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Marine Algae as a Natural Source for Antiviral Compounds

Amar S. Musale, G. Raja Krishna Kumar, Ajit Sapre, Santanu Dasgupta*

Reliance Research & Development Centre, Reliance Corporate Park, Thane-Belapur Road, Ghansoli, Navi Mumbai 400 701, India

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ABSTRACT

Coronavirus or COVID-19 is started from the China, Wuhan city in December 2019 and soon later, spread around 190 countries and declared as pandemic on March 11, 2020 by WHO. Healthcare systems all over the world are fighting against this pandemic. Most of the countries are lockdown for uncertain periods to protect their people from this pandemic as a result the world economy is struggling to cope up with the current situation. Several countries have conducted research studies to produce vaccine or antiviral drug but there is still no specific solution for the prevention or treatment of COVID-19 infection in general. Along with other treatment methods, many countries are fuelling their demand for antiviral compounds from natural resources due to coronavirus. Microalgae and cyanobacteria are excellent source of antiviral activity. Several cyclic or linear peptides and depsipeptides isolated from cyanobacteria are protease inhibitors, which is considered as significant antiviral candidate. Micro and macroalgae were one of the first sources of natural compounds showing in vitro anti-HIV activity. Numerous in vitro or in vivo studies has shown the potential of algae against wild range of viruses. The use of natural products in the manufacturing of drugs is an ancient and well-established practice. Marine microorganisms are known producers of pharmacological and anti-viral agents and may provide unlimited biological resources to produce therapeutic drugs for the treatment and control of viral diseases in humans. Our major intention to write this review to bring world's attention in terms of public health and public policy practices across the world to grab an opportunity from this known healthcare practices, and conventional platform to produce vaccine or antiviral medicine to overcome COID-19.

Keywords: Corona, COVID-19, Pandemic, Antiviral, Public health, Algae, compounds

1 Introduction

The coronavirus 2 (SARS-CoV-2) or severe acute respiratory syndrome was first identified in a few rare pneumonia patients linked to the Wuhan seafood wholesale market in China in December 2019 (Chen et al., 2020; Gorbalenva et al., 2020). Soon later, the corona virus disease 2019 (COVID-19) spread all around the world listed 190 countries and was declared a pandemic on March 11, 2020 (WHO report, 2020). The whole world's healthcare systems are struggling to overcome this pandemic. (WHO report 2020). Due to mandatory isolation or quarantines, millions of lives have been affected seriously. The current effect of the COVID-19 outbreak have brought far reaching consequences on the global economy if spread is not controlled in time (Gorbaleva, et al., 2020; Kupferschmidt, et al., 2020; Corona report). Coronaviruses infect both humans and animals, bats are the major mammals that host the largest variety of coronaviruses appear to be immune to coronavirus-induced illness. (Anthony, et al., 2017). The worlds medical systems

are working hard and fast to control this pandemic by each means, since there are no specific treatments for CoV infection and preventive vaccines are still being explored.

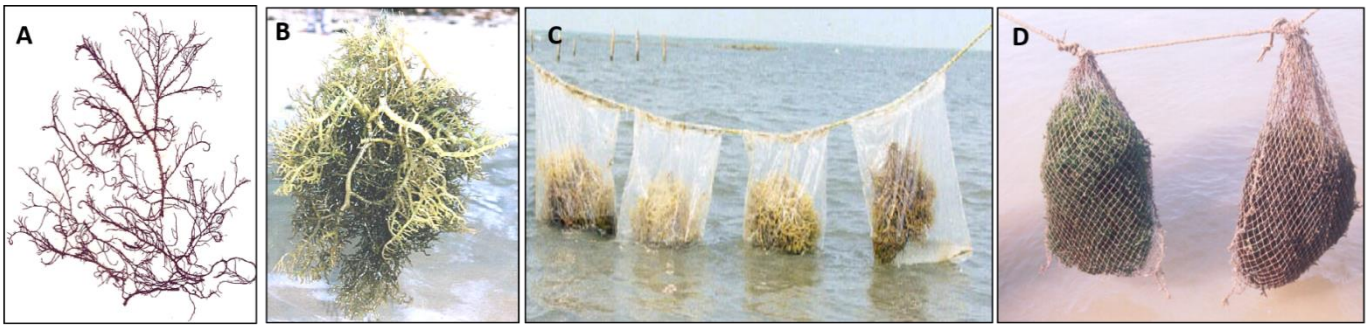
Algae is the major component of any water bodies, ocean, rivers, estuaries etc. Both marine and fresh water algae, cyanobacteria, diatoms have certain crucial compounds that can be effective or act as inhibitory against many viruses. For this pandemic coronavirus numerous research activities are on-going worldwide and the studies have shown that protease inhibitors, which make up the major part of plant derivatives can therefore be very effective in controlling virus-induced infection. The recent study on eight secondary metabolites from conventional medicinal plants on COVID-19 virus protease were performed by using molecular docking analysis. The outcome of the study says that, the compounds investigated can interact with major amino acids in the enzyme flap to inhibit the new coronavirus protease enzyme. Among these secondary metabolites, Curcumin, the secondary metabolite of turmeric has the strongest interaction with the protease enzyme COVID-19. (Mohammadi, et al., 2020).

Blue green algae, Cyanobacteria has protease inhibitors which are very effective against antiviruses. Several cyclic or linear peptides and depsipeptides isolated from cyanobacteria are protease inhibitors, used for the treatment of diseases such as strokes, coronary artery occlusions and pulmonary emphysema (Skulberg, 2004; Singh et al., 2005). Micro and macroalgae were one of the first sources of natural compounds showing in vitro anti-HIV activity (Schaeffer and Krylov, 2000). The antibacterial activity of an aquatic microalgae was first reported for *Chlorella vulgaris* (Pratt and Fong, 1940). An early report of the antimicrobial properties of seaweed extracts was published a decade later (Pratt et al., 1951), and several other papers appeared in the next two decades (Burkholder and Sharma, 1969). This published literature and their results highlights the significance of algae as antiviral, antibacterial and antimicrobial activities. The present review will highlight some of the antiviral activities of algae, which is one of the vast aquatic organisms and which can help in controlling the present pandemic COVID-19. Many countries are looking for some of the strategies or organisms containing antiviral compounds or activities to develop vaccines or antiviral drugs and sanitisers to control this extreme situation. This review could help to the ongoing research efforts on COVID-19, public health and public policy practices across the world.

2 Literature Review & Discussion

2.1 Antiviral Activities of Algae

Microalgae and cyanobacteria are excellent source of antiviral activity. Silva et al., 2018 have shown in his study that, more than 80% inhibition of seasonal influenza A and B replication in MDCK cells occurred from seven extracts derived from microalgae and cyanobacteria in ethyl acetate solvent. Two extracts from Leptolyngbya sp. (cyanobacteria) and Chlorellaceae family (microalgae) inhibited influenza A and B replication and neuraminidase activity, from OST-sensitive and resistance strains and lineages. Thus, these organisms are important for bioprospecting in antiviral research. Similarly, Algae-derived polysaccharides were successfully introduced by Gerber and et al., 1958 as an antiviral agent. They found significant inhibition of mumps and Influenza B virus. Later, red algae polysaccharide fractions were tested as a potent source of antiviral agents against HSV and other viruses in the next two decades. Since then, numerous studies have published for the antiviral potential of various algae-derived polysaccharides. Red macro algae like *Kappaphycus alvarezii, Hypnea musciformis* (carrageenophytes) (Picture 1) cell wall contains sulphated polysaccharides has similar property like porphydium as a potential antiviral drug. (Burkholder & Sharma, 1969; Deig et al., 1974; Ehresmann et al., 1977; Richards et al., 1978, Reddy et.al., 2003; Reddy et al., 2005 (US patent); Gaikwad et al., 2009).



Picture 1: Macro algae A. *Hypnea musciformis* B. *Kappaphycus alvarezii*, Macroalgae cultivation methods C. In plastic bags, D. in nylon bags (Reddy et.al., 2003; 2005)

Table 1: Antivirals derived from marine algae (Lu et al., 2010)

Compound	**Common name**	**Organism**	**Virus**	**Reference**
A1	Microalgae	*Cochlodinium polykrikoides*	Influenza virus A and B; RSV A and B; HSV-1	Hasui et al. (1995)
A2	Microalgae	*Cochlodinium polykrikoides*	Influenza virus A and B; RSV A and B; parainfluenza type 2	Hasui et al. (1995)
AcDa-1		Dictyota menstrualis	HIV-1 replication and RNA-dependent DNA polymerase activity of the viral RT	Pereira et al. (2004)
Calcium spirulan	Cynobacteria	Arthrospira platensis (previously called Spirulina platensis)	HSV-1 replication; Measles replication; Mumps replication; Influenza replication; Polio replication; Coxsackie replication; HIV-1 replication; HCMV replication; Selectively inhibition of penetration into host cells	Hayashi et al. (1996)
Cyanovirin-N Da-1	Cynobacteria	Nostoc ellipsosporum	HIV-1 and HIV-2 and SIV fusion, replication and CPE HIV-1 replication and RNA-dependent DNA polymerase activity of the viral RT	Boyd et al. (1996) Pereira et al. (2004)
Fucoidan	Brown seaweed	Fucus vesiculosus	HSV-1 and HSV-2; HCMV; VSV; Sinbis virus; HIV-1 RT	Béress et al. (1993), Moen and Clark (1993)
Galactan Sulfate	Red seaweed	Agardhiella tenera	HIV-1 and HIV-1 CPE and syncytia formation; HIV-1 binding to host cells; Binding of anti-gpl20 mAb to HIV-1 gpl20; Other enveloped viruses (herpes viruses, togaviruses, arenaviruses, etc.)	Witvrouw et al. (1994)
Griffithsin	Red alga	Griffithsia sp.	HIV-1 glycoproteins (e.g., gpl20, gp41 and gpl60)	Mori et al. (2005)
Naviculan	Diatom	Navicula directa	HSV-1 and HSV-2 adhesion, penetration and replication	Lee et al. (2006)
SAE	Red alga	Schizymenia pacifca	HIV RT; AMV RT; RMLV RT	Nakashima et al. (1987a, b)

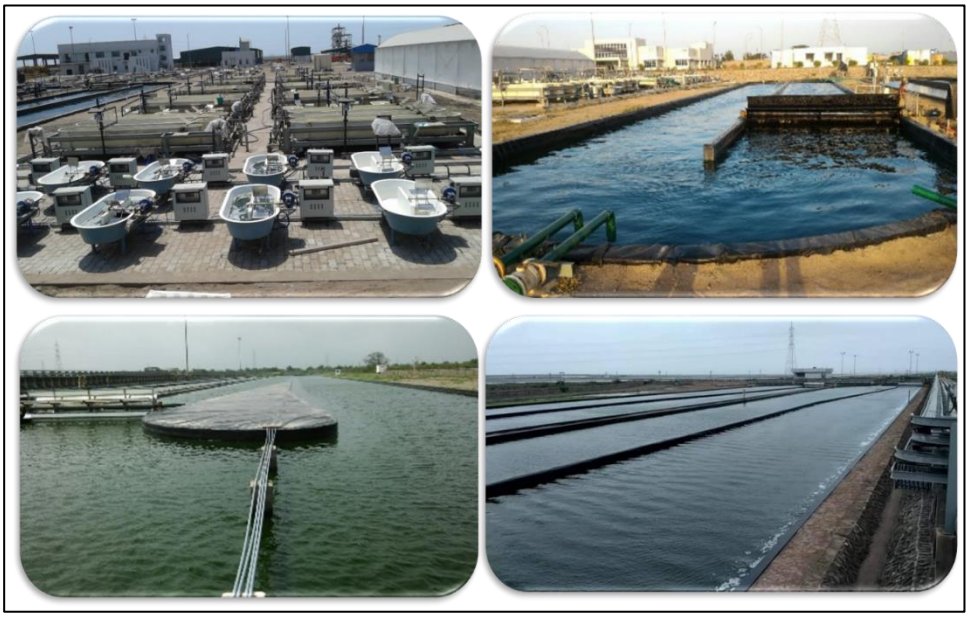
2.2 Future Prospectus of Marine Antiviral Drugs

Numerous in vitro or in vivo studies has shown the potential of algae against wild range of viruses (Table 1). The use of natural products in the manufacturing of drugs is an ancient and well-established practice (Roussis, 2005). Marine microorganisms are known producers of pharmacological and anti-viral agents and may provide unlimited biological resources to produce therapeutic drugs for the treatment and control of viral diseases in humans, livestock and marine farming species, as well as ever more novel compounds. (Bhadury et al., 2006).

However, due to lack of enough knowledge in terms of micro and macro algae cultivation pharmaceutical industries have discouraged from pursuing commercialization of marine-derived bioactive molecules. So far, these industries have focussed their research on limited organisms (Tziveleka et al., 2003), especially whichever is available near shores or collected seasonally or randomly. Along with large scale cultivation of marine algae for the large-scale production of these compounds for the clinical trials, drug development, combinatorial genetics and metabolic engineering could be the future solution for commercial production of these compounds. Another important challenge, as with any antiviral drugs, will be the development of resistance by various viruses. However, when considering the numerous undiscovered organisms in the marine environment, along with their unique metabolites, it is probable that increasing numbers of novel drugs will be discovered that viruses have not yet developed resistance to. It is also important to note that many organisms of different species produce similar classes of compounds, each suited for their unique composition and living environment. The fact that varying derivatives of a common class of compound are being produced by multiple organisms may be a solution. A virus that has developed resistance to a typical drug may not be resistant to other naturally occurring derivatives, which have the potential to possess similar, if not identical, antiviral activities. Should no alternatives be found occurring in nature, the application of biochemical technologies will allow the manipulation of naturally occurring compounds to produce chemical derivatives that are far superior to the original (Bhadury et al., 2006).

2.3 Status of Research and Development Centre, Reliance Industries Limited

Reliance Industries Research and Development center has its diverse germplasm repository of algal strains. Reliance biology R & D team is continuously running 20-acre open pond algae facility (Picture 2) last from few years, without crash. This huge algae cultivation facility is unique in the world and the produced algal biomass can be utilized for the pharmaceutical production of different drugs including antivirals with appropriate regulatory approval.



Picture 2: Reliance algae cultivation facility

3 Conclusion

To the best of our knowledge, Microalgae and cyanobacteria are excellent source of antiviral activity. Several cyclic or linear peptides and depsipeptides isolated from cyanobacteria are protease inhibitors, which is considered as significant antiviral candidate. Micro and macroalgae were one of the first sources of natural compounds showing in vitro anti-HIV activity. Numerous in vitro or in vivo studies has shown the potential of algae against wild range of viruses. The use of natural products in the manufacturing of drugs is an ancient and well-established practice. Marine microorganisms are known producers of pharmacological and anti-viral agents and may provide unlimited biological resources to produce therapeutic drugs for the treatment and control of viral diseases in humans and probably in recent pandemic, COVID-19.

4 Declarations

4.1 Acknowledgments

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4.2 Authors Contribution

All authors equally contributed in the work which is reported in the present manuscript. Before publication of this manuscript all the authors sincerely agreed with the terms and conditions of *AIJR Preprints*.

4.3 Competing Interests

The authors declared that there is no conflict of interest exist in the publication.

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