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R&D Trends of Brown Algae as Potential Candidates in Biomedical Application

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Abstract Seaweeds contain various bioactive compounds. Especially, brown algae (Phaeophyceae), the second abundant group of seaweeds, contain numerous nutraceutical and pharmaceutical substances. In this review, we investigated on the brown algae-related patents and literature. Consequently, the research and development (R&D) trends of patent related to brown algae showed that the large majority was applied as the composition of stem cell culture medium and mostly used as active substances. In conclusion, we suggested that many researchers try to investigate and develop applications of brown algae as the sophisticated-level biomedical materials because brown algae are actively developing as simple-level biomedical materials.

Keywords : R&D trends, Brown algae, Patent, Biomedical materials

Introduction

Brown algae are the secondary large group of mostly seaweeds and contain a valuable pigment, fucoxanthin [127,129]. They inhabit all over the world and some of them are investigated pharmacologically owing to their commercial value [16,129]. In previous studies, it contains a variety of nutrients and biological compounds including different polysaccharides, pigments, and unique secondary metabolites (Table 1) and it is known that their content varies depending on the season, age, species, geographical area, and environmental factors [7,11,28,29,118]. Due to their valuable and biomedical potentials, they are mainly consumed as functional foods, medicine ingredients, and gelling agents in worldwide including China, European countries, Japan, and Korea [43,54,73].

Biomedical engineering is a multidisciplinary field that combines various principles and techniques related to chemistry, medicine, biology, and engineering science. The main goal of biomedical engineering is improvement and treatment of the function of diseased or damaged organs through mimicking and fabricating tissue-like biological constructs. The key elements of biomedical engineering are known as scaffold, cell, and signal. Since biomaterial is applied as a material of scaffold and signal, the development of biomaterial is important in biomedical engineering [31,35,89,92].

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Table 1. Brown algae-derived bioactive compounds

Classification	Compounds	Biological properties	References
Polyphenolic compounds	6,6'-bieckols, Eckol, Eckstolonol, Dieckol, Diphlorethohydroxycarmalol, Fucodiphlorethol-G, Phlorofucofuroeckol, and Triphlorethol-A	Anticancer, anti-inflammatory and antioxidant activities	[2,53,106]
Polysaccharides	Alginate, Laminarin, and Fucoidan	Anti-angiogenesis, anti-apoptotic, antibacterial, anticoagulant, antioxidant, antitumor, antiviral, and immunomodulation activities	[1,9,12,13,15, 23,24,32,34, 40-42,44,47,50, 52,72,74-77, 79,83-85,94-98, 100,102,104, 107-109,111, 121,123-125, 128,133,134]
Pigments	β-carotene, Chlorophyll, and Fucoxanthin	Antibacterial, anti-diabetic, antifungal, anti-inflammatory anti-matrix metalloproteinases, antioxidant, anti-photoaging, and antitumor activities	[14,26,30,33, 48,49,80,82, 91,99,103,120, 122,132,135]

Several biomaterials including alginate, chitin, polycaprolactone (PCL), and poly (vinyl alcohol) (PVA) were used to produce cell scaffolds for bone and skin regeneration [35,89,92,93]. Besides, other biomaterials such as peptides, phenolic compounds, and polysaccharides were applied for regeneration or treatment of the diseased and/or damaged organs [8,93]. Due to these biomedical potentials, many researchers investigated biomedical applications of biomaterials and their effects.

To analysis the research an development (R&D) trends of the brown algae in biomedical application, the patent analysis was performed within a predetermined search range considered the number of patents related to brown algae. We analyzed brown algae-related patents among applied for and registered patents at patent offices of China (SIPO), Europe (EPO), Japan (JPO), Korea (KIPO), and United States (USPTO) until June 2015 as subjects of analysis (Table 2). Patents were classified through search formula and scientific names (Table 3). 254 patents related to biomedical applications were classified, but several patents were applied with the same content at different counties by the same inventor. Therefore, patents with the same content and family patent numbers were counted as one patent except patents applied for the different goals and/or materials form.

Therefore, the objective of this review was compiling all recent patents related to the biomedical materials containing brown algae-derived bioactive compounds to examine and understand the R&D trends concerning brown algae-derived biomedical material and then to suggest the future development direction of brown algae in the biomedical engineering industry.

Table 2. Research information for patent database

Classification	Country	Research data base	Analysis range	Research range
Publicized· Registration patent	America China Europe Japan S. Korea	Wipson	~ 2016. 02	Entire document of publicized and registration patents

R&D trends of marine brown algae

1. The major species of brown algae in biomedical application

We analyzed to genera and species of brown algae. The result indicated that 29 genera of brown algae including *Doctyota*, *Eisenia*, *Ecklonia*, *Pelvetia*, and *Sargassum* were used in patents (Table 4A). 19 genera were only used one species in 62 patents. In addition, only *Eisenia bicyclis* was used in 27 patents across all applications, respectively. (Table 4B and 5). In the other case, 4 genera of brown algae (*Dictyota*, *Ecklonia*, *Ishige*, and *Petalonia*) were applied for patents more than 5 patents (Table 4B). Other patents used other genera were applied for less than 5 patents despite the use of several species.

Table 3. Search formula and scientific names

Scientific name	Research formula
Dictyopteris prolifera (Okamura in De Toni & Okamura)	(Hera* adj yahazu*) (Dictyopteris* near prolifera*).key,cla.
Ecklonia cava Kjellman in Kjellman & Petersen	(Kajime* (Ecklonia* near (cava* cova* Kjellman*))).key,cla.
Dictyota okamurae (Dawson) Hörnig, Schnetter, et Prud'homme van Reine	(Dictyotae*Dilophusokamurae*).key,cla.
Petalonia fascia (O. F. Müller) Kuntze	(Petalonia* near fascia*).key,cla.
Scytosiphon lomentaria (Lyngbye) J. Agardh	(Whio near tube) (Scytosiphon* near (lomentaria* Lyngbye*).key,cla.
Elachista orbicularis (Ohta) Skinner	(Elachista* near (orbicularis* Ohta* Skinner*)).key,cla.
Ecklonia stolonifera	(Kelp* (Ecklonia* near stolonifera*).key,cla.
Halothrix lumbricalis (Kützing) Reinke	(Halothrix* near lumbricalis*).key,cla.
Sargassum horneri (Turner) C. Agardh	((sea near lentil) (Sargassum* near horneri*).key,cla.
Agarum clathratum (Dumortier)	(Aname* (Agarum* near (clathratum* Dumortier*))).key,cla.
Corynophlaea globulifera (Ruprecht) Perestenko	(Corynophlaea* near (globulifera* Ruprecht* Perestenko*)).key,cla.
Sphacelaria californica Sauvageau exSetchell & Gardner	(Mitsumata* adj kurogashira*) (Sphacelaria* near (californica* Sauvageau*)).key,cla.
Hydroclathrus clathratus (C. Agardh) Howe	(Hydroclathrus* near clathratus*).key,cla.
Dictyota friabilis Setchell	(Dictyota* near friabilis*).key,cla.
Colpomenia bullosa	(Colpomenia* adj bullosa*).key,cla.
Sargassum siliquastrum (Mertens exTurner) C. Agardh	(Yoremoku* (Sargassum* near siliquastrum*)).key,cla.
Chorda filum (Linnaeus) Stackhouse	(Bootlace* near (weed* Sea-twine*)) (Chorda* near (filum* Linnaeus* Stackhouse*)).key,cla.
Ectocarpus arctus Kützing	(Ectocarpus* near arctus*).key,cla.
Undariopsis peterseniana (Kjellman in Kjellman & Petersen) Miyabe et Okamura in Okamura	(Undariopsis* near peterseniana*).key,cla.
Punctaria latifolia Greville	(Punctaria* near (latifolia* Greville*)).key,cla.
Dictyopteris latiuscula (Okamura) Okamura	(Dictyopteris* near latiuscula*).key,cla.
Shige sinicola (Setchell et Gardner) Chihara	(shige* near (sinicola* Chihara*)).key,cla.
Dictyota cervicornis Kützing	(Dictyota* near cervicornis*).key,cla.
laminaria ochotensis	(laminaria* near ochotensis*).key,cla.
Undaria crenata Y. Lee in Lee & Yoon	(Undaria* near crenata*).key,cla.
Colpomenia expansa (Saunders)	(Colpomenia* near (expansa* Saunders*)).key,cla.
Desmarestia tabacoides Okamura	(Desmarestia* near tabacoides*).key,cla.
Eisenia bicyclis	(sea near oak) (Eisenia* near bicyclis*).key,cla.
Punctaria plantaginea (Roth) Greville	(Punctaria* near (plantaginea* Roth* Greville*)).key,cla.
Distromium decumbens (Okamura) Levring	(Distromium* near decumbens*).key,cla.
Pelvetia siliquosa	(Seaweed near wrightii) (Pelvetia* near siliquosa*).key,cla.
Scytosiphon canaliculatus (Setchell et Gardner in Setchell) Kogame	(Scytosiphon* near (canaliculatus* Setchell*)).key,cla.
Ralfsia expansa (J. Agardh) J. Agardh	(Ralfsia* near expansa*).key,cla.
Spatoglossum solieri (Chauvin ex Montagne) Kützing	(Spatoglossum* near solieri*).key,cla.
Sargassum fulvellum (Turner) C. Agardh	(Gulf* near weed*) (Sargassum* near (fulvellum* Turner*)).key,cla.
Sargassum muticum (Yendo) Fensholt	(Sargassum* near muticum*).key,cla.

Table 3. Search formula and scientific names (continued)

Scientific name	Research formula
Nemacystus decipiens (Suringar) Kuckuck	(Nemacystus* near (decipiens* Suringar* Kuckuck*)).key,cla.
Dictyopteris divaricata (Okamura) Okamura	(Dictyopteris* near divaricata*).key,cla.
Petalonia binghamiae (J. Agardh) Vinogradova	(Petalonia* near binghamiae*).key,cla.
Hincksia mitchelliae (Harvey) Silva inSilva, Meñez, & Moe	(Hincksia* near (mitchelliae* Harvey*)).key,cla.
Chordaria flagelliformis (Müller) C. Agardh	(Chordaria* near flagelliformis*).key,cla.
Sphacelaria rigidula Kützing	(Mitsumata* adj kurogashira*) (Sphacelaria* near rigidula*))).key,cla.
Halopteris filicina (Grateloup) Kützing	(Sea near (Fern Weed*) (Halopteris* near (filicina* Grateloup*)).key,cla.
Leathesia difformis (Linnaeus) Areschoug	(Leathesia* near (difformis* Linnaeus* Areschoug*)).key,cla.
Myelophycus simpelx (Harvey) Papenfuss	(Myelophycus* near (simpelx* Harvey* Papenfuss*)).key,cla.
Petrospongium rugosum (Okamura) Setchell et Gardner	(Petrospongium* near rugosum*).key,cla.
Zonaria diesingiana J. Agardh	((Zonaria* near diesingiana*).key,cla.
Colpomenia peregrina Sauvageau	(Colpomenia* near (peregrina* Sauvageau*)).key,cla.
Punctaria flaccida Nagai	(Punctaria* near (flaccida* Nagai*)).key,cla.
Padina arborescens Holmes	(Padina* near (arborescens* Holmes*)).key,cla.
Tinocladia crassa (Suringar) Kylin	(Tinocladia* near (crassa* Suringar* Kylin*).key,cla.
Padina crassa Yamada	(Padina* near crassa*).key,cla.
Colpomenia sinuosa (Martens ex Roth) Derbès et Solier in Castagne	(Oyster* near thief*) (Colpomenia* near sinuosa*).key,cla.
Halothrix rectiuscula Y. Lee	(Halothrix* near rectiuscula*)).key,cla.
Sphacelaria fusca (Hudson) Gray	(Sphacelaria* near (fusca* Hudson* Gray*)).key,cla.
Acinetospora crinita (Carmichael exHarvey inHooker) Kormann	(Acinetospora* near crinita*) (Carmichael* near exHarvey*).key,cla.
Desmarestia viridis	((Color near changer) (Desmarestia* near viridis*)).key,cla.
Sargassum patens C. Agardh	(Sargassum* near patens*).key,cla.
Padina gymnospora (Kützing) Sonder	(Padina* near gymnospora*).key,cla.
Sargassum confusum C. Agardh	(Sargassum* near confusum*).key,cla.
Elachista tenuis Yamada	(Elachista* near tenuis*).key,cla.
Punctaria projecta Yamada	(Punctaria* near projecta*).key,cla.
Papenfussiella kuromo (Yendo) Inagaki	(Papenfussiella* near (kuromo* Yendo* Inagaki*)).key,cla.
Elachista nipponica Umezaki	(Elachista* near (nipponica* Umezaki*)).key,cla.
Myagropsis myagroides (Martens ex Turner) Fensholt	(Myagropsis* near myagroides*).key,cla.
Corynophlaea verruculiformis (Lee et Lee)	(Corynophlaea* near verruculiformis*).key,cla.
Scytosiphon lomentaria (Lyngbye) Link	(Scytosiphon* near (lomentaria* Lyngbye*)).key,cla.
Spatoglossum latum Tanaka	(Spatoglossum* near latum*).key,cla.
Dictyopteris undulata Holmes	(Dictyopteris* near (undulata* Holmes*)).key,cla.
Carpomitra costata (Stackhouse) Batters	(Carpomitra* near (costata* Stackhouse* Batters*)).key,cla.
Sargassum thunbergii (Mertens ex Roth) Kuntze	(Sargassum thunbergii Mertens ex Roth Kuntze*).key,cla.
Sargassum hemiphyllum (Turner) C. Agardh	(Sargassum* near hemiphyllum*).key,cla.
Dictyopteris pacifica (Yendo)	(Dictyopteris* near pacifica*).key,cla.
Dictyota coriacea (Holmes)	(Dictyota* near (coriacea* Holmes*)).key,cla.
Dictyota dichotoma (Hudson) Lamouroux	((Divided* Net) adj Weed*) (Dictyota* near (dichotoma* Hudson* Lamouroux*))).key,cla.
Ectocarpus siliculosus (Dillwyn) Lyngbye	(Molnslick* (Ectocarpus* near (siliculosus* Dillwyn* Lyngbye*)).key,cla.
Sporochnus radiciformis (R. Brown ex Turner) C. Agardh	(Sporochnus* near radiciformis*).key,cla.
Cutleria cylindrica Okamura	(Cutleria* near cylindrica*).key,cla.
Sargassum macrocarpum C. Agardh	(Sargassum* near macrocarpum*).key,cla.
Sargassum coreanum J. Agardh	(Sargassum* near coreanum*).key,cla.
Sargassum fusiformis (Harvey) Okamura	(Sargassum* near fusiformis*).key,cla.
Proselachista taniaeformis (Yamada)	(Proselachista* near taniaeformis*).key,cla.
Ishige okamurae Yendo	(Ishigee* near okamurae*).key,cla.
Colpomenia tuberculata Saunders	(Colpomenia* near (tuberculata* Saunders*)).key,cla.
Spatoglossum crassum Tanaka	(Spatoglossum* near crassum*).key,cla.

Table 4. Analysis of species. The number of (A) species and (B) patents

(A)

Genus	Number of species
Sargassum	9
Dictyopteris	4
Dictyota	3
Chorda	2
Colpomenia	2
Desmarestia	2
Ecklonia	2
Ishige	2
Padina	2
Petalonia	2
Agarum	1
Carpomitra	1
Chordaria	1
Cutleria	1
Ectocarpus	1
Eisenia	1
Halopteris	1
Hydroclathrus	1
laminaria	1
Leathesia	1
Myagropsis	1
Myelophycus	1
Nemacystus	1
Pelvetia	1
Punctaria	1
Scytosiphon	1
Sporochnus	1
Tinocladia	1
Undariopsis	1

(B)

Genus of brown algae	Number of patent
Eisenia	27
Sargassum	19
Ecklonia	19
Dictyota	10
Petalonia	7
Chordaria	6
Ishige	5
Scytosiphon	5
Chorda	4
Dictyopteris	4
Colpomenia	3
Ectocarpus	3
Sporochnus	3
Desmarestia	2
Leathesia	2
Nemacystus	2
Padina	2
Undariopsis	2
Agarum	1
Carpomitra	1
Cutleria	1
Halopteris	1
Hydroclathrus	1
laminaria	1
Myagropsis	1
Myelophycus	1
Pelvetia	1
Punctaria	1
Tinocladia	1

2. R&D trends by filing year

The classified patents were analyzed every three years. Patents related to biomedical applications as extract-level fractions were intensively applied from 2002 to 2004 (Figure 1B). Unlike, patents related to biomedical application as stem cell culture medium were increased from 2011 to 2016. It was applied poorly previously and the patents related to biomedical devices based on various polysaccharides were intermittently applied (Figure 1B).

3. Patent trends of brown algae in biomedical applications

In our study, we classified the patent application form following 1) Biomedical applications as extract-level fractions; 2) Biomedical applications as stem cell culture medium; 3) Biomedical devices based on various polysaccharides. After that, we analyzed in detail to describe contents of patents.

3-1. Biomedical applications as extract-level fractions

One patent [126] used 39 brown algae as extract sources of elastase inhibitor, the additives to obtain a synergy effect with fish-derived collagen. In addition, *Ectocarpus siliculosus* was applied as a host cell system to produce hyaluronic acid in the bacterial cell [25]. In a patent [86], the gel sheet is able to contain both hydrophilic and hydrophobic drugs and contains lipid peptide-type gelling agent and various brown algae extract to enhance some properties such as biocompatibility and biostability. *Sargassum fulvellum*

Table 5. Biomedical applications and number of patents

Scientific name	Materials	Application	Number of patents
Eisenia bicyclis		Component of sheet-form cell culture carrier	17
	Alginic acid	Composition for cartilage regeneration and arthritic disorder treatment	3
		Component of a bio-inorganic compound complex for hyperthyroidism treatment	1
	Elastase inhibitor	Additives to obtain a synergy effect with fish-derived collagen	1
	Fucoidan	Enhancing stem cell mobilization and proliferation	2
		Preparation of iPSC*	1
		Prophylactic or therapeutic agent for diseases associated with cartilage damage	1
	Acidic polysaccharides	Composition of culture medium for antigen-specific cytotoxic T cell	1
Ecklonia cava Kjellman in Kjellman & Petersen	Alginic acid	Material of hydrogel for wound healing	1
		Composition of culture medium for stem cell	1
	Extract	Differentiation of iPSC induced from other stem cells	11
		Preparation of iPSC	15
	Phlorotannin fraction	Preparation of iPSC	1
Petalonia fascia (O. F. Müller) Kuntze	Elastase inhibitor	Additives to obtain a synergy effect with fish-derived collagen	1
	Fucoidan	Enhancing stem cell mobilization and proliferation	6
Sargassum horneri (Turner) C. Agardh	Elastase inhibitor	Additives to obtain a synergy effect with fish-derived collagen	1
	Extract	Active ingredient on the composition for enhancing bone mass	1
	Fucoidan	Enhancing stem cell mobilization and proliferation	2
		Prophylactic or therapeutic agent for diseases associated with cartilage damage	1
	Phlorotannin fraction	Preparation of iPSC	1
Dictyota dichotoma (Hudson) Lamouroux	Elastase inhibitor	Additives to obtain a synergy effect with fish-derived collagen	1
	Fucoidan	Enhancing stem cell mobilization and proliferation	4
	Phlorotannin fraction	Preparation of iPSC	1
Chordaria flagelliformis (Müller) C. Agardh	Elastase inhibitor	Additives to obtain a synergy effect with fish-derived collagen	1
	Fucoidan	Enhancing stem cell mobilization and proliferation	4
Sargassum fulvellum (Turner) C. Agardh	Elastase inhibitor	Additives to obtain a synergy effect with fish-derived collagen	1
	Extract	Component for producing a bio-inorganic compound complex	2
	Fucoidan	Enhancing stem cell mobilization and proliferation	1
		Prophylactic or therapeutic agent for diseases associated with cartilage damage	1
Scytosiphon lomentaria (Lyngbye) Link	Fucoidan	Enhancing stem cell mobilization and proliferation	4
Sporochnus radiciformis (R. Brown ex Turner) C. Agardh	Arginine kinase	Production of polysaccharides	1
	Alginic acid	Carrier for enzyme embedding	1
	Elastase inhibitor	Additives to obtain a synergy effect with fish-derived collagen	1
Chorda filum (Linnaeus) Stackhouse	Elastase inhibitor	Additives to obtain a synergy effect with fish-derived collagen	1
	Fucoidan	Enhancing stem cell mobilization and proliferation	2
Pelvetia siliquosa	Elastase inhibitor	Additives to obtain a synergy effect with fish-derived collagen	1
	Fucoidan	Enhancing stem cell mobilization and proliferation	2
Ectocarpus siliculosus (Dillwyn) Lyngbye	Extract	Removal or inactivation of pyrogens or target molecule	1
	Peptides	Base material for silica synthesis	2
Ishige okamurae Yendo	Elastase inhibitor	Additives to obtain a synergy effect with fish-derived collagen	1
	Extract	Compositions for wound healing and skin regeneration	1
	Phlorotannin fraction	Preparation of iPSC	1
Sargassum patens C. Agardh	Elastase inhibitor	Additives to obtain a synergy effect with fish-derived collagen	1
	Fucoidan	Prophylactic or therapeutic agent for diseases associated with cartilage damage	1
	Phlorotannin fraction	Preparation of iPSC	1

Table 5. Biomedical applications and number of patents (continued)

Scientific name	Materials	Application	Number of patents
Colpomenia bullosa	Elastase inhibitor	Additives to obtain a synergy effect with fish-derived collagen	1
	Extract	Compositions for wound healing and skin regeneration	1
Undariopsis peterseniana (Kjellman in Kjellman & Petersen)	Elastase inhibitor	Additives to obtain a synergy effect with fish-derived collagen	1
	Extract	Removal or inactivation of pyrogens or target molecule	1
Shige sinicola (Setchell et Gardner) Chihara	Elastase inhibitor	Additives to obtain a synergy effect with fish-derived collagen	1
	Extract	Compositions for wound healing and skin regeneration	1
Nemacystus decipiens (Suringar) Kuckuck	Extract	Polymeric compound of gel sheet	1
	Fucoidan	Prophylactic or therapeutic agent for diseases associated with cartilage damage	1
Leathesia difformis (Linnaeus) Areschoug	Extract	Compositions for wound healing and skin regeneration	1
		Removal or inactivation of pyrogens or target molecule	1
Sargassum thunbergii (Mertens ex Roth) Kuntze	Elastase inhibitor	Additives to obtain a synergy effect with fish-derived collagen	1
	Fucoidan	Prophylactic or therapeutic agent for diseases associated with cartilage damage	1
Dictyota coriacea (Holmes)	Elastase inhibitor	Additives to obtain a synergy effect with fish-derived collagen	1
	Phlorotannin fraction	Preparation of iPSC	1
	Alginic acid	Material of hydrogel for wound healing	1
Other	Elastase inhibitor	Additives to obtain a synergy effect with fish-derived collagen	22
	Extract	Compositions for wound healing and skin regeneration	1
		Tissue regeneration composition for fat transplant	1
	Fucoidan	Enhancing stem cell mobilization and proliferation	2
		Prophylactic or therapeutic agent for diseases associated with cartilage damage	1
	Phlorotannin fraction	Preparation of iPSC	1

*iPSC : induced pluripotent stem cell

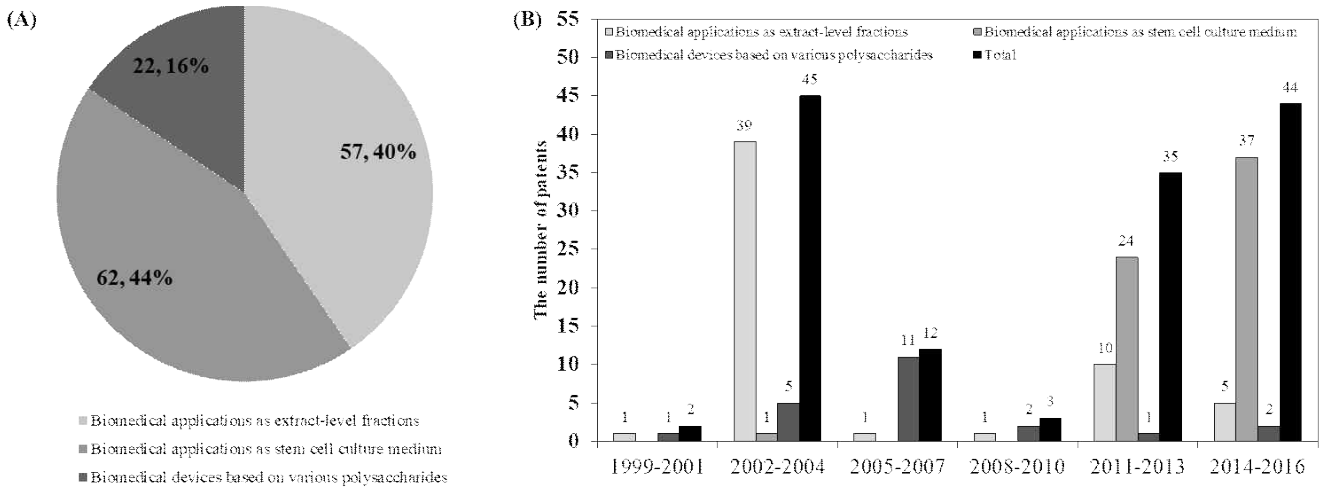

Figure 1. R&D trends of brown algae in biomedical application. The number of valid patents was calculated by considering the redundant patents. (A) Number and percentage of applied patents using brown algae in biomedical application. (B) The number of patents using brown algae as medical material according to filing year.

was used as the component of a bio-inorganic compound complex for hyperthyroidism treatment by reducing reactive oxygen species [87,88]. Furthermore, a patent [90] related to the silica synthetic method used *E. bicyclis* derived peptides as the base material of silica synthesis to convert the silica precursor into silica under an aqueous solution. Two patents [130,131] were applied arginine kinase extracted from *Sporochnus radiciformis* to producing polysaccharides. A patent [17] intended for removal or inactivation of pyrogens or target molecules through utilization of brown algae-derived extract. In addition, extract from several brown algae were used as compositions for wound healing and skin regeneration [39]. In a patent [138], *Sargassum horneri* extract was used as the active ingredient on the composition for enhancing bone mass due to anti-osteoporosis effect.

3-2. Biomedical applications as stem cell culture medium

In a patent [101], acidic polysaccharides (fucoidan and sulfate polysaccharides) were used as culture medium ingredients to culture antigen-specific cytotoxic T cells. In another patent [137], fucoidan from *E. bicyclis* plays the role of the differentiation-inducing agent from induced pluripotent stem cell (iPSC) to ectodermal cells. Additionally, two patents [18,19] extracted fucoidan from various brown algae to enhance mobilization and proliferation of stem cell. Moreover, three patents [20-22] used 7 brown algae for fucoidan extraction to enhance mobilization and proliferation of several stem cell lines. Summarizing applications as stem cell culture medium, fucoidan mainly was used in stem cell-related patents. Additionally, brown algae were used multiple applications as extract. *Ecklonia cava* extract extensively was used described following 1) Mesenchymal stem cell (MSC) culture medium [55]; 2) iPSC induction medium [56-63,67]; 3) iPSC differentiation medium into several cell lines including adipocyte, hepatocyte, osteoblast, neuron, and chondrocyte [63-65,68-70]. *E. cava* extract, as well as phlorotannins extracted from numerous brown algae, were used to induce iPSC from MSC [66,71]. Whereas, a patent [105] used *Sargassum confusum* extract as an active ingredient to enhance proliferation of fat cell after fat transplant.

3-3. Biomedical devices based on various polysaccharides

In a patent [81], fucoidan was extracted from 7 brown algae and used for the prophylactic or therapeutic agent to treatment cartilage damage-associated diseases, since it is widely known that fucoidan promotes cartilage regeneration through enhancing the production of glycosaminoglycan and proteoglycan. Alginate extracted from *E. bicyclis* was used to form the complex with protamine for reducing intense astringency and inhibiting lipase activity [110]. In addition, patent related with alginic acid extracted from *E. bicyclis* and it used as the component of sheet-form cell culture carrier to enhance stratification of the cell layer [27]. In several patents [3-6,45,46,78,112-117,119,136], alginic acid extracted from *E. bicyclis* was used as a base material of an aqueous polymer to make suitable for chitosan-containing polymer gel or cell culture carrier for lamination cell culture method. Another patent [139] described that wound dressing containing alginic acid has a proper effect for the relatively deep wound due to its hemostatic function, high absorption rate, and flexibility. In a patent related to wound healing, alginate extracted from *E. cava* and *Ecklonia stolonifera* was modified using tyramine and then applied on the hydrogel preparation [51]. Similarly, two patents [36-38] was used *E. bicyclis* for the alginic acid extraction to regenerate cartilage or treat arthritic disorders.

Conclusion

In the present study, R&D trends of brown algae were analyzed to forecast potential in biomedical applications through patents analysis. As a result,

application as stem cell culture medium is occupied the highest percentage among various application fields. However, the interest in the development of brown algae-derived polysaccharides in biomedical applications obtained comparatively less attention and then led to have only few patents over the last decades. Moreover, over the period, numerous studies have been conducted to extraction and isolation of bioactive materials indicating a huge potential for biomedical applications, yet there is no real application in tissue engineering including fabrication of engineered 3D scaffolds, nano-fibrous and so on. Hence, current patent analysis study indicates an infinite potential of brown algae-derived materials in regenerative medicine, especially in tissue engineering applications.

Although researchers were increasingly interested in applications of brown algae in biomedical engineering, there is no patent applied to biomedical engineering technology. In conclusion, this study suggested that brown algae have infinite potential for the R&D investigation in the future.

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