

# Algal Bioactive Compounds against Sexually Transmitted Diseases

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<http://dx.doi.org/10.13005/bbra/3009>

(Received: 30 April 2022; accepted: 20 September 2022)

Sexually transmitted diseases (STDs) are one of the major global health issues which is either ignored or gets suppressed due to difficulty in bringing forth the discussion in public domain. However, with the advent of time, naturally obtained solutions are making their mark in diagnostic areas. Algae and its bioactive compounds are amongst the natural and environment-friendly compounds which might provide solutions to the global challenges presented by STDs. Recent studies on efficacy of seaweeds as antiviral components exemplify the undivided attention within the area. The marine seaweeds like red, brown green algae, and cyanobacteria, have therapeutic preeminent compounds like lectins, sulfated polysaccharides, carrageenan, carotenoids, fucoidans, cyanovirin N, malyngamide F acetate which has broad antiviral properties. The present review aims on the understanding of the function and potency of bioactive marine algal compounds which might be studied further in an expansive way to be used as a potential drug against various STDs. An effort has been made to decode the composition as well as the constitution of various types of algae that furnish an elevated level of different prospects which can help in paving the way in diversified areas in scientific and medical assistance.

**Keywords:** Antiviral Peptide; Bioactive Compound; Cyanobacteria Seaweed; Sexually Transmitted Diseases.

As per the recent global data, it has been deciphered that sexually transmitted diseases like gonorrhea, chlamydia, syphilis has reached its peak in the past decades in countries like the U.S, particularly in 2018<sup>1</sup>. Modern lifestyle and its ways has increased the transmission in our new generation. The disease has been spreading more prevalently among the teens and young adults aged between 21-25 years<sup>1</sup>. Most of the sexually transmitted diseases (STDs) go unreported due to various underlying reasons like, lack of awareness and knowledge about the disease, lack of any

serious symptoms, difficulty in bringing fore the discussion about the sexual diseases. These STDs are generally caused by various prevalent microbes like viruses, bacteria as well as some parasites. Some of the common STDs are, chlamydia, genital warts caused by human papillomavirus (HPV), acquired immune deficiency syndrome (AIDS) caused by human immunodeficiency virus (HIV), gonorrhea, genital herpes, syphilis etc. The studies that have been done so far are few in number. In a report it has been found that sulfated polysaccharides extracted from different

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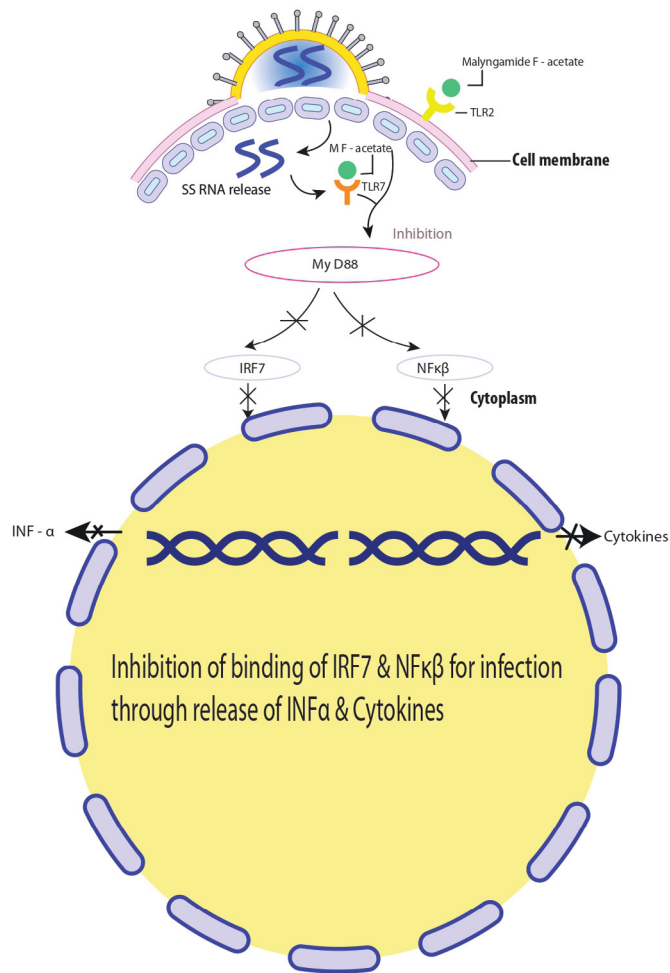


algae show broad spectrum antiviral activity against HIV-1 and HIV-2 *in vitro*<sup>2</sup>. The report says, cyanovirin N, a potential antiviral peptide obtained from cyanobacteria, affects the membrane fusion process during the entry of HIV-1 into the host cells<sup>2</sup>. Another important bioactive compound, sulfoquinovosyldiacylglycerol (sulfolipid) discovered from cyanobacteria species inhibits the reverse transcriptase activity of HIV-1 and HIV-2<sup>2</sup>. In the past decades many active compounds have been discovered from many microorganisms including marine animals, fungi, bacteria, and algae<sup>3</sup>. But both cyanobacteria and eukaryotic algae perform better than other marine organisms<sup>3</sup>.

In the present review we have highlighted the role of cyanobacteria and seaweeds and their potential derivatives to cure STDs. This work will be supportive in terms of future study and to make people aware about the STDs.

**Algal derived compounds as treatment**

The Algal world has proven to bring forth a long term blend of solutions against environmental pollution to biodiversity sustainability. Algae possess a wide range of bioactive compounds with diverse therapeutic benefits<sup>3,4</sup>. Right from microalgae including cyanobacteria to macro seaweeds, most of them possess sources of antiviral, anti-inflammatory compounds as well



**Fig. 1.** Bioactive compound Malyngamide F acetate- mediated inhibition of IRF7 and NFκB

as immune modulators against serious viral infections related to STDs as well as those caused by coronavirus<sup>5,6,7,8,9</sup>. The algal derived bioactive compounds has the ability to not only impede replication cycle but also delay the rate of infection caused by the viruses by blocking the area through which the viruses enter the cells, hence, providing a new therapeutic window in treatment against viral as well as sexually transmitted infections<sup>10,11,12</sup>.

### Cyanobacteria and marine algae and their metabolites

#### Microalgae

Microalgae generally include blue green algae or cyanobacteria, diatoms, and dinoflagellates<sup>3,4,7</sup>. These microalgae have broad spectrum bioactive molecules which have immense potential against viral activity particularly in treatment of HIV. Cyanobacteria like *Rivularia* sp., *Lyngbya majuscula*, have significant amount of anti-inflammatory properties<sup>8</sup>.

In general, in HIV infection, the virus impairs the CD4<sup>+</sup> T cell recovery. In B-cell signaling, the infection process is found to be reversed by the action of malyngamide F acetate, which binds with the Toll like receptors for example TLR2 or TLR7 that activate the MyD88 pathway, thereby inhibiting the function of IRF7 and NFκB response. Hence, the compound initiates the restoration of immune function and ultimately virus clearance<sup>13,14</sup>.

#### Macroalgae

These are generally multicellular organisms and classified according to their pigments-green algae, red algae, brown algae. These macroalgae have influential perspectives of antibacterial, antiviral and antifungal activity<sup>15,16,17,18</sup>. In accordance with the report provided by Deepa *et. al.* (2017), *Gracilaria corticata* has commanding power in the treatment of various infectious diseases like HIV<sup>19</sup>. In the

**Table 1.** Bioactive compound from cyanobacteria

Compound	Cyanobacteria species	Function	References
Bis-bromoindole	<i>Rivularia</i> sp.	Anti-inflammatory	11
Malyngamide F-acetate	<i>Lyngbya majuscula</i>	Inhibit production of NO, blocking MyD88 inflammatory pathway	13

**Table 2.** Bioactive compounds from macroalgae

Compound	Algal Species	Function	References
Galactan sulfate	<i>Agardhiella tenera</i>	Activity against HIV-1, HIV-2	8,20
Sulfated xylomannan	<i>Scinaia hatei</i>	Inhibition of HSV-1 HSV-2	3,25
Polysaccharide	<i>Sphaerococcus coronopifolius</i> , <i>Boergeseniella thuyoides</i>	Antiviral against HIV, HSV-1	8,26
Phlorotannin derivatives	<i>Ecklonia cava</i>	Anti HIV property, inhibits reverse transcriptase	22
Fucoidans	<i>Dictyota mertensii</i> <i>Fucus vesiculosus</i>	Prohibit reverse transcriptase HIV-1 activity	23,24
Sulfated polysaccharide	<i>Caulerpa brachypus</i> <i>Caulerpa okamurai</i> <i>Chaetomorpha crassa</i> <i>Monostroma nitidum</i> <i>Hydroclathrus clathrus</i>	Acts against type-1 herpes virus activity	8,27
Rhamnan sulfate	<i>Monostroma nitidum</i>	Active against type-2 herpes Virus	28
Lectin	<i>Boodlea coacta</i>	Shows antiviral function against infection caused by HIV-1	29

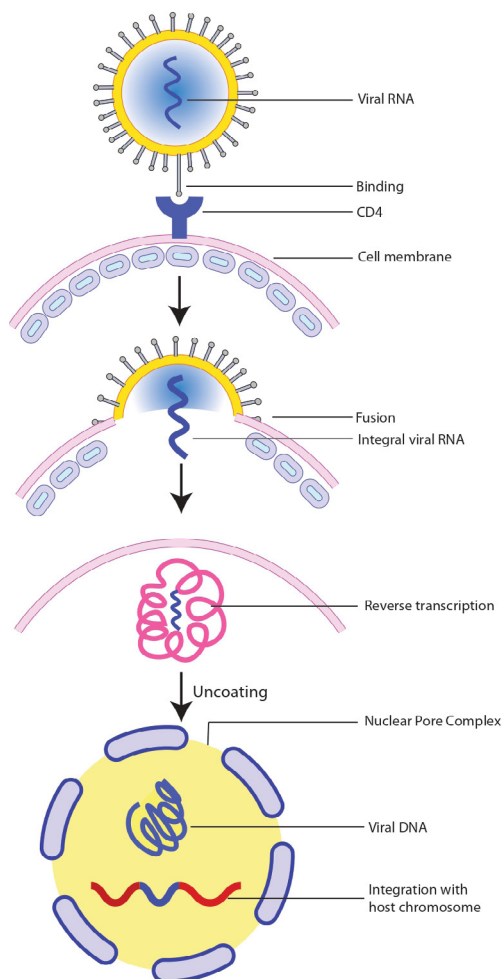
opinion of Witvrouw et. al. (1994), galactan sulfate from *Agardhiella tenera* has the capability to act against HIV-1, HIV-2, with IC50 value of 0.5 and 0.05 ug/l respectively<sup>20</sup>. Similarly, *Sphaerococcus coronopifolius*, *Boergeseniella thuyoides* has antiviral properties against HIV and herpes simplex virus (HSV-1)<sup>3</sup>. Laminarin, found in brown algae, has been found to function as an antiviral, anti-inflammatory agent<sup>5</sup>. It has also been found, fucoidan has antiviral as well as antibacterial properties and therefore, could be used to treat a wide range of infections and long term infectious diseases<sup>21</sup>. Derivatives of phlorotannin of *Ecklonia cava* contain 8,4'-dieckol and 8,8'-bieckol, which showed inhibitory function against viral reverse transcriptase and protease as anti-HIV-1 property

at the concentrations of 5.3 and 0.5 uM in IC50<sup>22</sup>. It was also found by Hayashi et. al. (2008) through various studies, fucoidan, generally found in *Undaria pinnatifida*, has defensive diagnostics against HSV infections<sup>23</sup>. Fucans from *Fucus vesiculosus* have shown to possess inhibitory properties against reverse transcriptase of HIV-1<sup>24</sup>.

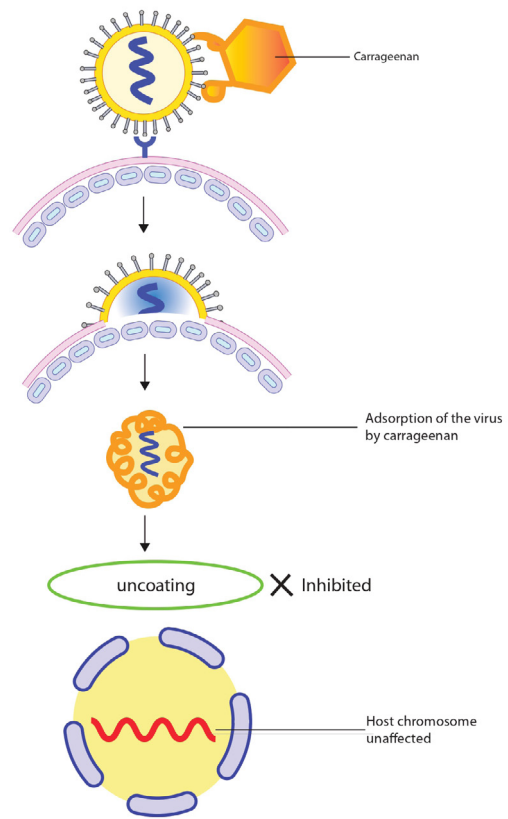
**Properties of some algal derived biochemical compounds**

**Carrageenan**

It is a type of linear sulfated polysaccharide generally found in Red algae. This polysaccharide has the ability to inhibit the entry of viral genes in the host genome at various phase points of HIV-1 infection. Capsid is known to show one of the important analytical functions at different stages of the viral replication cycle. Soon after the entry of the virus and subsequent fusion in target cell membranes, the capsid core is released into the cytoplasm and disassembles, which is known as the uncoating<sup>30</sup>.



**Fig. 2a.** HIV-1 viral entry in normal condition



**Fig. 2b.** Carrageenan activity against HIV-1

Carrageenan, by directly binding to the virus, can initiate the adsorption of the virus and ultimately ceases the process of uncoating of the virus particle<sup>8,31</sup>.

#### **Galactan**

According to Sansone *et al.* (2020), Galactan has been able to successfully pinpoint some encouraging results against HIV by blocking its attachment to the host cell and thus preventing subsequent adhesion of HIV gp120 on CD4<sup>+</sup> T cells<sup>32</sup>. It has also been established through reports by Matsuhiro *et al.* (2005), that galactan isolated from *Schizymenia binderi* has the ability to exhibit specificity in antiviral activity with regard to HSV by occluding the adhesion of viruses on the surface of the host cell<sup>33</sup>. Sulfated polysaccharide derived from *Hydroclathrus clathratus*, a brown algae, has inhibitory properties against HSV-1, HIV-1 as well as human cytomegalovirus (HCMV) where EC50 value count has shown to be low<sup>34</sup>.

#### **Lectins**

Griffithsin (GRFT), a group of lectin, derived from red algae, exerts inhibitory effects on viruses which not only cause hepatitis C, HIV, murine herpes simplex virus Type-2 but Middle East respiratory syndrome coronavirus (MERS-CoV) as well. The reason behind the usage of GRFT is because it possesses a high safety profile with almost zero toxicity. The structure of the HIV-1 virion particle comprises 14 spikes. However, out of fourteen, four spikes are essentially required for successful infection caused by the virus. Therefore, GRFT subsequently requires four spikes to neutralize and inhibit the HIV virion-causing infection as followed in the reports of Huskens and Schols (2012)<sup>35</sup> and subsequently by Lee (2019)<sup>36</sup>.

#### **CONCLUSION AND FUTURE PROSPECTS**

Through various inclusive studies, it can be derived that marine algal bioactive molecules present several advantages as potential new therapeutic drugs. Most of the molecules exhibit a broad spectrum antiviral activity against various sexually transmitted diseases especially HIV, HSV and also hepatitis related diseases. They act against the virus by inhibiting their entry and subsequent replication. Biomolecules like lectins present a promising candidate for the prevention of HIV transmission by interacting with the HIV gp

120<sup>14</sup>. Carrageenan in particular has successfully expressed some definite positive effects in inhibiting the HIV activity by blocking the virus from the uncoating stage<sup>8,31,37</sup>. It has also been established that among all the variants of seaweeds, red algae possess the maximum number of biomolecules with potential and powerful antiviral activities against STDs. The previous studies performed by researchers were mainly based on antiviral or antimicrobial properties of seaweeds in general. However, we must make people aware about STDs, and follow the thumb rule of 'prevention is better than cure' by using algae regularly in their diet. Our present study is still an unopened and unexplored book, where we have tried to highlight some active components and their sources briefly, so that budding researchers can get familiar with the topic. Further extensive studies are required in order to bring forth the efficacy of the biomolecules as potential therapeutic treatment on a large scale.

#### **ACKNOWLEDGEMENT**

The Department of Botany, Bangabasi Evening College is acknowledged for its laboratory facilities.

#### **Conflict of interest**

Authors declare that there is no conflict of interest.

#### **Funding resource**

This research did not receive any financial assistance.

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