Algal Bioactive Compounds against Sexually Transmitted Diseases

Sunipa Sen¹, Gour Gopal Satpati¹* and Pritha Basu²

¹Department of Botany, Bangabasi Evening College, 19, Rajkumar Chakraborty Sarani, Kolkata-700009, West Bengal, India.
²Cryptogamic Unit, Central National Herbarium, Botanical Survey of India, Howrah-711103, West Bengal, India.

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

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 also known as plants of the sea like, blue green algae; red, brown and green algae, have therapeutic preeminent compounds like lectins, sulfated polysaccharides, carrageenans, carotenoids, fucoidans, 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; 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 2018¹. 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 years¹. 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 forth 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
algae show broad spectrum antiviral activity against HIV-1 and HIV-2 in vitro. 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. Another important bioactive compound, sulfoquinovosyldiacylglycerol (sulfoglycolipid) discovered from cyanobacteria species inhibits the reverse transcriptase activity of HIV-1 and HIV-2. In the past decades many active compounds have been discovered from many microorganisms including marine animals, fungi, bacteria, and algae. But both cyanobacteria and eukaryotic algae perform better than other marine organisms.

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. Right from microalgae to macro seaweeds, most of them possess sources of antiviral, anti-inflammatory compounds as well as immune modulators against

---

**Fig. 1.** Bioactive compound Malyngamide F acetate- mediated inhibition of IRF7 and NFκB
serious viral infections related to STDs as well as those caused by coronavirus\textsuperscript{5,6,7,8,9}. 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\textsuperscript{10,11,12}.

**Marine Algae and their Metabolites**

**Microalgae**

Microalgae generally include blue green algae or cyanobacteria, diatoms, and dinoflagellates\textsuperscript{3,4,7}. 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\textsuperscript{8}.

In general, in HIV infection, the virus impairs the CD4\textsuperscript{+} 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 NFkâ response. Hence, the compound initiates the restoration of immune function and ultimately virus clearance\textsuperscript{13,14}.

**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\textsuperscript{15,16,17,18}. In accordance with the report provided by Deepa et. al. (2017), *Gracilaria corticata* has commanding power in the treatment

### Table 1. Bioactive compound from microalgae

| Compound                        | Algal species                          | Function                                           | References |
|---------------------------------|----------------------------------------|----------------------------------------------------|------------|
| Bis-bromoindole                 | *Rivularia* sp.                        | Anti-inflammatory                                   | 11         |
| Malyngamide F-acetate           | *Lyngbya majuscula*                    | Inhibit production of NO, blocking MyD88 inflammatory pathway | 13         |

### Table 2. Bioactive compounds from macroalgae

| Compound                  | Algal Species                          | Function                                           | References |
|---------------------------|----------------------------------------|----------------------------------------------------|------------|
| Galactan sulfate          | *Agardhiella tenera*                   | Activity against HIV-1, HIV-2                      | 8,20       |
| Sulfated xylomannan       | *Scinaia hatei*                        | Inhibition of HSV-1 HSV-2                          | 3,25       |
| Polysaccharide            | *Sphaerococcus coronopifolius, Boergeseniella thuyoides* | Antiviral against HIV, HSV-1                       | 8,26       |
| Phlorotannin derivatives  | *Ecklonia cava*                        | Anti HIV property, inhibits reverse transcriptase   | 22         |
| Fucoidans                 | *Dictyota mertensii*                   | Prohibit reverse transcriptase                      | 23,24      |
|                           | *Fucus vesiculosus*                    | HIV-1 activity                                     |            |
|                           | *Caulerpa brachypus*                   | Acts against type-1 herpes virus activity          | 8,27       |
|                           | *Caulerpa okamurai*                    |                                                    |            |
|                           | *Chaetomorpha crassa*                  |                                                    |            |
|                           | *Monostroma nitidum*                   |                                                    |            |
|                           | *Hydroclathrus clathrus*               |                                                    |            |
| Rhamnan sulfate           | *Monostroma nitidum*                   | Active against type-2 herpes Virus                  | 28         |
| Lectin                    | *Boodlea coacta*                       | Shows antiviral function against infection caused by HIV-1 | 29         |
of various infectious diseases like HIV\(^\text{19}\). In the opinion of Witvrouw et. al. (1994), galactan sulfate from \textit{Agardhiella tenera} has the capability to act against HIV-1, HIV-2, with IC\textsubscript{50} value of 0.5 and 0.05 ug/l respectively\(^\text{20}\). Similarly, \textit{Sphaerococcus coronopifolius}, \textit{Boergeseniella thuyoides} has antiviral properties against HIV and herpes simplex virus (HSV-1)\(^\text{3}\). Laminarin, found in brown algae, has been found to function as an antiviral, anti-inflammatory agent\(^\text{4}\). 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\(^\text{21}\). Derivatives of phlorotannin of \textit{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 IC\textsubscript{50}\(^\text{22}\). It was also found by Hayashi et. al. (2008) through various studies, fucoidan, generally found in \textit{Undaria pinnatifida}, has defensive diagnostics against HSV infections\(^\text{23}\). Fucans from \textit{Fucus vesiculosus} have shown to possess inhibitory properties against reverse transcriptase of HIV-1\(^\text{24}\).

**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\(^\text{26}\).

**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 particle8,31.

**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+ T cells32. 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 cell33. 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 low34.

**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)35 and subsequently by Lee (2019)36.

**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 gp12014. Carrageenan in particular has successfully expressed some definite positive effects in inhibiting the HIV activity by blocking the virus from the uncoating stage33,37. 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. Authors also thank many researchers from India and abroad for their active guidance and support.

**Conflict of interest**

Authors declare that there is no conflict of interest.

**Funding resource**

This research did not receive any financial assistance.

**REFERENCES**

1. https://www.yalemedicine.org/conditions/sexually-transmitted-diseases. Accessed on 02.05.2022.
2. Luescher-Mattli M. Algae, a possible source for new drugs in the treatment of HIV and other viral diseases. Curr. Med. Chem.-Antinfect. Agents, 2003; 2(3): 219-225.
3. Barzkar N., Jahromi S.T., Poorsaheli H.B. and Vianello F. Metabolites from marine microorganisms, micro, and macroalgae: immense scope for pharmacology. Mar. Drugs, 2019; 17: 464.
4. Imhoff J.F., Labes A. and Wiese J. Bio-mining the microbial treasures of the ocean: new natural products. Biotechnol. Adv., 2011; 29: 468–482.
5. Satpati G.G. Algal sulfated polysaccharides: potent immunomodulators against COVID-19 in pandemic 2020. Biosciences Biotechnol. Res. Asia, 2020; 17(3): 601-605.

6. Satpati G.G. A preliminary report on plant based immunity against SARS-CoV-2 (COVID-19) in pandemic 2020. Res. J. Biotechnol., 2020; 15(10): 174-176.

7. Debbab A., Aly A.H., Lin W.H. and Proksch P. Bioactive compounds from marine bacteria and fungi. Microbiol. Biotechnol., 2010; 3: 544-563.

8. Pal A., Kamthania M.C. and Kumar A. Bioactive compounds and properties of seaweeds-a review. Open Access Libr. J., 2014; 1: 1.

9. Besednova N.N., Zvyagintseva T.N., Kuznetsova T.A., Makarenkova I.D., Smolina T.P., Fedyanina L.N., Kryzhanovsky S.P. and Zaporozhets T.S. Marine algae metabolites as promising therapeutics for the prevention and treatment of HIV/AIDS. Metabolites, 2019; 87-104.

10. Lin L.T., Hsu W.C. and Lin C.C. 2014. Antiviral natural products and herbal medicines. J. Tradit. Complement. Med., 4: 24-35.

11. Nunnery J.K., Mevers E. and Gerwick W.H. Biologically active secondary metabolites from cyanobacteria. Curr. Opin. Biotechnol., 2010; 21(6): 787-793.

12. Zhou Y. and Simmons G. Development of novel entry inhibitors targeting emerging viruses. Expert Rev. Anti. Infect. Ther., 2012; 10: 1129–1138.

13. Villa F.A., Lieske K. and Gerwick L. Selective myd88-dependent pathway inhibition by the cyanobacterial natural product malyngamide F acetate. Eur. J. Pharmacol., 2010; 629: 140–146.

14. Prasanta K.D., Bhavesh D.K., Hang S., Mary G.B. and Howard E.G. Pathways towards human immunodeficiency virus elimination. eBioMedicine, 2020; 53: 102667.

15. Motuhu S.E., Mehiri M., Payri C., La Barre S. and Bach S. Marine natural products from new caledonia- a review. Mar. Drugs, 2016; 14: 60.

16. Deepa S., Bhuvana B., Hemamalini S., Janet C. and Kumar S. Therapeutic potential and pharmacological significance of the marine alga Gracilaria corticata. Pharm. Biol. Eval., 2017; 4: 68–72.

17. Witvrouw M., Este J., Mateu M., Reynen D., Andrei G., Snoeck R., Ikeda S., Pauwels R., Bianchini N.V. and Desmyter J. Activity of a sulfated polysaccharide extracted from the red seaweed Agardhiella tenera against human immunodeficiency virus and other enveloped viruses. Antivir. Chem. Chemother. 1994; 5: 297–303.

18. Lutay N., Nilsson I., Wadström T. and Ljungd Å. Effect of heparin, fucoidan and other polysaccharides on adhesion of enterohemorrhagic helicobacter species to murine macrophages. Appl. Biochem. Biotechnol., 2011; 164: 1–9.

19. Ahn M.J., Yoon K.D., Min S.Y., Lee J.S., Kim J.H., Kim T.G., Kim S.H., Kim N.G., Huh H. and Kim J. Inhibition of hiv-1 reverse transcriptase and protease by phlorotannins from the brown alga Ecklonia cava. Biol. Pharmaceut. Bull., 2004; 27: 544-547.

20. Hayashi K., Nakano T., Hashimoto M., Kanekiyo K. and Hayashi T. Defensive effects of a fucoidan from brown alga Undaria pinnatifida against herpes simplex virus infection. Int. Immunopharmacol., 2008; 8: 109-116.

21. Béress A., Wassermann O., Bruhn T., Béress L., Kraiselburd E.N., Gonzalez L.V., de Motta G.E. and Chavez P.J. A new procedure for the isolation of anti-hiv compounds (polysaccharides and polyphenols) from the marine alga Fucus vesiculosus. J. Nat. Prod., 1996; 59: 552.

22. Mandon P., Pujol C.A., Carlucci M.J., Chattopadhyay K., Damonte E.B. and Ray B. Anti-herpetic activity of a sulfated xylomannan from Scinaia hatei. Phytochemistry, 2008; 69: 2193-2199.

23. Bouhilal R., Haslin C., Cherermann J.C., Collic-Jouault S., Sinquim C., Simon G., Cerantola S., Riadi H. and Bourgougnon N. Antiviral activities of sulfated polysaccharides isolated from Sphaerococcus coronopifolius (Rhodophyta, Gigartinales) and Boergeseniella thuyoides (Rhodophyta, Ceramiales). Mar. Drugs, 2011; 9: 1187-1209.

24. Lee J.B., Koizumi S., Hayashi K. and Hayashi T. Therapeutic potential of seaweed derived bioactives to treat non-communicable diseases. Mar. Drugs, 2016; 14: 60.
Carbohydr. Polym., 2010; 81: 572-577.

29. Sato Y., Hirayama M., Morimoto K., Yamamoto N., Okuyama S. and Hori K. High mannose-binding lectin with preference for the cluster of α1–2-mannose from the green alga Boodlea coacta is a potent entry inhibitor of hiv-1 and influenza viruses. J. Biol. Chem., 2011; 286: 19446-19458.

30. Thenin-Houssier S. and Valente S.T. HIV-1 capsid inhibitors as antiretroviral agents. Curr. HIV Res., 2016; 14(3): 270-282.

31. Neushul M. Antiviral carbohydrates from marine red algae. Springer, Netherlands, Dordrecht, 1990; 99–104.

32. Sansone C., Brunet C., Noonan D.M. and Albini A. Marine algal antioxidants as Potential vectors for controlling viral diseases. Antioxidants, 2020; 9: 392-404.

33. Matsuhiro B., Conte A.F., Damonte E.B., Kolender A.A., Matulewicz M.C., Mejias, E.G., Pujol C.A. and Zuniga E.A. Structural analysis and antiviral activity of a sulfated galactan from the red seaweed Schizymenia binderi (Gigartinales, Rhodophyta). Carbohydr. Res., 2005; 340(15): 2392-2402.

34. Wang H., Ooi E.V. and Ang P.O. Antiviral polysaccharide isolated from Hong Kong brown seaweed Hydroclathrus clathratus. Sci. China Ser. C., 2007; 50(5): 611-618.

35. Huskens D. and Schols D. Algal lectins as potential HIV microbicide candidates. Mar. Drugs, 2012; 10: 1476-1497.

36. Lee C. Griffithsin, a highly potent broad-spectrum antiviral lectin from red algae: from discovery to clinical application. Mar. Drugs, 2019; 17(10): 567.

37. Balzarini J., van Laethem K., Peumans W.J., van Damme E.J., Bolmstedt A., Gago F. and Schols D. Mutational pathways, resistance profile, and side effects of cyanovirin relative to human immunodeficiency virus type 1 strains with N-glycan deletions in their gp120 envelopes. J. Virol., 2006; 80: 8411-8421.