Can sulphated polysaccharides from seaweed provide prophylactic and/or therapeutic solution to COVID-19 pandemic?

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The novel corona virus or severe acute respiratory syndrome virus or SARS-CoV-2 has spread throughout the world in a very short period. Till date, there is no approved medicine or pharmaceuticals product found to be effective against COVID-19. Sulphated polysaccharides from seaweed possess antiviral, anti-inflammatory, anticoagulant, antinociception, antitumor, antiallergic and immunological activities which can be useful to fight corona virus COVID-19 pandemic.

Corona virus is an enveloped virus with a positive sense single stranded RNA as its genetic material. The name corona comes from a peculiar crown-like spikes over its outer surface. The novel coronavirus or severe acute respiratory syndrome coronavirus or SARS-CoV-2 is a new coronavirus originated in Wuhan, China in December 2019 and has soon spread throughout the world. As it is an etiological agent for Corona Virus Disease-19 (COVID-19), a contagious disease which can spread from person to person, the World Health Organization declared it as pandemic and a public health emergency. COVID-19 is characterized by mild to a severe disorder of the upper respiratory tract which can even manifest severe interstitial pneumonia and acute respiratory distress syndrome (ARDS)[1]. Though it is believed that the COVID-19 is a respiratory tract infection, a study has shown that it should be considered as a systemic disease which includes almost all the systems and involve respiratory, gastrointestinal, neurological, cardiovascular, hematopoietic and immune system[2]. Older people with comorbidities like hypertension, diabetes, heart ailment and lung disorder are at higher risk but at the same time the younger population without any noticeable health issue may also face lethal complications such as myocarditis and disseminated intra vascular coagulopathy (DIC) which is characterized by the presence of small blood clots in blood stream, ultimately blocking the small blood vessels.

Unfortunately, according to WHO till date, there is no approved medicine or pharmaceuticals product found to be effective for the treatment of COVID-19 and the commonly used medicines are considered as ‘off label’ by the regulatory authority. But the experts and medical practitioners of different countries are using a treatment on trial and error basis. The information available in the scientific domain suggests that there are a number of potential drugs available but their efficacy for the treatment of COVID-19 is yet to be established. Some of the important drugs used against COVID-19 are chloroquine, hydroxy chloroquine, remdesivir, ribavirin, ritonavir, favipiravir, Umifenovir interferon-β1, lopinavir, aerosolized interferon α, oseltamivir, etc.[3]. In many countries including India, plasma therapy has also been tried. Among the common line of medication, chloroquine and hydroxyl chloroquine are approved medicines for prophylactic and therapeutic uses in malaria[3] but the anti-inflammatory and broad spectrum antiviral activities of these medicines have supposed to be a role in the treatment of COVID-19 patient[4]. Remdesivir, ribavirin, ritonavir and favipiravir are antiviral drugs which inhibit the viral replication probably by blocking viral RNA polymerase[3].

Sulphated polysaccharide

The marine environment is a natural habitat for a great variety of living organisms and contains more than 80% of plant and animal species in the world[5]. Such a genetic diversity renders chemical diversity which is a promising source for new drug development. The enormous ecological resources of the sea have been exploited since ancient times and included the use of marine animals and algae as the sources of medicine. Marine life forms are evolved to have the capability to grow and reproduce in extreme environments like high salinity, temperature and pressure. These organisms possess unique metabolic and physiological properties to thrive under the extremities through their metabolic processes generating various metabolites. Seaweed is easily accessible and one of the most abundant life forms of the marine ecosystem. In general, they are classified based on their photosynthetic pigments as red seaweeds (Rhodophyta), brown seaweeds (Phaeophyta) and green ceaweeds (Chlorophyta). Besides being a source of healthy food due to low calorie and significantly higher mineral and fibre content, it is an important resource of diverse kinds of bioactive principles. Derivatives of seaweeds are known to have a variety of activities such as anticoagulant, antioxidant, antibacterial, antiviral, anticancer, anti-hyperlipidemic, antihepatotoxic properties, etc.[6]. The sulphated polysaccharide is one such molecule present in seaweed having immense pharmacological activities which have generated interest among researchers. Sulphated polysaccharides are complex poly-anionic macromolecules containing sulphate moieties and sugar backbone. Due to their unique chemical structures, these compounds can interact with a wide variety of matrix and cellular proteins[7] which manifest different pharmacological and therapeutic properties.

The common sulphated polysaccharide of red seaweeds are agaran and carrageenan, whereas fucoidans, laminaran and alginates are from the brown seaweeds and ulvans from the green seaweeds.

Several studies have been conducted to affirm the bioactivities of sulphated polysaccharide from marine seaweeds[8]. It has attracted the attention of scientists throughout the world for its diverse bioactive properties.

Sulphated polysaccharide from seaweed has been used for the pharmaceutical purposes[9]. The probable mechanism of antibacterial activity is attributed to the glycoprotein receptors on the surface of polysaccharide which bind to the bacterial cell wall compound, which in turn increases the permeability of cytoplasmic membrane causing protein leakage and binding to bacterial DNA. Fucoidan and laminarin from brown seaweed have been used as oral antibiotics to inhibit the growth of *Staphylococcus aureus* and *E. coli*[9]. Several polysaccharides isolated from red and green seaweeds have been evaluated for its antiviral activities[10]. They are known to inhibit enveloped viruses like retro viruses HIV type 1 type 2, cytomegaloviruses, herpesviruses (HSV type 1 and 2), pseudorabbies virus, flaviviruses (dengue virus type 2), orthomyxoviruses (influenza A virus) and few other viruses[11]. The inhibitory effect of sulphated polysaccharides mainly depend on their ability to inhibit the initial attachment of the virus to the target cells which in turn block the viral entry[11]. Carrageenan, a sulphated polysaccharide from red seaweed, has been tried as a therapeutic agent for respiratory weaknesses like the common cold, influenza virus H1N1. *In vitro* study has shown that iota-carrageenan is active against novel pandemic H1N1/2009 influenza[12]. Its effect on herpes, hepatitis A, dengue viruses has also been evaluated. Carrageenan, in spite of inhibiting the penetration of virus on host cells, inhibits the synthesis of viral protein inside the cells. The sulphated polysaccharide from red and brown seaweeds exhibits excellent total antioxidant capacity, hydroxyl radical scavenging activity, superoxide radical scavenging, ferrous chelating ability and reducing power activity[13].

Anticoagulant activity of the sulphated polysaccharide is proven, it is understood that the sulphated polysaccharide interferes with coagulation factor and prolong or inhibit the coagulation. The underlying mechanism of coagulation is by inhibition of thrombin, a blood coagulation factor. Different variants of carrageenan have different anticoagulant properties. A study has shown that the most active carrageenan (λ) fraction has one fifteenth of the activity of heparin which means λ carrageenan has mild anticoagulation property[14]. Immunomodulatory role of sulphated polysaccharide is well studied[15]. It is observed that some of the sulphated polysaccharides modulate the immunological principle by inducing nitric oxide (NO) and various cytokine production through upregulation of mRNA expression. The study also shows that the use of sulphated polysaccharide increases the secretions of interferon and interleukins, suggesting that it is a strong immune-stimulator[13].

The available knowledge has shown that the sulphated polysaccharide is a wonder molecule with immense medicinal properties and it works on different types of bacteria and enveloped viruses which are similar to the SARS-CoV-2. Therefore in a world where more than 5 million infected people are struggling to get some relief and medical professionals and researchers are still fighting to reach any conclusive solution or effective medicine for SARS-CoV-2, sulphated polysaccharide from seaweeds can be a potent molecule to fight against COVID-19 pandemic. Even molecules like carbohydrate binding proteins, lectins could also be used as tool against SARS-CoV-2. A carbohydrate binding protein, Griffithsin, derived from red algae *Griffithsia* sp. – has shown *in vitro* and *in vivo* antiviral activity against enveloped viruses, and has registered low host toxicity[16], making it a candidate molecule to be studied against SARS-CoV-2.

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