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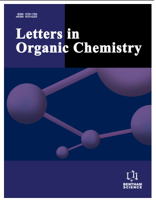
RESEARCH ARTICLE



Novel Persian Gulf Aminated Alginate Derivatives from Sargassum Bovaneum: Synthesis and Characterization

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Abstract: ***Aims*:** The aim of the study was to extract and characterize alginate from a new source, conduct synthesis and characterization of novel aminated alginate derivatives, make a comparison of physicochemical properties of extracted sodium alginate with its aminated derivatives, and investigate the effect of diamines chain length on physicochemical properties of newly synthesized derivatives.

***Background*:** Alginate is a natural biopolymer found in marine brown seaweeds. Alginate is widely used in the industry due to its features, such as gelling ability, biocompatibility, biodegradability, hydrophilicity, and non-toxicity. Alginate has two types of functional groups, free hydroxyl and carboxyl groups, which can be modified.

***Methods*:** In this study, sodium alginate was extracted from *sargassum boveanum* in basic media and characterized by physical and spectral properties. In order to prepare alginate precursors with clickable groups for hydrogel cross-linking application, extracted sodium alginate was further treated with two different diamines, diaminoheptane (DAH) and diaminopropane (DAP), in the presence of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC) and N-hydroxysuccinimide (NHS) to form amide linkages on the alginate backbone and synthesise aminated derivatives. The products were characterized by techniques, such as FTIR, ^{1}HNMR, TGA, XRD, and elemental analysis.

***Results*:** The average molar weight and the intrinsic viscosity of alginate from *Sargassum bovaneum* with a yield of 24.38% were 41.53 kDa and 0.9 dL/g 105 cps (2.5% C). Results showed that as the alginate concentration increased, the flow rate decreased with a mild slope.

***Conclusion*:** Elemental analysis (CHNS) of alginate derivatives indicated the percent of amine groups to be increased after amination reaction in comparison to corresponding alginates. The thermal analysis results indicate that the thermal stability of the sodium alginate is better than graft copolymers. Synthetic derivatives showed no particular sensitivity to environmental stimuli, such as temperature and pH changes.

Keywords: Alginate, extraction, isolation, *Sargassum bovaneum*, brown seaweeds, amination reaction.

1. INTRODUCTION

Marine waters, covering two-thirds of the Earth's surface, contain secret treasures, which accommodate numerous species of plants and animals that provide large amounts of chemical compounds. Marine biomaterials are used as raw materials in many industries, ranging from medicine to textile. For instance, chitin, a biopolymer obtained from sea crustaceans, can be used in textile finishing processes or in the form of fibers. It is also possible to obtain fibers from alginate, which is present in seaweeds. Alginate is used in medical, technical textiles, and textile printing [1]. As shown in Fig. (**1**), sodium alginate has a linear copolymer composed of two different monomers: mannuronic acid (M) and guluronic acid (G) [2-4]. Each seaweed can present a specific proportion of M and G units in alginate polymer [5, 6]. This kind of material can form non-toxic and biodegradable hydrogels in optimal conditions that have high porosity.

Alginate is derived from algae and bacteria. Biopolymer composition, viscosity, sequence of monomers, and molecular weight vary depending on the source and species producing it. In order for conventional alginate production in alginate pro-

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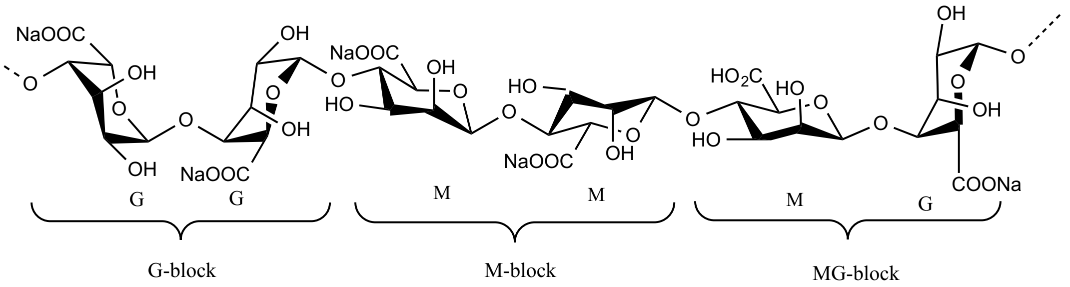


Fig. (1). Structure of sodium alginate: chain conformation, M: mannuronic, and G: guluronic acid sodium salt residue.

duction processes to extract and remove potential contaminants, such as polyphenols, fucoidans, and laminarins, dilute acid is used for converting insoluble alginate salts into alginic acid, which is then easily converted into soluble sodium alginate in the presence of sodium carbonate [7].

Alginate has some free hydroxyl and carboxyl groups distributed along the backbone; thus, it is an ideal candidate for chemical functionalization. By forming alginate derivatives through functionalizing available hydroxyl and carboxyl groups, the properties, such as solubility, hydrophobicity, physicochemical, and biological characteristics, may be modified for drug delivery and health applications [8-10]. The carboxyl and hydroxyl groups on the alginate backbone make it a suitable candidate for chemical functionalization. By functionalizing these groups, some properties of alginate, such as hydrophobicity, solubility, viscosity, and other physicochemical properties, can be improved and make it a suitable material for use in drug delivery systems and health applications [8-10]. The chemical reaction of alginate has been achieved using techniques, such as oxidation, sulfonation, esterification, amidation, nanocomposite synthesis, or grafting methods [11, 12]. These reactions can be performed in the C2 and C3 hydroxyl groups and the C-6 carboxylate group, requiring the dissolution of sodium alginate in organic solvents or water [13]. The ease of dissolving alginate in aqueous media has led to the application of aqueous carbodiimide chemistry to synthesize new alginate derivatives [14-16]. The reaction of the carboxylate groups on the alginate backbone with long-chain alkylamines to form hydrophobically substituted alkylamides is an example of such reactions [17]. In this work, Persian Gulf aminated alginate derivatives are synthesized with linear alkyl diamines by EDC and NHS as coupling agents to form amide linkages on the alginate backbone. Products are characterized by elemental analysis, FTIR, ^{1}HNMR, XRD, and TGA.

2. RESULTS AND DISCUSSION

2.1. Synthesis of Crosslinked Alginate

When the carboxyl group of the alginate backbone reacts with the amino group of the aliphatic diamine, the amide bond is synthesized. EDC and NHS catalyze the formation of this reaction, as shown in Scheme **1**.

2.2. Yield, Molecular Weight, and Viscosity of Extracted Sodium Alginate

The extracted alginate was obtained at 73.14 g from 300 g of defatted *Sargassum bovaneum* seaweeds with a yield of 24.38%. Alginate viscosity was measured for 0.3, 0.6, and 1% solutions in 0.1 M NaCl and evaluated. The results showed that as the alginate concentration increased, the flow rate in the extracts decreased with a mild slope. The viscosity of alginate *Sargassum bovaneum* in the PS is 0.9 dL/g 105 cps (2.5% C), which is relatively less than the other species of this family. The viscosity of alginate in *Sargassum spp.* is about 6.3-15.2 dL/g [18, 19].

The average molecular weight (M_r) of sodium alginate was determined using obtained viscosity (η) using the Mark-Houwink equation (1):

$$[\eta] = K.M_r^a \qquad (1)$$

Where η=105, a = 0.984 and k = 0.023. The average molar weight of alginate from *Sargassum bovaneum* was determined to be 41.53 kDa. The molecular weights of alginate extracted from *Fucus vesiculosus* and *Ascophyllum nodosum* with a sequential extraction were 154.9 and 177.3 kDa [20, 21].

2.3. FTIR Spectra of Sodium Alginate Derivatives

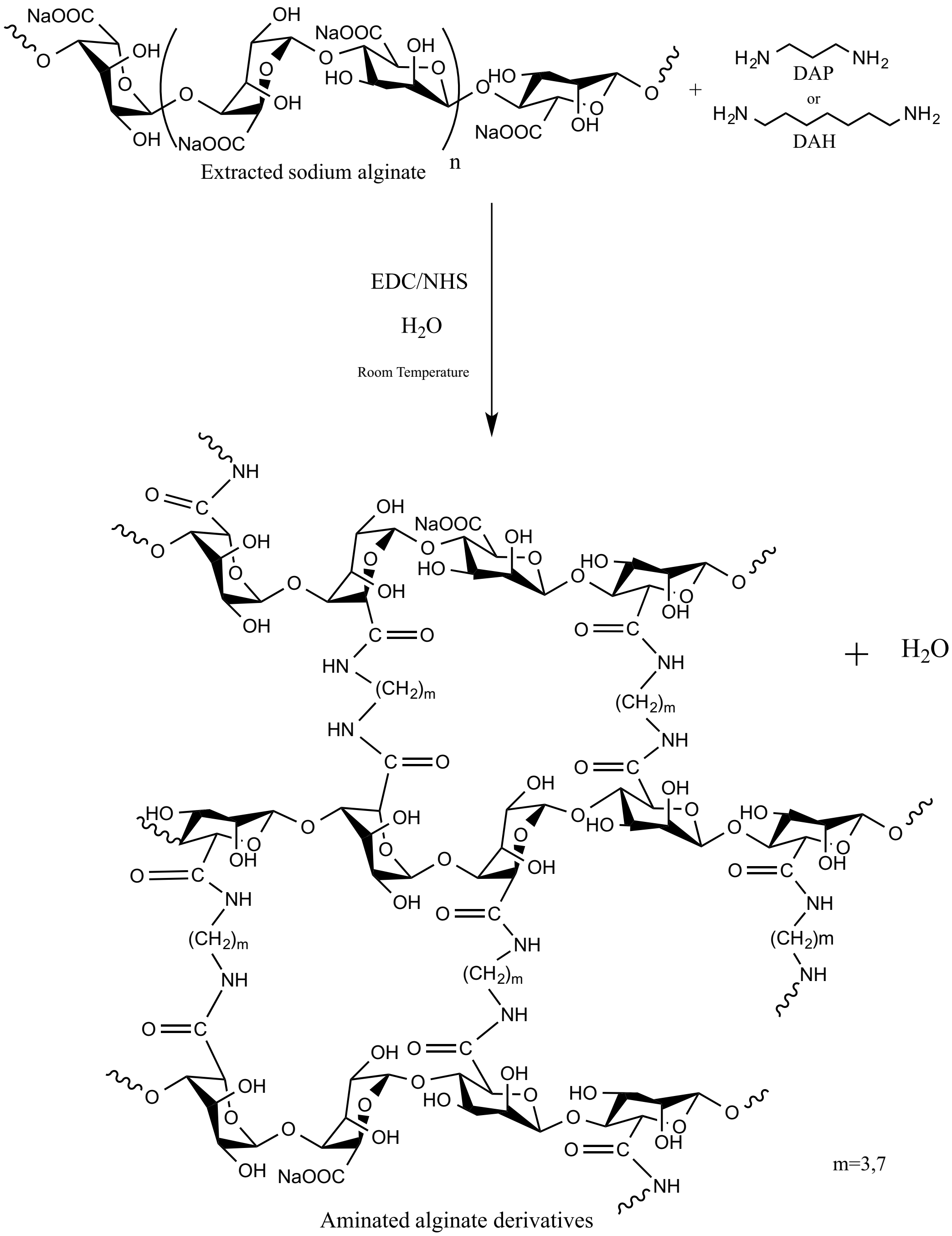
As presented in Fig. (**2**) and Table **1**, the FTIR spectra of Alg_{EX} showing a broad peak in the region 3000-3800 cm^{-1} were assigned to stretching vibrations of O–H, the signals at 2422.33 cm^{-1} were suggested as the C–H, and a sharp peak at 1610.78 cm^{-1} was attributed to carboxylate group. Vibrational bands at 1414.62 cm^{-1} were assigned to bending C–H. The band located at 1030 cm^{-1} could be assigned to C–O stretching vibrations, and the other peak at 912 cm^{-1} assigned to the C–O stretching vibration of the uronic acid residues. A band at 667 cm^{-1} could be assigned to the mannuronic acid residues. Our results are in agreement with the previous reports [22, 23].

2.4. ^{1}HNMR Spectra of Sodium Alginate Derivatives

The ^{1}HNMR spectra of sodium alginate and its derivatives with specific characteristic signals are shown in Figs. (**3-5**). The anomeric protons in the glucuronic acid and the mannuronic acid were identified using peaks assigned by Grasdalen [21]. The peak at 4.61 ppm belongs to anomeric hydrocarbons of the G-1*(glucuronic acid), and the other sharp peak at 4.92 ppm is assigned to M-1*(mannuronic acid), according to the previous studies [21].

^{1}HNMR spectra of alginate products with characteristic signals:

^{1}H NMR (D_2O), Alg_{EX} (ppm): δ 3.76 (s,2H, J 1.00 Hz, H-2, H-3), 3.92 (s, 1H, J 1.04 Hz, H-4), 4.02 (m, 1H, J 1.04 Hz, H-5).



Scheme 1. Schematic representation of aminated alginate derivatives.

Table 1. Infrared absorption frequencies of alginate derivatives.

Samples Wavenumber Functional Groups	Alg_{EX} (cm^{-1})	Alg_{EX}-DAP (cm^{-1})	Alg_{EX}-DAH (cm^{-1})
H_2O, OH M, G	3000-3800	3000-3800	3000-3800
–COOH	1610-1700	-	-
CH Bending	1414.62	1028.83	1029.80
CH Vibration	2935	1903.39	2189.53-2280.58
C=O, N-H bending (Amide)	-	1687.00, 1404.37	1623.42, 1504.37
CH_2 (Diamines)	-	1900-2400	1900-2400

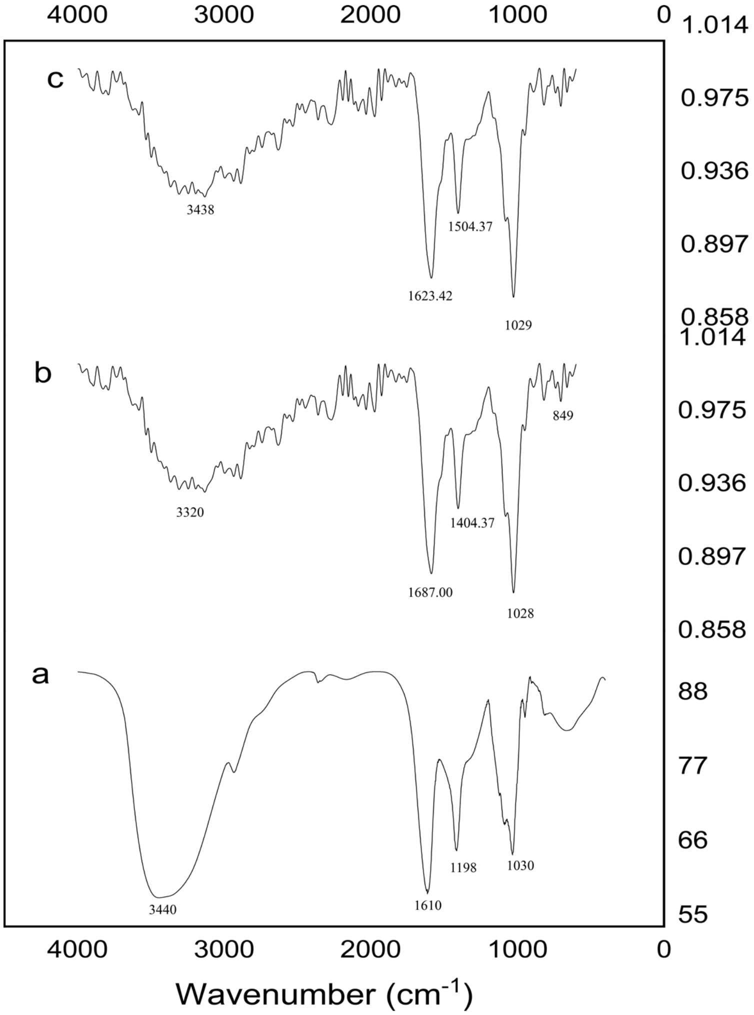


Fig. (2). FTIR spectra of (**a**) Alg_{EX}, (**b**) Alg_{EX}-DAP and (**c**) Alg_{EX}-DAH. (*A higher resolution/colour version of this figure is available in the electronic copy of the article*).

^{1}H NMR (D_2O), Alg_{EX}-DAP (ppm): δ 1.06 (m, 2H, J 0.73, H-C), δ 1.85 (s, 2H, J 0.52 Hz, H-b), 2.68 (s, 1H, J 1.09 Hz, H-a)

^{1}H NMR (D_2O), Alg_{EX}-DAH (ppm): δ 0.95 (td, 2H, J1.20, H-d), 1.26 (s, 2H, J 5.45 Hz, H-e), 1.54 (m, 2H, J3.67 Hz, H-f), 1.78 (m, 2H, J 0.97 Hz, H-g), 2.76 (m, 1H, J 5.15 Hz, H-h).

These results are also similar to previous reports [24, 25].

2.5. X-ray Diffraction (XRD) of Alginate Derivatives

The crystalline structures of the extracted sodium alginate shown in Fig. (**6**) indicated diagnostic crystalline peaks at 2θ at 22.8°, 29.6°, and 47.4° for Alg_{EX}; these results are in accordance with the previous reports. Due to impurities in the extracted alginate, the crystallinity of Sigma alginate is higher than the extracted alginate. Spectral data indicate that the extracted alginate has a semi-crystalline structure [17].

After modification with DAP and DAH, the spectrum of samples displayed little peaks. The reaction performance on the alginate backbone can be detected by the disappearance of some peaks in the resulting XRD spectra. This matter is related to the hydrogen bond cleavage that arranges the crystalline structure of the hydrocarbon chains in pure alginate [17].

XRD pattern of alginate products with characteristic peaks:

Alg_{EX} (2θ): 22.8°, 29.6°, 47.4°.

Alg_{EX}-DAP (2θ): 21.6°, 24.8°, 28.6°.

Alg_{EX}-DAH(2θ): 21.5, 24.8°, 28.7°, 35.6°.

2.6. TGA of Alginate Derivatives

Thermogravimetry analysis (TGA) of extracted sodium alginate and its derivatives is shown in Fig. (**7**). TGA curves of Alg_{EX} showed three mass loss steps. The first mass loss for Alg_{EX} in a solid state of about 15.2% at 25-237.7°C was due to dehydration, and the second mass loss of about 26.3% in the range 237.7-275.5°C was due to the destruction of samples and production of CH_4, water, and CO_2. The third mass loss of about 16.9% in the range 275.5-636°C was due to the degradation of polymer chains and the formation of carbonaceous residue. The temperature at which 50% mass loss of samples occurred was 420°C for extracted alginate.

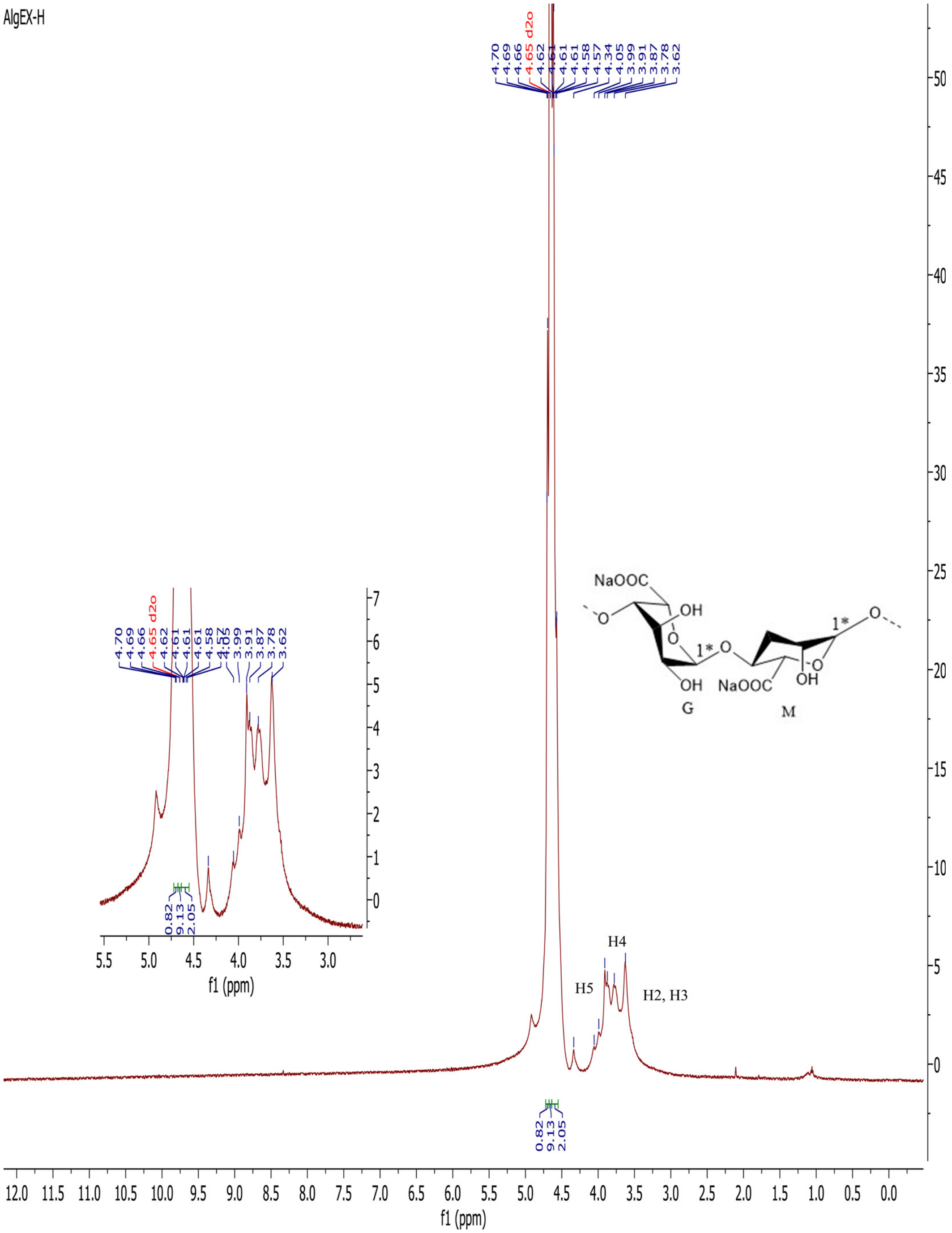


Fig. (3). ^{1}H NMR spectra of Alg$_{EX}$ with D_2O as a solvent. (*A higher resolution/colour version of this figure is available in the electronic copy of the article*).

In the case of Alg$_{EX}$-DAP and Alg$_{EX}$-DAH, the first weight losses of about 12%, starting from 37.98 to 190°C, and 8%, starting from 37.8 to 175°C, were due to evaporation of moisture [1, 26]. The second mass losses for Alg$_{EX}$-DAP of about 58% in the range 190-350°C and Alg$_{EX}$-DAH of about 58% in the range 175-370°C were due to degradation of carboxylate groups and the formation of CO_2, CH4, and H_2O. The third step of weight loss for Alg$_{EX}$-DAP of about 73% started from 350 to 606°C, and for Alg$_{EX}$-DAH, about 74% started from 370 to 608°C. This can be attributed to the decomposition of grafted diamino hydrocarbon chains and char formation. 50% mass losses of samples were at temperature 295°C for Alg$_{EX}$-DAP, and 290°C for Alg$_{EX}$-DAH, indicating the thermal stability of the sodium alginate to be better than graft copolymers.

2.7. Elemental Analyses (CHNS) of Alginate Derivatives

Anal. Calcd for $C_6H_9NaO_7$ (Alg$_{EX}$): C, 33.35; H, 4.19; Na,10.64; N,0; O, 51.82; S, 0. Found: C, 21.61; H, 3.13; N, 1.08; S, 0.38.

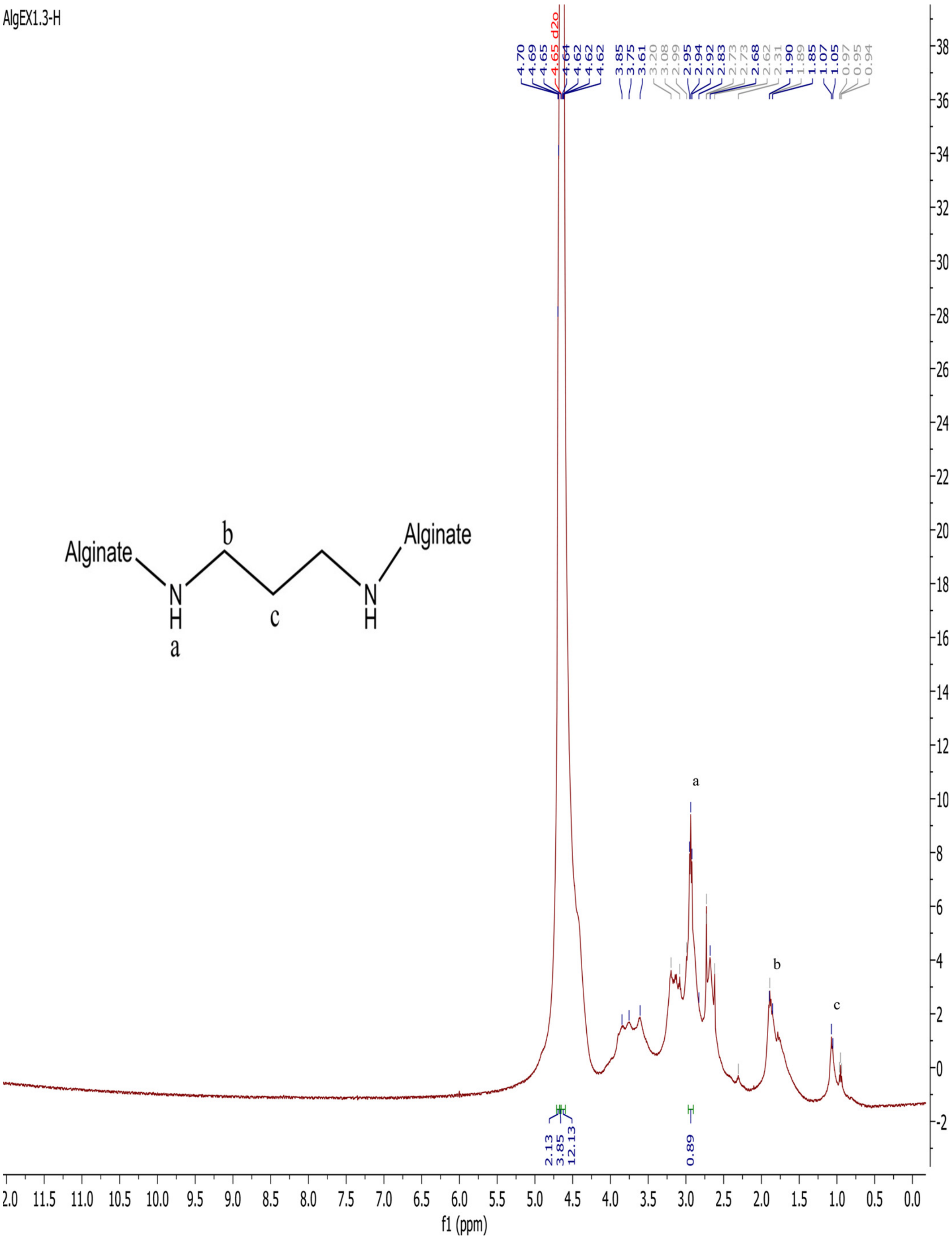


Fig. (4). ^{1}H NMR spectra of Alg$_{EX}$-DAP with D_2O as a solvent. (*A higher resolution/colour version of this figure is available in the electronic copy of the article*).

Table 2. Elemental analyses (CHNS).

Sample	%C	%H	%N	%S
Alg$_{EX}$	21.61	3.13	1.08	0.38
Alg$_{EX}$-DAP	37.48	6.82	6.47	0.1
Alg$_{EX}$-DAH	39.10	6.41	6.72	0.14

Elemental analysis of alginate derivatives.

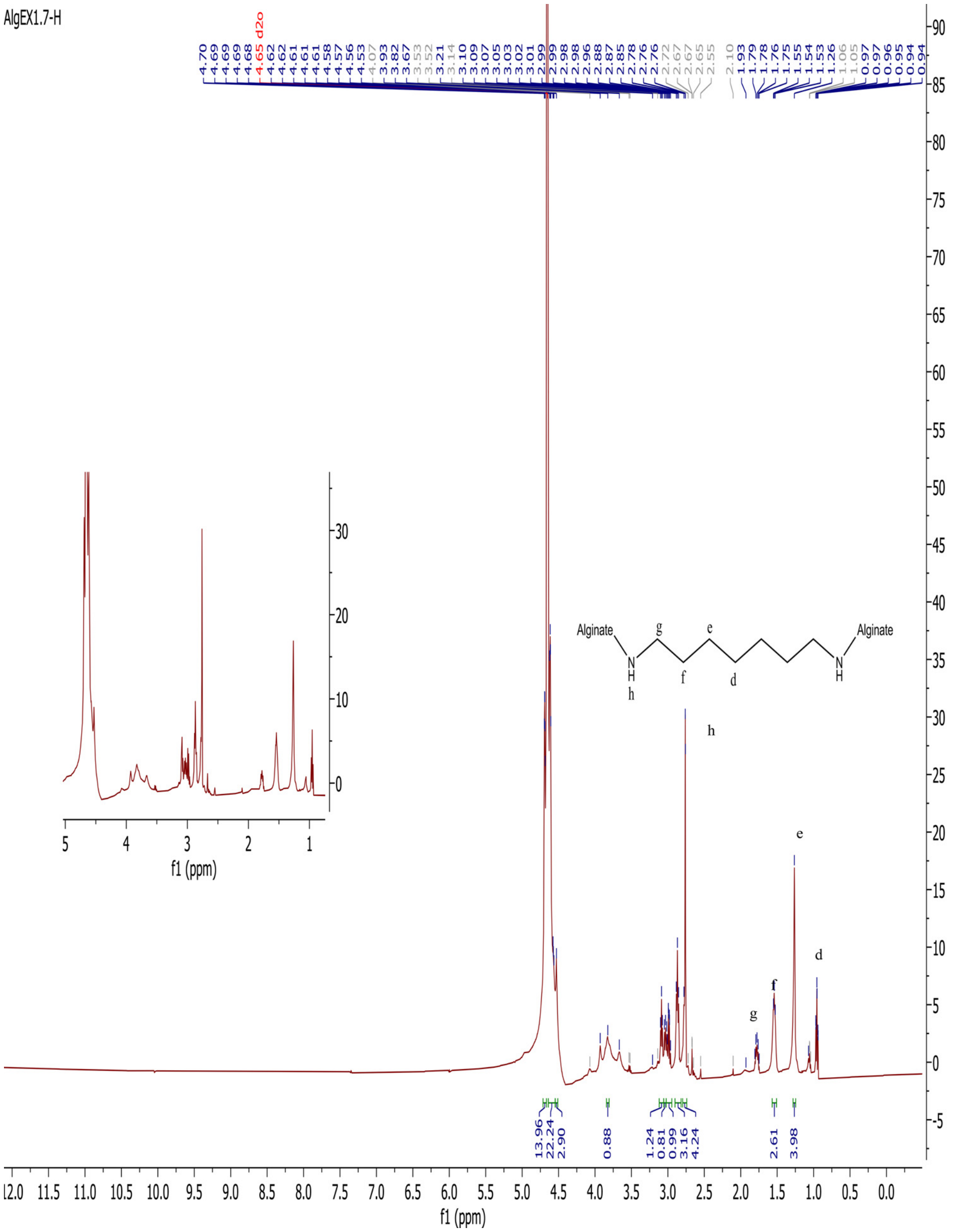


Fig. (5). ^{1}HNMR spectra of Alg$_{EX}$-DAH with D_2O as a solvent. (*A higher resolution/colour version of this figure is available in the electronic copy of the article*).

Anal. Calcd for $C_9H_{19}N_2O_6$ (Alg$_{EX}$-DAP): C, 43.02; H, 7.62; N,11.15; O, 38.21; S, 0. Found: C, 37.48; H, 6.82; N, 6.47; S, 0.1.

Anal. Calcd for $C_{13}H_{27}N_2O_6$ (Alg$_{EX}$-DAH): C, 50.80; H, 8.85; N,9.11; O, 31.23; S, 0. Found: C, 39.10; H, 6.41; N, 6.72; S, 0.14.

The elemental analysis results (Table **2**) indicated that the percentage of amine groups approximately increased after the amination reaction compared to corresponding alginates [27].

2.1. Materials and Methods

Sargassum boveanum was collected from the coastal area of the Persian Gulf (Chabahar coasts); 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC), N-hydroxysuccinimide (NHS), 1,3-Diaminopropane (DAP), and 1,7-Diaminoheptane (DAH) were obtained from Merck Co. (Germany). Other reagents of analytical grade were used without modification or purification.

2.2. Instrument

Elemental analysis instrument (Italy) Costech ECS 4010 was used for CHNS analysis. Infrared spectra were obtained on Bruker Vertex70 FT-IR (Germany) spectrophotometer (400 and 4000 cm^{-1}). ^{1}HNMR spectra were recorded on a Varian-INOVA 500 MHz spectrometer (England). XRD spectrum of alginate and its derivatives was investigated using X-ray powder diffractometer Seifert XRD 3003 (Germany). Samples were scanned in the region between 5^o and 50^o and a scan speed of 1.2^o per minute using a 50 mA generator

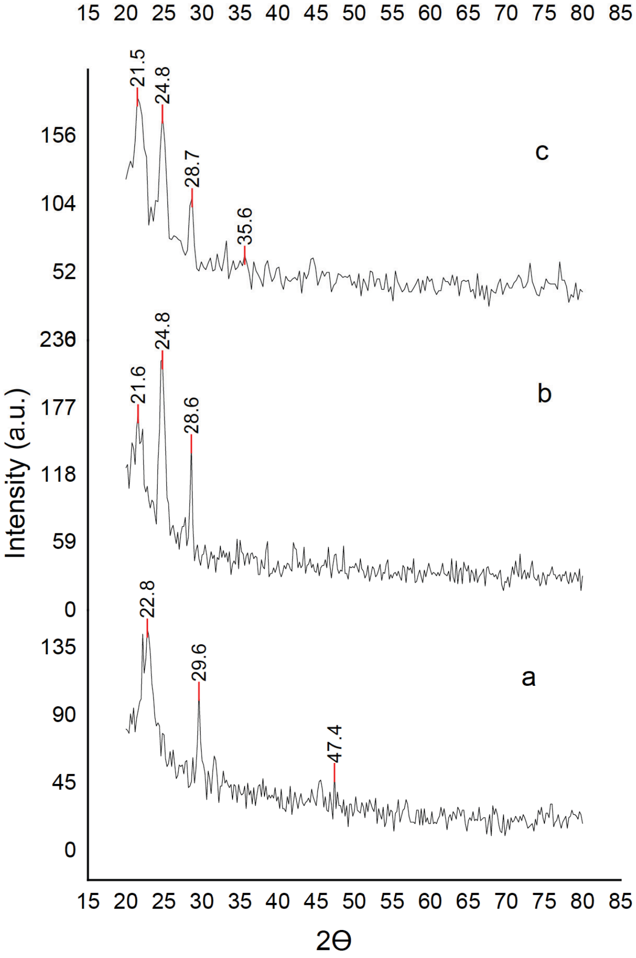


Fig. (6). XRD patterns of (**a**) Alg_{EX}, (**b**) Alg_{EX}-DAP, and (**c**) Alg_{EX}-DAH. (*A higher resolution/colour version of this figure is available in the electronic copy of the article*).

current. TGA thermograms were carried out using an SDT-Q600 simultaneous TGA, DTA thermal analyzer, TA instruments (America). 5 mg of sample masses were kept in an Al_2O_3 sample holder with a heating rate of 10°C min^{-1} from 35 to 700 under a nitrogen atmosphere (100 ml min^{-1}).

2.3. Seaweed Collection and Preparation

Brown seaweeds *Sargassum Boveanum* were collected on Persian Gulf coasts in December 2018. A researcher at Khorramshahr University of Marine Sciences and Technology performed scientific identification of seaweeds using Taylor's (1979) classification key and standard literature [28]. Seaweeds were washed with tap water to remove salts, sands, and epiphytes, and they were dried and milled into a fine powder using a home blender, and samples were stored in the refrigerator until extraction [29].

2.4. Extraction of Alginate

The seaweed extraction was performed with alkaline and acidic solutions with a few changes. Before alginate extraction, 300 g of dried seaweeds were washed with 1500 ml of sodium hypochlorite solution and 2.5% distilled water, respectively. Seaweeds were treated with an ethanol solution of 80% at ambient temperature for 24 hours. Seaweeds were refined and then washed with distilled water. Seaweeds, using an ultrasonic bath (60 Hz), were extracted twice with HCl 0.1 M at 70°C for 6 hours. Algal residue in an ultrasonic bath was treated twice with 1500 ml of Na_2CO_3 solution (2%) at 60°C for 4 hours. The residues were filtered by adding ethanol (98%), and sodium alginate was precipitated [30].

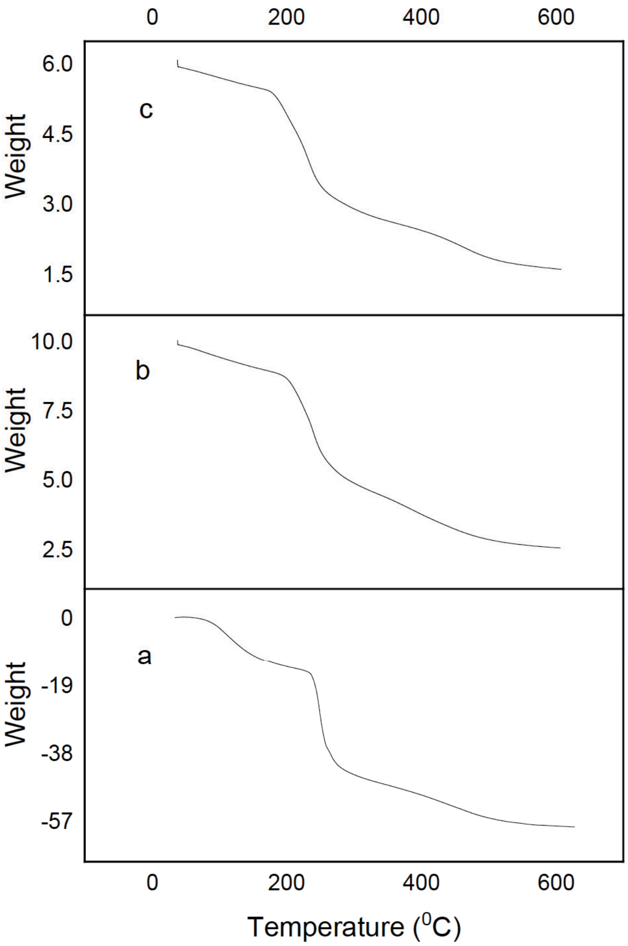


Fig. (7). TGA curves of (**a**) Alg_{EX}, (**b**) Alg_{EX}-DAP, and (**c**) Alg_{EX}-DAH. (*A higher resolution/colour version of this figure is available in the electronic copy of the article*).

2.5. Synthesis of Aminated Alginate Derivatives

Amination of extracted alginate from *Sargassum Boveanum* was carried out by Elsayed's 2016 method with slight modification. Briefly, 0.5 g of extracted sodium alginate was dissolved in 50 ml of distilled water, and then 1.16 g EDC and 0.14 g NHS were added to the reaction container at ambient temperature and stirred until a homogeneous solution was obtained. In the next step, the solution of 0.09 M aliphatic diamine in dilute 0.1 M HCl was added to the reaction mixture and stirred for 24 hours at ambient temperature. Aminated alginate derivatives were precipitated by adding excess acetone, rinsed with ethanol, and ultimately dried at 40°C. Products were characterized by ^{1}HNMR, FT-IR, XRD, TGA, and Elemental analysis.

CONCLUSION

Brown seaweeds demonstrate immense sources of alginate, which are used in various industrial fields, such as pharmaceuticals, food, and cosmetics. Sodium alginate and its derivatives also have good potential for drug delivery applications. The yield of extraction alginate in this work was 24.38%, and the molecular weight of extracted sodium alginate was estimated at 41.53 kDa. The supernatant fluid of the extract was rich in antioxidant and polyphenol content that can be used as a future source of natural polyphenols after purification. Alkylamine derivatives of alginate are prepared in EDC and NHS as coupling agents to form the amide structure of the alginate backbone. In this study, we investigated and compared the properties of alginates by varying the chain length of the cross-linking alkylamines. Elemental analysis (CHNS) of alginate derivatives indicated that the percent of amine groups increased by increasing the length of the alkylamine chain after the amination reaction compared to corresponding alginates. These synthetic derivatives showed no sensitivity to environmental stimuli, such as temperature and pH. All products were characterized by elemental analysis, FTIR, ^{1}HNMR, XRD, and TGA.

AUTHORS' CONTRIBUTION

Mohammad Reza Shoshizadeh contributed to the conception and design of the study and manuscript preparation. Shokouh Khodayar performed experiments, graphing and data analysis, and wrote the manuscript. Elham Tahanpesar revised the manuscript and supervised the study. Behzad Sharif Makhmalzadeh contributed to the design of the study. Haleh Sanaeishoar supervised the study. All the authors read and approved the final manuscript.

LIST OF ABBREVIATIONS

Alg_{EX} = Extracted Alginate
Alg_{EX}-DAH = 1,7-Diaminoheptane Cross-linked to Extracted Alginate
Alg_{EX}-DAP = 1,3-Diaminopropane Cross-linked to Extracted Alginate
DAH = 1,7-Diaminoheptane
DAP = 1,3-Diaminopropane
EDC = 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide
FTIR = Fourier Transform Infrared Spectroscopy
^{1}HNMR = ^{1}H Nuclear Magnetic Resonance
NHS = N-hydroxy Succinimide
TGA = Thermogravimetric Analysis
XRD = X-ray Diffraction

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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