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Review Article

Marine Algae: Natural Source for Antiviral Compounds to Combat COVID-19

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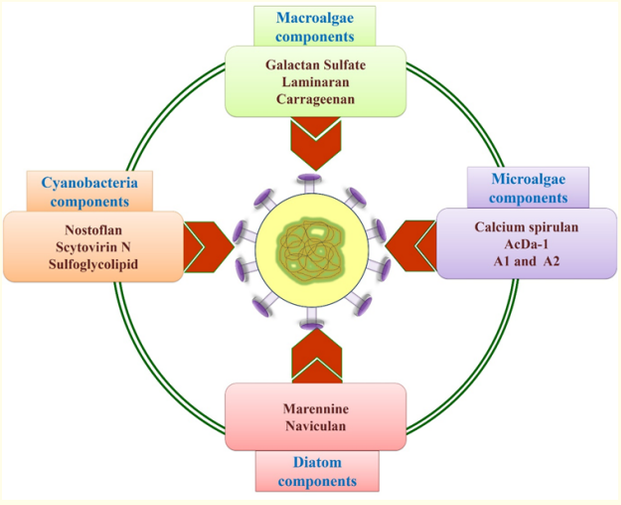
Graphical Abstract



Abstract

The global outbreak of a new coronavirus resulted in a health crisis and declared as a pandemic by World Health Organization, (WHO). To manage the extensive morbidity and mortality rates in humans, is a healthcare solution that provides adaptive immunity during different exposure levels. Healthcare specialists around the world are working to develop an effective vaccine. In cases where humans are resistant to therapy and prophylaxis, harnessing natural sources for chemically diverse antiviral lead entities, has a potential for therapeutic development against deadly diseases. Marine microorganisms are known producers of such unique biomolecules with pharmacological properties with the potential for the treatment and control of various human diseases. In this direction, microalgae, *Cyanobacteria* and macroalgae are an untapped resources for potential antiviral molecules. Several cyclic or linear peptides and depsipeptides isolated from these sources have demonstrated antimicrobial activity, in *in vitro* and *in vivo* studies which has their potential as therapeutic drugs. This review summarizes the current state of understanding of marine-derived biomolecules and their potential as therapeutic drugs. It is assumed that this comprehensive information will encourage scientists and healthcare professionals to research further to understand the potential of these biomolecules for future development towards improving life.

Keywords: COVID-19; Antiviral; Marine Algae; *Cyanobacteria*; Biomolecules; Vaccine; Therapeutic Drugs

Highlights

- Overview of global outbreak COVID-19 pandemic.
- Review of marine algal-derived biomolecules and their potential as antivirals and therapeutic drugs.
- Several cyclic or linear peptides and depsipeptides isolated from *Cyanobacteria* are protease inhibitors which are very effective against viral diseases.
- Reviewed comprehensive information will encourage scientists and healthcare professionals to research further to understand the potential of these biomolecules for addressing present and future corona virus and related issues.
- Implementation of synthetic biology and digital platforms could be very rapid and accurate ways for the production of antiviral drugs to fight against pandemics.

Introduction

Many diseases are infectious and severely affect the health of humans, animals and plants. For example, viral diseases such as Diarrhoea (*Rotaviruses*), Respiratory (*Hantavirus*), *Influenza*-A/H5N1, SARS coronavirus, 2003, AIDS (*Retrovirus*), etc. are few of them. In humans, infectious diseases are responsible for 15 million out of 57 million annual deaths in a global population of 6.2 billion people [1]. Each year, about 2 million people die from acquired immune deficiency syndrome (AIDS), 1.7 million people die from tuberculosis (caused by a mycobacterium, *Mycobacterium tuberculosis*), and more than 1.6 million people die from diarrheal disease caused by infectious pathogens [2].

The SAR- CoV-2 (COVID-19) has spread across the globe and declared as a pandemic by World Health Organization (WHO). The whole world is struggling to overcome this health issue. Due to mandatory isolation or quarantines, millions of lives have been affected financially, socially and emotionally all around the world. The current COVID-19 outbreak have brought far-reaching consequences to the global economy and could have much serious if the spread is not controlled in time [3,4]. Scientists and medical professionals all over the world are working aggressively to control this pandemic.

In an effort to fight against different infectious diseases, scientific advances and efforts have made few major progress. For example, during 1980. the most significant achievement was to overcome the smallpox by vaccination. Again, Polio, Tetanus, Flu Influenza, Hepatitis-A, Hepatitis-B, Rubella, Measles, Chickenpox, etc., have been significantly controlled globally with the help of vaccines. Some diseases like cancer, HIV virus are still remaining throughout the globe. HIV virus alone has killed more than 25 million people in last 25 years. All the scientific efforts are ongoing globally to overcome these diseases.

For many centuries, different natural plant-based medicines are used against various diseases. These medicines have produced by diverse medicinal plants including algae which is one of the best natural source. Algae are the significant component of water bodies such as ocean, rivers, estuaries etc. Both marine and fresh water algae, *Cyanobacteria*, diatoms have certain compounds (Table 1-3) that can be effective or act as inhibitory agents against many infectious diseases or viruses. To overcome the present coronavirus pandemic, numerous research efforts are on-going globally and the studies have shown that protease inhibitors, which make up the major part of plant derivatives can be very effective in controlling virus-induced infection. Recent studies on eight secondary metabolites from conventional medicinal higher plants on COVID-19 virus protease were performed by using molecular docking analysis. The outcome of the study indicates 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 COVID-19 protease enzyme [5].

Cyanobacteria has protease inhibitors which are very effective against viruses. 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 [6,7]. Many published literature and their results highlight the significance of algae as antiviral, antibacterial and antimicrobial activities [8]. The present review will highlight some of the antiviral activities of algae which can possibly help in controlling the current pandemic COVID-19. This review could help to the ongoing research efforts on COVID-19, public health and public policy practices across the world in terms of the usages of natural compounds to overcome the viral diseases like recent COVID-19.

Marine algae of interest

Marine algae are available in ample quantity ranging from diatoms, which are aquatic, microscopic, unicellular organisms, to seaweeds extending over 30 meter. Algae are of economic importance as food, fertilizer, agar-agar, or sources of iodine. Both micro and macroalgae are used for diverse applications such as for human consumption as food and medicines. These algae provide promising source of fatty acids, steroids, carotenoids, polysaccharides, lectins, amino acids, polyketides, agar, alginic acid, carrageenan etc.

[9]. Seaweeds, due to its various biological properties have been recognized as rich and valuable natural resources of bioactive compounds [10].

Bioactive compounds are a secondary metabolite which at low concentrations applies either beneficial or harmful effects on living organisms. Thus, these bioactive compounds obtained from algae are of interest for potential industrial or medical applications [11]. The natural products which have been discovered from both terrestrial and marine living organisms are more than 1 million. Out of which, 20-25% have shown antimicrobial, antifungal, anti-protozoan, anti-nematode, anticancer, antiviral or anti-inflammatory properties [12].

Macroalgae

Macroalgae or seaweeds may be classified into three categories such as *Chlorophyceae* (Green algae), *Pheophyceae* (brown algae), and *Rhodophyceae* (red algae) according to their pigmentation [13]. Seaweeds are being used since many centuries for different purposes such as food, medicines, therapeutics and herbalism, etc. [14].

Sulphated polysaccharides and other bioactive compounds obtained from macroalgae have long been recognized for medical applications. The global utilization of macroalgae is a multi billion dollar industry in terms of its farming, various products and compounds [15]. The interest in same remains high and prior to the 1950's, the products are also increasingly being used in medical and biochemical research however, which was restricted to the traditional and folk medicines [16]. During the 1980s and 90s, the compounds with biological activities or pharmacological properties were discovered in marine bacteria, invertebrates and algae [10]. During 1977-1987 algae have been the source of about 35% of the newly discovered chemicals [17], followed by sponges and cnidarians (22%). However, since 1995, new products from seaweeds started decreasing and attention has now shifted to marine micro-organisms [18]. However, marine algae especially macroalgae contains polysaccharides which has bioactive compounds and highly potential for pharmaceutical or therapeutic industries. Over the last three decades, macroalgae used for the discovery of metabolites and bioactivities has been increased significantly. Many modern research techniques are available to extract the chemicals or natural bioactive compounds of interest from macroalgae [19].

Microalgae

Microalgae is a diverse group of photosynthetic microorganisms that converts CO_2 into valuable compounds such as, biofuels, foods, feed and pharmaceuticals etc. [20]. For many centuries, microalgae have been used as food in ancient civilizations in Asia, Africa and South America. However, in the middle of the last century microalgae biotechnology began to develop and started extensive screening of novel compounds which may leads to the therapeutically useful agents [21].

Microalgae offer an excellent opportunity for the isolation of natural compounds of significant commercial interests in diversified industries such as pharmaceuticals, cosmetics etc. This encouraging fact makes microalgae as potential raw material with a great deal of added value [22]. Many researchers have already shown that, algae may produce antiviral compounds [23,24].

Other selective algae

Cyanobacteria

Cyanobacteria are prokaryotic photosynthetic, oldest microorganism present on the earth [25], which are diverse, highly specialized and well adapted group to various ecological habitats. *Cyanobacteria* are potentially very rich source of diverse chemical compounds with various industrial applications [26,27]. *Cyanobacteria* are one of the best model organisms for various studies and thus, it is well studied group from a biotechnology point of view. Many scale-up technologies such as open pond, photobioreactors (PBR's) have been developed by algae researchers worldwide [28], due to its high value of future novel therapeutic or pharmaceutical compounds exploration point of view.

Cyanobacteria have been considered a rich source of secondary metabolites with potential diverse biotechnological applications in the pharmacological field. Thus, production of bioactive compounds with commercial and medical applications has increased interest in studying these organisms [27]. *Cyanobacteria* has rich source of novel compounds with broad spectrum activities such as antiviral, anti-inflammatory, protease inhibition, antimicrobial, immune stimulating agents, antitumor, anticancer, anti-HIV (human immunodeficiency virus), anticoagulant, antifungal, antimalarial, antiprotozoal, and antituberculotic which have been yet unexplored except very few of them [29,30].

Diatom

Diatoms are diverse and well nanostructured cell wall organisms which has potential bio-geo chemical properties. The photoautotrophic diatoms play significant role in ocean biogeochemical regulation by carbon fixation, which produces oxygen by carbon sequestration through uptake of carbon dioxide and sunlight in the environment. The biggest advantage for pharmaceutical industries from diatoms which holds high contents of oil, saturated

and unsaturated fatty acids, steroids, lipids and other primary and secondary metabolites. Bioactive metabolites of diatoms can be act as anticancer, antioxidant and antibacterial drugs [31]. Marine microorganisms or diatoms are known for its proteins, polysaccharides and bioactive compounds which acts as a platform to combat pathogens, chronic diseases and viruses. Diatom derived bioactive compounds have been used in various therapeutic applications [32].

Antiviral compounds :General mode of action of antiviral compounds

In the prevention of life-threatening bacterial diseases, the use of microbial of synthetically produced antibiotics are being commonly used from many decades. The development of drugs to effectively combat viral diseases, however has proven to be much more difficult. However, the advanced microbial techniques such as the coupling of three-dimensional structure and replication cycles of viral molecules, are now making possible the development of highly specific and effective antiviral drugs.

Generally, a drug molecule, without being too toxic to the body's cells can act as an antiviral drug if, inhibits some stage of the virus replication cycle. Further, the possible mode of actions of anti-viral agents may include- active extracellular virus particles, prevent viral entry or attachment, prevent replication of the viral genome, prevent synthesis of specific viral proteins, prevent assembly of release of new infectious virions and act as a protease inhibitor.

For example, the new drug Rupintrivir (Pfizer) is an inhibitor of rhinovirus protease 3C which act as a protease inhibitor and protease action to cut a polyprotein into individual viral proteins [33]. In another study researchers have described the genotype and pathogenesis of an inhibitor resistant coronavirus. Further, they showed that the inhibitor-resistant virus is attenuated both in cell culture and in infected mice [34].

Macro algae-derived antiviral compounds

Polysaccharides or glycans, are the most abundant form of carbohydrate materials in the nature which has gained significant applications in biomedical and pharmaceutical industries [35]. Algae-derived polysaccharides were successfully introduced as an antiviral agent [36]. 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 Herpes Simplex Virus (HSV) and other viruses in the next two decades. Since then, numerous studies have been published for the antiviral potential of various algae-derived polysaccharides. Red macro algae like *Kappaphycus alvarezii, Hypnea musciformis* (carrageenophytes) (Figure 2) cell wall contains sulphated polysaccharides, has similar property like Porphydium as a potential antiviral drug [8,37-40].

Three extracts (Diethyl ether, acetone and ethanol) of ten marine macroalgae belonging to Chlorophyceae, *Rhodophyceae* and *Phaeophyceae* isolated from Red sea, for its antibacterial, antifungal and antiviral activities against different organisms including Newcastle Disease Virus (NDV)-(Paramyxoviridae) which is responsible for acute respiratory distress in chicken [41]. Selectively, as far as antiviral activity is concerned, the result of the ethanol extracts showed that seven of the ten tested algal extracts have strong activities against NDV. In another review article they have explained in detailed about various algal polysaccharides containing antiviral activities, including carrageenan, alginate, fucan, and laminaran [35] (Figure 1). Moreover, different mechanisms of action for these polysaccharides, such as inhibiting the binding of virus into the host cells or suppressing DNA replication and protein synthesis. The entire review gives insightful view about antiviral studies of algae derived polysaccharides, mechanism of action towards their development as natural antiviral agents (Table 1).

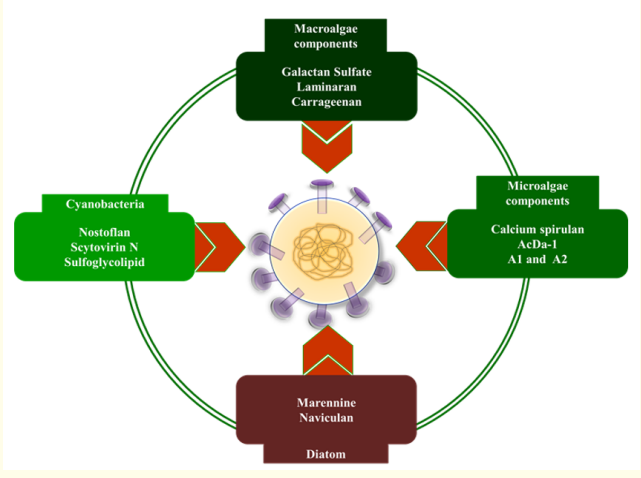


Figure 1: Schematic representation of biologically derived antiviral components against viruses.

Porphyridium cruentum, marine red algae have medicinally significant compounds in its exopolysaccharides [42]. During the growth when it reaches to the stationary phase it secretes exopolysaccharide (EPS) with sulphated polysaccharides which has the potential of antibacterial, antiviral and anti-inflammatory activity against human and animal viruses [43]. The antiviral activity of the red microalga *Porphyridium* sp. was also confirmed against herpes simplex virus [44].

Compound	Common name	Organism	Virus	Reference
Galactan Sulfate	Red alga	*Agardhiella tenera*	HIV-1 and HIV-1 CPE and syncytia formation; Other enveloped viruses (herpes viruses, togaviruses, arenaviruses, etc.)	[45]
Griffithsin	Red alga	*Griffithsia sp.*	HIV-1 glycoproteins (e.g., gpl20, gp41 and gpl60)	[46]
Sea Algae extract	Red alga	*Schizymenia pacifca*	HIV RT; AMV RT; RMLV RT	[47]
Carrageenan	Red alga	*Chondrus*, *Gigartina*, *Hypnea*, and *Eucheuma*	Influenza virus, DENV, HSV-1, HSV-2, HPV, HRV, HIV	[48]
	Red alga	*Porphiridium sp.*	Herpes simplex virus.	[44]
Galactan	Red algae	*Callophyllis variegate, Agardhiella tenera, Schizymenia binderi, Cryptonemia crenulata*	HSV-1, HSV-2, HIV-1, HIV-2, DENV, HAV	[49]
Fucoidan	Brown alga	*Fucus vesiculosus*	HSV-1 and HSV-2; HCMV; VSV; Sinbis virus; HIV-1 RT	[50]
Alginate	Brown alga	*Laminaria hyperborea*, *Laminaria digitata*, *Laminaria japonica*, *Ascophyllum nodosum*, *Macrocystis pyrifera*	HIV, IAV, HBV	[51]
Fucan	Brown alga	*Adenocytis utricularis*, *Undaria pinnatifida*, *Stoechospermum marginatum*, *Cystoseira indica*, *Cladosiphon okamuranus*, *Fucus vesiculosus*	HSV-1, HSV-2, HCMV, VSV, Sindbis virus, HIV-1	[52]
Laminaran	Brown alga	*Fucus vesiculosus*, *Saccharina longicruris*, *Ascophyllum nodosum*	Influenza A virus	[53]

Table 1: Antivirals derived from marine macro algae.

Micro algae-derived antiviral compounds

Algae may produce antiviral compounds is a known fact [23]. However, there is yet to be an opportunity to hunt for many unknown bioactive compounds from these natural resources. A sulphated polysaccharide, calcium spirulan (Ca-SP) isolated from *Spirulina platensis* has been showed to possess antiviral activities (Figure 1). This study reveals that, a sulphated polysaccharide composed of different compounds which was found to be inhibit the several enveloped viruses such as, Herpes simplex type-1, Human cytomegalovirus, measles virus, mumps virus, influenza-A virus and HIV-1 [54,55].

The aqueous extracts of *Porphyridium cruentum, Chorella autotrophica* and *Ellipsoidon* sp. showed significant inhibition of the *in vitro* replication of haemorrhagic septicemia virus and African swine fever virus [56]. The production of retroviruses (murine leukemia virus- MuLV) were significantly inhibited by red microalgal polysaccharides and cell transformation by murine sarcoma virus (MuSV-124) in cell culture. Polysaccharides derived from red microalgae significantly inhibited the production of retroviruses (MuLV) and cell transformation by MuSV-124 in cell culture [57] (Table 2).

Other selective marine algae-derived antiviral compounds

Microalgae and *Cyanobacteria* are known to produce many antioxidant molecules including antimicrobial, anticancer and antiviral activities [41]. Hence, the usages of these organism have increased for research and development purposes. Similarly, compared to other higher plants microalgae and *Cyanobacteria* can be scaled up in minimum period with significant growth rate to produce antiviral compounds [60]. The sulphated polysaccharides of *Cyanobac-*

Compound	Common name	Organism	Virus	Reference
A1	Microalgae	*Cochlodinium polykrikoides*	Influenza virus A and B; RSV A and B; HSV-1	[58]
A2	Microalgae	*Cochlodinium polykrikoides*	Influenza virus A and B; RSV A and B; parainfluenza type 2	[58]
AcDa-1		*Dictyota menstrualis*	HIV-1 replication and RNA-dependent DNA polymerase activity of the viral RT	[59]
Calcium spirulan	Microalgae	*Spirulina* platensis	Herpes simplex virus type 1, human cytomegalovirus, measles virus, mumps virus, influenza A virus, and HIV-1	[54-55]
	Microalgae	*Chlorella autotrophica* and *Ellipsoidon* sp.	Haemorrhagic septicemia virus and African swine fever virus	[56]
	Microalgae	*Porphyridium* sp.	MuSV-124, MuSV/MuLV	[57]
	Microalgae	P. *aerugineum*	MuSV-124, MuSV/MuLV	[57]
	Microalgae	*Rhodella reticulata*	MuSV-124, MuSV/MuLV	[57]

Table 2: Antivirals derived from marine microalgae.

teria, Spirulan has a potential antiviral activity against herpes simplex virus type 1 (HSV-1) and the human immunodeficiency virus type 1 (HIV-1) [61].

In one study, more than 80% inhibition of seasonal influenza A and B replication in Madin-Darby-Canine Kidney (MDCK) cells occurred from seven extracts derived from microalgae and *Cyanobacteria* in ethyl acetate solvent [62]. Two extracts from *Leptolyngbya* sp. (*Cyanobacteria*) and *Chlorellaceae* family (microalgae) inhibited influenza A and B replication and neuraminidase activity, from the oseltamivir, (OST, a neuraminidase inhibitor) sensitive and resistance strains and lineages. Thus, these organisms are important for bioprospecting in antiviral research. Similarly, an *in vitro* study has showed that, red and blue green algae has potential antiviral lectins which can combat against Hepatitis C viruses [63]. Spirulan and Ca-spirulan from significant antiviral cancer polysaccharides are from *Spirulina* sp. These compounds from the extracts of *Cyanobacteria* showed potent and broad-spectrum activity against HIV-1, HIV-2, H, influenza and a series of other enveloped viruses. At the same time components such as cynovirin-N and scytovirin, the carbohydrate binding proteins are being developed as potential virucidal drugs [64] (Table 3).

The extraction of polysaccharides marine microalgae viz. Naviculum from diatom *Navicula directa*, A1 and A2 from dinoflagellates, *Cochlodinium polykrikoides* showed antiviral activities against several enveloped viruses, such as HIV-1, HSV-1 or influenza virus type A (IFV-A) [65]. Diatoms has excellent antiviral properties with polyphenolic and antioxidant compounds e.g. diatoms, *Haslea* sp. [66]. An antiviral and antioxidant potential of marine microorganisms which can be useful to develop a natural "antiviral pharmacy" to combat against diverse viruses [67] (Figure 1).

Molecular tool development for targeted drugs (Synthetic biology and digital platform)

In current pandemic to fight against COVID-19 the molecular farming community is extensively active in establishing plant-based processes to produce diagnostic and therapeutic proteins. Currently, two EU consortia viz. H2020 projects Pharma-Factory and Newcotiana are focusing on molecular farming to establish plant-based platforms for the industrial applications to develop such proteins on high priority. At present, manufacturing of protein antigens and antibodies for diagnostic kits, therapeutic products, antiviral drugs, vaccines and scalable production systems is global urgency hence cooperation with such production companies for product formation and its commercialization is very crucial. Such opportunity creations or models will not only help in this present COVID-19 situation but also in future pandemics [70].

Recently, due to rapid applications of biotechnological or molecular tools in drug discovery and vaccine development, pharmaceutical companies are in a decent position in quality drugs production at industrial scales in stipulated time. Before the dawn of biotechnology era, drug discovery and development took many decades to produce effective medicines against different types of infectious diseases. Advancement in genomics, proteomics,

Compound	Common name	Organism	Virus	Reference
Calcium spirulan	*Cyanobacteria*	*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	[54]
Cyanovirin-N Da-1	*Cyanobacteria*	*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	[68] [59]
Spirulan	*Cyanobacteria*	*Spirulina* sp.	HIV-1 and HIV-2 (inhibit reverse transcriptase) HSV, influenza	[64]
Nostoflan	*Cyanobacteria*	*Nostoc flagilliforme*	HSV-1 (HF), HSV-2 (UW-268), HCMV(Towne) Influenza (NWS), Adeno (type 2), Coxsackie (Conn-5)	[64]
Scytovirin N	*Cyanobacteria*	*Scytonema varium*	HIV-1 (interacts with oligosaccharides conaining a1-2, a1-2, a1-6 tetramannose units of envelope glycoproteins, gp120, gp160, gp41)	[64]
Sulfoglycolipid	*Cyanobacteria*	*Scytonema* sp.	HIV-1 (inhibit reverse transcriptase and DNA polymerases)	[64]
Marennine	Diatoms	*Haslea* sp.	HSV-1	[66]
Naviculan	Diatom	*Navicula directa*	HSV-1 and HSV-2 adhesion, penetration and replication	[69]

Table 3: Antivirals derived from other marine algae.

Artificial Intelligence (AI) based modelling and prediction helped further to expedite drug development and vaccine production. *In vitro* studies of sulphated Polysaccharide extracted from the seaweed *Saccharina japonica* effectively bind to the S-protein of SARS-CoV-2 with less toxicity when compared to Remdesvir medicine [71]. Recently researchers from Western University (Canada) and Suncor have jointly proposed to use micro algae as diagnostic kits for COVID 19. In another study by University of Pittsburgh School of Pharmacy planned to express Q-griffithsin molecule from Griffithsia in tobacco plant and use as nasal drops. Further, it has compared the over expression of Griffithsin in various expression systems [72]. In *E. coli* (fermenter based) yield was 819 mg/L and after purification 542 mg/L; tobacco leaves yield 1g/kg and after purification 300mg/kg; in rice seeds yield was 301 mg/kg dry seed and after purification 223 mg/kg. Countries like Israel and Italy working on micro algae as edible drugs [73]. Docking and *in silico* toxicity assessment of 3 molecules of phycocyanobilin, phycoerythrobilin and folic acid from *Arthrospira* showed anti-SARS-CoV-2 activity [74].

Another recent studies state that, Guangxi University and Huazhong Agriculture university researchers used a 3D homology model of the sequence to screen against more than 32,000 potential antiviral phytochemicals and traditional Chinese medicinal compounds. This effort led to 9 specific plant molecules that may be used to develop drugs against COVID 19 [75]. Indonesian researchers used molecular docking to search for potential inhibitors of COVID-19 main protease (Mpro), a potential drug target. They searched a bioactive compound in which luteolin-7-glucoside, demethoxycurcumin, apigenin-7-glucoside, oleuropein, curcumin, catechin, and epicatechin-gallate have the best potential to act as COVID-19 Mpro inhibitors. Further studies have suggested for its confirmations and potential medicinal usages [76]. University of Maragheh also conducted molecular docking study which led to nine neutral and low risk drugs that have inhibitory activities against COVID-19 protease [77]. These advanced synthetic biology and digital platform approaches may help to produce targeted medicines at industrial scales in very less time to combat against infectious viral and other diseases.

Conclusion

The present COVID-19 pandemic has highlighted the importance and priority of discovery compounds from marine natural

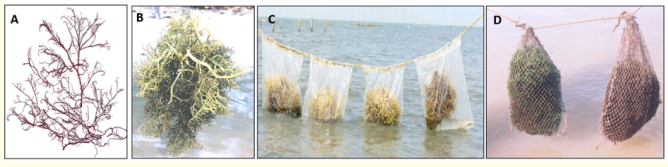


Figure 2: Macro algae A. *Hypnea musciformis*. B. *Kappaphycus alvarezii*, Macroalgae cultivation methods. C. In plastic bags. D. in Nylon bags [38,39].

resources for the prevention and treatment of severe and acute viral infections. To the best of our knowledge, Macro algae, micro-algae, *Cyanobacteria* and diatoms 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. Numerous *in vitro* or *in vivo* studies has shown the potential of algae against wide range of viruses. The use of natural products in the manufacturing of drugs is an ancient and well-established practice. In our opinion, the pharmaceutical potential of marine algae deserves more scientific attention, inter-disciplinary research along with its diverse habitat explorations to find novel compounds to control viral diseases in humans and probably in recent pandemic, COVID-19.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

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