Anticoagulant and antilipaemic activities of polysaccharides from marine algae

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Abstract

In this review the research on the anticoagulant and antilipaemic activity of sulfated and synthetically modified polysaccharides extracted from marine macro algae between 1913 and 2018 was summarized and the results were compared with a long known natural polysaccharide from animal sources, heparin which contain N-sulfate group. The highest anticoagulant activity of algal sulfated polysaccharide was obtained from Dictyota menstrualis, red alga, found to be 4.8 times more active than heparin. Antilipaemic activity of some algal sulfated polysaccharides showed similar activity as heparin.

Keywords: Anticoagulant, antilipaemic, polysaccharides

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Introduction

Anticoagulants are important therapeutic agents for thrombotic disorders. The first natural anticoagulant is glucosamine and galactose sulfate ester, which was isolated from liver, heart and bovine of animals and activities were determined (McLean 1916; Howell and Holt 1918). The well known anticoagulant heparin contains O-sulfate and N-sulfate groups in the carbohydrate skeleton, on the other hand, sulfate containing algal polysaccharides have various carbohydrate components without N-sulfate groups.

The assessment of anticoagulation properties of sulfate containing polysaccharides from marine algae has been conducted by several medical assays such as Heptest, Hepocloth, thrombin time (TT) (Pitney and Dacie 1953), the Prothrombin time (PT) (Quick 1945), the partial thromboplastin time (PTT) and activated partial thromboplastin time (aPTT) (Margolis 1958) to measure
how quickly blood clotting takes place and to compare with heparin. The fibrinolytic activity is measured with fibrin plat method (Astrup and Mullertz 1952) and platelet aggregation for blood clotting assays (Deacon-Smith and Rogers 1982).

Antilipaemic agents are lipid-lowering substances that are used in the treatments of hyperlipidemia. This activity is measured by Baker method (Baker 1957).

Algal polysaccharides were identified based on metachromasy (Lison 1935). This phenomenon was found by Ehrlich (1877). Agar, alginic acid and carrageenan (including iota-, lambda- and kappa-) were identified by this method (Güven and Güvener 1985a; 1985b). Sulfate content of polysaccharides were determined as inorganic sulfate liberated after acid hydrolysis (Dodgson and Price 1962).

In this paper, anticoagulant and antilipaemic activities of algal polysaccharides were reviewed in accordance with their taxa, that is, class order, family, and species as well as active compounds.

**Anticoagulant activities of macro algal polysaccharides**

**Chlorophyta**

Marine green algae especially *Monostroma, Ulva, Enteromorpha, Codium* and *Caulerpa* are very important sources of sulfate containing polysaccharides.

Maeda *et al.* (1991) examined 23 green algae for anticoagulant activity and the extract of *Monostroma nitidum* had 3.3-fold higher activity than that of standard heparin. Hayakawa *et al.* (2000) found the same activity for this alga. A high anticoagulant activity was found in *M. latissimum* (Maeda *et al.* 1991; Hayakawa *et al.* 2000; Zhang *et al.* 2008). Two fractions of *M. nitidum* extract including 1,2- linked 1-rhamnose substituted sulfate group at C-3/C-4 position exhibited a high activity (Mao *et al.* 2008; 2009).

Another study reported *C. divaricatum* possesses a high anticoagulant activity *in vitro* of which sulfated polysaccharide mainly composed of (1→3)-β-d-galactopyranose residues, branched by single (1→)-β-d-galactopyranose units attached to the main chain at C-4 positions (Li et al. 2015). *C. divaricatum* also had *in vitro* fibrinolytic enzyme with a high anticoagulant activity (Matsubara et al. 2000).

The anticoagulant activity of some extracts of *Caulerpa* species *C. cupressoides*, *C. prolifera*, *C. sertularioides* were assayed by PPT and PT, but only *C. cupressoides* was found active (Costa et al. 2010; Selim et al. 2015). A certain polysaccharide with high sulfate value from *C. cupressoides* was found with an anticoagulant activity (Rodrigues et al. 2011). *C. peltata* showed the highest activity among *Caulerpa* species with heparin unit of ~151 I.U./mg (Shanmugam et al. 2001c) but *C. okamurae* had a weak activity (Maeda et al. 1991). *C. cupressoides*, *Anadyomene stellata* presented potent anticoagulant activities same as heparin (De Lara-Isassi et al. 2004). *C. lentillifera* has a potential anticoagulant activity as heparin (Arenajo et al. 2017).

A water soluble polysaccharide isolated from *Enteromorpha clathrata* showed high activity (Qi et al. 2012). Two sulfated polysaccharides with anticoagulant activity were isolated from *E. linza* (Qi et al., 2013) and one was effective in *in vitro* APTT and TT assays (Wang et al. 2013). *E. compressa* and *E. intestinalis* exhibited weak activities (Maeda et al. 1991).

*Ulva conglobate* with high anticoagulant activity (Mao et al. 2006), *U. lactuca* crude extract with some anticoagulant properties (Elmegeed et al. 2014) a weak activity of *U. arasakii* (Maeda et al. 1991) and a prolonged APTT for a sulfated polysaccharide from *U. fasciata* have been reported (Shonima et al. 2012; Faggio et al. 2016; Ibrahim et al. 2016). *U. pertusa* showed good anticoagulant properties (Kang et al. 2016).

The other examined algae *Udotea indica*, *U. flabellum*, *Cladophora fascicularis*, *C. gracia*, *Boodlea composita*, *Chaetomorpha media*, *C. torta*, *Valoniopsis pachynema* and *Bryopsis plumosa* were found with moderate activities (Shanmugam et al. 2001c). *Cladophora flexuosa* var. *densa*, *Cladophora rugulosa*, *Chaetomorpha crassa* showed a potent activity whereas the extracts of *Chaetomorpha spiralis*, *Spongomorpha duriuscula*, *Bryopsis maxima* showed weak activities (Maeda et al. 1991). A sulfated polysaccharide containing rhamnose (49.7%), galacturonic and glucuronic acid (32% of total sugar) with 20% sulfate content with an anticoagulant activity mediated by heparin cofactor II was obtained from *Arthrospira platensis* (Majdoub et al. 2009).
Phaeophyta

Brown algae are rich sources of sulfated fucans (fucoidans) which are potent anticoagulant agents with heterogeneous structures that contain sulfate ester groups and L-fucose units. The most studied group of fucoidan was first isolated by Kylin (1913) named as fucodin from *Laminaria digitata* and later anticoagulant activity of fucoidan isolated from green, red and especially brown algae: *Fucus serratus*, *F. platycarpus*, *Halidrys silicuosa*, *Laminaria saccharina*, *Himanthalia lerea*, *Ascophyllum nodosum* and *Cordaria flagelliformis* demonstrated by Elsner (1938). Crude and purified fucoidans possess antithrombin activities (Schuler and Springer 1957; Springer et al. 1957; Bernardi and Springer 1962). The fucoidans have the potent anticoagulant activity mediated by antithrombin and heparin cofactor II (Mourao 2004). The anticoagulant activity of fucoidan was found to be more potent than heparin for the first time by Springer et al. (1957).

Many studies have been published on anticoagulant activity of fucoidans and it was found that the sulfate content/position (Dobashi et al. 1989; Nishino et al. 1989; Kitamura et al. 1991; Chevolot et al. 1999; Pereira et al. 1999; Haroun-Bouhedja et al. 2000; Pereira et al. 2002a; Albuquerque et al., 2004; Mourao 2004; Cumashi et al. 2007; Zhang et al. 2014), and molecular weight (Chandía and Matsuhiro 2008) play an important role for the activity. The relationship between structure and anticoagulant activity of algal fucans is not simply a function of charge density, but depends critically on the pattern of sulfation and monosaccharide composition (Mourao 2004). Fucoidan expresses both antithrombin activity (Mourao 2004) and platelet aggregation (Cheng and Wang 2003; Yoon et al. 2007; Li et al. 2008). PT, TT test of fucoidans showed similar activity with heparin (Athukorala et al. 2006). A study demonstrated that fucoidan is not toxic in Sprague–Dawley rats (Kim et al. 2010). Fractionation of enzyme hydrolysate of fucoidan isolated from *Ascophyllum nodosum* brought out the structure may be responsible for anticoagulant activity (Mauray et al. 1995; Nardella et al., 1996; Chevolot et al. 1999; Millet et al. 1999; Chevolot et al. 2001; Trento et al. 2001; Collic-Jouault et al. 2003; Cumashi et al. 2007; Durand et al. 2008). Heterofucans from the brown algae *Canistrocarpus cervicornis* with its anticoagulant activities were reported (Camara et al. 2011). Fucan isolated from *Cordaria firma* has an anticoagulant activity (Takemori 1957a; 1957b). A galactofucan fraction of *Dictyota menstrualis* polysaccharide was 4.8 times more active than the low molecular weight heparin (Albuquerque et al. 2004). The sulfated heterofucans of *D. cervicornis*, *D. deliculata*, *D. mertensis* showed important activities (Costa et al. 2010). Fucoidan, laminaran and mannuronan mixture from *Dictyopteris polyodioides* has a significant activity (Karaki et al. 2013). Enzymatic hydrolysate of sulfated polysaccharide from *Ecklonia cava* was found as active as heparin (Athukorala et al. 2006;
Jung et al. 2007; Wijesinghe et al. 2011). A high anticoagulant activity of sulfated fucoidans and their fractions from E. kurome (Nishino et al. 1989; 1999) and Eisenia bicyclis (Usui et al. 1980) was reported.

Fucoidan from Fucus vesiculosus showed similar anticoagulant activity to heparin (Soeda et al. 1992; Nishino et al. 1994; Trento et al. 2001; Kuznetsova et al. 2003; Costa et al. 2010). Highly purified fucoidan fraction obtained from F. vesiculosus showed potent anticoagulant and fibrinolytic properties with only minor platelet activating effect (Durig et al. 1997). F. evanescens, F. serratus and F. distichus fucoidans (Cumashi et al. 2007) and F. serratus and F. spiralis extracts (Deacon-Smith and Rogers, 1982; Deacon-Smith et al. 1985a; 1985b) exhibited strong antithrombin activity in platelet aggregation. Anticoagulant activity of fucoidan from Hizikia fusiforme (Dobashi et al. 1989; Li et al. 2008) and H. fusiformis were reported (Athukorala et al. 2007).

Laminaria angustata var. longissima (Kitamura et al. 1991) showed high anticoagulant activity. The fucoidan with low sulfate content from L. brasiliensis has a very high activity (Pereira et al. 1999). Fucan containing 2,3-disulfated, 4-linked unit from L. cichorioïdes has a potent anticoagulant activity in APTT assay (Yoon et al. 2007). L. digitata, L. hyperborea and L. saccharina extracts completely inhibited platelet aggregation of Ristocetin (Deacon-Smith and Rogers 1982; Deacon-Smith et al. 1985a; 1985b; Cumashi et al. 2007). The fucoidan fraction from L. bongardiana had a very strong anticoagulant activity (Bilan et al. 2016). Low molecular weight fucoidan fractions from L. japonica and L. ochotensis showed high activities (Athukorala et al. 2007; Wang et al. 2010). Fucans from L. saccharina (Ushakova et al. 2009) and Lessonia vadosa presented a good inhibition of coagulation (Chandía and Matsuhiro 2008).

Padina gymnospora contains heterofucans which are compounds of glucuronic acid, L-fucose and D-xylose units with sulfation at C-3 positions of L-fucose and presented anticoagulant activity (Silva et al. 2005). Anticoagulant and antithrombin activities of low molecular weight fucoidan extracted from Pelvetia canaliculate, xylofucan sulfate and Punctaria plantaginea were reported (Colliec et al. 1991; Ustyuzhanina et al. 2016).

Sargassan is a sulfated polysaccharide with a high anticoagulant activity and isolated from Sargassum linifolium (Abdel-Fattah et al. 1973; 1974). Fermentation process of S. fulvellum increased the anticoagulant activity of its sulfated polysaccharide (de Zoysa et al. 2008). Sulfated polysaccharide fucan isolated from S. vulgare exhibited high antithrombin action and prolonged APTT (Dore et al. 2013). Low molecular weight (LMW) polysaccharides from S. fusiforme possessed anticoagulant activity (Sun et al. 2018). Hot water extracts of S. horneri and S. siliquastrum showed high activities. On the other
hand, hot water extracts of *S. thunbergii*, *S. fulvellum*, *S. coreanum* and *Scytosiphon lomentaria* presented weak anticoagulant activity (Athukorala et al. 2007). Antithrombotic features of algal sulfated galactofucan from the *Spatoglossum schröederi* have been reported (Rocha et al. 2005; Almeida-Lima et al. 2010; 2011).

Orally administrated fucoidan from *Undaria pinnatifida* had also significant effect on coagulation assays (Irhimeh et al. 2009; Faggio et al. 2015).

**Rhodophyta**

Activity mechanisms and potency of red algal polysaccharides were discussed as follows. A sulfated galactan extracted from *Botryocladia occidentalis* with 2,3-disulfated and 2-sulfated of each 1/3 ratio were found that its anticoagulant activity was attributed mostly to the 2,3-disulfated units (Farias et al. 2000; Pereira et al. 2002a). Investigation on the mechanisms of anticoagulant activity of sulfated galactans is achieved mainly through potentiation of plasma cofactors which are the natural inhibitors of coagulation proteases. Anticoagulant activity of sulfated galactan was attributed to the sulfation at O-2 and O-3 position of the α-D-galactopyranosyl residues requiring molecular size between 16 and 46 kDa (Melo et al. 2004).

Sulfated polysaccharides contained in red algae are galactans, carrageenan, agar, porphyrans, funoran and other specific polysaccharides (Percival and McDowell 1967). These polysaccharides contain –O–SO₃H group which is important for inhibition of blood clotting (Demole and Reinert 1930; Fischer 1931; Chargaff et al. 1936). Earlier red algal anticoagulant activity studies showed galactans from *Iridae laminarioides* (Chargaff et al. 1936), carrageenan, agar and galactan (Elsner et al. 1937).

Galactan was first isolated from *Iridae laminarioides* (Hassid 1933). Carrageenan of *Corallina rubens* was more active than that of galactan (Guven et al. 1974b). A sulfated galactan of *B. occidentalis* has the same anticoagulant potency with heparin (Farias et al. 2000; 2001; Melo et al. 2004).

Carrageenan is a linear sulfated polysaccharide built up of alternative 1-3 and 1-4 linked β- or α-galactopyranosyl units. The former contains 2- and 4-sulfates or not, 1-4 linked contains 2- and 6- mono or disulfates, 2,6-anhydride and 3,6-anhydride 2-sulfate. It has various types depending on the sulfate content, gelling properties and substitution as: λ- (lambda), κ- (kappa), τ- (iota), μ- (mu), ν- (nu), θ- (theta), ζ- (xi). Carrageenan from *Delesseria sanguinea* (Elsner, 1938), *Chondrus crispus* and *L. laminarioides* (Springer et al. 1957) expressed anticoagulant activity. *Furcellaria festigiate*, *Eucheuma spinosum*, *Gigertina acicularis*, *G. pistillata*, *G. radula* extracts were compared and the highest
anticoagulant activity was shown by the extract from *G. acicularis* which was more active than heparin (Houck *et al.* 1957). Anticoagulant activity of *Phyllophora nervosa* extract was demonstrated by Howell time test on rabbit (Güven and Aktin 1962). A degraded carrageenan from *Eucheuma spinosum*, λ- and κ-carrageenan from *C. crispus*, *Polyides rotundus* showed anticoagulant activity in rabbits. The degraded carrageenan was less toxic and λ-carrageenan was more toxic than κ-carrageenan (Anderson *et al.* 1965). *Corallina rubens* extract and its fraction showed high anticoagulant and fibrinolytic activity (Güven *et al.* 1973). In contrary to these findings, anticoagulant and fibrinolytic activities of carrageenan rank as λ-, κ-, ι-carrageenan (Sigma), carrageenan from *Grateloupia dichotoma* and alginic acid (Roth) were tested and *G. dichotoma* carrageenan and λ-carrageenan (Sigma) showed similar anticoagulant and fibrinolytic activity in all biological tests applied (Güven *et al.* 1991). Sulfated polysaccharides from the clonned *G. filicina* had a good potential as anticoagulant agents (Chen 2015).

Carrageenans prolonged the clotting time, inhibited amidolytic activity of thrombin coagulation factor x-(Xa)-catalyzed amidolysis potentiated the *in vitro* inactivation of thrombin and Xa by antithrombin III (Kindness *et al.* 1979a; 1979b). Carrageenan does not have an antithrombin effect, it inhibits fibrin aggregation or polymerization and its effect can be blocked by protamine (Schimpf *et al.* 1969). It activates Hageman factor in human plasma and promotes blood coagulation (Schwartz and Kellermeyer 1969). According to the activity degrees of carrageenan λ-type was the most potent followed by ι-type and κ-type (Hawkins and Leonard 1962; 1963; Anderson *et al.* 1965). Other studies proposed that the potency of the types were as ι>λ>κ (Winter *et al.* 1962; McMillan *et al.* 1979). In contrary to these findings, anticoagulant and fibrinolytic activities of carrageenan rank as λ>κ>ι (Güven *et al.* 1991).

Purified sulfated polysaccharide isolated from *Grateloupia indica* possesses potent PT, CT, BT and hemostatic activities (Sen *et al.*, 1994). *G. elliptica*, *G. lanceolate*, *Sinkoraena lancifolia*, *Halymenia dilatata*, *Lomentaria catenata*, *Martensia denticulate*, *Schizymenia dubyi*, *Chondrus crispus* showed the highest anticoagulant activities than the other examined algae species *Pterocladia capillacea*, *Prionitis cornea*, *Capopeltis affinis*, *Gloiopeltis furcata*, *Laurencia okamurae*, *Gelidium amansii*, *Ahnfeltiopsis flabelliformis*, *Gracilaria textori*, *Chondria cassicaulis*, and *Acrosorium flabellatum*. Enzymatic digestion of *S. dubyi* and *L. catenata* polysaccharide fractions exhibited the most potent anticoagulant activity (Lee *et al.* 2008). A sulfated polysaccharide of *Botryocladia occidentalis* was found more potent than *Gelidium crinale* extract (Pereira *et al.* 2005). A fraction of *Pterocladiad capillacea* (*G. latifolium*) extract showed anticoagulant activity by RT, PT, ELT assays (Güven *et al.* 1979b; Abou Zeid *et al.* 2014).
The fraction obtained by depolymerization of the sulfated galactan from *Schizymenia binderi* showed anticoagulant activity (Zúñiga et al. 2006). A degraded fraction of porphyran isolated from *Porphyra haitanensis* showed anticoagulant activity (Zhao et al. 2006). Porphyran isolated from *P. haitanensis* after alkali treatment and resulfation showed anticoagulant activity (Zhang et al. 2010; Liu et al. 2015). The other red algae reported possessing anticoagulant activity were *Lomentaria catenata* (Pushpamali et al. 2008), *Gigartina skottsbergii* (Carlucci et al., 1997), *Schizymenia binderi* (Zuniga et al. 2006), *P. haitanensis* (Zhang et al. 2010) and *Nothogenia fastigiata* (Kolender et al. 1997). *Hypnea esperi* methanol extract effectively prevented the blood clotting time (Selim et al. 2015).

**Anticoagulant activity of synthetically sulfated algal polysaccharides**

Synthetically sulfated polysaccharides were first prepared by Bergström in 1935 and 1936 (Bergström 1935; 1936). A sulfated alginate had much lower anticoagulant activity and much more toxic than heparin (Molho and Cotte 1951). When containing two sulfate groups per glucose units the alginate gave the highest anticoagulant activity (Dewar 1956). High sulfate content and low molecular weight sulfated alginates has a good anticoagulant activity (Fan et al. 2011). Many studies were published on synthetic laminarin sulfate which was extracted from *Laminaria* sp. and preparations with the highest sulfate groups per glucose residue had anticoagulant activities of 25-30% that of a standard heparin (O'Neill 1955) and sulfonic acid derivatives were more active than the sulfate esters (Hawkins and O'Neill 1955). A derivative of laminarin contained 1.83 sulfate groups per glucose unit showed third as potent as heparin in rabbit test and it was extremely toxic to guinea pigs (Adams and Thorpe 1957). Laminarin sulfate s.c. and i.m. applications showed some anticoagulant activity (Hawkins and Leonard 1958). Enhancement of anticoagulant properties of polysaccharides upon sulfation was shown by several authors (Doctor et al. 1991). Laminarin sulfates were synthesized and increasing content of sulfate groups increased the anticoagulant activity, highest activity was obtained with 1.49 sulfate groups per glucose unit (Alban et al. 1992). Synthetically sulfated polysaccharide from *Enteromorpha linza* showed anticoagulant activity and it was found that the activity was related to degree of sulfation and molecular weight (Wang et al. 2013). Sulfated alginate has 8.1 and 2.9 folds activity (Pulsawat and Tongmalee 2014).

On the contrary, native alginate did not demonstrate anticoagulant activity (Güven et al. 1991). After structural modifications, such as sulfonation, oxidation, and reduction, laminarans exhibited anticoagulant activity (Kraan et al. 2012).
Antilipaemic activity of macro algal polysaccharides

Antilipaemic activity is clearing of visible lipemia and used in the treatment of atherosclerosis. The origin of this subject was due to realize lipase from heparin hydrolyzes triglycerides finalize with free fatty acids liberation (Shore et al. 1953) and free acids were determined (Duncombe 1963; 1964; Güven et al. 1979a).

The antilipaemic activity of fucoidan was first demonstrated and found as active as heparin and probably acts by the release of the clearing factor (Schuler and Springer 1957). Fucoidan fraction with MW 5000-15000 possesses antilipaemic activity (Springer et al. 1957).

This review is not only focused on the sulphated polysaccharides but synthetically sulfated algal polysaccharides as well (Besterman and Evans 1957). Laminaran is a non-sulfated polysaccharide found in brown algae. There are two forms of laminaran as soluble and non-soluble. A low level of sulfation gave laminarin antilipaemic properties similar to those of heparin (Besterman and Evans 1957). Total fat, β-lipoprotein, esterified cholesterol levels decreased after parenteral administration of laminarin sulfate or of heparin (Mookerjea and Hawkins 1958). Sulfated alginic acid showed some antilipaemic potency as heparin (Constantinides et al. 1954). Clearing effects of various algae Furcellaria festigiate, Eucheuma spinosum, Gigartina acicularis, G. pistillata, G. radula and Iridae sp. were examined and found no activity (Houck et al. 1957). Synthetically sulfated polysaccharide polymannourides depresses hyperlipidemia in human (Constantinides et al. 1960). Laminaran sulfate prepared by sulfation of polysaccharides of the brown alga, Eisenia bicyclis, Laminaria digitata and carrageenan obtained from Chondria crispus showed antilipaemic and anti atherogenic activities in rabbit (Murata 1961; 1962). Degraded polysaccharides isolated from L. cloustoni were sulfated and examined their antilipaemic activities (Adams et al. 1962). Sulfated laminarin prepared from L. cloustoni is valuable in the treatment of lipemia and atherosclerosis (Gollin et al. 1965). Zha et al. (2012) reported that crude polysaccharides from L. japonica at a dose of 400 mg/kg/day caused a reduction in total serum cholesterol, TG, high density lipoprotein (HDL)-cholesterol, and LDL in serum. Lipolytic activity of algal extracts: some fractions of Phyllophora nervosa (Güven et al. 1972), Corallina rubens (Güven et al. 1973; 1974b; 1975), Pterocladia capillacea (Gelidium latifolium) (Güven et al. 1979b), Sargassum vulgare, Polisiphonia subuliera (Aktin and Güven 1965), Haloptysis curvus (Güven and Kızıl 1986), Cystoseira barbata (Güven and Aktin 1964; Güven et al. 1974a), C. crinite (Ben-Gara et al. 2017), Gracilaria verrucosa and Gelidium latifolium (Aktin and Güven 1969) extracts showed activities. Various algae (1 green, 21 brown and 4 red) were investigated for
their antilipemic activities and found appreciable suppression were observed (Ren et al. 1994). The polysaccharide Ulvan from *Ulva pertussa* has been utilized in old China for various medicinal purposes and this polysaccharide decreased LDL-cholesterol level and has antilipemic effect (Pengzhan et al. 2003). The acetylation of ulvans from *U. pertusa* by acetic anhydride showed higher antihyperlipidemic activity than natural ulvans, especially with regard to causing a decrease in TG and LDL-cholesterol levels (Yu et al. 2017). Polysaccharides extracted from *U. prolifera* exhibited pancreatic lipase inhibition activity (Yuan et al. 2018). Cao et al. (2016) reported that porphyran from *Pyropia yezoensis* at a dose of 200 mg/kg/day can decrease the percentage of body weight gain and serum lipid profiles of mice, similar to the effect of a hypolipidemic drug.

In conclusion, the first anticoagulant agent heparin was introduced for thrombosis therapy. The clearing of visible fat in the blood by heparin is accompanied by changes in lipoprotein metabolism. Chemically it is a sulfated polysaccharide and composed of sulfated uronic acid and *N*-sulfate-glucosamine. On the other hand, algal sulfated polysaccharides contain only -O-SO$_3$H groups and these groups were essential for the anticoagulant effect and may be important for antilipemic effect, thus many studies have been undertaken on the algal polysaccharides. However, these experiments were only on animals, these polysaccharides have very high molecular weights (100,000-300,000) and they have high toxicities.

Deniz alglerinden elde edilen polisakkaritlerin antikoagülan ve antilipemik etkileri

Öz


Anahtar kelimeler: Antikoagülan, antilipemik, polisakkaritler
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