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## REVIEW ARTICLE

### A Review of Anticoagulant Activity of a Fucoidan from *Undaria Pinnatifida* Sporophy II

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#### ABSTRACT

*Undaria pinnatifida* is brown sea weed. Fucoidan is a group of marine sulfated polysaccharides of the cell-wall matrix of brown algae, containing large proportion of L-fucose and sulfate, together with minor amounts of other sugar like xylose, galactose, glucose, mannose, uronic acid, and rhamnose. Fucoidan medically used as anti-inflammatory, antiviral, anticoagulant, antitumor and antiangiogenesis. Fucoidan changes the liquid form of blood into gel type leads to blood clotting. Blood coagulation involve complex interactions between platelets, coagulation factors and injured vessel wall. Platelets are disc shape elements they aggregate or clump together during blood clotting. Many studies on this activity of fucoidan have proved effect on blood coagulation. It has been proposed as alternatives to the anticoagulant heparin.

**Keywords:** *Undaria pinnatifida*, Fucoidan, uronic acid, anticoagulant activity

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#### 1. Introduction

**Biology:** *Undaria pinnatifida* is brown sea weed, gold – brown in macroscopic stage and microscopic stage. A macroscopic stage (sporophyte) produces zoospores microscopic in nature, it can germinate and grow in microscopic gametophytes. this stage is present at the spring and summer seasons. when all the spores released it dies. The gametophyte (microscopic) release sperm and

eggs, When favourable conditions are present the macroscopic plant is develop after fertilization. Sporophyte is yellow in color and also 1-3 cm wide mid rib present which forms a continuation of the stip(stem). Sporophylls present at the base of the stem. Above the stem mid rib runs the entire length of a large leaf like lamina, which is 50-100 cm long, feathery in nature. Heptera one of the special

structure help for the attachment of algae to the substratum, yendo cells also present.

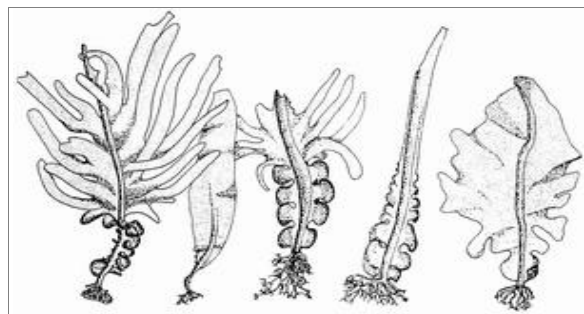


Fig 1: En -Wakame, Fr - Wakamé, Es - Abeto Marino

Chemical Structure of Several Main Active Compounds Of Undaria Pinnatifid

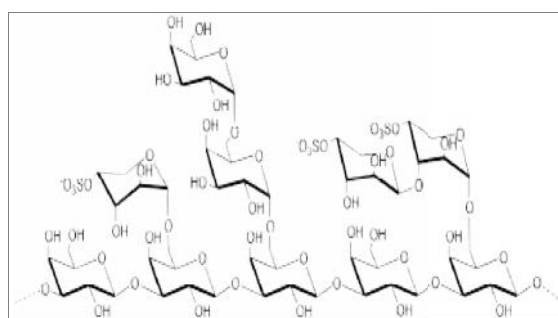


Fig 2: Sulfated poly saccharides

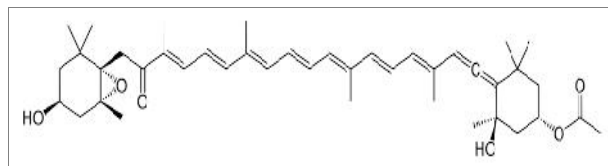


Fig 3: Fucoxanthin

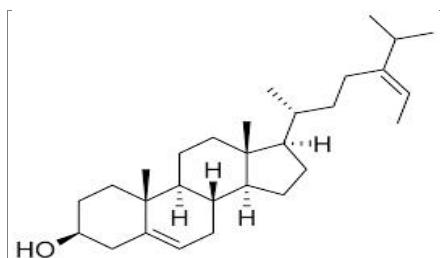


Fig 4: Fucosterol

Table 1: Biological activities of main chemical components of undaria pinnatifida

Active compounds	Biological activities
Sulfated poly saccharides	anti oxidant, Immune stimulating, Anti tumor, Anti influenza, Anti coagulating, Anti cancer
Fucoxanthin	anti obesity, Anti diabetic
Fucosterol	Anti inflammatory
Phenols	Anti microbial, Anti viral

### Coagulation

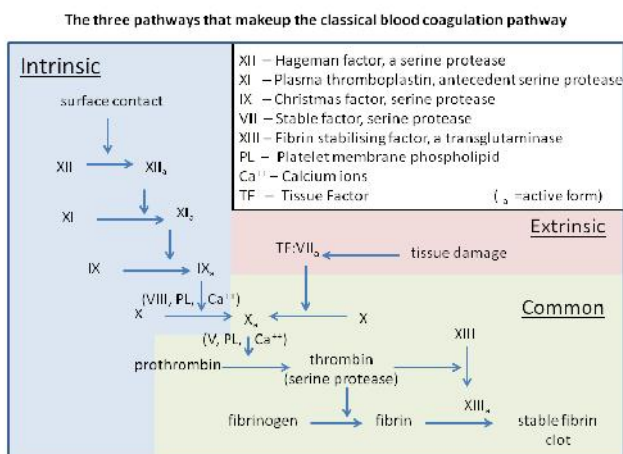
Blood coagulation involve complex interactions between platelets , coagulation factors and injured vessel wall. Platelets are disc shape eliments they aggregate or clump together during blood clotting. Fibrin is an insoluble protein develop from fibrinogen in blood that forms mesh like structure to strengthen the platelet plug by depositing. When platelets come into contact with damaged tissue thrombin is formed as a result of series of coagulation cascade that culminate in the formation of fibrin from fibrinogen.coagulation factors are the proteins mainly developed from liver. They were originally numbered based on their discovery, traditionally using roman numerals from I to XIII.

Table 2: Coagulation factors

Factor	Name
Factor-I	Fibrinogen
Factor-II	Prothrambin
Factor-III	Tissue thromboplastin
Factor-IV	Calcium
Factor-V	Proaccelerin, Labile factor
Factor-V	Accelerin
Factor-VII	Serum prothrambin, stable factor antihemophilic
Factor-VIII	Anti hemophilic A, Anti hemophilic Globulin, Anti hemophilic factor
Factor-IX	Plasma thrombo plastin components, Anti hemophilic factor B or Christmas factor
Factor-X	Stuart power factor
Factor-XI	Anti hemophilic factor C
Factor-XII	Hageman factor
Factor-XII	Fibrin stabilizing factor

### Coagulation Pathways

Blood clotting is a sequential process that involves interaction of blood components. This process can be initiated by activation of two separate pathways, Extrinsic and intrinsic. Both pathways result the production of factor X. In the coagulation process extrinsic pathway is first pathway and is stimulated in response to a protein called tissue factor . When the blood vessel breaks and these cells come in to contact with blood, tissue factor activates factor VII it forms factor VIIa . Finally rapid production of factor X occur. When the blood vessel is internally injured the intrinsic path way occur. Blood circulates over injured internal surface of vessel the activation of factor XII (Hugeman factor) may occur. So the intrinsic path way is starts with activation of factor XII . This intrinsic path way components may also activated by extrinsic path way. When factor X produced results in cleavage of factor II (prothrambin) to factor IIa(thrombin) this factor IIa catalyze the conversion of factor I(fibrinogen) into factor Ia(fibrin ) .Fibrin is insoluble plasma protein it is a long sticky threads like structure . This fibrin threads forms a mesh like structure that traps blood cells ,platelets and plasma within minutes, the fibrin mesh work contract, squeezing out its fluid contents this process is called clot retraction , it is the final step , it yield a in soluble clot that can withstand friction of blood flow called resilient.



**Fig 5:** Coagulation pathways

### Heparin Action

Heparin is discovered in 1916 by medical student Mc Lean, Howell and Holt named it as heparin. It is non uniform mixture of straight chain mucopoly saccharides with M.V 10,000 TO 20,000 . It contain polymers of two sulfated disaccharide units that is D-glucosamine-L- iduronic acid, D-glucosamine –D- glucuronic acid. Heparin present in all tissues containg mast cells, lungs , liver , intestinal mucosa. It activates the plasma antithrombin III .The Heparin –AT III complex then binds to clotting factors of both intrinsic and extrinsic pathways (Xa,IIa,IXa,XIa,XIIa and XIIIa) and inactivates them but factor VII a operative in extrinsic path way. At low level of heparin ,factor Xa mediated conversions that is thrombin from prothrambin is affected .The anticoagulation activity is occur mainly by inhibition of factor thrombin(II a) as well as factor Xa. Factor thrombin converts the fibrinogen to fibrin. Low concentration of heparin prolongs aPTT but not prolong PT. High concentration prolongs both Aptt and PT . so low concentration interfere selectively with intrinsic pathway affecting amplification and aontinuation of clotting occur. But high concentration affect the common pathway as well.Heparin one of strong anti coagulaent thus has been widely used in hemodialysis patients but many clinical trails have claimed that it show potentially serious side effects like thrombocytopenia, hemorrhage, osteoporosis. More over heparin produce from mammalian mucosa has potential risk of contamination by many prions and virises.

### Fucoidan

Fucoidan is a group of marine sulfated poly saccharide of cell wall matrix of brown alage L-fucose, sulfate and small amount of sugars like xylose, galactose, glucose, mannose, uronic acid, rhamnose present. The skeleton structure of fucoidan is 1,3-linked –L-fucose-4-sulfate.Because of presence of these poly saccharides fucoidan shows more physiological and biological activities example anti coagulant activity. Fucoidan is obtain from vegetable origin that is sporophyll of undaria pinnatifida contain less infectious agents like animal viruses or prions. Because of these reasons it is suggested that the fucoidan of undaria pinnatifida sprophyll would be promising candidate for development of anti-coagulant.

### Purification of Fucoidan

Fucoidan was extracted from sporophyll of undaria pinnatifida , these are collected from a southern coastal area of wando, korea. Approximately 250g of dried sporophyll was cut into small chips (size should be 3x3 cm)and kept in 4 L of 0.1 N HCL at ambient temperature for 24 hrs. Then filtered through a typical woman’s nylon socks and the filtrate was neutralized with 1 N NaoH and fucoidan were precipitated with 3 volumes of ethanol .The precipitate was redissolved in water after centrifugation for 30 min at 6,000 x g . The p<sup>H</sup> was adjusted to 2.0 CaCl<sub>2</sub> was also added to the final concentration of 4 M. Again centrifugation was performed and precipitate was removed then supernatant was treated with 3 volumes of ethanol . The precipitation of ethanol was repeated twice and precipitate was re dissolved in water ,dialyzed at 4°c in water for 48 h and then freeze-dried.Column chromatography was used for the purification of crude fucoidan for this 100mg of crude fucoidan was dissolved in 10 ml of water (ph 2.0) and applied to DEAE- cellulose column (3x42 cm) preequilibrated by water(ph 7.0 adjusted with 0.1 NaoH) and eluted with same buffer containg increasing concentration of NaCl like 0.5,1.0,1.5,2.0,2.5,3.0 cm until no more carbohydrates was detected.

### 2. Conclusions

The fucose, sulphate, and uronic acid content of crude fucoidan extracted from *Undaria pinnatifida* grown around the coastal waters were comparable to other published studies. The anticoagulant activity of the purified fucoidan was significantly prolonged the clotting time. The anticoagulant activity of the purified fucoidan increased with increasing concentration of the fucoidan. Blood coagulation involve complex interactions between plate lets, coagulation factors and injured vessel wall. Platelets are disc shape eliments they aggregate or clump together during blood clotting. Many studies on this activity of fucoidan have proved effect on blood coagulation. It has been proposed as alternatives to the anticoagulant heparin.

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