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Spirulina (Arthrospira Spp) as A Complementary Covid-19 Response Option: Early Evidence of Promise

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Abstract

The COVID-19 pandemic poses a profound threat to human health across the world. A growing body of evidence suggests that dietary choice can support pandemic response efforts. This paper asks whether spirulina, a type of edible microalgae, may offer a means of reducing COVID-19 risk. This question follows from spirulina's observed antiviral effects vis-à-vis other viral diseases. Questions about possible complementary therapies remain important due to the ongoing threat posed by COVID-19, given major gaps to vaccine rollout and the proliferation of mutant variants. The paper is based on a narrative review of the academic literature relevant to this question. The 25 papers identified were grouped and summarised, then discussed. The evidence reported suggests spirulina may have prophylactic and therapeutic efficacy against SARS-CoV-2 via several pathways, though further investigation is needed to verify the linkages identified. Incorporating spirulina into diet might thus offer a way to lower COVID-19 risk. This option may moreover be particularly helpful for at-risk populations, such as those in the Global South where many remain unvaccinated and food insecurity is widespread. This review reports findings in non-technical language and could inform actions by diverse stakeholders, including researchers, governments and households.

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Introduction

Covid-19 Continues to Pose a Threat to Lives and Livelihoods

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus. The COVID-19 pandemic has had profound adverse impacts across the world. As of 7 February 2022, 387 million confirmed cases have been recorded worldwide along with 5.7 million deaths,[1] though other metrics suggest excess deaths since the pandemic's onset number 24.3 million.[2]

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Some COVID-19 survivors are left with lasting health problems notably 'long COVID', which can have life-derailing symptoms such as breathing problems, deep fatigue, joint pain, brain fog and heart palpitations.[3] The pandemic is also having devastating impacts on jobs, businesses and economies.[4]

The process of vaccinating the world's population is well underway, with over 10.2 billion doses administered as of 7 February 2022 and vaccinations proceeding at an average rate of 28 million per day.[5] While national vaccination campaigns are making headway, full roll-out will take time. Worryingly, this process remains starkly inequitable, as reflected in counts of 'fully vaccinated' persons in countries from different income categories. As of 7 February 2022, these counts were: high income (72%), upper-middle income (75%), lower-middle income (42%) and low income (6%).[6]

Figure 1 illustrates these trends and breaks them down by country category. It shows that high income countries are consistently well vaccinated, while low income countries are consistently poorly vaccinated. The two intermediate categories are more mixed, but in both cases one large country (represented by a big dot) stands out as better vaccinated than others and raises the average for its category, namely China for upper-middle income countries (UMICs) and India for lower-middle income countries (LMICs).

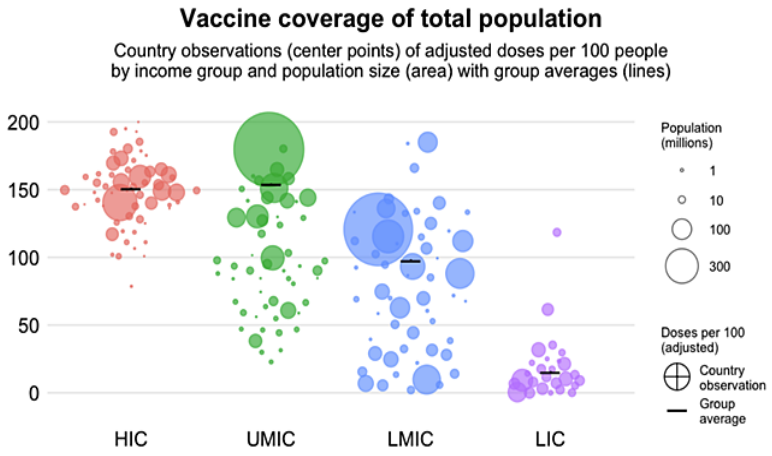

Fig. 1: Vaccine coverage of population in different country categories, as of 7 February 2022[7]

Such inequities sadly seem to be accepted by some news outlets.[8] Meanwhile, a joint statement by leaders from the charitable sector has argued that "in our interdependent world no one is safe until everyone is safe".[9]

Vaccination efforts also face major challenges. Some countries continue to experience supply constraints, while many children remain ineligible for vaccines.[10] Vaccine scepticism by some communities complicates uptake, especially when rooted in negative past experiences with the medical system.[11] The proliferation of mutant SARS-CoV-2 variants raises thorny questions, such as implications for the infection rate, severity of illness and continued efficacy of vaccines.[12,13] In the meantime, the unvaccinated arguably face greater risks than ever,[5] even as some experts suggest vaccine escape is 'inevitable'.[14]

If vaccination will take time and could prove complicated, relying chiefly on vaccinations to control the pandemic is risky.[15] In such a scenario, examining complementary pandemic response options seems prudent.

Dietary Measures as Possible Pandemic Response Options

Dietary measures including use of nutritional supplements offer possible pandemic response options that could complement medical and public health measures like vaccination and social distancing.

The capacity of diet and nutrition to support immune-system function vis-à-vis viral diseases is well-established. A recent review of evidence from humans and animals concluded that dietary supplements can offer a safe, effective and low-cost means to build immune resistance to viral diseases, and recommended nutrition be incorporated into government strategies to limit the impact of viral infections including COVID-19.[16] A review of clinical trials examined the scope for supplements such as vitamins, minerals, nutraceuticals and probiotics to enhance immunity to viral infections like COVID-19. It found various supplements helped prevent or manage such infections and suggested they may be useful against COVID-19.[17] In vivo experiments with mice found that dietary supplements can help them cope with coronavirus and other viral infections, and identified several as especially promising, including elderberry, selenium and spirulina.[18]

Conversely, deficiencies in protein, carbohydrates or nutrients can impair immune system function, and are associated with higher rates of viral infection and increased risk of morbidity and mortality.[17] COVID-19 risk factors like obesity and metabolic syndrome are also linked in part to diet.[19,20] Poor nutrition can moreover delay COVID-19 recovery and compound complications for survivors.[21]

One scenario in which using foods or their bioactive extracts to boost immune function could be key to reducing disease risk is where communities face malnutrition, since this condition can impair the immune system, suppressing immune functions that are fundamental to host protection. Various studies have demonstrated that adding deficient nutrients into human or animal diets can improve their immune function and resistance to infections.[22]

An estimated 811 million people currently face hunger while 2 billion are malnourished.[23] Widespread micronutrient deficiencies notably in parts of the Global South contribute to problems like intellectual impairment and decreased capacity for work.[24] Deficiencies of key nutrients – e.g., calcium, dietary fibre, omega-3 fatty acids – are also common in the Global North, notably among vulnerable groups.[25]

This set of factors has led to calls for more research on the linkages between diet and disease, as well as stronger national programmes on diet.[26] The World Health Organization (WHO) issued dietary guidelines for the COVID-19 pandemic that call for eating certain foods while limiting use of others to reduce infection risk.[27] Target foods include fresh fruits and vegetables, whole grains, beans, nuts, fish and unsaturated fats. Those to eat less of include processed foods, salt, sugar and saturated fats like those found in fatty meats or butter.

This diet resembles the 'healthy reference diet' elaborated by the Lancet Commission,[28] an expert body that issued a landmark report in 2019. This report sought to provide an "evidence-based starting point" for addressing current realities of poor nutrition and unsustainable agricultural production.[29] It suggested that changes to diet and food production could create 'win-win' outcomes for human and planetary health.[30]

Microalgae as a Possible Target Food

Algae is a term that covers a diverse group of aquatic organisms ranging from freshwater microalgae to large seaweeds. Like plants, algae typically generate energy from sunlight via photosynthesis, but they differ from plants in basic ways, such as growing in water and lacking rigid cell walls. Some algae are seen as harmful, such as those that cause 'algal blooms' which can kill aquatic organisms by depleting oxygen.[31] Others can be used to meet key human needs like food, feed and energy supply.

This review paper focuses on microalgae from the genus Arthrospira, which are commonly known as spirulina. These freshwater algae grow in alkaline water and are used as a dietary supplement, among other applications. Spirulina has been a traditional food for centuries in places where it occurs naturally, such as for the Kanembu people of Chad, and it was a key food for the Aztec civilisation.[32]

Two factors explain the paper's focus on spirulina as a possible pandemic response option. First, a pre-pandemic body of evidence suggested spirulina has antiviral efficacy against several viral diseases, making its efficacy against SARS-

CoV-2 an obvious question. Second, a significant body of research and experience with spirulina already exists, so any evidence on its relevance to COVID-19 could be set in context.

Materials and Methods

The present analysis asked whether spirulina may have efficacy as a means of reducing COVID-19 risk, given pre-existing evidence of its antiviral effects vis-à-vis other diseases. It examined this question via a narrative review of the academic literature conducted using Web of Science, Pub Med, Cochrane, Scopus and Google Scholar. Two sets of searches were conducted, namely "spirulina AND COVID" and "spirulina AND pandemic". All 25 papers identified were included in the analysis, given the small size of the evidence base in light of the short time for such evidence to accrue. All were published in academic journals except for one pre-print.[33]

Analysis of the 25 papers identified included grouping them into categories then summarising their headline findings vis-à-vis spirulina and COVID-19, followed by a discussion. Aspects of findings most relevant to debates on pandemic response efforts were emphasised. The general benefits and risks of spirulina consumption were also briefly described.

This review has several characteristics that distinguish it from the prior reviews it cites. While some prior reviews considered whether different algae species might offer options to help manage COVID-19, this review focuses on one widely available alga that has been extensively studied. It aims to glean headline findings from studies along with their practical implications rather than report detailed technical analysis. It shares findings in non-technical language to foster wider access beyond academics in relevant disciplines. It considers how this alga may be particularly useful to pandemic response efforts in countries with large at-risk populations.

This review also builds on these earlier reviews. Notably, it distils provisional lessons to support COVID-19 response efforts by public health authorities and households looking to manage pandemic risk. It also flags the need for further research into these linkages in terms that could resonate with potential enablers such as government officials and funding agencies.

The approach followed aims to foster wider recognition of this body of work to maximise the likelihood of follow up actions. It fits with the growing calls for opening up disciplinary 'silos' and embracing more holistic framings of issues to help address key societal challenges. An example is the call from some thought leaders to adopt a One Health perspective to address interlinked health, agricultural and environmental problems.[34]

Results

The technological characteristics of spirulina include its profile as a crop and a food, among others. This paper focuses on spirulina as a dietary supplement, since this is the aspect that emerged from the review process.

Before reporting the review findings, the wider literature on the benefits of consuming spirulina is briefly summarised. The possible risks of spirulina consumption are also highlighted in the following discussion.

Wider Literature on Spirulina Consumption

A significant body of literature exists on the health benefits of consuming spirulina.

A recent review of laboratory studies, *in silico* analysis and human trials assessed the health benefits of spirulina and its food industry applications.[35] Spirulina was reported to be the best known and most widely cultivated microalga worldwide whose use as a food supplement has been extensively studied. Its nutritional profile includes high protein content and diverse bioactive compounds including essential amino acids, minerals, B vitamins, pigments, and lipids like gamma linolenic acid and polyunsaturated fatty acids. Spirulina also demonstrates anti-oxidation, anti-inflammation, and anti-tumour activity and can reduce risks from various diseases or conditions, such as type-2 diabetes, obesity or hypertension.

Other sources likewise suggest spirulina can mitigate disease risk. One review of *in vivo* and *in vitro* studies mapped its pharmacological profile and reported various benefits, including antiviral, antibacterial, anticancer, immune-stimulant, antioxidant and metalloprotective (i.e., prevention against heavy metal poisoning) effects.[36] Another literature review found spirulina showed strong biological activity against various conditions while also promoting growth of beneficial gut microflora.[37] A third review found spirulina use was linked to antioxidant, immunomodulatory and anti-inflammatory effects, and suggested it offers a promising therapy for various diseases and conditions.[38] A review of randomised controlled trials on the efficacy of spirulina for treating diseases suggested it may ameliorate symptoms and have anticancer, antiviral and antiallergic effects.[39] Finally, spirulina use was found to boost immune system function of senior citizens and to slow age-related system decline.[40]

The wider literature encompasses diverse studies that found spirulina boosted resistance to specific diseases. Examples include exhibiting anticancer activity of clinical significance,[41] inhibiting replication of HIV-1/AIDS[42] and foot-and-mouth virus,[43] helping patients cope with hepatitis C,[44] and improving blood parameters of patients with chronic obstructive pulmonary disease.[45] Some studies examined spirulina's effects on influenza, another respiratory disease caused by an encapsulated RNA virus. For instance, one study reported that feeding spirulina to influenza-infected mice improved their survival rates, and suggested it might offer a safe and effective therapeutic agent to help manage influenza outbreaks and hence merits further clinical investigation.[46]

Review Findings on Spirulina and Covid-19

The early evidence on spirulina and COVID-19 was examined to assess the viability of this microalgae as the basis of possible response options to the pandemic.

The paper belongs to the literature on food supplements or extracts providing protection against pathogens like bacteria or viruses. Modes of action vis-à-vis viruses include boosting immune system function and interfering with viral pathways.[47] Interference with pathways can occur at different stages of viral infection, such as entering the body, transport through the body, infecting target cells or reducing disease severity.[48] Studies showing algal compounds exerting antiviral effects at different stages of viral pathogenesis suggest algae offer a highly promising source of antiviral compounds.[49]

Consuming spirulina seems to help combat COVID-19 in different ways. One is supporting general immune system function thanks to being a potent nutritional supplement. Another is protecting against the SARS-CoV-2 virus via distinct anti-viral pathways. This evidence on COVID-19 and spirulina comes from human trials as well as *in vivo, in vitro* and *in silico* studies.

The three key categories into which the 25 papers identified fall are (i) examining antiviral properties vis-à-vis COVID-19 of compounds derived from spirulina; (ii) examining biological mechanisms linking spirulina with resistance to COVID-19; and (iii) spirulina as a potential COVID-19 response option of particular relevance to at-risk populations.

One group of papers explored how spirulina and perhaps also other algae might help society cope with COVID-19 via the antiviral properties of compounds derived from these organisms. Some of these papers are reviews of laboratory studies and/or human trials (Table 1), while others are based on computer modelling (Table 2).

Table 1: Antiviral activity of spirulina's constituent compounds vis-à-vis COVID-19 based on diverse studies

First author	Key findings
Rosales-Mendoza (2020)[50]	Reviewed evidence from *in vivo* and *in vitro* studies to see if different types of algae including spirulina might help combat COVID-19 thanks to activity against enveloped viruses. Reported that algae are a valuable source of antiviral and anti-inflammatory compounds for either direct use or drug development but observe direct use avoids the need for costly purification while facilitating treatment.

El-Sheekh (2020)[51]	Reviewed laboratory studies and human trials on the antiviral activity of spirulina and reported that it contains compounds like sulfated polysaccharides and calcium spirulan which inhibit replication of diverse viruses including coronaviruses. Argued it offers "a gleam of hope as a therapeutic agent for COVID-19" but that this needs thorough clinical investigation.
Alam (2021)[52]	Reviewed evidence from *in vitro*, *in vivo* and *in silico* studies to assess whether algae-derived molecules could be used against COVID-19. Found some of these molecules (including those from spirulina) can improve immunity and suppress viral activity and may thus help prevent COVID-19.
Bhatt (2020)[53]	Reviewed *in vivo* and *in vitro* studies on utilization of algal compounds like sulfated polysaccharides as therapeutics for SARS-CoV-2 and other viruses. Reported that compounds derived from spirulina, among other types of algae, show antiviral activity and suggested further investigation of these linkages is merited as possible options to tackle SARS-CoV-2.
Santos (2020)[54]	Reviewed diverse evidence from the literature on whether polyphenols might reduce COVID-19 illness severity and described several ongoing clinical trials to test this hypothesis. This includes a clinical trial of COVID-19 patients with comorbidities such as obesity and diabetes using polyphenols derived from spirulina. Suggested these bioactive substances may offer scope to control or reverse COVID-19 effects like changes to ACE-2 receptors and elevated production of pro-inflammatory cytokines. Concluded that polyphenols show potential for treating COVID-19 patients and hope clinical trials will elucidate this.
Reynolds (2021)[49]	Reviewed early evidence from pre-clinical and clinical studies on algal compounds as a basis for antiviral drugs, given the various such studies suggesting these compounds can exert antiviral effects at different stages of viral pathogenesis. Assessed such effects at each stage of viral infection in humans, including evidence on algal compounds that may interfere with infection pathways of SARS-CoV-2. Identified promising algal sources for anti-SARS-CoV-2 drugs, which included spirulina.

Table 2: Antiviral activity of spirulina's constituent compounds vis-à-vis COVID-19 based on modelling

First author	Key findings
Pendyala (2020)[33]	Conducted an *in silico* study to assess whether phycocyanobilin derived from spirulina could inhibit SARS-CoV-2 infection. Found this bioactive compound showed higher binding affinity to SARS-CoV-2 targets than recognised antiviral drugs like remdesivir, lopinavir and nelfinavir, and concluded further research is needed to assess its potential to reduce COVID-19 risk.
Petit (2021)[55]	Used computer modelling to assess the antiviral potential vis-à-vis COVID-19 of molecules derived from spirulina. Found that four such molecules showed "great aptitude" to inhibit the spike protein receptor targeted by SARS-CoV-2 and call for *in vivo* and *in vitro* studies on this. They suggest photosynthetic aquatic organisms hold "tremendous" but "little exploited" potential to help combat COVID-19.
Raj (2020)[56]	Used *in silico* analysis to assess whether C-Phycocyanin derived from spirulina could help society combat COVID-19. Found that it binds to the active site of a

	protein targeted by this virus – NSP12 – and could therefore inhibit viral replication in infected persons. Stressed further research is needed but suggested spirulina use in the meantime. Also noted India's Central Food Technological Research Institute recommends spirulina use to support immune system function and reduce risk of COVID-19 infection.

Another group of papers explored biological mechanisms via which spirulina might help people cope with COVID-19. Some of these papers simply discuss relevant mechanisms and how they might prove useful (Table 3). Other papers discuss these mechanisms but also suggest that consuming spirulina or algal extracts could help people manage COVID-19 risk pending the outcome of further research on these linkages (Table 4). Notably, some authors also suggest spirulina might help people cope with mutant variants.

Table 3: Evidence on biological mechanisms via which spirulina might help people cope with COVID-19

First author	Key findings
Ferreira (2020)[57]	Reviewed laboratory studies on 12 'therapeutic agents' (e.g., zinc, vitamin D3, spirulina) to assess how they interact with viruses including SARS-CoV-2 and hence whether they might help prevent COVID-19 infection or support its treatment. Reported that spirulina boosted immune system function in relevant ways including macrophage activation, increased NK cells, activation of NK cells, improved T-cell function, supporting antibody production and neutrophil function. Found it also hampered virus replication in the body by boosting type 1 interferon response and helped control hyperinflammation and reduce oxidative stress. Concluded spirulina could play a beneficial role in combatting COVID-19 but that controlled, randomized clinical trials are needed to confirm its therapeutic potential.
Chei (2020)[58]	Demonstrated the anti-inflammatory potential of spirulina in both human and mouse macrophages, including suppressing proinflammatory cytokines, thus offering hope that spirulina might suppress the cytokine 'storm' associated with severe cases of COVID-19.
McCarty (2020)[18]	Assessed the scope for different food supplements to enhance the capacity of mice to cope with SARS-CoV-2 and other RNA viruses via laboratory experiments. Found spirulina showed promise as a means to blunt the cytokine storm induced by COVID-19 via boosting type-1 interferon response to SARS-CoV-2. Suggested spirulina may "help prevent and control RNA virus infections" and called for further research on such effects.
Jeswin (2021)[59]	Generated pseudotyped viruses including SARS-CoV-2 that mimic live viruses but allow experiments without the need for sophisticated biocontainment facilities. Used these to screen for antiviral activity of natural products including spirulina and green tea extracts via *in vitro* experiments. Found both foods inhibited virus entry into cells of the target host by binding to their receptors (i.e., spike proteins) and concluded such foods could be useful tools for managing COVID-19 and other emerging viruses.
Svyatchenko (2021)[60]	Evaluated the efficacy against COVID-19 of the drug radachlorin derived from spirulina based on experiments with monkey cells *in vitro*. Found it provided protection to cells against infection by SARS-CoV-2 while also inhibiting viral replication within cells, suggesting radachlorin may be a promising option to prevent and treat COVID-19.

Table 4: Evidence on biological mechanisms that is coupled with recommendations on early use of spirulina

First author	Key findings
Sangtani (2020)[61]	Reviewed evidence from *in vivo, in vitro* and human studies to assess the potential of algae as a basis for broad spectrum antiviral therapeutics, given fears new COVID-19 variants could compromise the efficacy of vaccines and/or therapies. Reported "outstanding results of virucidal activity by algal polysaccharides", including one spirulina extract that was found to suppress proliferation of enveloped viruses like herpes simplex, HIV-1, influenza A and measles. Suggested algal extracts could help prevent or treat viral infections including COVID-19 and called for further research on this.
Tzachor (2021)[62]	Conducted an *in vitro* study which found spirulina reduced the cytokine storm that is central to COVID-19 by 40-70%. Suggested spirulina might offer a robust therapeutic intervention that could be orally administered and dispensed widely and safely. Speculated it may also be unaffected by mutations to SARS-CoV-2 and called for animal studies and clinical trials to verify these findings.
Rahman (2021)[63]	Reviewed evidence from laboratory studies and human trials on the capacity of selected traditional foods to combat viral infections, including coronaviruses. Reported that spirulina interferes with viral access to host cells and inhibits viral replication, including against HIV, mumps, measles, herpes, influenza. Reported it also has relevant immune-modulating properties such as mobilisation of macrophages and T cells, accumulation of natural killer cells and antibody generation. Suggested spirulina may thus help "shield" against COVID-19 and recommended that people consume spirulina and certain other foods to reduce COVID-19 risk.
Ratha (2021)[64]	Reviewed evidence from *in vivo, in vitro*, *in silico* studies and human trials on algal nutraceuticals as possible options to combat COVID-19 and related viral infections, and report that some (including those derived from spirulina) acted as immune-boosting and therapeutic agents against such infections, thus limiting fatalities. This includes strengthening adaptive and innate immunity and providing bioactive compounds with antiviral properties, such as angiotensin converting enzyme (ACE) inhibitor peptides, sulfated polysaccharides and calcium spirulan. The authors lament that use of such therapies remains limited in national pandemic response efforts and argue such foods warrant "urgent attention and clinical research".
Pothula (2020)[65]	Reviewed human and animal studies on how spirulina interacts with viruses including SARS-CoV-2. Reported it can inhibit viral replication by augmenting interferon-gamma and natural killer cell cytotoxicity, while also activating T-cells that can suppress SARS-CoV-2. Called for randomized controlled trials to establish spirulina's efficacy against COVID-19, but suggested its use could help protect people in the interim, though they also flagged risks to those with serious allergies or autoimmune disorders.
DiNicolantonio (2020)[66]	Reviewed evidence from animal studies on spirulina consumption and thrombosis, given the status of COVID-19 as a risk factor for thrombosis. Reported spirulina has potential to mitigate this risk and recommended consuming one tablespoon of it per day.

A third group of papers reported evidence of linkages between spirulina use and COVID-19 while specifying that this microalga could be particularly relevant to at-risk populations as a COVID-19 response option (Table 5). This includes populations where vaccination rates remain low and/or where many face food insecurity.

Table 5: Evidence on spirulina as a COVID-19 response option that emphasises its utility to at-risk populations

First author	Key findings
Elaya (2020)[67]	Reviewed evidence from laboratory studies and human trials to assess algae as a source of compounds to help combat COVID-19. Reported that spirulina can improve immune function and supress viral activity, including that of enveloped RNA viruses, and suggested it might both reduce infection risk and help those affected to fight this disease. Suggested it may be especially useful to vulnerable groups, given evidence spirulina use improved immune function of malnourished and HIV-infected people.
Sami (2021)[68]	Reviewed *in vivo* and *in vitro* studies on different types of algae and their relevance to COVID-19. Reported that algae – including spirulina –offer a “fruitful reservoir” of compounds with strong antiviral activity and immune boosting effects that may inhibit SARS-CoV-2. Suggested algae could help people withstand COVID-19 and may be especially useful in countries facing challenges to vaccination, and recommended that governments “supply raw algae powders/ capsules” to their populations.
Singh (2020)[69]	Reviewed evidence from laboratory studies and human trials on the nutritional and therapeutic profile of spirulina. Suggested it could help combat COVID-19, given its anti-viral, anti-inflammatory and immunomodulatory properties. Argued it may be especially useful where vaccination levels remain low, since avoiding infection and strengthening immune response could be key in such places.
Chinsembu (2020)[70]	Reviewed evidence on various medicinal plants from *in vivo*, *in vitro*, *in silico* and human studies to assess their capacity to inhibit SARS-CoV-2, whether in their natural form or as a basis of drug development. Found they offer a “library” of promising COVID-19 response options, including reporting that spirulina enhanced the immune status of COVID-19 patients, though its data are mostly from pre-clinical studies. Suggested the need for such products is especially great in Africa due to its under-resourced health systems.

Finally, one paper identified diverged from the others, as it found no linkages between spirulina and COVID-19.[71] It screened 51 medicinal plants via *in silico* analysis for their potential as a basis of drug development for COVID-19, but spirulina was not among those identified as particularly promising.

Discussion

Spirulina and Covid-19 Risk

Given complications with pandemic response efforts, risks from COVID-19 could persist over time, creating scope for measures like dietary change to play a valuable role in pandemic response efforts. The findings of this review suggest spirulina may represent a useful complementary COVID-19 response option.

The evidence summarised suggests two ways in which consuming spirulina or its extracts may help reduce peoples’ COVID-19 risk. One is that it could support general health and immune system function, given its rich nutritional profile. Another is that it may also inhibit SARS-CoV-2 via distinct antiviral mechanisms. Based on these early findings, it seems that incorporating spirulina into diet might offer scope to decrease the risk or severity of COVID-19 disease, and hence reduce associated morbidity and mortality. Further research is needed to verify the linkages identified and their apparent prophylactic and therapeutic effects, as called for by the authors cited. Some of these authors (e.g., Table 4) nonetheless also recommended consuming spirulina in the interim as a safe means to potentially reduce pandemic risk.

Spirulina might be particularly useful vis-à-vis COVID-19 for populations in the Global South, notably those in poorer countries or districts. In such areas many face delays to vaccination and/or have limited access to medical care. Some also struggle to access ample, nutritious food. These risks could heighten vulnerability to COVID-19, but consuming spirulina may offer scope to mitigate such risks.

Even if spirulina has potential, accessing it could be a challenge given the high cost of most commercially available spirulina powders and tablets. This mirrors a problem with the Lancet healthy reference diet, where an examination of data from 159 countries suggested this diet could be unaffordable to many of the world's poor.[72] One possible solution would be to foster local production of target foods to facilitate access. For spirulina, such efforts could build on the work of charitable projects like Antenna Foundation in Niger[73] or Nasio Trust in Kenya[74], which promote community-based production.

Given its apparent potential, using spirulina as a dietary supplement may offer scope for people to enhance their resilience with regard to COVID-19. Resilient systems are defined as those able to withstand shocks without losing their functionality.[75] Resilience building measures can minimise damages from a shock, for instance to health or assets, but may also foster positive outcomes like enhanced functionality. Resilience is a timely concept in a world facing growing instability and shocks. Resilience building is also central to the United Nations Sustainable Development Goals as both a poverty reduction measure and facet of climate action.[76]

Caveats to these Findings and Possible Risks

While the evidence cited offers grounds for hope that spirulina could help combat COVID-19, two caveats regarding these findings should be noted.

One crucial caveat is that evidence on the health effects of consuming spirulina is limited and often based on laboratory studies. Critically, there is a dearth of evidence based on randomised controlled trials, which are key to verifying the efficacy of health-related interventions. Spirulina should thus be viewed as a possible pandemic response option requiring further investigation rather than a proven one.

Another caveat is that while spirulina may offer scope to reduce COVID-19 risk, it mustn't be seen as a substitute for proven preventative measures like getting vaccinated and social distancing. A related concern is that bold claims about 'miracle foods' being able to prevent COVID-19 have been circulating on social media despite a lack of solid evidence.[77] While regrettable, the fact that some people make irresponsible claims must not be allowed to derail sober consideration of promising options and their potential significance.

Spirulina is deemed safe for human consumption by regulators in leading countries,[78] which fits with its status as a traditional food in some cultures. Two potential risks should however be noted: Those with auto immune disorders could have an adverse reaction to it,[79] while poor cultivation practices could produce spirulina that is contaminated with toxins like heavy metals[80] or biological agents like microcystins.[81,82] Risks from heavy metals due to spirulina consumption appear low, however. Al-Dhabi[83] examined the heavy metal concentrations in 25 commercial spirulina products from different countries and found concentrations were significantly below allowable daily intake levels. Minimising contamination risk during production is nonetheless important. One factor that reduces risk of biological contamination is that spirulina grows in highly alkaline water,[84] which is not tolerated by most aquatic organisms.[85] Biological risks can also be reduced by varying the temperature or salinity of the culture medium in ways spirulina can tolerate but other organisms may not.[86]

Scope for Action

Although the available evidence on spirulina and COVID-19 remains thin and provisional, it nonetheless suggests several concrete actions as part of COVID-19 response efforts. Notably, governments could support further research on spirulina or launch healthy eating campaigns including this microalgae, while households and communities could consume–and perhaps also produce – spirulina as a potential means of lowering their pandemic risk.

Despite its potential, use of spirulina as a dietary supplement remains low across the world. Its limited market penetration to date is reflected in a global market of just $102 million per annum in 2017, which for comparison was dwarfed by the $2 billion garlic market.[88] Global farmed spirulina production was 69,600 tonnes live weight in 2018, though this is deemed an underestimate due to missing data from key producers like France, India, Israel, Italy, Japan, Malaysia and the USA.[89]

Several research priorities follow from this analysis, notably (i) further research on the antiviral activity of spirulina vis-à-vis SARS-CoV-2, including randomised controlled trials; (ii) assessing the efficacy of spirulina vis-à-vis other emerging viral diseases; (iii) identifying ways to ensure spirulina production meets safety standards, and (iv) better understanding spirulina's low market penetration despite its technological promise.

Some authorities have warned pandemics could become increasingly common in future due to factors like deforestation, industrial farming and climate change that are destabilising natural systems and making it easier for diseases of animal origin to jump between species. International trade and travel may then facilitate their rapid spread. Such diseases disproportionately affect the poor and those in less-developed countries. The 'One Health' approach holds promise for minimising such dangers by emphasising the interlinkages between human, animal and environmental health and addressing these issues synergistically.[90,91] Further investigations into the scope for microalgae to help address COVID-19 and other novel diseases would fit with such efforts.

Conclusions

The COVID-19 pandemic creates threats on several levels, notably to lives and livelihoods. COVID-19 risks could persist over time, given the complexities surrounding vaccination and mutant variants, among other issues. National responses have tended to focus on measures like vaccination and social distancing, but dietary change offers possible complementary response options. Spirulina is an edible alga that merits greater attention as a potential means of lowering pandemic risk. One priority is further investigating its promise and limits as a dietary supplement, including its anti-viral effects vis-à-vis SARS-CoV-2 and other pathogens.Pending the outcome of such research, early use of spirulina may offer a way for people to boost their capacity to resist COVID-19. One demographic that might particularly benefit is populations facing elevated pandemic risk due to factors like low vaccination rates or food insecurity – realities common in parts of the Global South.

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Conflict of Interest

The authors declare no conflict of interest.

References

1. WHO Coronavirus (COVID-19) Dashboard. Geneva: World Health Organization; 2022. WHO Coronavirus (COVID-19) Dashboard | WHO Coronavirus (COVID-19) Dashboard With Vaccination Data. Updated 7 Feb 2022. Accessed 7 Feb 2022.
2. COVID-19 Data: The Pandemic's True Death Toll. *The Economist*. https://www.economist.com/graphic-detail/coronavirus-excess-deaths-estimates. Published 2 Sept 2021. Updated 7 Feb, 2022. Accessed 7 Feb 2022.
3. Marx, V. Scientists set out to connect the dots on long COVID. *Nature Methods.* 2021; 18: 449-453. https://doi.org/10.1038/s41592-021-01145-z
4. Schotte, S.; Danquah, M.; Osei, R.D.; Sen, K. Report: How COVID-19 is affecting workers and their livelihoods in urban Ghana. Helsinki: United Nations University World Institute for Development Economics Research (WIDER);2021.41 pages. DOI https://doi.org/10.35188/UNU-WIDER/2021-rep-1.

Published March 2021. Accessed 7 February 2022.

5. Bloomberg Vaccine *Tracker. Bloomberg.* More Than 10.2 Billion Shots Given: Covid-19 Vaccine Tracker (bloomberg.com). Updated 7 Feb 2022. Accessed 7 Feb 2022.
6. Daily COVID-19 Vaccination Progress. *Our World in Data*. https://twitter.com/vaccc progress. Updated 7 Feb 2022. Accessed 7 Feb 2022.
7. Schellekens, P. Data insight: Vaccine equity needs a boost. *Pandem-ic* website. Vaccine equity needs a boost (pandem-ic.com). Updated 7 Feb 2022. Accessed 7 Feb 2022.
8. Sandset, T. The necropolitics of COVID-19: Race, class and slow death in an ongoing pandemic. *Global Public Health*. 2021; 16(8-9): 1411-1423. DOI: 10.1080/17441692.2021.1906927
9. No-on is safe until everyone is safe – why we need a global response to COVID-19 (statement from religious and civil society leaders). Geneva: United Nations International Children's Emergency Fund; 2021.https://wcmssec4.unicef.org/press-releases/no-one-safe-until-everyone-safe-why-we-need-global-response-covid-19. Published 23 May 2021. Accessed 10 Nov 2021.
10. Fox, K. The Countries that are Vaccinating Children Against COVID-19. *Cable News Network.* https://edition.cnn.com/2021/09/17/world/covid-vaccine-children-countries-intl-cmd/index.html. Published 7 Sept 2021. Accessed 10 Nov 2021.
11. Batelaan, K. It's not the science we distrust, it's the scientists: Reframing the anti-vaccination movement within black communities. *Global Public Health.* 2021: 1-14. DOI: 10.1080/17441692.2021.1912809
12. Chen, J.; Gao, K.; Wang, R.; Wei, G.W. Prediction and mitigation of mutation threats to COVID-19 vaccines and antibody therapies. *Chemical Science.* 2021; 12(20): 6929-6948. DOI: 10.1039/d1sc01203g
13. Weber, S.; Ramirez, C.M.; Weiser, B.; Burger, H.; Doerfler, W. SARS-CoV-2 worldwide replication drives rapid rise and selection of mutations across the viral genome: A time-course study potential challenge for vaccines and therapies. *EMBO Molecular Medicine.* 2021; 13(6), e14062: 1-35. DOI: https://doi.org/10.15252/emmm.202114062
14. Hainey, F. Seven things we learned from leading Covid scientists today – from 'mythical' herd immunity to 'inevitable' vaccine-escaping variants. *Manchester Evening News.* Seven things we learned from leading Covid scientists today - from 'mythical' herd immunity to 'inevitable' vaccine-escaping variants - Manchester Evening News. Published 10 Aug 2021. Accessed 10 Nov 2021.
15. Oliu-Barton, M.; Pradelski, B.S.R.; Aghion, P.; Artus, P.; Kickbusch, I.; Lazarus, J.V.; Sridhar, D.; Vanderslott, S. SARS-CoV-2 elimination, not mitigation, creates best outcomes for health, the economy and civil liberties. *The Lancet.* 2021; 397(10291): 2234-2236. DOI: https://doi.org/10.1016/S0140-6736(21) 00978-8
16. Calder, P.C.; Carr, A.C.; Gombart, A.F.; Eggersdorfer, M. Optimal nutritional status for a well-functioning immune system is an important factor to protect against viral infections. *Nutrients.* 2020; 12(4): 1181. DOI: https://dx.doi.org/10.3390%2Fnu12041181
17. Jayawardena, R.; Sooriya arachchi, P.; Chourdakis, M.; Jeewandara, C.; Rana singhe, P. Enhancing immunity in viral infections, with special emphasis on COVID-19: A review. *Diabetes & Metabolic Syndrome.* 2020; July-Aug 14(4): 367-382. DOI: https://dx.doi.org/10.1016%2Fj.dsx.2020.04.015
18. McCarty, M.F.; DiNicolantonio, J.J. Nutraceuticals have potential for boosting the type 1 interferon response to RNA viruses including influenza and coronavirus. *Progress in Cardiovascular Disease.* 2020; 63(3): 383-385. DOI: 10.1016/j.pcad.2020.02.007
19. Zabetakis, I.; Lordan, R.; Norton, C.; Tsoupras, A. COVID-19: The Inflammation Link and the Role of Nutrition in Potential Mitigation. *Nutrients.* 2020; 12(5), 1466: 1-28. DOI: 10.3390/nu12051466 (doi.org)
20. Malhotra, A. COVID-19 and the Elephant in the Room. *European Scientist*. https://www.europeanscientist.com/en/article-of-the-week/covid-19-and-the-elephant-in-the-room/. Published 16 April 2020. Accessed 1 Nov 2021.
21. *Food Security and COVID-19.* Washington DC: The World Bank; 2021. Food Security and COVID-19 (worldbank.org). Published 23 May 2021. Accessed 10 Nov 2021.

22. Calder, P.C.; Kew, S. The immune system: A target for functional foods? *The British Journal of Nutrition.* 2002; 88, Supplement 2: 165-177. DOI: 10.1079/BJN2002682
23. *Zero Hunger. Geneva:* World Food Programme. Zero Hunger | World Food Programme (wfp.org). Accessed 10 Nov 2021
24. Bailey, R.L.; West, K.P.; Black, R.E. The Epidemiology of global micronutrient deficiencies. Annals of *Nutrition and Metabolism.* 2015; 66 (supplement 2): 22-33. DOI: 10.1159/000371618
25. Bruins, M.J.; Bird, J.K.; Aebischer, C.P,; Eggersdorfer, M. Considerations for secondary prevention of nutritional deficiencies in high-risk groups in high-income countries. *Nutrients*. 2018; 10(47): 1-15. DOI: 10.3390/nu10010047
26. Jayawardena, R.; Misra, A. Balanced diet is a major casualty in COVID-19. Diabetes and Metabolic Syndrome: *Critical Research and Reviews.* 2020; 14: 1085-1086. DOI: https://doi.org/10.1016/j.dsx.2020.07.001
27. *Nutrition advice for adults during the COVID-19 outbreak.* World Health Organization. WHO EMRO | Nutrition advice for adults during the COVID-19 outbreak | COVID-19 | Nutrition site. Accessed 10 Nov 2021.
28. Lucas, T.; Horton, R. The 21st Century Great Food Transformation. *The Lancet.* 2019; 393(10170): 386-387. DOI: https://doi.org/10.1016/S0140-6736(18)33179-9
29. Willett, W.; Rockstrom, J.; Loken, B.; Springmann, M.; Lang, T.; Vermulen, S.; Garnett, T.; Tilman, D.; DeClerck, F.; Wood, A.; Jonell, M.; Clark, M.; Gordon, L.J.; Fanzo, J.; Hawkes, C.; Zurayk, R.; Rivera, J.A.; De Vries, W.; Sibanda, L.M.; Afshin, A.; Chaudhary, A.; Herrero, M.; Agustina, R.; Branca, F.; Lartey, A.; Fan, S.; Crona, B.; Fox, E.; Bignet, V.; Troell, M.; Lindahl, T.; Singh, S.; Cornell, S.E.; Reddy, K.S.; Narain, S.; Nishtar, S.; Murray, C.J.L. Food in the Anthropocene: the EAT-Lancet Commission on Healthy Diets from Sustainable Food Systems. *The Lancet.* 2019; 393(10170): 447-492. DOI: https://doi.org/10.1016/S0140-6736(18)31788-4
30. The Lancet. 2019: The Year for Nutrition (editorial). *The Lancet.* 2019; 393(10168): 200. DOI: https://doi.org/10.1016/S0140-6736(19)30080-7
31. Shaw, G.R.; Moore, D.P.; Garnett, C.M. Eutrophication and Algal Blooms. In *Encyclopedia of Life Support Systems* (EOLSS), Volume II, Environmental and Ecological Chemistry. Paris: United Nations Educational, Scientific and Cultural Organization, 2003.http://www.eolss.net/Sample-Chapters/C06/E6-13-04-04.pdf. Accessed 1 Nov 2021.
32. Habib, M; Parvin, M., Huntington, T.; Hasan, M. *A Review on Culture, Production and Use of Spirulina as Food for Humans and Feeds for Domestic Animals and Fish.* Rome: Food and Agriculture Organization of the United Nations; 2008. http://www.fao.org/3/a-i0424e.pdf. Accessed 10 Nov 2021.
33. Pendyala, B.; Patras, A. In silico screening of food bioactive compounds to predict potential inhibitors of COVID-19 Main protease (Mpro) and RNA-dependent RNA polymerase (RdRp). ChemRxiv [*Preprints*]. 2020: 1-11. DOI: 10.26434/chemrxiv.12051927.v2
34. Capua, I. Circular Health: *Empowering the One Health Revolution.* Padua: Bocconi University Press, 2020.Circular Health - Ilaria Capua
35. Lafarga, T.; Fernandez-Sevilla, J.M.; Gonzalez-Lopez, C.; Acien-Fernandez, F.G. Spirulina for the food and functional food industries. *Food Research International.* 2020; 137, 109356: 1-10. DOI: 10.1016/j.foodres.2020.109356
36. Hoseini, S.M.; Khosravi-Darani, K.; Mozafari, M.R. Nutritional and medical applications of spirulina microalgae. *Mini Reviews in Medicinal Chemistry.* 2013; 13(8): 1231-1237. Nutritional and Medical Applications of Spirulina Microalgae: Ingenta Connect
37. Furmaniak, M.A.; Misztak, A.E.; Franczuk, M.D.; Wilmotte, A.; Waleron, M., Waleron, K.F. Edible cyanobacterial genus Arthrospira: Actual state of the art in cultivation methods, genetics, and application in medicine. *Frontiers of Microbiology.* 2017; 8(2541): 1-21. DOI: https://doi.org/10.3389/fmicb.2017.02541
38. Qinghua, W.; Lian, L.; Miron, A.; Klimova, B.; Wan, D.; Kuca, K. The antioxidant, immunomodulatory, and anti-inflammatory activities of spirulina: An overview. *Archives of Toxicology.* 2016; 90(8): 1817-1849. DOI: 10.1007/s00204-016-1744-5
39. Karkos, P.D.; Leong, S.C.; Karkos, C.D.; Sivaji, N.; Assimakopoulos, D.A. Review article: Spirulina in clinical practice: Evidence-based human applications. *Evidence-based Complementary and Alternative Medicine.*

2011; Article ID 531053: 1-4. DOI: https://dx.doi.org/10.1093%2Fecam%2Fnen058

40. Selmi, C.; Leung, Patrick S.C.; Fischer, L.; German, B.; Yang, C.Y.; Kenny, T.P. The effects of spirulina on anemia and immune function in senior citizens. *Cellular and Molecular Immunolpogy.* 2011; 8(3): 248-254. DOI: 10.1038/cmi.2010.76
41. Ramakrishnan, R. Anticancer properties of blue-green algae Spirulina platensis – A review. *International Journal of Medicine and Pharmaceutical Science.* 2013; 3(4): 159-169. Anticancer Properties of Blue Green Algae Spirulina platensis - A Review (researchbib.com)
42. Ayehunie, S.; Belay, A.; Baba, T.W.; Ruprecht, R.M. Inhibition of HIV-1 replication by an aqueous extract of Spirulina platensis (Arthrospira platensis). J*ournal of Acquired Immune Deficiency Syndromes and Human Retrovirology.* 1998; 18(1): 7-12. https://pubmed.ncbi.nlm.nih.gov/9593452/
43. Daoud, H.M.; Soliman, E.M. Evaluation of Spirulina platensis extract as natural antivirus against food and mouth disease virus strains (A, O, SAT2). *Veterinary World.* 2015; 8(10): 1260-1265. DOI: 10.14202/vetworld.2015.1260-1265
44. Yakoo, M.; Salem, A. Spirulina platensis versus silymarin in the treatment of chronic hepatitis C virus infection. A pilot randomized, comparative clinical trial. *BMC Gastroenterology.* 2012; 12:32: 1-9. DOI: 10.1186/1471-230X-12-32 (doi.org)
45. Ismail, M.; Hossain, M.F.; Tanu, A.R.; Shekhar, H.U. Effect of spirulina intervention on oxidative stress, antioxidant status, and lipid profile in chronic obstructive pulmonary disease patients. *BioMed Research International.* 2015; Article ID 486120: 1-7. DOI: https://doi.org/10.1155/2015/486120
46. Chen, Y.H.; Chang, G.K.; Kuo, S.M.; Huang, S.Y.; Hu, I.C.; Lo, Y.L.; Shih, S.R. Well-tolerated Spirulina extract inhibits influenza virus replication and reduces virus-induced mortality. *Scientific Reports.* 2016; 6:24253: 1-11. DOI: 10.1038/srep24253
47. Sultan, M.T.; Butt, M.S.; Qayyum, M.M.N.; Suleria, H.A.R. Immunity: Plants as effective mediators. Critical Reviews in *Food Science and Nutrition.* 2014; 54(10): 1298-1308. DOI: 10.1080/10408398.2011.633249
48. Mrityunjaya, M.; Pavithra, V.; Neelam, R.; Janhavi, P.; Halami, P.M.; Ravindra, P.V. (2020). Immune-boosting, antioxidant and anti-inflammatory food supplements targeting pathogenesis of COVID-19. *Frontiers in Immunology.* 2020; 07. DOI: 10.3389/fimmu.2020.570122
49. Reynolds, D.; Huesemann, M.; Edmundson, S.; Sims, A.; Hurst, B.; Cady, S.; Beirne, N.; Freeman, J.; Berger, A.; Gao, S. Viral inhibitors derived from macroalgae, microalgae and cyanobacteria: A review of antiviral potential throughout pathogenesis. *Algal Research.* 2021; 57, 102331. DOI: 10.1016/j.algal.2021.102331
50. Rosales-Mendoza, S.; García-Silva, I.; González-Ortega, O.; Sandoval-Vargas, J.M.; Malla, A.; Vimolmangkang, S. The potential of algal biotechnology to produce antiviral compounds and biopharmaceuticals. *Molecules.* 2020; 25(18), 4049: 1-25. DOI: https://doi.org/10.3390/molecules25184049
51. El-Sheekh, M.; Abomohra, A.E. The therapeutic potential of spirulina to combat COVID-19 infection. *Egyptian Journal of Botany.* 2020; 60(3): 605-609. DOI: https://doi.org/10.21608/ejbo.2020.49345.1581.
52. Alam, M.A.; Parra-Saldivar, R.; Bilal, M.; Afroze, C.A.; Ahmed, M.N.; Iqbal, H.M.N.; Xu, J. "Algae-derived bioactive molecules for the potential treatment of SARS-CoV-2." *Molecules.* 2021; 26(8): 2134. DOI: 10.3390/molecules26082134
53. Bhatt, Ankita; Arora, Pratham; Prajapati, Sanjeev Kumar. "Can algae-derived bioactive metabolites serve as potential therapeutics for the treatment of SARS-CoV-2 like Viral Infection?" *Frontiers of Microbiology.* 2020: 1-5. DOI: 10.3389/fmicb.2020.596374
54. Santos, J.C.; Ribeiro, M.L.; Gambero, A. The impact of polyphenols-based diet on the inflammatory profile in COVID-19 elderly and obese patients. *Frontiers in Physiology.* 2020; 11(612268): 1-12. DOI: https://dx.doi.org/10.3389%2Ffphys.2020.612268
55. Petit, L.; Vernes, L. ; Cadoret, J.P. Docking an in silico toxicity assessment of Arthrospira compounds as potential antiviral agents against SARS-CoV-2. *Journal of Applied Phycology.* 2021; Mar 20: 1–24. DOI: 10.1007/s10811-021-02372-9 (doi.org)
56. Raj, K.; Rajamani, R.; Basalingappa, K.M.; Thangaraj, G. C-Phycocyanin of Spirulina platensis inhibits NSP12 required for replication

of SARS-COV-2: A novel finding in-silico. *International Journal of Pharmaceutical Sciences and Research.* 2020; 11(9): 271-278. DOI: 10.13040/IJPSR.0975-8232.11(9).4271-78

57. Ferreira, A.O.; Polonini, H.C.; Dijkers, E.C. Postulated adjuvant therapies for COVID-19. *Journal of Personalized Medicine.* 2020; 10(3): 1-33. DOI: 10.3390/jpm10030080
58. Chei, S.; Oh, H.J.; Song, J.H.; Seo, Y.J.; Lee, K.; Kim, K.J. Spirulina maxima extract prevents activation of the NLRP3 inflammasome by inhibiting ERK signaling. *Scientific Reports.* 2020; 10(1): 2075. DOI: https://doi.org/10.1038/s41598-020-58896-6
59. Jeswin, J.; Karthika, T.; Akshay Das, V.R.; Raj, V.S. The use of pseudotyped coronaviruses for the screening of entry inhibitors: Green tea extract inhibits the entry of SARS-CoV-1, MERS-CoV and SARS-CoV-2 by blocking receptor-spike interaction. Current Pharmaceutical *Biotechnology.* 2021; August. DOI: 10.2174/1389201022666210810111716 (doi.org)
60. Svyatchenko, V.A.; Nikonov, S.D.; Mayorov, A.P.; Gelfond, M.L.; Loktev, V.B. Antiviral photodynamic therapy: Inactivation and inhibition of SARS-CoV-2 in vitro using methylene blue and radachlorin. Photodiagnosis and *Photodynamic Therapy.* 2021; 33, 102112: 1-5. DOI: 10.1016/j.pdpdt.2020.102112 (doi.org)
61. Sangtani, R.; Ghosh, A.; Jha, H.C.; Parmar, H.S.; Bala, K. Potential of algal metabolites for the development of broad-spectrum antiviral therapeutics: Possible implications in COVID-19 therapy". *Phytotherapy Research.* 2020; Nov 18: 2296-2316. DOI: 10.1002/ptr.6948.
62. Tzachor, A.; Rozen, O.; Khatib, S.; Jensen, S.; Avni, D. Photosynthetically controlled spirulina, but not solar spirulina, inhibits TNF-a secretion: Potential implications for COVID-19 related cytokine storm therapy. *Marine Biotechnology.* 2021; 23(1): 149–155. DOI: 10.1007/s10126-021-10020-z (doi.org)
63. Rahman, M.M.; Mosaddik, A.; Alam, A.H.M.K. Traditional foods with their constituent's antiviral and immune system modulating properties. *Heliyon,* 2021; 7(1), e05957: 1-10. DOI: https://doi.org/10.1016/j.heliyon.2021.e05957
64. Ratha, S.K.; Renuka, N.; Rawat, I.; Bux, F. Prospective options of algae-derived nutraceuticals as supplements to combat COVID-19 and human coronavirus disease. *Nutrition;* 2021, 83: 1-6. DOI: 10.1016/j.nut.2020.111089
65. Pothula, P. Spirulina extract enhances T-cell responses targeting spike protein of severe acute respiratory syndrome coronavirus 2: A potential drug candidate for treatment of COVID-19. *American-Eurasian Journal of Toxicological Sciences.* 2020; 12(1): 08-13. DOI: 10.5829/idosi.aejts.2020.08.13 (doi.org)
66. DiNicolantonio, J.J.; McCarty, M. "Thrombotic complications of COVID-19 may reflect an upregulation of endothelial tissue factor expression that is contingent on activation of endosomal NADPH oxidase". *Open Heart.* 2020; 7(1): 1-4. DOI: 10.1136/openhrt-2020-001337
67. Elaya Perumal, U.; Sudararaj, R. Algae: A potential source to prevent and cure the novel coronavirus – A review. *International Journal on Emerging Technologies.* 2020; 11(2): 479-483. https://www.semanticscholar.org/paper/Algae%3A-A-potential-source-to-prevent-and-cure-the-%E2%80%93-Perumal-Sundararaj\a1cbadc577a9799b0a1c42795acc3385892e5b
68. Sami, N.; Ahmad, R.; Fatma, T. Exploring algae and cyanobacteria as a promising natural source of antiviral drug against SARS-CoV-2. *Biomedical Journal.* 2021; 44(1): 54–62. DOI: https://dx.doi.org/10.1016%2Fj.bj.2020.11.014
69. Singh, S.; Dwivedi, V.; Sanyal, D.; Dasgupta, S. Therapeutic and Nutritional Potential of Spirulina in Combating COVID-19 Infection. *International Journal of Creative Research Thoughts.* 2020; 8(9): 4051-4063.DOI: 0.13140/RG.2.2.16527.41127
70. Chinsembu, K.C. Coronaviruses and nature's pharmacy for the relief of coronavirus disease 2019. *Revista Brasileira de Farmacognosia.* 2020; Oct 6: 1–19. DOI: https://dx.doi.org/10.1007%2Fs43450-020-00104-7
71. Upadhyay, S.; Tripathi, P.K.; Singh, M.; Raghavendhar, S.; Bhardwaj, M.; Patel, A.K. Evaluation of medicinal herbs as a potential therapeutic option against SARS-CoV-2 targeting its main protease. *Phytotherapy Research.* 2020; Aug 4: 3411-3419. DOI: 10.1002/ptr.6802 (doi.org)
72. Hirvonen, K.; Bai, Y.; Headey, D.; Masters, W.A. Affordability of the EAT-Lancet reference diet: A global analysis. *The Lancet Global Health.* 2020; 8(1): E59-E66. DOI: https://doi.org/10.1016/S2214-109X(19)30447-4

73. Charity Non-Governmental OrganisationFighting Child Malnutrition in Niger. *Antenna France.* Antenna France - Charity NGO fighting child malnutrition in Niger (antenna-france.org). Accessed 7 Feb 2022.
74. Spirulina Production Project. *The Nasio Trust.* https://www.thenasiotrust.org/projects/spirulina-production/. Accessed 7 Feb 2022.
75. *Glossary of Key Terms.* Bonn: United Nations Framework Convention on Climate Change. Glossary of key terms (unfccc.int). Accessed 10 Nov 2021.
76. *Sustainable Development* – The 17 Goals. New York: United Nations Department of Economic and Social Affairs.
77. THE 17 GOALS | Sustainable Development (un.org). Accessed 7 Feb 2022.
78. Ibitoye, T. Coronavirus: There are no miracle foods or diets that can prevent or cure COVID-19. *The Conversation.* Coronavirus: there are no miracle foods or diets that can prevent or cure COVID-19 (the conversation.com). Published 21 April 2020. Accessed 10 Nov 2021.
79. Marles, R.J.; Barrett, M.L.; Barnes, J.; Chavez, M.L.; Gardiner, P.; Ko, R; Mahady, G.B.; Dog, T.L.; Sarma, N.D.; Giancaspro. G.I.; Sharaf, M.; Griffiths, J. United States pharmacopeia safety evaluation of spirulina. *Critical Review in Food Science and Nutrition.* 2011; 51(7): 593-604. DOI:https://doi.org/10.1080/10408391003721719
80. Lee, A.N.; Werth, V.P. Activation of auto immunity following use of immunostimulatoryherbal supplements. *Archives of Dermatology.* 2004 Jun; 140(6): 723-727. DOI: 10.1001/archderm.140.6.723
81. *'Spirulina'.Drugs.com.* Spirulina Uses, Benefits & Dosage - Drugs.com Herbal Database. Accessed 10 Nov 2021.
82. Jiang, Y.; Xie, P.; Chen, J.; Liang, G.Detection of the hepatotoxic microcystins in 36 kinds of cyanobacteria spirulina food products in China. *Food Additives and Contaminants Part A, Chemistry, Analysis, Control, Exposure & Risk Assessment.* 2008; 25(7): 885-894. DOI: 10.1080/02652030701822045
83. Roy-Lachapelle, A.; Solliec, M.; Bouchard, M.F.; Sauve, S. Detection of Cyanotoxins in Algae Dietary Supplements. *Toxins.* 2017; 9(76): 1-17. DOI: 10.3390/toxins9030076
84. Al-Dhabi, N.A. Heavy metal analysis in commercial Spirulina products for human consumption. *Saudi Journal of Biological Sciences.* 2013; 20(4): 383-388. DOI: 10.1016/j.sjbs.2013.04.006.
85. Gumbo, J.R.; Nesamvuni, C.N. Spirulina a source of bioactive compounds and nutrition. *Journal of Chemical and Pharmaceutical Sciences.* 2017; 10(3): 1317-1325. https://www.semanticscholar.org/paper/A-Review%3A-Spirulina-a-source-of-bioactive-compounds-Gumbo-Nesamvuni/1c87ac9dc43df2f209246b142c933a03181ff4d0
86. Spirulina Growing Manual. *JustSpirulina.* JustSpirulina | Spirulina Growing Manual. Accessed 1 Nov 2021.
87. Wang, L.; Yuan, D.; Li, Y.; Ma, M.; Hu, Q.; Gong, Y. Contaminating microzooplankton in outdoor microalgal mass culture systems: An ecological viewpoint. *Algal Research.* 2016; 20: 258-266. DOI: https://doi.org/10.1016/j.algal.2016.10.013
88. Spirulina Sales and Consumption 2017 Market Research Report. *WiseGuyReports.* https://www.newsmaker.com.au/news/335559/global-spirulina-sales-and-consumption-2017-market-research-report#.Xz1eDqeSIPY. Published 12 Dec 2017. Accessed 1 Nov 2021.
89. FAOSTAT *crops and livestock products*: Database. Rome: Food and Agriculture Organization of the United Nations. http://www.fao.org/faostat/en/#data/TP. Accessed 1 Nov 2021.
90. *The State of World Fisheries and Aquaculture: Sustainability in Action.* Rome: Food and Agriculture Organization of the United Nations; 2020. https://doi.org/10.4060/ca9229en. Accessed 1 Nov 2021.
91. *Preventing the next pandemic: Zoonotic diseases and how to break the chain of transmission.* Nairobi: United Nations Environment & the International Livestock Research Institute, 2020. Preventing the next pandemic: Zoonotic diseases and how to break the chain of transmission (unep.org)
92. Coronaviruses: Are they here to stay? *United Nations Environment Programme News,* 3 April 2020. https://www.unenvironment.org/news-and-stories/story/coronaviruses-are-they-here-stay