REZMER, Jakub, WASILEWSKA, Inga, HOMA, Wojciech, WANAT, Joanna, KOBIERNIK, Adam and FORTUNIAK, Weronika. Harnessing marine microorganisms in the battle against the influenza virus. Journal of Education, Health and Sport. 2025;80:59423 eISSN 2391-8306.
https://doi.org/10.12775/JEHS.2025.80.59423
https://apcz.umk.pl/JEHS/article/view/59423

The journal has had 40 points in Minister of Science and Higher Education of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 05.01.2024 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical culture sciences (Field of medical and health sciences); Health Sciences (Field of medical and health sciences).
Punkty Ministerialne 40 punktów. Załącznik do komunikatu Ministra Nauki i Szkolnictwa Wyższego z dnia 05.01.2024 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).
The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 13.03.2025. Revised: 04.04.2025. Accepted: 20.04.2025. Published: 23.04.2025.

Harnessing marine microorganisms in the battle against the influenza virus

1. **MD Jakub Rezmer**
   Samodzielny Publiczny Specjalistyczny Zakład Opieki Zdrowotnej
   ul. Węgrzynowicza 13, 84-300 Lębork, Poland
   https://orcid.org/0000-0002-0717-9061
   jakubrezmer1@gmail.com - corresponding author

2. **MSD Inga Wasilewska**
   Indywidualna Praktyka Lekarska lek. stom Marlena Wilczyńska-Rezmer
   ul. Bohaterów Monte Cassino 15D, Lębork, Poland
   https://orcid.org/0000-0002-0864-9993
   wasilewskainga@gmail.com

3. **MD Wojciech Homa**
   Wojewódzki Szpital Specjalistyczny
   al. Kraśnicka 100, 20-718 Lublin, Poland
   https://orcid.org/0000-0003-2177-8818
   wojciech.homa2@gmail.com

4. **Joanna Wanat**
Medical University of Lublin
Aleje Racławickie 1, 20-059 Lublin, Poland
https://orcid.org/0009-0009-3349-3618
asiawanat2000@gmail.com

5. **MD Adam Kobiernik**
Southern Warsaw Hospital
Rotmistrza Witolda Pileckiego 99, 02-781 Warsaw, Poland
https://orcid.org/0009-0003-4879-6837,
adam.kobiernik@gmail.com

6. **MD Weronika Fortuniak**
Samodzielny Publiczny Szpital Kliniczny im. prof. W. Orłowskiego Centrum Medycznego Kształcenia Podyplomowego
Czerniakowska 231, 00-416 Warsaw, Poland
https://orcid.org/0009-0006-4765-6164
fortuna.wf@gmail.com

Abstract:

The Orthomyxoviridae family of RNA viruses is responsible for influenza. Both influenza A and B strains induce seasonal influenza illnesses, whereas influenza C typically only results in minor respiratory sickness. Coughing and sneezing can spread the disease, and direct touch can transmit the virus. Although a few authorized anti-influenza drugs accessible such as oseltamivir, amantadine, and rimantadine, are available, due to the expanding drug resistance, they are becoming less efficient and effective.

Microorganisms living in the marine environment can produce unique chemical compounds with potent biological activity, including antiviral. Natural antiviral substances can be used against various viruses pathogenic to humans, including influenza.

This review aimed to search for potential anti-influenza properties of different substances derived from marine microorganisms.

The literature review was conducted using the PubMed scientific database.

The authors propose a great variety of substances that could be potentially helpful in the fight against influenza. Starting from abyssomycins, polysaccharides, and spirostaphylotrichin, through violapyrones, polyketides indole diterpenoids, finishing with microalgae and cyanobacteria extracts and others. Some of them directly target the viral adsorption and internalization processes, inhibit viral polymerase activity, or stimulate the immune system of the host.

In the future, potential drugs that could be used to improve the treatment of influenza are believed to be obtained from marine sources, which could be used for the creation of innovative pharmaceuticals. The authors of the studies strongly advise additional *in vitro* and *in vivo* research on substances with potential antiviral properties.

Keywords: influenza, antiviral compounds, marine microorganisms, novel pharmaceuticals, immune system modulation, marine, microorganisms

Introduction

Influenza, which is caused by RNA viruses from the Orthomyxoviridae family has the ability to affect both humans and animals. Influenza A and B strains induce seasonal influenza illnesses, whereas influenza C typically only results in minor respiratory sickness. [1]

The disease can spread through coughing, sneezing, and direct contact. [2] Although there are some approved medications such as oseltamivir, amantadine and rimantadine for treating influenza their effectiveness is decreasing due to the emergence of drug-resistant strains. [3]

This review aimed to investigate substances derived from microorganisms that may possess anti-influenza properties.

Materials and Methods

The literature review was carried out by utilizing the PubMed database, specifically focusing on studies published in the English language. The primary search terms used were "influenza" and "influenza virus," supplemented by the inclusion of the term "marine." Following the initial search, the appropriate articles meeting the criteria were selected for further examination and review.

Results

Marine products, which can serve as a resource for medicinal purposes, can produce lots of natural compounds with potential therapeutic properties. Sulfated compounds derived from marine organisms have emerged as a potent and promising source of antiviral agents, demonstrating significant inhibitory activity against influenza *in vitro* and *in vivo.* Kim, Meehyein et al. 2012 conducted research about sulfated polysaccharide p-KG03, derived from the marine microalga *Gyrodinium impudium*, which demonstrates significant inhibitory activity against influenza type A virus. It targets viral adsorption and internalization steps, making it a potent influenza A viral entry inhibitor. [4] In the study by Ogura, Fumie et al. 2010 the hot-water extract of *Aphanothece sacrum*, specifically the non-dialyzable portion containing sulfated polysaccharides (ASWPH), demonstrated a remarkable inhibitory effect on the replication of influenza virus type A (IFV-A, H1N1) *in vitro*. ASWPH was found to inhibit viral adsorption to the receptor of host cells involved in the replication process of the virus, but not significantly suppress the penetration stage. These findings suggest that ASWPH could be a promising candidate for preventing infectious diseases caused by IFV-A. [5]

The sulfated polysaccharide fucoidan extracted from brown sea algae *Laminaria japonica* demonstrated potent antiviral activity against the highly virulent avian influenza virus H5N1. Fucoidan effectively protected the cell cultures from the cytopathogenic effects of the influenza virus at a low viral dose. It also suppressed the production of the H5N1 virus within 24 hours of infection when used in prophylactic or therapeutic-and-prophylactic treatment regimens. [6]

As mentioned before, sulfated polysaccharides exhibited their antiviral activity *in vivo* as well. Fucoidan KW, derived from brown algae *Kjellmaniella crassifolia*, exhibits strong anti-influenza A virus activity with low toxicity. It effectively blocks viral infection both *in vitro* and *in vivo.* Fucoidan KW has a broad anti-influenza A spectrum and a low likelihood of inducing viral resistance, making it better than amantadine - a conventional anti-influenza A drug. The mechanism of action involves inactivating virus particles before infection, blocking stages after adsorption, and inhibiting viral neuraminidase activity to prevent virus release. Intranasal administration of fucoidan KW in mice infected by influenza A significantly improves survival and reduces viral titers. These findings suggest that fucoidan KW has the potential to be developed into a novel nasal drop or spray for preventing and treating influenza infections in the future. [7] These results from mentioned studies indicate that fucoidan shows potential as a prospective antiviral agent for preventing and treating infections caused by influenza viruses.

Another *in vivo* study was conducted using Rhamnan sulfate (RS), a sulfated polysaccharide derived from alga *Monostroma nitidum*, which demonstrated significant antiviral activity against influenza A virus infection both *in vitro* and *in vivo*. RS showed inhibitory effects on viral proliferation and blocked virus adsorption and entry. In mice, oral administration of RS effectively suppressed viral proliferation in both immunocompetent and immunocompromised groups, while also stimulating neutralizing antibody production. [8] Furthermore, Lambda-carrageenan (λ-CGN), a sulfated polysaccharide derived from marine red algae, exhibits broad-spectrum antiviral activity against influenza A and B viruses. It effectively inhibits viral replication by targeting viral attachment to cell surface receptors and prevents virus entry. Importantly, λ-CGN showed no toxicity to host cells at tested concentrations. In an *in vivo* experiment, intranasal administration of λ-CGN protected mice from influenza A viral infection, reducing infection-mediated weight loss and virus-induced mortality. [9]

Chen, Yi-Hsiang et al. 2016 researched that the spirulina cold water extract demonstrated significant anti-viral properties against a broad range of influenza viruses, including oseltamivir-resistant strains. It showed low cellular toxicity and was well-tolerated in animal models. The extract acted at an early stage of infection, reducing virus yields in cells and improving survival in influenza-infected mice. These findings suggest that the Spirulina extract could be a promising and safe therapeutic agent for managing influenza infections. [10] Another *in vivo* study showed that the sulfated exopolysaccharide from the halophilous cyanobacterium *Aphanothece halophytica* (EPAH) has significant antiviral activity against

influenza virus A FM (H1N1) in FM1-induced pneumonia in mice. EPAH effectively inhibited pneumonia when administered before and simultaneously during the viral infection. It also showed immune-modulating effects, enhancing the release of IL-2 and resuming the cytolytic activity of natural killer cells, which are important components of the host immune response against viral infections. The results suggest that EPAH could be a potential therapeutic agent against influenza virus A infections and may act by interacting with the virus and modulating the host immune system. [11]

Two studies were conducted by Nakashima Ayaka to examine the anti-influenza activity of *Euglena gracilis*, a microalga. In research from 2021 euglena extract showed strong antiviral activity against various influenza virus strains, including drug-resistant ones. The extract's mechanism of action appears to involve activating host cell defense mechanisms rather than directly targeting the virus. Additionally, the presence of zinc in the extract was found to contribute to its antiviral activity. [12] This study supported a previous paper from this author from 2017 that demonstrates that *Euglena gracilis* Z and her carbohydrate storage substance, the paramylon, have protective effects against influenza virus infection in mice. The administration of them resulted in higher survival rates and significantly lower virus titers in the lungs of infected mice.[13] The results indicate that the Euglena might be a potent candidate for treating influenza.

HESA-A is a natural compound of herbal-marine origin and shows potential as an effective treatment for influenza A, preventing virus penetration and adsorption to cells. It also exhibits anti-inflammatory effects without any toxic impact on cell viability. [14] Moreover, HESA-A was found to suppress the expression of pro-inflammatory cytokine TNF-α and by modulating the host immune response, could be a potent treatment option for influenza A infections. [15] Further research and clinical trials are needed to fully explore its antiviral properties and therapeutic potential.

Green algae have emerged as a promising source of marine-derived compounds that exhibit potential anti-influenza activity. A study conducted by Komatsu, Takayuki et al. 2013 demonstrates that the acidic polysaccharide fraction from the green alga *Coccomyxa gloeobotrydiformi* (CmAPS) possesses potent antiviral activity against various strains of influenza A virus, including the pandemic strains. CmAPS inhibits viral growth and yield by preventing the interaction between the virus and the host cells. Therefore, it prevents hemagglutination and hemolysis of the erythrocyte induced by the virus. [16] A lectin isolated from the green alga *Halimeda renschii*, HRL40, effectively inhibits the infection of influenza virus (A/H3N2/Udorn/72) by high-affinity binding to viral envelope hemagglutinin. [17] *In*

silico studies have demonstrated that certain lectins can interact with the glycans of the spike glycoprotein of SARS-CoV-2, potentially neutralizing coronavirus infection.[18]

The polysaccharide derived from *Durvillaea Antarctica* green algae, known as *Duvira Antarctic* polysaccharide (DAPP), has demonstrated antiviral activity against H1N1 influenza virus. The study found that DAPP showed no toxicity to MDCK cells at a concentration of 32 μg/mL and reduced cell apoptosis by inhibiting the ERK signaling pathway. Additionally, DAPP increased the expression of STAT3 and significantly inhibited proinflammatory cytokines. [19]

Red algae were examined for its anti-influenza activity as well. κ-carrageenan demonstrates potent antiviral activity against the swine pandemic 2009 H1N1 influenza virus (SW731) and A/California/04/2009 H1N1 (CA04) in a dose-dependent manner. The compound exhibits no cytotoxicity at concentrations below 1000 μg/ml. It specifically targets the HA of SW731 and CA04, which are pandemic H1N/2009 viruses, without affecting other influenza virus strains. Mechanism studies indicate that κ-carrageenan interferes with adsorption, transcription, and viral protein expression. [20] The red alga lectin ESA-2 also demonstrated potent antiviral activity not only against the H1N1-2009 but also against various other influenza strains. It exhibited a high affinity for viral hemagglutinin (HA) through binding to high mannose (HM)-glycans present on the viral envelope. ESA-2 effectively inhibited virus entry into host cells.[21] These findings indicate that algae have the potential to be an abundant source for the anti-influenza substances.

The aciduric fungal strain *Penicillium camemberti* OUCMDZ-1492 showed promising potential in producing bioactive compounds. Fan, Yaqin et al. identified six new indole-diterpenoids, along with five already known analogs. Several of identified compounds, exhibited significant activity against the H1N1 virus, but there is a need of the specific substitutions, such as 3-oxo, 4b-hydroxy, and 9-isopentenyl groups, in enhancing the anti-H1N1 activity of hexacyclic indole-diterpenoids. [22] Another marine-derived fungus, *Cochliobolus lunatus* SCSIO41401, yielded a novel spirocyclic γ-lactam, spirostaphylotrichin X with three known analogs. Spirostaphylotrichin X demonstrated significant inhibitory activity against multiple influenza virus strains by targeting the polymerase PB2 protein and interfering with viral RNA production. [23] In virtual screening research by Mia, Md Mukthar et al. 2022. fungal-derived natural compounds as potential inhibitors for nucleoprotein and neuraminidase of H5N1 and H5N8 subtypes were examined. Chevalone E, Brevione F, Brocazine-A, Penilactone-A, Aspergifuranone, Estramustine, Iloprost, Butorphanol, Desvenlafaxine,

Zidovudine, Nadolol, Sitaxentan, Ergoloid mesylate, Capecitabine, and Fenoterol emerge as possible candidates for further drug development against these influenza subtypes. [24]

Mangroves serve as a rich and diverse origin of fungi, offering plenty of potential bioactive compounds. A study of the fungus *Penicillium polonicum* MCCC3A00951, isolated from a sediment of the mangrove forest in China, led to the discovery of isolated cyclopenin, that exhibited potent inhibition of influenza neuraminidase. The comprehensive characterization and molecular docking simulation suggest that cyclopenin holds promise as a potential candidate for the development of anti-influenza neuraminidase therapeutics. Further optimization of cyclopenin may lead to the development of effective treatments for influenza infections. [25] Luo, Xiaowei et al isolated and identified polyketides and congeners from a mangrove-associated fungus *Diaporthe* sp. SCSIO 41011 and four compounds showed promising activity against multiple influenza A virus subtypes. [26] Li, Jing et al. focused on the evaluation of analogs synthesized from a natural isoprenyl phenyl ether found in a mangrove-derived fungus, for their inhibitory activity against influenza H1N1 neuraminidase. Among these analogs, 3-(allyloxy)-4-hydroxybenzaldehyde demonstrated the most potent inhibitory activity against H1N1 neuraminidase. Molecular docking studies provided valuable insights into the compounds' SAR and offer a basis for future structure modifications to develop more effective neuraminidase inhibitors for combating influenza infections. [27]

The deep-sea derived fungus *Spiromastix* sp. yielded a novel class of phenolic lactones called spiromastilactones A-M. Among these compounds, spiromastilactone D demonstrated potent inhibitory activity against a wide panel of influenza A and B viruses, including drug-resistant clinical isolates. This compound exhibited its antiviral effects by disrupting the interaction between the viral hemagglutinin protein and sialic acid receptors, which is crucial for viral attachment and entry. Additionally, it was found that compound 4 also targeted the viral RNP complex, inhibiting viral genome replication. [28] Marine, sponge-associated fungus *Epicoccum* sp. JJY40 is a source of pyronepolyene C-glucoside (iso-D8646-2-6) and D8646-2-6 compound. They showed some anti-influenza A H1N1 activities. [29]

Two studies made by Hou Lukuan examined the potential of type III polyketide synthases (PKSs). Heterologous expression of the type III polyketide synthase gene vioA in marine-derived *Streptomyces youssoufiensis* OUC6819 led to the production of six violapyrones (VLPs), which have demonstrated significant anti-influenza A (H1N1 and H3N2) virus activity, with methylated VLPs generally displaying better anti-virus activity than their non-methylated VLPs. VLP S showed the most potent anti-influenza activity. [30] By

overexpressing the VioA gene in different hosts, fourteen violapyrone compounds were identified, with some demonstrating considerable anti-H1N1 activity. [31]

The study conducted by Zainuddin E N et al. 2002 demonstrated that cyanobacteria of several genera possess *in vitro* antiviral activity against influenza A virus, with the most active extracts derived from Microcystis species. The observed antiviral activity was associated with protease inhibitory activity, which significantly reduced virus replication. [32] Another research explored the potential of microalgae and cyanobacteria extracts, revealing promising anti-influenza properties in a considerable number of tested extracts. [33] These findings suggest that cyanobacteria can produce compounds with potential clinical interest as antiviral agents.

Through the investigation of marine *Verrucosispora* sp. MS100137, Zhang, Jingyu et al. 2020 discovered a new polycyclic metabolite named abyssomicin Y, along with six previously known abyssomicin and proximicin analogs. Abyssomicin Y is classified as a type I abyssomicin, featuring an epoxide group at C-8 and C-9. Three compounds exhibited potent inhibitory effects against the influenza A virus. [34]

Discussion

The results of this review show that marine-based substances have great potential in becoming effective antiviral agents against influenza. The wide variety of sources from the sea and their unique chemical compositions offer promising opportunities for developing safe and efficient therapies to combat influenza infections.

While the findings presented in this review are promising, it's important to recognize the limitations and challenges when applying these results in a clinical setting. Further research is needed to fully understand how these marine based compounds work, conduct studies on their toxicity and evaluate their impact on pharmacokinetics and pharmacodynamics. Additionally, it's crucial to develop methods for extracting and producing these compounds in a scalable and sustainable manner for potential use in pharmaceuticals.

Conclusion

Marine microorganisms residing in the oceanic environment have the capability to produce exceptionally distinct chemical compounds with potent biological activity, including

antiviral properties. These natural antiviral substances hold the potential for combatting various viruses that are harmful to humans, including influenza.

The authors propose a wide array of substances that could be promising in the fight against influenza. These include abyssomycins, polysaccharides, spirostaphylotrichin, violapyrones, polyketides, indole diterpenoids, as well as extracts from microalgae and cyanobacteria, among others.

These substances exhibit various mechanisms of action, such as directly targeting viral adsorption and internalization processes, inhibiting viral polymerase activity, or stimulating the host's immune system.

The authors of the studies strongly recommend further *in vitro* and *in vivo* investigations on substances showing potential antiviral properties.

Disclosure

Author's contribution

Conceptualization, Jakub Rezmer and Inga Wasilewska and Wojciech Homa and Joanna Wanat ; methodology Jakub Rezmer and Wojciech Homa and Adam Kobiernik; check, formal analysis Jakub Rezmer and Inga Wasilewska and Weronika Fortuniak, investigation Jakub Rezmer and Inga Wasilewska and Wojciech Homa, resources, Jakub Rezmer and Inga Wasilewska; data curation, Jakub Rezmer and Wojciech Homa and Joanna Wanat; writing - rough preparation - Jakub Rezmer, writing - review and editing - Inga Wasilewska and Adam Kobiernik and Weronika Fortuniak. All authors have read and agreed with the published version of the manuscript.

Funding

The research received no external funding

Institutional Revier Board Statement

Not applicable.

Informed Consent Statement

Not applicable.

Data Availability Statement

Not applicable.

Conflicts of Interest

The authors declare no conflict of interest.

References:

1. Abdullahi H, Elnahas A, Konje JC. Seasonal influenza during pregnancy. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2021;258:235–239.
2. Kumar, Virendra. “Influenza in Children.” Indian journal of pediatrics vol. 84,2 (2017): 139-143. doi:10.1007/s12098-016-2232-x
3. Smyk, Julia M et al. “Evolution of Influenza Viruses-Drug Resistance, Treatment Options, and Prospects.” International journal of molecular sciences vol. 23,20 12244. 13 Oct. 2022, doi:10.3390/ijms232012244
4. Kim, Meehyein et al. “In vitro inhibition of influenza A virus infection by marine microalga-derived sulfated polysaccharide p-KG03.” Antiviral research vol. 93,2 (2012): 253-259. doi:10.1016/j.antiviral.2011.12.006
5. Ogura, Fumie et al. “Evaluation of an edible blue-green alga, Aphanothece sacrum, for its inhibitory effect on replication of herpes simplex virus type 2 and influenza virus type A.” Bioscience, biotechnology, and biochemistry vol. 74,8 (2010): 1687-90. doi:10.1271/bbb.100336
6. Makarenkova, I D et al. “Antiviral activity of sulfated polysaccharide from the brown algae Laminaria japonica against avian influenza A (H5N1) virus infection in the cultured cells” Voprosy virusologii vol. 55,1 (2010): 41-5.
7. Wang, Wei et al. “Inhibition of Influenza A Virus Infection by Fucoidan Targeting Viral Neuraminidase and Cellular EGFR Pathway.” Scientific reports vol. 7 40760. 17 Jan. 2017, doi:10.1038/srep40760
8. Terasawa, Masahiro et al. “Anti-Influenza A Virus Activity of Rhamnan Sulfate from Green Algae Monostroma nitidum in Mice with Normal and Compromised Immunity.” Marine drugs vol. 18,5 254. 13 May. 2020, doi:10.3390/md18050254
9. Jang, Yejin et al. “Antiviral activity of lambda-carrageenan against influenza viruses and severe acute respiratory syndrome coronavirus 2.” Scientific reports vol. 11,1 821. 12 Jan. 2021, doi:10.1038/s41598-020-80896-9
10. Chen, Yi-Hsiang et al. “Well-tolerated Spirulina extract inhibits influenza virus replication and reduces virus-induced mortality.” Scientific reports vol. 6 24253. 12 Apr. 2016, doi:10.1038/srep24253
11. Zheng, Weifa et al. “Oral administration of exopolysaccharide from Aphanothece halophytica (Chroococcales) significantly inhibits influenza virus (H1N1)-induced pneumonia in mice.” International immunopharmacology vol. 6,7 (2006): 1093-9. doi:10.1016/j.intimp.2006.01.020

12. Nakashima, Ayaka et al. “Antiviral Activity and Underlying Action Mechanism of Euglena Extract against Influenza Virus.” Nutrients vol. 13,11 3911. 30 Oct. 2021, doi:10.3390/nu13113911
13. Nakashima, Ayaka et al. “Oral administration of Euglena gracilis Z and its carbohydrate storage substance provides survival protection against influenza virus infection in mice.” Biochemical and biophysical research communications vol. 494,1-2 (2017): 379-383. doi:10.1016/j.bbrc.2017.09.167
14. Mehrbod, Parvaneh et al. “Prophylactic effect of herbal-marine compound (HESA-A) on influenza A virus infectivity.” BMC complementary and alternative medicine vol. 14 131. 7 Apr. 2014, doi:10.1186/1472-6882-14-131
15. Mehrbod, Parvaneh et al. “Attenuation of influenza virus infectivity with herbal-marine compound (HESA-A): an in vitro study in MDCK cells.” Virology journal vol. 9 44. 16 Feb. 2012, doi:10.1186/1743-422X-9-44
16. Komatsu, Takayuki et al. “Antiviral activity of acidic polysaccharides from Coccomyxa gloeobotrydiformi, a green alga, against an in vitro human influenza A virus infection.” Immunopharmacology and immunotoxicology vol. 35,1 (2013): 1-7. doi:10.3109/08923973.2012.710636
17. Mu, Jinmin et al. “A Novel High-Mannose Specific Lectin from the Green Alga Halimeda renschii Exhibits a Potent Anti-Influenza Virus Activity through High-Affinity Binding to the Viral Hemagglutinin.” Marine drugs vol. 15,8 255. 16 Aug. 2017, doi:10.3390/md15080255
18. Naik, Sanjay, and Sanjit Kumar. “Lectins from plants and algae act as anti-viral against HIV, influenza and coronaviruses.” Molecular biology reports vol. 49,12 (2022): 12239-12246. doi:10.1007/s11033-022-07854-8
19. Su, Jingyao et al. “Duvira Antarctic polysaccharide inhibited H1N1 influenza virus-induced apoptosis through ROS mediated ERK and STAT-3 signaling pathway.” Molecular biology reports vol. 49,7 (2022): 6225-6233. doi:10.1007/s11033-022-07418-w
20. Shao, Qiang et al. “Specific Inhibitory Effect of κ-Carrageenan Polysaccharide on Swine Pandemic 2009 H1N1 Influenza Virus.” PloS one vol. 10,5 e0126577. 13 May. 2015, doi:10.1371/journal.pone.0126577
21. Sato, Yuichiro et al. “Entry Inhibition of Influenza Viruses with High Mannose Binding Lectin ESA-2 from the Red Alga Eucheuma serra through the Recognition of Viral Hemagglutinin.” Marine drugs vol. 13,6 3454-65. 29 May. 2015,

doi:10.3390/md13063454

22. Fan, Yaqin et al. “Indole-diterpenoids with anti-H1N1 activity from the aciduric fungus Penicillium camemberti OUCMDZ-1492.” Journal of natural products vol. 76,7 (2013): 1328-36. doi:10.1021/np400304q
23. Wang, Jianjiao et al. “Spirostaphylotrichin X from a Marine-Derived Fungus as an Anti-influenza Agent Targeting RNA Polymerase PB2.” Journal of natural products vol. 81,12 (2018): 2722-2730. doi:10.1021/acs.jnatprod.8b00656
24. Mia, Md Mukthar et al. “Inhibitory Potentiality of Secondary Metabolites Extracted from Marine Fungus Target on Avian Influenza Virus-A Subtype H5N8 (Neuraminidase) and H5N1 (Nucleoprotein): A Rational Virtual Screening.” Veterinary and animal science vol. 15 100231. 6 Jan. 2022, doi:10.1016/j.vas.2022.100231
25. Liu, Shun-Zhi et al. “Bioactive compounds derived from the marine-derived fungus MCCC3A00951 and their influenza neuraminidase inhibition activity in vitro and in silico.” Natural product research vol. 35,24 (2021): 5621-5628. doi:10.1080/14786419.2020.1817015
26. Luo, Xiaowei et al. “Structurally Diverse Polyketides From the Mangrove-Derived Fungus Diaporthe sp. SCSIO 41011 With Their Anti-influenza A Virus Activities.” Frontiers in chemistry vol. 6 282. 12 Jul. 2018, doi:10.3389/fchem.2018.00282
27. Li, Jing et al. “Studies on synthesis and structure-activity relationship (SAR) of derivatives of a new natural product from marine fungi as inhibitors of influenza virus neuraminidase.” Marine drugs vol. 9,10 (2011): 1887-1901. doi:10.3390/md9101887
28. Niu, Siwen et al. “Spiromastilactones: A new class of influenza virus inhibitors from deep-sea fungus.” European journal of medicinal chemistry vol. 108 (2016): 229-244. doi:10.1016/j.ejmech.2015.09.037
29. Peng, Jixing et al. “Pyronepolyene C-glucosides with NF-κB inhibitory and anti-influenza A viral (H1N1) activities from the sponge-associated fungus Epicoccum sp. JJY40.” Bioorganic & medicinal chemistry letters vol. 22,9 (2012): 3188-90. doi:10.1016/j.bmcl.2012.03.044
30. Hou, Lukuan et al. “Generation of methylated violapyrones with improved anti-influenza A virus activity by heterologous expression of a type III PKS gene in a marine Streptomyces strain.” Bioorganic & medicinal chemistry letters vol. 28,17 (2018): 2865-2868. doi:10.1016/j.bmcl.2018.07.029
31. Silva, Thauane et al. “Inhibitory effect of microalgae and cyanobacteria extracts on influenza virus replication and neuraminidase activity.” PeerJ vol. 6 e5716. 26 Oct. 2018,

doi:10.7717/peerj.5716

32. Zainuddin, E N et al. “Cyanobacteria a potential source of antiviral substances against influenza virus.” Medical microbiology and immunology vol. 191,3-4 (2002): 181-2. doi:10.1007/s00430-002-0142-1
33. Silva, Thauane et al. “Inhibitory effect of microalgae and cyanobacteria extracts on influenza virus replication and neuraminidase activity.” PeerJ vol. 6 e5716. 26 Oct. 2018, doi:10.7717/peerj.5716
34. Zhang, Jingyu et al. “A new abyssomicin polyketide with anti-influenza A virus activity from a marine-derived Verrucosispora sp. MS100137.” Applied microbiology and biotechnology vol. 104,4 (2020): 1533-1543. doi:10.1007/s00253-019-10217-2