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Anticoagulant Properties from Marine Algae – A Systemic Review

Pandian P*, Srinivasan N

Department of Pharmacy, Annamalai University, Annamalainagar-608002, Chidambaram, Tamil Nadu, India

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Abstract

The anticoagulants are used to eliminate mainly blood clots. They are offered to patients who are at risk of developing clots, in order to improve their general wellbeing. Anticoagulant namely heparin, has many disadvantages like thrombocytopenia, antithrombin defensives, bleeding disorders and etc. The marine algae are sulphated polysaccharides has many advantages from commercially available anticoagulant which is derived from the animal's sources. The anticoagulant is found in various species of marine algae, mainly from the red, brown and green algae and its determined by various methods, namely APTT, PT, TT, CT. The marine algae species are *Padina tetrastromatica, Ulva fasciata,Corallina, Asparagopsis taxiformis, Grateloupia filicina*, *Ulva rigida, Bursatella leachii, Agardhiella subulate, Turbinaria ornate, Monostroma angicava, Arthrospira platensis, Sargassum tenerrimum, Sargassum wightii, Turbinaria conoides, Lomentaria catenate, Gracilaria debilis*, and *Monostroma nitidum* are some of the species revealed its anticoagulant properties. The anticoagulant produced by the marine species are compared with standard namely heparin by in vitro and in vivo methods and the review result reveal that the anticoagulant values produced are nearer to the standard and in some species, the value are more than that of standard. The sample are crude extracted one and some samples are isolated from different fraction.

*Corresponding Author

Name: Pandian P
Phone: +919942055172
Email: pandian0071@rediffmail.com

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INTRODUCTION

Marine sources are very valuable for anticoagulant properties, which has novel structure and activities. The anticoagulant produced from the marine source has safer biomolecules when compare to terrestrial mammals' counterparts (Senni *et al.*, 2011).

There are three main classes of eukaryotic algae, green algae, brown algae, and red algae. The marine algae are rich in sulphated polysaccharide, which is a key factor for an anticoagulant property and the green algae have less amount of sulphated polysaccharide compared to the other two algae because of its colour. More than 50 years, an anticoagulant is used commercially to prevent venous thromboembolic disorders. However, anticoagulant namely heparin has many disadvantages like thrombocytopenia, antithrombin defensives, bleeding disorders and etc (Pereira *et al.*, 2002). In sulphated polysaccharide the anticoagulant activity is widely used (Costa *et al.*, 2010). The sulfated galactans, fucoidans, are some other anticoagulant isolated and characterized from marine algae of the sulphated polysaccharides, respectively (Carlucci *et al.*, 1997). The marine algae of sulphated polysaccharide are identified and significant for anticoagulant activity (Chevolot *et al.*, 1999).

Furthermore, heparin is derived from animal origins, like meat animals such as source from heparin found in the intestines of swine and lungs of pigs are purified and the yield of the heparin are low or poor. The anticoagulant generated from aquatic algae and is given as a substitute to replace the blood's anticoagulant. This alternative for heparin has many reasons because of the certain religious groups believe the use of heparin from animal sources and also, this anticoagulant is likely linked with fatal disorders. The Latest findings have found that chronic heparin administration to patients with thrombocytopenia is linked with elevated mortality rates in critical care patients (Liu *et al.*, 2020). As a consequence of these drawbacks, scientists have been working on better solutions (Du *et al.*, 2019).

Anticoagulant from *Padina tetrastromatica, Ulva fasciata*

In all the coagulation parameters studied, in *Padina tetrastromatica, Ulva fasciata* and heparin decreased the fibrin clotting time by 40% as compared to the control. For PT assays, slight variations in results were observed between groups when compared to APTT assay. Moreover, the antithrombotic activity of the combination of *Padina tetrastromatica* and *Ulva fasciata* (P1U1) was found to be significantly higher ($p<0.05$) to that of heparin activities in terms of PT and APTT. These results further confirmed the results of in vitro anticoagulant studies (Mourão, 2015).

Effect of SPSs on thrombus formation in Wessler's rat thrombosis model

The effect of individual SPSs and their combinations on the thrombus formation in rats were evaluated by % thrombosis occurred in inferior vena cava (IVC) of experimental rats and by determining thrombotic index. The % thrombosis in thrombus control is taken as 100 %. Thrombus scoring determines the extent of occurrence of thrombus in the IVC segments after the induction of experimental thrombosis. For the thrombus control group, the thrombus score was obtained as 4, which confirmed complete thrombus formation in the IVC by the surgical procedure. PSPS, USPS and P1U1 treatments significantly reduced ($p<0.05$) the thrombotic index and thereby reduced the % thrombosis.

The treatment with *Padina tetrastromatica* and *Ulva fasciata* significantly reduced ($p<0.05$) the thrombus size induced by thrombogenic stimuli in Wessler's rat model. As in the in vitro study, the combined effect of both SPSs dominates over the activity of individual compounds and standard drug heparin. The study results confirmed that the anticoagulant efficacy of the marine algal SPSs through the antithrombotic mechanism. The study results substantiated the data in the article, which discussed the perspectives on the use of sulfated polysaccharides from the marine world as a new source of antithrombotic drugs (Lekshmi and Kurup, 2019).

Anticoagulant from of red algae *Corallina*

Therefore, we studied the polysaccharides isolated from *corallina* species for the anticoagulant activity of the APTT assay. The CT was measured and calculated By using the ratio APTT/control = APTT/34; we can find a heparin equivalent. The APTT is from 28-38 seconds and is determined by the form of the lab, and the reagents are chosen. A noticeable slowing effect is seen when the concentration ratio is 1.2 or higher. The concentrations of sulfated galactans increased from 0.05 to 5 μg and the ratio increased from 1.21 to 3.07; as a result, the anticoagulant effect became greater. The results were based on the recently published research (Sebaaly *et al.*, 2014).

Anticoagulant activity of the purified polysaccharide of *Asparagopsis taxiformis*

The potency of the polysaccharide purified was determined by detecting the anticoagulant (Manilal *et al.*, 2012) activity (APTT assay) for a varied concentration of the polysaccharide. The CT of the sample was compared with increasing concentration series of the standard heparin. In both sample and heparin, the CT was increased by its concentration was found. The purified concentration polysaccharide at a level of 48.00 ug/mL. showed a clotting time over 1000 sec. Whereas standard heparin showed a similar operation at a level of 60 ng/mL. Statistically, the difference between purified polysaccharide of clotting time and heparin significantly not differ ($p= 0.373$). Thus, the purified polysaccharide has a similar anticoagulant property to that of commercial heparin. The inhibition pathway polysaccharide purified from *A. taxiformis* was performed by triggered partial thromboplastin times and prothrombin times. The addition of polysaccharide prolonged the coagulation time in both complete and partial thromboplastin time assays envisaging the inhibition of both intrinsic and extrinsic pathways of coagulation.

Furthermore, the PT assay of relative clotting factor are within the normal range as per the recommended manufacturer guidelines (Caporiccio *et al.*, 2009) reported that armatan, isolated from red algae *Asparagopis armata* to find sulphated polysaccharides that increase the coagulation time of rat plasma as in-vivo assays. In *Asparagopsis*, the anticoagulant activity was reported to more or less to similar algal species. According to the present study,

the seaweed *A. taxiformis* might be a natural source for developing anticoagulant in future. Therefore, bioassay to identify the fractionation guided by the anticoagulant principles of *A. taxiformis* are needed in the subsequent investigation.

Anticoagulant Activity Assays from Cloned *Grateloupia filicina*

The GSP activities of anticoagulant (*Grateloupia* sulphated polysaccharide) were determined by Athukorala *et al.* (2008) the active thrombin time, prothrombin time and activated partial thromboplastin time immunoassays of coagulation process of different stages in vitro that characterize by anticoagulation activity. Results were illustrated by prolong the APTT, TT and PT of GSP, but the value showed are different between among each other and also the PT are more obvious than APTT and TT. In the concentration of 15 ug/mL (32.4s), the clotting time prolong more obviously and in Nacl, 0.9% was 24.5s when compare to standard (heparin) clotting time, 3.3 ug/mL (40.8s). At a concentration of 80 ug/mL of GSP, the prolonged clotting time was 17s, in 0.9%Nacl 14.5s and in standard 50 ug/mL was 26.8s. The GSP concentration was 110 ug/mL, which caused the blood clotting time to be extended (14.1 seconds), and heparin (7 ug/mL) was 15.6 seconds. The sulphated polysaccharide of *Grateloupia filicina* shows good results from the above values.

The values obtained from the seaweeds are weaker when compare to the standard. In GSP for APTT assay, the anticoagulant potential of anticoagulant activities are increased as the concentration values increase. In case of TT and PT assays display a propensity of the anticoagulant GSP to extend its clotting plasma duration, and it is acceptable when compared to the previous reference reported in sulphated polysaccharide from marine algae, which shows the inhibition of intrinsic pathway of anticoagulant activity (Chen *et al.*, 2015).

Anticoagulant Activity Isolated from the *Ulva rigida*

In these algae, using a chemical solvents cleaning technique its to determine the sulfate content of the sulphated polysaccharide (Adrien *et al.*, 2019). The obtained fraction are containing the chemical sulfate of doubling the polysaccharides from sulfate content and also the same in the second fraction also. Using different assay, both fractions are assessed for its anticoagulant activities with the targeting of intrinsic or common APTT extrinsic PT and the TT pathway. The antithrombin specific dependent pathway inhibits the activation of both the coagulation cascade and these are compared with commercial standard preparations. The results obtained from chemically sulfated ulvan fraction are more potent than standard in both coagulation pathway of intrinsic and extrinsic. These are more interesting in chemically sulfated fraction for an alternative therapy to heparins with different achievements and more anticoagulant activity.

Anticoagulant Activity of *Bursatella leachii* Viscera

Using APTT and TT in-vitro studies of BLVP (*Bursatella leachii* Viscera polysacharride) for anticoagulant studies were done Dhahri *et al.* (2020). The results was conducted in triplicate and standardised to the mean and variance with a t-test. In a various anticoagulant test, the BLVP polysaccharides prolonged the CT and also APTT, TT. The BLVP indicates blocking intrinsic and common pathways. The BLVP polysaccharides at APTT and TT concentration are increased concentration at or above 5 μg/mL for APTT, and the maximum time was achieved at 10 μg/mL for TT. The BLVP effectively increase the APTT and PT concentrations compare to standard heparin sodium. In addition of 5 μg/mL concentration, the TT has twice the prolonged time of BLVP and in a concentration of 25 μg/mL of APTT has a four to five-time increased of BLVP polysaccharides. From marine algae, the SPS of anticoagulant activity was less when compared to *B.leachii* polysaccharides (Song *et al.*, 2019). For instance, Song et al. the anticoagulant activity of *Patinopecten yessoensis* viscera concentration are increased three-time respectively, at 200 and 1000 μg/mL. This test in vitro can rely on the high level of sulphates (Tang *et al.*, 2017) and high molecular weights (Nogueira *et al.*, 2017), and This indicates antithrombus activity in vivo.

Anticoagulant activity of *Ulva fasciata* and *Agardhiella subulate*

In human RBC, no cytotoxic effect was observed in algal polysaccharides when it tested. In the extract, the APTT value was increased by 80sec. In the Table 1, the anticoagulant is summarized. The results show that the algae collected from Ganzirri lake (*Ulva fasciata* and *Agardhiella subulate*) have anticoagulation relative to normal heparin at APTT and TT assayed. The coagulation was inhibited by prolongation of PT in the extrinsic pathway and APTT inhibition in intrinsic or common pathways (Faggio *et al.*, 2016).

Anticoagulant behaviour brown algae *Turbinaria ornate*

Anticoagulant activity of the algal extract in the blood plasma of four different concentration was tested and shown in Table 2. The positive control at

Table 1: Tests conducted on blood samples treated with *U. aspera* and *A.subulata* extracts by PT and APTT

Algal extracts	PT (%) Normal values 70–120	APTT (s) Normal values 28–40
Ulva fasciata (10 mg/ml)	60	92
Ulva fasciata (20 mg/ml)	57	88
Agardhiella subulata (10 mg/ml)	48	>100
Agardhiella subulata (20 mg/ml)	43	>100

more than 1500 sec at 100 μg/mL of heparin shows more clotting time than a sample. The resting APTT value at 1125 sec after exposure to 1000 μg/ml. The APTT measurement is poor at 150 seconds at 125 μg/mL. Whereas PT activity can be observed in concentrations up to 1000 μg/ml. The TT assay showed the limit at 320 seconds at 1000 micrograms per ml in general. The entire respective assay, the higher activity recorded at increasing concentration of crude polysaccharides (Arivuselvan *et al.*, 2011).

Anticoagulant from phlorotannins

The currently used anticoagulant drugs from sulfated polysaccharides is heparin and low molecular heparin. In marine algae, the anticoagulant derived from sulfated polysaccharides possess the same to that of or higher heparin.24 from the information it suggests that the sulphated polysaccharides from seaweeds has potential anticoagulant agent which will be used in the pharma industry Phlorotannins from *S. thunbergii* was used as an anticoagulant as invitro and in vivo activity. At a concentration of 1mg/ml, the seaweeds have potential anticoagulant of increase in APTT, PT and TT. The phloroglucinol was developed as a novel anticoagulant in pharmaceutical research (Costa *et al.*, 2010).

Anticoagulant activity of *Monostroma angicava*

In Table 3, the APTT, TT and TT assay with PF2 based on anticoagulant activity are listed in the PT test of PF2 has no clotting inhibition in the concentration used in the experiments and shows that PF2 does not stop the coagulation pathway of extrinsic. More than 200sec, the concentration at 150 μg/mL of the APTT and TT prolonged by PF2 in increased the concentration of polysaccharides, the inhibition of intrinsic or coagulation pathway common in APTT. The same manner in 120sec at 100 μg/mL concentration increases the concentration of polysaccharide by PF2 significantly at TT. The TT increase shows that stop the fibrin polymerization or thrombin in clotting time thrombin inhibition factor. Finally, the results of PF2 inhibit the internal or coagulation common pathway of thrombin activity for convert from fibrinogen to fibrin (Bae, 2011).

Anticoagulant activity of green alga *Arthrospira platensis*

The anticoagulant activity of a fraction eluting at high ionic strength at 1.5 M was named PUF2 and PUF2 was performed by APTT and TT assays with reference standard from heparin and DS of procine intestinal mucosa. In standard heparin for APTT and TT assays, the value obtained from this is equal to that of the PUF2 five and seven times higher concentration was equal to that of standard, respectively. During the assay the there is no inhibition in incubated thrombin in sulfated polysaccharides alone in various concentration of tested one. In 35U/mg of extract of *A.platensis* (PUF2), in a concentration of the sample was compared to APTT activity of heparin at 173u/mg using the parallel standard curve. These sulphated polysaccharides is more effective in enhancing the APTT and TT than porcine DS. Moreover, the in porcine intestinal mucosa need four times higher concentration when compared to PUF2 for APTT and TT (Li *et al.*, 2017).

The anticoagulation activity of crude SPS of *Sargassum tenerrimum, Sargassum wightii, Turbinaria conoides, Turbinaria ornata* and *Padina tetrastromatica*

Blood coagulation is the formation of a number of enzyme active forms, including a proenzyme and other enzyme forms. The fibrinogen to fibrin is the final step to convert next to cross-linked fibrin and clot types (Majdoub *et al.*, 2009). The in vitro anticoagulant assays from sulphated polysaccharides are checked for APTT and PT. The test was used for assessing SPS behaviour and it is so difficult to sensitizes the test analysis in any change in blood coagulation in internal pathway coagulation, and the factors VIIIa, IXa, XIa, and XIIa are inhibited, which may reduce the capacity of the factors Xa, Va, and IIa (Koch and Biber, 2007). In factor VIIa the coagulation protein of the PT pathway is monitered the integrity of the external pathway (Duxbury and Poller, 2001). The APTT assay is performed in anticoagulant to note the considerable differences in the

Table 2: Anticoagulant activities of from *T. ornata*, determined by the APTT, PT, and TT assays (s)

Sample at different conc (μg/ml)	APTT(s)	PT(s)	TT(s)
Heparin 100(μg/ml)	>1500	>1202	>1500
125	170	6	36
250	240	15	72
500	502	39	153
1000	1126	81	320

Table 3: Anticoagulant behaviour dependent on APTT, TT, and PT studies with PF2

Clotting Time [a] (s)	Polysaccharides	Concentration (μg/mL)					
		0	10	20	50	100	150
APTT	PF2	32.5± 2.2	44.9± 2.6	64.8±3.2	125.7±3.1	174.5±4.3	>200
	Heparin	36.4±2.4	78.6±3.1	128.7±3.5	>200	>200	>200
TT	PF2	18.5±2.2	36.4±2.4	9.7± 3.5	103.2±3.7	>120	>120
	Heparin	18.5±2.3	42.2±3.2	89.2±3.2	>120	>120	>120
PT	PF2	13.3±1.5	14.2±1.2	15.1±2.0	15.8± 2.0	15.5±1.8	16.1± 2.3
	Heparin	14.2±1.3	36.4±2.3	57.8±2.8	87.2± 3.1	>120	>120

A three samples were prepared for assays for all attributes. The data were stated as means ± standard deviation (SD)

SPS produced by different algae. The high value implies S. *tenerrimum* has more anticoagulant activity 134 ± 1.73 when compared to other species, especially 122 ± 1 in *S.wightii*, 117.6 ± 1.52 in *T.ornata*, (108 ± 1.41) in *T.conoides* and 89.3 ± 1.52 in *P.tetrasromatica*. In the internal anticoagulant pathway, the APTT attributed interference with prolongation of its time. Though the inhibition in prothrombin time by SPS is not relevant, the same with our control PT at 12 sec and at 12 to 16 sec by crude extract of *S. wightii, T. conoides, P. tetrastromatica, Sidney. Teeternium* and *T. ornata* ranged from 14 to 16 s in length (Table 4). The lengthened CT is due to intrinsic behaviour.

The results suggest that it inhibit the intrinsic or common coagulation pathway in sulphated polysaccharides and does not inhibit the extrinsic coagulation pathway in anticoagulant activity. In the coagulation cascade, the targeted proteins allows the interaction of sulphation of pattern in an anticoagulation property (Church *et al.*, 1989). The anticoagulant activity results shown by these crude SPS is in good correlation with the metachromasia effect and sulphate to sugar molar ratio. It shows high sulphate/sugar of sulphated polysaccharides of *S.tenerrium*, and among five species, the APTT values are high (134s). The sulphated polysaccharides See the order of sulphate/sugar ratio in the crude extract. When the sugar/sulphate molar ratio is high, the anticoagulant activity is higher. The anticoagulant activity is low in *T. conoides* and higher the sulphate/sugar ratio at *P.tetrastromatica* The FTIR analysis of crude SPS suggests vibrations of sulphate at 820 cm-1 *Sargassum tenerrimum, Sargassum wightii, Turbinaria conoides, Turbinaria ornata*, which indicates sulphation at the equatorial position, while the sulphate vibration was found at 850 cm-1 in *P. tetrastromatica* which indicates sulphation at the axial position.

In sulphated polysaccharides, the anticoagulant activities of while the addition of sulphur to sugars is also essential (Chevolot *et al.*, 1999). The sulphated polysaccharides near of the concentration of C2 sulphate and C-2,3 disulphate, but also the 2,3-disulphate sugar residue is the typical structural characteristic of the anticoagulant activity of fucoidan (Yoon *et al.*, 2007). In *P. tetrastromatica*, the activation of anticoagulation is low, with the sulphation in the axial position. The levels of heparin activity in purified crude heparinoid were measured using the relative clotting factor and substituted in the heparin norm.

Crude sulphated polysaccharides with heparinoid activity for S are shown in Table 5. *Tennerimum* is high (25.47 heparin USP units/mg) and the anticoagulant is lower in decreasing order for the marine species of *S. Wightii, T. Ornamented, P. tetrastromatica, T.Conoides*. Unlike the anticoagulant activity of heparin, the anticoagulant activity of these crude SPS varied from 10% to 18% of the activity

of heparin (Table 5). The same experiments were conducted for fucoidan brown algae anticoagulants with values of 33, 24.2, 26.9, 19.1, 9.4 and 13.4 USP/mg for *Laminaria sacchrina, Laminaria digitata, Fucus distichus, Fucus serratus, Fucus vesiculosus* and *Ascophyllum nodosum* fucoidan, respectively. The heparinoid activity of the results is compared with fucoidan by the sulphated polysaccharides algae species. The values are followed as per the S comparison. Tennerimum (25.47 units/mg of heparin USP) and S. Wightii (22.52 units/mg heparin USP) with L fucoidan. Digitata (24.2 units/mg USP heparin). Yeah. The *T. Ornata* (21,45 units/mg of heparin USP), *T. Conoids* (19.1 units/mg of heparin USP) with Fucoidan *F. Seratus* (19.1 units of heparin USP/mg) and also *P. tetrastromatica* (14.51 units of heparin USP/mg) with fucoidan. *A.Nodosum* (13.41 units/mg of heparin USP) (Manoj *et al.*, 2013).

Anticoagulant Polysaccharides

Much of marine algal anticoagulants are sulfated glycosaminoglycans, which are sulfated linear polysaccharides. Three cell divisions produce three algal divisions known as the red algae, brown algae and green algae (green algae). Natural polysaccharides derived from marine algae used in a range of cosmetics, medicinal and food products. Several anticoagulant polysaccharides from marine algae have been isolated. The well-known anticoagulants from marine algae are carrageenan and fucose. They reflect a popular gas-substance complex of galactose and/or fucose. On the other side, green algae were not historically known to contain anticoagulant polysaccharides, demonstrating how little we know about algae. Deacon-Smith *et al.* (1985) concluded that the Codium fragile ssp. Contained anticoagulant activity. As for green algae, the major attention has been centred on it, and several anticoagulant polysaccharides have been discovered. The majority of anticoagulants are present in green algae, but homogenous galactan was recently discovered. The studies go into the mechanisms by which the anticoagulant function of the algae is exerted. As the mechanisms of algal anticoagulant polysaccharides were thought close to that of heparin, the effects on thrombin and factor Xa and on AT III and HC II activity were mainly examined (Figure 1). The relationship of platelets inside the wound and how they lead to hemostasis was investigated (Matsubara, 2004).

Anticoagulant from red seaweed *Lomentaria catenate*

The series of mechanism factors affect intrinsic and extrinsic pathways of the blood coagulation system. Anticoagulants inhibit or inactivate these factors by one or both pathways. As intrinsic pathway was measured by APTT by its Clotting time, and Prothrombin time are linked by their clotting time. There the TT pathway is most commonly present in intrinsic and extrinsic pathways. In Table 6, the APTT, PT, TT was assayed for purified anticoagulant activity of L. catenate a proteoglycan. 40Ig/ml of test values for activated partial thromboplastin time and prothrombin time assessed for polysaccharides concentration and in PT assay, it shows no clotting inhibition was observed. Due to the high heparin activity of L. catenate (183 IU/mg) than standard, it is used in the blood coagulation system in intrinsic and traditional pathways. PT studies suggest that there is no evidence of an inherent pathway of coagulation.

Anticoagulant activity of sulfated polysaccharide from *Gracilaria debilis*

The *G.debilis* of the anticoagulant activity of purified sulphated polysaccharides of clotting factors of human blood are performed by assays testing activated partial thromboplastin time and prothrombin time. In a concentration of 25 μg/ml of APTT test, the intrinsic pathway of *G.debilis* anticoagulant activity was 14.11 units and followed by 8.23units at the same concentration for the PT test evaluated for the extrinsic coagulation pathway. The APTT and PT are measured for an intrinsic and extrinsic pathway for clotting time-dependent.

The red seaweed species *Lomentaria catenate* with a concentration of 40 μg/ml of APTT are prolonged of polysaccharides, and in PT there was no inhibition was observed (Costa *et al.*, 2010). In 25 μg/ml of both Enabled partial thromboplastin time (APTT) and prothrombin time (PT) of *G.debilis* in crude and purified polysaccharides, there is a heparin relation to inhibition to coagulation discreat the activity. The *Botryocladia occidentalis* is a red alga and sulfated galactan with an anticoagulant activity where heparin is isolated. The polysaccharides which has individuals response in forming the complex with an inhibitor of plasma and target protease and also the anti-thrombin heparin of sulfated polysaccharides cannot be extended to other polysaccharides (Farias *et al.*, 2000). The oligosaccharides, polysaccharides have different sulfate group, molar mass and structure which shows different anticoagulant and antithrombin activity. This activity is stereospecific with target proteases in coagulation co-factor in the interaction of structural requirements in the sulfate content and their charge density (Melo *et al.*, 2004). Consequently, the sulfated polysaccharides of *G.debilis* at present result signifies as an potent

Table 4: APTT detection of crude sulphated polysaccharides

Crude SPS	APTT (seconds)	RCF	PT (seconds)	RCF
S. tennerimum	134±1.73	4.47	16	1.33
S. wightii	122±1	4.07	15	1.25
T. ornata	117.6±1.41	3.92	15	1.25
T. conoides	108±1.41	3.6	15	1.25
P. tetrastromatica	89.3±1.52	2.98	15	1.25
H1	33	1.1	13	1.08
H2	55.8	1.86	15	1.25
H3	82.8	2.76	18	1.5
H4	115.8	3.86	21	1.75
H5	148.8	4.96	24	2
Control	30	1	12	1

H1 to H5 = heparin (10, 25, 50, 75,100 μg/ml respectively); Sample 500 = μg/ml

Table 5: The behaviours of various crude SPS expressed in units of heparin

Crude SPS fraction	Anticoagulation activity [heparin units]	Percentage of heparin activity of crude SPS
S. tennerimum	25.46±0.42	18.15
S. wightii	22.52±0.24	16.05
T. ornata	21.46±0.37	15.25
T. conoides	19.18±0.28	13.61
P. tetrastromatica	14.53±0.37	10.34

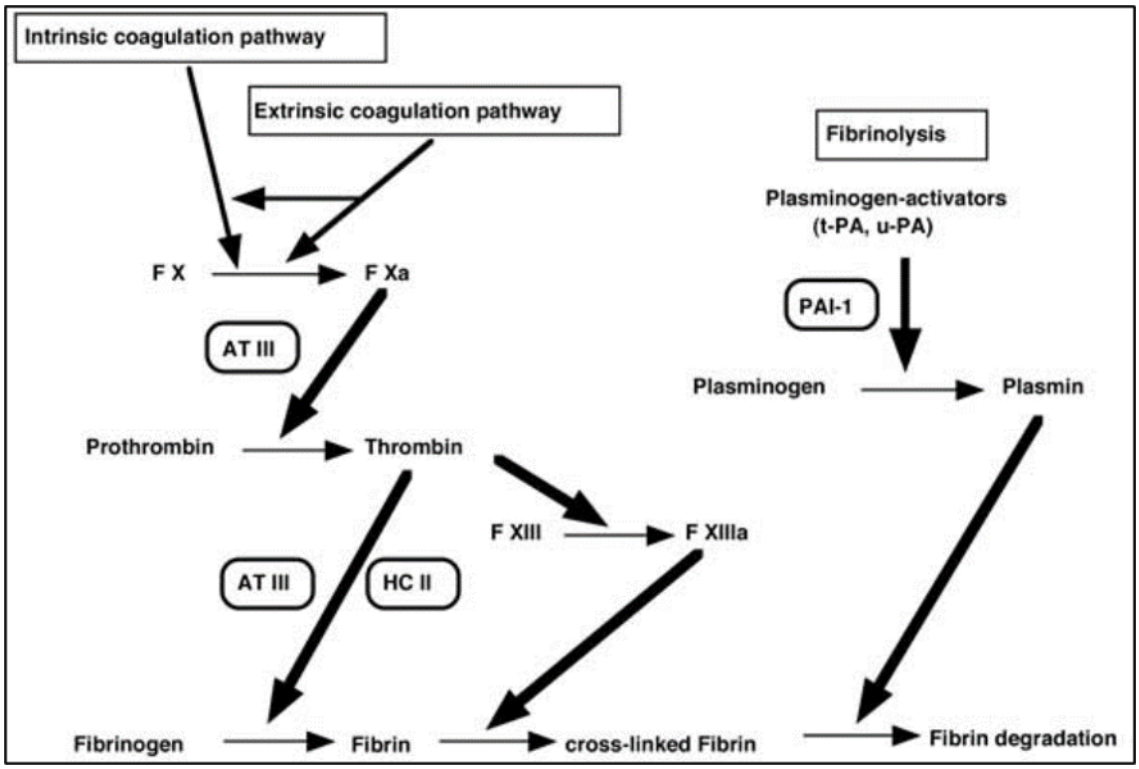

Figure 1: Blood coagulation and fibrinolysis pathways

Table 6: The anticoagulant function of distilled polysaccharide from fermented *L. catenata* and contrast with heparin(183 IU/mg)

Sample	Concentration (lg/mL)	Clotting time (s)		
		APTT	PT	TT
L. catenata	12	348	14.3	670
	25	576	18.2	841
	40	>1000	19.8	>1000
Heparin[a]	31.25	409	197	574
	62.5	>1000	779	>1000
Water[b]		36.8	11.4	12.1

All the values were the mean of threedifferent experiments;
[a] Heparin (183 IU/mg) is used as thepositive control; [b]Water was the control

anticoagulant as replacing the existing anticoagulant (Sudharsan *et al.*, 2015).

Anticoagulant behaviours of the sulfated polysaccharides. of *Monostroma nitidum*

Anticoagulant activities based on the APTT and TT assays which measure fraction WF1 and fraction WF3. Their behaviour against heparin, a classical anticoagulant, were contrasted. APTT and TT were prolonged by the vitamins WF1 and WF3. The signals for WF1 and WF3 were saturated at concentrations of 200 g/ml and 100 g/ml, respectively, at two-time points of 120 seconds and at 150 seconds. The fraction of WF1 and WF3 anticoagulant activity are less when compare to heparin; in order to get the same effect, the fraction concentration are increased. In extrinsic and intrinsic or common pathway, it includes the coagulation process, which is combined with the coagulant factor sequentially. When the APTT is increase it shows the inhibition of internal and common pathway and same as TT inhibit the thrombin activity or fibrin polymerization, as well as it is useful in investigate the thrombin accelerated clot Shape in the sample results of weak plasma. The WF1 and WF3 fractions to control the activity of thrombin. And the conversion of fibrinogen to fibrin in both intrinsic and/or typical coagulation pathways. The two fractions differ from heparin in PT, the absence of the fraction has not been detected, and the findings indicate that the extrinsic coagulation process has not been prevented by the two fractions. The variations between the two fractions were pronounced. WF3 has a higher concentration of anticoagulant activity in the APTT assay than WF1, and the same results occur in the TT assay. This occurs because of the variance in structural properties in the contrast between anticoagulant activities (Mao *et al.*, 2008).

CONCLUSIONS

The review concluded that the anticoagulant is the best source from the marine algae when compare to the commercial anticoagulant, which has more disadvantage. The anticoagulant derived from marine algae has less disadvantage and the molecular weight are less than 10,000 Daltons and in commercial the molecular weight more than 10000 Dalton. The disadvantage was depending on the molecular weight, the assay value like APTT, TT, CT, PT are under the reference value are within the range when compared to standard.

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Conflict of Interest

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