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Review

Biological activities and potential industrial applications of fucose rich sulfated polysaccharides and fucoidans isolated from brown seaweeds: A review

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ABSTRACT

Brown seaweeds are rich in sulfated polysaccharides that could potentially be exploited as functional ingredients for human health. Over the years, sulfated polysaccharides with potential pharmacological, nutraceutical, functional food and cosmeceutical properties have been isolated from brown seaweeds. In the present review, attempts have been made to discuss the functional properties of brown algal fucoidans and fucose rich sulfated polysaccharides. Anticoagulant, antithrombotic, immunomodulation, anticancer and anti-proliferative activities are the most extensively studied biological activities of fucoidans. The profound functional properties of fucoidans have proven to be invaluable and could be employed in the potential industrial applications as natural functional ingredients to obtain possible health benefits. For such applications, the reviewed literature in this communication may provide valuable basic information.

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Contents

1. Introduction

While marine algae have traditionally formed part of the oriental diet, especially in Asian-pacific region; their major use in Western countries has traditionally concentrated on the extraction of compounds used by pharmaceutical, cosmetics, and food industries (Ordonez, Escrig, & Ruperez, 2010). Nowadays, the field of marine natural products becomes more sophisticated. Seaweeds produce a variety of biologically active components with different structures and interesting functional properties (Amarowicz, Pegg, Rahimi-Moghaddam, Barl, & Weil, 2004; Choi et al., 2002; Kong, Kim, Yoon, & Kim, 2009; Kim & Bae, 2010; Shibata, Ishimaru, Kawaguchi, Yoshikawa, & Hama, 2008). The bioactive components of seaweeds include polyphenols, peptides, polysaccharides, *etc.* Many of these active compounds found to be useful functional ingredients with numerous health benefits.

Brown seaweeds belong to a very large group and it is the second most abundant group of seaweeds (Davis, Volesky, &

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Mucci, 2003; Mestechkina & Shcherbukhin, 2010; Reddy & Urban, 2009). Most brown seaweeds contain the pigment fucoxanthin, which is responsible for the distinctive greenish-brown colour that gives them their name. Brown seaweeds also produce a range of active components including unique secondary metabolites such as phlorotannins and many of which have specific biological activities that give possibilities for their economic utilization.

Polysaccharides produced by seaweeds expand the economically important and global industries. Significant amounts of seaweed derived polysaccharides are used in food, pharmaceuticals and other products for human consumption. Thus, the global seaweed polysaccharide industry operates in a highly regulated environment (Renn, 1997). Over the last decade, bioactive sulfated polysaccharides isolated from brown seaweeds have attracted much attention in the fields of pharmacology and biochemistry. Functional polysaccharides such as fucans and alginic acid derivatives produced by brown seaweeds are known to exhibit different biological properties including anticoagulant, anti-inflammatory, antiviral and antitumoral activities (Boisson-Vidal et al., 1995; Costa et al., 2010; Lee, Athukorala, Lee, & Jeon, 2008). In the recent years, sulfated polysaccharides, fucoidans have been isolated from different brown algal species such as *Ecklonia cava*, *Ascophylum nodusum*, and *Undaria pinnatifida* (Athukorala, Jung, Vasanthan, & Jeon, 2006; Matou, Helley, Chabut, Bros, & Fischer, 2002). This gives brown seaweeds great value as potential sources of fucoidans for the development of health promoting natural products. Therefore, as will be discussed in this review, the functional properties of fucoidans from brown seaweeds could be contributed to the development of pharmaceuticals, cosmeceuticals and functional foods. Taken together, this communication focuses on recent efforts in discovering the biological aspects associated with brown algal fucoidans. In addition, some important perspectives on the potential industrial uses of fucoidans for the development of functional ingredients are also discussed and summarized.

2. Fucose rich sulfated polysaccharides/fucoidans

Polysaccharides are the most abundant among the natural products produced by plants and they widely exist in plants, animals, microorganisms and algae (Paulsen, 2002; Yang & Zhang, 2009). These polymeric carbohydrate structures, usually composed of various monosaccharides linked with different glucosidic bonds (Holdt & Kraan, 2011). Depending on the structure, polysaccharides can have distinct functional properties from their building blocks. Sulfated polysaccharides are among the most abundant and broadly studied polysaccharides from non-animal origin (Pereira, Silva, Valente, & Mourao, 2002). Most naturally occurring sulfated polysaccharides are complex mixtures of molecules showing wide variations in their structure as well as their activities (Alban, Schauerte, & Franz, 2002). They are widespread in nature. Seaweeds are recognized as a major source of sulfated polysaccharides with various biological activities. Thus, sulfated polysaccharides are of special interest in the search of natural products.

Fucoidan (Fig. 1) is a type of complex sulfated polysaccharide, mainly found in the cell-wall matrix of various brown seaweed species (Kim, Lee, & Lee, 2010; O'Connell, Murray, Piggot, Hennequart, & Tuohy, 2008; Teruya, Konishi, Uechi, Tamaki, & Tako, 2007). It contains substantial percentages of L-fucose and sulfate ester groups (Jiang et al., 2010; Li, Lu, Wei, & Zhao, 2008; Matou et al., 2002). Fucose is a hexose deoxy sugar with the chemical formula $C_6H_{12}O_5$ and is the fundamental sub unit of the fucoidan polysaccharide. For the past decade fucoidan has been extensively studied due to its numerous biological activities. Recently researches for new drugs have raised interest in fucoidans. In the past few years, several fucoidans' structures have been isolated, and

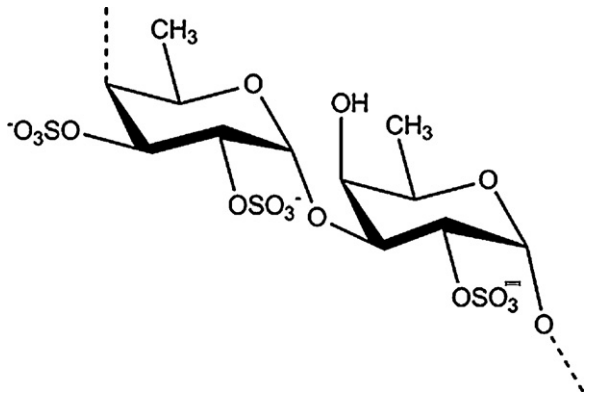

Fig. 1. Chemical structure of fucoidans.

many aspects of their biological activity have been elucidated (Li et al., 2008). Previous studies have clearly shown that the composition and complexity of fucoidans from different brown seaweeds can vary considerably (O'Connell et al., 2008).

3. Isolation and purification of fucoidans from brown seaweeds

Investigation of seaweed derived chemical compounds, a different source of natural products, has proven to be a promising area of functional ingredient studies. Therefore, over the years, isolation and chemical characterization of active substances from seaweeds have gained much attention. Seaweeds appear to be good sources of active polysaccharides presenting great chemical, physico-chemical and rheological diversities (Lahaye, 1991). Naturally occurring sulfated polysaccharides are today among the most talked about classes of bioactive natural products. These sulfated polysaccharides might be very important functional ingredients in various industrial applications.

Extraction is influenced by the chemical nature of the components, the extraction method employed and the presence of interfering substances (Chirinos, Rogetz, Campos, Pedreschi, & Larondelle, 2007). The polysaccharide content of seaweeds varies according to the species. Generally these polysaccharides have been extracted using water or aqueous organic solvents (Albuquerque et al., 2004). However, since the cell wall consists of complex polymers, it is not easy to extract active polysaccharides using solvent extraction process. The production of different bioactive polysaccharides with lyases is required in order to increase the extraction efficiency of more functional ingredients from seaweeds. Therefore, enzyme-assisted extraction (EAE) technique can be employed as an alternative method to enhance the extraction efficiency of bioactive polysaccharides from seaweed sources for industrial use (Athukorala et al., 2009; Kang et al., 2011; Wijesinghe & Jeon, 2011a).

The detailed experimental procedures of the isolation and purification of fucoidans from seaweeds have been well described in earlier studies (Athukorala, Jung, Vasanthan, & Jeon, 2006; Matsubara, Matsuura, Hori, & Miyazawa, 2000). The purity of the sample can be confirmed by agarose gel electrophoresis, and the molecular weight of the sample can be determined by gel filtration chromatography (GFC) system. In addition, fucoidanase can be used to hydrolyze fucoidan to produce low molecular weight fucoidans. Therefore, it could additionally be used as a tool for elucidating the structure of fucoidans (Wu et al., 2011). Fig. 2 shows the essential steps involved in the isolation and purification of fucoidans from brown seaweeds.

Table 1
Possible health effects of fucose rich sulfated polysaccharides and fucoidans isolated from different brown seaweed species.

Possible health effect	Source	Reference
Anticoagulant/antithrombotic	*E. cava*	Athukorala et al. (2006)
	E. cava	Jung et al. (2007)
	F. evanescens	Kuznetsova et al. (2003)
	E. cava	Wijesinghe et al. (2011)
	P. gymnospora	Silva et al. (2005)
	A. nodosum	Chevolot et al. (1999)
	S. fulvellum	De Zoysa et al. (2008)
	Hizikia fusiforme	Dobashi et al. (1989)
	Laminaria cichorioides	Yoon et al. (2007)
Immunomodulation	*F. vesiculosus*	Kim et al. (2008)
	F. vesiculosus	Do et al. (2010)
	F. vesiculosus	Jintang et al. (2010)
	U. pinnatifida	Yoo et al. (2007)
	F. vesiculosus	Yang et al. (2008)
Anti-inflammation	*L. japonica*	Li et al. (2011)
	E. cava	Kang et al. (2011)
Antitumor/anti-proliferation/anticancer	*U. pinnatifida*	Synytsya et al. (2010)
	E. cava	Athukorala et al. (2009)
	F. evanescens	Alekseyenko et al. (2007)
	L. guryanovae	Lee, Ermakova, et al. (2008)
	C. okamuranus TOKIDA	Teruya et al. (2007)
	C. okamuranus TOKIDA	Heneji et al. (2005)
Angiogenesis	*A. nodosum*	Matou et al. (2002)
Cardioprotection	*C. okamuranus* TOKIDA	Thomes et al. (2010)
Antivirus	*U. pinnatifida*	Hemmingson et al. (2006)
Gastric mucosal protection	*C. okamuranus* TOKIDA	Shibata et al. (2000)
Neuroprotection	*Laminaria japonica*	Luo et al. (2010)

4. Biological activities of fucoidans and possible health effects

During the last decades various carbohydrate polymers have been shown to be responsible for biological effects, either by exhibiting the effect themselves or by inducing effects *via* complex reaction cascades (Paulsen, 2002). Fucose-containing sulfated polysaccharides from brown seaweeds might exhibit interesting biological properties (Matsuhiro, Zuniga, Jashes, & Guacucano, 1996). The prominent biological activities of the sulfated polysaccharides are probably due to the presence of sulfate groups in varying amounts. In addition, positions of the sulfated groups along the macromolecular backbone also play a significant role in their functional properties. Among the sulfated polysaccharides, often called fucoidans found in seaweeds, are well-known to have various biological activities (Table 1) and the potent biological properties of fucoidans seem to be determining by their high degree of sulfation, fine structure and molecular weight (Jiang et al., 2010; Wijesinghe & Jeon, 2011b; Zvyagintseva et al., 2003). However, the composition of algal fucans varies according to several factors such as species, extraction procedure, season of harvest and climatic conditions (Dietrich et al., 1995; Grauffel, Kloareg, Mabeau, Durand, & Josefonficz, 1989). Thus, each newly isolated and described fucans are unique compounds with unique structural features, consequently having the potential of being used as novel functional ingredients in pharmaceutical, cosmeceutical or food industries (Kumar et al., 2010; Silva et al., 2005).

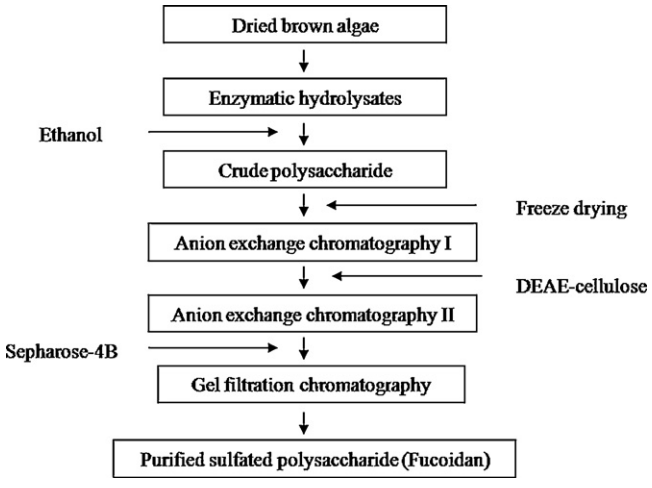

Fig. 2. Essential steps involved in purification of fucoidans from brown seaweeds.

4.1. Anticoagulant and antithrombotic activity

Disorders in blood coagulation can lead to an increased risk of bleeding (hemorrhage) or clotting (thrombosis) (Rivas, Gutierrez, Arteaga, Mercado, & Sanchez, 2011). Anticoagulants are substances that prevent coagulation; that is, they stop blood from clotting (Desai, 2004). Therefore, they are a group of pharmaceuticals that can be used *in vivo* as a medication for thrombotic disorders. Heparin, a highly sulfated polysaccharide present in mammalian tissues, is one of the commonly and widely used drugs for anticoagulant therapy for more than 50 years (Fan et al., 2011; Lee, Athukorala, et al., 2008). However, there are some well-documented problems such as risk of excessive bleeding and heparin induced thrombocytopenia related to the clinical use of heparin as an antithrombotic drug. Considerable efforts have been made in recent years to obtain safer anticoagulants with less hemorrhagic risk, while retaining a good antithrombotic activity (Alban et al., 2002; Mansour et al., 2010). Therefore, recently alternative drugs for heparin are in high demand due to its bad and long-term side effects (Athukorala, Lee, Kim, & Jeon, 2007). Marine algae are a rich source of sulfated polysaccharides with novel structures, and these compounds have anticoagulant properties. Various anticoagulant polysaccharides, especially from red and brown seaweeds have been isolated and characterized (De Zoysa, Nikapitiya, Jeon, Jee, & Lee, 2008; Mao, Zang, Li, & Zhang, 2006). The ability of sulfated polysaccharides to interfere with biological systems has a longstanding record, as illustrated with heparin (Huynh, Chaubet, & Jozefonvicz, 2001). In addition, anticoagulant and antithrombotic

activities are among the most widely studied properties of sulfated polysaccharides. With the evidence from previous studies, brown algal sulfated polysaccharide, fucoidan attracted extensive interest in anticoagulative drug discovery.

Anticoagulant activity of fucose containing sulfated polysaccharide isolated from brown seaweed *E. cava* including activated partial thromboplastin time (APTT), thrombin time (TT) and prothrombin time (PT) was reported (Athukorala et al., 2006). According to their results the isolated pure compound showed almost similar anticoagulant activity to that of heparin. Further study demonstrated that fucose containing sulfated polysaccharide isolated from *E. cava* strongly inhibits the activities of coagulation factors *via* interaction with antithrombin III in both the extrinsic and common coagulation pathways (Jung et al., 2007). Fucoidans enhance ATIII-mediated coagulation factor inhibition in coagulation pathways. This contributes to its high anticoagulant activity. Another recent study demonstrated *in vivo* anticoagulant activity of isolated fucose rich sulfated polysaccharide obtained from *E. cava* (Wijesinghe, Athukorala, & Jeon, 2011). In that study, similar transmittance was observed in Fourier transform infrared spectroscopy (FT-IR), for the commercial fucoidan and isolated polysaccharide with an intense absorption band at 1240 and 820 cm^{-1} indicating its high sulfate content. Nishino and Nagumo (1992) reported anticoagulant and antithrombin activities of over sulfated fucans having different sulfate contents. Their results showed that heparin cofactor II-mediated antithrombin activity of the over sulfated fucans also increased significantly with increase in sulfate content. In addition it was reported that the major antithrombin activity by fucoidan was mediated by heparin cofactor II (Qui, Amarasekara, & Doctor, 2006).

Partial characterization and anticoagulant activity of a heterofucan from the brown seaweed, *Padina gymnospora* were also reported (Silva et al., 2005). According to their report, 3-*O*-sulfation at C-3 of 4-α-L-fucose-1 → units was responsible for the anticoagulant activity of fucoidan from the particular seaweed species. De Zoysa et al. (2008) reported the isolation and characterization of fucose containing sulfated polysaccharide as an anticoagulant agent from the edible brown seaweed *Sargassum fulvellum* by using a simple fermentation process and chromatography technique. Further they have reported that fermentation could offer a tool to increase the bioactive potentials of seaweeds. Thus, the report facilitates further screening and mass production of the bioactive substances from fermented seaweeds in the future.

4.2. Anti-proliferative/antitumor/anticancer activity

During the search for natural anticancer compounds, crude extracts and pure compounds from marine organisms have been the object of many investigations (Moreau et al., 2005). Over the past years, it has been reported that fucose rich sulfated polysaccharides isolated from brown seaweeds exhibited anticancer activity, which is one of the most important biological activities of seaweeds.

Teruya et al. (2007) reported the anti-proliferative activity of over sulfated fucoidan from commercially cultured *Cladosiphon okamuranus* TOKIDA in U937 cells. Their results indicated that the over sulfated fucoidan induced apoptosis *via* caspase-3 and -7 activation-dependent pathways. In addition, fucoidan extracted from *C. okamuranus* TOKIDA induces apoptosis of human T-cell leukemia virus type 1-infected T-cell lines and primary adult T-cell leukemia cells (Heneji et al., 2005). Their results indicated that fucoidan is a potentially useful therapeutic agent for patients with adult T-cell leukemia. The brown seaweed *C. okamuranus* TOKIDA is commercially cultured around the Okinawa Island, Japan. Fucoidans, sulfated polysaccharides of brown seaweed *C. okamuranus* TOKIDA, have attracted steady attention in the last few years. In fact a fucoidan has been prepared on an industrial scale from *C. okamuranus* TOKIDA and used as an additive to health foods, drinks and cosmetics in Japan (Teruya et al., 2007).

Antitumor activity of fucoidan from *U. pinnatifida* in PC-3, HeLa, A549 and HepG2 cancer cells in similar pattern to that of commercial fucoidan was reported (Synytsya et al., 2010). According to another recent study, fucose rich sulfated polysaccharide from *E. cava* has antiproliferative effects on murine colon carcinoma (CT-26), human leukemic monocyte lymphoma (U-937), human promyelocytic leukemia (HL-60), and mouse melanoma (B-16) cell lines (Athukorala et al., 2009). Fucoidan was found to inhibit proliferation and induce apoptosis in human lymphoma HS-Sultan cell lines (Aisa et al., 2004). According to their results, fucoidan-induced apoptosis was accompanied with the activation of caspase-3. Another *in vitro* study demonstrated the inhibitory effects of fucoidan on activation of epidermal growth factor receptor and cell transformation in JB6 C141 cells (Lee, Ermakova, et al., 2008). Their results provided the first evidence that fucoidan from *Laminaria guryanovae* exerted a potent inhibitory effect on EGF-induced phosphorylation of epidermal growth factor receptor (EGFR). The EGFR, one of the receptor tyrosine kinases, plays an important role in regulating cell proliferation, differentiation, and transformation (Chen et al., 1987). Therefore, it is an important target for cancer therapy (Yarden & Sliwkowski, 2001). In another recent study, antitumor and antimetastatic activities of fucoidan, isolated from brown seaweed *Fucus evanescens* was studied in C57Bl/6 mice with transplanted Lewis lung adenocarcinoma (Alekseyenko et al., 2007).

Identification of novel effective cancer chemopreventive agents has become an essential worldwide strategy in cancer prevention (Eldeen, Ahmed, & Zeid, 2009). Anti-proliferative and antitumor properties of fucoidan were reported for several studies (Itoh, Noda, Amano, & Ito, 1995; Maruyama, Tamauchi, Hashimoto, & Nakano, 2003; Maruyama, Tamauchi, Iizuka, & Nakano, 2006). Fucoidans inhibit tumor growth and metastatic process both by direct action on tumor cells or by the enhancement of immune response (Khotimchenko, 2010). Therefore, finding of anticancer properties of brown algal fucoidans could elevate the value of brown seaweeds as functional ingredients in pharmaceuticals or functional foods.

4.3. Immunomodulatory activity

Immunomodulation refers to the action undertaken by the medication on auto regulating processes that steer the immunological defense system. Many polysaccharides obtained from natural sources are considered as biological response modifiers and have been shown to enhance various immune responses (Li et al., 2008). According to the previous studies, oligosaccharides have been shown to have a variety of effects on the immune system, such as inhibition of cancer metastasis, antitumor activity, immunological activity, and complement activation, and may be effective candidates for tumor immunotherapy (Yuan, Song, Li, Li, & Liu, 2011). Therefore, besides of direct anticancer or antiproliferative properties, fucoidans can also suppress the development of tumor cells through enhancing body's immunomodulatory activity.

Immunomodulatory effects of fucoidan purified from brown seaweed *Fucus vesiculosus* on dendritic cells were reported (Kim & Joo, 2008). In addition, they suggested that the fucoidan has immunostimulating and maturing effects on bone marrow-derived dendritic cells, *via* a pathway involving at least NF-κB. Choi, Kim, KIm, and Hwang (2005). investigated the immunomodulating effects of arabinogalactan and fucoidan *in vitro*. Their data suggest that arabinogalactan and fucoidan are activators of lymphocytes and macrophages. This property may contribute to their effectiveness in the immunoprevention of cancer.

According to Yang et al. (2008), fucoidan may be used on dendritic cells-based vaccines for cancer immunotherapy. In their study, effects of fucoidan on maturation process and activation of human monocyte-derived dendritic cells were demonstrated. Their results suggest that dendritic cells appear to be a potential target for the immunomodulatory capacity of fucoidan. Do, Kang, Pyo, Billiar, and Sohn (2010) reported the effect of fucoidan on Nitric Oxide (NO) production induced by IFN-γ and the molecular mechanisms underlying these effects in two types of cells including glia (C6, BV-2) and macrophages (RAW264.7, peritoneal primary cells). The authors have reported that the effects of fucoidan on inducible Nitric Oxide Synthase (iNOS) expression through IFN-g-mediated signaling between two cell types and suggested the possibility of fucoidan not only as a promising candidate for treating inflammatory-related neuronal injuries, but also as an immune modulating nutrient for altering sensitivity of cells.

It is reported that fucoidan post-translationally regulated MMP-9 secretion from U937 cells (Jintang et al., 2010). Matrix metalloproteinase-9 (MMP-9) is a secreted multidomain enzyme which plays an important role in the migration of immune cells. Fucoidan isolated from *U. pinnatifida* possesses immunomodulating activity to produce cytokines and chemokines from macrophages and splenocytes (Yoo et al., 2007). Immunological activity of fucoidan against aspirin-induces gastric mucosal damage was documented recently (Raghavendran, Sriniwasan, & Rekha, 2011). In that study immunity changes in stomach tissues of rats were assessed. Their findings collectively indicate that the gastro protective effect of fucoidan against aspirin-induced ulceration in rats is mediated through its immunomodulatory properties.

4.4. Anti-inflammatory activity

The inflammatory process involves a series of events that can be elicited by numerous internal or external stimuli. Therapy of inflammatory diseases is usually directed at the inflammatory processes. Anti-inflammatory refers to the property of a substance or treatment that reduces inflammation. Macrophages are key players in inflammation (Kazlowska, Hsu, Hou, Yang, & Tsai, 2010). Since the synthetic anti-inflammatory drugs are known to provoke gastrointestinal irritations, search for alternative anti-inflammatory drugs and medicines among the bounties of natural herbs is required (Nguemfo et al., 2007).

Kang et al. (2011) successfully investigated potent effect of the fucose containing sulfated polysaccharide from *E. cava* on anti-inflammatory activity in lipopolysaccharide (LPS)-stimulated RAW 264.7 cells. According to their results, isolated sulfated polysaccharide containing fucose, dose-dependently inhibited the LPS-induced iNOS and cyclooxygenase-2 (COX-2) gene expression, as well as the subsequent production of NO and prostaglandin E_2 (PGE_2) by LPS in RAW 264.7 macrophages. Recent *in vivo* study revealed that the administration of fucoidan, isolated from brown seaweed *Laminaria japonica* could regulate the inflammation response *via* HMGB1 and NF-κB inactivation in I/R-induced myocardial damage on rats (Li et al., 2011). According to the Senni et al. (2006) fucoidan from *Ascophyllum nodosum* is a potent modulator of connective tissue proteolysis. In addition, the authors suggested that fucoidan could be used for treating some inflammatory pathologies in which uncontrolled extracellular matrix degradation takes place. Connective tissue destruction during inflammatory diseases, such as chronic wound, chronic leg ulcers, or rheumatoid arthritis, is the result of continuous supply of inflammatory cells and exacerbated production of inflammatory cytokines and matrix proteinases (Senni et al., 2006).

4.5. Other biological activities of fucoidan

Thomes, Rajendran, Pasanban, and Rengasamy (2010) studied cardioprotective activity of fucoidan extracted from *C. okamuranus* TOKIDA in isoproterenol induced myocardial infarction in rats. According to the authors, briefly, fucoidan treatment reduced myocardial damage, which has been reflected by improvement in parameters such as creatinine phosphokinase, lactate dehydrogenase, alanine transaminase and aspartate transaminase. In addition, fucoidan improved the antioxidant defense system in treated animals and considerably reduced the oxidative stress exerted by isoproterenol. Properties of fucoidan from *C. okamuranus* TOKIDA in gastric mucosal protection were also reported (Shibata et al., 2000). Their results suggested that *Cladosiphon* fucoidan is a safe substance with potential for gastric protection.

In one of the recent efforts to explore new drugs for Parkinson's disease treatments, fucoidan from *L. japonica* has drawn attention (Luo et al., 2009). The findings of this study suggested that fucoidan had protective effect on 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (a neurotoxin)-induced nurotoxicity in Parkinson's disease *via* its antioxidant activity.

Fucoidan can enhance vascular tube formation induced by fibroblast growth factor-2 (FGF-2) with a modulation of the expression of surface proteins involved in angiogenesis (Matou et al., 2002). The authors reported the effect of fucoidan from *A. nodosum* on FGF-2-induced proliferation and differentiation of human umbilical vein endothelial cells. In another study however, smooth muscle cell proliferation was inhibited by fucans, suggesting an antiproliferative effect (Logeart, Prigeant-Richard, Jozefonvicz, & Letourneur, 1997). Together with these results Matou et al. (2002) suggested a potentially preventive effect of fucoidan on restenosis.

Hemmingson, Falshaw, Furneaux, and Thompson (2006) demonstrated the potential antiviral activity of galactofucan sulfates extracted from *U. pinnatifida* against herpes viruses HSV-1, HSV-2 and HCMV. In recent years, few other antivirus activities of sulfated polysaccharides containing fucose have been demonstrated (Hayashi, Nakano, Hashimoto, Kanekiyo, & Hayashi, 2008; Mandal et al., 2007).

Despite these biological activities, detailed study on the toxicology of brown algal fucoidan was performed (Kim, Lee, Lee, & Lee, 2010). They have tested the toxicity of a four-week oral trial of fucoidan extracted from the *U. pinnatifida* in Sprague-Dawley rats. The study showed that fucoidan from *U. pinnatifida* is not toxic when orally administered at 150, 450, and 1350 mg/kg bw/day for four weeks, and does not have anticoagulant activity, reducing concern about adverse effects related to excess bleeding.

5. Potential industrial applications of fucoidans

In the recent years, there are significant developments in the fields of pharmaceutical, nutraceutical, cosmeceutical and functional food. There is a growing interest among producers and the public in those areas that may provide health benefits beyond basic nutrition. Increasing awareness among consumers about health promoting foods has aroused interest in food supplement research worldwide (Kumar et al., 2010). This fact has brought great interest for searching new functional ingredients that can contribute to develop new opportunities in the relevant applications. Therefore, today, in the modern market, novel products are available with functional ingredients from different natural sources. Over the years, seaweeds are extensively used for the production of industrially useful ingredients. Research during past decade has provided extensive scientific evidence for the health benefits of brown algal fucose rich sulfated polysaccharides and fucoidans. Discussed biological properties of brown algal fucoidans

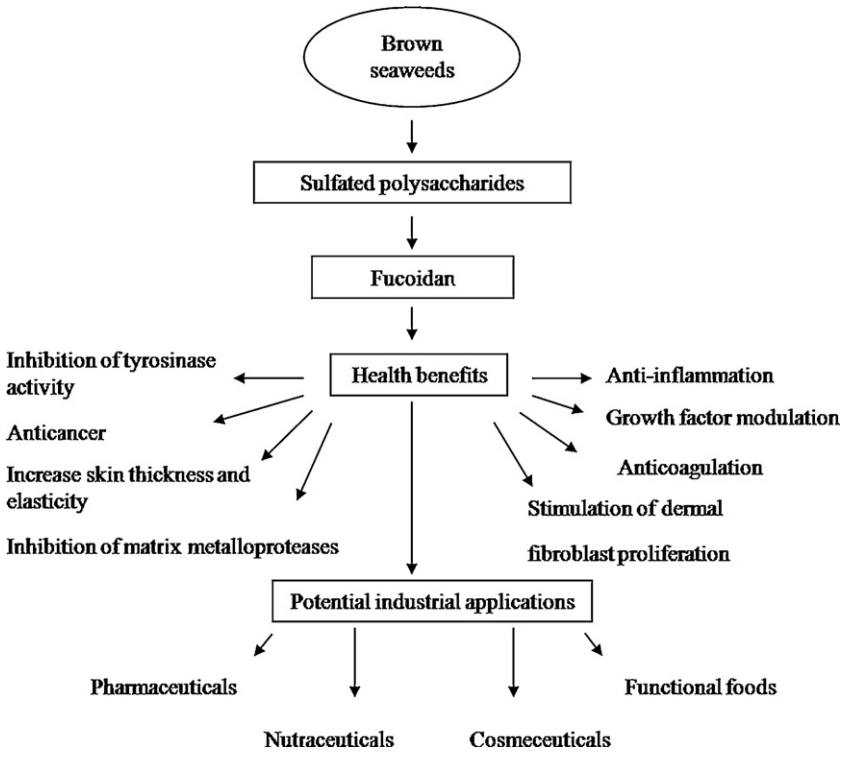

Fig. 3. Biological properties and potential industrial uses of fucoidans.

have opened up potential opportunities in drug, nutraceutical, cosmeceutical and functional food industries (Fig. 3). However, it is important to study how these active polysaccharides can retain their functional properties in different processing steps of the particular industrial applications. In addition, during the production of functional foods or cosmeceuticals containing fucoidans, processing methods should be developed to enhance their bioavailability as functional ingredients. Since these components may cause color or flavor problems, it is also important to identify the appropriate form of the components prior to incorporate with pharmaceuticals, nutraceuticals, functional foods or cosmeceuticals. These factors should carefully be taken into consideration when looking for possible industrial applications of fucose rich sulfated polysaccharides and fucoidans from brown seaweeds. Moreover, development of required processing technologies will ensure the exploitation of a variety of potential value-added products with these functional ingredients.

6. Conclusion

Brown seaweeds have been identified as easily accessible producers of sulfated polysaccharides. This review paper explores the functional properties of brown algal fucoidans, as well as outlines the potential uses as active ingredients in industrial applications. In addition, here we discussed the isolation and purification of the sulfated polysaccharides, fucoidans together with its numerous biological properties. The potent biological activities of brown algal fucoidans may represent an interesting advance in the search for novel functional applications in the relevant industrial uses including pharmaceuticals, nutraceuticals, cosmeceuticals and functional foods.

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