E-ISSN: 2347-5129
P-ISSN: 2394-0506
(ICV-Poland) Impact Value: 5.62
(GIF) Impact Factor: 0.549
IJFAS 2020; 8(3): 663-666

www.fisheriesjournal.com
Received: 19-03-2020
Accepted: 23-04-2020

Dian Yuni Pratiwi
Lecturer of Faculty of Fisheries and Marine Science, Universitas Padjadjaran, Indonesia

Fittrie Meyllianawaty Pratiwy
Lecturer of Faculty of Fisheries and Marine Science, Universitas Padjadjaran, Indonesia

Corresponding Author:
Dian Yuni Pratiwi
Lecturer of Faculty of Fisheries and Marine Science, Universitas Padjadjaran, Indonesia

A review: The potential of algae to increase immunity system

Dian Yuni Pratiwi and Fittrie Meyllianawaty Pratiwy

Abstract
The function of immune system is to protect the body from various pathogens such as viruses, bacteria, parasites. If the immune system is good, the protection from various pathogens that cause disease will be increasingly. However, the immune system can also be weakened. Factors that influence the work of the immune system are age, nutrition, exercise, hormones, and emotions. Eating nutritional food is one way to improve the immune system. Algae, which is commonly known as seaweed, is an aquatic commodity that has many benefits and potential to increase the immune system. Several studies have shown that algae can have potential to increase the immune system in humans. Types of algae that have been proven to have the potential to increase the immune system are *Spirulina platensis*, *Eucheuma cottonii*, *Laminaria* sp, *Gracilaria* sp, *Chlorella* sp and others. The other advantages of Algae are growing rapidly along the coastal areas and being a food resources as human consumption. Therefore, the purpose of this article is to review the potential of various algae as antiviral, anticancer and antibacterial in an effort to improve the immune system.

Keywords: Algae, immunity, antiviral, antibacterial, anticancer

1. Introduction
The immune system is an important system for human health. The function of the immune system is to protect the body from various pathogens, maintain the body's homeostasis, and get rid of toxic and allergenic substances. The mechanism of the immune system in protecting the body consists of innate and adaptive immunity. Innate immunity is non-specific. Innate immunity mechanism uses physical (skin, cilia, mucous membranes), chemical (lysozyme, lactoferrin, neurominic acid, interferon, cytokines, chemokines), cells (macrophages, neutrophils, dendritic cells, and natural killer (NK) cells). Adaptive immunity is specific. The defense mechanisms of adaptive immunity are carried out by antibody and cellular (T lymphocytes). However, the immune system can also be weakened. One way to improve the immune system is to eat nutritious foods [1] such as algae. Algae contain various nutrients such as polysaccharides, proteins, and fatty acids [2]. Algae also are a source of several bioactive compounds such as vitamins, pigments, and secondary metabolites. Several studies showed that algae raw extracts had biological activities [3], such as anticancer [4], anti-microbial [5], anti-inflammatory [6], and immunomodulatory activities [7]. This review emphasizes on the potentiality of algae in food and how it can improve the immunity system of human.

2. Algae
Algae belong to the kingdom Protista with cells that have a nucleus. The characteristics of algae are the body of the talus, multicellular/ unicellular, free living and some can symbiosis with other organisms to form lycenes. Algae are photosynthetic organisms that can make their own food). Algae can be grouped into Chlorophyta (Green algae), Chrysophyta (golden algae), Phaeophyta (Brown algae), Rhodophyta (Red algae), Euglenophyta, Pyrrophyta (Fire algae), Bacillariophyta (diatoms) [8].
There are a lot of algae species which can be consumed by human. *Ulva lactuca* is a green algae usually cooked as an ingredient in soup. *Saccharina japonica* is brown algae which can be used to make broth. *Pyropia yezoensis* can be used as nori to wrap rice in Japan. *Gracilaria* sp as ingredients for jelly [9]. *Spirulina platensis* and *Chlorella* sp are commonly used as a single cell protein supplement [10].

Several studies have shown that algae have the potentiality to increase the immune system in humans. Bioactive compounds in Algae can be used for increase immunity system. These contents have the potential to be antiviral, antibacterial, and anticancer [2].

2.1 Antiviral Agent

Viral disease has remained the leading causes death globally. Bird flu of Influenza A virus subtype (H5N1) had a fatality rate of 60% percent [11]. Global HIV statistics reports that at the end of 2018, 77 million people died from AIDS-related illnesses [12]. By the end of 2019, Covid 19 caused by the corona virus had spread in the city of Wuhan, Hubei, China. Since then, covid 19 has continued to spread to various countries. On 11 March 2020, it was declared a pandemic by WHO. Until May 26, 2020, the number of people infected with covid 19 worldwide was 5,406,282 cases and 343,562 people had died [13].

Virus infected host cell by some stages. Stages 1, the virus attaches to host cells (adhesion). Stages 2, viral nucleic acids enter the host cell (adsorption). Stages 3, replication of the genome virus (eclipse phase). Stages 4, maturity of the particle virus. Stages 5, virus particle release from host cell and induce host cell death. The virus induces host cell death by apoptosis or pyroptosis. Even though antiviral agents have discovered, the resistance and the side effects of drug might trigger the failure of antiviral therapy [14]. Therefore, the antiviral agents still needs to be examine.

Algae contains various ingredients that have the potential to become antiviral agents. The content in several types of algae that can act as antivirals are carrageenan, galactan, alginate, fucoidan, fucan, laminar, and calcium spirulan. Carrageenan blocked the binding of viruses (adhesion) into the host cell or the internalization of the virus into the host cells. Galactan potential as an antiviral agent because can blockage of the virus adhesion and replication into the host cell. Alginate can inhibit the inverse transcriptase in RNA viruses. Fucan Inhibition of cell adhesion and blockage of the reverse transcriptase. Laminaran can blockage of the reverse transcriptase activity. *Calcium spirulan* can inhibit the attachment, penetration, and replication of viruses in host cells [14].

*Spirulin*a has been shown to have antiviral potential. A study on the potential of *Spirulina* sp cold water extract at a dose of 5,000 mg/kg, or 3,000 mg/kg/day for 14 successive days has been conducted. The results showed that *Spirulina* sp extract inhibited viral plaque formation in a broad range of influenza viruses and reduced yields in cells [15].

Not only *Spirulina*, some species of algae have also antiviral potential. *Gracilaria tenuistipitata* has been shown to inhibit HCV protein synthesis, RNA replication, and HCV infection [16]. *Laminaria japonica* contains fucoidan which has antiviral activity. Fucoidan with a concentration of 50 to 500 µg/ml can inhibit influenza A/H5N1 virus production within 24 hours of infection [17]. Fucoidan form *Fucus vesiculosus* can also suppress HBV replication [18].

2.2 Antibacterial Agent

Bacteria infection is responsible for illnesses in humans. Some diseases can affect death such as tuberculosis, and pneumonia. Various antibiotics have been used to fight bacterial infections. However, some microbes are resistant to ingredients. Therefore, natural ingredients that have antibacterial potential need to be found [19].

Algae are abundant biological resources which contain potential bioactive compounds as antibacterial. Bioactive compounds found in algae include alkaloids, flavonoids, steroids, tannins, phenols, saponins [20], and glycosides [21].

Research on the potentiality of antibacteria in seaweed have been widely carried out. The first genus is Gracilaria. There are many species from genus *Gracilaria*, which have antibacterial activities. *Gracilaria* sp extract with a concentration of 0.05% has been shown to inhibit the growth of *Escherichia coli*, *Staphylococcus aureus* [22]. *Gracilaria verrucosa* extracted with methanol: aquades (75:25) for 72 hours can inhibit the growth of *E. coli* and *Salmonella typhimurium* [23]. The isoamyl alcohol extract of *G. verrucosa*, *G. foliifera*, *G. corticata*, *G. crassa* and *G. edulis* have potential to inhibit growth of *Pseudomonas aeruginosa*, *Enterobacter aerogenes*, *S. typhi* and *S. aureus* [24]. The methanol extract of *G. corticata* can inhibit growth of *S. aureus*, *Bacillus subtilis*, *Streptococcus pneumonia*, *Enterococcus faecalis*, *Klebsiella pneumoniae* and *Proteus mirabilis* [25]. A research about the effect on bacterial growth of a crude sulfated polysaccharide (SP) from the red marine alga *G. ornata* has been conducted in 2012. The result showed that *G. ornata* can inhibit growth of *E. coli* [26].

The other genus of algae which have antibacterial activity is Eucheuma. *Eucheuma cottonii* is one of algae from genus Eucheuma that can produce secondary metabolites that act as antibacterial. *E. cottonii* can inhibit growth of *S. aureus*, *E. coli*, *V. cholera*, and *S. typhosa* [27]. The minimum inhibitory concentration of *E. cottonii* to *E. coli*, *S. aureus* and *V. cholera* were at 1% concentration while *S. typhosa* was at 5% concentration [27]. *E. spinosum* and *E. denticulatum* also have antibacterial activity. *E. spinosum* can inhibit growth of *S. aureus* [28] and *Porphyromonas gingivalis* [29]. *E. denticulatum* can inhibit growth of *S. aureus* and *S. pyogenes* [30].

Ulva also shows antibacterial activity. *Ulva rigida* can inhibit growth of *E. coli*, *Vibrio tapetis*, *Pseudomonas cepacia, P. aeruginosa*, *Aeromonas hydrophila*, *Salmonella typhymurium*, *S. aureus*, *E. faecalis* [31]. The n-butanolic extract *Ulva reticulata* has antibacterial activity against *S. typhi*, *S. aureus*, *E. coli*, *P. aeruginosa*, *V. cholerae*, *Vibrio parahaemolyticus*, *B. cereus* and *Listeria monocytogenes*. The highest inhibition of *U. reticulata* was exhibited against *E. coli* and *B. cereus* [32]. The chloroform and ethyl acetate extract of *U. lactuca* can act as antibacterial against *E. fecalis*, *K. pnumoniae*, *S. aureus*, and *E. coli*. The ethyl acetate extract of *U. lactuca* was more effective as antibacterial than chloroform extract [33].

Antibacterial agents can act as bacteriocidal (kill bacteria), bacteriostatic (inhibit bacterial growth) or inhibit the germination of bacterial spores. Antibacterial kills or inhibits bacterial growth by inhibiting cell wall synthesis [34], changing the permeability of bacterial cells, diffusing into membranes and interacting with genetic material causing mutations [35].

2.3 Anticancer Agent

Cancer occurs because of abnormalities in the cell cycle regulation system so that cell division is not controlled. One of the causes of cancer is ROS (Reactive Oxygen Species). ROS (Reactive Oxygen Species) cause DNA mutation. DNA mutations can occur in tumor suppressor gene and make this gene inactivation [36].

Bioactive compounds in algae have potential as anticancer. They can act as anticancer by inducing apoptotic pathway of cancer cells [36], and inhibitory ROS (Reactive Oxygen

Species) activity and trigger antioxidant gene expression. Apoptotic pathways can be induced by caspase dependent or caspase independent pathways. Bioactive compounds can act as antioxidant which inhibit Reactive Oxygen Species (ROS) activity by exchanging one of their own electrons with the free radical molecules to stabilize them [37].

There are a lot of research about algae as potential agent for anticancer. A research to about anticancer effect of methanol extracts from *E. cottonii*, red algae on cervix cancer Hela cells has been conducted. The concentration of 0.5, 0.7, 0.9 and 1.0 mg/mL treated for 24 hours. The result showed that methanol extracts from *E. cottonii* can inhibit the proliferation of HeLa cells and induced apoptosis to the HeLa cells [38]. The ethanol extract of *E. cottonii* also effective in inhibiting mammary tumor growth and more effective than tamoxifen and displayed little toxicity to the liver and kidneys [39]. *E. cottonii* can also inhibit proliferation of breast MCF-7 and colorectal HCT-116 cancer cells [40]

Brown algae, *S. japonica* anticancer activities. *S. japonica* with dose of 20 and 30 µg/ml of the extract for 24 can induces apoptosis and cell cycle arrest in 267B1/K-ras human prostate cancer cells [41]. *S. japonica* can also inhibit growth and induced apoptosis nasopharyngeal carcinoma cell lines [42], human hepatocellular carcinoma cells [43].

Green algae, *U. lactuca* also has anticancer activity. *U. lactuca* contains polysaccharides, steroids, glycosides, flavonoids, and tannins that can act as anticancer [40]. The effects of polysaccharides, ulvan on *U. lactuca* on human breast cancer cell line (MCF-7) has been conducted. The result showed that ulvan polysaccharides at the level of initiative and promotion might have potential chemopreventive effects against breast carscinogenesis [44]. *U. lactuca* can also inhibit the growth of human leukemia cell lines, human throat cancer cells (hep2), breast human cancer (MCF7), and colocteral (HT29) cancer cell lines [45]. The other green algae, *Chlorella vulgaris* also has anticancer activities against human breast cancer (MCF7) cell lines [46], human liver cancer cell line (HepG2) [47], murine melanoma B16F10 cell line [48].

3. Conclusion

In conclusion, the development of new antiviral and antibacterial agents with diverse kinds of actions is widely developed. The examination for new agents focuses on not only synthetic compounds but also natural products such as animals, and plants. This review paper has a great deal of interest regarding the marine algae as potential antiviral and antibacterial agents to increase the immune system in human's body based on its components.

4. References

1. Cruvinel WM, Junior DM, Araujo JAP, Catelan TTT, Silva de Siuza AW, Pereira de Silva N *et al*. Immune system – Part I Fundamentals of innate immunity with emphasis on molecular and cellular mechanisms of inflammatory response. Brazilian Journal Rheumatology. 2010; 50(4):434-461.
2. Ganesan AR, Tiwari U, and Rajauria G. Seaweed nutraceuticals and their therapeutic role in disease prevention. Food Sciences and Human Wellness. 2019;8(3):252-263.
3. Martinez AKA, Lauritano C, Romano G, Ianora A. Marine microalgae with anti-cancer properties. Marine Drugs. 2018; 16(5):165.
4. Chen X, Song L, Wang H, Liu S, Yu H, Wang X *et al.* Partial characterization, the immune modulation and anticancer activities of sulfated polysaccharides from filamentous microalgae *Tribonema* sp. Molecules. 2019; 24:322.
5. Martinez KA, Lauritano C, Druka D, Romano G, Grohmann T, Jaspars M *et al*. Amphidinol 22, a New Cytotoxic and Antifungal Amphidinol from the Dinoflagellate Amphidinium carterae. Marine Drugs. 2019; 17:385.
6. Rodriguez-Luna A, Avila-Roman J, Gonzalez-Rodriguez ML, Cozar MJ, Rabasco AM, Motilva V *et al*. Fucoxanthin-containing cream prevents epidermal hyperplasia and uvb-induced skin erythema in mice. Marine Drugs. 2018; 16:378.
7. Manzo E, Cutignano A, Pagano D, Gallo C, Barra G, Nuzzo G *et al*. A new marine-derived sulfoglycolipid triggers dendritic cell activation and immune adjuvant response. Scientific Reports. 2017; 7:6286.
8. Quick dissolving tablets. http://www.materiipa.com. 16 June, 2020.
9. Wells ML, Potin P, Craigie JS, Raven JA, Merchant SS, Helliwell KE *et al.* Algae as nutritional and functional food sources: revisiting our understanding. The Journal of Applied Phycology. 2017; 29:949-982.
10. Ritala A, Hakkinen ST, Toivari M, and Wiebe MG. Single cell protein- State of the art industrial landscape and patent 2001-2016. Frontiers in Microbiology. 2017; 8:1-18.
11. Quick dissolving tablets. https://www.who.int. 9 June, 2020
12. Quick dissolving tablets. https://www.unaids.org/en. 9 June, 2020
13. Quick dissolving tablets. https://covid19.who.int. 27 Mei, 2020
14. Sansone C, Brunet C, Noonan DM, and Albini A. Marine Algal Antioxidants as Potential Vectors for Controlling Viral Diseases. Antioxidants. 2020; 9(392):1-12.
15. Chen YH, Chang GK, Kuo SM, Huang SY, Hu LC, Lo YL *et al.* Well tolerated *Spirulina* extract inhibits influenza virus replication and reduces virus induced mortality. Scientific Reports. 2016; 6:1-11.
16. Chen KJ, Tseng CK, Chang FR, Yang JL, Yeh, CC, Chen WC *et al*. Aqueous extract of the edible *Gracilaria tenuistipitata* inhibits Hepatitis C viral replication via cyclooxygenase-2-suppression and reduces virus induced inflamation. Plos One. 2013; 8(2)(e57704):1-8.
17. Makarenkova ID, Deriabin PG, L'Kov DK, Viagintseva TN, Besednova NN. Antiviral Activity of Sulfated Polysaccharide from the Brown Algae *Laminaria Japonica* Against Avian Influenza A (H5N1) Virus Infection in the Cultured Cells. Voprosy virusologii. 2010; 55(1):41-45.
18. Li HF, Li JR, Tang Y, Lin L, Xie ZL, Zhou J *et al.* Fucoidan from *Fucus vesiculosus* suppresses hepatitis B virus replication by enhancing extracellular signal regulated Kinase activation. Virology Journal. 2017; 14(178):1-8.
19. Zaman S, Hussain MA, Nye R, Mehta V, Mamun KT, Hossain N. A review on antibiotic resistance: Alarm bells are ringing. Cureus. 2017; 9(6):e1403.
20. Singkoh O, Mantiri DMH, Lumenta C, and Manoppo H. Identification bioactive compounds of algae *Halymenia durvillei*. Journal Bios Logos. 2019; 9(1):83-90.

21. Riwanti P, and Izazih F. Phytochemical Screening of 96% Ethanol Extract *Sargassum polycystum* and Profile with Infrared Spectrophotometry. Acta Holistica Pharmaciana. 2019; 1(1):34-41.
22. Melki, Wike Ayu EP, Kurniati. Antibacterial Test of *Gracilaria* sp. Extract. (Seaweed) Against *Escherichia coli* and *Staphylococcus aureus*. Ocean Sciences Study Program FMIPA Sriwijaya University, Palembang, 2011.
23. Dayuti S. Antibacterial activity of red algae (*Gracilaria verrucosa*) extract against *Escherichia coli* and *Salmonella typhimurium*. Aseanfen International Fisheries Symposium, 2017.
24. Prasad MP, Sushant S, Ganesh R. Antibacterial activity of seaweed (*Gracilaria*) extracts against human pathogens. Asian Journal of Biological Sciences. 2012; 1(3):219-222.
25. Balasankar T, Pushparaj A. Antimicrobial activity of red seaweed *Gracilaria corticata* against human pathogenic bacterial strains. World Journal of Pharmaceutical Sciences. 2014; 2(12):2321-3310.
26. Amorim *et al*. Antimicrobial Effect of a Crude Sulfated Polysaccharide from the Red Seaweed *Gracilaria ornata*. Brazilian Archives of Biology and Technology. 2012; 55(2):171-181.
27. Sartika R, Melki, Anna IS, Purwiyanto. Antibacterial activity of *Eucheuma cottoni* seaweed extract against bacteria *Escherichia coli*, *Staphylococcus aureus*, *Vibrio cholera* and *Salmonella typhosa*. Maspari Journal. 2013; 5(2):98-103.
28. Safitri A, Srihardyastutie A, Roosdiana A, and Sutrisno. Antibacterial activity and phytochemical analysis of edible seaweed *Eucheuma spinosum* against *Staphyloccocus aureus*. Journal of Pure and Applied Chemistry Research. 2018; 3:301-315.
29. Mattulada IK, Trilaksana AC, Abduh DA. Antibacterial effectivity of red algae extract (*Euchema spinosum*) to inhibit the growth of bacteria *Porphyromonas gingivalis*. Makassar Dental Journal. 2018; 7(1):40-45.
30. Al-Haj NA, Mashan NI, Shamsudin MN, Mohamad H, Vairappan CS, Sekawi Z. Antibacterial activity in marine algae *Eucheuma denticulatum* against *Staphylococcus aureus* and *Streptococcus pyogenes*. Research Journal of Biological Sciences. 2009; 4(4):519-524.
31. Ismail A, Ktari L, Rhomdane YBR, Aoun B, Sadok S, Boudabous A *et al*. Antimicrobial fatty acids from green alga *Ulva rigida* (Chlorophyta). Hindawi BioMed Research International, 2018.
32. Ravikumar S, Anburajan L, and Meena B. Antibacterial activity of *Ulva reticulata* from southwest coast of Kanyakumari, India. Journal of Coastal Life Medicine. 2018; 4(3):246-247.
33. Habbu P, Warad V, Shastri R, Sevant C, Madagundi S, Kekare P. *In vitro* and *in vivo* antimicrobial activity of *Ulva lactuca* Linn. (Green algae) associated endophytic bacterial Strains. Journal of Applied Pharmaceutical Science. 2016; 6(10):138-146.
34. Pelczar MJ, Chan. Fundamentals of Microbiology. UI-Press, Jakarta, 2015.
35. Edberg SC. Antimicrobial susceptibility test in antibiotics and infection. Penerbit Buku Kedokteran, Jakarta, 1983.
36. Majumder I, Paul S, Kundu R. Anti cancerous and anti tumorous activity of algae- a review. International Journal of Innovative Pharmaceutical Sciences and Research. 2015; 3(2):72-89.
37. Sanchez C. Reactive oxygen spesies and antioxidant properties from mushrooms. Synthetic and System Biotechnology. 2017; 2(91):13-22.
38. Lee JW, Teo SS. *In vitro* cytotoxicity and anticancer activity of *Eucheuma Cottonii* extracts against hela cell line. Malaysian Journal of Science. 2013; 32:213-220.
39. Shamsabadi A, Khoddami A, Fard SG, Abdullah R, Othman HH, Mohamed S. Comparison of tamoxifen with edible seaweed (*Eucheuma cottonii* L.) Extract in suppressing breast tumor. Nutrition and Cancer. 2013; 65(2):255–262.
40. Arsianti *et al*. Phytochemical composition and anticancer activity of seaweeds *Ulva lactuca* and *Eucheuma cottonii* against breast MCf-7 and colon HCT-116 cells. Asian Journal of Pharmaceutical and Clinical Research. 2016; 9(6):115-119.
41. Jo MJ, Kim HR, Kim GD. The anticancer effect of *Saccharina japonica* on 267BI/K-ras human prostate cancer cells. International Journal of Oncology. 2012; 41(5):1789-1797.
42. Wei F, L X, Lin Y, Guo M, Sun W. Effect and mechanism of *Laminaria japonica* polysaccharide (LJP) on apoptosis and cycle of nasopharyngeal carcinoma cells. Biomedical Research. 2017; 28(15):6706-6710.
43. Jung HI, Jo MJ, Kim HR, Choi YH, Kim GD. Extract of *Saccharina japonica* induces apoptosis companied by cell cycle arrest and endoplasmic reticulum stress in SK-Hep1 human hepatocellular carcinoma cells. Asian Pacific Journal of Cancer Prevention. 2014; 15(7):2993-2999.
44. Ellatef GE, Ahmed OM, Reheim ESA, Hamid A, and Hamid A. *Ulva lactuca* polysaccharides prevent wistar rat breast carcinogenesis through the augmentation of apoptosis, enhancement of antioxidant defense system, and suppression of inflammation. Breast Cancer - Targets and Therapy. 2017; 9:67-83.
45. Devi JS, Bhimba BV. Anticancer activity of silver nanoparticles synthesized by the seaweed *Ulva lactuca in vitro*. Open Access Scientific Reports. 2012; 1(4):1-4.
46. Ghosh P, and Das S. Exploitation of *Chlorella Vulgaris* for treatment of breast cancer. Proceedings of International Conference on Drug Discovery (ICDD), 2020.
47. Yusof YAM, Saad SM, Makpol S, Shamaan NA, Ngahl WWW. Hot water extract of *Chlorella vulgaris* induced DNA damage and apoptosis. Clinics. 2010; 65(12):1371-1377.
48. Gupta P, Sinha D, Bandopadhyaya R. Isolation and screening of marine microalgae *Chlorella* sp for anticancer activity. International Journal of Pharmacy and Pharmaceutical Sciences. 2014; 6(10):517-519.