Marine Biological Macromolecules as Matrix Material for Biosensor fabrication

Namita Bedi[1], Dhaval Srivastava[1], Arti Srivastava[1], Supratim Mahapatra[2], Pranjal Chandra[2], and Ashutosh Srivastava[1]

[1]Amity University
[2]Indian Institute of Technology BHU Varanasi

January 17, 2022

Abstract

The Ocean covers two-third of our planet and has great biological heterogeneity. Marine organisms like algae, vertebrates, invertebrates, and microbes are known to provide many natural products with biological activities as well potent sources of biomaterials for therapeutic, biomedical, biosensors, and climate stabilization. Over the years, the field of biosensors have gained huge attention due to their extraordinary ability in providing early diseases diagnosis and treatment as well as environmental pollutants. This review focuses on various biomaterials (Carbohydrtae polymers, proteins, polyacids etc) of marine origin such as Alginate, Chitin, Chitosan, Fucoidan, Carrageenan, Chondroitin Sulfate (CS), Hyaluronic acid (HA), Collagen, marine pigments, marine nanoparticles, Hydroxyapatite (HAp), Biosilica, lectins, and marine whole cell. Further, it mentions the source of such marine biomaterials and their promising evolution for the development of biosensors that are potent to be employed in the biomedical, environmental science and agricultural sciences domains.

Marine Biological Macromolecules as Matrix Material for Biosensor fabrication Namita Bedi[1,] Dhaval Kumar Srivastava[1], Arti Srivastava[1], Supratim Mahapatra[2,] Pranjal Chandra[2], Ashutosh Srivastava[1,3*]

[1]Amity Institute of Biotechnology, Amity University Uttar Pradesh, Sector 125, Noida- INDIA

[2]Laboratory of Bio-Physio Sensors and Nanobiotechnology, School of Biochemical Engineering, Indian Institute of Technology (BHU) Varanasi, Varanasi, Uttar Pradesh, INDIA

[3]Amity Institute of Marine Science and Technology, Amity University Uttar Pradesh, Sector 125, Noida-INDIA

* Corresponding author: asrivastava4@amity.edu; Phone no: +91-120-4735688

AbstractThe Ocean covers two-third of our planet and has great biological heterogeneity. Marine organisms like algae, vertebrates, invertebrates, and microbes are known to provide many natural products with biological activities as well potent sources of biomaterials for therapeutic, biomedical, biosensors, and climate stabilization. Over the years, the field of biosensors have gained huge attention due to their extraordinary ability in providing early diseases diagnosis and treatment as well as environmental pollutants. This review focuses on various biomaterials (Carbohydrtae polymers, proteins, polyacids etc) of marine origin such as Alginate, Chitin, Chitosan, Fucoidan, Carrageenan, Chondroitin Sulfate (CS), Hyaluronic acid (HA), Collagen, marine pigments, marine nanoparticles, Hydroxyapatite (HAp), Biosilica, lectins, and marine whole cell. Further, it mentions the source of such marine biomaterials and their promising evolution for the development of biosensors that are potent to be employed in the biomedical, environmental science and agricultural

sciences domains.**Keywords-** Marine Biomaterials, Polysaccharides, Proteins, Biosensors, Biomedical and Environment

Introduction

Biomaterials can be defined as any material, engineered, or natural in origin, that can supplement human body parts partly to sustain the standard of human life. These biomaterials should be secure, dependable, inexpensive, and biologically suitable and should not link with the host's biological system. Synthetic materials are usually metallic, polymeric, and ceramic, or can be composite. These biomaterials are derived from marine microbes like fungi and bacteria, vertebrates like fish, mammals, and invertebrates like corals. Fish skin is a rich source of collagen and bone for hydroxyapatite (Boaventura, et al., 2020) Marine algae such as blue-green algae are reported as an excellent source of various polysaccharides, it includes alginate, chitin, chitosan, and fucoidan (Venkatesan et al., 2015). Studies have found that these marine biomaterials, such as surgery, tissue engineering, and medicaments, are frequently used for biomedical applications. Marine Biomaterials in accordance with chemical nature are categorized into six classes. (Figure 1).**Figure 1: Classification of Marine Biomaterials based on chemical nature**

1. Biomaterials from Marine sources

Marine organism's diversity offers a huge list of biomaterials with varied properties and characteristics for biological and biomedical applications. Different biomaterials from varied marine sources have been described in this review.

1.1. Marine polysaccharide

1.1.1. Alginate:

Alginates are components of the cell wall of seaweeds including*Laminaria, Macrocystis, Ascophyllum, Eclonia, Lessonia, Durvellia, Sargassum* as magnesium, calcium and sodium salts of alginate. These are anionic, nontoxic, biocompatible, biodegradable, polysaccharides with controlled porosity (Gomez et al., 2009). Algin is formed by copolymerization of β-D- mannuronate and α-1-guluronate (1-4')-linkage and gelation is affected by pH. Alginates drawn out from various sources have different lengths and varying compositions of monosaccharides. Purified alginates may be applied to form different structures like fibers, beads, hydrogels or films.

Alginate hydrogels are formed by various cross-linking associations of anionic and multivalent inorganic cationic alginates. Hydrogels have a structural resemblance to extracellular matrices of living tissues and are widely studied as a scaffold. The mechanical toughness of hydrogels helps in maintaining their structure in membranes, avoids breaking when in use, and after tissue adherence. Drug delivery through alginate hydrogels is pH sensitive and in acidic conditions, gel deters the drugs tight and in neutral conditions, carboxylic group on alginate deprotonates leading to network swelling and drug release (Silva et al., 2008). Some limitations of alginate hydrogels are low porosity, swelling, degradation, mechanical rigidity, cell attachment or detachment of bio-active molecule by physical or chemical modification. Alginate biomaterial has an application in the biomedical field (Rossi et al.,2018), tissue regeneration, wound healing (Campiglio et al., 2020), three dimensional (3D) printing (Wang et al., 2018), *in vitro* modeling (Chu et al., 2018), and biosensing (Sun et al., 2020) .

1.1.2 Chitin and Chitosan

It is the second plentiful polysaccharide associated with marine species. It is reported from the exoskeleton of *Arthropoda* , which includes *Arachnids* , *Myriapods* , *Crustaceans*(Bastiaens et al., 2019), Fungi, algae, protozoa, *Onychophora* ,*Entroprocta* (horseshoe worms), *Ectoprocta* (lamp shell),*Bryozoa* (Kaur & Dhillom, 2014), *Porifera* , *Mollusca*(Rahman & Halfar, 2014), and phylum *Cnidaria* (Bo et al., 2012). Chitin is acetylated polymer made by N-acetyl-d-glucosamine and chitosan is formed by chemical or enzymatic deacetylation of chitin (Verma & Fortunati, 2019). As per micro-fibril orientations of chitin, it has three different forms α-, β- and γ. Both the polymers are highly porous, biodegradable, biocompatible, structural dependable, non-toxic, chemically inert and less soluble.

Chitin and Chitosan's physiochemical and biochemical qualities provide ease for molding it into membranes, gels, beads and nanoparticles (Ifuku et al., 2009). Both are applicable in transducer surface modifiers, biosensors, drug and gene delivery, tissue engineering, stem cell technology, surgical dressings, and scaffolds (Elieh-Ali-Komi & Michael 2016). Polymeric scaffolds of chitin and chitosan are utilized successfully for tissue repair and regeneration. Nanosilver composite scaffolds of both are used for wound healing. They have an antibacterial activity and blood clotting ability as well (Madhumathi et al., 2009).

Chitosan combines with other materials like collagen or polyvinyl alcohol and improves its strength and cell attachment potential. In addition chitosan is capable to form tough hydrogel thin film, which can be used for electrodeposition on electrode surfaces for fabrication of micro and nano biosensors. Chitosan-derived immobilized matrices on a biosensor surface have shown excellent accuracy, selectivity and reliability for the recognition of a varied range of biomolecules (Jiang & Wu, 2019). Chitosan can be applied in the diagnostic, protein attachment in biological processes and surface adaptation of cells as well

1.1.3. Fucoidans

Fucoidan is a fucose-rich sulfated sugar present in the cell wall of a huge number of seaweed including *Fucus vesiculosus, Sargassum stenophyllum, Fucus distichus, Hizikia fusiforme, Padina gymnospors, Analipus japonicas, chorda filum, Caulerpa recemosa,* and*Kjellmaniella crassifolia* . Fucoidan has varied monosaccharides including xylose, galactose, mannose and glucuronic acid. Fucoidan structure and activity vary with geographical area and seaweed source. It has several combined applications documented with nanoparticles, hydrogels, microspheres, drug-releasing systems, nanofibers, scaffolds and microsphere for tissue design and wound dressing (Venkatesan et al., 2019).

1.1.4 Carrageenan

Carrageenan is a negatively charged linear sulfur sugar acquired from algae such as *Chondrus cripus* , *Gigartina stellate* ,*Hypnea* , *Halurus* and *Solieria* (Prajapati et al., 2014). Carrageenan is made up of 3,6 anhydro galactopyranose and galactose linked by galactose α-1,3 and β -1, 4 glycosidic bonds. The residue 3, 6-anhyro-D-galactose is essential for forming gel by carrageenan (Venkatesan et al., 2015). Carrageenans are easily soluble in water, biocompatible, nontoxic, highly viscous, high gelling capacity and stable in a wide pH range. It exists in the form of nanoparticles, hydrogels, microspheres, nanofibers, wafers, films, pellets and microspheres and it has an application in tissue designing, drug transport, wound healing, pharmaceutical formulations, and biosensing (Pacheco-Quito et al., 2020).

1.2. Marine ceramics

1.2.1 Hydroxyapatite (HAp)

HAp chemical nature is calcium phosphate and it is retrieved from varied sources which includes mammalian sources such as bone from camel, bovine, horse, marine sources like fish scale, shells, marine plants, algae, and mineral sources. Certain red algal forms such as*Phymatolithon calcareum* (Kusmanto et al., 2008), *Amphiroa ephedra* (Oliveira et al., 2007) have calcium carbonate in their structure and are precursors of Hap.

Hydroxyapatite is a biocompatible, porous, renewable and bioactive polymer and has been used as bone filler material. HAp can be mixed with a polycaprolactone to manufacture mechanically strong and porous scaffolds. Hydroxyapatite prepared from aquatic sources is thermostable at higher temperatures of 1200°C (Piccirillo et al., 2013). Hydroxyapatite (HAp) provides efficient absorption surface for functional biomolecules such as protein, DNA and so on and it influences the HAp surface electronic state. Surface electrical properties of HAp such as resistivity and capacitance can be useful as receptors and transducers of biosensors.

1.2.2. Marine Calcium carbonate ($CaCO_3$ or calcite):

Calcite is a precursor molecule for hydroxyapatite and isolated from different marine corals (*Lithothamnion glaciale* , *Coralline officinallis,* and *Phymatholithon calcareum*), calcifying algae, sponges, echinoderms, foraminifera, mollusks (*Ostrea sdulis, Pinctada maxima, Mytilus galloprovincialis*) bryozoans, fish bones, and Crustaceans shells (Andersson & Gledhill, 2013). Calcite has a resemblance to trabecular bones and suitable for orthopedics and dentistry (Srivastava et al., 2015). It has an advantage of porosity and pore interconnectivity as well as a demerit of fast dissolution and poor structural stability (Ben-Nissan, 2003).

1.2.3. Biosilica:

Biosilica is formed by biomineralization of silica known as frustules and formed by sponges, diatoms, radiolarians, and choanoflagellates (Schröder et al., 2008). The silica frustule structure varies in diatom species. There are approximately 3000 species of diatoms with silica exoskeleton. Some of them are *Aulacoseria ambigua* ,*stephanodiscus minutulus* , *Melosira undulata,* and*Cocconeis placentula* . Diatom silica has advantages of high surface area, porous, chemically inert, biocompatible, thermomechanical stability, lightweight, optophotonics features and it acts as ideal biomaterial for tissue designing, drug deliverables, and biosensors. The addition of various metals in silica frustules improves its physiochemical attributes as nanomaterial.

Delasoie and Zobi (2019) revealed the application of biosilica frustule of genera *Aulacoseira graulata* as drug delivery vehicles to colorectal cancer cells. Other diatom species such as*Thalassiosira weissflogii, Coscinodiscus concinnus, Thalassiosira pseudomonas* and *Nitzschia* species also can deliver drugs and*Phaeodactylum tricornutum,* and *Odontella* are considered suitable for semiconductors (Tramontano et al., 2020). Surface functionalization as well provides a unique opportunity for sustained and controlled drug release capacities and delivery potential.

1.3. Marine proteins

1.3.1 Collagen

Collagen is a high molecular weight proteinaceous biomaterial, component of connective tissues of humans, vertebrates and invertebrates. The shape and structural properties of collagen are established by triple helix domain. Collagens are divided into five different groups based on their structure, function, location and other characteristics. Type I and V collagen group is allied with bone, dermis, tendon, ligaments, cornea and Type II cartilage is associated with cartilage, nucleus pulposus, vitreous body and Type III is obtained from vessel wall, skin, reticular fibers of lung, liver and spleen and Type IV in basement membranes.

Collagen extracted from calfskin and bones are the primary sources of industrial collagen and have a high risk of bovine spongiform encephalopathy. To overcome these problems, related to vertebrate collagen, alternative of marine collagen from skin, bones, fin and scales of sponges and jellyfishes has been provided. Marine collagen from *Ircinia fusca* shows similarity with type I human collagen and other marine sponges *Chondrosia reniformis* collagen resembles type IV human collagen (Panagiotis, 2015). It shows that marine collagen is having similarities to human collagen and safer alternatives to the potential harmful bovine-originated collagen. Marine collagen can be recovered from marine vertebrates, algae, and invertebrates including jellyfish, sea urchin, Octopus, Squid, Cuttlefish, sea anemone, prawn, starfish (Barzideh et al., 2014; Jankangram et al., 2016; Langasco et al., 2017).

Collagen from marine origin has many advantages over higher vertebrate collagen. It is pure, safe, thermostable, with interconnected porosity, and has higher denaturation temperature due to more cross-linking (Panagiotis, 2015). Collagen of Type I is paramount and has huge applications in biomedical science. Collagen can be structurally converted into porous sheets and gels. Collagen has a wide application in cosmetics, drug delivery, surgery, bio-prosthetic implants, food supplements, and tissue engineering. Collagen appears as a potential biomaterial as scaffold in corneal, wound healing, dental, vascular tissue, and corneal damage tissue engineering. *Chondrosia reniformis* collagen has an application in preparation of moisturizers. There is a good evidence for the application of collagen biomaterials in drug delivery of target drugs to specific body parts (Patra et al., 2018).

Though collagen has some disadvantages as it can interact with cells and alter its growth or movement. To overcome this problem in collagen scaffolds, it is crosslinked with another suitable material. 3D printed fish collagen scaffold shows biocompatibility with human mesenchymal cells and fibroblast.

1.3.2. Lectins :

Lectins are the diverse group of carbohydrate-binding proteins that bind through high affinity and specific molecular sites. These lectins interact reversibly with high specificity to mono or oligosaccharides through non-covalent linkages. Lectins can recognize and attach to specific proteins on various cell types and can identify cell development stages through flow cytometry, histochemical applications and lectin microarrays. Lectins can indicate pathological conditions by identifying altered surface glycoproteins and glycolipids. Lectin has a multivalent binding site for the sugar moiety. Lectins are associated with varied taxa of microbes, plants and animals. Marine lectins are structurally diverse and grouped according to structural similarity of carbohydrate recognition domain (CRD) into Fucolectin type lectin, C-type lectins (CTLs), rhamnose binding lectin (RBL) Lily type, Ricin type and Tectonin type lectins.

Lectin producing marine species are *Aphrocallistes vastus, Axinella polypoides, Geodia cydoniu, Ptilota filicina, Tridacna maxima, Haliotis laevigata, Megabalanus rosa* , *Balanus rostratus, Tachypleus tridentatus,* and *Cucumaria echinate* (Ogawa et al., 2011), *Palmaria palmate, Solieria robusta, Gracilaria verrucosa, Cystoclonium purpureum, Bryothamnion seaforthii, B.triquetrum, solieria filiformis, Enantiocladia duperreyi, Amansis multifidi, Hypnea musciformis,* and green algae of genus *Codium, Ulva lactuca, Caulerpa cupressoides, Entermorpha prolifera, Ulva pertusa, Bryopsis plumose, Bryopsis hypnoides* and marine algal genus *Ptilota*(Teixeira et al., 2012).

Lectins have shown varied applications in the field of biomedical, drug delivery systems, diagnostic markers, anticancer drugs, and therapeutic activities. Cyanobacteria *Nostoc ellipsosporum* and red algae*Griffithsia sps* were used to obtain Anti-HIV and HCV lectins. Marine lectins have great potential as antiviral drugs against the transmission of enveloped viruses by preventing viral entry into host cells. Marine lectin has also shown antiparasitic, immunoenhancing, immunomodulating, mitogenic, cardiogenesis, and vasorelaxant activities. In diagnostic application, lectin specificity can be utilized to differentiate between carcinoma and normal human lymphocytes and fibroblasts. Altered glycan on cells or tissues surface can be recognized using lectin-based methods such as biosensors and histochemistry. Lectin and glycan interaction in biosensors can be analyzed by signals (Dan et al., 2016).

1.4. Marine peptidoglycan : Chondritin sulfate and hyaluronic acid are heteropolysaccharides of class glycosaminoglycan.

1.4.1. Chondroitin Sulfate:

Chondroitin sulfate (CS) is a sulfated polymer of glucoronate and N-acetylglucosamine linked by β-(1-3) glycosidic linkage. CS are classified according to attachment of sulfate group on Carbon atom into CS-A, CS-C, CS-E, CS-D and Cs-B respectively. Marine CS has been isolated from marine vertebrates including Whale, squid, salmon, skate, shark, king crab, sea cucumber and marine invertebrates like*Cnidaria, Mollusca* and *Polychaeta* . Shark fins of varied species including *Dasyatis akajei, Scyliorhinus torazame, Surus oxyrinchus, Prionace glauca* , *Dalatias licha* ,*Mitsukurina owatoni* are used as commercial sources of CS (Abdallaha et al., 2020).

Marine CS has many advantages as it is non-immunogenic, biocompatible, non-toxic, anti-inflammatory, and helps in cellular communication. Marine CS has an application in nerve regeneration, anti-inflammatory, anti-metastatic activity, tissue engineering scaffolds, anticoagulant activity, and biosensors. In tissue engineering, it is applied for bone repair, cartilage, and cutaneous wounds. To control biodegradability CS can be mixed with other polymers to make scaffolds. CS also has pharmacological applications such as coating material for implants and hydrogel in controlled drug release (Benito-Arenas et al., 2019).

1.4.2. **Hyaluronic acid (HA)** :

Hyaluronic acid is a natural nonsulfated polysaccharide made up of α-1,4 D glucuronic acid and β-1,3-N-acetyl-D-glucosamine, linked by (1-3)bonds. It is part of intracellular matrix of cartilage, umbilical cord connective tissue, skeleton and vitreous humor of cartilaginous fishes and the cell wall of marine bacteria *Streptococcus zooepidemicus* (Murado et al., 2012).

The HA activity is dependent on its size (Liao et al., 2005). HA can hold water molecules and this property of HA gives a large range of physical, chemical and biological activity such as biocompatibility, angiogenic, viscoelasticity and immune-stimulation. HA is also having shock-absorbing activities and acts as a lubricant for joint movement. In the skin, HA scavenges free radicals generated by the UV rays from sunlight and prevents cells from oxidative stress. HA has an application in the diagnosis of rheumatoid arthritis, cancer, and live pathologies, cosmetic fields such as plastic surgery, anti-aging cosmetics, arthritis treatment intraocular surgery, and drug delivery (Srivastava et al., 2015; Vázquez et al., 2013). Though data are scarce on biosensors.

1.5. Marine Nanoparticles:

In recent years, researchers have shown the great potential of marine sources in synthesis of nanoparticles (Asmathunisha & Kathiresan, 2013), as marine nanoparticles are both biocompatible and biodegradable. These include various marine species producing nanoparticles with sizes ranging from 1 to 100 nm. Microbe-based nanoparticle synthesis allows for greater size control due to periplasmic space and vesicle compartmentalization. pH, substrate concentration, temperature, and duration of exposure to the substrate are all variables that influence intracellular particle production (Gericke & Pinches, 2006). With diverse antibacterial applications, the mangrove-derived microorganisms*Aspergillus niger* , *Penicillium fellutanum* , and*Escherichia coli* can degrade silver ions at a quicker pace (Singh et al., 2015). Other mangrove-derived yeast-like species*Rhodosporidium diobovatum* and *Pichia capsulate* are also capable of synthesizing nanoparticles (Manivannan et al., 2010; Seshadri et al., 2012). Marine origin nanoparticles have shown significant applications in biomedical and biological streams including tissue engineering, cancer therapy, sensors, catalysis, drug delivery, electronic materials and wastewater treatment (Chaudhary et al., 2020).

Table 1: List of some marine organisms producing nanoparticles (Singh et al., 2015).

	Species	**Nanoparticles secreted**
Algae	*Tubinaria conoides*	Silver, Gold
	Colpomenia sinuosa	Silver
	Padina gymnospora	Silver
	Sargassum cinereum	Silver
	Gracilaria corticata	Gold
	Turbinaria conoldes	Gold
	Sargassum ilicifolium	Silver
	Ulva fasciata	Silver
	Ulva lactuca	Silver
	Urospora sp.	Silver
Cyanobacteria	*Microcoleus sp.*	Silver
	Turbinana conoides	Gold
	Phormidium tenue	Cadmium
	Phormidium tenue	Silver
Marine animals	*Saccostera cucullata*	Silver
	Acanthella elongata	Gold
	Cod liver oil (Fin Fish*)*	Silver

1.6. Marine pigments:

The pigment is a secondary metabolite produced by microbes. Pigments are the mixture of chemical compounds with varied biological activities. Marine bacteria *Rubritalea squalenifaciens Planococcus mar-*

*itimus*produces acetylenic carotenoids, *Flavobacterium dehydrogenase, Halococcus, Halobacteria, Actinomycetales,* produces aryl carotenoids such as 3-hydroxy-isorenieratene, isorenieratene and *Streptomyces mediolani* , *Monascus, Rhodotorula Brevibacterium linens, Mycobacterium aurum* , marine *Pseudoalteromonas* , marine*Actinomycetes* , and marine blue-green algae produce 3,3'-di-hydroxy-isorenieratene carotenoid.

Carotenoids extracted from *Phaffia rhodozyma* and*Haematococcus pluvialis* are used in aquaculture pharmaceuticals and food additives. *H.pulvialis* produces astaxanthins, which have an application in aquaculture feeds as well as a role in memory improvement and antiaging (Ramesh et al., 2019). As a food additive, Xanthan gum, an exopolysaccharide generated by *Xanthomonas campestris* , is utilized. Flexirubin, which is generated by Chryseobacterium and Flavobacterium, is used to treat chronic skin illness, dermatitis, stomach ulcers, and other conditions. Marine bacterial pigments can be used as pollution indicators in biosensors (Venil et al., 2014).

2. Biosensors:

A biosensor is a self-sufficient tool with a high specificity and sensitivity for quantitative estimation of specific chemical or organism and its toxicity (Purohit et al., 2020). Physiochemical transducing element of biosensor gives quantifiable estimation about the analyte in the form of electric signal. It should be specific, sensitive, portable and independent of physical parameters such as temperature and pH. They can measure the analyte in complex matrix with least sample preparation (Chandra, 2016). It is has both in vivo and in vitro applications (Noh et al., 2012; Baranwal, 2018).

Biosensors are categorized based on different parameters like bioreceptors, transducing elements, signal transduction and biorecognition principles. The transducer is an element that changes one form of energy to another and produces measurable signals. Biosensors are classified according to the type of transducer they use: optical, electrochemical, piezoelectric, and thermal. The basic principle of electrochemical biosensors is to convert biological events into electrons on an electrode, which are then converted into electric signals (Kumar et al., 2019; Turner, 2000). By measuring current as a function of applied voltage, voltammetric potential determines an analyte. Amperometric biosensors detect the current created when an electroactive biological element is oxidized or reduced. Potentiometric biosensors biorecognition element with a transducer recognizes the deviation in ion concentration.

An optical biosensor's primary goal is to provide a signal proportional to the concentration of the chemical being analyzed (analyte). The optical biosensor may employ biorecognition components from different biological materials like enzymes, antibodies, antigens, receptors, nucleic acids, entire cells, and tissues. Surface plasmon resonance (SPR), evanescent wave fluorescence, and optical waveguide interferometry detect the interaction of the biorecognition element with the analyte by utilizing the evanescent field near the biosensor surface. There are several variants in the design of optical biosensors, and this study will concentrate on a few that have been chosen for their extensive use and proclivity for detecting physiologically relevant chemicals.

An optical biosensor is an analytical device having a biorecognition sensing element integrated with an optical transducer system. Optical based biosensors are based on the principle of simple light absorption, fluorescence, reflectance, Raman scattering, chemoluminescence, surface Plasmon resonance (SPR), optical resonators, optical waveguides, optical resonators, photonic crystals, and optical fibers (Chen & Wang 2020). Optical biosensors can detect chemical changes in an analyte or organism by estimating the variation in the absorption of light or bioluminescence (Velasco-Garcia, 2009).

Physical factors such as acceleration, tension, and pressure may be converted into an electrical charge using piezoelectric biosensors. This bio element is coupled with piezoelectric components such as quartz crystal coated with gold electrodes. These crystals will vibrate at specific frequency depending on crystal mass as well electrical frequency of crystal and produce electrical signal of a specific frequency directly equivalent to the vibration. Though piezoelectric sensor has disadvantage too, as the surface charged produced due to oscillation, can be neutralized easily by environmental charges and current leakage. These biosensors are sensitive to temperature, as they can lead to crystal deformation and finally an electrical output (Paul & Dertein, 2018).The Cantilever biosensor is the new group of emerging micromechanical biosensors, having microfabricated silicon technology. This biosensor responds to physical (PH and temperature) and chemical changes into a mechanical bending and it can be estimated easily. Thermometric biosensors are the one which measures the temperature change due to heat production or evolution, by analyzing enzymatic reactions.

Figure 2: Schematic representation of working of biosensor

Bioreceptors are the biocatalytic molecule including enzymes, cells, antibodies, nucleic acids, and microbes that recognizes the analyte. According to the bioreceptors component, biosensors will be classified into DNA biosensors, enzymatic biosensors, non-enzymatic biosensors and immunosensors, and whole-cell biosensors. Enzymatic biosensors are the one which combines enzyme with transducer. The specific immobilized enzyme identifies a specific substrate and produces a signal, the substrate can be identified by any of the transducers (optical, electrochemical, thermal and Piezoelectric) and converted into electric signal. The non-enzymatic biosensor has metal like platinum integrated with a transducer. Non-enzymatic sensors are without biological functional units and can be beneficial in terms of structural simplicity and mass production (Mehrotra, 2016).

Immunosensors are selective, specific, and flexible biosensors that recognize a stable compound of particular antigens or antibodies. DNA biosensors are categorized by spontaneous hydrogen bonding of the target DNA with its complementary strand based on the detection of nucleic acid sequences from infectious microbes and tiny contaminants (Asal et al., 2018).

Whole-cell biosensors are those that use living organisms as the recognition component, such as bacteria, yeast, fungus, plant and animal cells, or even tissue slices, by monitoring the initial inputs into a biological response. Whole-cell biosensors have an advantage of providing sensitive, selective, real-time, rapid and unique data as compared to conventional chemical-based biosensors. A marine algae*Spirulina subsala* has an application in detecting metals and pesticides (Tonnina et al., 2002). As biosensors are cost-effective and sensitive, their applications have increased rapidly in environment, medical and industrial applications (Anand Raj et al., 2020).

3. Fabrication of biosensors using biomaterials

3.1. Polysaccharide biosensor:

Polysaccharides such as alginate, chitin, chitosan, agarose, cellulose, dextran and hyaluronic acid are biomaterials with the unique property of forming hydrogels. These polysaccharide hydrogels are attractive biomaterials for biosensors because of their hydrophilicity, high protein affinity, heavy metal ion chelation, biocompatibility, ease to modify surface chemical group, low cost, acceptable mechanical properties and facile fabrication method.

There is much evidence of application of polysaccharide-based hydrogels as immobilized biomaterial for fabrication of bioreceptors (Tavakoli & Youhong, 2017). Physical absorption, trapping, covalent bonding, crosslinking, and other approaches can be used to immobilize bio receptors on the hydrogel surface. Irreversible immobilization of bioreceptor prevents detachment of it from the biosensor and if it gets detached, the hydrogel microstructure or bio receptor activity will be destroyed (Mousty et al., 2001).

3.1.1 Alginate based Biosensor :

Alginate-based biosensors have applications in the detection of bacterial contamination in milk (Kikuchi et al., 2020), water quality estimation and biomedical applications. To determine glucose level in blood, alginate microsphere glucose oxidase-based biosensor was designed, which utilizes glucose oxidase enzyme to estimate the glucose in vivo glucose monitoring system (Chaudhary et al., 2010). Cell-based Microarray is designed by applying alginate and antibodies for application in drug discovery, toxicology and stem cell research. Alginate-based 3D microarrays are developed for pancreatic cancer detection (Fernandes et al., 2008; 2009).

Additional evidence has been found for the detection of heavy metals by*Aliivibrio fischeri* in water, based on alginate microsphere Luminescence Fiber-Optic Biosensor (Futra et al., 2014). The *A. fischeri* bacteria could maintain their metabolic activity for a longer time, without any change in bioluminescence. A low limit of detection for heavy metals, such as copper, cadmium, plum, chromium, gold, cobalt and nickel, may be observed using an alginate-based biosensor ranging from 1:56 µg/L to 3100 µg/L.

Turemis et al. (2018) employed a Calcium-alginate fluidic flow cell with built-in detector *Chlorella volgaris* and the *Tetrahymen pyriformis* algae to estimate marine contaminants in real-time, using fluorescent photosynthetic photosystem II analysis. The other algal species *Laminaria hyperborean* pyeroalginate conjugate biomaterial was used for physical entrapment of polyphenol oxidase (PPO). These amperometric biosensors can be used for determining catechol as analyte, producing the sensitivity of 80 and 350 µA M-1 cm-2, respectively (Abu-Rabeah et al., 2005).

3.1.2 Chitin and chitosan biosensor:

Chitin and chitosan hydrogels are biocompatible and easy to modify chemically. There are 5 categories of the chitin-based biosensor (Kittle et al., 2012).

3.1.2.1. Electrochemical biosensor:

Chitosan is often used in the construction of electrochemical biosensors due to its solubility in moderately acidic aqueous solutions and simplicity of usage under physiological settings (Bhatnagar et al., 2018; Baranwal et al., 2018; Kashish et al., 2017). Chitin requires partly deacetylated chitin's amine and hydroxyl functionalities, as well as glyoxal, carbodiimide, or epichlorohydrin to cross-link individual chitin chains and bind enzymes to chitin networks. For electrostatic immobilization of enzymes, thin chitin or chitin dispersed in carbon/platinum paste are acceptable matrices (Kittle et al., 2012). Chitosan to show electrical conductivity, combine with nanoparticles like graphene, multiwall carbon nanotubes, polypyrrole, polyaniline to enhance its electrical properties for sensing applications.

The glucose oxidase-loaded chitin films are used for quantifying the pH, oxygen and hydrogen peroxide changes in traditional glucose sensors. Lou et al. (2020) developed electrochemical biosensor for amlodipine identification for pharmaceutical applications using nickel molybdate nanosheets chitosan nanocomposite. Another application of chitosan-based electrochemical biosensor with graphene was reported by Shen et al. (2020) and for the detection of dopamine by exhibiting good sensitivity with a low detection limit of 0.29 µM.

3.1.2.2. Chitosan-Based Electrochemical Nucleic Acid Biosensors:

Chitosan-based DNA biosensors are formulated by surface fixing of biotinylated probe DNA by its anionic phosphate to cationic amino group of chitosan either by covalent bonding or affinity conjugation. This sensor was used to detect Gonorrhea (a sexually transmitted illness), as reported by Singh et al, (2011). Another application of chitosan-based nucleic acid biosensor was used for detecting Salmonella typhi by immobilizing ss DNA of infectious agent on graphene oxide/chitosan/ITO nanocomposite (Singh et al., 2013). Complementary, noncomplementary, and one base mismatch sequences may all be distinguished by the biosensor. For the detection of E. coli 0157:H7, a comparable electrochemical DNA biosensor was created by immobilizing SS E. coli DNA using a graphene oxide chitosan hybrid nanocomposite (Xu et al., 2017).

3.1.2.3. Chitosan-Based Electrochemical Immunosensors:

Electrochemical immunosensors based on Chitosan are created by immobilizing antibodies or antigens on the electrode surface of Chitosan. One of the advantages of chitosan is that the number of amino sites accessible for covalent protein attachment to chitosan materials may be varied across a large range merely by changing the degree of deacetylation of the variety. The fungal hepatocarcinogen aflatoxin B1 (Masoomi et al., 2013), botulisum neurotoxin A (Afkhami et al. 2017), diarrhea triggering bacteria *Shigella flexneri,* Ochratoxin A, hepatitis B biomarkers, cancers and iron content of blood (Liang et al., 2014) are detected and monitored by using electrochemical immunosensors.

Figure 3 : **DNA immobilization on electrode surfaces using chitosan.**

3.1.2.4. Chitosan-Based Electrochemical Enzyme Biosensor:

Chitosan appears as a porous polymer for adherence of enzymes by its polycationic chains to form the biosensor. Cross-linking drugs such as GL, carbodiimide, NH, epichlorohydrin or GL, NH or cyanuric acid are suitable for this attachment eg., a cross-link such as GL and GL. The adhesion does not interfere with enzyme movement and function. The important aspect in connecting Chitosan with various chemical groups is the abundance of functional groups and pH solubility. Many applications of chitosan-based electrochemical enzyme biosensor were reported, including for dopamine release in the brain of rats (Njagi et al.,2008), detection of hydrogen peroxide via catalase immobilized on chitosan-β-cyclodextrin (Dong et al., 2017) and chlorophenol determination via laccase immobilized on ZnO-Chitosan nanocomposite (Mendes et al., 2017).

3.1.2.5. Chitosan-Modified Voltammetric Electrodes for Trace Analysis:

Chemically modified Chitosan with electrochemical voltammetry has enormous potential as efficient sorbent material for the detection of environmental pollutants including pesticides, heavy metals and dyes. The current difference between the reference and working electrodes created by the reduction or oxidation of an electrochemical biosensor is measured using a voltammetric biosensor. Anodic stripping voltammetry, sweep voltammetry and cyclic voltammetry are used for determining heavy metals with great sensitivity. Janegitza et al. (2009) demonstrated the use of chitosan-supported adsorptive stripping voltammetry for the quantification of Cu (II), Cd (II), and Hg (II) with good sensitivity in electroanalysis of heavy metals.

Nickle oxide coupled chitosan electrochemical biosensor has been applied for the estimation of an infective pathogen like *E. coli* and*Salmonella typhi* from environment and clinical samples (Solanki et al., 2015). A large number of chitin and chitosan-based biosensors have been designed till now and the above mentioned are the some of the representative in this category (Suginta et al., 2013).

3.1.3. Fucoidan biosensor:

For the manufacture of the drug delivery system, Kurosaki et al. (2009) used fucoidan as a matrix material. Berger et al. (2010) has also used fucoidan and dextran sulfate as a biomaterial for HGF sensor coating. HGF has been attached specifically to sulfated polysaccharide fucoidan for the identification of hepatocyte growth factor in the serum-containing medium of a small bioreactor for culturing hepatocytes. Fucoidan coated HGF biosensor has shown highest sensitivity and low-cost alternative to the use of antibodies (Berger et al., 2010).

3.1.4. k-Carrageenan Biosensor:

For nonaqueous solvents, k-Carrageenan gel has been considered as an appropriate choice for enzyme immobilization in organic phase electrode construction (Campanella et al.,1999). In another study, Campanella et al. (2000) have reported, carrageenan biomaterial as immobilizing membrane for superoxide dismutase enzyme, which determines superoxide radical received through amperometric gaseous electrode for oxygen or hydrogen peroxide. Other biosensor application includes reduction of pathogen contamination in poultry food (Medina, 2004), radical scavenging properties in hydrophobic compounds (Campanella et al., 2001) and low-level urea detection (Taşaltın et al., 2020). Another enzymatic biosensor for glucose detection from glucose-spiked saliva samples is a bio nanocomposite film comprising a polyelectrolyte complex (PEC) doped with gold nanoparticles containing glucose oxidase (Rassas et al., 2019).

3.2. Marine protein Biosensor

3.2.1. Lectin biosensor:

Lectin-based biosensors determines the measurable signal by estimating the conversion of lectin-carbohydrate interactions. Lectins have a high affinity to multivalent oligosaccharides. Lectins' extremely specific binding to terminal carbohydrate moieties on cell surfaces and protein aggregates is used in physiological and pathological studies, such as virus and bacterium detection and glycol profiling of serum glycoproteins. Electrochemical lectin-based biosensors can be used to diagnose illness and pathogens by detecting biomarkers (Coelho et al., 2017), as well as biorecognition of glycan in viral proteins (Cesewski & Johnson, 2020).

SARS-COV-2 envelope glycoprotein might be exploited for early detection using lectin-based biosensors. Another use of lectin-based electrochemical biosensors includes the use of cyclic voltammetry and impedance to detect norovirus (nonenveloped virus) in feces samples without showing cross-reactivity with hepatitis A or E (Hong et al., 2015). The impedimetric lectin-based biosensor can also be applied for differentiating chikungunya virus, Zika virus, yellow fever and DENV-2 in serum-based samples (Simao et al., 2020).

Liao et al. (2016) described a lectin-based biosensor made from the marine mollusk *Crenomytilus grayanus* (CG) that may be used to diagnose and treat cancer. The CGL crystal can attach to three ligands: galactose, galactosamine, and globotriose (Gb3), and it may be utilized to recognize Gb3 on the surface of breast cancer cells, causing them to die. Peiris et al. (2012) developed a lectin-based biosensor using N-acetylgalactosamine lectin from the Roman snail Helix pomatia agglutinin (HPA) (Helix pomatia). This HPA based biosensor can have an affinity for metastatic SW620 cells and non-metastatic SW480 in different molar ranges.

This approach is the latest approach for the selective determination and quantification of cancer-specific glycans and lectin.

3.2.2. Collagen-based biosensor:

Marine collagen is reported to be non-toxic, environmental friendly, low inflammatory response and biocompatible. There are many reports of marine collagen biomaterial in tissue engineering, though there is a scarcity of data on the marine collagen-based biosensor.

Zong et al. (2006) reported a biosensor using chrome waste from leather waste in a tannery. The collagen grafted biosensor which has been discovered is found to be biocompatible, thermally stable, highly sensitive, and with improved selectivity. Due to the advantages offered by hybrid collagen, zirconia nanoparticles collagen composite was reported to prepare amperometric glucose biosensors.

3.3. Marine ceramics-based biosensors:

3.3.1. Hydroxyapatite (HAp) based biosensors :

Hydroxyapatite surface provides excellent ability to absorb functional molecules such as proteins, DNA, etc. Nishikawa et al. (2006) have shown that sodium hydroxyapatite is one of the most effective biomaterials for biosensor applications. By utilizing hydroxyapatite nanoparticles and chitosan nanocomposite, Lu et al. (2010) created a new tyrosinase-based biosensor. By monitoring the reduction signal of the bio-catalytically generated quinone species at -0.2 V, the constructed biosensor was used to identify phenolic chemicals (vs. saturated calomel electrode). Sudhan et al. (2019) utilized the tannery hydroxyapatite-graphene multi-walled carbon nanotube's sensing capability to detect a chemical that represents risk factors for sudden infant death syndrome (SIDS). This sensor helps in estimating the risk factors associated with SIDS.

3.3.2 Biosilica based biosensors:

Diatom frustules are composed of nanostructured amorphous silica, and their surface may be functionalized and tailored for biosensor applications. Due to the easy availability of diatom frustules in every pond water, it assures its low cost. Rea & De Stefano, (2019) reported the fabrication of silver nanoparticles on the diatom surface, which produces huge plasmonic hotspots that increase the Raman effect. The molecular probes are covalently attached to the diatom cell wall (DNA strands, proteins, enzymes, antibodies, and so on). Selvaraj et al. (2018) found that nitroaromatic compounds could be identified with excellent sensitivity and specificity using amine-removed diatom frustules from *Nitzschia sp* They also reported the detection of*Salmonella typhi* by same diatomic species. Leonardo et al. (2017) reported fixation of antibody functionalized diatoms on gold electrodes. Changing the electrodeposition parameters can influence diatom immobilization, orientation, and yield. For methyl parathion electrochemical detection, Gannavarapu et al. (2019) utilized a diatom*Phaeodactylum tricornutum* surface reformed by ZrO_2 by precipitating in a solution. The hybrid diatom-based electrode offers the benefit of detecting pollutants, chemicals, and enzymes at the picomolar level.

3.4. Marine peptidoglycan-based biosensors

3.4.1. Hyaluronic acid-based biosensors :

Hyaluronic acid, is an anionic, nonsulfated glycosaminoglycan, antifoulant biomaterial for electrochemical biosensors (Liu et al., 2014). HA disaccharide unit facilitates the hydrogen bonding of bioreceptors. Joung et al. (2013) developed an impedimetric label-free immunosensor by utilizing nano-porous hyaluronic acid (HA) membrane for detection of *E.coli* O157:H7 pathogen from whole milk.

3.4.2. Chondroitin sulfate-based biosensors:

Zhao et al. (2020) have reported ultrasensitive and ultra-selective polyethylene glycol (PEG) chondroitin sulfate (CS) biosensor, for identification of *Mycoplasma ovipneumonia* . This sensor is more sensitive than the earlier sensors in detecting *Mycoplasma ovipneumonia* in whole serum thus, offering a wide range of applications. The Chondroitin sulfate-based biosensor exhibits high selectivity, reproducibility, storage stability, and analytical performance with a wide range of concentrations (1017 M – 1012 M) in the buffer.

3.5. Marine nanoparticles-based biosensors:

Marine Nanomaterial based biosensors should be integrated within tiny biochips, which enhances functionality of biosensors as well as made portable, pocket friendly and easy to use (Singh et al., 2015).

Elgamouz et al. (2020) have prepared *Noctiluca scintillans* -mediated AgNP's biosensor for sensing hydrogen peroxide. It was discovered that the breakdown of hydrogen peroxide on AgNP's catalytic surface is pH, temperature, and time-dependent. Using Abs calibration curves, the test assay correctly predicts repeatable levels of H_2O_2 in unlabeled samples in three distinct ranges— mM, M, and nM.

Algal synthesized gold nanoparticles are utilized in the biosensing of cancer diagnostics by analyzing the type and quantity of hormones in the human body. The algae-produced nano Au-Ag alloy has substantial electrical catalytic activity against 2-butanones and offers a platform for the early phase cancer development in which the biosensor detects the initial stages by recognizing the presence of malignant cells.

In separate research, the AuNPs biosensor from *Hypnea Valencia*was shown to be capable of detecting human chorionic gonadotrophin (HCG) in urine samples from pregnant women in an HCG blood pregnancy kit (Kuppusamy et al., 2014). Platinum NPs from *S. myriocystum* can be used as biosensors to track the amount of adrenaline in the body, which is a hormone-based medicine used to treat allergies, asthma, and heart attacks (Sharma et al., 2019).

3.6. Marine pigment-based biosensors :

A whole-cell biosensor for cadmium assessment utilizing a colorimetric technique has been created using a genetically engineered red pigment generating bacterium *Deinococcus radiodurans* (Joe et al., 2012). Lac Z reporter gene cassettes were created by combining the promoter regions of inducible genes that detect high levels of Cd. The reporter cassettes were transplanted into *D. radiodurans* R1 to assess promoter activity and specificity. It can detect cadmium in concentrations ranging from 1mM to 10mM. LacZ expression was increased up to 100 lM Cd, but it swiftly decreased with increasing concentrations. The presence of Cd reforms the color of the sensor bacterium strain (KDH081) from light yellow to red, but the addition of other metals have no impact. With a Cd detection range of 50nM to 1mM, the color shift is produced by the formation of red pigment and can be observed with the naked eye. By introducing a promoter region that may be utilized as a possible colorimetric system-based biosensor, there is a good chance of developing a novel pigment-based vector and host system.

Table 2: List of marine biomaterial-based biosensors

Biosensor Source	**Biomaterial**	**Type of Biosensor**	**Purpose of Biosensor**	**Reference**
Spectral emission of Lux recombinant of 11 bacterial species from four genera *Vibrio photobacterium, Alteromonas, Photorhabdus* found in marine habitats.	Whole-cell, DNA based	Bioluminescent Biosensor	Heavy- metal Indicator	Thouand et al., 2003
Microtox and luxCDABE and modified Ps. Fluorescent	Transposon DNA based	Bioluminescent, Whole-cell Biosensor	To assess the organotonins and their breakdown products tributylin, dibutyltin, triphenyltin,diphenyltin	Boyd et al., 1997
lux CDABE modified Ps. Fluorescent	DNA based	Bioluminescent, Whole-cell Biosensor	Identifies restrictions to bioremediation of BTEX contaminated sites.	Sousa et al., 1998
luxCDABE modified Ps. fluorescent	DNA based biosensor	Bioluminescent, Whole-cell Biosensor	Estimation of heavy metal toxicity in sewage sludge.	McGrath et al., 1999
Pseudomonas. fluorescent HK44 genetically modified with luxCDABE	DNA based biosensor	Bioluminescent Whole-cell biosensor.	Detection of polycyclic aromatic hydrocarbons.	Ripp et al., 2000
Fabrication of a hydroxyapatite based membrane originated from fish scales for designing of electrochemical membrane for detection of KIM-1	Hydroxyapatite is sourced from natural fish scales.	Electrochemical Biosensor	Sensitive determination of Kidney injury molecule 1 (KIM-1)	Zhang et al., 2014

Biosensor Source	Biomaterial	Type of Biosensor	Purpose of Biosensor	Reference
The Biosensor was developed using sulfated polysaccharides such as fucoidan and Dextran sulfate and antibodies for HGF were immobilized on the membrane via dicarboxy polyethylene.	Dextran sulfate and fucoidan used as sensor coatings	Electrochemical Biosensor	A surface acoustic wave biosensor has been used for identifying hepatocyte growth factor (HGF/SF) in the serum-containing medium of a miniature bioreactor.	Berger et al., 2010
Marine microalgal biosensors bound to the marine buoys for the detection of Pesticides inhibiting photosynthesis of marine organisms.	Marine microalgae from *Chlorophyceae, Trebouxiophyceae,Dinoflagellates, Diatoms, and Eustimatophyceae.*	Whole-cell biosensor	Detection of photosynthetic inhibiting pesticides includes Diuron, Simazine, Irgarsol in marine water.	Moro et al., 2018
Microbial fuel cell (MFC) based biosensors for determining the concentration of organic carbon.	The biofilm for the biosensor has been forming from marine sediment in the anodic compartment.	Electrochemical Biosensor	Has the ability to provide an early indication of biofouling in seawater, optimize the pretreatment method for high organic carbon and monitor its effectiveness.	Quek et al., 2015
Marine hydrocarbon classic bacteria as a whole-cell biosensor for n-alkanes.	Marine bacteria *Alcanivorax borkumensis*	Whole-cell Biosensor	Used for detection of alkanes	Sevilla et al., 2015
Microalgal-based recombinant bioluminescence based biosensor for estimating antifouling biocides.	Recombinant Marine green alga *Ostreocccus tauri.*	Whole cell luminescent biosensor	Application in determining antifouling biocides i.e diuron and Irgasol.	Sanchez-Fernandin et al., 2013

Biosensor Source	Biomaterial	Type of Biosensor	Purpose of Biosensor	Reference
Sea urchin application in assessment of macrozoobenthos health state.	*Paracentrotus lividus* coelomocytes	Whole-cell Biosensor	Application in estimation of macrobenthos health state.	Pinsino et al., 2008
Nanostructured silica frustules of the Marine diatoms as optical biosensors	Modified frustule of *Coscinodiscus concinnus* bound to a specific bioprobe as antibody.	Optical Biosensors	For antibody detection	De Stefano et al., 2009
Helix pomatia agglutinin	*Helix pomotia*	Electrochemical Biosensor	Colorectal cancer	Peiris et al., 2012

4. Future prospects and Conclusion

Marine Biomaterials are attracting tremendous attention from researchers as they offer a cost-effective and biocompatible potent source for therapeutics, regenerative medicine, the food industry, and biosensors. The interdisciplinary approach is appreciated in the field of biosensor designing. Biomaterials are widely used in biosensing prototypes as polymeric fibers, polymer composites, and conducting materials. Biosensors made from marine biomaterials are biocompatible, thermally stable, and have excellent specificity and selectivity. The significant field of biosensors and the principles of their operation were covered in this study. Varied types of biosensors are available based on biological components, biomaterial type, and transducers. Comparing the sensitivity and effectiveness of sensor systems based on various types of marine biomaterials is very intriguing. Even though there are considerable advances in the field of biomaterials used in the biosensor, a lot more remains to be achieved.

Acknowledgment

The Authors of this review article are extremely thankful to Amity University Uttar Pradesh, for its support and encouragement towards this review and for providing all kinds of Research/ Study materials for helping towards the fulfillment of this article. Dr. Pranjal Chandra thanks Prof. Pramod Kumar Jain, Director IIT (BHU) for encouragement and for providing the necessary facility for the completion of this work.

References

1. Abdallaha, M. M., Fernández, N., Matiasa, A. A., & Bronze, M. R. (2020). Hyaluronic acid and Chondroitin sulfate from marine and terrestrial sources: Extraction and purification methods. *Carbohydrate Polymers,* 243, 116441. doi: 10.1016/j.carbpol.2020.116441
2. Abu-Rabeah, K., Polyak, B., Ionescu, R. E., Cosnier, S., & Marks, R. S. (2005). Synthesis and Characterization of a Pyrrole-Alginate Conjugate and Its Application in a Biosensor Construction. *Biomacromolecules* , 6, 3313–3318. https://doi.org/10.1021/bm050339j
3. Afkhami, A., Hashemi, P., Bagheri, H., Salimian, J., Ahmadi, A., & Madrakian, T. (2017). Impedimetic immunosensor for the label-free and direct detection of botulinum neurotoxin serotype A using Au nanoparticles/graphene-chitosan composite. *Biosens Bioelectron* . 93, 124–131. doi: 10.1016/j.bios.2016.09.059
4. Anand Raj, M. K., Rathanasamy, R., Kaliyannan, G. V., & Thangamuthu, M. R. (2020). Research Insights on the Development of Biosensors, in: Inamuddin, A. Asiri (Eds), *Nanosensor Technologies for Environmental Monitoring. Nanotechnology in the Life Sciences* , Springer, Cham.
5. Andersson, A. J., & Gledhill, D. (2013). Ocean Acidification and Coral Reefs: Effects on Breakdown, Dissolution, and Net Ecosystem Calcification. *Annual Review of Marine Science* , 5, 321-348.

https://doi.org/10.1146/annurev-marine-121211-172241
6. Asal, M., Ozen, O., Şahinler, M., Polatoğlu, İ. (2018). Recent Developments in Enzyme, DNA and Immuno-Based Biosensors. *Sensors (Basel)* , 18, 1924. doi: 10.3390/s18061924
7. Asmathunisha, N., & Kathiresan, K. A. (2013). Review on biosynthesis of nanoparticles by marine organisms. *Colloids surf B, Biointerfaces* , 103, 283–287. doi: 10.1016/j.colsurfb.2012.10.030
8. Baranwal, A., & Chandra, P., (2018). Clinical implications and electrochemical biosensing of monoamine neurotransmitters in body fluids, in vitro, in vivo, and ex vivo models. Biosensors and Bioelectronics, 121, 137-152. DOI: 10.1016/j.bios.2018.09.002
9. Baranwal, A., Kumar, A., Priyadharshini, A., Oggu, G. S., Bhatnagar, I., Srivastava, A., & Chandra, P. (2018). Chitosan: An undisputed Bio-fabrication material for tissue engineering and bio-sensing applications. *International Journal of Biological Macromolecules* . 110, 110-123. https://doi.org/10.1016/j.ijbiomac.2018.01.006
10. Barzideh, Z., Latiff, A. A., Gan, C. Y., Abedin, M. Z., & Alias, A. K. (2014). ACE Inhibitory and Antioxidant Activities of Collagen Hydrolysates from the Ribbon Jellyfish (Chrysaora sp.). *Food Technol. Biotechnol* , 52, 495–504. doi: 10.17113/ftb.52.04.14.3641
11. Bastiaens, L., Soetemans, L., D'Hondt, E., & Elst, K. (2019). Sources of Chitin and Chitosan and their Isolation, In: van den Broek, L. A. M., Boeriu, C. G., Stevens, C. V. (Eds), *Chitin and Chitosan Properties and Applications,* Wiley Publication , 1–34.
12. Benito-Arenas, R., Zárate, S. G., Revuelta, J., & Bastida, A. (2019). Chondroitin sulfate-degrading enzymes as tools for the development of new pharmaceuticals. *Catalysts* , 9, 322. https://doi.org/10.3390/catal9040322
13. Ben-Nissan, B. (2003). Natural bioceramics: from coral to bone and beyond. *Curr. Opin. Solid State Mater. Sci,* 7, 283– 288. DOI: 10.1016/j.cossms.2003.10.001
14. Berger, M., Welle, A., Gottwald, E., Rapp, M., & Länge, K. (2010). Biosensors coated with sulfated polysaccharides for the detection of hepatocyte growth factor/scatter factor in cell culture medium.*Biosensors & bioelectronics* , 26, 1706–1709. doi: 10.1016/j.bios.2010.07.065
15. Bhatnagar, I., Mahato, K., Ealla, K. K., Asthana, A., & Chandra, P. (2018). Chitosan stabilized gold nanoparticle mediated self-assembled glip nanobiosensor for diagnosis of invasive aspergillosis.*International Journal of Biological Macromolecules* . 110, 449-456. https://doi.org/10.1016/j.ijbiomac.2017.12.084
16. Bo, M., Bavestrello, G., Kurek, D., Paasch, S., Brunner, E., Born, R., Galli, R., Stelling, A. L., Sivkov, V. N., Petrova, O. V., Vyalikh, D., Kummer, K., Molodtsov, S. L., Nowak, D., Nowak, J., & Ehrlich, H. (2012). Isolation and identification of chitin in the black coral*Parantipathes larix* (Anthozoa: Cnidaria). *Int. J. Biol. Macromol.* 51, 129–137. https://doi.org/10.1016/j.ijbiomac.2012.04.016
17. Boaventura, T. P., Peres, A. M., Gil, V. S. B. , Gil, C. S. B., Oréfice, R. L., & Luz, R. K. (2020). Reuse of collagen and hydroxyapatite from the waste processing of fish to produce polyethylene composites. *Química Nova* , 43, 168-174. https://doi.org/10.21577/0100-4042.20170475
18. Boyd, E. M., Killham, K., Wright, J., Rumford, S., Hetheridge, M., Cumming, R., & Meharg, A. A. (1997). Toxicity assessment of xenobiotic contaminated groundwater using lux modified*Pseudomonas fluorescens* . *Chemosphere* , 35, 1967-85. doi: 10.1016/s0045-6535(97)00271-3.
19. Campanella, L., De Luca, S., Favero, G., Persi, L., & Tomassetti, M. (2001). Superoxide dismutase biosensors working in non-aqueous solvent. *Fresenius. J. Anal. Chem.,* 369, 594–600. doi: 10.1007/s002160000672
20. Campanella, L., Favero, G., Persi, L., & Tomassetti, M. (2000). New biosensor for superoxide radical used to evidence molecules of biomedical and pharmaceutical interest having radical scavenging properties. *J. Pharm. Biomed. Anal.,* 23, 69–76. DOI: 10.1016/s0731-7085(00)00276-4.
21. Campanella, L., Favero, G., Sammartino, M., & Tomassetti, M. (1999). Enzymatic immobilisation in kappa-carrageenan gel suitable for organic phase enzyme electrode (OPEE) assembly. *J. Mol. Catal. B: Enzym* ., 7, 101–113. https://doi.org/10.1016/S1381-1177(99)00035-1
22. Campiglio, C. E., Bidarra, S. J., Draghi, L., & Barrias, C. C. (2020). Bottom-up engineering of cell-laden hydrogel microfibrous patch for guided tissue regeneration. *Mater. Sci. Eng. C Mater. Biol. Appl.*

, 108, 110488. doi: 10.1016/j.msec.2019.110488

23. Cesewski, E., & Johnson, B. N. (2020). Electrochemical biosensors for pathogen detection. *Biosens Bioelectron* . 159, 112214. doi: 10.1016/j.bios.2020.112214.
24. Chandra, P. (2016). Nanobiosensors for personalized and onsite biomedical diagnosis. London, United Kingdom: The Institution of Engineering and Technology.
25. Chaudhary, A., McShaneb, M. J., & Srivastava, R. (2010). Glucose response of dissolved-core alginate microspheres: Towards a continuous glucose biosensor. *Analyst* , 135, 2620-2628. https://doi.org/10.1039/C0AN00109K
26. Chaudhary, R., Nawaz, K., Khan, A. K., Hano, C., Abbasi, B. H., & Anjum, S. (2020). An Overview of the Algae-Mediated Biosynthesis of Nanoparticles and Their Biomedical Applications.*Biomolecules,* 10, 1498. https://doi.org/10.3390/biom10111498
27. Chen, C., & Wang, J. (2020). Optical Biosensors: an exhaustive and comprehensive review. *The Analyst* , 145, 1605- 1628 doi:10.1039/c9an01998g
28. Chu, Y. P., Li, H. C., Ma, L., & Xia, Y. (2018). Establishment of a tumor neovascularization animal model with biomaterials in rabbit corneal pouch. *Life Sci.* , 202, 98–102. doi: 10.1016/j.lfs.2018.03.043
29. Coelho, L. C., Silva, P. M., Lima, V. L., Pontual, E. V., Paiva, P. M., Napoleão, T. H., & Correia, M.T. (2017). Lectins, Interconnecting Proteins with Biotechnological/Pharmacological and Therapeutic Applications. *Evidence-Based Complementary and Alternative Medicine* , 1594074. doi: 10.1155/2017/1594074
30. Dan, X., Liu, W., & Ng, T. B. (2016). Development and Applications of Lectins as Biological Tools in Biomedical Research. *Med Res Rev* ., 36, 221-47. doi: 10.1002/med.21363
31. De. Stefano, L., Rotiroti, L., De. Stefano, M., Lamberti, A., Lettieri, S., Setaro, A., & Maddalena, P. (2009). Marine diatoms as optical biosensors. *Biosens Bioelectron* ., 24, 1580-1584. doi: 10.1016/j.bios.2008.08.016.
32. Delasoie, J., & Zobi, F. (2019). Natural Diatom Biosilica as Microshuttles in Drug Delivery Systems. *Pharmaceutics* , 11(10), 537. doi: 10.3390/pharmaceutics11100537
33. Dong, W. B., Wang, K. Y., Chen, Y., Li, W. P., Ye, Y. C., & Jin, S. H. (2017). Construction and characterization of a chitosan-immobilized-enzyme and beta-cyclodextrin-included-ferrocene-based electrochemical biosensor for H_2O_2 detection. *Materials* , 10, 868. doi: 10.3390/ma10080868.
34. Elgamouz, A., Idriss, H., Nassab, C., Bihi, A., Bajou, K., Hasan, K., Abu Haija, M., & Patole, S.P. (2020). Green Synthesis, Characterization, Antimicrobial, Anti-Cancer, and Optimization of Colorimetric Sensing of Hydrogen Peroxide of Algae Extract Capped Silver Nanoparticles. *Nanomaterials* , 10, 1861. doi: 10.3390/nano10091861
35. Elieh-Ali-Komi, D., & Michael, R. H. (2016). Chitin and Chitosan: Production and Application of Versatile Biomedical Nanomaterials. *International journal of advanced research* ,. 4, 411-427.
36. Fernandes, T. G., Diogo, M. M., Clark, D. S., Dordick, J. S., & Cabral, J. M. (2009). High-throughput cellular microarray platforms: Applications in drug discovery, toxicology and stem cell research.*Trends Biotechnol* ., 27, 342-349. doi: 10.1016/j.tibtech.2009.02.009
37. Fernandes, T. G., Kwon, S., Lee, M., Clark, D. S., Cabral, J. M., & Dordick, J. S. (2008). On-Chip, cell-based microarray immunofluorescence assay for high-throughput analysis of target proteins. *Anal. Chem.* , 80, 6633-6639. doi: 10.1021/ac800848j
38. Futra, D., Heng, L. Y., Surif, S., Ahmad, A., & Ling, T. L. (2014). Microencapsulated *Aliivibrio fischeri* in alginate microspheres for monitoring heavy metal toxicity in environmental waters. *Sensors* , 14, 23248-23268. doi: 10.3390/s141223248
39. Gannavarapu, K. P., Ganesh, V., Thakkar, M., Mitra, S., & Dandamudi, R.B. (2019). Nanostructured Diatom-ZrO_2 composite as a selective and highly sensitive enzyme free electrochemical sensor for detection of methyl parathion. *Sens. Actuators B Chem.* 288, 611–617. doi: 10.1016/j.snb.2019.03.036
40. Gericke, M., & Pinches, A. (2006). Microbial production of gold nanoparticles. *Gold Bulletin* , 39, 22-28. https://doi.org/10.1007/BF03215529
41. Gomez, C. G., Lambrecht, M. V. P., Lozano, J. E., Rinaudo, M., & Villar, M. A. (2009). Influence of the extraction– purification conditions on final properties of alginates obtained from brown algae

(*Macrocystis pyrifera*). *Int. J. Biol. Macromol.,* 44, 365–371. doi: 10.1016/j.ijbiomac.2009.02.005

42. Hong, S. A., Kwon, J., Kim, D., & Yang, S.A. (2015). A rapid, sensitive and selective electrochemical biosensor with concanavalin a for the preemptive detection of norovirus. *Biosens Bioelectron* , 64, 338-344. doi: 10.1016/j.bios.2014.09.025
43. Ifuku, S., Nogi, M., Abe, K., Yoshioka, M., Morimoto, M., Saimoto, H., & Yano, H. (2009). Preparation of chitin nanofibers with a uniform width as alpha-chitin from crab shells. *Biomacromolecules,* 10, 1584–8. doi: 10.1021/bm900163d.
44. Janegitza, B. C., Marcolino-Juniorb, L. H., Campana-Filhoc, S. P., Fariaa, R. C., & Fatibello-Filhoa, O. (2009). Anodic stripping voltammetric determination of copper(II) using a functionalized carbon nanotubes paste electrode modified with crosslinked chitosan.*Sens Actuat B* , 142, 260. doi: 10.1016/j.snb.2009.08.033
45. Jankangram, W., Chooluck, S., & Pomthong, B. (2016). Comparison of the Properties of Collagen Extracted from Dried Jellyfish and Dried Squid. *Afr. J. Biotechnol* ., 15, 642–648. DOI: 10.5897/AJB2016.15210
46. Jiang, Y., & Wu, J. (2019). Recent development in chitosan nanocomposites for surface-based biosensor applications.*Electrophoresis* , 40, 2084-2097. https://doi.org/10.1002/elps.201900066
47. Joe, M. H., Lee, K. H., Lim, S. Y., Im, S. H., Song, H. P., Lee, I. S., & Kim, D. H. (2012). Pigment-based whole-cell biosensor system for cadmium detection using genetically engineered *Deinococcus radiodurans* . *Bioprocess Biosyst Eng* ., 35, 265-72. doi: 10.1007/s00449-011-0610-3.
48. Joung, C. K., Kim, H. N., Lim, M. C., Jeon, T. J., Kim, H. Y., & Kim, Y. R. (2013). A nanoporous membrane-based impedimetric immunosensor for label-free detection of pathogenic bacteria in whole milk.*Biosensor Bioelectron* , 44, 210-5. doi: 10.1016/j.bios.2013.01.024
49. Kashish, Bansal, S., Jyoti, A., Mahato, K., Chandra, P., & Prakash, R. (2017). Highly sensitive in vitro biosensor for enterotoxigenic escherichia coli detection based on ssdna anchored on ptnps-chitosan nanocomposite. *Electroanalysis* , 29, 2665-2671. https://doi.org/10.1002/elan.201600169
50. Kaur, S., & Dhillon, G. S. (2014). The versatile biopolymer chitosan: Potential sources, evaluation of extraction methods and applications.*Crit. Rev. Microbiol.* , 40, 155–175. doi: 10.3109/1040841X.2013.770385.
51. Kikuchi, N., May, M., Zweber, M., Madamba, J., Stephens, C., Kim, U., & Mobed-Miremadi, M. (2020). Sustainable, Alginate-Based Sensor for Detection of Escherichia coli in Human Breast Milk. *Sensors,*20, 1145. https://doi.org/10.3390/s20041145
52. Kittle, J. D., Wang, C., Qian, C., Zang, Y. F., Zang, M. Q., Roman, M., Morris, J. R., Moore, R. B., & Esker, A. R. (2012). Ultrathin Chitin Films for Nanocomposites and Biosensors.*Biomacromolecules* , 13, 714-718. https://doi.org/10.1021/bm201631r
53. Kumar, A., Purohit, B., Maurya, P. K., Pandey, L. M., & Chandra, P. (2019). Engineered nanomaterial Assisted Signal-amplification strategies for Enhancing Analytical performance of Electrochemical Biosensors. *Electroanalysis* , 31, 1615-1629. https://doi.org/10.1002/elan.201900216
54. Kuppusamy, P., Mashitah, M. Y., Maniam, G. P., & Govindan, N. (2014). Biosynthesized gold nanoparticle developed as a tool for detection of HCG hormone in pregnant women urine sample. *Asian Pac. J. Trop. Dis* ., 4, 237.
55. Kurosaki, T., Kitahara, T., Kawakami, S., Nishida, K., Nakamura, J., Teshima, M., Nakagawa, H., Kodama, Y., To, H., & Sasaki, H. (2009). The development of a gene vector electrostatically assembled with a polysaccharide capsule. *Biomaterials* , 30, 4427–4434. https://doi.org/10.1016/j.biomaterials.2009.04.041
56. Kusmanto, F., Walker, G., Gan, Q., Walsh, P., Buchnan, F., Dickson, G., McCaigue, M., Maggs, C., & Dring, M. (2008). Development of composite tissue scaffolds containing naturally sourced microporous hydroxyapatite. *Chemical Engineering Journal* , 139, 398–407. https://doi.org/10.1016/j.cej.2007.11.041
57. Langasco, R., Cadeddu, B., Formato, M., Lepedda, A. J., Cossu, M., Giunchedi, P., Pronzato, R., Rassu, G., Manconi, R., & Gavini, E. (2017). Natural Collagenic Skeleton of Marine Sponges in Pharmaceutics: Innovative Biomaterial for Topical Drug Delivery. *Mater. Sci. Eng. C Mater. Biol.*

Appl., 70, 710–720. doi: 10.1016/j.msec.2016.09.041

58. Leonardo, S., Garibo, D., Fernandez-Tejedor, M., O'Sullivan, C. K., & Campas, M. (2017). Addressed immobilization of biofunctionalized diatoms on electrodes by gold electrodeposition. *Biofabrication* , 9, 015027. doi: 10.1088/1758-5090/aa6400.
59. Liang, S., Xueming, L., Chen, F., & Chen, Z. (2014). Current microalgal health food R&D activities in China. *Hydrobiologia* , 512, 45–48. https://doi.org/10.1023/b:hydr.0000020366.65760.98
60. Liao, J. H., Chien, C. T. H., Wu, H. Y., Huang, K. F., Wang, I., Ho, M. R., Tu, I .F., Lee, I. M., Li, W., Shih, Y. L., Wu, C. Y., Lukyanov, P. A., Hsu, S. T. D., & Wu, S.H. (2016). A Multivalent Marine Lectin from *Crenomytilus grayanus* Possesses Anti-cancer Activity through Recognizing Globotriose Gb3. *Journal of the American Chemical Society,* 138, 4787–4795. doi: 10.1021/jacs.6b00111
61. Liao, Y. H., Jones, S. A., Forbes, B., Martin, G. P., & Brown, M. B. (2005). Hyaluronan: Pharmaceutical characterization and drug delivery.*Drug Deliv* ., 12, 327– 342. doi: 10.1080/10717540590952555
62. Liu, X., Huang, R., Su, R., Qi, W., Wang, L., & He, Z. (2014). Grafting Hyaluronic Acid onto Gold Surface to Achieve Low Protein Fouling in Surface Plasmon Resonance Biosensors. *ACS applied materials & interfaces,* 6,13034-13042. doi: 10.1021/am502921z.
63. Lou, B., Rajaji, U., Chen, S., & Chen, T. (2020). A Simple Sonochemical Assisted Synthesis of Porous NiMoO4/chitosan Nanocomposite for Electrochemical Sensing of Amlodipine in Pharmaceutical Formulation and Human Serum. *Ultrason. Sonochem,*64, 104827. https://doi.org/10.1016/j.ultsonch.2019.104827
64. Lu, L., Zhang, L., Zhang, X., Huan, S., Shen, G., & Yu, R. (2010). A novel tyrosinase biosensor based on hydroxyapatite-chitosan nanocomposite for the detection of phenolic compounds. *Anal Chim Acta* . 665, 146-51. doi: 10.1016/j.aca.2010.03.033
65. Madhumathi, K., Binulal, N. S., Nagahama, H., Tamura, H., Shalumon, K. T., Selvamurugan, N., Nair, S. V., & Jayakumar, R. (2009). Preparation and characterization of novel beta-chitin-hydroxyapatite composite membranes for tissue engineering applications. *International Journal of Biological Macromolecules* , 44, 1–5. doi: 10.1016/j.ijbiomac.2008.09.013
66. Manivannan, S., Alikunhi, N. M., & Kandasamy, K. (2010). In vitro synthesis of silver nanoparticle by marine yeasts from coastal mangrove sediment. *Adv. Sci. Lett.,* 3, 428-433. https://doi.org/10.1166/asl.2010.1168
67. Masoomi, L., Sadeghi, O., Banitaba, M. H., Shahrjerdi, A., & Davarani, S. S. H. (2013). A non-enzymatic nanomagnetic electro-immunosensor for determination of Aflatoxin B-1 as a model antigen. *Sensor Actuat B-Chem.* 177, 1122–1127. doi: 10.1016/j.snb.2012.11.067
68. McGrath, S. P., Knight, B., Killham, K., Preston, S., Paton, G. I.(1999). Assessment of the toxicity of metals in soils amended with sewage sludge using a chemical speciation technique and a lux-based biosensor. *Environmental Toxicology and Chemistry* , 18, 659-663. https://doi.org/10.1897/1551-5028(1999)018<0659:AOTTOM>2.3.CO;2
69. Medina, M. B. (2004). Binding interaction studies of the immobilized*Salmonella typhimurium* with extracellular matrix and muscle proteins, and polysaccharides. *Int. J. Food Microbiol,* 93, 63–72. doi: 10.1016/j.ijfoodmicro.2003.10.008.
70. Mehrotra, P. (2016). Biosensors and their applications - A review. *Journal of oral biology and craniofacial research* , *6* , 153–159. doi: 10.1016/j.jobcr.2015.12.002
71. Mendes, R. K., Arruda, B. S., de Souza, E. F., Nogueira, A. B., Teschke, O., Bonugli, L. O., & Etchegaray, A. (2017). Determination of chlorophenol in environmental samples using a voltammetric biosensor based on hybrid nanocomposite. *J Brazil Chem Soc* ., 28, 1212–1219. https://doi.org/10.21577/0103-5053.20160282
72. Moro, L., Pezzotti, G., Turemis, M., Sanchis, J., Farre, M., Denaro, R., Giacobbe, M. G., Crisafi, F., & Giardi, M. T. (2018). Fast pesticide pre-screening in marine environment using a green microalgae-based optical bioassay. *Mar Pollut Bull* ., 129, 212-221. doi: 10.1016/j.marpolbul.2018.02.036
73. Mousty, C., Lepellec, A., Cosnier, S., Novoa, A., & Marks, R.S.(2001). Fabrication of organic phase biosensors based on multilayered polyphenol oxidase protected by an alginate coating. *Electrochemistry communications* , 3, 727-732. https://doi.org/10.1016/S1388-2481(01)00252-1

74. Murado, M. A., Montemayor, M. I., Cabo, M. L., Vazquez, J. A., & Gonzalez, M. P. (2012). Optimization of extraction and purification process of hyaluronic acid from fish eyeball. *Food Bioprod. Proc.* , 90, 491–498. https://doi.org/10.1016/j.fbp.2011.11.002
75. Nishikawa, H., Okumura, D., Kusunoki, M.,& Hontsu, S. (2006). Application of hydroxyapatite thin film as a biosensor. *American Physical Society.* APS March Meeting, March 13-17, V16.011.
76. Njagi, J., Ispas, C., & Andreescu, S. (2008). Mixed ceria-based metal oxides biosensor for operation in oxygen restrictive environments.*Anal Chem.* , 80, 7266–7244. doi: 10.1021/ac800808a
77. Noh, H., Chandra, P., Moon, J.O., & Shim, Y. (2012). In vivo detection of glutathione disulfide and oxidative stress monitoring using a biosensor. *Biomaterials,* 33, 2600-2607. doi: 10.1016/j.biomaterials.2011.12.026
78. Ogawa, T., Watanabe, M., Naganuma, T., & Muramoto, K. (2011). Diversified carbohydrate-binding lectins from marine resources. *Journal of amino acids* , 1, 838914. https://doi.org/10.4061/2011/838914
79. Oliveira, J. M., Grech, J. M. R., Leonor, I. B., Mano, J. F. M., & Reis, R. L.(2007). Calcium-phosphate derived from mineralized algae for bone tissue engineering applications. *Materials Letters* , 61, 3495–3499. DOI: 10.1016/j.matlet.2006.11.099
80. Pacheco-Quito, E. M., Ruiz-Caro, R., & Veiga, M. D. (2020). Carrageenan: Drug Delivery Systems and Other Biomedical Applications.*Marine Drugs* , 18, 583. https://doi.org/10.3390/md18110583
81. Panagiotis, B. (2015). Marine Collagen: Extraction and Applications. In: *Research Trends in Biochemistry, Molecular Biology and Microbiology* .
82. Patra, J. K., Das, G., Fraceto, L. F., Campos, E. V. R., del Pilar Rodriguez-Torres, M., Acosta-Torres, L. S., Diaz-Torres, L. A., Grillo, R., Swamy, M. K.,Sharma, S., Habtemariam, S., & Shin, H. S. (2018). Nano based drug delivery systems: Recent developments and future prospects. *J. Nanobiotechnol,* 16, 71. https://doi.org/10.1186/s12951-018-0392-8
83. Paul, R., & Dertein, E. (2018). Piezoelectric sensors, In: Sensors for Mechatronics (second edition).
84. Peiris, D., Markiv, A., Curley, G. P., & Dwek, M. V. (2012). A novel approach to determining the affinity of protein–carbohydrate interactions employing adherent cancer cells grown on a biosensor surface. *Biosensors and Bioelectronics* , 35, 160-6. doi: 10.1016/j.bios.2012.02.037
85. Piccirillo, C., Pintado, M., & Castro, P. (2013). Hydroxyapatite and calcium phosphates from marine sources: Extraction and characterization. In: Kim, S. K. (Ed), *Marine Biomaterials: Characterization, Isolation and Applications* , CRC Press Boca Raton, FL, 29–44.
86. Pinsino, A., Torre, C. D., Sammarini, V., Bonaventura, R., Amato, E., & Matranga, V. (2008). Sea urchin coelomocytes as a novel cellular biosensor of environmental stress: a field study in the Tremiti Island Marine Protected Area, Southern Adriatic Sea, Italy. *Cell Biol Toxicol* ., 24, 541-52. doi: 10.1007/s10565-008-9055-0.
87. Prajapati, V. D., Maheriya, P. M., Jani, G. K., & Solanki, H.K.(2014). Carrageenan: A natural seaweed polysaccharide and its applications. *Carbohydr. Polym.* , 105, 97–112. doi: 10.1016/j.carbpol.2014.01.067
88. Purohit, B., Vernekar, P. R., Shetti, N. P., & Chandra, P. (2020). Biosensor nanoengineering: Design, operation, and implementation for biomolecular analysis. *Sensors International,* 1, 100040. https://doi.org/10.1016/j.sintl.2020.100040
89. Quek, S. B., Cheng, L., & Cord-Ruwisch, R. (2015). Microbial Fuel Cell Biosensor for Rapid Assessment of Assimilable Organic Carbon under Marine Conditions. *Water research* , 77, 64-71. https://doi.org/10.1016/j.watres.2015.03.012
90. Rahman, M. A., & Halfar, J. (2014). First evidence of chitin in calcified coralline algae: New insights into the calcification process of *Clathromorphum compactum* . *Sci. Rep.* 4, 6162. https://doi.org/10.1038/srep06162
91. Ramesh, C., Vinithkumar, N. V., Kirubagaran, R., Venil, C. K., & Dufosse, L. (2019). Multifaceted applications of microbial pigments: current knowledge, challenges and future directions for public health implications. *Microorganisms* . 7(7), 186. https://doi.org/10.3390/microorganisms7070186
92. Rassas, I., Braiek, M., Bonhomme, A., Bessueille, F., Raffin, G., Majdoub, H., & Jaffrezic-Renault, N.

(2019). Highly Sensitive Voltammetric Glucose Biosensor Based on Glucose Oxidase Encapsulated in a Chitosan/Kappa-Carrageenan/Gold Nanoparticle Bionanocomposite. *Sensors (Basel)* , 19, 154. doi: 10.3390/s19010154.

93. Rea, I., & De Stefano, L. (2019). Recent Advances on Diatom-Based Biosensors. *Sensors* , 19, 5208. https://doi.org/10.3390/s19235208
94. Ripp, S., David, E. N., Ahn, Y., Werner, C., Jarrell, J., Easter, J. P., Cox, C. D., Burlage, R. S., & Sayler, G. S. (2000). Controlled Field Release of a Bioluminescent Genetically Engineered Microorganism for Bioremediation Process Monitoring and Control. *Environmental Science & Technology, 34,* 846-853. https://doi.org/10.1021/es9908319
95. Rossi, S., Mori, M., Vigani, B., Bonferoni, M. C., Sandri, G. Riva, F. Caramella, C. & Ferrari, F. A. (2018). Novel dressing for the combined delivery of platelet lysate and vancomycin hydrochloride to chronic skin ulcers: hyaluronic acid particles in alginate matrices. *Eur. J. Pharm., Sci.* 118, 87–95. DOI: 10.1016/j.ejps.2018.03.024
96. Sanchez-Ferandin, S., Leroy, F., Bouget, F. Y., & Joux, F. A. (2013). New, sensitive marine microalgal recombinant biosensor using luminescence monitoring for toxicity testing of antifouling biocides.*Applied and environmental microbiology* , 79, 631-638. doi: 10.1128/AEM.02688-12.
97. Schroder, H. C., Wang, X. H., Tremel, W., Ushijima, H., & Muller, W.E.(2008). Biofabrication of biosilica-glass by living organisms.*Nat. Prod. Rep* , 25, 455–474. doi: 10.1039/b612515h
98. Selveraj, V., Thomas, N., Anthuvan, A. J., Nagamony, P., & Chinnuswamy, V. (2018). Amine-functionalized diatom frustules: A platform for specific and sensitive detection of nitroaromatic explosive derivative. *Env. Sci. Pollut. Res* ., 25, 20540–20549. https://doi.org/10.1007/s11356-017-0916-z
99. Seshadri, S., Prakash, A., & Kowshik, M. (2012). Biosynthesis of silver nanoparticles by marine bacterium, Idiomarina sp. PR58-8. *Bulletin of Materials Science* , 35, 1201-5.
100. Sevilla, E., Yuste, L., & Rojo, F. (2015). Marine hydrocarbonoclastic bacteria as whole-cell biosensors for n-alkanes. *Microb Biotechnol* , 8, 693-706. doi: 10.1111/1751-7915.12286.
101. Sharma, D., Kanchi, S., & Bisetty, K. (2019). Biogenic synthesis of nanoparticles: A review. *Arab. J. Chem.* 12, 3576–3600. https://doi.org/10.1016/j.arabjc.2015.11.002
102. Shen, X., Ju, F., Li, G., & Ma, L. (2020). Smartphone-based electrochemical potentiostat detection system using pedot: Pss/chitosan/graphene modified screen-printed electrodes for dopamine detection. *Sensors (Switzerland)* , 20, 2781. https://doi.org/10.3390/s20102781
103. Silva, E. A., Kim, E. S., Kong, H. J., & Mooney, D. J. (2008). Material-based deployment enhances efficacy of endothelial progenitor cells. *Proc Natl Acad Sci USA.* 105, 14347–14352. https://doi.org/10.1073/pnas.0803873105
104. Simao, E. P., Silva, D. B. S., Cordeiro, M. T., Gil, L. H. V., Andrade, C. A. S., & Oliveira, M. D. L. (2020). Nanostructured impedimetric lectin-based biosensor for arboviruses detection.*Talanta* , 208, 120338. doi: 10.1016/j.talanta.2019.120338
105. Singh, A., Sinsinbar, G., Choudhary, M., Kumar, V., Pasricha, R., Verma, H. N., Singh, S. P., & Arora, K. (2013). Graphene oxide-chitosan nanocomposite based electrochemical DNA biosensor for detection of typhoid. *Sensor Actuat B-Chem.,* 185, 675–684. https://doi.org/10.1016/j.snb.2013.05.014
106. Singh, C. R., Kandasamy, K., & Sekar, A. (2015). A review on marine based nanoparticles and their potential applications. *African Journal of Biotechnology* , 14, 1525-32. https://doi.org/10.5897/AJB2015.14527
107. Singh, R., Verma, R., Kaushik, A., Sumana, G., Sood, S., Gupta, R. K., &. Malhotra, B. D. (2011). Chitosan-iron oxide nano-composite platform for mismatch-discriminating DNA hybridization for Neisseria gonorrhoeae detection causing sexually transmitted disease. *Biosens. Bioelectron* , 26, 2967–2974. doi: 10.1016/j.bios.2010.11.047
108. Solanki, P. R., Patel, M. K., Ali, M. A., & Malhotra, B. D. (2015). A chitosan modified nickel oxide platform for biosensing applications.*Journal of Materials Chemistry B,* 3, 6698-708. https://doi.org/10.1039/C5TB00494B
109. Sousa, S., Duffy, C., Weitz, H., Glover, L. A., Bar, E., Henkler, R., & Killham, K.(1998). Use of a lux-modified bacterial biosensor to identify constraints to bioremediation of btex-contaminated

sites.*Environmental Toxicology and Chemistry.* 17, 1039-1045.doi: 10.1002/etc.5620170609

110. Srivastava, A., Srivastava, A., Srivastava, A., & Chandra, P. (2015). Marine biomaterials in therapeutics and diagnostic, In: Kim, S. K. (Ed), *Springer Handbook of Marine Biotechnology,* Springer, Berlin, Heidelberg, pp. 1247-1263.
111. Sudhan, N., Lavanya, N., Leonardi, S. G., Neri, G., & Sekar, C. (2019). Monitoring of Chemical Risk Factors for Sudden Infant Death Syndrome (SIDS) by Hydroxyapatite-Graphene-MWCNT Composite-Based Sensors. *Sensors (Basel)* , 19, 3437. doi: 10.3390/s19153437
112. Suginta, W., Khunkaewla, P., & Schulte, A. (2013). Electrochemical biosensor applications of polysaccharides chitin and chitosan. *Chemical reviews* , 113, 5458-5479. doi: 10.1021/cr300325r
113. Sun, J., Yu, J., Jiang, Z., Zhao, Z., & Xia, Y. (2020). Fluorescent carbonized polymer dots prepared from sodium alginate based on the CEE effect. *ACS Omega* , 5, 27514-27521. https://doi.org/10.1021/acsomega.0c03995
114. Taşaltın, N., Aydın, E., Karakuş, S., & Kilislioğlu, A. (2020). K-carrageenan/PVA/nano-eggshell biocomposite-based non-enzymatic electrochemical biosensor for low-level urea detection. *Appl. Phys. A* , 126, 827. https://doi.org/10.1007/s00339-020-03960-1
115. Tavakoli, J., & Youhong, T. (2017). Hydrogel Based Sensors for Biomedical Applications: An Updated Review. *Polymers* , 9, 364. doi: 10.3390/polym9080364
116. Teixeira, E. H., Arruda, F. V. S., do Nascimento, K. S., Carneiro, V. A., Nagano, C. S., Rocha da Silva, B., Sampaio, A. H., & Cavada, B.S. (2012). Biological applications of plants and algae lectins: an overview. In: Chang, C. F. (Ed), *Carbohydrates-Comprehensive Studies on Glycobiology and Glycotechnology* , InTech, Rijeka, Croatia.
117. Thouand, G., Daniel, P., Horry, H., Picart, P., Durand, M. J., Killham, K., Knox, O. G. G., DuBow, M. S., & Rousseau, M. (2003). Comparison of the spectral emission of lux recombinant and bioluminescent marine bacteria. *Luminescence* , 18, 145-55. doi: 10.1002/bio.716.
118. Tonnina, D., Campanella, L., Sammartino, M. P., & Visco, G. (2002). Integral toxicity test of sea waters by an algal biosensor. *Annali di chimica.* 92, 477-484.
119. Tramontano, C., Chianese, G., Terracciano, M., Napolitano, M., De Stefano, L., & Rea, I. (2020). Nanostructured Biosilica of Diatoms: From Water World to Biomedical Applications. *Appl. Sci* ., 10, 6811. https://doi.org/10.3390/app10196811
120. Turemis, M., Silletti, S., Pezzotti, G., Sanchís, J., Farré, M., & Giardi, M.T. (2018). Optical biosensor based on the microalga-paramecium symbiosis for improved marine monitoring. *Sensors and Actuators B: Chemical* , 270, 424-432. https://doi.org/10.1016/j.snb.2018.04.111
121. Turner, A. P. (2000). Biosensors–sense and sensitivity,*Science* , 290, 1315-1317. DOI: 10.1126/science.290.5495.1315
122. Vázquez, J. A., Rodríguez-Amado, I., Montemayor, M. I., Fraguas, J., del Pilar González, M., & Murado, M. A. (2013). Chondroitin sulfate, hyaluronic acid and chitin/chitosan production using marine waste sources: Characteristics, application and ecofriendly processes: A review. *Mar. Drugs* , 11, 747–774. doi: 10.3390/md11030747
123. Velasco-Garcia, M. N. (2009). Optical biosensors for probing at the cellular level: A review of recent progress and future prospects.*Semin Cell Dev Biol,* 20, 27–33. doi: 10.1016/j.semcdb.2009.01.013
124. Venil, C. K., Aruldass, C. A., Dufossé, L., Zakaria, Z. A., & Ahmad, W. A. (2014). Current perspective on bacterial pigments: emerging sustainable compounds with coloring and biological properties for the industry – an incisive evaluation. *RSC Adv.,* 4, 39523. https://doi.org/10.1039/C4RA06162D
125. Venkatesan, J., Lowe, B., Anil, S., Manivasagan, P., Kheraif, A. A. A., Kang, K., & Kim, S. (2015). Seaweed polysaccharides and their potential biomedical applications, *Starch,* 67 (5–6) 381-390. https://doi.org/10.1002/star.201400127
126. Venkatesan, J., Manivasagan, P., & Kim, S. K. (2015). Marine Microalgae Biotechnology: Present Trends and Future Advances. In: Kim, S. K. (Eds), *Handbook of Marine Microalgae* , 1-9.
127. Venkatesan, J., Sukumaran, A., Rao, S., & Kim, S. K. (2019). Macroalgal Fucoidan for Biomedical Applications. In: Ravishankar, G. A., & Ambati, R. R. (Eds). *Handbook of Algal Technologies and Phytochemicals.* Volume I, Food, Health and Nutraceutical Applications. CRC Press pp. 13-24.

128. Verma, D., & Fortunati, E. (2019). Biopolymer processing and its composites: An introduction. In: Biomass, Biopolymer-Based Materials, and Bioenergy*,* Woodhead Publishing Series in Composites Science and Engineering, pp. 3-23.
129. Wang, L., Xu, M. E., Luo, L., Zhou, Y., & Si, P. (2018). Iterative feedback bio-printing-derived cell-laden hydrogel scaffolds with optimal geometrical fidelity and cellular controllability. *Sci. Rep.,* 8, 2802. https://doi.org/10.1038/s41598-018-21274-4
130. Xu, S. C., Zhang, Y. Y., Dong, K., Wen, J. N., Zheng, C. M., & Zhao, S. H. (2017). Electrochemical DNA biosensor based on graphene oxide-chitosan hybrid nanocomposites for detection of*Escherichia coli* O157:H7. *Int J Electrochem Sc.* , 12, 3443–3458. doi: 10.20964/2017.04.16
131. Zhang, Y., Zhnag, W., Zhnag, Q., Li, K., Liu, W., Liu, Y., & Banks, C. E. (2014). Green electrochemical sensing platforms: utilizing hydroxyapatite derived from natural fish scales as a novel electrochemical material for the sensitive detection of kidney injury molecule 1 (KIM-1). *Analyst,* 139, 5362-5366. DOI https://doi.org/10.1039/C4AN00957F
132. Zhao, S., Zhou, Y., Wei, L., & Chen, L. (2020). Low fouling strategy of electrochemical biosensor based on chondroitin sulfate functionalized gold magnetic particle for voltammetric determination of mycoplasma ovipneumonia in whole serum. *Analytica chimica acta* , 1126, 91–99. doi: 10.1016/j.aca.2020.06.015.
133. Zong, S., Cao, Y., Zhou, Y., & Ju, H. (2006). Zirconia nanoparticles enhanced grafted collagen tri-helix scaffold for unmediated biosensing of hydrogen peroxide. *Langmuir: the ACS journal of surfaces and colloids* , 22, 8915–8919. doi: 10.1021/la060930h.