# Could microalgae-derived antiviral compounds combat SARS-CoV-2 and other viruses?

By Dr. Liji Thomas, MD Jun 28 2021

With the emergence of the ongoing coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a frantic search for effective and safe antivirals was initiated. In the absence of any major successes, vaccines have become the predominant means of pandemic management worldwide.

A new review article published in the journal *Antibiotics* reports the presence of a large number of bioactive compounds in microalgae that target chemical structures present only in their structure.

*Study: Evaluation of Microalgae Antiviral Activity and Their Bioactive Compounds. Image Credit: Chokniti Khongchum / Shutterstock*

## Background

Marine algae already contribute almost a tenth of biomedical molecules, for some of which scientists depend entirely on these microcellular organisms. Secondly, microalgae proliferate abundantly at low energy costs, while producing high amounts of medicinal compounds.

Microalgae produce a variety of such chemicals, such as carbohydrate-binding proteins, called lectins, that bind directly to viral glycoproteins added post-translationally via specifically-oriented carbohydrate recognition domain (CRDs); polysaccharides with sulfate groups and acidic polysaccharides; pigments; peptides and proteins; flavonoids and polyphenols; and glycolipids.

# Types of antiviral compounds

Cyanobacterial lectins include Agglutinin OAA, Cyanovirin-N (CV-N), Microcystis Viridis Lectin (MVL), Microvirin, and Scytovirin, from species such as *Oscillatoria agardhii* strain NIES-204, *Nostoc ellipsosporum* and *Microcystis aeruginosa* PCC7806. These inhibit a range of viruses such as human immunodeficiency virus (HIV) 1 and 2, hepatitis C virus (HCV), the hemorrhagic fever virus ZEBOV, influenza A, B viruses, and herpes virus simplex (HSV).

Polysaccharides are produced by the well-known *Spirulina* and *Porphyridium* microalgae. Sulfate polysaccharides may occupy the viral attachment sites on the viral envelope via the negative charge on the sulfate group that binds to the positive charges on the envelope, creating a non-reversible complex.

Other promising sulfate-polysaccharides from *Spirulina* include the calcium-spirulan (Ca-SP), which is active against HIV1 and HSV, as well as the cytomegalovirus (CMV), mumps virus and influenza virus. *Porphyridium* is red, whereas the other is green. The former has an envelope rich in sulfate polysaccharides that inhibit tumor growth, bacterial and viral growth.

The Varicella zoster (HH3), murine leukemia virus and HSV are also inhibited by *Porphyridium* species. Other microalgae produce sulfate polysaccharides that inhibit picornaviruses (causing diverse conditions ranging from myocarditis and encephalitis, through neurological and reproductive diseases, to diabetes), and parainfluenza viruses, responsible for severe pediatric respiratory disease, as well as HIV, HSV, and mumps viruses.

A well-known acidic polysaccharide from this class of organisms includes Nostoflan from a *Nostoc* species, highly active against HSV by inhibiting the viral envelope glycoprotein synthesis.

Microalgal pigments such as pheoporbide and carotenoids are used in biomedical applications on a wide scale. These may inhibit viral entry as well as having post-viral entry effects.

## Carotenoids inhibit cytokine storm

Carotenoids, in particular, may counteract the cytokine storm implicated in severe COVID-19 by inhibiting the excessive production of antiviral reactive oxygen species (ROS) and reactive nitrogen-oxygen (RNS). While these are useful in reducing viral replication, they also activate transcription nuclear factor-KB (NF-KB), inducing the JAK/STAT inflammation pathway.

Since the cytokine storm also induces life-threatening acute respiratory distress syndrome (ARDS), and acute lung injury (ALI), associated with multi-organ damage, carotenoids may have a still higher utility beyond their direct effects on the virus.

Other pigments with antioxidant and antiviral activity include phycobiliproteins and astaxanthin. The latter is reported to reduce both ARDS and ALI.

Some microalgae produce peptides that show antiviral activity in aquaculture and in silkworms. Flavonoids have potent antiviral activity, such as marennine, a bluish-grey pigment from *Haslea ostrearia*, active against HIV and HSV. This can be manufactured in a bioreactor and is used in food, coloring agents and cosmetics. It

Glycolipids are also produced by microalgae, and some show potent virucidal effects against HSV2 and HIV, using different mechanisms of action such as DNA polymerase inhibition or damaging the viral envelope to promote viral lysis.

## Potential for vaccine production

Apart from microalgal compounds, they have the ability to act as vectors expressing double-stranded RNA in viruses and thus interfere with viral mRNA to inhibit viral replication. One example is the green microalga *Chlamydomonas reinhardtii*, used against a shrimp virus, the yellow head virus.

Other vaccines could be created using microalga bioengineered in other ways.

## Dietary supplements with anti-SARS-CoV-2 activity

Microalgal supplements could be used in the diet to counteract SARS-CoV-2 infection. Spirulina, already known for its high nutritional value, also activates the immune system by virtue of its Braun-type lipoproteins that trigger Toll-like receptors. A spirulina-rich diet may help fight HIV infection, which may be linked to the lower incidence of HIV infection in some parts of the world, including Asia, where spirulina is consumed in larger amounts.

Spirulina improves the leukocyte count. Its fatty acids are generally linked to a higher number of immune cells and may also help to degrade the viral lipid membrane and envelope.

Additionally, spirulina enhances insulin sensitivity because of the antioxidant effects of the phycobiliproteins, thus regulating interleukin-6, a mediator in insulin signaling, and increasing lipoprotein lipase activity, which is typically abnormal in these patients. Moreover, it may prevent side effects following vaccination. Finally, its antioxidant content is high.

An asthaxanthin-rich diet could also help modulate cytokine release and improve the outcomes in SARS-CoV-2 infection. Increased immune activity, especially an increase in lymphocytes, is also seen with this nutrient, and is relevant in this infection, typically characterized by lymphopenia.

A diet enriched with *Chlorella* and *Hematococcus pluvialis* could also help prevent severe symptomatic COVID-19, therefore. *Chlamydomonas reinhardtii* also improves gut health via its phenolic compounds, again benefiting patients with COVID-19 who frequently have an altered gut microbiome.

Other microalgal products already used in foods, such as chitosan and carrageenan, are also worth further examination for their activity against SARS-CoV-2. The former regulates cholesterol levels.

## Conclusion

Overall, therefore, microalgae "*display eco-friendly and eco-sustainable characteristics, produce a high variety of antiviral compounds, and can be used as a supplement in diets without collateral effects. Moreover, these organisms are considered very good candidates for the genetic engineering approach*."

**Journal reference:**


- Carbone, D. A. et al. (2021). Evaluation of Microalgae Antiviral Activity and Their Bioactive Compounds. *Antibiotics*. https://doi.org/10.3390/antibiotics10060746, https://www.mdpi.com/2079-6382/10/6/746.



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