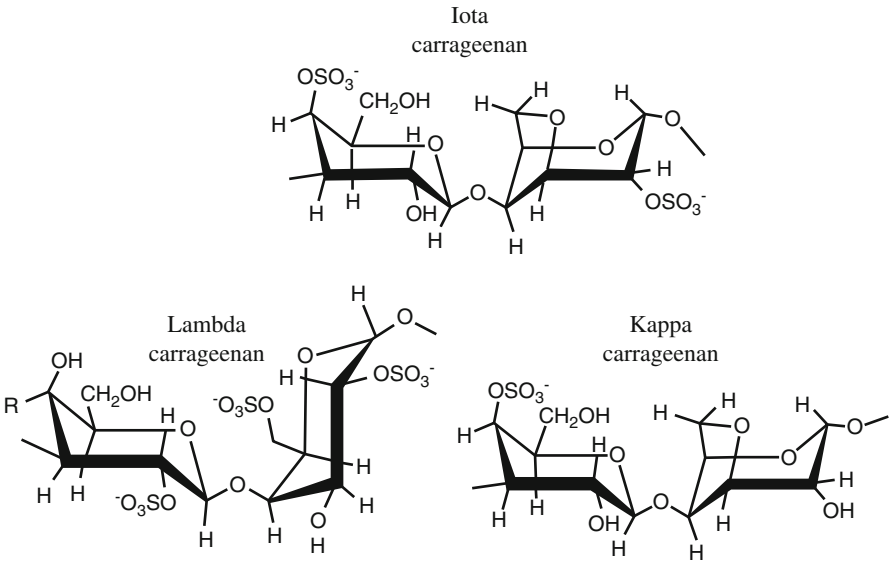



**Fig. 5.6** Types of carrageenan

**Table 5.5** Marine organisms derived sulfated polysaccharides with nanotechnological, biological and pharmaceutical applications

| Type of SPS | Nanotechnology application | Biological and pharmaceutical applications |
|---|---|---|
| Carrageenans | Capping agent for biomineralizing metal oxides<br>Composite gels<br>Composite nanoparticles<br>Drug encapsulation and delivery<br>Gelling agent<br>Hydrogels<br>Microbeads for controlled release<br>Stabilizing agent<br>Stabilizing micelles<br>Thickening agent | Anti-coagulant activity<br>Anti-oxidant activity<br>Anti-viral activity<br>Free radical scavenging activity<br>Microbicidal activity<br>Prevention of sexually transmitted diseases<br>Vaginal gel formulation |
| Fucoidans | Stabilizing agent<br>Fucospheres or microspheres | Anti-angiogenic activity<br>Anti-coagulant activity<br>Anti-inflammatory activity<br>Anti-oxidant activity<br>Anti-proliferative activity<br>Anti-tumor activity<br>Anti-viral activity<br>Immunomodulating property<br>Treating dermal burns in rabbit |
| Ulvan | Nanofibrous scaffolds | Resist attack of necrotic pathogens in plants<br>Antifungal activity |

safety. CS, carrageenan, and cross linking agent tripolyphosphate based nanoparticles was investigated by Rodrigues et al. [131] for their stability smaller size and strong positive surface. In this study prepared nanoparticles were used for purpose in mucosal delivery of macromolecules. Metallic nanoparticles for gastrointestinal release using modified kappa-carrageenan was investigated to study the effect of genipin cross-linking and it was proved that metallic nanoparticles seem significantly improve gastrointestinaltract-controlled drug delivery [132]. Salgueiro et al. [133] studied the influence of introducing spherical and rod-shaped gold nanoparticles in the microstructure and thermomechanical properties of delta-carrageenan hydrogels. Moreover he has also investigated the effect of these nanoparticles in the release kinetics and mechanism of methylene blue from kappa-carrageenan nanocomposites. It was observed that hydrogel nanocomposites demonstrated enhanced viscoelastic properties in contrast with neat kappa-carrageenan, at the time they used with either with gold nanospheres and gold nanorods.

### *5.3.4 Agarose Nanoparticles*

3,6 anhydro galactose based natural polymer known as Agarose (Fig. 5.7) derived from red seaweeds, *Gracilaria sp*. and *Gelidium sp*. This 3,6 anhydro galactose based natural polymer is a linear polysaccharide made up of repeating units of

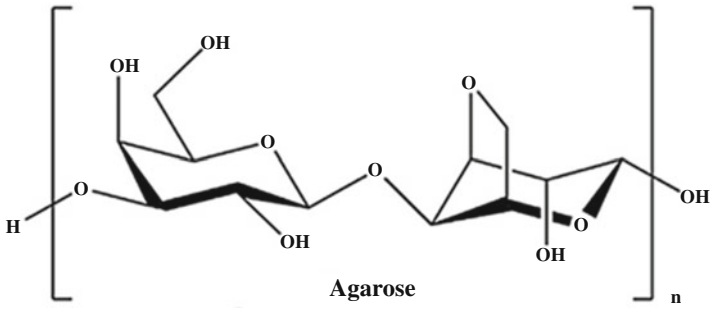



**Fig. 5.7** Structure of agarose

agarobiose, which is a disaccharide made up of D-galactose. Agarose is having various applications in biotechnology biochemistry and molecular biology field especially in different types of electrophoresis techniques (for the separation of nucleic acids). This red seaweed derived polysaccharide usually used for its gel-forming property to create semiconductor and metal nanoparticles. It was observed that this type of nanoparticle exhibit strong antibacterial activity against *Escherichia coli*. It has been also discovered that the agarose composite films can be rapidly transformed to carbon metal composites by carbonizing the films in nitrogen atmosphere [134]. Previous finding suggested the application of agarose-stabilized gold nanoparticles for the detection of micromolar concentrations of DNA nucleosides via surface-enhanced Raman spectroscopic detection [135]. Results suggested that agarose-stabilized goldnanoparticles yield higher surface-enhanced Raman spectroscopic detection for DNA nucleosides, which is used for on-chip biosensing applications.

### *5.3.5 Porphyran Based Nanoparticles*

Porphyran (Fig. 5.8) 3,6-anhydro galactose is a natural sulphated polysaccharides obtained from marine red seaweed, *Porphyra vietnamensis* [136]. Porphyran is a hot-water-soluble fraction of the cell wall having the similar characteristics like agar. It is the major constituent (40–50 %) of the marine *P. vietnamensis* and has nutritional value. It's a anionic disaccharide units consisting of 3-linked D-galactosyl residues alternating with 4-linked 3,6-anhydro-L-galactose and 6-sulfate residues. Porphyran can be extracted from various species of *Porphyra* and having some important pharmaceutical properties reported in various structural and functional studies.

Bhatia et al 2009 described biological properties emphasizing the role of porphyran in pharmaceutical world [137–143]. Bhatia et al (2010) demonstrated the structure based gelling and emulsifying properties of porphyran. Molecular weight based antioxidant property of porphyran was described by Bhatia et al. (2011) [137–143]. Further molecular weight dependent potential immunomodalation

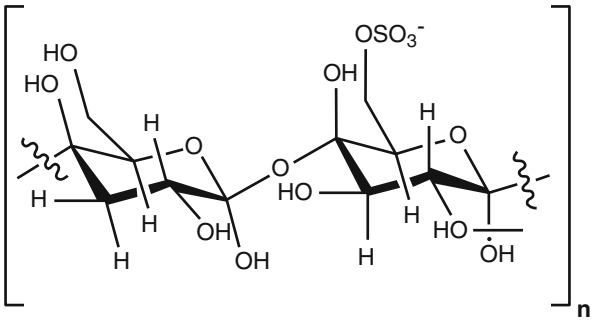



**Fig. 5.8** Structure of Porphyran

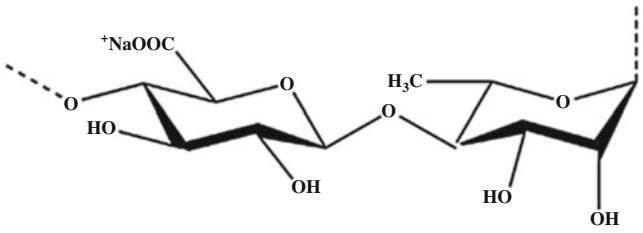
effect of porphyran was investigated by Bhatia et al. (2013). Porphyran molecular weight was modified and immunomodulation effects of modified and natural sample were investigated [137–143]. It was observed that alkali treated sample showed better immunomdulation effects then natural one. Bhatia et al. (2013) has examined the role of porphyran in development of oral amphotericin B loaded nanoparticles to reduce its toxicity and other associated problems [137–143]. In this study Amphotericin B was packed between two oppositely charged ions (chitosan and porphyran) by polyelectrolyte complexation technique with TPP as a crosslinking agent. Formulation was optimized using three-factor three-level (33) central composite design. High concentration of POR in NPs was confirmed by sulfated polysaccharide assay [137–143]. Degradation and dissolution studies suggested the stability of NPs over wide pH range. Hemolytic toxicity data suggested the safety of prepared formulation. In vivo and in vitro antifungal activity data suggested the high antifungal potential of optimized formulation when compared with standard drug and marketed formulations. Hence, these experimental oral NPs may represent an interesting carrier system for the delivery of AmB. Bhatia et al. (2015) investigated the factors influencing the molecular weight of porphyran and its associated antifungal activity. During this study various extraction methodologies have been employed to derive porphyran from high tide and low tide samples of *P. vietnamensis*. Results suggested that *P. vietnamensis* collected during low tide yields high percentage of porphyran with relatively low molecular weight and high sulfate content than the high tide sample. Among various extraction methodologies alkali modified POR yield slow molecular weight polysaccharide but surprisingly with high sulfate content which have shown improved physico-chemical and antifungal properties than chitosan without any toxicological affects. Bhatia et al. (2015) has established the relationship between structural features and pharmaceutical properties of porphyran [137–143]. This polysaccharide exhibit molecular weight dependent activity as highlighted in reports on the anticancer and antioxidant activities of porphyran [144]. Biosynthesis of gold nanoparticles using a porphyran and subsequent loading of Doxorubicin was investigated [145]. Toxicological data of porphyran-reduced gold nanoparticles was performed on normal monkey kidney cell line, which showed a non-toxic nature of nanoparticles [146].

### 5.3.6 *Nanofibers of Ulvan*

Ulvan (Fig. 5.9) is obtained from the cell walls of marine green algae (Ulvales, Chloro-phyta). It's a complex anionic sulfated polysaccharide contains sulfated, xylose, rhamnose, glucuronic, and iduronicacids. Ulvan is abundantly present in green algae especially Ulva rigida and have a low cost of production. These polysaccharides are still under-exploited and have been investigated as an antitumor, anticoagulant, antioxidant, and immune modulator [15]. Current utilization of ulvan in nanotechnology is especially towards preparation of nanofibers with the special interest in the biomedical engineering field because of their potential applications in tissue engineering, drug delivery and wound dressing. Due to some physicochemical and biological properties ulvan becomes good candidate for nanofiber production and has been successfully explored into nanobiotechnology for presenting novel promising biomaterials in biomedical applications, including drug delivery systems, wound dressing, and tissue engineering. Earlier report suggested that spinnability of *U. rigida* based polysaccharide can be used for the fabrication of nanofibers which imply that spinnability plays an important role in improving the properties of ulvan [147].

### 5.3.7 *Mauran Based Nanoparticles*

Just like other sulphated polysaccharides, mauran is *Halomonas maura* (halophilic bacterium) derived sulfated polysaccharide with high sulfate, phosphate, and uronic acid content. Moreover it has been also reported that mauran constitute mannose, glucose, galactose, and glucuronic acid. Recent research has explored the utilization of mauran for the biosynthesis of metal nanoparticles and their well known viscoelastic properties. Previous finding suggested the role of sulfated polysaccharide-based nanoparticles as a good biocompatible material for bioimaging, drug delivery and anticancer activity [1]. Additionally thixotropic and pseudoplastic properties of mauran make it a supreme molecule for material science applications [148].




**Ulvan**

**Fig. 5.9** Structure of Ulvan

### 5.3.8 Chitin and Its Nanoparticles

Chitin (Fig. 5.10) is one of the abundantly present biopolymer in nature [149], isolated from the various marine sources crab, shrimp, and lobster shells and their by-product in the seafood industry. Million tons of chitin per annum generated as waste by the seafood industry [150]. There are several methods involved in the production of chitin such as enzymatic methods, hydrolytic methods using boiling HCl and methods applied using chitin whiskers. Various applications of chitin in nanoscience are mentioned in Table 5.6.

### 5.3.9 Chitosan Based Nanoparticles

Chitosan is a naturally occurring linear polysaccharide which is composed of glucosamine and N-acetylglucosamine units via β-(1 → 4) linkages. These linkages are randomly or block-spread all over the polymer chain. Arrangement or distribution of these linkages is dependent on the extraction procedures to derive chitosan from chitin. Degree of deacetylation is known as the parameter that define molar ratio of glucosamine to N-acetyl glucosamine. Degree of deacetylation significantly determines the physicochemical properties and industrial applications of chitosan [126]. Once the chitosan get deactylated it can be easily dissolved in an acidic medium and develop into the only sulfated polysaccharide that possesses a

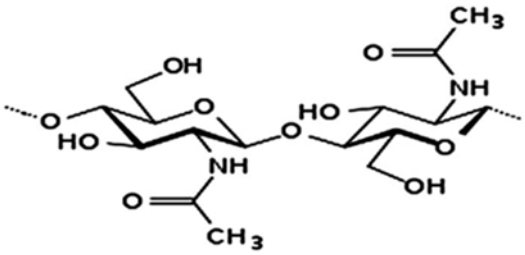



**Fig. 5.10** Structure features of chitin and chitosan

**Table 5.6** Chitin and its nano-applications

| Type of chitin | Method | NPs | Applications | Uses/benefits | References |
|---|---|---|---|---|---|
| Chitin | Ion cross linking agent | Chitin NPs | Reinforcing fillers in polymeric matrices | | [151] |
| Carboxy-methyl chitin | – | CMC NPs | Wound-healing dressings, exhibits good bio-compatibility | Nontoxic, water-soluble anionic derivative | [152] |
| Carboxymethyl chitin | Cross-linking approach with $FeCl_3$ & $CaCl_2$ | CMC NPs | Controlled drug delivery applications, in vitro cyto-toxicactivity against mouse L929 cell lines, NPs showed strong antibacterial activity against Staphylococcus. | Nontoxic, water-soluble anionic derivative | [153] |
| Amorphous chitin | Ionic cross-linking approach using pentasodium tripolyphosphate | Paclitaxel loaded amorphous chitin nanoparticles | For colon cancer drug delivery | Hemo-compatible & in vitro drug release exhibited a sustained release, enhanced efficacy | [154] |
| Amorphous chitin | Ionic cross-linking | Rifampicin-loaded amorphous chitin | Intracellular delivery of rifampicin inside polymorphonuclear leukocytes, anti-bacterial activity | Sustained drug delivery could reduce dosing frequency, lower toxicity, enable long-term treatment, & prevent potential side effects related to the free drug | [155] |

high density of positive charges. This positive charge is due to the protonation of amino groups on its backbone. In addition to its unique features chitosan has been reported to have various other essential properties such as good biocompatibility and biodegradability and non-toxicity [156]. There are different protocol reported for the preparation of various derivatives of chitosan (Figs. 5.11 and 5.12). Currently chitosan has offered significant applications (Table 5.7) in nanotechnological area especially in biomedical sector such as drug delivery [168], nutrition [169], and tissue engineering [170].

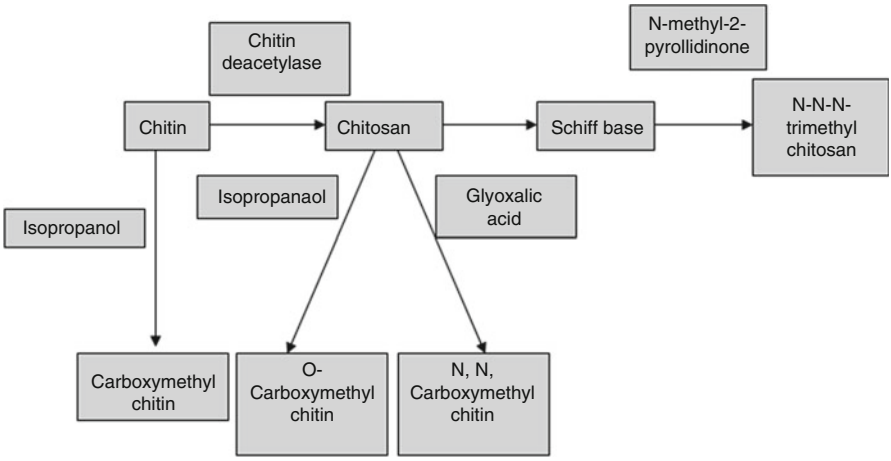



**Fig. 5.11** Steps involved in the chemical modification of chitin/chitosan

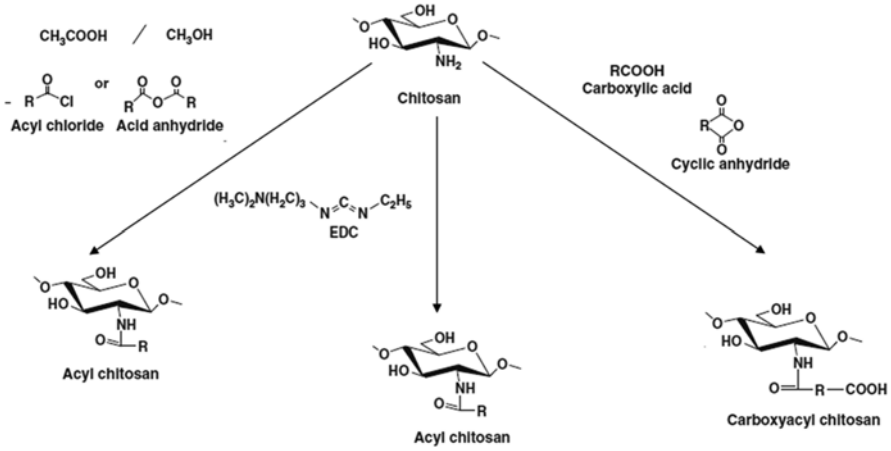



**Fig. 5.12** Protocol for the preparation of various chitosan derivatives

**Table 5.7** Applications of chitosan nanoparticles

| NPs type | Method | Model drug | Application | References |
|---|---|---|---|---|
| CS- and CS-gold nanoconjugates | Ionic gelation method | Salmon leutinizing hormone releasing hormone | Showed considerable reproductive efficacy in female fish (Cyprinus carpio) | [157] |
| CS-dextran sulfate NPs | Ionic gelation method | Doxorubicin | Anticancer activity (increase cytotoxicity activity) | [158] |
| Dextran-DOX encapsulated in CS nanoparticles | Reverse micro-emulsion | Doxorubicin | Improved antitumor activity in murine tumor models | [159] |
| CS NPs | | Immuno-suppressive peptide cyclosporin A | Targeted delivery of drugs to the ocular mucosa, | [160] |
| CS NPs cross-linked- glutaraldehyde | AOT/n hexane reversemicellar system | – | Particle size of CS NPs was mainly influenced by the degree of cross-linking | [161] |
| CS NPs Cu-loaded CS NPs | | Copper | Anti-antibacterial activity against pathogenic microorganisms | [162] |
| CS–TPP-NPs | polyanion-initiated elation | gene or protein macromolecules | Delivery of gene or protein macromolecules | [163] |
| CS NPs | Ionic gelation method | siRNA | Good vehicles for siRNA delivery | [164] |
| CS–TPP-NPs | Ionic gelation method | siRNA | CS–TPP-NPs proved as good vehicles for siRNA delivery then CS NPs | [165] |
| Hydrophobically modified glycol chitosan NPs | | Camptothecin | Substantial enhancement of antitumor activity | [165] |
| CS and silver-loaded CS NPs | | Silver | Antimicrobial textile applications, silver-loaded CS NPs exhibited synergistic antibacterial activity | [166] |
| CS NPs | Blank | | Hemolytic activity | [167] |

**Table 5.8** Various applications of COS nanoparticles

| Nanoparticles (NPs) | Applications/advantages | References |
|---|---|---|
| Hydrophobically modified amphiphilic COS derivatives for self-assembled polymeric NPs | Drug delivery in cancer therapy by improving the solubility of insoluble drugs, drug targeting, and absorption | [172] |
| Iron oxide loaded magnetic COS NPs | Colloidally stable in water and buffer & attractive for biomedical applications | [173] |
| CS oligosaccharide-stabilized ferri-magnetic iron oxide nanocubes | Efficient heat nano-mediator for cancer hyperthermia & exhibited strong antitumor activity without toxicity. | [174] |
| Multidentate dithiolanelipoic acid and phosphorylcholine conjugated CS oligosaccharide derivative to stabilize gold NPs | Used for bio-logical various applications | [175] |
| COS NPs polyelectrolyte complexes | Showed strong inhibition of the proliferation of HeLa & B16 melanoma cells. | [176] |
| COS-based multidentate NPs | Ultrastable, cytotoxicity & biocompatible | [177] |

### *5.3.10 Chitooligosaccharide Based Nanoparticles*

Chitooligosaccharide is low molecular weight polymer obtained by depolymerization of CS and offers various superior features such as biocompatiblity, water-solublity, biodegradablity and nontoxicity in nature. Chitosan has various applications in biomedical and pharmaceutical sectors and also exhibit unique biological activities such as immune-enhancing, antimicrobial, and antitumor activities. Recently this oligosaccharide is exploited for its polymer-drug conjugate applications. This is because of its accessibility for coupling with the primary amino groups and hydroxyl groups of each polymer subunit. Further the cationic nature of COS allows ionic crosslinking [171]. Different applications of COS are mentioned in Table 5.8.

## 5.4 Marine Polysaccharide-Based Nanomaterials and Its Biomedical and Biotechnological Applications

Marine polysaccharides especially algal polysaccharides based nanomaterials are considered as nanomedicine offering high possibilities for diagnosis and therapeutical applications. Current researches on these nanomaterails have attracted attention of all the researchers in the field of biotechnological and biomedical science [178]. Current researchers are working on the structural features of these polysaccharides to synthesize more potential derivatives that are suitable for various applications. Recent innovations in polymeric sciences lead to the production of potential lower molecular weight oligosaccharide derivatives which have shown to possess a

variety of biomedical applications. We have traced some of the important nanobiotechnological applications of these biopolymer based nanomaterials in the field of antimicrobial activity, drug delivery, gene delivery, tissue engineering, cancer therapy, wound dressing biosensors, and water treatment.

## *5.4.1 Biomedical Applications of Marine Polysaccharides*

### 5.4.1.1 Antimicrobial Activity

Marine organism has their potential antimicrobial activities since they live in such a dampish environment where moisture promotes the growth of microorganisms. Such type of organisms are usually found on intertidal zone. Antimicrobial therapy has been evolved in recent years with development of more resistance of pathogenic microorganisms against different types of antimicrobial agents. Prevailing resistance of many infectious microorganisms contributes a serious problem in clinical practice, therefore limits the development of novel drugs to fight against them [179]. Explorations of those substances which can prevent the development of resistant pathogenic species of microorganisms are more preferred nowadays. Potential effects of certain inorganic agents have been recently explored and it was found that these candidates can act effectively against resistant strains of microorganisms [180]. Among these candidates, silver compounds and their derivatives are extensively studied for antimicrobial activity. Moreover recent research is exploring these compounds and their derivatives in form of nanoparticles using marine polysaccharides as biopolymer, to enhance their antimicrobial potential more effectively [181, 182]. A report suggested the role of agar as biopolymer (derived from the red alga *Gracilaria dura*) in the synthesis of silver nanoparticles and nanocomposite material [182]. It was found that these silver loaded NPs showed potential antibacterial effect with 99.9 % reduction of bacteria over the control value. These types of nanocomposites may considered as effective antibacterial activity and may offer various applications in food preservation and wound dressing. Previous finding on green synthesis of silver nanoparticles using marine polysaccharide derived from red algae, *P. vietnamensis* suggested the dose-dependent effect of biosynthesized silver nanoparticles. This report has explored the effective anti-bacterial activity against Gram-negative bacteria compared with Gram-positive bacteria [183].

### 5.4.1.2 Marine Based Nanomaterials and Its Drug Delivery Applications

Development in nano-biotechnology allows the medicines to be administered in a more convenient and safe way. This can be achieved by the development of more efficient and advance drug delivery systems to diagnose, cure or to treat any disorder. Current research is more emphasizing on the safe and targeted delivery of many bioactive compounds for cancer treatment. Innovations in biomedical sciences are paying attention towards nanomaterials for reducing dosing frequency, their

**Table 5.9** Applications of algal based NPs in drug delivery system (DDS)

| Nanoparticles (NPs) | Applications in DDS | References |
|---|---|---|
| CS NPs | As novel drug delivery system for the ocular mucosa | [185] |
| CS NPs | Topical ocular route drug delivery system | [186] |
| DOX-loadedgold NPs using porphyran | Strong cytotoxicity on LN-229 cell line | [187] |
| Berberine-loaded CS/Fucodain–taurine complex NPs | Oral delivery of berberine (Ber). | [187] |

toxicity, and avoiding potential side effects however they do not recognize that delivery systems themselves may impose risks to the patient [184]. Various applications of algal based polysaccharides are mentioned in Table 5.9.

#### 5.4.1.3 Genetic Transformation

Developments in biotechnology endow different alternatives to treat the disease e.g. gene therapy can be utilized for correcting genetic disorders by use of genes itself. Genetic transformation can be successfully achieved by plasmid DNA. In this process plasmid DNA which carries gene of interest is introduced into the target cells. The introduced plasmid DNA should get transcribed and further the genetic information should finally be translated into the respective protein. There are number of obstacles to be overcome by the gene delivery device during this genetic transformation [171]. According to current research nucleic acids are being functionally utilized for both vaccination and therapeutic gene expression and chitosan nanoparticles have been suggested as promising non viral gene carriers. Chitosan-alginate NPs (core-shell structured) were fabricated using water-in-oil reverse microemulsion template and utilized to encapsulate a plasmid DNA for gene delivery through the cell endocytosis pathway [188]. Nevertheless it has been already reported that chitosan-DNA NPs can be easily fabricated by complex coacervation between the positively charged amine groups on CS and negatively charged phosphate groups on DNA [189]. Previous finding suggested that CS nanoparticles can potentially provide protection to encapsulated plasmid DNA from *nuclease* attack. This was established by evaluating degradation in the presence of *DNase* I. Further the incorporation of the plasmids with incubated nanoparticles was investigated by *galactosidase* assay. Plasmid DNA based model present as combination of both supercoiled and open circular forms. Utilization of si-RNA as a significant therapeutic agent for the management of several diseases is inadequate due to its rapid degradation and low intracellular organization in vitro and in vivo. Recent report suggested the role of chitosan–polyguluronate NPs in delivering siRNA to HEK 293 FTand HeLa cells [190]. To transport siRNA into cells, chitosan–polyguluronate NPs have a great promise and exhibit low cytotoxicity cells [190].

#### 5.4.1.4 Algal Polymers and Its Applications in Tissue Engineering

Algal polymers has their various applications in tissue engineering e.g. in the development of bio-artificial implants and/or promote modification in tissues with the objective of repairing, maintaining, replacing, or enhancing tissue or organ function. With the aid of bio-artificial constructs consisting living cells and biomaterials tissue engineering offers various applications in science and technology. According to report investigated by Noh et al. [191], cytocompatibility of etecrospinned chitin nanofibers for tissue engineering applications was established by cell attachment and spreading of normal human keratinocytes and fibroblasts. Similarly carboxymethyl chitin (CMC)/poly (vinyl alcohol) (PVA) blend was prepared by using electrospinning technique [192]. During this study it was observed that CMC/PVA scaffold supports cell adhesion/attachment and proliferation, and therefore, these scaffolds are useful for tissue engineering applications. CS–gelatin/nanophase hydroxyapatite composite scaffolds was developed by CS and gelatin with nanophasehydroxyapatite [193], exhibited well swelling characteristic, which could be modified by altering the quantity of chitosan and gelatin. Nanocomposite scaffolds showed superior response on MG-63 cells in terms og improved cell attachment, higher proliferation, and spreading than CS–gelatin scaffold.

#### 5.4.1.5 For Delivery of Anticancer Drugs

Cancer is a terrible human disease which when happens affects the immune system of whole body. One of the significant properties of nanomaterials is that they are highly preferable for parenteral injection of aqueous insoluble drugs. This property can be utilized for drug targeting applications because their particle sizes are less than 1000 nm. Potential anticancer drug like doxorubicin was incorporated in to nano-materials using methoxy poly (ethylene glycol)-grafted carboxymethyl chitosan nanoparticles to investigate antitumor activity. Possible interaction between these two ingredients was due to the presence of positive amine groups which lead to the formation of nanoparticles. These nanomaterials were tested against DOX-resistant C-6 glioma. It has been observed that these nanoparticles exhibited higher cytotoxicity to DOX alone [194]. In another finding it was reported that chitosan nanoparticles were utilized as carrier for the mitotic inhibitor paclitaxel. These nanoparticles were fabricated by a solvent evaporation and emulsification cross-linking method. It was observed that paclitaxel-loaded CS nanoparticles had higher cell toxicity than individual paclitaxel. Additionally confocal microscopy investigation confirmed strong cellular uptake efficiency [195]. Potential chemotherapeutic agent, doxorubicin was incorporated in to fucodain acetate to form nanoparticles. These nanoparticles were tested for immunotherapy and chemotherapy in cancer treatment. According to observation acetate nanoparticles showed important function in immunomodulation and drug efflux pump inhibition [196].

#### 5.4.1.6 Treatment of Infection and Wounds

According to current research antibacterial therapy-resistant pathogens is the most critical setback that requires more development in antimicrobial therapeutic agents in form of their formulation, delivery and physico-chemical properties. Advancement in this field lead to the development of newly designed wound dressing which has offered a main step forward for the treatment of infection and wounds. Current science is focusing on various strategies to develop novel therapies antibacterial agents to treat wounds infected with antibacterial treatment-resistant pathogens. Among the metallic nanoparticles silver nanoparticles are now become more effective bactericidal agents therefore exhibit various biomedical applications ranging from silver-based dressing to silver-coated therapeutic devices [197]. Various investigations are available on the utilization of chitosan scaffolds and membranes to treat patients with deep burns, wounds, etc. Electrospunned collagen-chitosan complex nanofibers were prepared by Chen et al. [198], showed positive effect on wound healing. Chitin scaffolds were utilized by Madhumathi et al. [21] for silver nanoparticles preparation. These nanoparticles showed effective wound-healing applications by showing antibacterial activity against pathogenic bacteria, with good blood-clotting ability. These outcomes proved that chitin/nanosilver composite scaffolds could be useful for wound-healing applications.

### *5.4.2 Role of Marine Based Polysaccharides for Biotechnological Applications*

#### 5.4.2.1 Biosensor Technology

Recent innovations in biosensor technology exploring its beneficial properties as analytical tools such as low cost, simple, portable, and laboratory-based well established method as well as allows miniaturization [199]. Several reports are available on chitosan nanofibrous membrane and its recent application in enzyme immobilization. Due to the favorable properties such as good biocompatibility, high surface, and large porosity of chitosan nanofibrous membrane has recently explored as better substrate for enzyme immobilization. The concentration of chitosan nanofibrous membrane that was utilized to immobilize lipase was 63.6 mg/g. Further the reported activity retention of the immobilized lipase was 49.8 % less than the optimum condition.

Developed chitosan based system can be used for biosensors [200]. According to previous investigation electrochemical tyrosinase biosensor showed good repeatability and stability. This electrochemical tyrosinase biosensor was used for determining phenolic compounds on the basic of the use of a glassy carbon electrode modified with tyrosinase-$Fe_3O_4$ magnetic nanoparticles-chitosan nanobiocomposite film. Such chitosan based novel tyrosinase biosensor offers wonderful applications for eco-friendly, fast and simple methods of phenolic contaminants in

ecological samples [201]. Amperometric biosensor was developed by Chauhan et al. [202] for the determination of glutathione by covalently immobilizing a glutathione oxidase onto the surface of gold-coated magnetic nanoparticles-modified Pt electrode. It was observed that glutathione oxidase/chitosan/gold-coated magnetic nanoparticles were an outstanding candidate for the production of extremely responsive glutathione biosensor.

#### 5.4.2.2 Waste Water Management

Current innovations in polymeric sciences lead to its exploration in waste water management. Owing to the presence of reactive amino groups chitosan is considered as potential candidate in waste water management. Chitosan and chitin both have been widely investigated for the removal of toxic elements such as heavy metal ions from waste water [203]. Chitosan bead-immobilized algae system with the association of *Scenedesmus* sp. was investigated for removing phosphate and nitrate from water and it was observed that this system was proved to be more efficient conventional free cell system [204]. Since waste contains large amount pathogenic bacteria, fungi, viruses, therefore efficient antimicrobial system is required to reduce chances of infections or any other disease. For these purpose silver nanoparticles using polysaccharide-based bioflocculant was developed by Manivasagan et al. [32]. These nanoparticles were synthesized using polysaccharide-based bioflocculant by *Streptomyces* sp. MBRC-91. Fabricated silver nanoparticles showed potential antibacterial activity in sewage water. Therefore these types of researches can make a new opportunity in the waste water management.

## 5.5 Marine Polysaccharide-Based Nanomaterials and Its Patents

There are almost fifty patents are existing on marine polysaccharides-based nanomaterials and their applications. Among these polysaccharides only few claimed that nanocomposite materials based on metallic nanoparticles were stabilized with branched polysaccharides. More specifically chitosan derivatives such as alditolic or aldonic monosaccharide and oligosaccharide and their products was obtainable with these polysaccharide sin the presence or absence of reducing agents claimed to be stabilized metallic nanoparticles in their matrix. In these studies polysaccharides applications were explored for antimicrobial activities and molecular biosensors by exploring their features associated with the nanometric dimensions and the presence of biological signals on polymeric chains [205]. Claimed protocol suggested that these polysaccharides based nanocomposite materials are present in the form of 3-dimensional structure. This structure is formed by a polymeric matrix consisting of a polysaccharidic composition of neutral or anionic polysaccharides and branched cationic polysaccharides. It has been claimed that metallic nanoparticles are homogeneously dispersed and stabilized in this 3-D matrix [206].

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