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Functional modification mediated value addition of seaweed polysaccharides - A perspective†

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A diverse array of functionally modified seaweed polysaccharide derivatives were prepared, which would be described in this account principally based on the reports published by us during the last decade. The modification reactions involved esterification, -C-N- bond formation and amidation reactions engaging the C-6 carbon of one of the repeating pyranose moieties of the polysaccharides of seaweed species growing in Indian waters, occasionally employing grafting and crosslinking reactions. The new functional properties that were imparted on the modified polysaccharides as a result, included fluorogenicity, thixotropicity, pH-responsiveness and gelling/swelling/metal ion absorbing properties. Of these, some properties were targeted, some were obtained fortuitously, and the latter included thixotropicity and photosensitizer activity. This article showcases various polysaccharide based new materials and the value added seaweed biomass, presenting potential opportunities in this area of research.

1. Introduction

Polysaccharides have polymeric carbohydrate structures, consisting of repeating units (either mono- or di-saccharides) joined together by glycosidic bonds and they are the oldest biopolymers present on earth. The basic function of polysaccharides in living systems is energy storage, besides providing structural strength. In seaweeds, polysaccharides prevent desiccation during their exposure at low tides. The structure of polysaccharides is often linear, but it may contain various degrees of branching. Most of the polysaccharides with some exceptions are soluble in water. After many years of oblivion, the area of polysaccharide chemistry is presently receiving renewed attention. This is mostly due to the increase in the understanding of the role of these polymers in various biological processes.

The majority of the polysaccharides have plenty of hydroxyl and/or carboxyl groups. The presence of these important functional groups made them amenable to chemical derivatization (cf. Fig. 1), resulting in derivatives with functional properties, which were different than those of the parent ones. Active research activities on the modification of polysaccharides are under way in various labs to explore the possibilities of their newer applications in fields such as in biomedical,[1-4] biochemical,[5-7] physicochemical[8] as well as in industrial applications,[9, 10] It has been demonstrated by researchers including us that derivatization of the gelling seaweed polysaccharides agar/agarose based materials results in new properties e.g. pH-stablity and/or pH-responsive,[11-13] fluorogenic,[14-18] self-assembled nano-material,[19] sweetening,[20] and controlled-release[15] properties. On the other hand, alginate derived materials exhibited the following properties: thixotropic,[21] fluorogenic,[22, 23] metal ion scavenging,[23, 24] sprayable soft gel,[25] controlled-release,[26] porous-catalytic,[27] properties. Further, carrageenan based new materials exhibited fluorogenic, gelling,[28] as well as absorbent[29, 30] properties.

In an article the work on alginate derivatization, their properties and applications have been eminently reviewed by Pawar *et al*., (2012)[31]. Singh *et al.* (2009) reviewed modification of polysaccharides and other polymeric compounds through different reactions including grafting reactions, which led to improved functions e.g. flocculating properties[32]. Mergy *et al*., (2012), described modification of several ene-functional charged and neutral polysaccharides, i.e., hyaluronic acid and dextran, by esterification reaction of the hydroxyl groups, which led to the synthesis of several functional biomaterials[33]. Recently, Cumpstey (2013) has summarized modification of polysaccharide structures by various reactions[34]. Kristi L. Kiick and co-workers have reported preparation of polysaccharides based new materials mainly by hybridization with synthetic polymers.[35, 36] Polysaccharides with tailored nanostructures for biomedical applications have also been reported by Boddohi *et al*., (2009)[37]. Terrestrial plant polysccharides as well as the marine derived ones have been chemically modified for biomedical applications.[38] Singh *et al*., (2010) have reported grafting of polysaccharides and applications of these new materials.[39] Potential uses of novel modified seaweed polysaccharides have been studied as flocculating[40] and antiviral agents.[41] Chemical modification of

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alginate by free-radical graft copolymerization has been reviewed.[42] Microwave-assisted alkaline modification of seaweed galactans has also been reported.[43] Esterification of various polysaccharides including seaweed polysaccharides has been reviewed by Heinze *et al*., (2006)[44] and Campo *et al.*, (2010) have reviewed biological properties, chemical modifications and structural characterization of carrageenan.[45] Another review article describes properties and application of seaweed polysaccharides e.g. agar/agarose, alginate and carrageenan.[46]

Unlike the terrestrial plant derived polysaccharides, the seaweed derived polysaccharides such as, agar and carrageenans are acid sensitive polymers and alginate on the other hand is stable in acid and alkali. The real challenge in the modification of these polymers lies in the fact that they enhance solution stability in a wide range of pH, modify gelling behavior, crystallinity and chiral disposition, which would make them amenable to diverse new applications.

Agarose is extracted from red seaweeds and it is widely used as gelling agent in biomedical and bioengineering applications. The basic disaccharide repeating units of agarose consist of (1, 3) linked β-D-galactose and (1, 4) linked α-L-3, 6-anhydrogalactose. Alginic acid is the major structural polysaccharide of brown algae belonging to the family Phaeophyceae. It is a linear block copolymer of two monomeric units, namely β-D-mannuronopyranosyl and α-L-guluronopyranosyl units. These monomers occur in three types of blocks one contains mostly mannuronic acid (M), or guluronic acid (G) and the third has intermediate composition (MG). Carrageenans represent yet another prominent class of gelling polysaccharide obtainable from red seaweeds. Major carrageenans are termed ι-, κ-, λ-carrageenans. Structurally, these carrageenans are consisted of sequences of: D-galactose-4-sulphate and 3,6-anhydro-D-galactose-2-sulphate (ι- carrageenan), D-galactose-4-sulphate and 3,6-anhydro-D-galactose (κ- carrageenan), D-Galactose-2-sulphate and D-galactose-2,6-disulphate (λ-carrageenan). Iota-, κ-carrageenans form stable gels in presence of metal ions e.g. potassium and calcium ions, whereas λ- carrageenan does not gel at all.

We have been successful to prepare a polysaccharide based material with thixotropic properties.[25] Such targeted attempts in our laboratory have been rewarded, e.g. introduction of amino groups on the polysaccharide backbone, some of which were subsequently cross-linked to afford new materials.[14, 22, 23] The studies described in this account primarily encompass commercially important seaweed polysaccharides as well as cellulose, which were used in the derivatization protocol (Fig. 1). Polysaccharide derivatives were prepared employing substrates say, hydrophobic, hydrophilic, aliphatic and aromatic compounds. The following advantages of these natural polymers under consideration basically motivated this work: (a) the resources are abundantly naturally occurring renewable biomass and are relatively cheaper; (b) their processing is fairly easy; (c) most of them are soluble in water. In the backdrop of the relevant body of works that has been done by other research groups in the realm of functional modification of seaweed polysaccharides, we present herein a perspective on our work in this area, which were carried out during the last decade, leading to value addition of seaweed bioresource.

2. Methodology

The seaweed polysaccharides agarose/agar, kappa-carrageenan and alginate were used for modification reactions. These polysaccharides, alginate (*Sargassum tenerrimum*), agarose (*Gracilaria dura*), carrageenan (*Kappaphycus alvarezii*) and agar (*Gelidiella acerosa and Gracilaria sp.*) were extracted from the seaweeds occurring in Indian waters, mentioned in the brackets, in our laboratory as reported earlier.[47, 48] The chemical modification work principally involved esterification, amide formation and C-N bond formation. Besides these, cross-linking reactions were employed using the natural cross-linker genipin involving suitable substrates such as various diamines. Chemical reactions for synthesizing the modified polysaccharides derivatives have been presented in Tables 1-4. The products were subsequently characterized employing various analytical methods e.g., Fourier transform infrared spectroscopy (FT-IR), nuclear magnetic resonance (NMR), UV-Vis spectrophotometry, inductively coupled plasma spectrophotometry (ICP), scanning electron microscopy (SEM), transmission electron microscopy (TEM), X-ray diffraction analysis (XRD), size-exclusion chromatography (SEC), electrospray ionization-mass spectrometry (ESI-MS), differential scanning calorimetry (DSC), thermogravimetric analysis (TGA), rheometry, fluorometry, circular dichroism-optical rotatory dispersion (CD-ORD) studies.

3. Discussion

The R&D works of this account can be divided in two parts: (a) Chemical bioprospecting of Indian seaweeds and (b) modification of polysaccharides.

In the process of chemical investigation of seaweeds followed by modification of polysaccharides, several materials with new functions were synthesized by us (cf. Fig. 1). One of the prominent outcomes of this work was identification of a little-known Indian seaweed species – *Gracilaria dura*, which produced superior quality agarose with excellent properties [low sulphate (ca. 0.2% w/w) and high gel strength of 2200 g cm^{-2} (1% gel, w/v) comparable to those available in the market, in a method using non-ionic surfactant induced freeze-thaw modification process.[48] Another significant spin-off was identification of an Indian seaweed species, a source of commercially important *iota*-carrageenan.[47]

Agarose or agar is as such an excellent gelling agent by itself – in water at a concentration of ca. 1% w/w, it forms strong gel. Aqueous solution of kappa-carrageenan (1% w/w) forms strong gel in presence of KCl or $CaCl_2$. Aqueous solution of sodium alginate forms viscous material, but in presence of $CaCl_2$ it forms strong gel. All these gelling seaweed

polysaccharides were chemically modified using several substrates, which resulted in new functional properties e.g. fluorogenic, swelling and metal ion scavenging properties, to name a few (Tables 1-4).

3.1 Fluorogenic

Agarose, carrageenan and alginate were modified to produce fluorogenic derivatives in a facile microwave induced method, which would be of potential utility in biomedical and pharmaceutical applications as sensors and radical scavengers. Agarose was modified using the nucleobases guanine, adenine and cytosine in a microwave mediated facile method. The new agarose derivatives exhibited significantly enhanced fluorescence intensities e.g. 85%, 30% and 143% enhancements respectively at a 5×10^{-5} M concentration, with regard to those of the pure nucleobases at a molar equivalent concentration that was present in the modified agarose solution. Similarly, *kappa*-carrageenan was modified with adenine and cytosine exhibiting 40% and 81% fluorsence enhancements respectively. These derivatives would be of potential utility in sensory applications (Fig 2)[16-18].

Carbodiimide (dicyclohexylcarbodiimide /4-dimethylaminopyridine) chemistry was employed to synthesize a fluorescent 6-*O*-naphthylacetyl agarose (NA-agarose), which under hydrolytic conditions released the plant growth regulator naphthyl acetic acid (NAA) in a controlled manner. Like in the case of modified agarose derivatives mentioned above, in a solution of NA-agrose derivative (1×10^{-3} M) an 82% enhancement of fluorescence was registered with respect to pure agarose at a specified concentration (0.08 mg), the molar equivalent present in NAA contnent in 1×10^{-3} M solution. This polymer derivative may find applications as a sustained release plant growth regulator and as sensor.[15]

A fluorescent agarose-L-tryptophan ester hydrogel was synthesized using carbodiimide chemistry. The hydrogel exhibited enhanced (65%) fluorescence emissions in aqueous solution (λ max 350 nm; 1×10^{-4}M), as opposed that of tryptophan at an equivalent concentration. A genipin crosslinked blue hydrogel was prepared with this ester hydrogel. Both the hydrogels exhibited similar gelling characteristics to agarose and they were stable across a wide range of pH media (pHs 1.2, 7.0 and 12.5) under ambient conditions.[49]

Amides of alginic acid (ALG) were synthesized using different diamines having varying numbers of carbon atoms and structure - hydrazine (HY), ethylenediamine (EDA), 1,6-hexanediamine (HDA), and 1,4-cyclohexanediamine (CHDA). All these amides underwent cross linking reaction with genipin involving the free pendant -NH_2 group of the amides, yielding fluorescent products. It may be noted that the amide ALG-EDA exhibited fluorescence while the other three amides did not. On the other hand all the genipin cross linked products showed significant fluorescence emissions, with ALG-EDA registering a three-fold enhancement in fluorescence intensity. There existed an inverse correlation of fluorescence intensity with the number of carbon atoms (Fig. 3).[22]

We intended to have a free -NH_2 group on to the backbone of agarose polymer, so that it can be functionalized further. In a facile Mitsunobu-inspired method 6-aminoagarose was synthesized for the first time under microwave irradiation. Amino-agarose may be deployed to generate cationic polysaccharide for possible applications as gene/drug delivery vehicles.[50, 51] 6-Aminoagarose was genipin cross linked to produce a blue hydrogel with similar characteristics as those of agarose. This aminoagarose was coupled with the biologically active substrates e.g. picolinic and nicotinic acids to afford corresponding fluorogenic amides. These amides exhibited enhanced (ca. 82% and ca. 90%) fluorescence emissions λ_{max} 430 and 412 nm at 1×10^{-3} M, respectively, compared to those of pure picolinic and nicotinic acids at molar equivalent concentrations (0.2 mg).[14]

So far it has been observed that in the fluorogenic agarose derivatives the fluorescence emissions are greater than that in the dilute solution (1×10^{-4} M) of modifying pure substrates. Oza *et al*.,[16] evoked that these enhancements were "at least partly due to the participation of fluorescent emissions (λ_{ex} = 266 nm) of water and highly diluted aqueous media, as described by Pershin (2002)[52] and Belovolova *et al*., (2009)[53] present in the polysaccharide-water matrix".

3.2 Photosensitizer activity

In the backdrop of our work on synthesizing alginic acid amides with aliphatic amines, in a strucutred approach, it was decided that a series of alginic acid amide derivatives would be synthesized using mono-, di- and trinuclear aromatic amines, and study their properties. Fortuitously, we chanced upon a few thixotropic alginate-phenyl/naphthyl amides, which would be discussed a little later (Fig. 4; sec. 3.3).

The ester and amide derivatives (Alg-Anth) of alginate (Alg) and 9-chloromethyl anthracene and 2-amino anthracene (Anth) respectively, did not exhibit any thixotropy. However, these derivatives showed photosensitizer activity as a "welcome bonus" instead, in presence of an acceptor pyrene in reasonably good efficiencies in transferring energy to the acceptor e.g. 63% with ester and 37% with amide. Hydrophilic–lipophilic balance (HLB) factor (> 10.0) of both the derivatives aptly qualified their suitability as solubilizers. These water soluble polysaccharide-based polymers may be used as sensor as well as these would be of potential utility as photosensitizers for reactions of organic compounds in aqueous media.[54]

3.3 Thixotropy

Thixotropic materials are those which starts to flow under shear by virtue of lesser viscosity than the initial value under zero shear stress. The material would attain the initial viscosity on withdrawal of shear. Different aromatic amides of alginate (Na-Alg) were synthesized. Anthryl amide was not thixotropic but it was photosensitizing, which is discussed above. Mononuclear aromatic amides viz. Na-Alg-Aniline amide (liquid) and Na-Alg-*p*-phenylene diamide (solid) were not thixotropic. The *o*-amino-benzoic (OABA) and *m*-amino benzoic

(MABA) acid amides of Na-Alg were thixotropic exhibiting 15 and 9 stucture recovery cycles in rheometric evaluations, whereas Na-Alg-1-naphthyl amide showed thixotropicity showing 9 stucture recovery cycles (Fig. 4 and Fig. 5).

These amides derived from *o*-amino-benzoic (OABA) and *m*-amino benzoic (MABA) acids exhibited adequate viscosity under a shear of ca. 32 mPa s at ca. 800 s^{-1} for Na-Alg/OABA, which may be suitable in sprayable formulations.[21, 25] The increase in the apparent viscosities of Na-Alg/OABA (822 ± 5.5 cP) and Na-Alg/MABA (315 ±5.0 cP) from that of Na-Alg (1% w/v) were attributed "to the formation of the stronger double helical structures through the participation of the -COOH group of OABA and MABA in the formation of hydrogen bonds subsequently increasing the number of junction zones in the gel network systems".

It prompts one to wonder if is it necessary to have amide functionality along with aromaticity (π-electron pool) in a compound to be thixotropic. Chejara *et al*., (2013)[21] sought to qualify the prerequisites with "the presence of favourable non-bonding or van der Waals' interactions between the amine/amide derivative and water (hydrophilic–lipophilic balance) instead must also be playing a crucial role for the formation of such thixotropic materials". New functional materials may be designed on the basis of this study for their potential applications as pharmaceuticals, sensors and actuators.

3.4 Absorbent hydrogel, pH-responsiveness and controlled-release properties

A blend of agar/Na-alginate was grafted with polyacrylamide to afford new interpolymeric materials with superior swelling properties. Further polysaccharide adducts (polyuronic acid/chitosan) exhibited superior swelling properties in aqueous media. These new materials would be of potential utility in pH-specific dosage delivery applications.

Meena *et al*., (2008) reported robust hydrogel formed by a material Agar/Na-Alg blend (1:3) grafted with polyacrylamide (PAAm).[55] This grafted product showed maximum swelling capacities of 24, 18 and 11 g g^{-1}, while Na-Alg swelled 14, 12 and 8.5 g g^{-1} in acidic, neutral and alkaline media, respectively. Similarly, using the blend employing polyacrylonitrile (PAN), Agar/Na-Alg-*graft*-PAN synthesized, which exhibited a relatively lower swelling capacity (8.5 g g^{-1} at pH 1.2).[56] Meena *et al*., (2008), reports that "enhanced swelling capacity of the blend in acidic pH 1.2 was presumably due to the presence of acidic pH stable sodium alginate.[55] It may be noted that one of the blend components was acid-labile agar, nonetheless the acid stability of the blend hydrogel product may be attributed to increased entanglements of the macromolecule chains within the blend hydrogel, causing slower diffusion in the aqueous medium".

Sodium alginate is constituted of polymannuronic acid (PMA) and polyguluronic acid (PGA). These acids were isolated from a sample of sodium alginate of Indian *Sargassum* seaweed species employing a microwave assisted method and the M/G ratio (0.38) was determined. Chitosan (CH) was used to synthesize super-swellable hydrogel adducts (CH-PMA and CH-PGA) of these polymeric acids in very high yields (95-97%) under microwave irradiation, which showed swelling ratios (2700–3000%). This outlines a superior method to the conventional thermal heating method.[57] The swelling behavior was harnessed to demonstrate controlled-release of structurally different drugs e.g., Paracetamol (PCT), indomethacin (IND), isoniazid (INH), atenolol (ATN) and pravastatin (PST). The release rate was pH- and structure-dependent. The drugs containing –NHCO- group (PCT, INH and ATN) release rate decreased with increasing pH i.e., highest at pH 1.2 and lowest at pH 7.4. However, the drugs having no (IND and PST) showed a reversed trend in release rate with pH. Chhatbar *et al*., (2013) noted that this phenomenon of pH-dependence to have an apparent correlation "with the structural features of the adducts and the drugs containing -NH-CO- groups, manifesting pH-dependent preferential interactions of -NH-CO- groups through intermolecular hydrogen bonding facilitated at a higher pH".[58]

3.5 Genipin cross-linking imparts unusual stability of galactans in acidic media

Genipin reacts with compounds containing free -NH_2 group and produces blue to deep blue cross-linked products.[59] Agar and kappa-carrageenan are extremely acid lable and do not contain any amino group on its backbone. They have been found to contain small amounts of proteins (0.25% and 2.0% respectively), apparently entangled in their polymer chains. On reaction of these polymers with genipin produced blue cross-linked products with remarkable acid stability. That the proteins participated in the genipin cross linking reaction was confirmed by the fact that on removal of proteins from the polysaccharides, genipin reaction did not afford any blue colored corss linked product. Genipin-fixed agarose hydrogel in various pH media (1.2, 7.0 and 12.5) swelled up to 1100-1500 min to achieve an equilibrium (swelling ratio 4000-5000%), when degradation of the polymer ensued.

Similarly, over a period of 1100-1500 min genipin cross linked kappa-carrageenan (kC) hydrogel swelled to produce equilibrium swelling ratios 4500-2400% in acidic, neutral and alkali media. The swollen carrageen hydrogel began to disintegrate beyond the point of equilibrium swelling in acidic medium (pH 1.2). By virtue of this significant stability and swelling capacity of genipin cross linked agarose and kappa-carrageenan based products in pH 1.2, these hydrogels would be of utility in sustained delivery pharmaceutical formulations.[60, 61]

A follow-up of the above work was reported by Meena *et al*., (2009) wherein genipin cross linked super-swellable hydrogel of agar-carrageenan blend (agar/kC) was described. The hydrogels were distinguished by their remarkable stability in various pH media and Ringer's solution. The swelling ratios were in the range 4500-2200% in different pH media 1.2 to 12.5 up to 20 h. These characteristics predispose this hydrogel for its potential utility in food applications.[11]

A pendant amino group was introduced on the agarose backbone by modifying it with L-phenylalanine to yield an ester derivative agarose-6-*O*-L-phenylalanine, which underwent cross linking reaction with genipin. Both the ester and cross linked hydrogels exhibited comparable gelling properties with those of agarose. Phenylalanine containing hydrogels can form hydrophilic interpenetrating network and may be used in biomedical devices e.g. contact lenses, scaffolds as well as in specific targeted delivery applications.[12]

3.6 Interpolymeric metal ion scavenging materials

Modified polysaccharide amide derivatives were prepared which were fluorogenic, which would be of potential utility as sensors and for metal ion scavenging from aqueous media offering an opportunity for their applications in the areas of water purification and environmental protection.

A novel rhodamine–alginate polymer-based highly fluorogenic compound was reported, which was immobilized on calcium alginate to generate colorimetric, chemosensor beads. These beads effectively extracted Hg^{2+} and Cr^{3+} ions from aqueous media at pH 7.1 (Fig. 6). The beads could be reused to extract the ions for 3 cycles employing KI washes for regeneration purpose.[24]

A new water soluble fluorogenic interpolymeric diamide was synthesized using alginic acid and polyglucuronic acid (PGA) amide of ethylenediamine (EDA), through a monoamide of PGCA and EDA, in greater than 80 wt % yields in each step. TEMPO (2,2,6,6-tetramethyl piperidine-1-oxyl radical) oxidation of cellulose of the halophytic plant *Salicornia brachiata*[62] was used to afford PGA. The monoamide of PGA exhibited 7-fold greater fluorescence emissions than those of the interpolymeric diamide. The monoamide showed superior heavy divalent metal ions (Pb^{2+} and Hg^{2+}) scavenging properties to those of the diamide, the optimum adsorptions of ions were 398.8 and 282.8 mg/g, respectively (Sanandiya and Siddhanta, 2013).[23]

3.7 Miscellaneous properties

3.7.1 Sweet agarose

Sweet agarose was prepared. This was synthesized in situ with agarose and saccharin to produce a water-soluble agarose-saccharate, which was sweeter in 150 ppm solution than sucrose although significantly less sweet than pure sodium saccharate. Agarose-saccharate did not have bitter aftertaste in 675 ppm solutions or in the solid state. Pure sodium saccharate, on the other hand tasted bitter under identical conditions. This sweet agarose would be of potential use as a food additive.[20]

3.7.2 Sugar reactivity of agar

Sugar reactivity of agar in presence of glucose was reported for the first time by Meena *et al*., (2006).[63] Agars of Indian agarophytes viz. *Gelidiella acerosa*, *Gracilaria edulis*, *Gracilaria crassa* and *Gelidium pusillum*, collected from the Gulf of Mannar, India, were used in this study. The sugar reactivity was more pronounced in presence of sucrose (ca. 25–45%) than glucose (19–34%) in terms of their increased gel strengths ca. 25–45% with sucrose vs. 19–34% with glucose, respectively. In this study Oxoid agar was used as reference material. This was a classic example of useful spin-offs of the chemical bioprospecting studies that were carried out in our lab on the polysaccharides of Indian seaweeds.[63]

3.7.3 Hydrophobization of agarose, kappa-carrageenan and a sulphated heteropolysaccharide and adhesive property

Agarose was hydrophobized with fatty acids affording a nano-material. Hydrophobically modified nano-sized particulate esters of agarose and stearic/palmitic acids (Ag-SA and Ag-PA), was achieved employing carbodiimide chemistry. This hydrophobized agarose formed self-assembled nano-sized particles. The aqueous solution of the modified polymer was studied by dynamic light scattering and transmission electron microscopy, which showed the presence of 4-5 nm micelles, and 220-250 nm polymeric vesicles. The self-aggregate was spherical in shape (TEM). These new nano-sized agarose based materials may be of potential utility as drug delivery vehicles.[19]

Recently, we have reported syntheses of agarose half-esters of succinic, phthalic and maleic acids, which formed nano-sized polymer vesicles (32-124 nm) in aqueous solution. "The aqueous solution of sodium salts of these esters exhibited enhanced electrical conductivity (ca. 17.5 mS/cm at 40 °C) as compared to those of the parent half-esters (ca. 0.3 mS/cm at 40 °C). These new agarose based nano-sized materials may have potential applications in electrochemical devices, sensors and as drug carriers".[64]

Besides our recent report on interpolymeric polysaccharide derivatives described in Section 3.6 above, earlier in a bid to have interpolymeric products involving seaweed polysaccharides and synthetic polymers, Prasad *et al*., (2006)[65] reported the syntheses of copolymer hydrogels e.g. agar-*graft*-PVP and kappa-carrageenan-*graft*-PVP (PVP = polyvinypyrrolidone) in a one-pot method. These hydrogels exhibited enhanced water-holding capacity and crystallinity. Similarly, Meena *et al*., (2006)[29] described the syntheses of *kappa*-carrageenan-*graft*-PMMA (PMMA = polymethyl methacrylate) and kappa-carrageenan-*graft*-PAAm (PAAm = polyacrylamide). The latter exhibited superior swelling property and maximum swelling was registered in alkaline pH 12.5 (22 g g^{-1}). This product demonstrated excellent binding properties, which held sheets of papers, polyethylene and pieces of wood. The binding property was comparable with those of Fevicol®, a commercially available adhesive (Pidilite Industries, Mumbai, India). Latterly, we have reported synthesis of a similar adhesive polysaccharide based grafted product wherein the sulphated heteropolysaccharide of the brown seaweed *Cystoseira indica* was grafted with PVP.[66]

3.7.4 Agar-surfactant interactions

It has been extensively reported that gelling characteristics of polymers in solutions can be modulated employing surfactants.[67] Surfactants have been reported to play an important role in facilitating gelation of associating polymers.[68] It was reported that non-ionic surfactants, Triton X-100 and

Brij 35, reduced the viscosity of agar extractive obtained from a red seaweed *Gelidiella acerosa*. Subsequently, we also observed Synperonic® 91/6, a polyoxyethylene (6) C9-C11 synthetic alcohol ethoxylate and Triton X-100 (octyl phenol ethoxylate), which are non-ionic in nature, precipitated agarose from the aqueous extractive of the seaweed *Gracilaria dura*. Repeated water and alcohol washes removed adhering surfactant from the agarose polymer.[69] Subsequently, development of a new process for agarose extraction from red seaweed was reported by Meena *et al*., (2014),[48] which did away with the use of conventional energy-intensive freeze-thaw method. In this energy-efficient process the seaweed extractive is treated with a non-ionic surfactant Triton X-100 under stirring at ambient conditions. Agarose got precipitated in an easily dispersible finely granular form, which was isolated by filtration. This agarose was benchmarked with commercially available products (Sigma and Merck), which was found to be exhibiting comparable performance to that of the commercial agarose. [48] This process was found to be suitable to only those agar polysaccharides containing very low sulphate (<0.2%).

In another study, Sing *et al*., (2007)[70] reported the process of complex formation, and phase separation in gelatin–agar aqueous solutions. Coacervation of agar, an anionic polysaccharide, ensued via associative complexation up on mixing with gelatins (Type-A and B; a polyampholyte) in aqueous solution employing an acid-base tritrimetric method. This was noted that "electrostatic and patch-binding interactions" led to the formation of coacervates.

3.7.5. Porous material and catalytic activity

Modification of alginic acid was reported using *ortho*-tolidine, a water soluble alginic acid-biphenyl, forming an amide conjugate under microwave irradiation at pH 4.0. A significant change in the optical rotation values of alginic acid (-30.82°) and the conjugate (+39.48°) confirmed that a significant chiroptical makeover had taken place. The conjugate had a porous structure and the porosity values decreased from 0.85 (parent alginic acid) to 0.67 (the amide conjugate). Alginic acid/*o*-tolidine conjugate (pK_b *ca.* 11.0) was used as a catalyst for direct asymmetric nitroaldol reaction (Henry reaction) of nitromethane with benzaldehyde yielding ca. 85% aldol product.[27] This amide conjugate provides an important clue for further investigation for developing organo-catalysts for synthetic purposes.

4. Outcomes

A summary of the various methods of functional modification of polysaccharides and the new effects generated has been presented in Table 5. The following are the important outcomes of the studies reviewed herein.

(a) The C-6 position of the pyranose moiety of the repeating units of polysaccharides is well disposed to access for modification reactions.

(b) Choice of substrates for tagging them on to the polysaccharide backbone is important for onward modification opportunities. For example, alginate based new porous material and a thixotropic amide were serendipitously engineered.

(c) Direct insertion of -NH_2 group onto the C-6 carbon would be extremely useful to a host of predictable consequences in generating new materials. Methylene(s) can be a useful group to serve as a spacer between the C-6 carbon and the -NH_2 group for modulating functional properties e.g. fluoroscence. Likewise, introduction of -SH- or -S- onto the polysaccharide structure would be of great value considering their biological significance.[33]

(d) Above all, these polysaccharide based materials would move the seaweed bioresources up the value chain (Table 5).

5. Future prospects

Some known methods reported in the literature were adapted to modify seaweed polysaccharides for bringing about new functional properties, which have been described in this account. Looking ahead, in the endeavor of striving towards materials security, efforts may be focused to look for new materials with a range of novel functions to contain the future demands of various dimensions. Several strategies can be employed to achieve this goal. There may be targeted strategies to engineer materials with desired functions, while on the other hand a considered approach may lead to serendipitous results of utility. These are likely to produce materials with various new properties and attributes, as described in this account for example, thixotropic, fluorescent, porous and photosensitizing materials.

A careful projection tells one that cross-linking reactions as well as inter-polymeric products would possibly be attractive choices with numerous possibilities. Seaweeds as sources of polysaccharides can play a significant role in this endeavor. In emerging economies like the one of India's, this work is expected to bring about a change in the scenario of seaweed based industries creating renewed employment opportunities in the country's coastal districts for the fisher folk who would participate in the large-scale mariculture activities for producing value added seaweed biomass. The latter would subsequently kick-start conventional allied chemical processing industries.

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Legends for figures

Fig. 1 Modification reaction of polysaccharides e.g. alginate, agarose, carrageenan and cellulose

Fig. 2 Fluorescence emissions of (a) agarose, 5×10^{-5} M; (b) κ-carrageenan, 5×10^{-5}M; (c) cytosine, 3.09×10^{-5} M, containing 0.030 mM cytosine; (d) cytosine, 3.5×10^{-5} M, containing 0.035 mM cytosine; (e) cytosine, 5×10^{-5} M, containing 0.048 mM cytosine; (f) agarosegraftcytosine, 5×10^{-5} M, containing 0.030 mM cytosine; (g) carrageenan-*graft*-cytosine, 5×10^{-5} M, containing 0.035 mM cytosine [Reproduced with permission from *Carbohydr. Polym.*, *87*(3), 1971-1979; Elsevier]

Fig. 3 Fluorescent properties of amide derivatives of alginic acid (ALG) with hydrazine (HY), etheylenediamine (EDA), hexamethylenediamine (HDA) and cyclohexanediamine (CHDA) and their genipin crosslinked derivatives.

Fig. 4 Structure-function relationship of sodium alginate based materials

Fig. 5 Thixotropic loops for (a) Na-Alg/OABA for 15 subsequent structure recovery cycles and (b) Na-Alg/MABA for 9 subsequent structure recovery cycles [Reproduced with permission from *Soft Matter*, 2012, *8*(6), 1837-1844; The Royal Society of Chemistry]

Fig 6 Schematic representation of the methodologies adopted for synthesis of receptor 1 and the formation of the rhodamine-alginate conjugate Gel Bead 1. R represents rhodamine B; G and M represent α-L-guluronate and β-D-mannuronate respectively [Reproduced with permission from *Chem. Comm.*, 2012, *48*(11), 1659-1661; The Royal Society of Chemistry]

Legends for Tables

Table 1 Derivatization of agarose via -C-N bond formation and amination reactions

Table 2 Derivatization of agarose via esterification and amidation reactions

Table 3 Derivatization of alginate/alginic acid via amidation and esterfication reactions

Table 4 Graft copolymerization of □-carrageenan with vinyl pyrrolidone and methyl methacrylate

Table 5 Polysaccharide derivatives with new functions

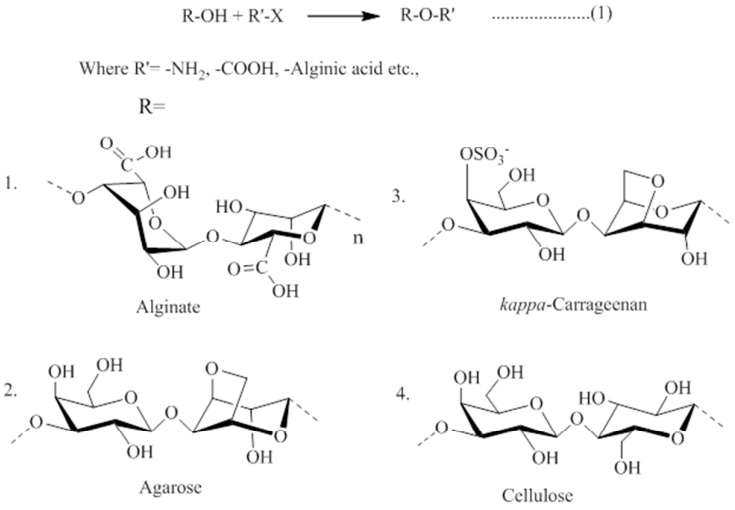


Fig. 1.

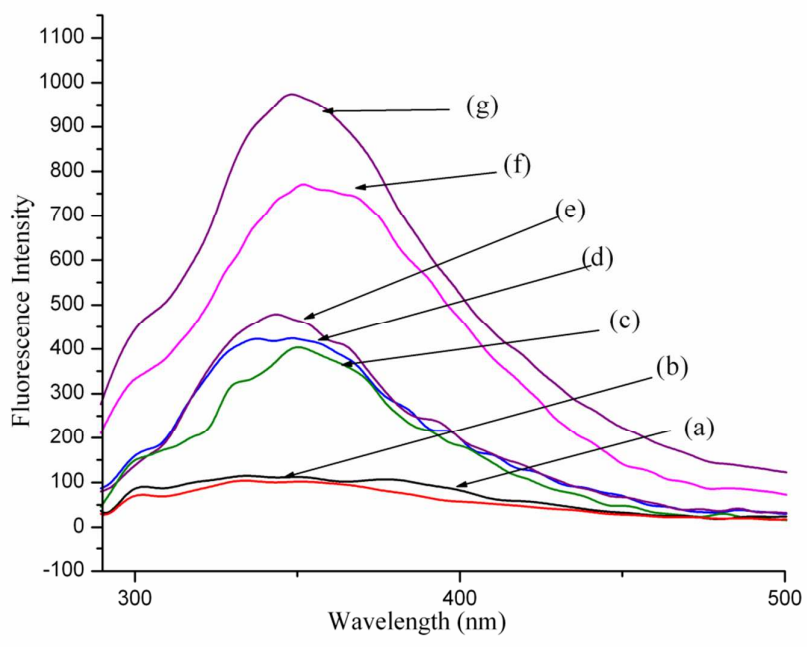


Fig. 2.

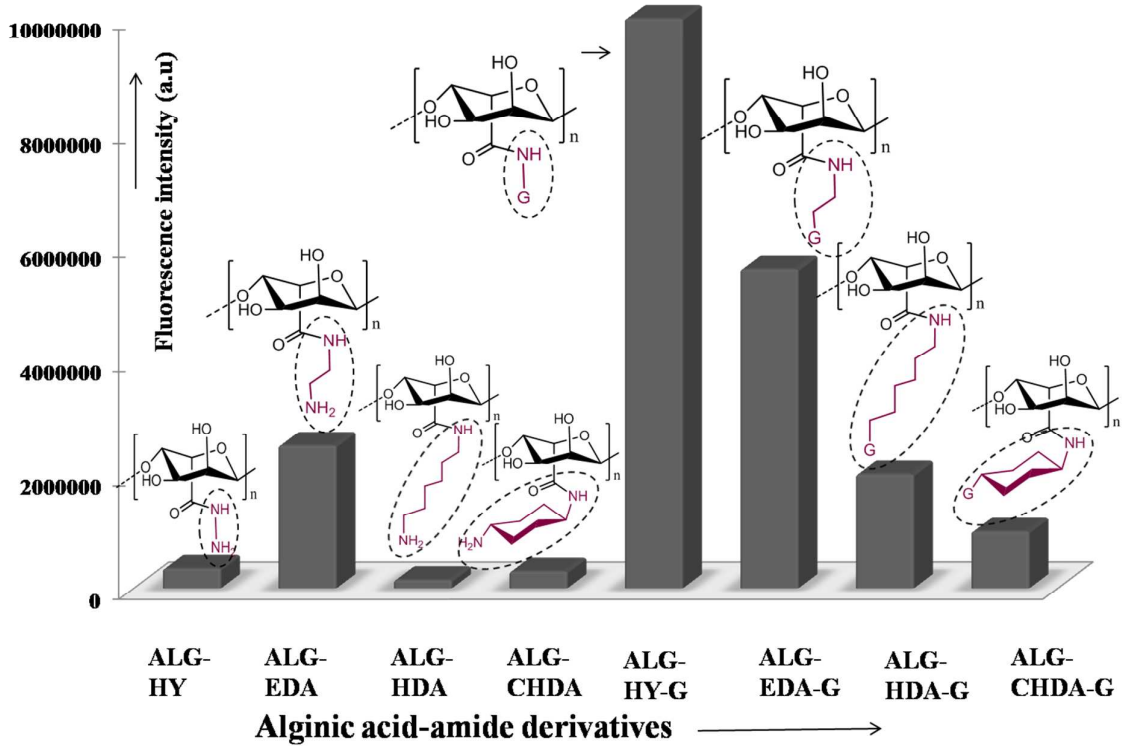


Fig. 3.

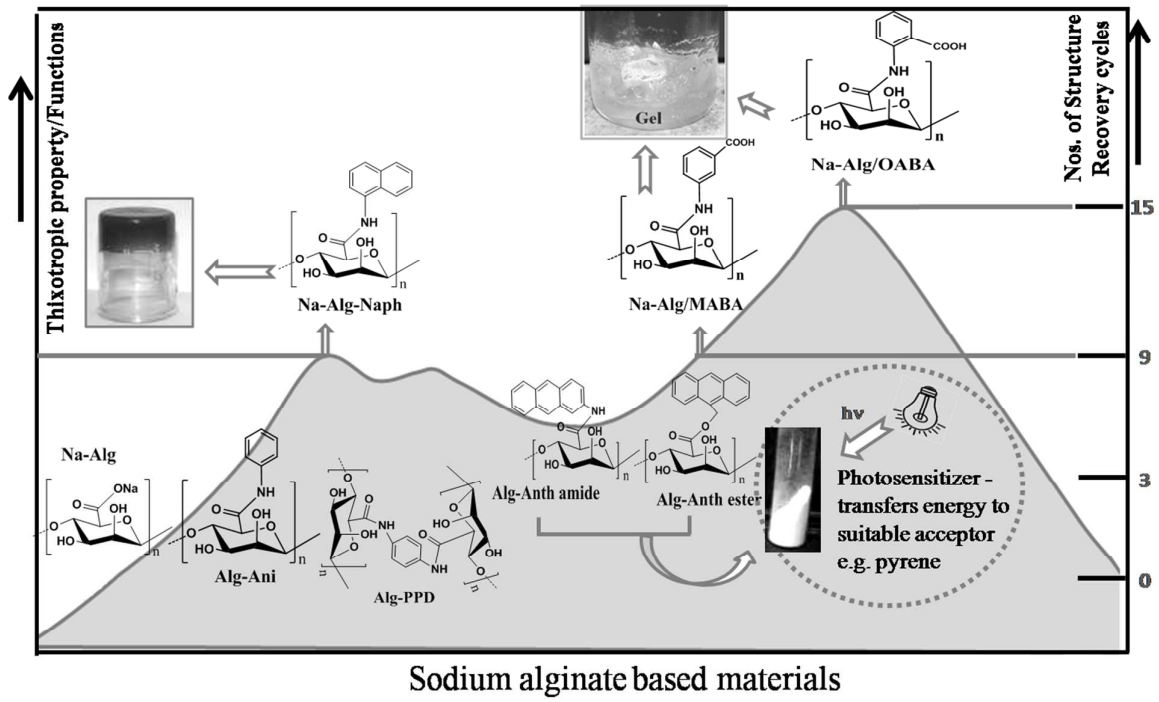


Fig. 4.

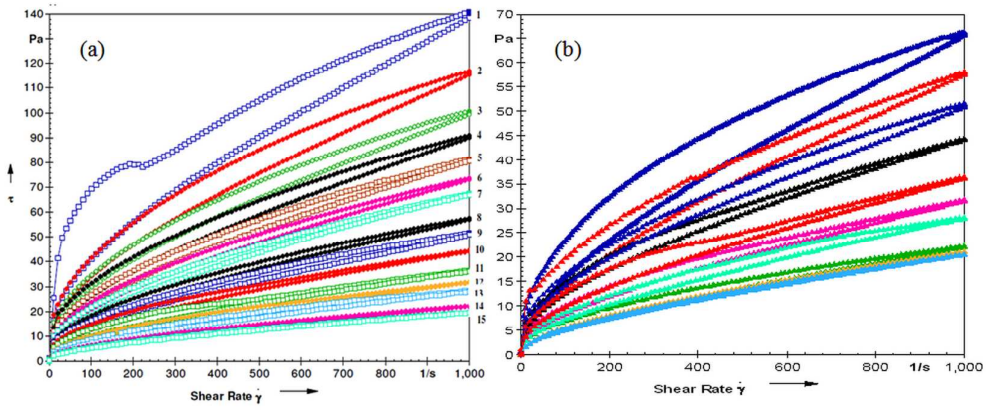


Fig. 5.

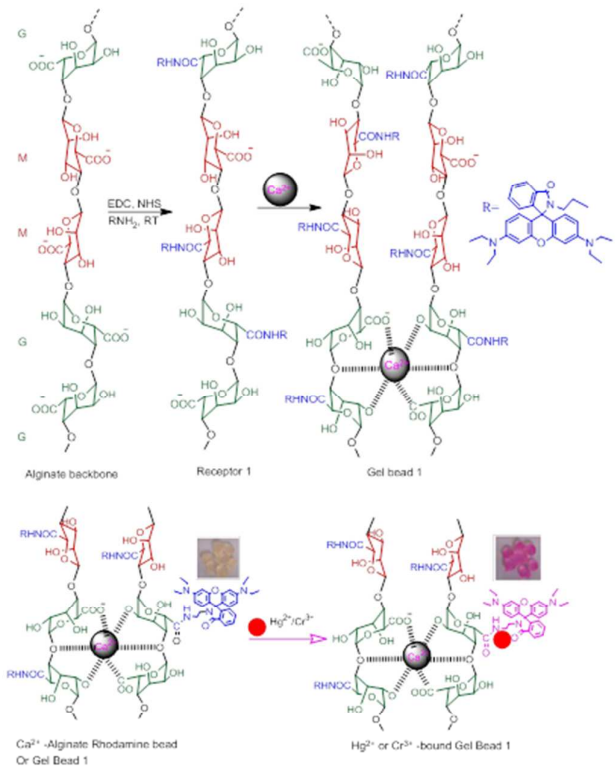


Fig 6.

Table 1

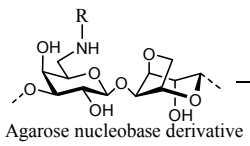
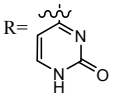
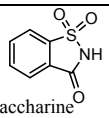
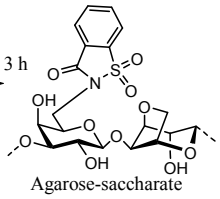
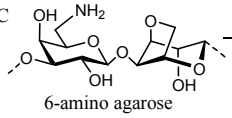
Polysaccharide	Reaction condition Substrates	Modified polysaccharide	New properties imparted	[Ref]
Agarose	C-N bond formation: KPS/MW, R-NH_2	 Agarose nucleobase derivative	Agarose nucleobase derivatives exhibited substantially enhanced fluorescence emission, than respective nucleobase	[16-18]
	C-N bond formation: R=  Cytosine, Guanine, Adenine			
	C-N bond formation: I_2/Ph_3P/pyridine 70° C, 3 h;  Saccharine	 Agarose-saccharate	Sweet Agarose: Agarose-saccharate, sweeter than saccharine; no bitterness	[20]
	Amination: (i)DIAD/$P(Ph)_3$/MW,100°C (ii)Hydrazinolysis/MW, 60°C; 	 6-amino agarose	Amino-agarose may be used to generate cationic polysaccharide for possible applications as gene/drug delivery vehicles	[14]

Table 2

Polysaccharide	Reaction condition Substrates	Modified polysaccharide	New properties imparted	[Ref]
Agarose (Esterification)	DCC/DMAP ; MW L-phenylalanine	Agarose-L-phenylalanine ester	Hydrogels were highly stable in all pH media (pH 1.2, 7.0 and 12.5)	[12]
Agarose (Esterification)	DCC/DMAP ; MW L-Tryptophan	Agarose-L-tryptophan derivative	Fluorescent hydrogel	[49]
Agarose (Esterification)	DCC/DMAP ; MW n= 6(Palmitic acid) 7(Stearic acid)	Agarose-fatty acid ester derivatives	Self-assembled nano particles in aquous phase	[19]
Agarose (Esterification)	DCC/DMAP ; MW 1-Naphthylacetic acid (NA)	Agarose-NA ester	On hydrolysis in heterogeneous aqueous phase releases the 1-naphthyl acetic acid, a plant growth regulators in a controlled manner	[15]
6-Amino agarose (Amidation)	EDC/NHS RT, 12 hrs Nicotinic acid Picolinic acid	Amide derivatives amino agarose	Both the amide derivatives exhibited enhanced (82-90%) fluorescence emissions.	[14]

Table 3

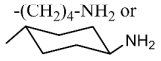
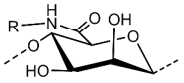
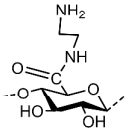
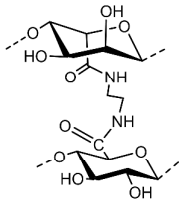
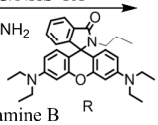
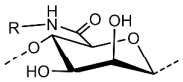
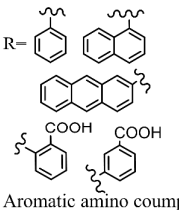
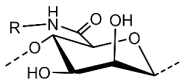
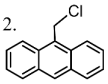
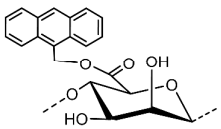
Polysaccharide	Reaction condition Substrates	Modified polysaccharide	New properties imparted	[Ref]
Alginic acid/alginate (Amidation)	$R\text{-}NH_2$ / MW R= $-NH_2$; $-(CH_2)_2\text{-}NH_2$; $-(CH_2)_4\text{-}NH_2$ or  Diamine compounds	 Alginic acid amide derivatives	Fluorogenic alginic acid amide derivatives	[22]
	MW  Cellulose alginic acids interpolymeric diamide		New interpolymeric diamide based on cellulose and alginic acids withfluorogenic metal scavenging properties	[23]
	EDC/NHS RT $R\text{-}NH_2$  Rhodamine B	 Alginate-rhodamine conjugate	Effective extraction of Hg^{2+} and Cr^{3+} ions from aqueous media by a novel rhodamine-alginate polymer based highly fluorogenic, as well as colorimetric chemosensor beads	[24]
	EDC/NHS RT $R\text{-}NH_2$ R=  Aromatic amino coumpound	 Alginic acid amide derivatives	Introduction of aromatic amino compound (Aniline, 1-Napthylamine, 2-Aminoanthracene, *m*-Aminobenzoic acid, *o*-Aminobenzoic acid) imparted thixotropicity on to sodium alginate	[21,25]
	1. IR resin/TBAB/ 2. DMSO 30°C  9-Chloro methyl anthracene	 Alginate-anthracene ester derivative	Efficient photosensitizing ability	[54]

Table 4

Polysaccharide	Reaction condition Substrates	Modified polysaccharide	New properties imparted	[Ref]
kappa-Carrageenan	Free radical graft-copolymerizations; $K_2S_2O_8/\triangle$; vinylpyrrolidone	κ-Carrageenan-*graft*-PVP	These hydrogels exhibited enhanced water-holding capacity; R= κ-Carrageenan	[65]
kappa-Carrageenan	Free radical graft-copolymerizations; $K_2S_2O_8/\triangle$; methylmeth-acrylate	κ-Carrageenan-*graft*-PMMA	Controlled microwave induced copolymerization; carrageenan remained undegraded; R= κ-Carrageenan	[29]

Table 5

Entry Effect/Properties	Remarks	References
Agarose hydrogel- effect of surfactant	Led to the development of a new process of agarose extraction	48,69, 70
Agar-sugar reactivity	Enhancement of gel strength with sugar	63
Hydrophobization- Enhanced crystallinity > orderliness>superior absorbent	Copolymer hydrogels: Carrageenan-PMMA; Agar-PVP & Carrageenan-PVP	28, 65
Hydrophobization- nano-size self-assembly	Agarose-fatty acid esters; and Electrically conductive agarose-half-esters	19, 64
Adhesive and absorbent hydrogel	κ-Carrageenan-*graft*-PAAm; and PVP-grafted sulphated polysaccharide of *Cystoseira indica*	29, 66
Swelling hydrogels	Genipin cross-linked hydrogel	11,12, 60, 61
Absorbent hydrogel – pH-responsive	Superior absorbent properties in acidic pH 1.2	11, 55, 56, 57
Fluorogenic polysaccharides	Significantly enhanced fluorescence in the derivatives-agarose: nitrogenous substrates compared to the substrate alone	16, 17, 18, 22, 49
Fluorogenic - slow release	Agarose-naphthyl acetyl – slow release of NAA on hydrolysis; Agarose-pyridine carboxylic acids	14, 15, 58
Fluorogenic interpolymer – metal ion scavenger	Scavenging of Hg(II) & Cr(III) by alginate-rhodamine complex; and Pb(II) & Hg(II) by an alginate-cellulose interpolymer	23, 24
Photosensitizer	Sodium alginate-anthracene derivative	54
Thixotropic	Thixotropic alginate-aromatics adducts	21,25
Sweet agarose	Agarose-saccharate derivative- maybe an alternative sweetener	20

Note: PMMA=Poly methyl methacrylate; PVP=Polyvinyl pyrrolidone; PAAm=Polyacrylamide; NAA=Naphthylacetic acid