CHAPTER SAMPLER

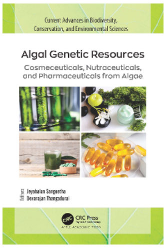
Plant Biotechnology

Routledge
Taylor & Francis Group

APPLE ACADEMIC PRESS

www.routledge.com

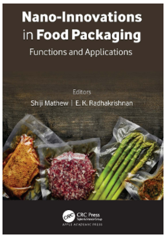
Contents



1. Algae as Nutraceutical, Functional Food, and Food Ingredient

By Umesh Pawar et al

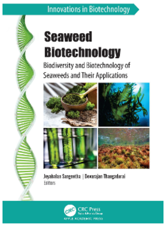
From Algal Genetic Resources Edited By Jeyabalan Sangeetha, Devarajan Thangadurai



2. Edible Nanocoatings and Films for Preservation of Food Matrices

By Shiji Mathew & E. K. Radhakrishnan

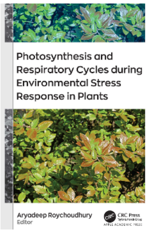
From Nano-Innovations in Food Packaging: Functions and Applications Edited By Shiji Mathew, E. K. Radhakrishnan



3. Seaweeds as a New Source of Bioactive Compounds and Potent Biotechnological Applications

By Fatima El Khalloufi and Brahim Oudra

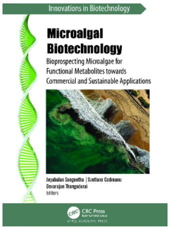
From Seaweed Biotechnology: Biodiversity and Biotechnology of Seaweeds and Their Applications Edited By Jeyabalan Sangeetha, Devarajan Thangadurai



4. Introduction to Plant Responses to Environmental Stress

By Preetha Bhadra, Sagar Maitra, and Masina Sairam

From Photosynthesis and Respiratory Cycles during Environmental Stress Response in Plants Edited By Aryadeep Roychoudhury



5. Microalgae: A Valuable Source of Natural Colorants for Commercial Applications

By Chidambaram Kulandaisamy Venil, Matheswaran Yaamini and Laurent Dufossee

From Microalgal Biotechnology: Bioprospecting Microalgae for Functional Metabolites towards Commercial and Sustainable Applications Edited By Jeyabalan Sangeetha, Svetlana Codreanu, Devarajan Thangadurai

Request your free Inspection Copy and discover more of our free resources for Faculty on our Instructor Hub.

CHAPTER 2

ALGAE AS NUTRACEUTICAL, FUNCTIONAL FOOD, AND FOOD INGREDIENTS

UMESH PAWAR,[1] NIVAS DESAI,[1] UTTAM DETHE,[1]
VISHAL APARADH,[1] and DATTATRAY GAIKWAD[2]

[1]*Department of Botany, S.P.K. College, Sawantwadi–416510, Maharashtra, India*

[2]*Sub-Center, Babasaheb Ambedkar Marathwada University, Aurangabad, Osmanabad–413501, Maharashtra, India*

ABSTRACT

The increasing demand of algal food supplement is growing tremendously. Algae are being consumed for functional benefits beyond the traditional considerations of nutrition and health. There is considerable evidence for the health benefits of algal-derived food products, but there remain considerable challenges in quantifying these benefits, as well as possible adverse effects. Algae are primary producers presenting a remarkable source of different nutrients. The high protein content of algal species is one of the main reasons to consider them as an important source of proteins, oils from microalgae rich in some PUFAs seem particularly suitable for children, pregnant women, vegetarians, and patients with fish allergies. Algae also represent an important source of vitamins, minerals, antioxidants, and natural colorants, the incorporation of the whole biomass in food and feed could be used to provide the color, increment nutritional value, and improve texture or resistance to oxidation.

2.1 INTRODUCTION

Algae are the most abundant primary producers on the global surface. The algae are the lower plants which contain chlorophyll in cells and are typical inhabiting in aquatic environment (freshwater and saline ocean waters) (Blazencic, 2007), and on the basis of dimensions they are divided into macroalgae and microalgae. There are three main classes, or phyla, of seaweed: Phaeophyceae (brown algae), Rhodophyta (red algae), and Chlorophyta (green algae). Thousands of species comprise each phylum (Rindi et al., 2012; Guiry and Guiry, 2019). A special group of microalgae are blue-green algae, also called cyanobacteria because of their prokaryotic cell type, group of organisms for the isolation of novel and biochemically active natural products (Singh et al., 2005). Algae have been consumed by coastal localities worldwide since the beginning of human civilization (Dillehay et al., 2008). Microalgae are also utilized in the cosmetics industry or as animal feed (Huntley et al., 2015; Ariede et al., 2017).

2.1.1 NUTRITIONAL VALUE

Algae are a rich and varied source of pharmacologically active natural products and nutraceuticals. While nutraceutical and pharmaceutical content in the baseline algae strain is very small, current market values for these products are extremely high. The major products currently being commercialized or under consideration for commercial extraction include carotenoids, phycobilins, fatty acids (FAs), polysaccharides, vitamins, sterols, and biologically active molecules for use in human and animal health. The upcoming sections will bring into focus the use of algae as a potential source of pharmaceutical and nutraceutical ingredients. The growing use of algae biomass for nutraceutical purposes is expected to provide an attractive revenue stream for algae producers. While nutraceutical content in the baseline algae strain is very small, current market values for these products are extremely high. Physiologically-active nutraceuticals from algae include food supplements, dietary supplements, value-added processed foods as well as non-food supplements such as tablets, soft gels, capsules, etc.

Some of the noteworthy products that can be derived from algae: omega-3 polyunsaturated fatty acids (PUFA), carotenoids, astaxanthin, and β-carotene.

The markets for both pharmaceuticals and nutraceuticals are growing quickly worldwide, and it is this global scope that particularly attracts marketers. A growing proportion of today's promising pharmaceutical and nutraceutical research focuses on the production of promising compounds from algae. Thus, the untapped potential of algae in the field of pharmaceuticals and nutraceuticals has to be still explored to grow and capitalize on tremendous global marketing opportunities.

2.1.2 FUNCTIONAL FOOD AND INGREDIENTS

At the beginning of the 1980s, the functional food concept first time came in Japan. The meaning of that concept was protecting the health of people and to reduce the high health costs (Arai, 1996). Functional food is defined as food that contains more functional ingredients that provide additional health benefits (Lordan et al., 2011). Nowadays, a wide variety of compounds such as polyphenols, PUFA, or phytosterols obtained, for example, from wine, fish byproducts, or plants are utilized to prepare new functional foods (Plaza et al., 2009). Algae play an important role in human diet in recent years (Turner, 2003; Craigie, 2010). The algal metabolite compounds are a vital source of ingredients for the development of food products they are also good source of proteins, minerals, vitamins, amino acids, lipids, fatty acids, polysaccharides, nucleic acid, and carotenoids, etc., which have huge value as nutraceuticals (Tokuşoglu and Una, 2003; Priyadarshani and Rath, 2012).

2.2 ALGAE AS NUTRACEUTICAL

In the last few decades, interest has grown in seaweeds as nutraceuticals, or functional foods, which gave dietary benefits beyond their macronutrient content. In addition, seaweed has been explored for metabolites with biological activity, to produce therapeutic products (Davis and Vasanthi, 2011; Zerrifi et al., 2018). Throughout human history, seaweeds have been used as food, folk remedies, dyes, and mineral-rich fertilizers (Shannon and Abu-Ghannam, 2019). Marine algae present a good antioxidant activity (Biriș-Dorhoi et al., 2019). They are an important source of vitamins, minerals, proteins, PUFA, antioxidants, etc., (Blazencic, 2007; Gouveia et al., 2008).

Seaweeds are also rich in bioactive compounds, including polyphenols, polysaccharides (Teng et al., 2013), peptides, sterols, flavonoids, alkaloids, proteins, and other bioactive compounds (Jmel et al., 2019; Randhir et al., 2020).

Algae contain enormous bioactive compounds having wide biological activities such as antioxidant, anti-bacterial, anti-viral, anti-carcinogenic, etc. Some algae contain high fiber content in the form of sulfated galactans or carragenates in red algae, fucans, alginates, and laminarin, etc. The intake of high fiber diet has a progressive effect on the human body that curtails the risks of cancer, diabetes, obesity, and hypercholesterolemia. The high fiber content diet showed a good immunological activity (German et al., 2013). Alginate in *Undaria pinnatifida* showed a positive effect on cardiovascular disease, and alginic acid demonstrated to reduce hypertension in hypertensive rats (Ikeda et al., 2006). Alginic acid, xyloglucans in *Sargassum vulgare* and sulfated fucans in *Undaria pinnatifida* have anti-viral activity against herpes type-1 and cytomegalovirus in humans (Thompson and Dragar, 2004; Hemmingson et al., 2006). The fucoidans from algae acts as anti-coagulant, anti-thrombotic agents and also showed anti-tumoral properties in rat model studies (Lee et al., 2013; Maruyama et al., 2013; De Jesus Raposo et al., 2015). A sulfated polysaccharide from the *Porphyra* sp. has apoptotic property in carcinogenic cells (Maruyama et al., 2013; Raposo et al., 2015).

2.2.1 ANTIOXIDANTS

The in vitro antioxidant activities were proved by different studies. Marine algae are rich sources of antioxidant compounds. Microalgae and macroalgae contain antioxidant organic compounds and enzymes that control the oxidative damage (Cornish and Garbary, 2010). There are two broad categories of antioxidant activity of algae, and they are decreasing oxidative stress on the gut microbiome by limiting reactive oxygen species (ROS) within the digestive tract and transportation of epithelial cells into the blood for distribution throughout the body (Gobler et al., 2011). Natural antioxidants, found in many algae, are important bioactive compounds that play an important role against various diseases and aging processes through the protection of cells from oxidative damage. The detected antioxidant compounds in algae from these genera and others have potential anti-aging, dietary, anti-inflammatory, anti-bacterial, antifungal, cytotoxic, anti-malarial, anti-proliferative, and anticancer properties (Zubia et al., 2007).

2.2.2 PROTEINS

Protein constitutes 5–47% of seaweed dry mass. Red seaweeds have the greatest protein content, while green has less, and brown the least (Cerna, 2011). Of the total amino acids (aa) in seaweeds, approximately 42% to 48% are essential aa (Wong and Cheung, 2000). In terms of a score (on a scale of 0.0–1.0), where egg protein has a score of 1.0, most seaweeds have a higher score than all plant-based proteins, with the exception of soy, which has a score of 1.0. *Undaria pinnatifida* has an amino acid score of 1.0, equal to that of egg and soy, *Pyropia/Porphyra* 0.91, and *Laminaria saccharina* 0.82 (Murata and Nakazoe, 2001). However, the high polyphenolic content of seaweeds can reduce the digestibility of algal proteins, giving a slightly lower score on the protein digestibility-corrected aa scale (Wong and Cheung, 2001). Despite this, seaweeds still represent a viable alternative to animal-derived protein; if other high-aa scoring vegan foods, such as soy or mycoprotein, are included in the diet. Nori, a dried sheet product of *Porphyra yezoensis* is known to contain an exceptionally high (12.5–51.5% w/w) protein content among seaweeds and can be expected to produce a high quantity of free amino acids after degradation (Uchida et al., 2017). *Spirulina* as a plant-based source of complete protein, makes it an ideal dietary supplement choice for vegetarians (De Marco et al., 2014).

2.2.3 LIPIDS

Lipids play a vital role for all living organism as it is component of cell membrane, actively engaged in cell signaling (Eyster, 2007). Algal lipids consist of phospholipids, glycolipids, and non-polar glycerolipids. Phospholipids and glycolipids are important for membrane function. Lipid membranes contain sterols such as fucosterol and β-sitosterol (Fahy et al., 2005) and it has health benefits (Arul et al., 2012). Algae contain many of the major lipids of plants, such as the glycosylglycerides and the usual phosphoglycerides. In addition, more unusual compounds such as the betaine lipids, chlorosulfolipids or various other sulfolipids may be major components of some species or orders. These acyl lipids have characteristic fatty acid compositions and are often highly enriched in PUFAs. PUFA are vital components in human nutrition and are known to have several beneficial effects for human health. Betaine lipids are widely distributed in algae, where they display different functions as donors of diacylglycerols and fatty acids (FAs) to be used in the biosynthesis of other lipid classes (Rey et al., 2019).

2.2.4 CARBOHYDRATES

The photosynthate produced during photosynthesis is the major carbohydrates in the algae. Mostly these carbohydrates are used for building structural element and also energy storage. The main polysaccharides obtained from marine algae are: alginate, agar, and carrageenan. Those hydrocolloids are commonly used in food, pharmaceutical industries, and in biotechnology, among others, due to their ability to form highly viscous solutions and gels. Agar and carrageenan form thermoreversible gels. However, agar melts at a higher temperature than carrageenan (Hernández-Carmona et al., 2013).

2.2.5 ALKALOIDS

Alkaloids have been isolated from macroalgae. Marine algae contain 44 alkaloids, consisting of 1 phenylethylamine, 41 indole, and 1 naphthyridine derivates. In the halogenated alkaloid group, there can be found 25 bromine-containing compounds, among which 7 have chlorine and 5 have sulfur, additionally. In brown algae are rarely found, but in red algae, alkaloids are more abundant than in green algae. Some alkaloids were produced by host organisms on algae. Like communes in which was isolated from the mycelium of a strain of *Penicillium* sp. on the *Enteromorpha intestinalis*, Ascosalipyrrolidinone was isolated from fungus *Ascochyta salicornia* on green alga *Ulva* sp. and citrinadin A was isolated from *Penicillium citrinum* separated from a marine red alga (Guven et al., 2013).

2.2.6 MINERALS AND VITAMINS

Marine algae in particular often contain a wide range of minerals (magnesium, selenium, chromium, zinc) (Sugimura et al., 1976; Thomson et al., 1996; Mouritsen, 2013). Processed seaweeds are widely used as mineral and metal nutritional supplements (Kay, 1991). Some minerals may be excessively concentrated by algae. Iodine is often found in algae at levels greater than recommended for human consumption, causing thyroid problems in regular consumers (Phaneuf et al., 1999). Cesium is also concentrated in seaweed, which is of concern only when the water is contaminated with radioactive Caesium. Algae are also rich in many vitamins, such as A, C, B1, B2, B3, and B6, as well as minerals, such as iodine, calcium, potassium, magnesium, and iron. They can be consumed from cooked to dried or raw

(Siva et al., 2015). Algae are used for some products such as medicines, vitamins, vaccines, nutraceuticals, and other nutrients. Many types of algae and the products derived from them have shown medicinal values and nutritional applications.

2.3 FUNCTIONAL FOOD INGREDIENTS

The increased interest in functional food ingredients and other natural food products has been recognized to promote excellent health, decrease the risk of mainly non-communicable diseases, and enhance cost effective care by promoting a quality of life (Shahidi, 2008). The positive impact of nutritious foods on human health has been long realized, which has led to the development of several innovative functional ingredients and functional food products. Functional foods have been linked with health improvement, quality of life, and decrease illness risk (Gouveia et al., 2010). Algae-derived nutrients and bioactive compounds are being investigated for their potential biological activities (Batista et al., 2013; Nuno et al., 2013). Edible algae can be directly consumed or used as a raw material for preparing food. Nowadays, there are diverse species of edible seaweeds be cultured as large-scale including *Porphyra yezoensis*, *Saccharina japonica*, and *Undaria pinnatifida*. Seaweeds contain a large amount of nutrient contents such as proteins, dietary fiber, vitamins, and minerals. Regular consumption of seaweeds has many benefits. As an addition to these benefits, the medicinal properties of seaweed bioactive have been recognized. Seaweeds are used for treatment and or for prevention of goiter, which is caused by the lack of iodine in the diet. Several studies have shown various remedial effects of algal species against non-communicable diseases such as inflammation, obesity, diabetes, hypertension, and viral infections (Shao et al., 2017). A clinical study showed that regular consumption of *Undaria* seaweed can effectively minimize the risk of breast cancer in women, while an oral administration of seaweed extracts (*Fucus vesiculosus*, *Macrocystis pyrifera* and *Laminaria japonica*) with zinc, manganese, and vitamin B6, potentially decreased osteoarthritis symptoms in a mixed population. Seaweeds are well-known for their antioxidant capacities and bioactive polyphenolic compounds (Ganesan et al., 2019). *Gracilaria canaliculata* can be used up in the form of powder added to food items and ready to use (Madhu et al., 2011). In coastal areas of all continents, seaweeds are used in human and animal nutrition, so that they are widely cultivated algal crops.

Species such as *Porphyra* sp., *Chondrus crispus*, *Himanthalia elongata*, and *Undaria pinnatifida* are very interesting to consumers and the food industry due to their low content in calories and high content in vitamins, minerals, and dietetic fiber (Plaza et al., 2008). On the other hand, microalgal biomass is usually available in the form of powder, tablets, capsules, liquids, and, also, it can be incorporated into different food products. However, the consumption of microalgal biomass is restricted to very few taxa, and the most important in human nutrition are *Spirulina* and *Chlorella* genera. *Spirulina* as a superfood is a plant that can nourish the body by providing most of the protein require by the body. It helps to prevent the annoying sniffling and sneezing of allergies, reinforces the immune system, helps to control high blood pressure and cholesterol, and helps to protect against cancer. The recommended daily dose is typically 3–5 grams, which can be spread out twice to thrice a day (Oluwakemi and Sharma, 2017). *Spirulina* comes in capsules, tablets, powders, and flakes. *Spirulina* is a safe source of protein, nutrients, vitamins, and minerals that has been used for centuries, though there are no known side effects associated with spirulina, the body may react to it based on individual current state of health. The reactions can be reduced by increasing the water intake, reducing stress levels, eating according to nutritional type, and getting plenty of rest.

2.4 CONCLUSION

Algae are a sustainable source of bioactive compounds for human health and functional food applications. The global burden of diseases such as type 2 diabetes, hypertension, obesity, cancer, antibiotic resistance, and heart disease places a huge strain on the finances and resources of health services in affected countries. This may be improved by the inclusion of algal-based supplements in the diet, as part of overall lifestyle improvement. 'Algal Food as Pharma' could be promoted in terms of the natural health and nutritional benefits of dietary macroalgae based on epidemiological studies. Having reviewed the literature on the benefits of algae consumption, data from scientific medical studies may inform public health systems in the design of dietary intervention plans and may be beneficial for policymakers, educators, practitioners, researchers, and academics who contribute to the promotion of public health. The functional properties of seaweed can be incorporated into food, from fat replacers to antioxidant, fiber, and antimicrobial enhancers. We should focus on the marine agronomy, mariculture, and bioengineering of algae for future prospecting and challenges.

KEYWORDS

- **algae**
- **alkaloids**
- **antioxidants**
- **carbohydrates**
- **food ingredients**
- **functional food**
- **lipids**
- **minerals**
- **nutraceuticals**
- **nutrients**
- **proteins**
- **seaweeds**
- **vitamins**

REFERENCES

Arai, S., (1996). Studies of functional foods in Japan; State of the art. *Biosci. Biotechnol. Biochem., 60*, 9–15.

Ariede, M. B., Candido, T. M., Jacome, A. L. M., Velasco, M. V. R., De Carvalho, J. C. M., & Baby, A. R., (2017). Cosmetic attributes of algae: A review. *Algal Res., 25*, 483–487.

Arul, A. B., Al Numair, K., Al Saif, M., & Savarimuthu, I., (2012). Effect of dietary beta-sitosterol on fecal bacterial and colonic biotransformation enzymes in 1,2-dimethylhydrazine induced colon carcinogenesis. *Turk. J. Med. Sci., 42*, 1307–1313.

Batista, A. P., Gouveia, L., Bandarra, N. M., Franco, J. M., & Raymundo, A., (2013). Comparison of microalgal biomass profiles as novel functional ingredients for food products. *Algal Research, 2*(2), 164–173.

Biriș-Dorhoi, E., Michiu, D., Taloș, I., & Tofa, M., (2019). Algae as functional food: Review. *Hop and Medicinal Plants, 28*, 1–2.

Blazencic, J., (2007). *Sistematika Algi*. Beograd: NNK International.

Cerna, M., (2011). Seaweed proteins and amino acids as nutraceuticals. In: Kim, S. K., (ed.), *Advances in Food and Nutrition Research* (pp. 297–312). Academic Press, San Diego, California, USA.

Cornish, M. L., & Garbary, D. J., (2010). Antioxidants from macroalgae: Potential applications to human health and nutrition. *Algae, 25*, 155–171.

Davis, G. D. J., & Vasanthi, A. H. R., (2011). Seaweed metabolite database: A database of natural compounds from marine algae. *Bioinformation, 5*, 361–364.

De Jesus, R. M. F., De Morais, A. M., & De Morais, R. M., (2015). Marine polysaccharides from algae with potential biomedical applications. *Marine Drugs, 13*(5), 2967–3028.

De Marco, E. R., Steffolani, M. E., Martinez, C. S., & Leon, A. E., (2014). Effects of spirulina biomass on the technological and nutritional quality of bread wheat pasta. *LWT-Food Sci. Technol., 58*, 102–108.

Dillehay, T. D., Ramirez, C., Pino, M., Collins, M. B., Rossen, J., & Pino, N. J., (2008). Monte Verde: Seaweed, food, medicine, and the peopling of South America. *Science, 320*, 784–786.

Eyster, K. M., (2007). The membrane and lipids as integral participants in signal transduction: Lipid signal transduction for the non-lipid biochemist. *Adv. Physiol. Educ., 31*, 5–16.

Fahy, E., Subramaniam, S., Brown, H. A., Glass, C. K., Merrill, A. H., & Murphy, R. C., (2005). A comprehensive classification system for lipids. *J. Lipid Res., 46*, 839–861.

Ganesan, A. R., Uma, T., & Gaurav, R., (2019). Seaweed nutraceuticals and their therapeutic role in disease prevention. *Food Science and Human Wellness, 8*, 252–263.

German, J. B., Zivkovic, A. M., Dallas, D. C., & Smilowitz, J. T., (2013). Nutrigenomics and personalized diets: What will they mean for food? *Annual Review of Food Science Technology, 2*, 97–123.

Gobler, C. J., Berry, D. L., Dyhrman, S. T., Wilhelm, S. W., Salamov, A., & Lobanov, A. V., (2011). Niche of the harmful alga *Aureococcus anophagefferens* revealed through ecogenomics. *Proc Natl. Acad. Sci. USA., 108*, 4352–4357.

Gouveia, L., Batista, A. P., Sousa, I., Raymundo, A., & Bandarra, N. M., (2008). Microalgae in novel food products. In: Papadoupoulos, K., (ed.), *Food Chemistry Research Developments* (pp. 75–112). New York: Nova Science Publishers.

Gouveia, L., Marques, A. E., Sousa, J. M., Moura, P., & Bandarra, N. M., (2010). Microalgae-source of natural bioactive molecules as functional ingredients. *Food Science and Technology Bulletin, 7*(2), 21–37.

Guiry, M. D., & Guiry, G. M., (2019). *Algae Base*. National University of Ireland, Galway.

Hemmingson, J. A., Falshaw, R., Furneaux, R. H., & Thompson, K., (2006). Structure and anti-viral activity of the galactofucan sulfates extracted from *Undaria pinnatifida* (Phaeophyta). *Journal of Applied Phycology, 18*, 185–193.

Hernandez-Carmona, G., Freile-Pelegrin, Y., & Garibay, E., (2013). Conventional and alternative technologies for the extraction of algal polysaccharides. *Functional Ingredients from Algae for Foods and Nutraceuticals*, 475–516.

Huntley, M., Johnson, Z., Brown, S., Sills, D., Gerber, L., Archibald, I., Machesky, S., et al., (2015). Demonstrated large-scale production of marine microalgae for fuels and feed. *Algal Res., 10*, 249–265.

Ikeda, K., Kitamura, A., Machida, H., Watanabe, M., & Negishi, H., (2006). Effect of *Undaria pinnatifida* (Wakame) on the development of cerebrovascular diseases in stroke-prone spontaneously hypertensive rats. *Clinical and Experimental Pharmacology and Physiology, 30*(1, 2), 44–48.

Kay, R. A., (1991). Microalgae as food and supplement. *Crit. Rev. Food Sci. Nutr., 30*, 555–573.

Kwon, M. J., & Nam, T. J., (2006). Porphyran induces apoptosis related signal pathway in AGS gastric cancer cell lines. *Life Sciences, 79*(20), 1956–1962.

Lee, J. C., Hou, M. F., Huang, H. W., Chang, F. R., & Yeh, C. C., (2013). Marine algal natural products with anti-oxidative, anti-inflammatory, and anticancer properties. *Cancer Cell International, 13*(1), 55–62.

Lordan, S., Paul, R. R., & Stanton, C., (2011). Marine bioactives as functional food ingredients: Potential to reduce the incidence of chronic diseases. *Marine Drugs, 9*(6), 1056–1100.

Madhu, B. K., Bereket, T., Bikshal, B. K., Phani, R. S., & Ravi, A., (2011). Protein rich marine red algae-*Gracilaria canaliculata* as an additive for diet. *Journal of Pharmacy Research, 4*(11), 4306–4307.

Maruyama, H., Tamauchi, H., Hashimoto, M., & Nakano, T., (2013). Antitumor activity and immune response of Mekabu fucoidan extracted from sporophyll of *Undaria pinnatifida*. *In Vivo, 17*(3), 245–249.

Mouritsen, O. G., (2013). *Seaweeds, Edible, Available and Sustainable*. Chicago: University of Chicago Press.

Murata, M., & Nakazoe, J., (2001). Production and use of marine algae in Japan. *Japan Agricultural Research Quarterly, 35*, 281–290.

Nuno, K., Villarruel-Lopez, A., Puebla-Perez, A. M., Romero-Velarde, E., & Puebla-Mora, A. G., (2013). Effects of the marine microalgae *Isochrysis galbana* and *Nannochloropsis oculata* in diabetic rats. *Journal of Functional Foods, 5*(1), 106–115.

Phaneuf, D., Cote, I., Dumas, P., Ferron, L. A., & LeBlanc, A., (1999). Evaluation of the contamination of marine algae (seaweed) from the St. Lawrence River and likely to be consumed by humans. *Environmental Research, 80*, 175–182.

Plaza, M., Cifuentes, A., & Ibanez, E., (2008). In the search of new functional food ingredients from algae. *Trends in Food Science and Technology, 19*(1), 31–39.

Plaza, M., Herrero, M., Cifuentes, A., & Ibanez, E., (2009). Innovative natural functional ingredients from microalgae. *J. Agric. Food Chem., 57*, 7159–7170.

Priyadarshani, I., & Rath, B., (2012). Commercial and industrial applications of microalgae: A review. *Journal of Algal Biomass Utilization, 3*(4), 89–100.

Randhira, A., Laird, D. W., Maker, G., Trengove, R., & Moheimania, N. R., (2020). Microalgae: A potential sustainable commercial source of sterols. *Algal Research, 46*, 101772.

Rindi, F., Soler-Vila, A., & Guiry, M. D., (2012). Taxonomy of marine macroalgae used as sources of bioactive compounds. In: Hayes, M., (ed.), *Marine Bioactive Compounds* (pp. 1–53). Springer, New York, USA.

Shahidi, F., (2008). Nutraceuticals and functional foods: Whole versus processed foods. *Trends in Food Science and Technology, 20*(9), 376–387.

Shannon, E., & Abu-Ghannam, N., (2019). Seaweeds as nutraceuticals for health and nutrition. *Phycologia, 58*(5), 563–577.

Shao, L. L., Xu, J., Shi, M. J., Wang, X., Li, Y. T., Kong, L. M., & Zhou, T., (2017). Preparation, antioxidant, and antimicrobial evaluation of hydroxamated degraded polysaccharides from *Enteromorpha prolifera*. *Food Chem., 237*, 481–487.

Singh, S., Kate, B. N., & Banerjee, U. C., (2005). Bioactive compounds from cyanobacteria and microalgae: An overview. *Critical Reviews in Biotechnology, 25*(3), 73–95.

Slavin, J., (2013). Fiber and prebiotics: Mechanisms and health benefits. *Nutrients, 5*(4), 1417–1435.

Sugimura, Y., Suzuki, Y., & Miyake, Y., (1976). The content of selenium and its chemical form in seawater. *Journal of the Oceanographical Society of Japan, 32*, 235–241.

Thompson, K. D., & Dragar, C., (2004). Anti-viral activity of *Undaria pinnatifida* against herpes simplex virus. *Phytotherapy Research, 18*(7), 551–555.

Thomson, C. D., Smith, T. E., Butler, K. A., & Packer, M. A., (1996). An evaluation of urinary measures of iodine and selenium status. *Journal of Trace Elements in Medicine and Biology, 10*, 214–222.

Tokuşoglu, O., & Una, M. K., (2003). Biomass nutrient profiles of three microalgae: *Spirulina platensis*, *Chlorella vulgaris*, and *Isochrisis galbana*. *Journal of Food Science, 68*(4), 1144–1148.

Turner, N. J., (2003). The ethnobotany of edible seaweed (*Porphyra abbottae* and related species; Rhodophyta: Bangiales) and its use by first nations on the Pacific Coast of Canada. *Can. J. Bot., 81*, 283–293.

Uchida, M., Kurushima, H., Ishihara, K., Murata, Y., Touhata, K., Ishida, N., Niwa, K., & Araki, T., (2017). Characterization of fermented seaweed sauce prepared from nori (*Pyropia yezoensis*). *J. Biosci. Bioeng., 123*(3), 327–332.

Wong, K. H., & Cheung, P. C. K., (2001). Nutritional evaluation of some subtropical red and green seaweeds. Part II: *In vitro* protein digestibility and amino acid profiles of protein concentrates. *Food Chemistry, 72*, 11–17.

Wong, K., & Cheung, P. C., (2000). Nutritional evaluation of some subtropical red and green seaweeds: Part I: proximate composition, amino acid profiles and some physicochemical properties. *Food Chemistry, 71*, 475–482.

Zerrifi, S., El Khalloufi, F., Oudra, B., & Vasconcelos, V., (2018). Seaweed bioactive compounds against pathogens and microalgae: Potential uses on pharmacology and harmful algae bloom control. *Marine Drugs, 16*, 55.

Zubia, M., Robledo, D., & Freile-Pelegrin, Y., (2007). Antioxidant activities in tropical marine macroalgae from the Yucatan Peninsula, Mexico. *J. Appl. Phycol., 19*, 449–458.

CHAPTER 8

Edible Nanocoatings and Films for Preservation of Food Matrices

SHIJI MATHEW and E. K. RADHAKRISHNAN*

School of Biosciences, Mahatma Gandhi University, Kottayam 686560, Kerala, India

**Corresponding author. E-mail: radhakrishnanek@mgu.ac.in*

ABSTRACT

Edible packagings in the form of coatings and thin films are one among the leading interesting and attractive primary packaging approaches for optimization of food quality. Edible coatings/thin films are prepared from renewable natural biomaterials, such as polysaccharides, lipids, and proteins which can be applied directly on food products to improve their quality and shelf life. Edible packaging possesses the unique advantages of being edible along with the packed food, biodegradable, eco-friendly, and washable. Advanced research has shown that the incorporation of nanomaterials in edible films can make this venture more promising and efficient. Nanomaterials or nanocomposite-based edible films/coatings can offer better encapsulation of bioactive agents and confer controlled release of antioxidants, antimicrobials, nutraceuticals, and flavoring agents. Besides, edible nanocoatings/films can also lead to improvement of food functional aspects like sensory attributes, maintain natural appearance, as well as provide protection from microbial spoilage thereby preserving the food freshness. This chapter discusses about the general aspects of edible coating and edible nanocoating, various types of nano-based edible coating biomaterials used, methods of applying edible nanocoatings on fresh and processed foods, and the recent developments and successful applications in this area.

8.1 INTRODUCTION

The food from the producer has to be protected from various environmental factors until it reaches the consumer. Hence, food-packaging materials are considered to have a vital role in the food chain supplies. Edible packagings are thin layer of primary packaging composed of biopolymeric material that is used to coat/wrap the food directly to extend its shelf life without changing the original architecture of the food (Dehghani et al., 2018). These coatings form an integral part of the food such that it can be consumed along with the food. Edible packagings generally can be applied by two different ways: in the liquid form such that it forms a coat around the food or as thin solid film laminates which can be used to wrap the food (Falguera et al., 2011).

Edible coatings have been used since the 12th and 13th centuries in China in the form of waxes which were applied on lemons and oranges for increasing its shelf life (Zeuthen and Bøgh-Sørensen, 2003). Afterwards, edible coatings have received great attraction in various countries owing to their advantages that they can be consumed along with the food, leaving behind no waste to be discarded and also thereby lessening the environmental impact. Moreover, being simple process in application, this technology greatly influenced the consumer demands and new market requirements. With the incorporation of active agents (antimicrobials, antioxidants, and natural extracts), edible coatings can also be converted to active edible coatings which besides extending the product's shelf life, can also release the active agents in a controlled manner to improve the physical, chemical, sensory, and organoleptic properties of the food (Santos and Melo, 2020).

As we all are aware, in recent times, the study and application of nanotechnology in various fields, primarily in the food sector has increased with promising results. Due to their unique characteristics, nanomaterials when added to edible coatings can have a great impact, resulting in an upgrading of the functionalities and applications of edible coatings (González-Reza et al., 2018). Numerous studies have shown that the application of a bionanocomposite or nanomaterial-based edible coating/film over highly perishable fresh produces and processed foods can prevent their rapid spoilage, maintain freshness without affecting their original architecture, and also provides an extended shelf life.

This chapter provides an in-depth knowledge on the various advancements and practical aspects of nanomaterials-based edible packaging systems. The first section of this chapter mainly focuses on the important functions attributed by nano-based edible coatings/films as an ideal food packaging. This is followed by a detailed portion on the main strategies used for the preparation and application of edible nanocoatings or films on food matrices. Then, the different biomaterials used for the fabrication of nanostructure-based edible packaging materials are briefed with suitable examples. The later section covers the practical role and effect of edible nanocoatings/films in packaging of varied fresh and processed food products which are explained with appropriate examples.

8.2 MULTIFUNCTIONAL EDIBLE NANOCOATINGS

Edible nanocoats/films offer many advantages which make them attractive and convenient compared with synthetic packaging materials. Edible nano-based packagings are considered as a one-step solution which offers all the essential functions required for an ideal packaging. The multiple functions performed by nanostructure-based edible coatings are described below.

Edible: As the name indicates, the main advantage and attractive feature of using edible nano-based package is that it forms an integral part of the food and can be consumed along with the packaged product (Janjarasskul and Krochta, 2010) as these packagings are mainly composed of bio-based renewable and edible ingredients. **Protection:** Edible nanocoatings/films can give physical protection to foods and can also prevent the draining of liquid from it. They can also extend the food's shelf life by providing effective barrier to gases, light, and water. Moreover, these coatings can reduce the loss of moisture, aromas, and solutes from the food and allows selective and controlled exchange of gases involved in food respiration, such as O_2, CO_2, ethylene, etc. (Huber and Embuscado, 2009). **Eco-friendly:** Since these edible packages do not create any waste material of their own, they also play a major role in reducing the serious environmental impact of white pollution. **Preserves organoleptic properties:** Nanocomposites or nanostructured edible coating matrices act as a good medium for adding various additives and functional groups which can play a vital role in maintaining the original texture, taste, and odor of the packed foods (Bharti et al., 2020). **Antimicrobial performance:** The incorporation of biocidal nanomaterials in the coatings can impart antimicrobial ability and hence can function in greatly reducing microbial contamination of foods. **Antioxidant property:** With the inclusion of antioxidants, the edible coatings can have antioxidant ability which can result in the preservation of fresh produces and prevent them from browning. **Role as carrier:** Edible nanocoatings can act as carrier of many bioactive natural agents, such as antimicrobials, antioxidants, flavoring agents, dyes, plant/animal extracts, or prebiotic and probiotic agents. Such encapsulated nanocoatings can cause controlled release of these agents which can further enhance the nutritional value and boost up the sensory attributes of food. **Washable:** Some nanocoatings are even washable, so that they form an intact protective covering over the food surface and can be easily removed by washing prior to consumption of the coated food. **Sensorial ability:** Edible coatings can also be incorporated with certain nanosensors which can rapidly detect any possible spoilage or chemical changes on the coated fruit and immediately notify it to the consumer. Figure 8.1 summarizes the multiple functions of nano-based edible coatings.

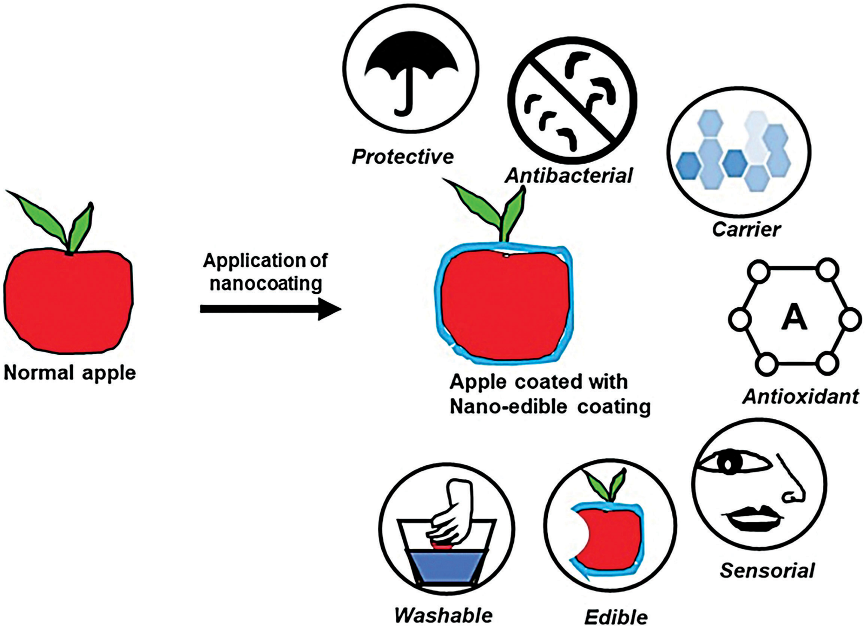


FIGURE 8.1 Multiple functions performed by edible nanocoatings on food materials

On the other side, certain limitations are also associated with the implementation of nanotechnological applications in foods. Regulation of the use and safety aspects of nano-based edible coatings is still a controversial issue. Currently, there are many uncertainties regarding their response to public health, impact on environment and occupational risks associated with their manufacturing (Zambrano-Zaragoza et al., 2018).

8.3 METHODS OF APPLYING EDIBLE NANOCOATINS/FILMS ON FOOD

Different methods are available for preparing nanolaminate food wraps and application of edible nanocoatings on the surface of food. The major methods for applying nanocoatings include dipping/drenching or immersing, coating (spray, spread, or spin rotation method), fluidized bed, and panning (Suhag et al., 2020; Yanyun Zhao, 2011). Similarly, the main methods that are followed for preparing nanolaminates or films include casting, extrusion, electrospinning, etc. In addition, multilayered nano-based edible coating can be prepared by dipping, layer-by-layer method, and co-extrusion technology. The selection of these methods depends upon the nature of the food to be coated, objective of coating process, and surface attributes of coating process, such as surface tension, density, and viscosity (Andrade et al., 2012). The major steps involved in these procedures are illustrated in Figure 8.2. Dipping, spraying, and solvent casting methods are discussed in detail in the following section.

8.3.1 DIPPING OR IMMERSING

Dipping/drenching or immersing method of nanocoating aids in the formation of uniform coatings on the food surface (Lu et al., 2010). The first step in this process involves the development of a pH adjusted homogenous nanocoating solution/dispersion. Next step is the preparation of the food sample to be coated which includes its cleaning, cutting, drying, and weighing. After this step, the food is dipped/immersed in the nanocoating solution/dispersion for a desired time (30 s–30 min). Then the coating deposited food is taken out, the excess solution is drained off and then the solvent is allowed to dry by evaporation. Finally, the coated food can be stored in plastic or any other containers. The wetting capacity of

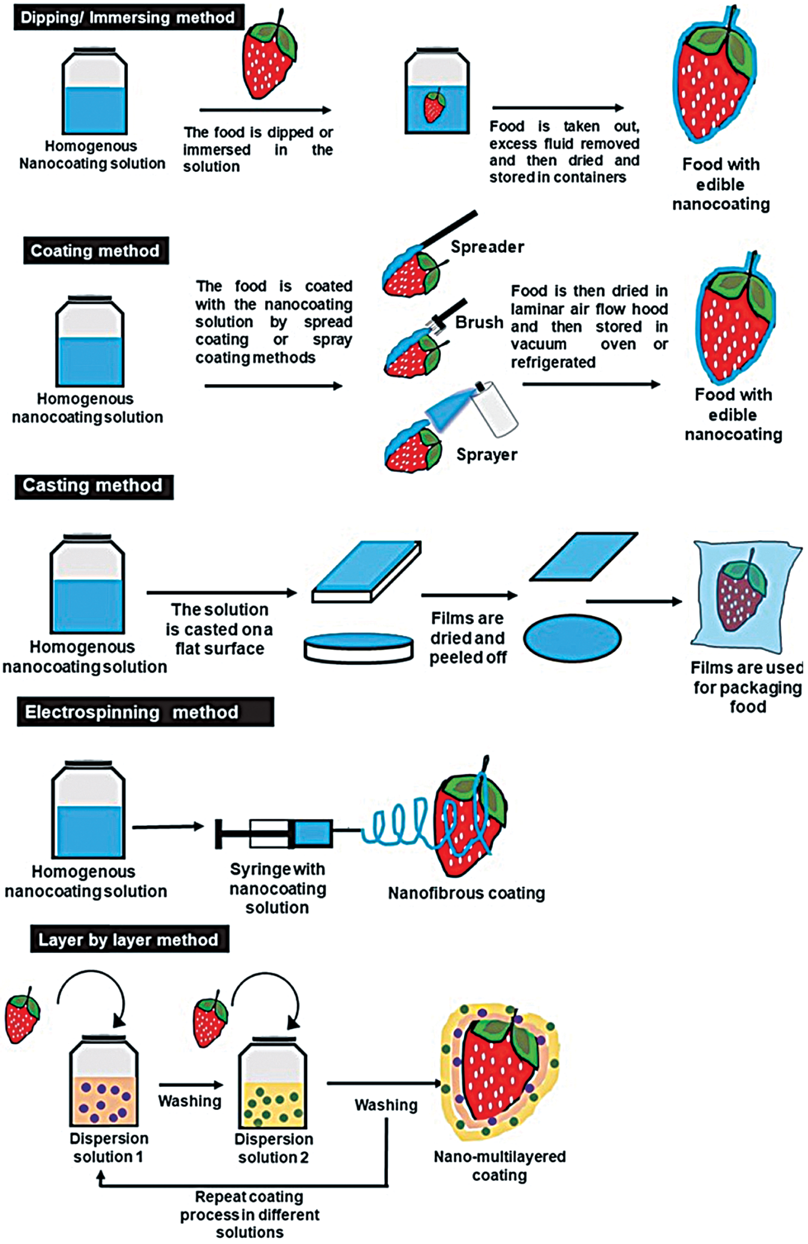


FIGURE 8.2 Different strategies used for application of edible nanocoatings on food surface. *Source:* Adapted and modified from Gheorghita (Puscaselu) et al. (2020), Zambrano-Zaragoza et al. (2020).

the food surface, processing, and draining time plays an important role in determining the success of this process. Immersion or dipping process is a simple procedure which provides better preservation of the coated foods, especially fresh produces. This method can also be employed to generate multiple layers of coating on the food, which may provide even better performance (Wang et al., 2018).

8.3.2 COATING

Coating is a method of applying the nano-based coats either directly on the surface of the food, such as fruits, meat, vegetables or indirectly on the surface of the packaging material. This can be done by three different ways: spread coating, spray coating, and spin coating.

Spread coating: Direct Spread coating on food surface can be done by the use of sterile tools, such as spreader, brush, or spatula. This type of coating is a potentially effective method in preserving the quality of the food and limiting the microbial growth. These direct spread coatings can also influence the gas permeability and thereby extend the shelf life of the coated products. Indirect spread coating of nanoformulations on packaging material can also offer better antibacterial property and can also be used as a method of fabricating multilayer sheets of coating on the packaging material (Guo et al., 2014).

Spray coating: Spraying can be done with a set of nozzles which forms droplets that can be dispensed on food surfaces. Spray coating can be attained with the use of tools, such as knapsack sprayer, compressed air-assisted sprayer, or copper backpack. Three types of spraying techniques for coating on foods include air spray atomization, air-assisted airless atomization, and pressure atomization (Gheorghita (Puscaselu) et al., 2020; Suhag et al., 2020).

8.3.3 CASTING

Casting or solvent casting is the most common method of preparing edible nanolaminates or films. This process involves three steps: (1) Solubilization process where the selected polymer and chosen nano-additives are dissolved or dispersed in a suitable solvent separately. (2) Casting process, in this process, the dissolved/dispersed polymer/solvent/additive mixture is poured onto a flat surface such as a petridish/Teflon plate. This is followed by the (3) drying process where the solvent gets removed by evaporation, leaving behind a thin film of the nanocomposite (Suhag et al., 2020). Finally, this film can be used to wrap the food.

8.4 MATRICES USED FOR EDIBLE NANOCOATINGS

Biopolymeric and easily available and renewable sources, such as polysaccharides, proteins, and lipids are generally employed for the fabrication of nanocomposite or nanostructured edible matrices. The following section discusses on the use of these important matrices for the development of a nano-based edible coating/film with certain examples.

8.4.1 POLYSACCHARIDES-BASED EDIBLE NANOCOATINGS

Being one of the most widely available biopolymers, polysaccharides of animal, plant, and marine origin are the extensively researched matrix for the development of nanomaterial-based edible packagings (Aguirre-Joya et al., 2018). The structure and properties of these polysaccharide favors the effective incorporation, as well as biological and molecular functioning of nanomaterials in this matrix (Zheng et al., 2015). The common polysaccharides exploited for the fabrication of nano-based edible coatings include pectin (Sucheta et al., 2019), starch (Escamilla-García et al., 2018), alginate (Emamifar and Bavaisi, 2020), chitosan (Ortiz-Duarte et al., 2019), gum xanthan (K. S. et al., 2020), and carrageenan. Definitely, starch-based edible nanocoatings/films are the most researched ones which are found to protect and act as efficient carriers of bioactive agents for controlled delivery.

Polysaccharide-based edible nanocoatings can be fabricated in two important ways: (1) exploitation of any polysaccharide matrix for the incorporation of various functional nanoparticles or (2) by nanostructuring of the polysaccharides itself, for example, use of cellulose nanocrystals. The nanomaterials often used as additives in polysaccharide matrix to provide functional characteristics include metallic nanoparticles, such as silver (Ortiz-Duarte et al., 2019), zinc oxide (Koushesh Saba and Amini, 2017), and titanium dioxide (Mozhgan Nasiri et al., 2019), solid lipid nanoparticles (Zambrano-Zaragoza et al., 2013), polymeric nanoparticles, such as nanochitosan (Mohammadi et al., 2016) or cellulose nanocrystals (Souza Vieira da Silva et al., 2019), essential oil nanoparticles (Zhang et al., 2019).

Many reports are available on the development and application of polysaccharide-based coatings/thin films for food packaging purpose. In a very recent work, a novel approach was reported where structured oil nanoparticles (SONs) fabricated from sunflower oil was used to improve the hydrophobicity of polysaccharide-based edible films (Ghiasi et al., 2020). Here, farsi gum (FG) was used as the polysaccharide matrix. Comparatively, the physicochemical, mechanical, and thermal properties of FG films with 0.5% SONs showed better performance over FG films with SONs with 0 and 1% (w/w) and sunflower oil-incorporated FG control films.

8.4.2 PROTEINS-BASED EDIBLE NANOCOATINGS

Recently, proteins derived from both animal and plant sources have been greatly used for the preparation of nano-based edible coatings/films as they offer hydrophilic surfaces providing improved water and gas barrier properties. The common protein matrices used for the preparation of nanomaterial-based edible food coatings include whey (Wang et al., 2020) and casein proteins (Bora and Mishra, 2016) from milk, zein from corn (Hager et al., 2019), gluten from wheat (Tanada-Palmu and Grosso, 2005), and gelatine from animal tissues (Zhang et al., 2017) and egg proteins.

Protein-based edible nanocoatings can be developed by three ways: (1) either by using an animal or plant-based protein matrix onto which various functional nanoparticles can be incorporated or (2) by using nanostructured form of proteins as an essential component of coatings (such as nanostructured zein, gelatin and bovine serum albumin), or (3) by the application of protein-based nanofibers such as electrospun whey nanofiber in edible coatings. Nanostructured zein is a highly attractive nanostructured protein candidate which is highly stable and an efficient vehicle for entrapping and controlled delivering of bioactive substances.

In a recent work, an interesting edible and washable poly (albumen)-based multifunctional bionanocomposite coating composed of egg white protein, glycerol, egg yolk, curcumin extract, and cellulose nanocrystals was reported by Jung and colleagues. For its practical application, perishable fruits, such as papaya, banana, strawberries, and avocado were coated by dipping method and the results showed that this nanocoating would preserve the cosmetic appearance of fruits as well as reduce microbial growth, dehydration, and respiration of fruits, thereby contributing to an extended fruit shelf life (Jung et al., 2020). Table 8.1 shows the list of protein-based edible nanocoatings and their practical applications in food preservation.

8.4.3 LIPIDS-BASED EDIBLE NANOCOATINGS

Many natural sources, such as plants, animals, and insects are rich in lipids. Recently, researchers have focused more on to the usage of lipids as edible coatings/thin films as a matrix for the inclusion of functional nanoparticles which in addition to act as efficient edible packaging, can also provide gloss, reduce moisture loss, and lessens the complexity and cost of packaging among others. The important lipids used for this purpose include oils, fats, waxes, essential oils, plasticisers, resins, and emulsifiers. In addition, nanostructured lipid matrices possess high encapsulation ability and impart controlled delivery of bioactive substances. Nanoemulsions of essential oils from various spices, nuts, and fruits are important examples of nanostructured lipid which forms an important ingredient in active nano-based edible coatings due to its potential antimicrobial and flavor enhancing capability. Table 8.2 summarizes various examples of edible coatings with nanoemulsions of essential oil and their potential applications.

8.5 DIRECT APPLICATION OF EDIBLE NANOCOATINGS ON FOODS

One of the most important applications of edible coatings/films comes in the case of perishable food stuffs, such as fresh produces like vegetables and fruits, meat and poultry, fish and marine foods, and eggs and dairy products. The section below details on the use of various nano-based edible coatings/thin films that have been applied for preservation and shelf life extension of both processed and fresh foods.

TABLE 8.1 List of Protein-Based Edible Nanocoatings and Their Practical Application.

Components of edible nanocoating	Preparation method	Functions performed	References
Hazelnut industry waste with nanoemulsions of clove essential oil	Ultrasonication	Provided better mechanical, antibacterial, and antioxidant properties	Gul et al. (2018)
Gluten films containing chitosan–gelatin nanofibers	Nozzle-less electrospinning	Improved mechanical properties	Ebrahimi et al. (2019)
Gamma-aminobutyric acid-rich edible films with soy fermented protein and chitosan	Casting method	Antimicrobial and antioxidant	Zareie et al. (2020)
Soy protein SiOx nanocomposite film	Casting method	Extended the shelf life of apples	Liu et al. (2017)
Whey protein concentrate-corn oil-TiO_2 nanoparticles	Casting method	Extended shelf life of cheese	Montes-de-Oca-Ávalos et al. (2020)
Chitosan–whey protein	Casting method	Chestnut preservation, antimicrobial properties	Huang et al. (2020)
Semolina protein with zinc oxide nanoparticles	Casting method	Improved mechanical and antibacterial properties	Jafarzadeh et al. (2017)

TABLE 8.2 List of Edible Food Coatings Composed of Nanoemulsions of Essential Oil for Food Packaging Application.

Edible coating matrix	Essential oil present	Preparation method	Functions performed	References
Whey protein films	Nanoemulsion of *Grammosciadium ptrocarpum* Bioss. essential oil	Casting	Lowered water permeability, improved mechanical, and antimicrobial performance	Ghadetaj et al. (2018)
Chitosan coatings	Nano-encapsulated *Paulownia tomentosa* essential oil	Casting	Improved shelf life of ready-to-cook pork chops	Aguilar-Sánchez et al. (2019)
Chitosan–gelatin coating	Nanoencapsulated tarragon essential oil	Ionic gelation	Preservation of pork slices	Zhang et al. (2020)
Pullulan films	Nanoemulsions of cinnamon essential oil	Ultrasonication	Antibacterial performance	Chu et al. (2020)
Whey protein isolate/chitosan	Nanoencapsulated garlic essential oil	Casting	Extended shelf life of vacuum-packed sausages	H. Esmaeili et al. (2020)
Sodium caseinate films reinforced with ZnO nanoparticles	Microencapsulated *Melissa officinalis* essential oil	Casting	High antioxidant and antibacterial properties	Sani et al. (2021)
Large mouth mass Fish sarcoplasmic protein–chitosan	Nanoemulsions of ginger essential oil	Casting	Extended shelf life of red sea bream fillets	Cai et al. (2020)
Chitosan films	Nanoemulsion of cumin essential oil	Casting	Improved quality of beef loins	Dini et al. (2020)
Banana starch films	Nanoemulsions of lemon grass and rosemary essential oils	Casting	Nanoemulsions increased the plasticity and decreased the water barrier properties of the films	Restrepo et al. (2018)

8.5.1 FRUITS AND VEGETABLES

Fruits and vegetables are one among the highly perishable food items wherein 40–50% of products are wasted every year. The factors which attribute to the rapid decay of fruits and vegetables during the postharvest management processes, such as handling, transportation, and storage include the presence of insects, microorganisms, loss of water, respiration, texture deterioration, transpiration, and senescence (Ali et al., 2010; Jung et al., 2020).

Many methods are adopted for preserving the freshness and to extend their shelf life of fruits and vegetables. Refrigeration is considered as the most common, traditional, and effective method to preserve fresh produces, but the process itself is not found to be sufficient enough. Other methods include the use of modified atmosphere packaging (MAP) and active coatings based on paraffin wax. Unfortunately, all these techniques possess the limitations of being expensive, time-consuming, and can also result in altering the texture and organoleptic properties of these produces. Another common method is waxing which involves coating fruit with preservatives containing weak acids and their derivatives, but is often associated with adverse effects in human body following its consumption. In this context, the use of bionanocomposite or nanostructure-based coatings is considered to be a promising alternative without causing any alteration to the physiological or physiochemical characteristics of the coated food. Numerous literatures have reported the preparation and application of nano-based edible coatings for the preservation of fruits and vegetables (Table 8.3). Few are discussed below.

In a recent study, different formulations based on chitosan nanoparticles and chitosan thyme essential oil (15%, 30%, and 45%) was used to develop natural edible nanocoatings by Correa-Pacheco et al., 2021. Then these formulations named CS15, CS30, CS45, TEO15, TEO30, and TEO45 were used to coat on fresh green bell peppers. Later, the quality and physiological parameters of coated and uncoated bell peppers inoculated and uninoculated with a common phytopathogen, *Pectobacterium carotovorum* was assessed for 12 days. Of all the formulations tested, preparation containing 15% chitosan nanoparticles (CS15) was considered as the highly efficient coating which showed lowest CO_2 production, reduced incidence of *P. carotovorum* infection. Figure 8.3 shows the severity of *P. carotovorum* infection on bell peppers. As indicated by this figure, no

TABLE 8.3 A Summary of Various Nano-Based Edible Coatings Used for Preservation of Fruits and Vegetables.

Components	**Fruit/vegetable treated**	**Effect introduced**	**References**
Carrageenan and ZnO nanoparticles	Mango	Reduced the total acidity, maintained firmness and delayed discoloration and decay and provided protection against microbes	Meindrawan et al. (2018)
Alginate-based limonene liposomes	Strawberry	The coated fruit showed lower respiration rates, pH and higher anthocyanin content	Dhital et al. (2018)
Beeswax solid lipid nanoparticles in xanthan gum and propylene glycol	Strawberry	The coated fruits showed less weight loss and decay and exhibited better firmness	Zambrano-Zaragoza et al. (2020)
Chitosan thyme essential oil nanocoating	Green bell pepper	Coated bell peppers showed lower CO_2 production, maintained firmness and weight loss and protected against bacteria *P. carotovorum*	Correa-Pacheco et al. (2021)
Chitosan and propolis nanocoatings	Fig fruit	Reduced weight loss and increased antioxidant capacity and antifungal activity	Aparicio-García et al. (2021)
Chitosan-based nano-TiO_2 and nano-SiO_2 coatings	Blueberry	Extended shelf life, delayed ripening and controlled spoilage organisms	Li et al. (2021)
Nanolaminate coatings based on alginate, chitosan, and antimicrobial extract of *Flournesia cernua*	Tomato	Improved WVP and O_2 permeabilities, inhibited microbes, extended shelf life and decreased weight loss	Salas-Méndez et al. (2019)
Chitosan, nisin, silicon dioxide nanocomposite coating films	Blueberry	Maintained fruit texture and acted as antimicrobial agent	Eldib et al. (2020)
Chitosan and alginate-based coatings with cinnamon essential oil microcapsules	Mango	Improvement in pH value, fruit firmness, vitamin C content, soluble solid contents and acid content were noticed	Yin et al. (2019)

TABLE 8.3 *(Continued)*

Components	Fruit/vegetable treated	Effect introduced	References
Chitosan nanoparticles and thyme essential oil nanocoating	Green Bell pepper	Extension of fruit shelf life without altering cellular or physicochemical properties with antibacterial effect against *Pectobacterium carotovorum*	Correa-Pacheco et al. (2021)
Alginate films with cellulose nanofibrils from cocoa by products	Wild Andean blueberries	Decreased water vapor permeability and transparency of films. decreased the weight loss, respiration rate, and improved the firmness of blueberries	Medina-Jaramillo et al. (2020)

infection was observed in the case of uninoculated control fruit. At the same time, the inoculated-uncoated fruit showed complete infection. The lowest incidence of infection was observed for CS15 coated fruit when compared with TEO30 coated ones.

FIGURE 8.3 Severity of *P. carotovorum* infection in (A) uninoculated control, (B) inoculated control, (C) CS15 coated, and (D) TEO30-coated bell pepper.

Source: Reprinted with permission from Correa-Pacheco et al. (2021). Copyrights @ 2020 Institute of Food Technologists.

Also, in recent years, there has been a growing consumer demand on fresh-cut vegetables and fruits. But the peeling and cutting process hastens the metabolic activities of plant tissue and then make them more perishable than the intact fruits and vegetables (Chiumarelli and Hubinger, 2012). In such cases, coating of fresh cut fruits or vegetables with edible nanocoatings has been used to prevent their quicker spoilage. Recently, Saravanakumar and coworkers developed nanocoatings composed of both biogenic and chemical silver nanoparticles polyvinylpyrrolidone-based glycerosomes (G/C-PVP–AgNPs) and compared their role in augmenting the shelf life of fresh cut yellow and red bell peppers (Saravanakumar et al., 2020). The biogenic silver nanoparticle-based coating showed more superior properties than the chemically synthesized one in terms of antibacterial and physicochemical attributes. Figure 8.4 shows the comparative changes in texture, color, moisture content, total dissolved solids, and antimicrobial analysis. After storing the fruits at 15°C for 15 days, G-PVP-AgNPs-coated fruits exhibited high efficiency in preventing the growth of gray molds when compared with control and C-PVP–AgNPs-coated fruits (Fig. 8.4a). At the same time, no detectable difference in controlling mould growth was seen in the case of red fresh cut bell peppers in all cases (Fig. 8.4b). In addition, the fruits coated with G-PVP-AgNPs maintained better firmness and played a significant role in extending the shelf life of coated fruits without altering the cellular and physicochemical nature of the fruits. Table below shows the development of various nanocomposite edible coatings for the fruits.

8.5.2 EGG AND DAIRY PRODUCTS

Egg

Eggs are worldwide available and acceptable food very high in nutritional and calorific values which are also easy to cook and ready to eat. As eggshell is very brittle and breathable material, it permits the entry of CO_2 and moisture, which can lead to significant weight loss of egg yolk. In such situations, when such pores can be sealed using an efficient edible coating, the internal changes occurring in the egg can be minimized, as well as the unexpected damage of eggshell can be avoided (Saeed et al., 2017).

In a study, an edible nanocoating based on whey protein isolate nanofibers with antibacterial agent carvacrol and glycerol as a plasticizer (WPNFs-CA/Gly) was developed to study its role in maintaining the texture of salted duck egg yolk (SDEY), a traditional pickled egg product (Wang et al., 2020). The WPNFs-CA/Gly-coated SDEY showed the lowest weight loss after 10 days of storage, which could be attributed to the unique dense structures and hydrophobicity of WPNFs (Fig. 8.5a). Moreover, WPNFs-CA/Gly coating resulted in reducing the sensory score of egg yolk in terms of hardiness, chewiness, and springiness. It also prevented the formation of cracks on the yolk as seen in Figure 8.5b.

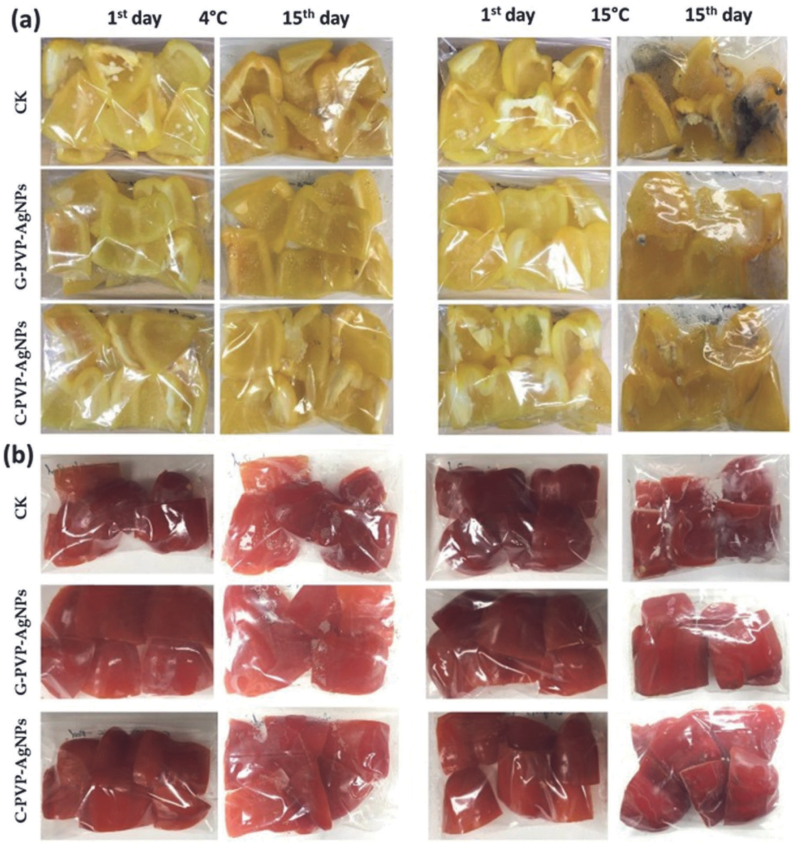


FIGURE 8.4 Effect of G–PVP-AgNPs and C-PVP–AgNPs-based nanocoatings on the shelf life of fresh cut bell peppers compared on 1st and 15th day.

Source: Reused with permission from Saravanakumar et al. (2020). Copyrights @ 2019 Elsevier B. V.

Dairy Products/Cheese

Among the varied dairy products, cheese is rich in protein, calcium, minerals, and vitamins and is one the most commonly consumed and regular part of human diet. Cheese gets spoiled rapidly by microbes when stored under inappropriate conditions and hence its safe packaging is of great importance. Edible coatings can be functionalized with nanostructured active agents to render them antibacterial, as a protective coating for cheese spoilage. The type of coatings/films used and the method of application must be selected depending on the type of cheese and storage conditions. The varieties of cheeses available are hard, soft, fresh, and pasteurized/processed cheeses (Ramos et al., 2016).

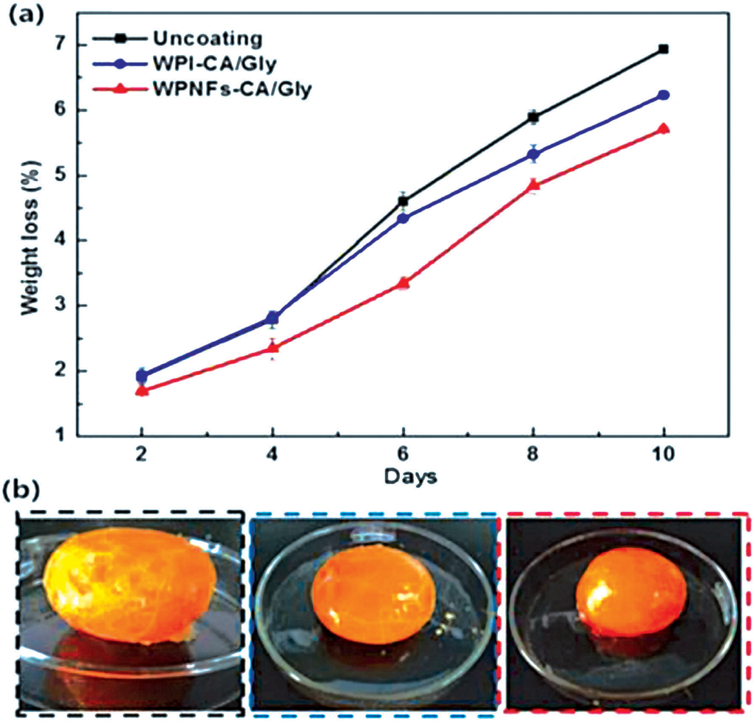


FIGURE 8.5 (a) Graph showing weight loss of uncoated and coated SDEYs stored for 10 days at 4°C, (b) digital image of SDEYS (starting from left to right) uncoated SDEY, WPI-CA/Gly-coated SDEY and WPNFs-CA/Gly-coated SDEY.

Source: Reprinted with permission from Wang et al. (2020), Open access.

Youssef et al. (2019) in their work developed a bionanocomposite coating composed of chitosan/ PVA/ TiO_2 nanoparticles and used it for protective coating on Ras cheese. Three different formulations were prepared using 0.5%, 1% and 2% (w/v) concentration of TiO_2 nanoparticle. The results showed that the coating with 2% TiO_2 nanoparticles showed the lowest weight loss and prevented the growth of mold on the cheese surface (Fig. 8.6). This study proved the efficiency of TiO_2-based edible nanocoating in extending the shelf life and limiting microbial contamination of cheese products.

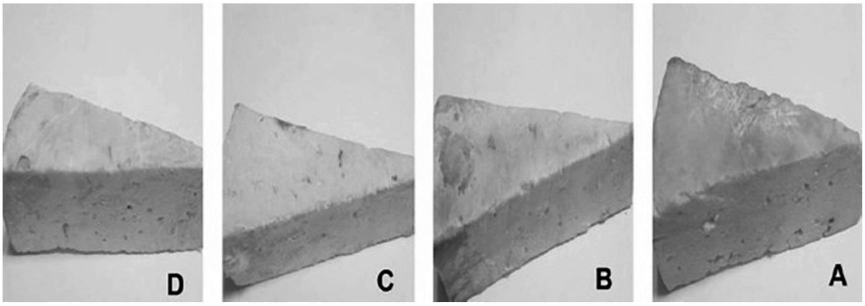


FIGURE 8.6 Changes observed on Ras cheese after coating with bionanocomposite containing TiO_2 nanoparticle concentrations (A) 0%, (B) 0.5%, (C) 1, and (D) 2%.
Source: Reprinted with permission from (Youssef et al., 2019). Copyrights @ 2018 Elsevier Ltd.

Recently, in a similar study, Ligaj et al. observed the impact of polyolefin foil with PLA coating and antibacterial nanocoating composed of polyolefin foil/PLA/zero-valent iron nanoparticle on inhibiting microbial growth on goat cream cheese (Ligaj et al., 2020). Figure 8.7a shows that after 5 weeks storage at chilled temperature, the cheese sample packed with polyolefin foil with PLA showed the presence of microorganisms, whereas the nanocoating film inhibited microbial growth both on the package and the cheese surface (Fig. 8.7b).

8.5.3 MEAT, POULTRY AND FISHERY PRODUCTS

Meat or muscle foods and fishery products form an important source of animal protein and hence they are influential ingredient of healthy and well-balanced diet. Meat and fish products are considered as the highly vulnerable to rapid microbial and oxidative deterioration during the preslaughter handling processes. Hence, muscle foods must be packaged in most appropriate manner that can prevent or delay its undesirable spoilage. From centuries onwards, edible coating techniques have been applied on meat and fishes to prevent shrinkage, discoloration, off-flavors, and microbial spoilage.

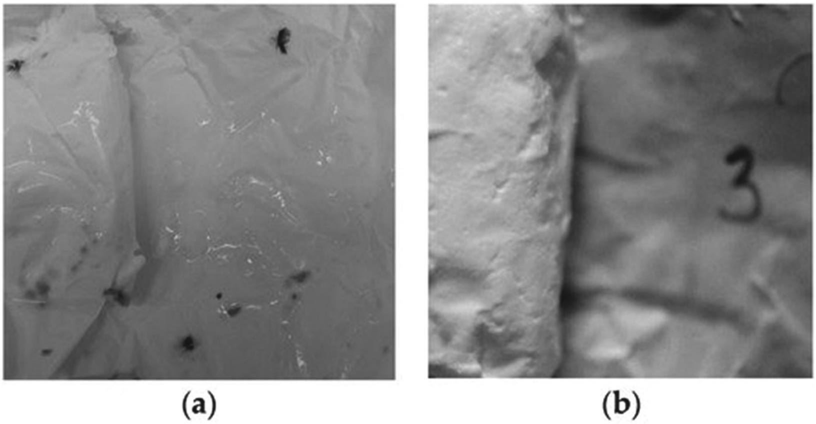

(a) (b)

FIGURE 8.7 Goat cream cheese wrapped with (a) polyolefin foil with PLA coating and (b) polyolefin foil with ZVI/PLA nanocoating.

Source: Reprinted with permission from Ligaj et al. (2020), Open Access Journal.

Meindrawan et al. reported the development of a bionanocomposite edible nanocoating made of gelatin–ZnO nanoparticle for preserving broiler chicken fillets (Meindrawan et al., 2020). Based on the concentration of ZnO nanoparticles, four different formulations of the coatings were prepared and were designated as F1 (0% w/w), F2 (0.024% w/w), F3 (0.048% w/w), and F4 (0.096% w/w). Figure 8.8 shows the physical appearance of chicken fillets uncoated and coated with gelatin–ZnO bionanocomposite. From the figure, it is clear that the fillets coated with F3 and F4 films maintained the freshness of the chicken as indicated by the reddish color of the meat. On the contrary, the uncoated, F1 and F2 formulation-coated samples showed yellow discoloration due to oxidative or microbial spoilage. The study concluded that the F3 film formulation was the best which provided lowest microbial count relatively high fillet firmness, and lowest weight loss. A handful of chapters have reported the preparation and application of nano-based edible coatings for preservation of meat and fishery products (Table 8.4).

8.6 CONCLUSION

Inclusion of nanomaterials in edible coating matrices is one of the most promising and advancing avenues in food nanotechnology. Nanomaterials in edible coatings/films not only improve the food shelf life, ensure food safety, but also can cause the enhancement of food quality and nutritive value. The main role of edible nanocoatings application is to preserve highly perishable food commodities like fresh and cut pieces of fruits and vegetables, meat, poultry, fish, egg and dairy products. Also, it is worth to mention that the selection of nanomaterials for use in edible coatings has to be made wisely as it should not impart any toxicity and do not interact with the functionalities of any natural additive compounds present in the coating.

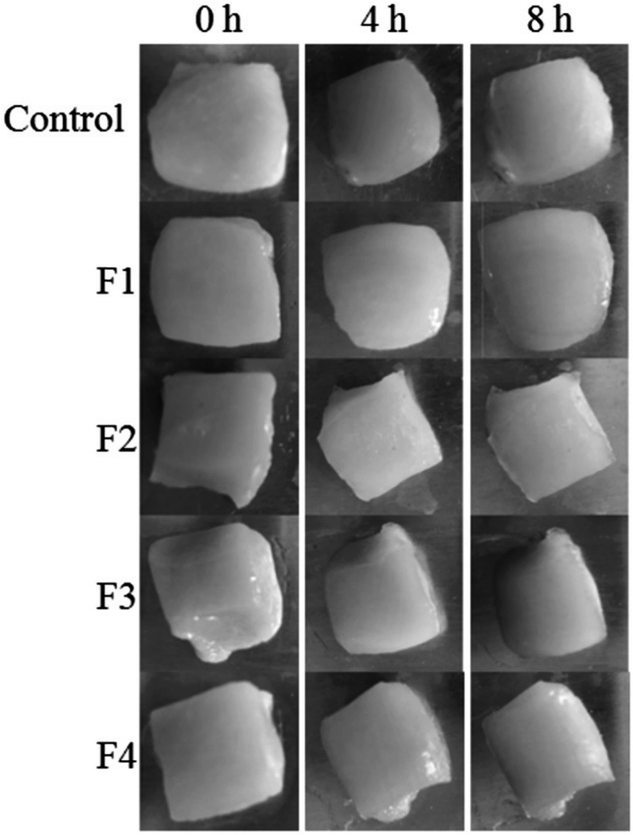


FIGURE 8.8 Physical appearance of chicken fillets coated with different formulations of gelatin–ZnO bionanocomposite coating.

Source: Reprinted with permission from Meindrawan et al. (2020). Copyrights @ 2020 WILEY VCH Verlag GmbH & Co. KGaA, Weinheim.

TABLE 8.4 List of Edible Nanocoatings Developed to Preserve Meat and Fishery Products.

Components	Meat treated	Effect introduced	References
Jujube gum and nettle oil-loaded nanoemulsion coatings	Beluga sturgeon fillets	Extended the fillet shelf life	Gharibzahedi and Mohammadnabi (2017)
Chitosan-based nanoliposome coating incorporated with *Satureja* plant essential oil	Lamb meat	Prolonged antimicrobial and antioxidant activity	Pabast et al. (2018)
Chitosan–montmorillonite-based nanocoatings with α tocopherol	Sliced dry-cured ham	Coated meat retained stronger radical-scavenging activity and showed lower thiobarbituric acid reactive substances	Yan et al. (2019)
Chitosan-*Lepidium sativum* sea gum nanocoating	Beef	Delayed microbial and oxidative spoilage of beef at three different storage temperatures	M. Esmaeili et al. (2020)
Nanochitosan incorporated with nanoliposome cumin	Sardine fish	antimicrobial and antioxidant activity	Homayounpour et al. (2020)
Chitosan zein coating with nanoencapsulated with *Pulicaria gnaphalodes (Vent.) Boiss*. aqueous extract	Rainbow trout fish	Showed lower thiobarbituric acid reactive substances and peroxide value	Mehdizadeh et al. (2021)
Low density polyethylene films with silver nanoparticles	Chicken breast fillets	Enhanced antimicrobial and antioxidant activity	Azlin-Hasim et al. (2016)
Thymol-loaded chitosan nanofiber coating	Gilthead sea bream fillets	Delayed chemical deterioration	Ceylan et al. (2017)
Whey protein nanofibrils with TiO_2 nanotubes	Chilled meat	Limited lipid peroxidation and promoted antioxidant activity in beef	Feng et al. (2019)

KEYWORDS

- **edible films**
- **nanocoatings**
- **food preservation**
- **solvent casting**
- **dipping method**
- **extension of food shelf life**
- **nanomaterials**

REFERENCES

Aguilar-Sánchez, R.; Munguía-Pérez, R.; Reyes-Jurado, F.; Navarro-Cruz, A. R.; Cid-Pérez, T. S.; Hernández-Carranza, P.; Beristain-Bauza, S. del C.; Ochoa-Velasco, C. E.; Avila-Sosa, R. Structural, Physical, and Antifungal Characterization of Starch Edible Films Added with Nanocomposites and Mexican Oregano (Lippia berlandieri Schauer) Essential Oil. *Molecules* **2019,** *24*, 2340.

Aguirre-Joya, J. A.; De Leon-Zapata, M. A.; Alvarez-Perez, O. B.; Torres-León, C.; Nieto-Oropeza, D. E.; Ventura-Sobrevilla, J. M.; Aguilar, M. A.; Ruelas-Chacón, X.; Rojas, R., Ramos-Aguiñaga, M. E.; Aguilar, C. N. Basic and Applied Concepts of Edible Packaging for Foods. In *Food Packaging and Preservation*; Elsevier, 2018; pp 1–61.

Ali, A.; Maqbool, M.; Ramachandran, S.; Alderson, P. G. Gum Arabic as a Novel Edible Coating for Enhancing Shelf-Life and Improving Postharvest Quality of Tomato (*Solanum lycopersicum* L.) Fruit. *Postharvest Biol. Technol.* **2010,** *58*, 42–47.

Andrade, R. D.; Skurtys, O.; Osorio, F. A. Atomizing Spray Systems for Application of Edible Coatings. *Compr. Rev. Food Sci. Food Saf.* **2012,** *11*, 323–337.

Aparicio-García, P. F.; Ventura-Aguilar, R. I.; del Río-García, J. C.; Hernández-López, M.; Guillén-Sánchez, D.; Salazar-Piña, D. A.; Ramos-García, M. de L.; Bautista-Baños, S. Edible Chitosan/Propolis Coatings and Their Effect on Ripening, Development of Aspergillus flavus, and Sensory Quality in Fig Fruit, during Controlled Storage. *Plants* **2021,** *10*, 112.

Azlin-Hasim, S.; Cruz-Romero, M. C.; Morris, M. A.; Padmanabhan, S. C.; Cummins, E.; Kerry, J. P. The Potential Application of Antimicrobial Silver Polyvinyl Chloride Nanocomposite Films to Extend the Shelf-Life of Chicken Breast Fillets. *Food Bioprocess Technol.* **2016,** *9*, 1661–1673.

Bharti, S. K.; Pathak, V.; Alam, T.; Arya, A.; Basak, G.; Awasthi, M. G. Materiality of Edible Film Packaging in Muscle Foods: A Worthwhile Conception. *J. Packag. Technol. Res.* **2020,** *4*, 117–132.

Bora, A.; Mishra, P. Characterization of Casein and Casein-Silver Conjugated Nanoparticle Containing Multifunctional (Pectin–Sodium Alginate/Casein) Bilayer Film. *J. Food Sci. Technol.* **2016,** *53*, 3704–3714.

Cai, L.; Wang, Y.; Cao, A. The Physiochemical and Preservation Properties of Fish Sarcoplasmic Protein/Chitosan Composite Films Containing Ginger Essential Oil Emulsions. *J. Food Process Eng*. **2020,** *43*.

Ceylan, Z.; Sengor, G. F. U.; Yilmaz, M. T. A Novel Approach to Limit Chemical Deterioration of Gilthead Sea Bream *(Sparus aurata)* Fillets: Coating with Electrospun Nanofibers as Characterized by Molecular, Thermal, and Microstructural Properties: Coating with Electrospun Nanofiber. *J. Food Sci.* **2017,** *82*, 1163–1170.

Chiumarelli, M.; Hubinger, M. D. Stability, Solubility, Mechanical and Barrier Properties of Cassava Starch—Carnauba Wax Edible Coatings to Preserve Fresh-Cut Apples. *Food Hydrocoll.* **2012,** *28*, 59–67.

Chu, Y.; Cheng, W.; Feng, X.; Gao, C.; Wu, D.; Meng, L.; Zhang, Y.; Tang, X. Fabrication, Structure and Properties of Pullulan-Based Active Films Incorporated with Ultrasound-Assisted Cinnamon Essential Oil Nanoemulsions. *Food Packag. Shelf Life* **2020,** *25*, 100547.

Correa-Pacheco, Z. N.; Corona-Rangel, M. L.; Bautista-Baños, S.; Ventura-Aguilar, R. I. Application of Natural-Based Nanocoatings for Extending the Shelf Life of Green Bell Pepper Fruit. *J. Food Sci.* **2021,** *86*, 95–102.

Dehghani, S.; Hosseini, S. V.; Regenstein, J. M. Edible Films and Coatings in Seafood Preservation: A Review. *Food Chem.* **2018,** *240*, 505–513.

Dhital, R.; Mora, N. B.; Watson, D. G.; Kohli, P.; Choudhary, R. Efficacy of Limonene Nano Coatings on Post-Harvest Shelf Life of Strawberries. *LWT* **2018,** *97*, 124–134.

Dini, H.; Fallah, A. A.; Bonyadian, M.; Abbasvali, M.; Soleimani, M. Effect of Edible Composite Film Based on Chitosan and Cumin Essential Oil-Loaded Nanoemulsion Combined with Low-Dose Gamma Irradiation on Microbiological Safety and Quality of Beef Loins during Refrigerated Storage. *Int. J. Biol. Macromol.* **2020,** *164*, 1501–1509.

Ebrahimi, S.; Fathi, M.; Kadivar, M. Production and Characterization of Chitosan-Gelatin Nanofibers by Nozzle-Less Electrospinning and Their Application to Enhance Edible Film's Properties. *Food Packag. Shelf Life* **2019,** *22*, 100387.

Eldib, R.; Khojah, E.; Elhakem, A.; Benajiba, N.; Helal, M. Chitosan, Nisin, Silicon Dioxide Nanoparticles Coating Films Effects on Blueberry (*Vaccinium myrtillus*) Quality. *Coatings* **2020,** 10, 962.

Emamifar, A.; Bavaisi, S. Nanocomposite Coating Based on Sodium Alginate and Nano-ZnO for Extending the Storage Life of Fresh Strawberries (Fragaria × ananassa Duch.). *J. Food Meas. Charact.* **2020,** *14*, 1012–1024.

Escamilla-García, M.; Rodríguez-Hernández, M.; Hernández-Hernández, H.; Delgado-Sánchez, L.; García-Almendárez, B.; Amaro-Reyes, A.; Regalado-González, C. Effect of an Edible Coating Based on Chitosan and Oxidized Starch on Shelf Life of *Carica papaya L.*, and Its Physicochemical and Antimicrobial Properties. *Coatings* **2018,** *8*, 318.

Esmaeili, H.; Cheraghi, N.; Khanjari, A.; Rezaeigolestani, M.; Basti, A. A.; Kamkar, A.; Aghaee, E. M. Incorporation of Nanoencapsulated Garlic Essential Oil into Edible Films: A Novel Approach for Extending Shelf Life of Vacuum-Packed Sausages. *Meat Sci.* **2020,** *166*, 108135.

Esmaeili, M.; Ariaii, P.; Nasiraie, L. R.; Pour, M. Y. Comparison of Coating and Nano-Coating of Chitosan- Lepidium Sativum Seed Gum Composites on Quality and Shelf Life of Beef. *J. Food Meas. Charact.* **2020**.

Falguera, V.; Quintero, J. P.; Jiménez, A.; Muñoz, J. A.; Ibarz, A. Edible Films and Coatings: Structures, Active Functions and Trends in Their Use. *Trends Food Sci. Technol.* **2011,** *22*, 292–303.

Feng, Z.; Li, L.; Wang, Q.; Wu, G.; Liu, C.; Jiang, B.; Xu, J. Effect of Antioxidant and Antimicrobial Coating based on Whey Protein Nanofibrils with TiO_2 Nanotubes on the Quality and Shelf Life of Chilled Meat. *Int. J. Mol. Sci.* **2019,** *20*, 1184.

Ghadetaj, A.; Almasi, H.; Mehryar, L. Development and Characterization of Whey Protein Isolate Active Films Containing Nanoemulsions of Grammosciadium Ptrocarpum Bioss. Essential Oil. *Food Packag. Shelf Life* **2018,** *16*, 31–40.

Gharibzahedi, S. M. T.; Mohammadnabi, S. Effect of Novel Bioactive Edible Coatings Based on Jujube Gum and Nettle Oil-Loaded Nanoemulsions on the Shelf-Life of Beluga Sturgeon Fillets. *Int. J. Biol. Macromol.* **2017,** *95*, 769–777.

Gheorghita (Puscaselu), R.; Gutt, G.; Amariei, S. The Use of Edible Films Based on Sodium Alginate in Meat Product Packaging: An Eco-Friendly Alternative to Conventional Plastic Materials. *Coatings* **2020,** *10*, 166.

Ghiasi, F.; Golmakani, M.-T.; Eskandari, M. H.; Hosseini, S. M. H. A New Approach in the Hydrophobic Modification of Polysaccharide-Based Edible Films Using Structured Oil Nanoparticles. *Ind. Crops Prod.* **2020,** *154*, 112679.

González-Reza, R.; García-Betanzos, C.; Sánchez-Valdes, L.; Quintanar-Guerrero, D.; Cornejo-Villegas, M.; Zambrano-Zaragoza, M. The Functionalization of Nanostructures and Their Potential Applications in Edible Coatings. *Coatings* **2018,** *8*, 160.

Gul, O.; Saricaoglu, F. T.; Besir, A.; Atalar, I.; Yazici, F. Effect of Ultrasound Treatment on the Properties of Nano-Emulsion Films Obtained from Hazelnut Meal Protein and Clove Essential Oil. *Ultrason. Sonochem.* **2018,** *41*, 466–474.

Guo, M.; Jin, T. Z.; Wang, L.; Scullen, O. J.; Sommers, C. H. Antimicrobial Films and Coatings for Inactivation of Listeria Innocua on Ready-to-Eat Deli Turkey Meat. *Food Control* **2014,** *40*, 64–70.

Hager, J. V.; Rawles, S. D.; Xiong, Y. L.; Newman, M. C.; Webster, C. D. Edible Corn-zein-based Coating Incorporated with Nisin or Lemongrass Essential Oil Inhibits *Listeria monocytogenes* on Cultured Hybrid Striped Bass, *Morone chrysops* × *Morone saxatilis*, Fillets during Refrigerated and Frozen Storage: Lemongrass Essential Oil Inhibits *Listeria*. *J. World Aquac. Soc.* **2019,** *50*, 204–218.

Homayounpour, P.; Jalali, H.; Shariatifar, N.; Amanlou, M.; Khanjari, A. Protective Effect of Nanochitosan Incorporated with Free/nanoliposome Cumin (*Cuminum cyminum* L.) Aqueous Extract on Sardine Fish. *J. Aquat. Food Prod. Technol.* **2020,** *29*, 949–961.

Huang, Y.; Gu, C.; He, S.; Zhu, D.; Liu, X.; Chen, Z. Development and Characterization of an Edible Chitosan–Whey Protein Nano Composite Film for Chestnut (*Castanea mollissima* Bl.) Preservation. *J. Food Sci.* **2020,** *85*, 2114–2123.

Huber, K. C.; Embuscado, M. E. *Edible Films and Coatings for Food Applications*; Springer: Dordrecht ; London, 2009.

Jafarzadeh, S.; Alias, A.; Ariffin, F.; Mahmud, S. Characterization of Semolina Protein Film with Incorporated Zinc Oxide Nano Rod Intended for Food Packaging. *Pol. J. Food Nutr. Sci.* **2017,** *67*, 183–190.

Janjarasskul, T.; Krochta, J. M. Edible Packaging Materials. *Annu. Rev. Food Sci. Technol.* **2010,** *1*, 415–448.

Jung, S.; Cui, Y.; Barnes, M.; Satam, C.; Zhang, S.; Chowdhury, R. A.; Adumbumkulath, A.; Sahin, O.; Miller, C.; Sajadi, S. M.; Sassi, L. M.; Ji, Y.; Bennett, M. R.; Yu, M.; Friguglietti, J.; Merchant, F. A.; Verduzco, R.; Roy, S.; Vajtai, R.; Meredith, J. C.; Youngblood, J. P.; Koratkar, N.; Rahman, M. M.; Ajayan, P. M. Multifunctional Bio-Nanocomposite Coatings for Perishable Fruits. *Adv. Mater.* **2020,** *32*, 1908291.

K. S., J.; Jose, J.; Li, T.; Thomas, M.; Shankregowda, A. M.; Sreekumaran, S.; Kalarikkal, N.; Thomas, S. Application of Novel Zinc Oxide Reinforced Xanthan Gum Hybrid System for Edible Coatings. *Int. J. Biol. Macromol.* **2020,** *151*, 806–813.

Koushesh Saba, M.; Amini, R. Nano-ZnO/Carboxymethyl Cellulose-Based Active Coating Impact on Ready-to-Use Pomegranate during Cold Storage. *Food Chem.* **2017,** *232*, 721–726.

Li, Y.; Rokayya, S.; Jia, F.; Nie, X.; Xu, J.; Elhakem, A.; Almatrafi, M.; Benajiba, N.; Helal, M. Shelf-Life, Quality, Safety Evaluations of Blueberry Fruits Coated with Chitosan Nano-Material Films. *Sci. Rep.* **2021,** *11*, 55.

Ligaj, M.; Tichoniuk, M.; Cierpiszewski, R.; Foltynowicz, Z. Efficiency of Novel Antimicrobial Coating Based on Iron Nanoparticles for Dairy Products' Packaging. *Coatings* **2020,** *10*, 156.

Liu, R.; Liu, D.; Liu, Y.; Song, Y.; Wu, T.; Zhang, M. Using Soy Protein SiOx Nanocomposite Film Coating to Extend the Shelf Life of Apple Fruit. *Int. J. Food Sci. Technol.* **2017,** *52*, 2018–2030.

Lu, F.; Ding, Y.; Ye, X.; Liu, D. Cinnamon and Nisin in Alginate–Calcium Coating Maintain Quality of Fresh Northern Snakehead Fish Fillets. *LWT—Food Sci. Technol.* **2010,** *43*, 1331–1335.

Medina-Jaramillo, C.; Quintero-Pimiento, C.; Gómez-Hoyos, C.; Zuluaga-Gallego, R.; López-Córdoba, A. Alginate-Edible Coatings for Application on Wild Andean Blueberries (Vaccinium meridionale Swartz): Effect of the Addition of Nanofibrils Isolated from Cocoa By-Products. *Polymers* **2020,** *12*, 824.

Mehdizadeh, A.; Shahidi, S.-A.; Shariatifar, N.; Shiran, M.; Ghorbani-HasanSaraei, A. Evaluation of Chitosan-zein Coating Containing Free and Nano-encapsulated *Pulicaria gnaphalodes (Vent.) Boiss*. Extract on Quality Attributes of Rainbow Trout. *J. Aquat. Food Prod. Technol.* **2021,** *30*, 62–75.

Meindrawan, B.; Putri, S.; Susanto, C. S.; Ofe, O.; Mangindaan, D.; Ayman, A.; Kasih, T. P. Bionanocomposite of Gelatin–ZnO Nanoparticles as Potential Edible Coating for Broiler Chicken Fillet. *Macromol. Symp.* **2020,** *391*, 1900165.

Meindrawan, B.; Suyatma, N. E.; Wardana, A. A.; Pamela, V. Y. Nanocomposite Coating Based on Carrageenan and ZnO Nanoparticles to Maintain the Storage Quality of Mango. *Food Packag. Shelf Life* **2018,** *18*, 140–146.

Mohammadi, A.; Hashemi, M.; Hosseini, S. M. Postharvest Treatment of Nanochitosan-Based Coating Loaded with Zataria Multiflora Essential Oil Improves Antioxidant Activity and Extends Shelf-Life of Cucumber. *Innov. Food Sci. Emerg. Technol.* **2016,** *33*, 580–588.

Montes-de-Oca-Ávalos, J. M.; Altamura, D.; Herrera, M. L.; Huck-Iriart, C.; Scattarella, F.; Siliqi, D.; Giannini, C.; Candal, R. J. Physical and Structural Properties of Whey Protein

Concentrate—Corn Oil—TiO_2 Nanocomposite Films for Edible Food-Packaging. *Food Packag. Shelf Life* **2020,** *26*, 100590.

Nasiri, M.; Sani, A. M.; Hakimzadeh, V.; Shahidi, M. Antimicrobial Effects of Edible Nano-Composite Based on Bean Pod Shell Gum, Nano-TiO_2, and Mentha Pulegium Essential Oil. *J. Appl. Biol. Biotechnol.* **2019,** *7*, 75–78.

Ortiz-Duarte, G.; Pérez-Cabrera, L. E.; Artés-Hernández, F.; Martínez-Hernández, G. B. Ag-Chitosan Nanocomposites in Edible Coatings Affect the Quality of Fresh-Cut Melon. *Postharvest Biol. Technol.* **2019,** *147*, 174–184.

Pabast, M.; Shariatifar, N.; Beikzadeh, S.; Jahed, G. Effects of Chitosan Coatings Incorporating with Free or Nano-Encapsulated Satureja Plant Essential Oil on Quality Characteristics of Lamb Meat. *Food Control* **2018,** *91*, 185–192.

Ramos, O.; Pereira, R. N. C.; Martins, J.; Malcata, F. Edible Packaging for Dairy Products. 2016.

Restrepo, A. E.; Rojas, J. D.; García, O. R.; Sánchez, L. T.; Pinzón, M. I.; Villa, C. C. Mechanical, Barrier, and Color Properties of Banana Starch Edible Films Incorporated with Nanoemulsions of Lemongrass (*Cymbopogon citratus*) and Rosemary (*Rosmarinus officinalis*) Essential Oils. *Food Sci. Technol. Int.* **2018,** *24*, 705–712.

Saeed, F.; Javaid, A.; Ahmed, N.; Nadeem, M. T.; Arshad, M. S.; Imran, A.; Sohaib, M.; Khan, A. U. Influence of Edible Coating Techniques on Quality Characteristics of Eggs: Influence of Edible Coating Techniques on Eggs. *J. Food Process. Preserv.* **2017,** *41*, e12815.

Salas-Méndez, E. de J.; Vicente, A.; Pinheiro, A. C.; Ballesteros, L. F.; Silva, P.; Rodríguez-García, R.; Hernández-Castillo, F. D.; Díaz-Jiménez, M. de L. V.; Flores-López, M. L.; Villarreal-Quintanilla, J. Á.; Peña-Ramos, F. M.; Carrillo-Lomelí, D. A.; Jasso de Rodríguez, D. Application of Edible Nanolaminate Coatings with Antimicrobial Extract of Flourensia Cernua to Extend the Shelf-Life of Tomato (*Solanum lycopersicum L.*) Fruit. *Postharvest Biol. Technol.* **2019,** *150*, 19–27.

Sani, I. K.; Marand, S. A.; Alizadeh, M.; Amiri, S.; Asdagh, A. Thermal, Mechanical, Microstructural and Inhibitory Characteristics of Sodium Caseinate Based Bioactive Films Reinforced by ZnONPs/Encapsulated *Melissa officinalis* Essential Oil. *J. Inorg. Organomet. Polym. Mater.* **2021,** *31*, 261–271.

Santos, A. M. P.; Melo, E. de A. Application of Edible Biopolymer Coatings to Extend the Storage Life of Fresh Fruits and Vegetables. In *Biopolymer Membranes and Films*; Elsevier, 2020; pp 505–513.

Saravanakumar, K.; Hu, X.; Chelliah, R.; Oh, D.-H.; Kathiresan, K.; Wang, M.-H. Biogenic Silver Nanoparticles-Polyvinylpyrrolidone Based Glycerosomes Coating to Expand the Shelf Life of Fresh-Cut Bell Pepper (*Capsicum annuum* L. var. grossum (L.) Sendt). *Postharvest Biol. Technol.* **2020,** *160*, 111039.

Souza Vieira da Silva, I.; Soares Prado, N.; Gontijo de Melo, P.; Campion Arantes, D.; Zeni Andrade, M.; Otaguro, H.; Pasquini, D. Edible Coatings Based on Apple Pectin, Cellulose Nanocrystals, and Essential Oil of Lemongrass: Improving the Quality and Shelf Life of Strawberries (Fragaria Ananassa). *J. Renew. Mater.* **2019,** *7*, 73–87.

Sucheta, Chaturvedi, K.; Sharma, N.; Yadav, S. K. Composite Edible Coatings from Commercial Pectin, Corn Flour and Beetroot Powder Minimize Post-Harvest Decay, Reduces Ripening and Improves Sensory Liking of Tomatoes. *Int. J. Biol. Macromol.* **2019,** *133*, 284–293.

Suhag, R.; Kumar, N.; Petkoska, A. T.; Upadhyay, A. Film Formation and Deposition Methods of Edible Coating on Food Products: A Review. *Food Res. Int.* **2020,** *136*, 109582.

Tanada-Palmu, P. S.; Grosso, C. R. F. Effect of Edible Wheat Gluten-Based Films and Coatings on Refrigerated Strawberry (*Fragaria ananassa*) Quality. *Postharvest Biol. Technol*. **2005,** *36*, 199–208.

Wang, H.; Qian, J.; Ding, F. Emerging Chitosan-Based Films for Food Packaging Applications. *J. Agric. Food Chem*. **2018,** *66*, 395–413.

Wang, Q.; Liu, W.; Tian, B.; Li, D.; Liu, C.; Jiang, B.; Feng, Z. Preparation and Characterization of Coating Based on Protein Nanofibers and Polyphenol and Application for Salted Duck Egg Yolks. *Foods* **2020,** *9*, 449.

Yan, W.; Chen, W.; Muhammad, U.; Zhang, J.; Zhuang, H.; Zhou, G.; Preparation of α-tocopherol-Chitosan Nanoparticles/Chitosan/Montmorillonite Film and the Antioxidant Efficiency on Sliced Dry-Cured Ham. *Food Control* **2019,** *104*, 132–138.

Yin, C.; Huang, C.; Wang, J.; Liu, Y.; Lu, P.; Huang, L. Effect of Chitosan- and Alginate-Based Coatings Enriched with Cinnamon Essential Oil Microcapsules to Improve the Postharvest Quality of Mangoes. *Materials* **2019,** *12*, 2039.

Youssef, A. M.; Assem, F. M.; Abdel-Aziz, M. E.; Elaaser, M.; Ibrahim, O. A.; Mahmoud, M.; Abd El-Salam, M. H. Development of Bionanocomposite Materials and Its Use in Coating of Ras Cheese. *Food Chem.* **2019,** *270*, 467–475.

Zambrano-Zaragoza, M. L.; Mercado-Silva, E.; Ramirez-Zamorano, P.; Cornejo-Villegas, M. A. Gutiérrez-Cortez, E.; Quintanar-Guerrero, D. Use of Solid Lipid Nanoparticles (SLNs) in Edible Coatings to Increase Guava (*Psidium guajava* L.) Shelf-Life. *Food Res. Int.* **2013,** *51*, 946–953.

Zambrano-Zaragoza, M. L.; Quintanar-Guerrero, D.; Del Real, A.; González-Reza, R. M.; Cornejo-Villegas, M. A.; Gutiérrez-Cortez, E. Effect of Nano-Edible Coating Based on Beeswax Solid Lipid Nanoparticles on Strawberry's Preservation. *Coatings* **2020,** *10*, 253.

Zambrano-Zaragoza, M.; González-Reza, R.; Mendoza-Muñoz, N.; Miranda-Linares, V.; Bernal-Couoh, T.; Mendoza-Elvira, S.; Quintanar-Guerrero, D. Nanosystems in Edible Coatings: A Novel Strategy for Food Preservation. *Int. J. Mol. Sci.* **2018,** *19*, 705.

Zareie, Z.; Tabatabaei Yazdi, F.; Mortazavi, S. A. Development and Characterization of Antioxidant and Antimicrobial Edible Films Based on Chitosan and Gamma-Aminobutyric Acid-Rich Fermented Soy Protein. *Carbohydr. Polym.* **2020,** *244*, 116491.

Zeuthen, P.; Bøgh-Sørensen, L., Eds. *Food Preservation Techniques, Woodhead Publishing in Food Science and Technology*; CRC Press; Woodhead: Boca Raton : Cambridge, 2003.

Zhang, H.; Li, X.; Kang, H. Chitosan Coatings Incorporated with Free or Nano-Encapsulated Paulownia Tomentosa Essential Oil to Improve Shelf-Life of Ready-to-Cook Pork Chops. *LWT* **2019,** *116*, 108580.

Zhang, H.; Liang, Y.; Li, X.; Kang, H. Effect of Chitosan-Gelatin Coating Containing Nano-Encapsulated Tarragon Essential Oil on the Preservation of Pork Slices. *Meat Sci.* **2020,** *166*, 108137.

Zhang, L.; Liu, A.; Wang, W.; Ye, R.; Liu, Y.; Xiao, J.; Wang, K. Characterisation of Microemulsion Nanofilms Based on Tilapia Fish Skin Gelatine and ZnO Nanoparticles

Incorporated with Ginger Essential Oil: Meat Packaging Application. *Int. J. Food Sci. Technol.* **2017,** *52*, 1670–1679.

Zhao, Y. *Application of Commercial Coatings, Edible Coatings and Films to Improve Food Quality*; CRC Press, 2011.

Zheng, Y.; Monty, J.; Linhardt, R. J. Polysaccharide-Based Nanocomposites and Their Applications. *Carbohydr. Res.* **2015,** *405*, 23–32.

CHAPTER 9

SEAWEEDS AS A NEW SOURCE OF BIOACTIVE COMPOUNDS AND POTENT BIOTECHNOLOGICAL APPLICATIONS

FATIMA EL KHALLOUFI[1] and BRAHIM OUDRA[2]

[1]Department of Geography, Biology, and Geology, Polydisciplinary Faculty of Khouribga (FPK), Sultan Moulay Slimane University of Beni-Mellal, Khouribga – 25000, Morocco

[2]Department of Biology, Faculty of Sciences Semlalia Marrakech, Cadi Ayyad University, Marrakech – 40000, Morocco

ABSTRACT

Seaweeds are considered a rich source of structurally different bioactive metabolites endowed with different biological activities. They have received more attention because of their potential activities, such as antibacterial, antifungal, antioxidant properties. Besides, they were highly coveted in agricultural, biomedical, and environmental domains. This current view leads to emphasize the importance of bioactive molecules derived from macroalgae. The development of these newly discovered molecules offers a promising future and prospects for biotechnological exploitation regarding their large spectrum of activities. Several research projects to highlight recent activities, in particular anti-obesity, anti-leishmanial, anti-malarial, and antiviral, are currently based on the exploration of seaweeds bioactive metabolites. In fact, it is the responsibility of applied scientific research, to promote sustainable development and to work on raising awareness on the different ways of developing and exploring these biological resources while proposing alternative solutions to the overexploitation of these capitals.

9.1 INTRODUCTION

Marine ecosystems present great biodiversity of significant natural resources that can be exploited. Most of this marine resource diversity is still unexplored despite their richness as a source of new metabolites likely to be the subject of various biotechnological applications. Seaweeds are among the significant currently exploited marine resources. They are very diverse and make up a heterogeneous group. About 9,000 species of algae have been identified and classified into three main divisions of red (Rhodophyta), green (Chlorophyta), and brown (Phaeophyta) based on their pigmentation (Miyashita et al., 2013).

Seaweeds had attracted increasing attention because of the chemical diversity within all taxonomic divisions offering a wide variety of metabolites (e.g., polysaccharides, proteins, and amino acids, phenolic compounds, pigments, and fatty acids) and gaining importance through several applications and biotechnological processes (Wang et al., 2017a; Zhao et al., 2018; Tanna and Mishra, 2019). Major compounds isolated from various seaweed species are reported to possess *in-vitro* and/or *in-vivo* biological properties and pharmacological activities, including antibacterial, antifungal, antiviral, anticancer, and others (Pérez et al., 2016; Wells et al., 2017; Zerrifi et al., 2018). These compounds represent the potential sources of new beneficial and therapeutic agents (Mayer et al., 2020). However, these biological activities could be influenced by different factors such as seaweed growth stages, life habitat, and season of collection and methods of extraction (Mishra et al., 2016). In fact, different other activities of seaweeds are explored, like anti-leishmanial, anti-malarial, and anti-obesity (Lehnhardt Pires et al., 2013; Murugan et al., 2016; Lee et al., 2020).

On the other side, seaweeds have been extensively exploited in the agriculture and environmental sectors. Farmers have used macroalgae for a long time as an amendment to improve soil structure or as a fertilizer to increase soil fertility (Alobwede et al., 2019). Seaweed-based biostimulants have been reported as environment-friendly strategies to improve crop yields and stresses tolerance (Frioni et al., 2018; Kulkarni et al., 2019). Bioactive compounds from seaweeds were also explored for their roles in plant protection, anti-phytopathogen activities, and induction of plants' resistance to biotic stress (Baloch et al., 2013; Ibraheem et al., 2017). As a potent biological eco-friendly process, seaweed bioactive metabolites have been exploited to deal with growing environmental concerns such as harmful algal blooms (HABs) and biofouling occurrence. Natural metabolites constitute a promising approach for controlling HABs and cyanobacteria in aquatic ecosystems (Schrader, 2003). Seaweeds have been shown to produce and release a wide range of allelopathic substances toxic to HABs species (red tides and HABs) (Jeong et al., 2000; Nakai et al., 2000). Considerable research based on the identification and the evaluation of the seaweeds antialgal potentials has been conducted (Sun et al., 2019) to develop an environmentally friendly, natural product-based antialgal agent. In addition, marine biofouling is considered a dominant phenomenon that occurs in the marine environment and causes serious problems worldwide. Bioactive substances from diverse seaweeds exhibit potential antifouling activity (Saha et al., 2018).

This chapter proposes a current review of the main biological applications of seaweeds bioactive metabolites by emphasizing the new molecules elucidated and the new perspectives for applications.

9.2 SEAWEEDS BIODIVERSITY

Algae are primary producers essential for the survival of many ecosystems. They colonize diverse environments and may establish a symbiotic association with fungi (lichens) (Suutari et al., 2010). Algae can be macroscopic or microscopic (from 0.5 microns to more than 60 meters). Macroalgae are macroscopic algae constituting a diverse multicellular polyphyletic group comprising photosynthetic eukaryotic organisms (Lee, 2008). They are structured on thallus with a holdfast, stipe, and blade; without true roots, stems, or leaves (Dhargalkar and Kavlekar, 2004).

Marine macroalgae or Seaweeds are photosynthetic non-flowering plant-like organisms. They are one among the dominant group of flora in the marine ecosystem (Ba-Akdah et al., 2016). These macroorganisms can be epiphytic, endophytic, endozoic or parasitic, but the majority of them are lithophytic. They are widely spread and sited in different zones, which range from tropical warm waters to freezing polar regions (Collins et al., 2016). The distribution and variety of marine algae are related to several environmental characteristics such as light exposure, temperature, depth, and tides. The habitat and location determine their content on different phytopigments because of the light intensity during the photosynthetic process. Therefore, species differ considerably in many ultrastructural and biochemical features.

More than 10000 species of seaweeds have been currently described worldwide (over 6000 of red algal species; approximately 2000 brown species; and around 1500 green algal species) (Collins et al., 2016; West et al., 2017). Classification of algae is based on their specific pigments (other than chlorophyll) besides other properties (cell wall chemistry, specific storage compounds, presence or absence of flagella, structure of their chloroplasts (Bocanegra et al., 2009). According to their specific pigments, they are then divided into three different divisions as Phaeophyceae (brown algae) which brown color is due to their fucoxanthin content, Chlorophyceae (green algae) dominated with Chlorophyll 'a' and 'b' and Rhodophyceae (red algae) comprising phycocyanin and phycoerythrin (Lee, 2008; Bocanegra et al., 2009; O'Sullivan et al., 2010; Collins et al., 2016).

9.3 SEAWEED BIOACTIVE METABOLITES

Nowadays, biological molecules have received more attention due to their biodegradability and their reduced environmental impact (Bilal et al., 2017). Nontoxic residues, short environmental longevity, and fewer environmental consequences are the primary qualities enhancing the importance of such molecules (Grzywacz et al., 2014). During normal growth conditions, primary metabolites of seaweeds like polysaccharides, proteins, and lipids take part in the main physiological functions. However, under stress conditions (ultraviolet radiation, salinity, water pressure) various secondary metabolites are produced (Senthilkumar et al., 2013; Lopes et al., 2016; Rosa et al., 2020). Based on their polyphyletic origin and their different marine environments; seaweeds are considered as a potential source of metabolites with more than 3000 different identified compounds in distinct seaweeds species (Leal et al., 2013; Belghit et al., 2017).

Seaweeds are endowed with a high number of bioactive compounds. They are rich in proteins (high content of essential amino acids), minerals (iodine, magnesium, iron, zinc, and calcium), vitamins, phytochemicals, polyunsaturated fatty acids (PUFA), and polysaccharides (carrageenan and alginate) (Jiao et al., 2011; Mohamed et al., 2012; Miyashita et al., 2013; Lange et al., 2015). To preserve a more adapted healthy lifestyle, they have been reported to produce several structural and chemical biomolecules for their defense mechanisms (Nylund et al., 2013; Sudatti et al., 2018). This production in terms of amount and type is species-dependent (Souza et al., 2011). Secondary metabolites like alkaloids, terpenes, pigments, polyphenols, and phlorotannins are largely distributed in seaweed species (Jormalainen and Honkanen, 2008; Antunes et al., 2011; Lange et al., 2015). Several bioactive metabolites from marine algae have been widely reported and reviewed for their biological activities. Those biomolecules included: Phlorotannins (Sanjeewa et al., 2016), polysaccharides (Wang et al., 2014), proteins, and peptides (Samarakoon and Jeon, 2012; Harnedy and FitzGerald, 2013), lipids, alkaloids (Güven et al., 2010), terpenoids (Wang et al., 2013) and pigments (Dumay et al., 2015).

9.3.1 SEAWEED POLYSACCHARIDES

Polysaccharides represent a very diverse group of molecules isolated from brown, green, or red macroalgae. Carbohydrates are present typically as sulfated and non-sulfated polysaccharides. They are considered as the major compounds in macroalgae; accounting for up to 76% dry weight (DW) (Holdt and Kraan, 2011; Paniagua-Michel et al., 2014). Seaweed's composition on polysaccharides is different depending on macroalgae species. Thereby Phaeophyceae are presenting alginic acid, laminarin, and fucoidan; Rhodophyceae contain mainly agar, carrageenans, xylans; whereas ulvans occur in Chlorophyceae (Kraan, 2012; Senthilkumar et al., 2017). The biological activities of polysaccharides are widely related to their structural properties (molecular type, size, glycosidic linkages, ratio of constituent monosaccharides, degree of sulfation, and distribution pattern of sulfate (Hu et al., 2013).

Seaweeds are a rich source of sulfated polysaccharides (PLS) (Cunha and Grenha, 2016) with several pharmacological activities (Lordan et al., 2011; de Souza et al., 2012; Aquib et al., 2019; Tanna and Mishra, 2019; Venkatesan et al., 2019; Cicinskas et al., 2020).

9.3.1.1 CARRAGEENANS

Carrageenans are PLS present in red seaweeds and account for 30–75% of algae DW (Vera et al., 2011). They are divided into six basic forms according to their structure. Carrageenans were found to contain repeating disaccharide units with 3-linked-β-D-galactopyranose, 4-linked-β-galactopyranose, or 3,6-anhydro-β-galactopyranose (Funami et al., 2007; Vera et al., 2011). The molecules feature a high molecular weight. κ-carrageenan and ι-carrageenan are mostly found in *Kappaphycus alvarezii* and *Eucheuma denticulatum*, respectively, while λ-carrageenan is more common to *Gigartina* and *Chondrus* (Campo et al., 2009).

9.3.1.2 FUCANS (FUCOIDAN)

Fucans are a group of important algal PLS. They constitute the major content of brown seaweed cell walls and occupy 5–20% of the seaweed DW (Cardoso et al., 2014). They are structured on 2-sulfate-O-fucose or 4-sulfate-O-fucose and ramifications at each two or three fucose residues, representing at all PLS with high molecular weight (Ale and Meyer, 2013). Fucans comprise xylofucoglycuronans, glycuronogalactofucans, and fucoidans.

Fucoidans represent the most studied group of fucans. The chemical structure of this compound is complex and different structures appear depending on the originated seaweed species (Zorofchian Moghadamtousi et al., 2014). They are primarily structured as the (1–3)-linked α-L-fucopyranosyl. The secondary structure consists of alternating α-(1–3) and α-(1–4)-linked L-fucopyranosyls (Pérez et al., 2016). In general, the composition of fucoidans varies with species and geographical origin (Cardoso et al., 2016). They are more abundant in *Ecklonia cava*, *Ascophyllum nodosum,* and *Undaria pinnatifida.*

9.3.1.3 ULVANS

Ulvans are the major polysaccharide isolated from green seaweeds (especially in the Ulvaceae family) representing 8–29% of algal DW (Andrieux et al., 1998). They are part of the cell wall composition with molecular weights varying from 189-8200 kDa. Ulvans are made up of repeating units of disaccharides (rhamnose and xylose) and iduronic acid or glucuronic acid (Lahaye and Robic, 2007; Rupérez et al., 2013; Cunha and Grenha, 2016).

9.3.2 SEAWEED LIPIDS AND FATTY ACIDS

Lipids are representing 0.6–4.14% of seaweeds DW (Rodrigues et al., 2015a). They are found as structural components of cellular membranes (polar lipids) and storage compounds (neutral lipids) (Pérez et al., 2016). The ability of algae to survive and proliferate in different environmental conditions is largely related to diversity and patterns of cellular lipid besides the modification of lipids metabolism in response to environmental variations (Guschina and Harwood, 2006). The average fatty acid profile of Chlorophyceae contains a proportion of 41.8% saturated, 14.1% monounsaturated, and 44.1% PUFA; Phaeophyceae shows 40% of saturated fatty acids, 20%

monounsaturated, and 40% PUFA. While Rhodophyceae shows a proportion of 42% of saturated fatty acids, 13% monounsaturated fatty acids, and 37% PUFA (Wielgosz-Collin et al., 2016). Despite the low algal lipid content, their constitution is interesting. Macroalgae receive more attention for their large and high amounts of PUFA (Kendel et al., 2015; Wielgosz-Collin et al., 2016). The PUFA content is similar to or higher than terrestrial plants (Kumari et al., 2010; Torres et al., 2019). α-linolenic acid (ω3), stearidonic acid (ω3), arachidonic acid (ω6) and eicosapentaenoic acid (EPA) (ω3) are among the most common PUFA found in marine macroalgae (Murata and Nakazoe, 2001; Dawczynski et al., 2007).

9.3.3 SEAWEED PROTEINS, PEPTIDES, AND AMINO ACIDS

Protein content and composition of seaweeds are species-dependent (Kumar et al., 2014). Red and green seaweeds have greater protein content (10–47% DW) unlike brown seaweeds (3–15% DW) (Wijesekara and Kim, 2015). The seaweed proteins content is generally a function of the species, season, and environment. Important bioactive proteins from red and green seaweeds including lectin, phycobiliprotein, and bioactive peptides from brown seaweeds have largely been studied.

The majority of seaweeds are an important source of essential and acidic amino acids such as glutamic acid and aspartic acid. Approximately 42% to 48% of the total amino acids in seaweeds are essential amino acids (Wong and Cheung, 2000). In the same way as the other metabolites, the amino acid composition of seaweed proteins is affected by seasonal variations and location (Marinho et al., 2015; Milledge et al., 2016).

9.3.4 SEAWEED PIGMENTS

Pigments in seaweeds comprise three classes: chlorophyll, carotenoid, and phycobiliproteins (phycocyanin and phycoerythrin). Chlorophyll is a green pigment with a fundamental role in the photosynthetic process (Aryee et al., 2018).

Carotenoids are a group of lipid-soluble compounds comprising carotenes (with carbon and hydrogen atoms) and xanthophylls (with at least one oxygen atom) (Tapiero et al., 2004; Krinsky and Johnson, 2005). The most common carotenes are β-carotene, while lutein, fucoxanthin, and violaxanthin belong to the xanthophylls class (Figure 9.1) (Zorofchian Moghadamtousi et al., 2014; Aryee et al., 2018). The importance of carotenoids such as β-carotene, α-carotene, β-cryptoxanthin, lycopene, and fucoxanthin, have been reported in different seaweeds species (Rodriguez-Amaya, 2016; Susanto et al., 2019). The β-carotene at the same time was found in several species, for example, *Fucus serratus*, *F. vesiculosus*, *Laminaria digitata*, *Ulva* sp., *Chondrus crispus*. Besides, fucoxanthin is considered one of the most abundant carotenoids found in brown algae and contributes over 10% total production of carotenoids in nature (Gullón et al., 2020). This kind of molecule is related to neuroprotective, photoprotective, and hepatoprotective effects; in addition to anti-inflammatory, anticancer, and anti-obesity activities (Bae et al., 2020; Liu et al., 2020; Miyashita et al., 2020).

On the other hand, phycobiliproteins (water-soluble pigment) contain three different structural classes of molecules: phycocyanins (blue pigment), allophycocyanins (light blue pigment), and phycoerythrins (red pigment), this latter being the most abundant (Aryee et al., 2018).

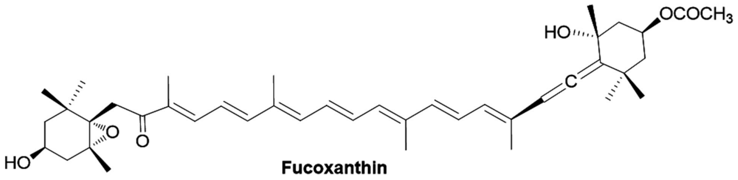


FIGURE 9.1 Chemical structure of fucoxanthin (Example of seaweed pigment) (from Liu et al., 2020).

9.3.5 PHENOLIC COMPOUNDS AND PHLOROTANNINS

Phenolic compounds are secondary metabolites widely distributed. They are divided into various groups and have several properties (Giada, 2013). In seaweeds, this group of compounds encompasses phenolic acids, tannins, flavonoids, catechins, and phlorotannins. The extent to which one type or another of phenolic compound is detected depends on the seaweed species.

The most studied algal polyphenolic compound is phlorotannins (Park et al., 2011). They are representing the major phenolic compounds found in brown algae (Steevensz et al., 2012; Machu et al., 2015). Whereas green and red algae contain mainly bromophenols, phenolic acids, and flavonoids (Gómez-Guzmán et al., 2018). Phlorotannins are reported to be extremely variable, heterogenic, and complex. This complexity is due to varying degrees of polymerization of phloroglucinol (1,3,5-trihydroxybenzene: the basic unit) (Kim et al., 2013). Nonetheless, the chemical properties of these marine polyphenols remind similar (Parys et al., 2007). Their molecular weight ranges from 126 Da to 650 kDa and they can be classified into four groups based on their linkages; (1) fuhalols and phlorethols (ether linkage), (2) eckols and carmalols (dibenzodioxin linkage), (3) fucophlorethols (ether and phenyl linkage), and (4) fucols (phenyl linkage) (Li et al., 2011; Martínez and Castañeda, 2013) (Figure 9.2). Phlorotannins were suggested to fulfill significant roles as basic components of the cell wall and function to provide chemical defenses against fluctuating environmental conditions (salinity level, nutrient, and light availability, ultraviolet (UV) radiation, and others) (Creis et al., 2015). To date, these compounds have been identified in many families of brown algae including the Alariaceae, Fucaceae, and Sargassaceae (Ferreres et al., 2012; Sathya et al., 2017). Several species like: *Ecklonia cava, Eisenia bicyclis*, *Sargassum thunbergii, Undaria pinnatifida,* and *Laminaria japonica;* have been cited for the pharmacological properties of phlorotannins (Rengasamy et al., 2014; Barbosa et al., 2019).

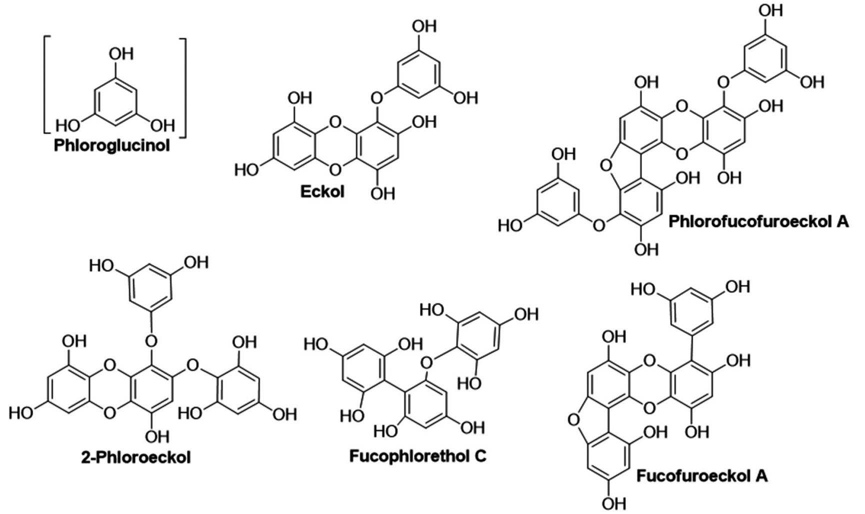


FIGURE 9.2 Chemical structures of Phloroglucinol (basic unit) and some Phlorotannins examples (Li et al., 2011; Barbosa et al., 2019).

Besides phlorotannins, other phenolic compounds have been reported in the composition of macroalgae (even less studied) (Farasat et al., 2014; Mannino et al., 2016). The presence of phenolic compounds such as gallic acid, hydroxybenzoic acid, catechin, epicatechin, has been revealed in different brown, red, and green species of macroalgae (Machu et al., 2015; Montero et al., 2018). Several studies have also reported the content of phenolic acids (Ying-Ying et al., 2015), flavonoids (Yoshie-Stark et al., 2003) and other phenolic compounds (Aigner et al., 2013). In fact, phlorotannins have been associated with different pharmacological and biological properties; among them the antimicrobial, antioxidant, anti-diabetic, anti-inflammatory, anti-allergic, and others (Lee et al., 2008; Heo and Jeon, 2009; Choi et al., 2010; Lee et al., 2012a,b; Wei et al., 2016; Sathya et al., 2017; Sugiura et al., 2018).

9.4 BIOMEDICAL AND PHARMACOLOGICAL SEAWEED EXTRACTS APPLICATIONS

In the last few years, seaweeds received more attention as a new promising source of novel bioactive compounds that can be used for drug development. Seaweeds may produce a wide range of bioactive compounds with a large spectrum of biological activities, such as antibacterial, antifungal, antiviral, antioxidant, anti-inflammatory, and anticancer (Kim et al., 2008; Pádua et al., 2015; Belattmania et al., 2016; Fu et al., 2016; Shi et al., 2017; Aquib et al., 2019; Antony and Chakraborty, 2020).

9.4.1 POTENTIAL ANTIMICROBIAL AND ANTIVIRAL SEAWEED ACTIVITIES

9.4.1.1 ANTIMICROBIAL ACTIVITY OF SEAWEEDS

Antibacterial activity of seaweed bioactive molecules was widely reported, as illustrated in Table 9.1. Extracts from 13 species of seaweeds were tested for their antimicrobial activities. Acetonic extracts of *Sargassum polyceratium* induced a strong antibacterial activity against *Staphylococcus aureus* (Borbón et al., 2012). In another study phlorofucofuroeckol-A, a polyketide from the brown alga *Eisenia bicyclis* has been tested against methicillin-resistant *Staphylococcus aureus* (MRSA). The obtained results revealed the inhibition of the methicillin resistance-associated genes expression at IC_{50} of 32 μg/ml and suppression of penicillin-binding protein 2a (PBP2a) production (Eom et al., 2014). Pereira et al. (2014) reported the inhibition of *Pseudomonas aeruginosa* biofilm formation by furanones (alkaloid) obtained from marine algae *Delisea pulchra* at 1.3 μM. Besides, aqueous extract of the genus *Sargassum* (*S. wightii*) showed moderate antibacterial activity against the Gram-negative bacteria *Escherichia coli* (Kumaresan et al., 2018). Methanol extract of *Laurencia iliformis* presented promising antibacterial activity against *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Streptococcus pyogenes*, and *Escherichia coli*; while the methanol extract of *Ulva reticulata* exhibited a strong effect against *Pseudomonas aeruginosa* (Begum et al., 2018). Mishra (2018) pointed out the positive results of four seaweeds *Sargassum wightii*, *Gracillaria edulis*, *Gracilaria corticata,* and *Ulva lactuca* from India, against *Pseudomonas aeruginosa, Escherichia coli,* and *Staphylococcus aureus.* It was suggested that the antibacterial activity of seaweeds was related to the ability of the active metabolite to bind with bacterial proteins such as enzymes and cell membranes (Pérez et al., 2016).

Biosynthesized nanoparticles (NPs), recognized as an effective antibiofilm, were tested against *Pseudomonas aeruginosa* biofilms responsible for antibiotic resistance (Khan et al., 2019). Gold NPs stabilized using fucoidan exerted activities in concentration depending manner with a MIC of 512 µg/ml. Antibacterial activity was detected at concentrations above MIC, whereas sub-inhibitory concentration inhibited biofilm formation without effect on bacterial growth (Khan et al., 2019). Most recently, silver nanoparticles (AgNPs) synthesized using the marine seaweed *Gracilaria corticata* have been tested against the biofilm-producing bacteria *Klebsiella pneumonia*. Significant antibacterial activity and biofilm reduction were recorded at 50 µg/mL and 100 µg/mL concentrations of Ag NPs respectively (Rajivgandhi et al., 2020). On the other side, marine natural products isolated from marine bacteria, dinoflagellates, sponges, sea cucumbers, and algae, are described to have a potent antifungal activity (Mayer et al., 2020). Through this section, only antifungal compounds from seaweeds are reported.

Seaweed's antifungal potential was highlighted in several studies (Peres et al., 2012; Arumugam et al., 2019; Arumugam and Rajendran, 2019). The antifungal activity of two new laurane-type sesquiterpenes: laurepoxyene, and 3 β-hydroxyperoxyaplysin, and a new PUFA ethyl ester isolated from the red alga *Laurencia okamurai* caused *Candida glabrata* inhibition with IC50 at 2–4 µg/ml (Yu et al., 2014; Feng et al., 2015). Lopes et al. (2013) screened antifungal activity of purified phlorotannins obtained from brown seaweeds (*Cystoseira nodicaulis, Cystoseira usneoides,* and *Fucus spiralis*). The obtained results showed fungistatic and fungicidal activity against yeast and dermatophytes, respectively. The most sensitive species were *Candida albicans* ATCC 10231, *Epidermophyton floccosum,* and *Trichophyton rubrum* (Lopes et al., 2013). The anti-candidal activity of the seaweeds

TABLE 9.1 Antibacterial Activity of Seaweeds

Seaweeds	Bioactive extract or molecule	Bacteria targeted	Main effects	References
Laurencia nangii	Neolaurene (Terpenoide)	*Salmonella typhi* and *Staphylococcus aureus*	Growth inhibition with IC_{50} of 7.5 µg/ml	Kamada and Vairappan, 2015
Sargassum wightii and *Halimeda gracilis*	Extracts	*Pseudomonas aeruginosa*, *Vibrio parahaemolyticus* and *Escherichia coli*	Antibacterial effect on gram-negative with MIC of 50 µg/ml Inhibition of bacterial pathogens at 25 and 50 µg/ml	Suganya et al., 2019
Sphaerococcus coronopifolius	Bromoditerpenes (Sphaerodactylomelol and 4 other sphaerane bromoditerpenes)	*Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus,* and *Candida albicans*	High antibacterial of Sphaerodactylomelol on *S. aureus* (IC_{50} 96.3 µM) High antibacterial activity of sphaerane bromoditerpene on *S. aureus* (IC_{50} 6.35 µM)	Rodrigues et al., 2015b
Sargassum tenerrimum	Fucoidan	*Enterococcus faecalis* and *Escherichia coli*	Potent antibacterial effect of depolymerized fucoidans	Ashayerizadeh et al., 2020
Dictyopteris polypodioides	Essential oil and volatile fraction	*Staphylococcus aureus, Agrobacterium tumefaciens, Salmonella typhimurium, Bacillus cereus, Micrococcus luteus* and *Escherichia coli*	High inhibitory effect of essential oil against all tested bacteria *S. aureus* the most sensitive with MIC of 1519 µg/ml	Riad et al., 2020

TABLE 9.1 *(Continued)*

Seaweeds	**Bioactive extract or molecule**	**Bacteria targeted**	**Main effects**	**References**
Sargassum latifolium, Sargassum platycarpum and Cladophora socialis	Methanol and acetone extracts	*Escherichia coli, Salmonella* sp., *Staphylococcus xylosus, Staphylococcus aureus, Bacillus subtilis, Enterococcus faecalis* and *Candida albicans*	*S. latifolium* and *S. platycarpum* methanolic extracts more active against gram-positive than gram-negative bacteria *C. socialis* methanolic extract with important effect on methicillin-resistant *Staphylococcus aureus* (MRSA)	Moubayed et al., 2017
Stypocaulon scoparium and *Halopitys incurvus*	Aqueous and Ethanol extract	*Staphylococcus aureus, Bacillus subtilis, Escherichia coli* and *Pseudomonas aeruginosa*	Ethanol extract of *S. scoparium* with remarkable antibacterial activity against all pathogenic bacteria	Khelil-Radji et al., 2017
Ulva lactuca	Methanol extract	*Bacillus subtilis, Corynebacterium diphtheria, Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa* and *Salmonella paratyphi*	Potent antibacterial activity against Gram-positive and Gram-negative bacteria strains	Alagan et al., 2017

IC_{50}: Concentration of a compound required for 50% inhibition *in vitro* and MIC: Minimum Inhibitory Concentration.

collected from the Gulf of Mannar (India) was evaluated with well diffusion and micro-dilution techniques. The methanolic extracts of *Dictyota bartayresiana* showed a zone of inhibition of 17.4 ± 0.62 mm against *Candida albicans*. Additionally, all tested extracts showed a fungistatic mechanism of inhibition of *Candida albicans* (Arumugam et al., 2019). In another study, Arumugam and Rajendran (2019) reported that *Stocheospermum marginatum* extracts showed a significant zone of inhibition up to 50 µg/ml against *Candida krusei* and other tested *Candida* strains.

Over all, seaweed's antimicrobial activity is influenced by different factors like the season of collection, the habitat, macroalgae growth stages, besides methods of extraction (Rosaline et al., 2012; Mishra et al., 2016).

9.4.1.2 ANTIVIRAL ACTIVITY OF SEAWEEDS

The marine environment is a rich source of biological and chemical compounds with antiviral activity. Secondary metabolites of algae have been tested as antiviral agents for different viruses of medical and veterinary importance (Aguilar-Briseño et al., 2015; Shi et al., 2017).

Seaweed polysaccharides have been extensively studied for medical antiviral activity as reported in Table 9.2. They have been described as inhibitors of viral attachment, internalization, uncoating, transcription, and replication (Shi et al., 2017). Gheda et al. (2016) evaluated the antiviral effects related to seaweed polysaccharides against Hepatitis C virus. *Sargassum vulgare* extract showed the potentiality to scavenge the free radicals (up to 81.5%) and *Laurencia obtusa* inhibited the Hepatitis C virus by 82.36% (Gheda et al., 2016).

Fucoidan extracted from *Dictyota bartayesiana* and *Turbinaria decurrens* were evaluated for anti-human immunodeficiency virus (anti-HIV) activity. Crude and purified fucoidan samples exhibited inhibitory activity of 90.5% and 89% for *Dictyota bartayesiana* and 89.7% and 92% for *Turbinaria decurrens* (Sanniyasi et al., 2019). Fucoidan was reported to inhibit HIV-1 and HIV-2 as well as further enveloped viruses like Herpes Simplex Virus type-1 (HSV-Type 1), Influenza virus A and B, Measles virus (MeV), and respiratory syncytial virus (RSV). The sulfated polysaccharide inhibited the fusion of the virus and the host cell and viral adsorption to the host cells (Esteves et al., 2011). PLS from *Sargassum fluitans* showed significant cytotoxic and antiviral activities against HSV-Type 1 with EC_{50} of 42.8 mg/ml and antiviral activity at a multiplicity of infection without cytotoxicity.

TABLE 9.2 Examples of Research on Antiviral Activity of Seaweed Compounds

Seaweeds	**Bioactive extract or molecule**	**Virus targeted**	**Main effects**	**References**
Dictyota pfaffii	Dolabelladienol A (Diterpene)	Human Immunodeficiency Virus 1 (HIV-1)	Virus inhibition with IC_{50} of 2.9 µM	Pardo-Vargas et al., 2014
Eisenia bicyclis	Phlorofucofuroeckol-A (Phlorotannin)	Murine norovirus	Virus inhibition with IC_{50} of 0.9 µM	Eom et al., 2015
Dictyota pfaffii	Dolabelladienetriol (Diterpene)	Herpes Simplex Virus-Type 1 (HSV-1)	Similar efficacy on the anti-HSV-1 activity to the Aciclovir drug	Garrido et al., 2017
Osmundaria obtusiloba	Ethanol extract	Chikungunya Virus (CHIKV)	CHIKV inhibition of 1.25 µg/mL	Cirne-Santos et al., 2019
Ecklonia cava	Phlorofucofuroeckol (Phlorotannin)	Influenza A viral strains (H1N1 and H9N2)	Potent antiviral activity with EC_{50} value of 13.48 ± 1.93 µM	Cho et al., 2019
Scytosiphon lomentaria	Galactofucan (Polysaccharide)	Herpes Simplex Virus-Type 1 and 2 (HSV-1 and HSV-2)	Fractions with different viral inhibitory properties	Ponce et al., 2019
Monostroma nitidum	Glucuronorhamnan (Polysaccharide)	Enterovirus 71 (EV71)	Inhibition of EV71 infection and down-regulation of host phosphoinositide 3-kinase / protein kinase B signaling pathway	Wang et al., 2020
Fucus vesiculosus	Fucoidan (Polysaccharide)	Hepatitis B Virus	Reduction of virus replication and activation of the extracellular signal-regulated kinase	Li et al., 2017

The observed activity was linked to the sulfatation, molecular weight, and carbohydrate nature of polysaccharides (Bedoux et al., 2017).

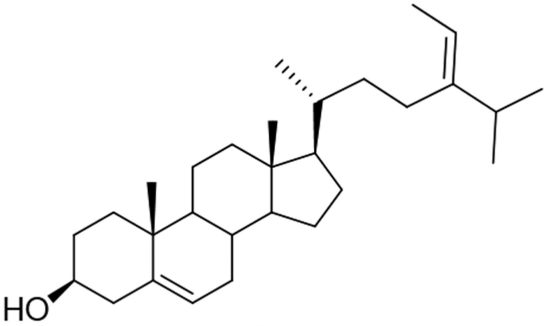
Pholorotannins also exhibited antiviral activity against several viruses like HIV-1, murine norovirus, human papilloma-virus (Ahn et al., 2004; Eom et al., 2015; Kim and Kwak, 2015). The antiviral activity of Polyphenol-rich extracts (PPs) from seaweeds was tested against MeV. Then the best polyphenols were combined with ribavirin and with PLS to discover potent antiviral properties (Morán-Santibañez et al., 2018). In this study, the virucidal activity of PPs extracts was reported by inactivating the viral particle. The observed inhibitory activity reached 83–89% of inhibition for both PPs (*Ecklonia arborea* and *Solieria filiformis*) (Morán-Santibañez et al., 2018).

The situation in 2020 with the global SARS-COV2 pandemic has more than ever emphasized the importance of having an arsenal of effective antiviral molecules to deal with emerging viral pathologies. At least, they are considered the only effective, but not foolproof, way to eradicate viruses, while waiting for the development of a vaccine (Roberts, 2020).

9.4.2 ANTIOXIDANT ACTIVITY OF SEAWEED EXTRACTS

Oxidative stress represents a state of imbalance between the production of radicals or reactive oxygen species (ROS) and the antioxidant cellular capacities in favor of ROS. The latter, are considered toxic products from normal oxygen metabolism and are significant contributors to many pathologies like cancer (Halliwell, 2013) and neurodegenerative diseases, mainly Alzheimer's and Parkinson's diseases (Clark et al., 2010).

Several studies have examined the antioxidant activity of seaweed derived natural products. Antioxidants are the most abundant among all biological compounds in seaweeds; including endogenous antioxidants (enzymes and proteins) and others exogenous (Polyphenols, vitamin C) (Chang and Teo, 2016). Lee et al. (2003) evaluated the antioxidant activity of fucosterol from *Pelvetia siliquosa* (Figure 9.3). They reported a significant increase of free radical scavenging enzyme activities like glutathione peroxidase (GPx), superoxide dismutase (SOD), and catalase (CAT). Zubia et al. (2007) reported the antioxidant potential of different seaweed species. *Avrainvillea longicaulis* portrayed the most potent one with high phenolic content (3.36 ± 0.05% DW) and low oxidation index EC_{50} (1.44 ± 0.01 mg/l). Extracts from *Chaetomorpha* were evaluated for their antioxidant activity using the 2, 2-diphenyl-1-picrylhydrazyl radical scavenging activity and total flavonoid, phenolic, and tannin content assays. The results revealed that ethanol extracts of *Chaetomorpha* exhibited higher antioxidant activity IC_{50} (9.41 ± 0.54 mg/ml) and showed totals of 189.14 ± 0.99 mg of Quercetin equivalent QE/g, 21.92 ± 0.43 mg of Gallic acid equivalent (mg GAE/g), and 21.81 ± 0.04 mg GAE/g of flavonoid, phenolic, and tannins contents respectively (Haq et al., 2019).



Fucosterol

FIGURE 9.3 Chemical structure of antioxidant compound Fucosterol (Lee et al., 2003).

The antioxidant capacities of seaweeds (*Sargassum polycystum, Eucheuma denticulatum, Kappaphycus alvarezzi* var. *Buaya,* and *Kappaphycus alvarezzi* var. *Giant*) were also documented (Fu et al., 2016). Among the tested species *Sargassum polycystum* exhibited the most antioxidant activities (2.00 ± 0.01 μmol TEAC/g DW and 0.84 ± 0.01 μmol TEAC/g DW). Umavandhana and Jayanthi (2018) evaluated the antioxidant activity for *Sargassum swartzi* and *Enteromorpha compressa*. The obtained results showed high free radical scavenging activity of *Sargassum swartzi* aqueous extract. In another work, seven green seaweeds were investigated for their total flavonoid and phenolic content, besides antioxidant, scavenging, and reducing activities (Tanna et al., 2018). *Caulerpa* spp. exhibited potential total antioxidant activity over 50%, high potential scavenging activity above 60%, and maximal reducing activity (>78%) (Tanna et al., 2018). Antioxidant potential of seaweeds was positively correlated to the total phenolic content (Chai et al., 2015; Pinteus et al., 2017), inversely other studies suggested no direct correlation between the antioxidant activity and phenolic content (Lim et al., 2002; Mamelona et al., 2007).

9.4.3 ANTICANCER POTENTIALS OF SEAWEEDS

Cancer is a complex disease in which cells divide uncontrollably, invade tissues, and form tumors. The causes can be infectious, medicinal, linked to environmental toxins, diet, and healthy lifestyle, hereditary genome mutations, hormones, or even diseases or failures of the immune system (Gutiérrez-Rodríguez et al., 2018). The cancer incidence is increasing with 18 million new cases worldwide, while the mortality due to cancer reached 9.6 million people (Bray et al., 2018). Chemotherapy on cancer cells is not specific, so way research on finding novel, efficient, and nontoxic chemotherapeutic drugs based on natural sources (like marine environments) has been of great interest (Vaikundamoorthy et al., 2018).

Several compounds isolated from macroalgae such as terpenes, polysaccharides, and polyphenols showed potent anticancer activity *in vivo* and *in vitro* as noted in Table 9.3 (Peng et al., 2011; Senthilkumar et al., 2013; Atashrazm et al., 2015).

Polysaccharides such as fucoidan, alginate, agarose, and carrageenan, which have immunomodulatory and anticancer effects, have attracted more consideration in the biochemical and medical fields (Ooi and Liu, 2000). Fucoidan and carrageenan obtained respectively from brown or red seaweeds exhibit antitumor and immunomodulating activities (Aquib et al., 2019; Cicinskas et al., 2020). Fucoidan has been reported with promising anticancer and antitumor activities (Lin et al., 2020). Multiple studies have indicated that fucoidan induces cytotoxicity against various cancer cells by preventing cell invasion, angiogenesis, metastasis, and cell cycle arrest; upregulating growth signaling molecules implicated in various cellular regulatory mechanisms; and inducing apoptosis (Senthilkumar et al., 2013).

The anticancer activity has been reported in different types of cancers such as lung cancer, gastric cancer, colon cancer, breast cancer, prostate cancer, and liver cancer (Han et al., 2008; Yamasaki-Miyamoto et al., 2009; Vishchuk et al., 2013; Mak et al., 2014; Choo et al., 2016; Hsu at al., 2017; Yan et al., 2019).

Fucoidan has potent antiproliferative activity against human lung adenocarcinoma cell line A549 (Boo et al., 2011). The sulfated polysaccharide isolated from *Undaria pinnatifida* displayed an anticancer effect against the breast cancer cell line T-47D and the melanoma cancer cell line SK-MEL-28 (Vishchuk et al., 2011). An anti-tumor effect was manifested by inhibition of cell aggregation for T-47D and SK-MEL-28 lines. They also inhibit the viability of B16 murine melanoma cell line by activating apoptosis (IC_{50} 530

TABLE 9.3 Potential Anticancer Activity of Seaweeds Metabolites

Seaweeds	Bioactive extract or molecule	Related disease	Cell lines tested	Main effects	References
Eucheuma cottonii	Polyphenol-rich extract	Breast adenocarcinoma	MCF7 and MDA-MB-231	- Apoptosis induction and downregulation of the endogenous estrogen biosynthesis - Antioxidative improvement	Namvar et al., 2012
Undaria pinnatifda	Fucoxanthin (Carotenoid)	Human gastric adenocarcinoma	SGC-7901 BGC-823	- Proliferation inhibition and apoptosis induction - Arrest of cell cycle at S phase for SGC-7901 cells and at G2/M phase for BGC-823 cells	Yu et al., 2018
Laminaria japonica	Fucoxanthin (Carotenoid)	Lung cancer	Human non-small cell lung cancer cells (NSCLC)	- *In vivo* anti-lung cancer and arrest cell cycle - Apoptosis induction	Mei et al., 2017
Sargassum muticum	Phlorotannins	Adenocarcinoma colon cancer	HT-29 cells	- Antiproliferative activity and cytotoxic potential	Montero et al., 2016
Ecklonia cava	Dieckol (Phlorotannin)	Ovarian cancer	A2780 and SKOV3	- Cytotoxic effect, SKOV3 apoptosis induction and tumor growth suppression - Mitochondrial dysfunction and suppression of anti-apoptotic proteins levels	Ahn et al., 2015

TABLE 9.3 *(Continued)*

Seaweeds	**Bioactive extract or molecule**	**Related disease**	**Cell lines tested**	**Main effects**	**References**
Fucus vesiculosus	Fucoidan (Product F5631)	Human leukemia	U937	- Inhibition of growth and induction of apoptosis - Activation of caspases and loss of mitochondria membrane potential	Park et al., 2013
Sphaerococcus coronopifolius	Bromoditerpenes (Sphaerodactylomelol and 4 other sphaerane bromoditerpenes)	Human hepatocellular carcinoma	HepG-2	- Inhibition of cell proliferation (IC_{50} 280 µM) and cytotoxicity (IC_{50} 720 µM) by sphaerodactylomelol	Rodrigues et al., 2015b

± 4.3 µg/ml) (Wang et al., 2017b). They seem to be involved in stopping or reducing cell proliferation, cell migration, tumor angiogenesis, invasion, and metastasis (Déléris et al., 2016). Besides, they showed the ability to stop the cell cycle in certain tumor cell lines, suggesting an effect on the cyclines (Déléris et al. 2016). Moreover, an extracted polysaccharide from *Sargassum vulgare* induced a potent inhibition on cells proliferation and antiangiogenic activity (Dore et al., 2013). Anticancer and apoptotic activity of fucoidan from *Sargassum cinereum* have been elucidated also against colon cancer cell line Caco-2 (Narayani et al., 2019). Caco-2 cell growth was inhibited in a dose-dependent manner with an IC_{50} concentration of 250 µg/ml. Besides, fucoidan induced cell apoptosis and increases ROS production and permeability of mitochondrial membrane (Narayani et al., 2019).

Oligo-fucoidan from *Sargassum hemiphyllum* was demonstrated to exhibit hepatocellular carcinoma apoptosis. Anti-hepatoma cell (HepG2 Cells) activity was revealed by cell cycle arrest and activation of caspases as apoptotic pathways inducing cell death (Yan et al., 2019). Carrageenans have an anti-angiogenesis and pro-apoptotic effect. Carrageenans obtained from *Kappaphycus alvarezii* effectively inhibited the growth of different cell lines (breast, colon, liver, and osteosarcoma) (Ariffin et al., 2014; Suganya et al., 2016). However, epidemiological data suggest a link between carrageenans (degraded and non-degraded) and intestinal ulcers and neoplasms (Déléris et al., 2016). Polysaccharides from *Ulva lactuca* exhibited an interesting anticancer activity against breast cancer (Abd-Ellatef et al., 2017).

More recently, seaweed polysaccharides from *Sargassum wightii, Enteromorpha compressa,* and *Acanthophora spicifera* (from India) were tested against the HT-29 human colon cancer cell line (Praveen et al., 2020). *Acanthophora spicifera* polysaccharide seaweed extract at 100 µg/ml presented a high *in vitro* cytotoxic effect on HT-29 cells up to 52.13 ± 1.4% (Praveen et al., 2020). Fucoxanthin, a non-polar carotenoid, was also reported to have an antiproliferative effect, inducing apoptosis and anti-angiogenesis and able to stop the cell cycle. This molecule, therefore, has significant potential in the prevention and treatment of cancer. The Fucoxanthin extracts from *Dictyota indica* (at 50 µg/ml) presented effective anticancer activity on the breast cancer cell line, without toxic effects to the normal cells (Karkhane Yousefi et al., 2018).

Phlorotannins from brown algae also show promising effects. It was emphasized that eckol isolated from *Ecklonia maxima* showed important cytotoxic activity against HeLa cells, H157, and MCF7 cell lines (Mwangi et al., 2017). Purified phlorotannin from *Ascophyllum nodosum* inhibited strongly the proliferation of colon cancer cells with IC_{50} values of 33 µg/ml (Nwosu et al., 2011). Furthermore, Alarif et al. (2016) reported the antiproliferative activity of three sesquiterpenoids (eudesma-4(15),7-diene-5,11-diol, teuhetenone, and chabrolidione B) from *Laurencia obtuse* against MCF-7 cell lines. As such, the most promising activity was shown by teuhetenone. Ethanol extracts of *Chaetomorpha* showed the highest anticancer activity through growth inhibition of MDA-MB-231 breast cancer cells. The low IC_{50} obtained was 225.18 ± 0.61 µg/ml. Extracts analysis indicated the presence of active antitumor compounds such as Dichloracetic acid, Oximes, and L-α-Terpinol (Haq et al., 2019).

9.4.4 ADDITIONAL POTENT BIOLOGICAL ACTIVITIES OF SEAWEED METABOLITES

Additionally to the above-cited activities, seaweeds have been explored for properties with potential health benefits in perspective of developing upcoming drug agents. A new path of the biological function of seaweed metabolites has emerged related to their potential applications in the treatment of diseases such as obesity, diabetes, malaria, leishmaniasis, as reported in Table 9.4.

TABLE 9.4 Summary of Potent Biological Activities of Seaweeds Biomolecules

Seaweeds	**Bioactive extract or molecule**	**Biological activity**	**References**
Ecklonia stolonifera	Phlorofucofuroeckol A (Phlorotannin)	Anti-obesity	Jung et al., 2014
Sargassum thunbergii	Indole derivatives	Anti-obesity	Kang et al., 2017
Plocamium telfairiae	Ethanol extracts	Anti-obesity	Lu et al., 2020
Grateloupia elliptica	Ethanol extracts	Anti-obesity	Lee et al., 2020
Ishige okamurae	Diphlorethohydroxycarmalol (Phlorotannin)	Anti-diabetes	Heo et al., 2009
Laminaria japonica and *Hizikia fusiforme*	Extracts	Anti-diabetes	Kang et al., 2018
Undaria pinnatifida	Fucoidan	Anti-diabetes	Sim et al., 2019
Sargassum confusum	Oligosaccharides	Anti-diabetes	Yang et al., 2019b
Undaria pinnatifida	Fucoidan	Anti-plasmodial Anti-malarial	Chen et al., 2009

TABLE 9.4 *(Continued)*

Seaweeds	**Bioactive extract or molecule**	**Biological activity**	**References**
S*argassum wightii*	Zinc oxide nanoparticles (ZnO NPs)	Anti-malarial	Murugan et al., 2018
Valoniopsis pachynema	CdS nanoparticles	Anti-malarial Anti-plasmodial	Sujitha et al., 2017
Laurencia dendroidea	Elatol (Sesquiterpene)	Anti-leishmanial	dos Santos et al., 2010
Solieria filiformis, *Botryocladia occidentalis*, *Caulerpa racemosa* and *Gracilaria caudata*	Sulfated polysaccharides	Anti-leishmanial	Lehnhardt Pires et al., 2013
Cystoseira baccata and *Cystoseira barbata*	Extracts	Anti-leishmanial	de Sousa et al., 2018

9.4.4.1 ANTI-OBESITY AND ANTI-DIABETIC ACTIVITIES OF SEAWEED EXTRACTS

Obesity is defined as the excessive or abnormal accumulation of body fat in the adipose tissue, energy imbalance, and lipogenesis (Ojulari et al., 2020). Different studies reported the anti-obesity effects of seaweed metabolites (Seca and Pinto, 2018).

The anti-obesity potential effect of *Ecklonia stolonifera* was related to phlorotannins by reducing lipid accumulation in 3T3-L1 cells. Phlorofucofuroeckol A was the most active with IC_{50} of 17.86 µM. The study reported that phlorotannins suppressed CCAAT/enhancer-binding protein α (C/EBP α) and peroxisome proliferator-activated receptor γ (PPARγ) expressions (Jung et al., 2014). Besides, fucosterol from *Ecklonia stolonifera* exhibited inhibition of adipogenesis preadipocytes of 3T3-L1 cells, downregulation of sterol regulatory element-binding protein 1 (SREBP1), and modulation of multiple signaling pathways (Lee et al., 2017).

Indole derivatives isolated from *Sargassum thunbergii* have been tested for their potential anti-obesity effects (Kang et al., 2017). The results showed inhibition of the 3T3-L1 adipocytes differentiation and lipid accumulation as well as downregulation of the expression of PPARγ and C/EBP α, and sterol regulatory element-binding protein 1c (SREBP-1c) (Kang et al., 2017). Sharma et al. (2017) showed that ethanol extract of *Caulerpa okamurae* induced significant inhibition of lipid accumulation and reduction of the expression of PPAR-γ, SREBP-1c, and C/EBPα in 3T3-L1 adipocytes. The *in vivo* conducted experiment revealed a decrease in body weight, fat weight, and liver weight in HFD-fed mice. Additionally, *Caulerpa okamurae* extracts caused a decrease in free fatty acids, triglyceride, total cholesterol, glucose, and insulin in the plasma (Sharma et al., 2017).

Recently, the anti-obesity effect of *Plocamium telfairiae* was evaluated by the optimal antiadipogenesis on 3T3-L1 cells and the anti-obesity properties in obese C57BL/6 mice (Lu et al., 2020). The obtained results indicated a decrease of fat accumulation and suppression in 3T3-L1 cells of the major adipogenesis factors expression, such as PPAR- γ, SREBP-1, C/EBPα, and phosphorylated ACC (Lu et al., 2020). Ethanolic extracts of *Plocamium telfairiae* resulted in a decrease of triglycerides, total cholesterol, adiponectin, and insulin in high-fat diet-induced obese mice (Lu et al., 2020). Similarly, ethanolic extract of *Grateloupia elliptica* caused inhibition of intracellular lipid accumulation in 3T3-L1 cells, and significant reduction of adipogenic protein expression. Meanwhile, *in vivo* experiments indicated a net reduction in body weight and white adipose tissue weight with downregulation of PPAR-γ and C/EBP-α mRNA (Lee et al., 2020).

Obesity is associated with lipid accumulation, oxidative stress and an increase in insulin resistance that results in diabetes (Yang et al., 2019a). Diabetes is a chronic metabolic disease that could develop with obesity and aging. Diabetes and obesity are closely interrelated disorders. Phlorotannins were reported for their anti-diabetic activity. Diphlorethohydroxycarmalol (DPHC) isolated from *Ishige okamurae* inhibited α-amylase and α-glucosidase (IC_{50} = 0.53 ± 0.08 and 0.16 ± 0.01 mM). The rise in postprandial blood glucose levels in both streptozotocin-induced diabetic and normal mice was also suppressed (Heo et al., 2009). While Lee et al. (2012c) indicated that DPHC treatment protected high glucose-induced damage in RINm5F pancreatic β-cells through the anti-oxidant effects. *Ishige okamurae* extract was shown to prevent insulin resistance and regulate blood glucose levels in hyperglycemia in C57BL/KsJ-db/db mice (Min et al., 2011).

The anti-diabetic effects of *Laminaria japonica* and *Hizikia fusiforme* extracts were assessed both *in vitro* and *in vivo* models (Kang et al., 2018). The study reported significant inhibition of the α-glucosidase activity (with best activities for *Hizikia fusiforme* extracts) and a net increase in glucose uptake. Besides, tested extracts induced phosphorylation of protein kinase B and AMP-activated protein kinase in skeletal muscle models (*in vivo* and *in vitro*) (Kang et al., 2018). Fucoidan isolated from *Undaria pinnatifida* has been reported to reduce blood glucose levels and improve insulin sensitivity in mice (Sim et al., 2019). The authors tested fucoidan anti-diabetic function with direct action on adipocytes in 3T3-L1 cells. The results showed a reduction in lipid accumulation and glycerol-3-phosphate dehydrogenase activity as well as suppression of the PPARγ expression, stimulation of glucose uptake in normal adipocytes, and restoration of insulin-stimulated glucose uptake in obesity-induced insulin-resistant adipocytes (Sim et al., 2019). *Sargassum confusum* oligosaccharides were evaluated for their anti-diabetic effects *in vivo* using high-fat/high-sucrose fed hamsters (Yang et al., 2019b). The oligosaccharides induced a significant decrease in fasting blood glucose levels and protected the cellular architecture of the liver. The main active anti-diabetic effect revealed in this study was the regulation of insulin receptor substrate 1/phosphatidylinositol 3-kinase and c-Jun N-terminal kinase pathways (Yang et al., 2019b).

9.4.4.2 ANTI-MALARIAL AND ANTI-LEISHMANIAL POTENTIALITIES OF SEAWEEDS

Malaria is caused by *Plasmodium* parasites, essentially *Plasmodium falciparum*, *Plasmodium vivax* and *Plasmodium malariae. Plasmodium* parasites are transmitted to vertebrates through the bites of infected *Anopheles* mosquitoes (Murugan et al., 2016). The treatment and control of malaria are facing different problems like the emergence of artemisinin and chloroquine resistance in *Plasmodium* parasites (Benelli and Mehlhorn, 2016).

Chen et al. (2009) through the evaluation of the anti-plasmodial activity *in vitro* and *in vivo* assessed the anti-malarial activity of fucoidan from *Undaria pinnatifida*. Significant inhibition of erythrocyte invasion by *Plasmodium falciparum* was recorded, the same as for the chloroquine-sensitive (CQ-s) *Plasmodium falciparum* 3D7 strain and the chloroquine-resistant (CQ-r) K1 strain. Besides, fucoidan induced 37% of suppressive effect in *Plasmodium berghei*-infected mice and had no toxic effects on RAW 264.7 cells (Chen et al., 2009). The green-synthesized zinc oxide nanoparticles (ZnO NPs) synthesized using S*argassum wightii* were tested against female anopheline mosquitoes *Anopheles stephensi* the vector of *Plasmodium* parasites (Murugan et al., 2018). Larvicidal and pupicidal toxicity on *Anopheles stephensi* were obtained with LC_{50} of ZnO NPs ranged from 4.330 (larva

I) to 7.430 ppm (pupa); as well as an important reduction of longevity and fecundity of *Anopheles stephensi* (Murugan et al., 2018). CdS NPs utilizing *Valoniopsis pachynema* extracts showed toxicity on *Anopheles stephensi* and *Anopheles sundaicus* young instars (Sujitha et al., 2017). The mosquitocidal effect of *Valoniopsis pachynema*-synthesized CdS NPs on *Anopheles stephensi* ranged from LC_{50} of 16.856 (larva I) to 30.301 µg/ml (pupa) and for *Anopheles sundaicus* from 13.584 to 22.496 µg/ml respectively. The anti-plasmodial response of the nano-synthesized product against CQ-r and CQ-susceptible (CQ-s) strains of *Plasmodium falciparum* was also evaluated. The results indicated that the IC_{50} of *Valoniopsis pachynema* extract was 58.1 µg/ml (CQ-s) and 71.46 µg/ml (CQ-r). Whereas, the IC_{50} of *Valoniopsis pachynema*-CdS NPs was 76.14 µg/ml (CQ-s) and 89.21 µg/ml (CQ-r) (Sujitha et al., 2017).

Leishmania parasites are the causative agents of Leishmaniasis. These pathologies are vector-borne diseases reported worldwide. Seaweeds, due to their composition of biomolecules, have been the subject of investigations relating to the anti-leishmanial activity. The anti-leishmanial activity of elatol a sesquiterpene from *Laurencia dendroidea* was investigated against *Leishmania amazonensis* (dos Santos et al., 2010). Elatol induced IC50 of 4.0 µM and 0.45 µM respectively, on promastigote and intracellular amastigote forms of *Leishmania amazonensis*. In addition, elatol induced several structural modifications in parasite like pronounced swelling of the mitochondrion, concentric membrane structures inside the organelle, destabilization of the plasma membrane, and formation of an extension of the endoplasmic reticulum (dos Santos et al., 2010).

In another study, PLS from *Solieria filiformis*, *Botryocladia occidentalis*, *Caulerpa racemosa,* and *Gracilaria caudata* were tested *in vitro* against *Leishmania amazonensis* promastigotes (Lehnhardt Pires et al., 2013). A purified polysaccharide from *Caulerpa racemosa* showed the most potent activity with an EC_{50} value of 34.5 µg/ml. Moreover, *in vitro* cytotoxic assays using peritoneal macrophages and J774 macrophages demonstrated a decrease in J774 cell survival with no notable effect on peritoneal macrophages (Lehnhardt Pires et al., 2013). de Sousa et al. (2019) in *in vitro* screening of anti-leishmanial properties of Iberian seaweed showed also cytotoxicity and strong morphological alterations in the parasites. Besides, seaweed extracts of *Cystoseira baccata* and *Cystoseira barbata* were also effective against intracellular amastigotes with respective IC_{50} values of 5.1 and 6.8 µg/ml.

9.5 AGRICULTURAL APPLICATIONS OF SEAWEEDS

Agriculture represents an economic sector of great importance. Global climate changes, environmental stresses and competition raise the evidence of searching for new plant growth-promoting substances to increase crops production.

9.5.1 SEAWEEDS BIOSTIMULANT EFFECTS

Biostimulants include diverse compounds, mainly organic, used in small doses through soil or foliar application to enhance plant growth and development (Schmidt et al., 2003). Plant growth biostimulants should improve plant resistance to stress, increase plant growth, and improve nutrient use efficiency of fertilizers. The major advantage of using this type of product is to reduce fertilizer utilization by increasing crop quality.

Agricultural use of biostimulants comprises obtained products from seaweeds with a significant positive impact on plant development, nutrients uptake, and resistance to abiotic and biotic stresses (Hamed et al., 2017). In agriculture, algae can be used in different forms, of which extracts appear to be the most effective (Khan et al., 2009; Chojnacka et al., 2015). Seaweed extracts could be applied on soil and/or on plants as a foliar spray (Du Jardin, 2015) and stated many potentialities such as plant growth regulation (auxin, cytokinin, gibberellins, betains) (Stirk et al., 2014), fungicides, and pesticides activities (Rengasamy et al., 2015a). Extracts from *Ascophyllum nodosum, Fucus* sp., *Laminaria* sp., and *Sargassum* are widely used in agriculture (Khan et al., 2009). The use of seaweed extracts in agriculture promotes improved germination, nutrient uptake, stimulation of root development and shoots elongation, and increased water holding capacity (Craigie, 2011). Algal extracts are involved in increasing plant growth and biomass, the content of chlorophyll, carotenoids, and improving root development (Khan et al., 2009; Michalak and Chojnacka, 2016).

9.5.1.1 SEAWEEDS CROP IMPROVEMENT

Seaweed-based biostimulants play a significant role in developing environment-friendly strategies to improve crop yields, stresses tolerance, and fruit quality (Frioni et al., 2018). Improving local yields through integrated nutrient management is pertinent to sustainable stewardship of agricultural ecosystems.

The bio-stimulating effects of seaweeds may be related to their content on polyphenols, polysaccharides, alginates, polyamines, pigments, free amino acids, betaines, vitamins, micro, and macro-nutrients, and natural phytohormones (cytokinins, auxins, and auxin-like compounds, indole acetic acid, abscisic acid) (Papenfus et al., 2012; Wally et al., 2013; Stirk et al., 2014). This mixture of useful biologically active substances led to different beneficial effects (Khan et al., 2009; Yusuf et al., 2012; Michalak et al., 2017). Several studies related to the ability of seaweed extract on enhancing plant growth, yield, and fruiting have been performed (Abd El-Gawad and Osman, 2014). Brown algae extracts have attracted great interest. They have been used extensively in sustainable and biological agriculture as either natural plant growth stimulants or bio-fertilizers (Hong et al., 2007; Craigie, 2011). *Ascophyllum nodosum* extract enhances growth and yield in many crops and improves quality.

Many studies have reported the positive and beneficial effects of seaweed extracts on the growth and yield of tomato (Demir et al., 2006), soybean (Rathore et al., 2009), wheat (Shah et al., 2013), eggplant (Abd El-Gawad and Osman, 2014), maize (Layek et al., 2015; Rengasamy et al., 2015b), red radish (Mahmoud et al., 2019) and others. Seed germination of *Cyamopsis tetragonoloba* was improved using seaweed fertilizers (Chithra et al., 2016). Godlewska et al. (2016) also emphasized the positive influence of the Baltics seaweeds (*Polysiphonia*, *Ulva,* and *Cladophora*) extract on *Lepidium sativum* seeds germination. An improvement in germination percentage and seedling vigor of rice (*Oryza sativa*) was recorded under *Kappaphycus alvarezii* and *Gracilaria edulis* saps (Layek et al., 2018). The application of seaweed extracts increased root growth and plants development (Khan et al., 2009; Alam et al., 2013; El Miniawy et al., 2014; Arioli et al., 2015).

Seaweed extract from a brown seaweed (*Ecklonia maxima*) has been reported as a plant biostimulant (Rouphael et al., 2017). A phlorotannin 'Eckol' was found to have auxin-like activities, and interesting growth-promoting activity (Rengasamy et al., 2015a, b). Moreover, spinach plants (*Spinacia oleracea*) showed a net increase in growth and biochemical parameters of plants exposed to eckol (from the seaweed *Ecklonia maxima*) a seaweed-based biostimulant (Kulkarni et al., 2019). Foliar applications of *Ascophyllum nodosum* extracts have been reported to affect plant hormone biosynthesis (Wally et al., 2013) and enhance crop tolerance to pathogens (Khan et al. 2009; Battacharyya et al. 2015). Seaweed extract from *Sargassum swartzii* significantly improved shoot length, leaves number, total phenolic content, proteins, and flavonoids of cowpea (*Vigna unguiculata*). The results highlighted that *Sargassum swartzii* application has significantly ameliorated the phytochemical contents and antioxidant activity in *Vigna unguiculata* (Vasantharaja et al., 2019).

More recently, arbuscular mycorrhizal fungus strain (*Rhizophagus irregularis*) combined with seaweed extract derived from *Fucus spiralis* induced significant increases in different growth, physiological, and histological parameters of the date palm (*Phoenix dactylifera* L.) (Anli et al., 2020).

9.5.1.2 SEAWEEDS APPLICATION AS BIO-FERTILIZER FOR SOIL QUALITY IMPROVEMENT

Even though seaweed extracts are mainly applied through foliar spray; they may have as well several effects on soil compartments. Seaweeds have been used as fertilizers and were applied to soils. Metabolites from algae such as polysaccharides (alginate, laminarin) have a positive effect on soil structure (Kraan, 2012) and are considered as perfect metal ion chelators.

The use of algal biomass for the improvement of soil quality for agricultural crop production has been reported (Cole et al., 2016). *Ascophyllum*-based composts used in the form of suspension, have improved the degraded soil structure (Alam et al., 2013). Algal biomass with its content of organic matter and other macronutrients (nitrogen, phosphorus, potassium, etc.); are useful for the improvement of soil quality and rhizosphere nutrients availability (Tabarsa et al., 2012). Seaweed extracts enhance rhizospheric microbes with plant growth-promoting traits and improve interaction with rhizosphere microorganisms and enzyme activity. When seaweed polysaccharides are applied in soils, they contribute to gel formation, water retention and soil aeration (Du Jardin, 2015), whereas the polyanionic compounds contribute to the cations fixation and exchanges closely related to the heavy metals fixation and soil remediation (Du Jardin, 2015). Some positive effects on the promotion of plant growth-promoting bacteria and pathogen antagonists in soils have also been reported. Alginate seaweed-based extracts increased rhizospheric-available phosphorus on *Chrysanthemum* plants, with no effects on microbial community (Ji et al., 2017). Recently, *Macrocystis pyrifera* biostimulant extracts have enhanced the hydrogenase activity of soil-degraded samples by erosion (Onet et al., 2019).

Application of seaweed fertilizers based on *Lessonia nigrescens* and *Lessonia flavicans* improved significantly beneficial microbes and fungi/bacteria ratio of *Malus hupehensis* rhizosphere (Wang et al., 2017c).

9.5.1.3 SEAWEEDS APPLICATION IN REALISTIC FIELD TRIALS

Mattner et al. (2018) showed the potential benefits of the integrated use of seaweed extracts in strawberry production. The biostimulatory effect of the seaweeds *Duvillaea potatorum* and *Ascophyllum nodosum* was manifested by an increase in root growth and fruit yield of strawberry. The extracts of *Ascophyllum nodosum* sprayed on grapevines were found to have positive effects, mainly on the quality of the wine grapes grown (Frioni et al., 2018). Foliar applications of *Ascophyllum nodosum* extracts resulted in a significant increase in tomato and sweet pepper plant growth parameters, including plant height, leaf number, plant dry biomass, root length, and chlorophyll content. The number of flower clusters, flower numbers, fruits per cluster, and total harvested fruit yield were also higher for plants treated with *Ascophyllum nodosum* extract in combination with fungicide treatment (Ali et al., 2019).

Layek et al. (2018) reported a high dry matter accumulation, chlorophyll index, crop growth rate, and rice yield after foliar spray of *Kappaphycus alvarezii* and *Gracilaria edulis* saps. Besides, the seaweed extracts increased the concentration of micronutrients (Fe, Cu, Zn, and Mn) and proteins in rice grains (Layek et al., 2018). On the other hand, seaweed extracts of *Ascophyllum nodosum* and *Sargassum muticum* used as biofertilizer, positively affected rice (*Oryza sativa*) and lettuce (*Lactuca sativa*) seed germination, plant development, and production (Silva et al., 2019). In another study, *Sargassum swartzii* extract enhanced *Vigna unguiculata* nutritional quality and yield (Vasantharaja et al., 2019).

9.5.1.4 SEAWEEDS ENHANCE ABIOTIC STRESS TOLERANCE

Crop productivity is negatively affected by different factors such as salinity, drought, extreme temperatures, and nutrient deficiencies inducing abiotic stresses. Abiotic stresses are associated with oxidative stress (ROS accumulation). ROS are reported to deteriorate biomolecules (DNA, proteins, and lipids) (Das and Roychoudhury, 2014). So, to prevent those negative effects, natural defense mechanisms are used for ROS scavenging. That includes enzymatic and non-enzymatic antioxidants such SOD, peroxidase, phenolic compounds, ascorbic acid, tocopherol, and others (Das and Roychoudhury, 2014). In order to mitigate abiotic stress, several studies were conducted. A positive impact of seaweed extract was also reported under stress conditions (abiotic and biotic) (Khan et al., 2009; Latique et al., 2014; Battacharyya et al., 2015). Their direct and indirect effects on plants under stress raised their role in alleviating stress conditions (Battacharyya et al., 2015). The extracts of *Ascophyllum nodosum, Laminaria digitata*, and *Fucus serratus* have been used as biofertilizers for their high content in betaines, organo-osmolytic compounds that play a crucial role in protecting plants against salt, drought, and extreme temperature stress (Blunden et al., 2010). Liu et al. (2019) reported that *Grateloupia filicina* polysaccharides alleviate salt stress on rice during the seed germination stage, and they stimulated rice seed development under salinity conditions. Polysaccharides extracted from *Lessonia nigrescens* were reported to enhance wheat seedlings adaptability to salt stress. Several plant parameters were improved under stress like shoot, root lengths and dry, fresh matters (Zou et al., 2019). On other study, *Ulva lactuca* and *Enteromorpha intestinalis* extracts significantly promoted diazotrophic bacterial growth and wheat seed germination under salt stress (Rai et al., 2018). Under drought stress, the application of *Gracilaria dura* extract induced an increase of wheat biomass and yield by 57% and 70% respectively (Sharma et al., 2019). Besides, *Ascophyllum nodosum* enhanced fresh biomass of lettuce exposed to potassium deficiency (Chrysargyris et al., 2018). A commercial extract of *Ascophyllum nodosum* evaluated for drought stress alleviation in soybean (*Glycine max*) was reported to induce higher relative water content and higher stomatal conductance under drought stress. The obtained results suggested that applications of *Ascophyllum nodosum* improved soybean drought tolerance through physiological changes and gene expressions (Shukla et al., 2018).

9.5.2 SEAWEEDS AGAINST PHYTOPATHOGENS

Phytopathogens like fungi and bacteria are responsible for serious diseases to humans and lead to great losses in crop productions (Ramaswamy et al., 2007). Natural products are then used as safer alternatives to antibiotics and chemical synthetic pesticides, commonly used for pest control (Derbalah et al., 2012). Several bioactive compounds obtained from seaweeds exhibit different biological activities. They were highlighted for their roles in plant protection, anti-phytopathogen activities, and induction of plant resistance to biotic stress as potential antimicrobial, anti-insecticidal, and anti-nematodal agents (Sahayaraj et al., 2012; Baloch et al., 2013; Ibraheem et al., 2017). Seaweed extracts are organic and cost-effective and offer a non-toxic alternative way for disease biocontrol (Baloch et al., 2013; Kulkarni et al., 2019).

9.5.2.1 ANTIMICROBIAL ACTIVITIES

Kumar et al. (2008) reported the activity of *Sargassum wightii* against *Pseudomonas syringae* responsible for leaf spot disease on *Gymnema sylvestre*. Moreover, *Sargassum swartzii* extracts were reported to inhibit the growth of *Xanthomonas oryzae* that causes bacterial blight of rice (Arunkumar et al., 2005). Also, the use of *Cystoseira myriophylloides* and *Fucus spiralis* extracts markedly decreased the severity of crown gall diseases caused by *Agrobacterium tumefaciens* on tomato (Esserti et al., 2017). Those extracts induced plant resistance against the crown gall diseases due to their high antioxidant content. The *Padina gymnospora* extracts exhibited significant antibacterial activity against the soil pathogenic bacteria *Ralstonia solanacearum* and *Pectobacterium carotovora* (Ibraheem et al., 2017). In addition, a recent study reported the pesticide effects of AgNPs synthesized using aqueous extracts of agar seaweeds (*Gracilaria corticata* and *Gracilaria edulis*) and carrageenan seaweeds (*Hypnea musciformis* and *Spyridia hypnoides*) (Roseline et al., 2019). The AgNPs exhibited effective antibacterial activities against *Xanthomonas axonopodis* and *Xanthomonas oryzae* (Roseline et al., 2019). On the other side, plant virus diseases are responsible for a great loss in agricultural production. Natural anti-viral substances are much sought to limit the development and progression of these diseases. Seaweed extracts, due to their content on proteins and polysaccharides, exhibited several antiviral activities (Zhao et al., 2017). *Durvillaea antarctica* extracts were able to reduce damages caused by tobacco mosaic virus in tobacco leaves (Jiménez et al., 2011).

Seaweeds also received much attention as a source of fungicidal compounds used to protect plants against several pathogenic fungi. Different seaweeds metabolites were reported efficient against common pathogens like *Fusarium solani*, *Rhizoctonia solani*, *Aspergillus* sp., *Fusarium oxysporum*, *Penicillium* sp., and *Botrytis cinerea* (Liu et al., 2014; Khallil et al., 2015; Ibraheem et al., 2017). Algal polysaccharides have been widely studied as a source of agricultural drugs against plant disease (Stadnik and Freitas, 2014). Polysaccharides from brown and red seaweeds can induce defense responses and plant resistance against phytopathogens (Vera et al., 2011). Polysaccharides stimulate pathogen-associated cellular changes, calcium concentration modifications as defense activation and pathogenesis-related proteins activation (Zhao et al., 2012). Jiménez et al. (2011) reported that *Gracillaria chilensis* impeded the growth of *Phytophthora cinnamomi* while *Lessonia trabeculata* suppressed the growth of *Botrytis cinerea* and reduced the necrotic lesion in tomato leaves. Laminarins (polysaccharides from brown seaweeds) elicit defense responses against *Botrytis cinerea* causing gray mold and *Plasmopara viticola* responsible for downy mildew in grapevine plants and suppressed infections (Copping, 2004). Liang et al. (2012) showed the fungicidal activity of laminarin at *Aspergillus flavus*, through reduction of mycelial growth and aflatoxin production. Extracts of *Laminaria digitata* and *Undaria pinnatifia* caused the growth and spore germination inhibition of *Botrytis cinerea*. A net reduction of wilt symptoms caused by *Verticillium dahliae* on olive twigs has been reported by applications of laminarin and alginate (Ben Salah et al., 2018).

On the other hand, carrageenans (red algae polysaccharides) induced protection against different kinds of pathogens like *Botrytis cinerea*, and *Pectobacterium carotovora* on tobacco (Vera et al., 2011). Brown seaweed *Hormophysa cuneiformis* was found to have potential antifungal activity against *Cladosporium herbarum* (Mohamed and Saber, 2019). Furthermore, glucuronan, and oligoglucuronans (saccharides from green algae), showed a reduction of the blue and gray mold (*Penicillium expansum* and *Botrytis cinerea*) severities on postharvest apple fruit (*Malus domestica*); with great effect achieved by oligoglucuronans (Abouraïcha a et al., 2017). Saccharides from green algae showed a protective effect on apple by the activation of related-defense responses such as antioxidant enzyme activities (CAT and SOD) and the levels of lignin and phenolic compounds (Abouraïcha et al., 2017). *Padina gymnospora*, *Sargassum latifolium*, and *Hydroclathrus clathratus* seaweed powders used as soil amendments, diminished the incidence of root rot disease in *Solanum melongena* (eggplant) caused by *Fusarium solani* (Ibraheem et al., 2017). Ammar et al. (2017) reported the fungicidal effect of the *Sargassum vulgare* extract on *Pythium aphanidermatum* by reducing mycelial growth and disease incidence. The sulfated polysaccharide from *Acanthophora spicifera* elicits defense responses on *Hevea brasiliensis* in response to *Phytophthora palmivora* infection (Pettongkhao et al., 2019). Roseline et al. (2019) showed interesting antifungal activity of AgNPs against *Ustilaginoidea virens* under *in vitro* conditions.

9.5.2.2 INSECTICIDAL ACTIVITY

Seaweed extracts have been integrated into pest management. They are considered as an eco-friendly environmental source of novel insecticidal substances. For instance, different seaweed extracts exhibited insecticidal activity against *Dysdercus* spp. (cotton insect pests) (Rajesh et al., 2011; Sahayaraj et al., 2012). *Sargassum swartzii* extracts induced a net reduction in male and female longevity of *Dysdercus cingulatus* (Asharaja and Sahayaraj, 2013). Foliar applications of ι-, κ-, and λ-carrageenans in *Arabidopsis* against the insect *Trichoplusia ni* showed interesting effects (Sangha et al., 2011). Treated plants with ι- and k-carrageenan manifested reduced feeding damage by *Trichoplusia ni* larvae, additionally to the reduction in larval weight under the same treatments (ι- and k-carrageenan) (Sangha et al., 2011).

9.6 SEAWEED-BASED PRODUCTS FOR ENVIRONMENTAL APPLICATIONS

9.6.1 SEAWEED ALGICIDAL ACTIVITY

In recent years, HABs have been reported as a serious hazard to aquatic ecosystems (freshwater and marine), the aquaculture industry and human health (Jeong et al., 2000). HABs are mainly due to the eutrophication of water bodies and climate changes (Paerl and Huisman, 2008; Ying-ying et al., 2015). Red tides or HABs correspond to a massive growth of toxic or non-toxic microalgae in coastal waters. While, harmful cyanobacterial blooms (Cyano HABs) are one of the most serious problems in drinking water resources and freshwater ecosystems (Harke et al., 2016). CyanoHABs are massive blooms of cyanobacteria produced primarily by potentially toxic species such as *Microcystis aeruginosa*, one of the most important freshwater cyanobacteria widely distributed worldwide (Catherine et al., 2013). Due to the undesirable effects caused by these HABs, extensive research in the control or mitigation of HABs has been conducted. Alamsjah et al. (2005) tested several macroalgae species (37 species) and reported that the strongest algicidal effect was obtained by *Ulva fasciata* extract. The growth of the microalgae *Heterosigma akashiwo* and *Alexandrium tamarense* was inhibited by *Sargassum thunbergii, Corallina pilulifera* and *Ulva pertusa* (Wang et al., 2007a). Wang et al. (2012) reported strong growth inhibition of

Heterosigma akashiwo by seaweed species like *Enteromorpha intestinalis, Ulva pertusa* and *Ulva linza.* Besides, the macroalgal extracts of *Porphyra tenera, Ulva pertusa,* and *Enteromorpha clathrata* showed strong growth inhibition on *Skeletonema costatum* (An et al., 2008).

Extract of *Stoechospermum marginatum* containing diethyl phthalate as a major constituent showed a significant algicidal effect on *Oscillatoria* sp. (Manilal et al., 2011). Sesquiterpenoids isolated from *Porphyra yezoensis* had significant selective antialgal activity against test red tide microalgae (Sun et al., 2018a). Growth inhibition or even cell mortality on different bloom-forming dinoflagellates species was significantly recorded by *Ulva pertusa* and *Gracilaria lemaneiformis* (Wang et al., 2007b). *Ulva prolifera* methanol extract also exhibited significant activity mainly against *Heterosigma akashiwo* and *Prorocentrum donghaiense* (Sun et al., 2016), whilst *Gracilaria tenuistipitata* affected the photosynthesis process of *Prorocentrum micans* (Ye and Zhang, 2013). *Ecklonia cava* (brown algae) also caused growth inhibition of *Cochlodinium polykrikide* and *Heterosigma akashiwo* (Chowdhury et al., 2014). Sun et al. (2018b) investigated the antialgal activities of nine novel isolated molecules from *Ulva pertusa* against common red tide microalgae. Selective antialgal effects were obtained for all red tide microalgae tested, suggesting *Ulva pertusa* as a new source of bioactive compounds with antialgal activity. In recent work, methanol extract of *Tricleocarpa jejuensis* was assayed to control the algicidal activity against the phytoplankton *Chattonella antiqua* (Zha et al., 2020). The highest activity was recorded for active compounds identified as (E)-9-hydroxyoctadec-10-enoic acid, (E)-10-hydroxyoctadec-8-enoic acid, (E)-11-hydroxyoctadec-12-enoic acid and (E)-12-hydroxyoctadec-10-enoic acid. The algicidal activity was then related to the presence of the hydroxyl group in the unsaturated fatty acids (Zha et al., 2020). Besides, significant seaweeds effects were reported against Cyano HABs such as *Microcystis aeruginosa* and *Phormidium* sp. Zerrif et al. (2018) reported that the methanol extract of the *Codium elongatum* collected from the coast of Morocco showed a significant progressive reduction in growth of the potential bloom-forming cyanobacteria *Phormidium* sp.

Recently, the potential algicidal activities of 14 species of seaweeds collected from the Moroccan coast were evaluated. Methanol extracts of *Bornetia secundiflora*, *Laurencia pinnatifida*, and *Gelidium pulchellum* induced a strong inhibitory activity against *Microcystis aeruginosa* on solid medium (27.33 ± 0.33 mm, 17.33 ± 0.33 mm, and 16.67 ± 0.33 mm, respectively) (Zerrifi et al., 2019). While in liquid culture medium, all tested methanol extracts showed a significant inhibitory effect on *Microcystis aeruginosa* compared to the negative control (Zerrifi et al., 2019). Seaweed extracts appear to have a positive impact on monitoring the growth of microalgae and on the development of highly effective and more specific eco-strategies for the biocontrol of HABs.

9.6.2 ANTI-BIOFOULING ACTIVITY OF SEAWEEDS

Biofouling is one of the most serious problems facing worldwide in the marine environment; corresponding to undesirable growth of micro and macroorganisms on submerged surfaces, considering man-made and living structures (Wahl, 1989). Bioactive compounds from diverse marine algae showed potential for unraveling this problem through the inhibition of the fouling process (Hellio et al., 2002). Genera like *Asparagopsis, Laurencia*, *Sargassum, Ulva,* and others are sources of active antifouling compounds. Different potential substances were identified. Dimethylsulphopropionate and proline qualified as surface-attached antifouling compounds were isolated from *Fucus vesiculosus* (Saha et al., 2012). In another study, acyclic linear diterpenoids from *Bifurcaria bifurcata* exhibited antifouling activity (Muñoz et al., 2013). Several studies reported also different antifouling compounds from *Sargassum* spp. such as phlorotannins (Nakajima et al., 2016). The potential antifouling activity was reported for the 3-bromo-5-(diphenylene)-2(5H)-furanone compound from *Ulva rigida* (Chapman et al., 2014). Whereas, Grosser et al. (2012) related the activity of *Ulva* sp. to β-carotene. Fatty acid derivatives like docosane, hexadecanoic acid, and cholesterol trimethylsilyl ether, were registered as cortical cell products and deposited on the surface of *Laurencia translucida* (Paradas et al., 2016). The same biological activity was reported for *Laurencia* sp. due to the presence of Omaezallene (Figure 9.4) (Umezawa et al., 2014). Greff et al. (2014) reported antimicrobial activity against both marine and terrestrial microorganisms owed to the highly brominated cyclopentenones: mahorone and 5-bromomahorone. The species belonging to *Cystoseira* (Fucales) are known to be a source of bioactive terpenoid derivates, particularly meroterpenoids and diterpenoids. Meroditerpenoid and Cystophloroketals A and B isolated from *Cystoseira tamariscifolia* have shown high potential activity. Potent inhibition activity against fouling microalgae and moderate antimicrobial activity against a diverse range of bacteria and fungi were reported (El Hattab et al., 2015).

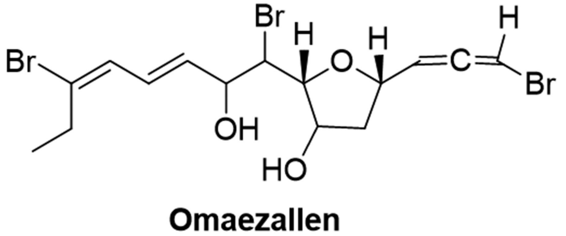


FIGURE 9.4 Omaezallene an anti-fouling compound from *Laurencia* sp. (Umezawa et al., 2014).

9.7 CONCLUSIONS AND FUTURE TRENDS

This chapter reviewed mainly recent studies related to seaweeds biodiversity and their richness on diverse and novel bioactive compounds with a wide large spectrum of biological properties. This suggests that macroalgae, within marine organisms, are the most coveted for possible biotechnological applications. The biological activities assigned to these seaweeds bioactive compounds are multiple like antibacterial, antifungal, antiviral, and anticancer activities.

Thereby, these various activities with different potent properties were investigated and involved in different domains of applications such as medicine, pharmacology, agricultural practice and environmental processes. Although there is much fundamental knowledge about the potential of seaweeds to play a key role as a new source of biomolecules with very interesting activities, there is a need for more investigations focused on the structural identification of novel substances and their mode of action to improve their biotechnological applications.

Seaweed bioactive molecules could gain importance and have greater value through the formulation of the natural product-based and environmentally friendly agents (designs of novel drugs and formulation of natural bio-control agents) to benefit the most from the biotechnological advantages offered by these bioactive compounds. The scientific communities must not only focus on the exploration of algal bio-compounds and the search for new biotechnological activities but also adopt alternative solutions for the efficient exploitation of these resources.

KEYWORDS

- **agricultural applications**
- **bioactive metabolites**
- **biological activities**
- **environmental uses of seaweeds**
- **minimum inhibitory concentration**
- **pharmacological potentialities**
- **seaweeds biotechnology**
- **seaweeds biodiversity**
- **seaweeds**
- **nanoparticles**
- **seaweeds extracts**

REFERENCES

Abd-Ellatef, G. E. F., Ahmed, O. M., Abdel-Reheim, E. S., & Abdel-Hamid, A. H. Z., (2017). *Ulva lactuca* polysaccharides prevent Wistar rat breast carcinogenesis through the augmentation of apoptosis, enhancement of antioxidant defense system, and suppression of inflammation. *Breast Cancer, 9,* 67–83.

Abouraïcha, E. F., El Alaoui-Talibi, Z., Tadlaoui-Ouafi, A., El Boutachfaiti, R., Petit, E., Douira, A., Courtois, B., et al., (2017). Glucuronan and oligoglucuronans isolated from green algae activate natural defense responses in apple fruit and reduce postharvest blue and gray mold decay. *J. Appl. Phycol., 29,* 471–480.

Aguilar-Briseño, J. A., Cruz-Suarez, L. E., Sassi, J. F., Ricque-Marie, D., Zapata-Benavides, P., Mendoza-Gamboa, E., Rodríguez-Padilla, C., & Trejo-Avila, L. M., (2015). Sulfated polysaccharides from *Ulva clathrata* and *Cladosiphon okamuranus* seaweeds both inhibit viral attachment/entry and cell-cell fusion, in NDV infection. *Marine Drugs, 13,* 697–712.

Ahn, J. H., Yang, Y. I., Lee, K. T., & Choi, J. H., (2015). Dieckol, isolated from the edible brown algae *Ecklonia cava*, induces apoptosis of ovarian cancer cells and inhibits tumor xenograft growth. *J. Cancer. Res. Clin. Oncology, 141,* 255–268.

Ahn, M. J., Yoon, K. D., Min, S. Y., Lee, J. S., Kim, J. H., Kim, T. G., Kim, S. H., Kim, N. G., Huh, H., & Kim, J., (2004). Inhibition of HIV-1 reverse transcriptase and protease by phlorotannins from the brown alga *Ecklonia cava*. *Biol. Pharm. Bull., 27,* 544–547.

Aigner, S., Remias, D., Karsten, U., & Holzinger, A., (2013). Unusual phenolic compounds contribute to ecophysiological performance in the purple-colored green alga *Zygogonium ericetorum* (Zygnematophyceae, Streptophyta) from a high-alpine habitat. *J. Phycol., 49,* 648–660.

Alagan, V., Valsala, R., & Rajesh, K., (2017). Bioactive chemical constituent analysis, *in vitro* antioxidant and antimicrobial activity of whole plant methanol extracts of *Ulva lactuca* Linn. *Br. J. Pharm. Res., 15,* 1–14.

Alam, M. Z., Brown, G., Norrie, J., & Hodges, D. M., (2013). Effect of *Ascophyllum* extract application on plant growth, fruit yield and soil microbial communities of strawberry. *Can. J. Plant. Sci., 93,* 23–36.

Alamsjah, M. A., Hirao, S., Ishibashi, F., & Fujita, Y., (2005). Isolation and structure determination of algicidal compounds from *Ulva fasciata*. *Biosci. Biotechnol. Biochem., 69,* 2186–2192.

Alarif, W. M., Al-Footy, K. O., Zubair, M. S., Halid, P. H. M., Ghandourah, M. A., Basaif, S. A., & Badria, F. A., (2016). The role of new eudesmane-type sesquiterpenoid and known eudesmane derivatives from the red alga *Laurencia obtusa* as potential antifungal-antitumor agents. *Nat. Prod. Res., 30,* 1150–1155.

Ale, M. T., & Meyer, A. S., (2013). Fucoidans from brown seaweeds: An update on structures, extraction techniques and use of enzymes as tools for structural elucidation. *RSC Adv., 3*, 8131–8141.

Ali, O., Ramsubhag, A., & Jayaraman, J., (2019). Biostimulatory activities of *Ascophyllum nodosum* extract in tomato and sweet pepper crops in a tropical environment. *PLoS One, 14*(5), e0216710.

Alobwede, E., Leake, J. R., & Pandhal, J., (2019). Circular economy fertilization: Testing micro and macro algal species as soil improvers and nutrient sources for crop production in greenhouse and field conditions. *Geoderma., 334,* 113–123.

Ammar, N., Jabnoun-Khiareddine, H., Mejdoub-Trabelsibi, B., Nefzi, A., Mahjoub, M. A., & Daami-Remadi, M., (2017). Pythium leak control in potato using aqueous and organic extracts from the brown alga *Sargassum vulgare* (C. Agardh, 1820). *Postharvest Biol. Technol., 130,* 81–93.

An, Z., Wang, Z., Li, F., Tian, Z., & Hu, H., (2008). Allelopathic inhibition on red tide microalgae *Skeletonema costatum* by five macroalgal extracts. *Front. Environ. Sci. Eng. China, 2,* 297–305.

Andrieux, C., Hibert, A., Houari, A. M., Bensaada, M., Popot, F., & Szylit, O., (1998). *Ulva lactuca* is poorly fermented but alters bacterial metabolism in rats inoculated with human faecal flora from methane and non-methane producers. *J. Sci. Food Agric., 77,* 25–30.

Anli, M., El Kaoua, M., Ait-el-Mokhtar, M., Boutasknit, A., Ben-Laouane, R., Toubali, S., Baslam, M., et al., (2020). Seaweed extract application and arbuscular mycorrhizal fungal inoculation: A tool for promoting growth and development of date palm (*Phoenix dactylifera* L.) *cv* Boufgous. *South African Journal of Botany, 132,* 15–21.

Antony, T., & Chakraborty, K., (2020). Anti-inflammatory polyether triterpenoids from the marine macroalga *Gracilaria salicornia*: Newly described natural leads attenuate proinflammatory 5-lipoxygenase and cyclooxygenase-2. *Algal Research, 47,* 101791.

Antunes, E. M., Afolayan, A. F., Chiwakata, M. T., Fakee, J., Knott, M. G., Whibley, C. E., Hendricks, D. T., et al., (2011). Identification and *in vitro* anti-esophageal cancer activity of a series of halogenated monoterpenes isolated from the South African seaweeds *Plocamium suhrii* and *Plocamium cornutum*. *Phytochemistry, 72,* 769–772.

Aquib, M., Farooq, M. A., Filli, M. S., Boakye-Yiadom, K. O., Kesse, S., Maviah, M. B. J., Mavlyanova, R., & Wang, B., (2019). A review on the chemotherapeutic role of fucoidan in cancer as nanomedicine. *Research Journal of Life Sciences, Bioinformatics, Pharmaceutical and Chemical Sciences, 5*(1), 512–539.

Ariffin, S. H. Z., Yeen, W. W., Abidin, I. Z. Z., Wahab, R. M. A., Ariffin, Z. Z., & Senafi, S., (2014). Cytotoxicity effect of degraded and undegraded kappa and iota carrageenan in human intestine and liver cell lines. *BMC Complementary and Alternative Medicine, 14,* 508.

Arioli, T., Mattner, S. W., & Winberg, P. C., (2015). Applications of seaweed extracts in Australian agriculture: Past, present and future. *J. Appl. Phycol., 27,* 2007–2015.

Arumugam, G., & Rajendran, R., (2019). Anti-candidal activity and synergetic interaction of antifungal drugs with differential extract of brown algae *Stocheospermum marginatum*. *Biocatal Agric. Biotechnol., 19,* 101145.

Arumugam, G., Rajendran, R., Khaleelullah, N. S., & Ramanathan, S., (2019). Anti-candidal and anti-virulence efficiency of selected seaweeds against azole resistance *Candida albicans*. *Biocatalysis and Agricultural Biotechnology, 20,* 101195.

Arunkumar, K., Selvapalam, N., & Rengasamy, R., (2005). The antibacterial compound sulphoglycerolipid 1-0 palmitoyl-3-0(6-sulpho-α-quinovopyranosyl)-glycerol from *Sargassum wightii* Greville (Phaeophyceae). *Botanica Marina, 40,* 441–445.

Aryee, A. N., Agyei, D., & Akanbi, T. O., (2018). Recovery and utilization of seaweed pigments in food processing. *Current Opinion in Food Science, 19,* 113–119.

Asharaja, A., & Sahayaraj, K., (2013). Screening of insecticidal activity of brown macroalgal extracts against *Dysdercus cingulatus* (Fab.) (Hemiptera: Pyrrhocoridae). *J. Biopest., 6,* 193–203.

Ashayerizadeh, O., Dastar, B., & Pourashouri, P., (2020). Study of antioxidant and antibacterial activities of depolymerized fucoidans extracted from *Sargassum tenerrimum*. *International Journal of Biological Macromolecules, 151,* 1259–1266.

Atashrazm, F., Lowenthal, R. M., Woods, G. M., Holloway, A. F., & Dickinson, J. L., (2015). Fucoidan and cancer: A multifunctional molecule with anti-tumor potential. *Marine Drugs, 13*(4), 2327–2346.

Ba-Akdah, M., Satheesh, S., & Al-Sofyani, A., (2016). Habitat preference and seasonal variability of epifaunal assemblages associated with macroalgal beds on the central Red Sea coast, Saudi Arabia. *J. Mar. Biol. Assoc. U.K., 96,* 1457–1467.

Bae, M., Kim, M. B., Park, Y. K., & Lee, J. Y., (2020). Health benefits of fucoxanthin in the prevention of chronic diseases. *Biochimica et Biophysica Acta (BBA) – Molecular and Cell Biology of Lipids, 1865*(11), 158618.

Baloch, G. N., Tariq, S., Ehteshamul-Haque, S., Athar, M., Sultana, V., & Ara, J., (2013). Management of root diseases of eggplant and watermelon with the application of asafoetida and seaweeds. *J. Appl. Bot. Food Qual., 86,* 138–142.

Barbosa, M., Lopes, G., Andrade, P. B., & Valentão, P., (2019). Bioprospecting of brown seaweeds for biotechnological applications: Phlorotannin actions in inflammation and allergy network. *Trends in Food Science and Technology, 86*, 153–171.

Battacharyya, D., Babgohari, M. Z., Rathor, P., & Prithiviraj, B., (2015). Seaweed extracts as biostimulants in horticulture. *Sci. Horticult., 196,* 39–48.

Bedoux, G., Caamal-Fuentes, E., Boulho, R., Marty, C., Bourgougnon, N., Freile-Pelegrín, Y., & Robledo, D., (2017). Antiviral and cytotoxic activities of polysaccharides extracted from four tropical seaweed species. *Natural Product Communications, 12*(6), 807–811.

Begum, S., Nyandoro, S., Buriyo, A., Makangara, J., Munissi, J., Duffy, S., Avery, V., & Erdelyi, M., (2018). Bioactivities of extracts, debromolaurinterol and fucosterol from macroalgae species. *Tanzania J. Sci., 44,* 104–116.

Belattmania, Z., Engelen, A. H., Pereira, H., Serrão, E. A., Barakate, M., Elatouani, S., Zrid, R., et al., (2016). Potential uses of the brown seaweed *Cystoseira humilis* biomass: 2-fatty acid composition, antioxidant and antibacterial activities. *J. Mater. Environ. Sci., 7,* 2074–2081.

Belghit, I., Rasinger, J. D., Heesch, S., Biancarosa, I., Liland, N., Torstensen, B., Waagbø, R., Lock, E. J., & Bruckner, C. G., (2017). In-depth metabolic profiling of marine macroalgae confirms strong biochemical differences between brown, red and green algae. *Algal Res., 26,* 240–249.

Ben, S. I., Aghrouss, S., Douira, A., Aissam, S., El Alaoui-Talibi, Z., Filali-Maltouf, A., & El Modafar, C., (2018). Seaweed polysaccharides as bio-elicitors of natural defenses in olive trees against Verticillium wilt of olive. *J. Plant Interact., 13,* 248–255.

Benelli, G., & Mehlhorn, H., (2016). Declining malaria, rising dengue and Zika virus: Insights for mosquito vector control. *Parasitol. Res., 115*(5), 1747–1754.

Bilal, H., Sahar, S., & Din, S., (2017). Bio-pesticides: New tool for the control of *Aedes* (*Stegomyia*) *albopictus* (Culicidae: Diptera) in Pakistan. *J. Arthropod. Borne. Dis., 11,* 278–285.

Blunden, G., Morse, P. F., Mathe, I., Hohmann, J., Critchleye, A. T., & Morrell, S., (2010). Betaine yields from marine algal species utilized in the preparation of seaweed extracts used in agriculture. *Nat. Prod. Commun., 5,* 581–585.

Bocanegra, A., Bastida, S., Benedí, J., Ródenas, S., & Sánchez-Muniz, F. J., (2009). Characteristics and nutritional and cardiovascular-health properties of seaweeds. *J. Med. Food, 12,* 236–258.

Boo, H. J., Hyun, J. H., Kim, S. C., Kang, J. I., Kim, M. K., Kim, S. Y., Cho, H., et al., (2011). Fucoidan from *Undaria pinnatifida* induces apoptosis in A549 human lung carcinoma cells. *Phytother. Res., 25,* 1082–1086.

Borbón, H., Herrera, J. M., Calvo, M., Sierra, H. T. L., Soto, R., & Vega, I., (2012). Antimicrobial activity of most abundant marine macroalgae of the Caribbean coast of Costa Rica. *Journal of Asian Scientific Research, 2,* 292–299.

Bray, F., Ferlay, J., Soerjomataram, I., Siegel, R. L., Torre, L. A., & Jemal, A., (2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer Journal for Clinicians, 68,* 394–424.

Campo, V. L., Kawano, D. F., Da Silva, D. B., & Carvalho, I., (2009). Carrageenans: Biological properties, chemical modifications and structural analysis – A review. *Carbohydrate Polymers, 77,* 167–180.

Cardoso, M. J., Costa, R. R., & Mano, J. F., (2016). Marine origin polysaccharides in drug delivery systems. *Marine Drugs, 14,* 34.

Cardoso, S. M., Carvalho, L. G., Silva, P. J., Rodrigues, M. S., Pereira, O. R., & Pereira, L., (2014). Bioproducts from seaweeds: A review with special focus on the Iberian Peninsula. *Current Organic Chemistry, 18,* 896–917.

Catherine, Q., Susanna, W., Isidora, E. S., Mark, H., Aurélie, V., & Jean-François, H., (2013). A review of current knowledge on toxic benthic freshwater cyanobacteria – Ecology, toxin production and risk management. *Water Res., 47*, 5464–5479.

Chai, T. T., Kwek, M. T., Ismail, N. I. M., Ooi, J. L. S., Amri, A. Y., Manan, F. A., Law, Y. C., & Wong, F. C., (2015). Antioxidant activities of methanol extract and solvent fractions of marine macroalga, *Avrainvillea erecta* (Berkeley) A. Gepp and E.S. Gepp (Dichotomosiphonaceae). *Trop. J. Pharm. Res., 14,* 503–509.

Chang, V. S., & Teo, S. S., (2016). Evaluation of heavy metal, antioxidant and anti-tyrosinase activities of Red Seaweed (*Eucheuma cottonii*). *Int. Food Res. J., 23*, 2370–2373.

Chapman, J., Hellio, C., Sullivan, T., Brown, R., Russell, S., Kiterringham, E., Le Nor, L., & Regan, F., (2014). Bioinspired synthetic macroalgae: Examples from nature for antifouling applications. *Int. Biodeterior. Biodegrad., 86,* 6–13.

Chen, J. H., Lim, J. D., Sohn, E. H., Choi, Y. S., & Han, E. T., (2009). Growth-inhibitory effect of a fucoidan from brown seaweed *Undaria pinnatifida* on *Plasmodium* parasites. *Parasitology Research, 104,* 245–250.

Chithra, K., Abraham, L. S., Thirugnanasambandham, R., & Prakash, P., (2016). A comparative analysis of the effect of seaweed fertilizers (Liquid and Paste) and vermiwash on seed germination of *Cyamopsis tetragonoloba. Biosciences Biotechnology Research Asia, 13,* 1089–1093.

Cho, H., Doan, T., Ha, T., Kim, H., Lee, B., Pham, H., Cho, T. O., & Oh, W. K., (2019). Dereplication by high-performance liquid chromatography (HPLC) with quadrupole-time-of-flight mass spectroscopy (qTOF-MS) and antiviral activities of phlorotannins from *Ecklonia cava*. *Marine Drugs, 17,* 149.

Choi, J. G., Kang, O. H., Brice, O. O., Lee, Y. S., Chae, H. S., Oh, Y. C., Sohn, D. H., et al., (2010). Antibacterial activity of *Ecklonia cava* against methicillin-resistant *Staphylococcus aureus* and *Salmonella* spp. *Foodborne Pathogens and Disease, 7,* 435–441.

Chojnacka, K., Michalak, I., Dmytryk, A., Gramza, M., Słowinski, A., & Górecki, H., (2015). Algal extracts as plant growth biostimulators. In: Kim, S. K., & Chojnacka, K., (eds.), *Marine Algae Extracts: Processes, Products, Applications* (pp. 189–211). Wiley-VCH Verlag GmbH and Co. KGaA: Weinheim, Germany.

Choo, G. S., Lee, H. N., Shin, S. A., Kim, H. J., & Jung, J. Y., (2016). Anticancer effect of fucoidan on DU-145 prostate cancer cells through inhibition of PI3K/Akt and MAPK pathway expression. *Marine Drugs, 14,* 126.

Chowdhury, M. T. H., Bangoura, I., Kang, J. Y., Cho, J. Y., Joo, J., Choi, Y. S., Hwang, D. S., & Hong, Y. K., (2014). Comparison of *Ecklonia cava*, *Ecklonia stolonifera* and *Eisenia bicyclis* for phlorotannin extraction. *J. Environ. Biol., 35,* 713–719.

Chrysargyris, A., Xylia, P., Anastasiou, M., Pantelides, I., & Tzortzakis, N., (2018). Effects of *Ascophyllum nodosum* seaweed extracts on lettuce growth, physiology and fresh-cut salad storage under potassium deficiency. *J. Sci. Food Agric., 98,* 5861–5872.

Cicinskas, E., Begun, M. A., Tiasto, V. A., Belousov, A. S., Vikhareva, V. V., Mikhailova, V. A., & Kalitnik, A. A., (2020). *In vitro* antitumor and immunotropic activity of carrageenans from red algae *Chondrus armatus* and their low-molecular weight degradation products. *Journal of Biomedical Materials Research Part A, 108*, 254–266.

Cirne-Santos, C. C., Barros, C. D. S., Nogueira, C. C. R., Azevedo, R. C., Yamamoto, K. A., Meira, G. L. S., Meira De, V. Z. F., et al., (2019). Inhibition by marine algae of Chikungunya virus isolated from patients in a recent disease outbreak in Rio de Janeiro. *Front. Microbiol., 10,* 2426.

Clark, T. A., Lee, H. P., Rolston, R. K., Zhu, X., Marlatt, M. W., Castellani, R. J., Nunomura, A., et al., (2010). Oxidative stress and its implications for future treatments and management of Alzheimer disease. *Int. J. Biomed. Sci., 6,* 225–227.

Cole, A. J., Roberts, D. A., Garside, A. L., De Nys, R., & Paul, N. A., (2016). Seaweed compost for agricultural crop production. *J. Appl. Phycol., 28*, 629–642.

Collins, K. G., Fitzgerald, G. F., Stanton, C., & Ross, R. P., (2016). Looking beyond the terrestrial: The potential of seaweed derived bioactives to treat non-communicable diseases. *Marine Drugs, 14,* 60.

Copping, L. G., (2004). *The Manual of Biocontrol Agents* (3^{rd} edn., p. 702). BCPC Publications, Alton.

Craigie, J. S., (2011). Seaweed extract stimuli in plant science and agriculture. *J. Appl. Phycol., 23,* 371–393.

Creis, E., Delage, L., Charton, S., Goulitquer, S., Leblanc, C., Potin, P., & Ar Gall, E., (2015). Constitutive or inducible protective mechanisms against UV-B radiation in the brown alga *Fucus vesiculosus*? A study of gene expression and phlorotannin content responses. *PLoS One, 10*, e0128003.

Cunha, L., & Grenha, A., (2016). Sulfated seaweed polysaccharides as multifunctional materials in drug delivery applications. *Marine Drugs, 14,* 42.

Das, K., & Roychoudhury, A., (2014). Reactive oxygen species (ROS) and response of antioxidants as ROS-scavengers during environmental stress in plants. *Front. Environ. Sci., 2,* 53.

Dawczynski, C., Schubert, R., & Jahreis, G., (2007). Amino acids, fatty acids, and dietary fibre in edible seaweed products. *Food Chemistry, 103,* 891–899.

De Sousa, C. B., Lago, J. H. G., Macridachis, J., Oliveira, M., Brito, L., Vizetto-Duarte, C., Florindo, C., et al., (2019). Report of *in vitro* antileishmanial properties of Iberian macroalgae. *Natural Product Research, 33*, 1778–1782.

De Souza, L. A. R., Dore, C. M. P. G., Castro, A. J. G., De Azevedo, T. C. G., De Oliveira, M. T. B., Moura, M. F. V., Benevides, N. M. B., & Leite, E. L., (2012). Galactans from the Red Seaweed *Amansia multifida* and their effects on inflammation, angiogenesis, coagulation and cell viability. *Biomed. Prevent. Nutr., 2,* 154–162.

Déléris, P., Nazih, H., & Bard, J. M., (2016). Seaweeds in human health. In: Fleurence, J., & Levine, I., (eds.), *Seaweed in Health and Disease Prevention* (pp. 319–367). San Diego, Academic Press.

Demir, N., Dural, B., & Yildirim, K., (2006). Effect of seaweed suspensions on seed germination of tomato, pepper and aubergine. *J. Biol. Sci., 6,* 1130–1133.

Derbalah, A. S., Elkot, G. A. E., & Hamza, A. M., (2012). Laboratory evaluation of botanical extracts, microbial culture filtrates and silver nanoparticles against *Botrytis cinerea*. *Ann. Microbiol., 62,* 1331–1337.

Dhargalkar, V. K., & Kavlekar, D. P., (2004). *Seaweeds – A Field Manual* (p. 42). National Institute of Oceanography. Dona Paula, Goa..

Dore, C. M. P. G., Alves, M. G. C. F., Santos, N. D., Cruz, A. K. M., Câmara, R. B. G., Castro, A. J. G., Alves, L. G., et al., (2013). Antiangiogenic activity and direct antitumor effect from a sulfated polysaccharide isolated from seaweed. *Microvasc. Res., 88,* 12–18.

Dos, S. A. O., Veiga-Santos, P., Ueda-Nakamura, T., Filho, B. P. D., Sudatti, D. B., Bianco, É. M., Pereira, R. C., & Nakamura, C. V., (2010). Effect of elatol, isolated from Red Seaweed *Laurencia dendroidea,* on *Leishmania amazonensis*. *Marine Drugs, 8,* 2733–2743.

Du Jardin, P., (2015). Plant biostimulants: Definition, concept, main categories and regulation. *Sci. Hortic., 196,* 3–14.

Dumay, J., Morançais, M., Nguyen, H. P. T., & Fleurence, J., (2015). Extraction and purification of R-phycoerythrin from marine red algae. *Nat. Prod. Mar. Algae.: Method. Protocol, 1308*, 109–117.

El Hattab, M., Genta-Jouve, G., Bouzidi, N., Ortalo-Magné, A., Hellio, C., Maréchal, J. P., Piovetti, L., et al., (2015). Cystophloroketals A–E, unusual phloroglucinol-meroterpenoid hybrids from the brown alga *Cystoseira tamariscifolia*. *J. Nat. Prod., 78,* 1663–1670.

El Miniawy, S. M., Ragab, M. E., Youssef, S. M., & Metwally, A. A., (2014). Influence of foliar spraying of seaweed extract on growth, yield and quality of strawberry plants. *J. Appl. Sci. Res., 10,* 88–94.

El-Gawad, H. G. A., & Osman, H. S., (2014). Effect of exogenous application of boric acid and seaweed extract on growth, biochemical content and yield of eggplant. *J. Hortic. Sci. Ornam. Plants, 6,* 133–143.

Eom, S. H., Lee, D. S., Jung, Y. J., Park, J. H., Choi, J. I., Yim, M. J., Jeon, J. M., et al., (2014). The mechanism of antibacterial activity of phlorofucofuroeckol-A against methicillin-resistant *Staphylococcus aureus*. *Appl. Microbiol. Biotechnol., 98,* 9795–9804.

Eom, S. H., Moon, S. Y., Lee, D. S., Kim, H. J., Park, K., Lee, E. W., Kim, T. H., et al., (2015). *In vitro* antiviral activity of dieckol and phlorofucofuroeckol-A isolated from edible brown alga *Eisenia bicyclis* against murine norovirus. *Algae, 30,* 241–246.

Esserti, S., Smaili, A., Rifai, L. A., Koussa, T., Makroum, K., Belfaiza, M., Kabil, E. M., et al., (2017). Protective effect of three brown seaweed extracts against fungal and bacterial diseases of tomato. *J. Appl. Phycol., 29*, 1081–1093.

Esteves, A. I. S., Nicolai, M., Humanes, M., & Goncalves, J., (2011). Sulfated polysaccharides in marine sponges: Extraction and anti-HIV activity. *Marine Drugs, 9,* 139–153.

Farasat, M., Khavari-Nejad, R. A., Nabavi, S. M. B., & Namjooyan, F., (2014). Antioxidant activity, total phenolics and flavonoid contents of some edible green seaweeds from northern coasts of the Persian Gulf. *Iran. J. Pharm. Res., 13,* 163–170.

Feng, M. T., Yu, X. Q., Yang, P., Yang, H., Lin, K., & Mao, S. C., (2015). Two new antifungal polyunsaturated fatty acid ethyl esters from the red alga *Laurencia okamurai*. *Chem. Nat. Compd., 51,* 418–422.

Ferreres, F., Lopes, G., Gil-Izquierdo, A., Andrade, P. B., Sousa, C., Mouga, T., & Valentao, P., (2012). Phlorotannin extracts from fucales characterized by HPLC-DAD-ESI-MSn: Approaches to hyaluronidase inhibitory capacity and antioxidant properties. *Marine Drugs, 10*, 2766–2781.

Frioni, T., Sabbatini, P., Tombesi, S., Norrie, J., Poni, S., Gatti, M., & Palliotti, A., (2018). Effects of a biostimulant derived from the brown seaweed *Ascophyllum nodosum* on ripening dynamics and fruit quality of grapevines. *Scientia Horticulturae, 232*, 97–106.

Fu, C. W. F., Ho, C. W., Yong, W. T. L., Abas, F., Tan, T. B., & Tan, C. P., (2016). Effects of phenolic antioxidants extraction from four selected seaweeds obtained from Sabah. *International Food Research Journal, 23*, 2363–2369.

Funami, T., Hiroe, M., Noda, S., Asai, I., Ikeda, S., & Nishinari, K., (2007). Influence of molecular structure imaged with atomic force microscopy on the rheological behavior of carrageenan aqueous systems in the presence or absence of cations. *Food Hydrocolloids, 21*, 617–629.

Garrido, V., Barros, C., Melchiades, V. A., Fonseca, R. R., Pinheiro, S., Ocampo, P., Teixeira, V. L., et al., (2017). Subchronic toxicity and anti-HSV-1 activity in experimental animal of dolabelladienetriol from the seaweed, *Dictyota pfaffii*. *Regulatory Toxicology and Pharmacology 86*, 193–198.

Gheda, S. F., El-Adawi, H. I., & EL-Deeb, N. M., (2016). Antiviral profile of brown and Red Seaweed polysaccharides against hepatitis C virus. *Iranian Journal of Pharmaceutical Research, 15*, 483–491.

Giada, M. D. L. R., (2013). Food phenolic compounds: Main classes, sources and their antioxidant power. In: Morales-Gonzalez, J. A., (ed.), *Oxidative Stress and Chronic Degenerative Diseases – A Role for Antioxidants* (pp. 87–112). Rijeka, Croatia: InTech.

Godlewska, K., Michalak, I., Tuhy, A., & Chojnacka, K., (2016). Plant growth biostimulants based on different methods of seaweed extraction with water. *BioMed Research International, 2016,* 5973760.

Gómez-Guzmán, M., Rodríguez-Nogales, A., Algieri, F., & Gálvez, J., (2018). Potential role of seaweed polyphenols in cardiovascular-associated disorders. *Marine Drugs, 16,* 250.

Greff, S., Zubia, M., Genta-Jouve, G., Massi, L., Perez, T., & Thomas, O. P., (2014). Mahorones, highly brominated cyclopentenones from the red alga *Asparagopsis taxiformis*. *J. Nat. Prod., 77,* 1150–1155.

Grosser, K., Zedler, L., Schmitt, M., Dietzek, B., Popp, J., & Pohnert, G., (2012). Disruption-free imaging by Raman spectroscopy reveals a chemical sphere with antifouling metabolites around macroalgae. *Biofouling, 28,* 687–696.

Grzywacz, D., Stevenson, P. C., Mushobozi, L. M., Belmain, S., & Wilson, K., (2014). The use of indigenous ecological resources for pest control in Africa. *Food Sec., 6,* 71–86.

Gullón, B., Gagaoua, M., Barbac, F. J., Gullón, P., Zhang, W., & Lorenzo, J. M., (2020). Seaweeds as promising resource of bioactive compounds: Overview of novel extraction strategies and design of tailored meat products. *Trends in Food Science and Technology, 100,* 1–18.

Guschina, I. A., & Harwood, J. L., (2006). Lipids and lipid metabolism in eukaryotic algae. *Progress in Lipid Research, 45*, 160–186.

Gutiérrez-Rodríguez, A. G., Juárez-Portilla, C., Olivares-Bañuelos, T., & Zepeda, R. C., (2018). Anticancer activity of seaweeds. *Drug Discovery Today, 23*, 434–447.

Güven, K. C., Percot, A., & Sezik, E., (2010). Alkaloids in marine algae. *Marine Drugs, 8*, 269–284.

Halliwell, B., (2013). The antioxidant paradox: Less paradoxical now? *Br. J. Clin. Pharmacol., 75,* 637–644.

Hamed, S. M., Abd, E. A. A., Abdel-Raouf, N., & Ibraheem, B. M. I., (2017). Role of marine macroalgae in plant protection and improvement for sustainable agriculture technology. *Beni-Suef University Journal of Basic and Applied Sciences, 7*, 104–110.

Han, J. G., Syed, A. Q., Kwon, M., Ha, J. H., & Lee, H. Y., (2008). Antioxidant, immunomodulatory and anticancer activity of fucoidan isolated from *Fucus vesiculosus*. *J. Biotechnol., 136*, S571.

Haq, S. H., Al-Ruwaished, G., Al-Mutlaq, M. A., Naji, S. A., Al-Mogren, M., Al-Rashed, S., Tul, A. Q., et al., (2019). Antioxidant, anticancer activity and phytochemical analysis of green algae, *Chaetomorpha* collected from the Arabian Gulf. *Sci. Rep., 9*, 18906.

Harke, M. J., Steffn, M. M., Gobler, C. J., Otten, T. G., Wilhelm, S. W., Wood, S. A., & Paerl, H. W., (2016). A review of the global ecology, genomics and biogeography of the toxic cyanobacterium, *Microcystis* spp. *Harmful Algae, 54*, 4–20.

Harnedy, P. A., & FitzGerald, R. J., (2013). Cardioprotective peptides from marine sources. *Curr. Protein Pept. Sci., 14,* 162–172.

Hellio, C., Pascal, B. J., Beaupoil, C., Le Gal, Y., & Bougougnon, N., (2002). Screening of marine algal extracts for anti-settlement activities against microalgae and macroalgae. *Biofouling, 18,* 205–215.

Heo, S. J., & Jeon, Y. J., (2009). Evaluation of diphlorethohydroxycarmalol isolated from *Ishige okamurae* for radical scavenging activity and its protective effect against H_2O_2-induced cell damage. *Process Biochem., 44,* 412–418.

Heo, S. J., Hwang, J. Y., Choi, J. I., Han, J. S., Kim, H. J., & Jeon, Y. J., (2009). Diphlorethohydroxycarmalol isolated from *Ishige okamurae*, a brown algae, a potent α-glucosidase and α-amylase inhibitor, alleviates postprandial hyperglycemia in diabetic mice. *Eur. J. Pharmacol., 615*, 252–256.

Holdt, S. L., & Kraan, S., (2011). Bioactive compounds in seaweed: Functional food applications and legislation. *J. Appl. Phycol., 23,* 543–597.

Hong, D. D., Hien, H. M., & Son, P. N., (2007). Seaweeds from Vietnam used for functional food, medicine and biofertilizer. *J. Appl. Phycol., 19,* 817–826.

Hsu, H. Y., Lin, T. Y., Lu, M. K., Leng, P. J., Tsao, S. M., & Wu, Y. C., (2017). Fucoidan induces Toll-like receptor 4-regulated reactive oxygen species and promotes endoplasmic reticulum stress-mediated apoptosis in lung cancer. *Sci. Rep., 7,* 44990.

Hu, D. J., Cheong, K. L., Zhao, J., & Li, S. P., (2013). Chromatography in characterization of polysaccharides from medicinal plants and fungi. *J. Sep. Sci., 36*, 1–19.

Ibraheem, B. M. I., Hamed, S. M., Abd, E. A. A., Farag, F. M., & Abdel-Raouf, N., (2017). Antimicrobial activities of some brown macroalgae against some soil borne plant pathogens and *in vivo* management of *Solanum melongena* root diseases. *Aust. J. Basic Appl. Sci., 11,* 157–168.

Jeong, J. H., Jin, H. J., Sohn, C. H., Suh, K. H., & Hong, Y. K., (2000). Algicidal activity of the seaweed *Corallina pilulifera* against red tide microalgae. *J. Appl. Phycol., 12,* 37–43.

Ji, R., Dong, G., Shi, W., & Min, J., (2017). Effects of liquid organic fertilizers on plant growth and rhizosphere soil characteristics of *Chrysanthemum*. *Sustainability, 9,* 841.

Jiao, G., Yu, G., Zhang, J., & Ewart, H. S., (2011). Chemical structures and bioactivities of sulfated polysaccharides from marine algae. *Marine Drugs, 9*, 196–223.

Jiménez, E., Dorta, F., Medina, C., Ramírez, A., Ramírez, I., & Peña-Cortés, H., (2011). Anti-phytopathogenic activities of macroalgae extracts. *Marine Drugs, 9*, 739–756.

Jormalainen, V., & Honkanen, T., (2008). Macroalgal chemical defenses and their roles in structuring temperate marine communities. In: Amsler, C. D., (ed.), *Algal Chemical Ecology* (pp. 57–90). Springer-Verlag, Berlin.

Jung, H. A., Jung, H. J., Jeong, H. Y., Kwon, H. J., Ali, M. Y., & Choi, J. S., (2014). Phlorotannins isolated from the edible brown alga *Ecklonia stolonifera* exert anti-adipogenic activity on 3T3 L1 adipocytes by downregulating C/EBP α and PPARγ. *Fitoterapia, 92,* 260–269.

Kamada, T., & Vairappan, C. S., (2015). New Laurene-type sesquiterpene from Bornean *Laurencia nangii*. *Nat. Prod. Commun., 10,* 843–844.

Kang, M. C., Ding, Y., Kim, E. A., Choi, Y. K., De Araujo, T., Heo, S. J., & Lee, S. H., (2017). Indole derivatives isolated from brown alga *Sargassum thunbergii* inhibit adipogenesis through AMPK activation in 3T3-L1 preadipocytes. *Marine Drugs, 15*, 119.

Kang, S. Y., Kim, E., Kang, I., Lee, M., & Lee, Y., (2018). Anti-diabetic effects and anti-inflammatory effects of *Laminaria japonica* and *Hizikia fusiforme* in skeletal muscle: *In vitro* and *in vivo* model. *Nutrients, 10,* 491.

Karkhane, Y. M., Seyed, H. M., Mashinchian, M. A., & Ghasempour, A. R., (2018). *In vitro* investigating of anticancer activity of focuxanthin from marine brown seaweed species. *Global J. Environ. Sci. Manage., 4,* 81–90.

Kendel, M., Wielgosz-Collin, G., Bertrand, S., Roussakis, C., Bourgougnon, N., & Bedoux, G., (2015). Lipid composition, fatty acids and sterols in the seaweeds *Ulva armoricana*, and

Solieria chordalis from Brittany (France): An analysis from nutritional, chemotaxonomic, and antiproliferative activity perspectives. *Marine Drugs, 13,* 5606–5628.

Khallil, A. M., Daghman, I. M., & Fady, A. A., (2015). Antifungal potential in crude extracts of five selected brown seaweeds collected from the western Libya coast. *J. Microbiol. Mod. Tech., 1,* 103.

Khan, F., Manivasagan, P., Lee, J. W., Pham, D. T. N., Oh, J., & Kim, Y. M., (2019). Fucoidan-stabilized gold nanoparticle-mediated biofilm inhibition, attenuation of virulence and motility properties in *Pseudomonas aeruginosa* PAO1. *Marine Drugs, 17*, 208.

Khan, W., Rayirath, U. P., Subramanian, S., Jithesh, M. N., Rayorath, P., Hodges, D. M., Critchley, A. T., et al., (2009). Seaweed extracts as biostimulants of plant growth and development. *J. Plant Growth Regul., 28,* 386–399.

Khelil-Radji, F., Belhouari, M. Y., Chemlal-Kherraz, D., Matallah-Boutiba, A., & Boutiba, Z., (2017). Antimicrobial activity of aqueous and ethanol extracts of two marine algae collected from Algerian west coast. *Int. J. Biosci., 10*, 217–222.

Kim, E., & Kwak, J., (2015). Antiviral phlorotannin from *Eisenia bicyclis* against human papilloma virus *in vitro*. *Planta Med., 81*.

Kim, M. S., Kim, J. Y., Choi, W. H., & Lee, S. S., (2008). Effects of seaweed supplementation on blood glucose concentration, lipid profile, and antioxidant enzyme activities in patients with type 2 diabetes mellitus. *Nutr. Res. Pract., 2,* 62–67.

Kim, S. M., Kang, S. W., Jeon, J. S., Jung, Y. J., Kim, W. R., Kim, C. Y., & Um, B. H., (2013). Determination of major phlorotannins in *Eisenia bicyclis* using hydrophilic interaction chromatography: Seasonal variation and extraction characteristics. *Food Chemistry, 138,* 2399–2406.

Kraan, S., (2012). Algal polysaccharides, novel applications and outlook. In: Chang, C. F., (ed.), *Carbohydrates – Comprehensive Studies on Glycobiology and Glycotechnology* (Vol. 22, pp. 489–532).

Krinsky, N. I., & Johnson, E. J., (2005). Carotenoid actions and their relation to health and disease. *Mol. Aspects Med., 26,* 459–516.

Kulkarni, M. G., Rengasamy, K. R. R., Pendota, S. C., Gruz, J., Plačková, L., Novák, O., Doležal, K., & Van, S. J., (2019). Bioactive molecules derived from smoke and seaweed *Ecklonia maxima* showing phytohormone-like activity in *Spinacia oleracea* L. *N. Biotechnol., 48,* 83–89.

Kumar, C. S., Raju, D., Sarada, V. L., & Rengasamy, R., (2008). Seaweed extracts control the leaf spot disease of the medicinal plant *Gymnema sylvestre*. *Indian J. Sci. Technol., 1,* 1–5.

Kumar, K. S., Ganesan, K., Selvaraj, K., & Rao, P. S., (2014). Studies on the functional properties of protein concentrate of *Kappaphycus alvarezii* (Doty) Doty – An edible seaweed. *Food Chemistry, 153,* 353–360.

Kumaresan, M., Vijai, A. K., Govindaraju, K., Tamilselvan, S., & Ganesh, K. V., (2018). Seaweed *Sargassum wightii* mediated preparation of zirconia (ZrO_2) nanoparticles and their antibacterial activity against gram positive and gram negative bacteria. *Microb. Pathog., 124,* 311–315.

Kumari, P., Kumar, M., Gupta, V., Reddy, C. R. K., & Jha, B., (2010). Tropical marine macroalgae as potential sources of nutritionally important PUFAs. *Food Chemistry, 120,* 749–757.

Lahaye, M., & Robic, A., (2007). Structure and functional properties of ulvan, a polysaccharide from green seaweeds. *Biomacromolecules, 8,* 1765–1774.

Lange, K. W., Hauser, J., Nakamura, Y., & Kanaya, S., (2015). Dietary seaweeds and obesity. *Food Sci. Human Wellness, 4,* 87–96.

Latique, S., Elouaer, M. A., Chernane, H., Hannachi, C., & Elkaoua, M., (2014). Effect of seaweed liquid extract of *Sargassum vulgare* on growth of durum wheat seedlings (*Triticum durum* L.) under salt stress. *Int. J. Innov. Appl. Stud., 7,* 1430–1435.

Layek, J., Das, A., Ramkrushna, G. I., Sarkar, D., Ghosh, A., Tukaram, Z. S., Lal, R., et al., (2018). Seaweed extract as organic bio-stimulant improves productivity and quality of rice in eastern Himalayas. *J. Appl. Phycol., 30,* 547–558.

Layek, J., Das, A., Ramkrushna, G. I., Trivedi, K., Yesuraj, D., Chandramohan, M., Kubavat, D., et al., (2015). Seaweed sap potential towards sustainable improvement of maize productivity: A dominant staple food crop of the North-east India. *Int. J. Environ. Stud., 72,* 305–315.

Leal, M. C., Munro, M. H. G., Blunt, J. W., Puga, J., Jesus, B., Calado, R., Rosa, R., & Madeira, C., (2013). Biogeography and biodiscovery hotspots of macroalgal marine natural products. *Nat. Prod. Rep., 30,* 1380–1390.

Lee, D. S., Kang, M. S., Hwang, H. J., Eom, S. H., Yang, J. Y., Lee, M. S., Lee, W. J., et al., (2008). Synergistic effect between dieckol from *Ecklonia stolonifera* and β-lactams against methicillin-resistant *Staphylococcus aureus*. *Biotechnol. Bioproc. Eng., 13,* 758–764.

Lee, H. G., Lu, Y. A., Li, X., Hyun, J. M., Kim, H. S., Lee, J. J., Kim, T. H., et al., (2020). Anti-obesity effects of *Grateloupia elliptica*, a Red Seaweed, in mice with high-fat diet-induced obesity via suppression of adipogenic factors in white adipose tissue and increased thermogenic factors in brown adipose tissue. *Nutrients, 12*, 308.

Lee, J. H., Jung, H. A., Kang, M. J., Choi, J. S., & Kim, G. D., (2017). Fucosterol, isolated from *Ecklonia stolonifera*, inhibits adipogenesis through modulation of FoxO1 pathway in 3T3-L1 adipocytes. *J. Pharm. Pharmacol., 69,* 325–333.

Lee, M. S., Shin, T., Utsuki, T., Choi, J. S., Byun, D. S., & Kim, H. R., (2012a). Isolation and identification of phlorotannins from *Ecklonia stolonifera* with antioxidant and hepatoprotective properties in tacrine-treated HepG2 cells. *J. Agric. Food Chem., 60,* 5340–5349.

Lee, R. E., (2008). *Phycology,* (4th edn., p. 560). Cambridge University Press: Cambridge, UK.

Lee, S. H., Choi, J. I., Heo, S. J., Park, M. H., Park, P. J., Jeon, B. T., Kim, S. K., et al., (2012b). Diphlorethohydroxycarmalol isolated from Pae (*Ishige okamurae*) protects high glucose-induced damage in RINm5F pancreatic β cells via its antioxidant effects. *Food Sci. Biotechnol., 21,* 239–246.

Lee, S. H., Choi, J. I., Heo, S. J., Park, M. H., Park, P. J., Jeon, B. T., Kim, S. K., et al., (2012c). Diphlorethohydroxycarmalol isolated from Pae (*Ishige okamurae*) protects high glucose-induced damage in RINm5F pancreatic β cells via its antioxidant effects. *Food Sci. Biotechnol., 21,* 239–246.

Lee, S., Lee, Y. S., Jung, S. H., Kang, S. S., & Shin, K. H., (2003). Anti-oxidant activities of fucosterol from the marine algae *Pelvetia siliquosa*. *Arch. Pharm. Res., 26,* 719–722.

Lehnhardt, P. C., Rodrigues, S. D., Bristot, D., Gaeta, H. H., De Oliveira, T. D., Lobo, F. W. R., & Toyama, M. H., (2013). Evaluation of macroalgae sulfated polysaccharides on the *Leishmania amazonensis* (L.) promastigote. *Marine Drugs, 11*, 934–943.

Li, H., Li, J., Tang, Y., Lin, L., Xie, Z., Zhou, J., Zhang, L., et al., (2017). Fucoidan from *Fucus vesiculosus* suppresses hepatitis B virus replication by enhancing extracellular signal-regulated Kinase activation. *Virology Journal, 14*, 178.

Li, Y. X., Wijesekara, I., Li, Y., & Kim, S. K., (2011). Phlorotannins as bioactive agents from brown algae. *Process Biochemistry, 46,* 2219–2224.

Liang, B. H., Hong, B. L., Jun, L. S., & Zeng, J., (2012). Effect of laminarin on *Aspergillus flavus* growth and aflatoxin production. *Adv. Mater. Res., 343, 344*, 1168–1171.

Lim, S. N., Cheung, P. C. K., Ooi, V. E. C., & Ang, P. O., (2002). Evaluation of antioxidative activity of extracts from a brown seaweed, *Sargassum siliquastrum*. *J. Agric. Food Chem., 50,* 3862–3866.

Lin, Y., Qi, X., Liu, H., Xue, K., Xu, S., & Tian, Z., (2020). The anti-cancer effects of fucoidan: A review of both *in vivo* and *in vitro* investigations. *Cancer Cell International., 20,* 154.

Liu, H., Chen, X., Song, L., Li, K., Zhang, X., Liu, S., Qin, Y., & Li, P., (2019). Polysaccharides from *Grateloupia filicina* enhance tolerance of rice seeds (*Oryza sativa* L.) under salt stress. *Int. J. Biol. Macromol., 124,* 1197–1204.

Liu, M., Li, W., Chen, Y., Wan, X., & Wang, J., (2020). Fucoxanthin: A promising compound for human inflammation-related diseases. *Life Sciences, 255,* 117850.

Liu, M., Wang, G., Xiao, L., Xu, A., Liu, X., Xu, P., & Lin, X., (2014). Bis (2,3-dibromo-4,5 dihydroxybenzyl) ether, a marine algae derived bromophenol, inhibits the growth of *Botrytis cinerea* and interacts with DNA molecules. *Marine Drugs, 12,* 3838–3851.

Lopes, G., Andrade, P. B., & Valentão, P., (2016). Phlorotannins: Towards new pharmacological interventions for diabetes mellitus type 2. *Molecules, 22,* 56.

Lopes, G., Pinto, E., Andrade, P. B., & Valentão, P., (2013). Antifungal activity of phlorotannins against dermatophytes and yeasts: Approaches to the mechanism of action and influence on *Candida albicans* virulence factor. *PLoS One, 8*(8), e72203.

Lordan, S., Ross, R. P., & Stanton, C., (2011). Marine bioactives as functional food ingredients: Potential to reduce the incidence of chronic diseases. *Marine Drugs, 9,* 1056–1100.

Lu, Y. A., Lee, H. G., Li, X., Hyun, J. M., Kim, H. S., Kim, T. H., Kim, H. M., et al., (2020). Anti-obesity effects of Red Seaweed, *Plocamium telfairiae*, in C57BL/6 mice fed a high-fat diet. *Food and Function, 11*, 2299–2308.

Machu, L., Misurcova, L., Vavra, A. J., Orsavova, J., Mlcek, J., Sochor, J., & Jurikova, T., (2015). Phenolic content and antioxidant capacity in algal food products. *Molecules, 20,* 1118–1133.

Mahmoud, S. H., Salama, D. M., El-Tanahy, A. M. M., & El-Samad, E. H. A., (2019). Utilization of seaweed (*Sargassum vulgare*) extract to enhance growth, yield and nutritional quality of red radish plants. *Annals of Agricultural Sciences, 64*, 167–175.

Mak, W., Wang, S. K., Liu, T., Hamid, N., Li, Y., Lu, J., & White, W. L., (2014). Anti-proliferation potential and content of fucoidan extracted from sporophyll of New Zealand *Undaria pinnatifida*. *Front. Nutr., 1,* 9.

Mamelona, J., Pelletier, É., Girard-Lalancette, K., Legault, J., Karboune, S., & Kermasha, S., (2007). Quantification of phenolic contents and antioxidant capacity of Atlantic sea cucumber, *Cucumaria frondosa*. *Food Chem., 104*, 1040–1047.

Manilal, A., Sujith, S., Seghal, K. G., Selvin, J., & Panikkar, M. V. N., (2011). Evaluation of seaweed bioactives on common aquatic floral and faunal weeds of shrimp ponds. *Thalassas, 27,* 47–56.

Mannino, A. M., Vaglica, V., Cammarata, M., & Oddo, E., (2016). Effects of temperature on total phenolic compounds in *Cystoseira amentacea* (C. Agardh). Bory. (Fucales, Phaeophyceae) from southern Mediterranean Sea. *Plant. Biosyst., 150,* 152–160.

Marinho, G. S., Holdt, S. L., & Angelidaki, I., (2015). Seasonal variations in the amino acid profile and protein nutritional value of *Saccharina latissima* cultivated in a commercial IMTA system. *J. Appl. Phycol., 27*, 1991–2000.

Martínez, J. H. I., & Castañeda, H. G. T., (2013). Preparation and chromatographic analysis of phlorotannins. *J. Chromatogr. Sci., 51*, 825–838.

Mattner, S. W., Milinkovic, M., & Arioli, T., (2018). Increased growth response of strawberry roots to a commercial extract from *Durvillaea potatorum* and *Ascophyllum nodosum*. *J. Appl. Phycol., 30,* 2943–2951.

Mayer, A. M. S., Guerrero, A. J., Rodríguez, A. D., Taglialatela-Scafati, O., Nakamura, F., & Fusetani, N., (2020). Marine pharmacology in 2014–2015: Marine compounds with antibacterial, antidiabetic, antifungal, anti-inflammatory, antiprotozoal, antituberculosis, antiviral, and anthelmintic activities; affecting the immune and nervous systems, and other miscellaneous mechanisms of action. *Marine Drugs, 18*, 5.

Mei, C. H., Zhou, S. C., Zhu, L., Ming, J. X., Zeng, F. D., & Xu, R., (2017). Antitumor effects of *Laminaria* extract fucoxanthin on lung cancer. *Marine Drugs, 15*, 39.

Michalak, I., & Chojnacka, K., (2016). The potential usefulness of a new generation of agro-products based on raw materials of biological origin. *Acta. Sci. Pol. Hortorum Cultus., 15*, 97–120.

Michalak, I., Chojnacka, K., & Saeid, A., (2017). Plant growth biostimulants, dietary feed supplements and cosmetics formulated with supercritical CO_2 algal extracts. *Molecules, 22*, 66.

Milledge, J. J., Nielsen, B. V., & Bailey, D., (2016). High-value products from macroalgae: The potential uses of the invasive brown seaweed, *Sargassum muticum*. *Reviews in Environmental Science and Bio/Technology, 15*, 67–88.

Min, K. H., Kim, H. J., Jeon, Y. J., & Han, J. S., (2011). *Ishige okamurae* ameliorates hyperglycemia and insulin resistance in C57BL/KsJ-db/db mice. *Diabetes Res. Clin. Pr., 93,* 70–76.

Mishra, A. K., (2018). *Sargassum*, *Gracilaria* and *Ulva* exhibit positive antimicrobial activity against human pathogens. *OALib., 5,* 1–11.

Mishra, J. K., Srinivas, T., & Sawhney, S., (2016). Antibacterial activity of seaweed *Halimeda opuntia* from the coasts of South Andaman. *Glob. J. Biosci. Biotechnol., 5,* 345–348.

Miyashita, K., Beppu, F., Hosokawa, M., Liu, X., & Wang S., (2020). Nutraceutical characteristics of the brown seaweed carotenoid fucoxanthin. *Archives of Biochemistry and Biophysics, 686*, 108364.

Miyashita, K., Mikami, N., & Hosokawa, M., (2013). Chemical and nutritional characteristics of brown seaweed lipids: A review. *J. Funct. Foods, 5,* 1507–1517.

Mohamed, S. S., & Saber, A. A., (2019). Antifungal potential of the bioactive constituents in extracts of the mostly untapped brown seaweed *Hormophysa cuneiformis* from the Egyptian coastal waters. *Egypt. J. Bot., 59*, 695–708.

Mohamed, S., Hashim, S. N., & Abdul, R. H., (2012). Seaweeds: A sustainable functional food for complementary and alternative therapy. *Trends Food Sci. Technol., 23,* 83–96.

Montero, L., Sánchez-Camargo, A. D. P., Ibáñez, E., & Gilbert-López, B., (2018). Phenolic compounds from edible algae: Bioactivity and health benefits. *Current Medicinal Chemistry, 25,* 4808–4826.

Montero, L., Sánchez-Camargo, A. P., García-Cañas, V., Tanniou, A., Stiger-Pouvreau, V., Russo, M., Rastrelli, L., et al., (2016). Anti-proliferative activity and chemical characterization by comprehensive two-dimensional liquid chromatography coupled to mass spectrometry of phlorotannins from the brown macroalga *Sargassum muticum* collected on North-Atlantic coasts. *J. Chromatogr. A, 1428*, 115–125.

Morán-Santibañez, K., Peña-Hernández, M. A., Cruz-Suárez, L. E., Ricque-Marie, D., Skouta, R., Vasquez, A. H., Rodríguez-Padilla, C., & Trejo-Avila, L. M., (2018). Virucidal and synergistic activity of polyphenol-rich extracts of seaweeds against Measles virus. *Viruses, 10,* 465.

Moubayed, N. M. S., Al Houri, H. J., Al Khulaifi, M. M., & Al Farraj, D. A., (2017). Antimicrobial, antioxidant properties and chemical composition of seaweeds collected from Saudi Arabia (Red Sea and Arabian Gulf). *Saudi J. Biol. Sci., 24,* 162–169.

Muñoz, J., Culioli, G., & Köck, M., (2013). Linear diterpenes from the marine brown alga *Bifurcaria bifurcata*: A chemical perspective. *Phytochem. Rev., 12,* 407–424.

Murata, M., & Nakazoe, J., (2001). Production and use of marine algae in Japan. *Japan Agricultural Research Quarterly, 35*, 281–290.

Murugan, K., Panneerselvam, C., Subramaniam, J., Madhiyazhagan, P., Hwang, J. S., Wang, L., Dinesh, D., et al., (2016). Eco-friendly drugs from the marine environment: Spongeweed-synthesized silver nanoparticles are highly effective on *Plasmodium falciparum* and its vector *Anopheles stephensi,* with little non-target effects on predatory copepods. *Environ Sci. Pollut. Res. Int., 23*, 16671–16685.

Murugan, K., Roni, M., Panneerselvam, C., Aziz, A. T., Suresh, U., Rajaganesh, R., Aruliah, R., et al., (2018). *Sargassum wightii* – synthesized ZnO nanoparticles reduce the fitness and reproduction of the malaria vector *Anopheles stephensi* and cotton bollworm *Helicoverpa armigera*. *Physiological and Molecular Plant Pathology, 101*, 202–213.

Mwangi, M. H., Njue, W. E., Onani, M. O., Thovhoghi, N., & Mabusela, W. T., (2017). Phlorotannins and a sterol isolated from a brown alga *Ecklonia maxima*, and their cytotoxic activity against selected cancer cell lines HeLa, H157 and MCF7. *Interdisciplinary Journal of Chemistry, 2,* 1–6.

Nakai, S., Inoue, Y., Hosomi, M., & Murakami, A., (2000). *Myriophyllum spicatum*-released allelopathic polyphenols inhibiting growth of blue-green algae *Microcystis aeruginosa*. *Water Res., 34,* 3026–3032.

Nakajima, N., Sugimoto, N., Ohki, K., & Kamiya, M., (2016). Diversity of phlorotannin profiles among sargassasacean species affecting variation and abundance of epiphytes. *Eur. J. Phycol., 51,* 307–316.

Namvar, F., Mohamed, S., Fard, S. G., Behravan, J., Mustapha, N. M., Alitheen, N. B. M., & Othman, F., (2012). Polyphenol-rich seaweed (*Eucheuma cottonii*) extract suppresses breast tumor via hormone modulation and apoptosis induction. *Food Chem., 130,* 376–382.

Narayani, S. S., Saravanan, S., Ravindran, J., Ramasamy, M. S., & Chitra, J., (2019). *In vitro* anticancer activity of fucoidan extracted from *Sargassum cinereum* against Caco-2 cells. *Int. J. Biol. Macromol., 1*, 618–628.

Nwosu, F., Morris, J., Lund, V. A., Stewart, D., Ross, H. A., & McDougall, G. J., (2011). Anti-proliferative and potential anti-diabetic effects of phenolic-rich extracts from edible marine algae. *Food Chem., 126,* 1006–1012.

Nylund, G. M., Enge, S., & Pavia, H., (2013). Costs and benefits of chemical defense in the red alga *Bonnemaisonia hamifera*. *PLoS One, 8*(4), e61291.

O'Sullivan, L., Murphy, B., McLoughlin, P., Duggan, P., Lawlor, P. G., Hughes, H., & Gardiner, G. E., (2010). Prebiotics from marine macroalgae for human and animal health applications. *Marine Drugs, 8,* 2038–2064.

Ojulari, O. V., Lee, S. G., & Nam, J. O., (2020). Therapeutic effect of seaweed derived xanthophyl carotenoid on obesity management: Overview of the last decade. *Int. J. Mol. Sci., 21*, 2502.

Onet, A., Dincua, L. C., Grenni, P., Laslo, V., Teusdea, A. C., Vasile, D. L., Enescu, R. E., & Crisan, V. E., (2019). Biological indicators for evaluating soil quality improvement in a soil degraded by erosion processes. *J. Soils Sediments, 19,* 2393–2404.

Ooi, V. E., & Liu, F., (2000). Immunomodulation and anti-cancer activity of polysaccharide-protein complexes. *Curr. Med. Chem., 7*, 715–729.

Pádua, D., Rocha, E., Gargiulo, D., & Ramos, A. A., (2015). Bioactive compounds from brown seaweeds: Phloroglucinol, fucoxanthin and fucoidan as promising therapeutic agents against breast cancer. *Phytochem. Lett., 14,* 91–98.

Paerl, H. W., & Huisman, J., (2008). Climate: Blooms like it hot. *Science, 320,* 57–58.

Paniagua-Michel, J. D. J., Olmos-Soto, J., & Morales-Guerrero, E. R., (2014). Algal and microbial exopolysaccharides: New insights as biosurfactants and bioemulsifiers. In: Kim, S. K., (ed.), *Advances in Food and Nutrition Research* (pp. 221–257). Academic Press, San Diego, California, USA.

Papenfus, H. B., Stirk, W. A., Finnie, J. F., & Van, S. J., (2012). Seasonal variation in the polyamines of *Ecklonia maxima*. *Bot. Mar., 55,* 539–546.

Paradas, W. C., Salgado, L. T., Pereira, R. C., Hellio, C., Atella, G. C., De Lima, M. D., Do Carmo, A. P. B., et al., (2016). A novel antifouling defense strategy from Red Seaweed: Exocytosis and deposition of fatty acid derivatives at the cell wall surface. *Plant Cell Physiol., 57,* 1008–1019.

Pardo-Vargas, A., De Barcelos, O. I., Stephens, P. R., Cirne-Santos, C. C., De Palmer, P. I. C., Ramos, F. A., Jiménez, C., et al., (2014). Dolabelladienols A-C, new diterpenes isolated from Brazilian brown alga *Dictyota pfaffii*. *Marine Drugs, 12,* 4247–4259.

Park, H. S., Hwang, H. J., Kim, G. Y., Cha, H. J., Kim, W. J., Kim, N. D., Yoo, Y. H., & Choi, Y. H., (2013). Induction of apoptosis by fucoidan in human leukemia U937 cells through activation of p38 MAPK and modulation of Bcl-2 family. *Marine Drugs, 11*, 2347–2364.

Park, H. Y., Han, M. H., Park, C., Jin, C. Y., Kim, G. Y., Choi, I. W., Kim, N. D., et al., (2011). Anti-inflammatory effects of fucoidan through inhibition of NF-IB, MAPK and Akt activation in lipopolysaccharide-induced BV2 microglia cells. *Food and Chemical Toxicology, 49*, 1745–1752.

Parys, S., Rosenbaum, A., Kehraus, S., Reher, G., Glombitza, K. W., & König, G. M., (2007). Evaluation of quantitative methods for the determination of polyphenols in algal extracts. *J. Nat. Prod., 70,* 1865–1870.

Peng, J., Yuan, J. P., Wu, C. F., & Wang, J. H., (2011). Fucoxanthin, a marine carotenoid present in brown seaweeds and diatoms: Metabolism and bioactivities relevant to human health. *Marine Drugs, 9*, 1806–1828.

Pereira, U. A., Barbosa, L. C., Maltha, C. R., Demuner, A. J., Masood, M. A., & Pimenta, A. L., (2014). Gamma-alkylidene-gamma-lactones and isobutylpyrrol-2(5H)-ones analogues to rubrolides as inhibitors of biofilm formation by gram-positive and gram-negative bacteria. *Bioorg. Med. Chem. Lett., 24,* 1052–1056.

Peres, J. C. F., De Carvalho, L. R., Goncalez, E., Berian, L. O. S., & Felicio, J. D., (2012). Evaluation of antifungal activity of seaweed extracts. *Cienc. Agrotec., 36*, 294–299.

Pérez, M. J., Falqué, E., & Domínguez, H., (2016). Antimicrobial action of compounds from marine seaweed. *Marine Drugs, 14*, 52.

Pettongkhao, S., Bilanglod, A., Khompatara, K., & Churngchow, N., (2019). Sulfated polysaccharide from *Acanthophora spicifera* induced *Hevea brasiliensis* defense responses against *Phytophthora palmivora* infection. *Plants, 8,* 73.

Pinteus, S., Silva, J., Alves, C., Horta, A., Fino, N., Rodrigues, A. I., Mendes, S., & Pedrosa, R., (2017). Cytoprotective effect of seaweeds with high antioxidant activity from the Peniche coast (Portugal). *Food Chem., 218,* 591–599.

Ponce, N. M. A., Flores, M. L., Pujol, C. A., Becerra, M. B., Navarro, D. A., Córdoba, O., Damonte, E. B., & Stortz, C. A., (2019). Fucoidans from the phaeophyta *Scytosiphon lomentaria*: Chemical analysis and antiviral activity of the galactofucan component. *Carbohydrate Research, 478,* 18–24.

Praveen, A. M., Parvathy, K. R. K., Patra, S., Khan, I., Natarajan, P., & Balasubramanian, P., (2020). Cytotoxic and pharmacokinetic studies of Indian seaweed polysaccharides for formulating raindrop synbiotic candy. *Int. J. Biol. Macromol., 154,* 557–566.

Rai, A., Cherif, A., Cruz, C., & Nabti, E., (2018). Extracts from seaweeds and *Opuntia ficus-indica* cladodes enhance diazotrophic-PGPR halotolerance, their enzymatic potential, and their impact on wheat germination under salt stress. *Pedosphere, 28,* 241–254.

Rajesh, S., Asha, A., Kombiah, P., & Sahayaraj, K., (2011). Biocidal activity of algal seaweeds on insect pest and fungal plant pathogen. *Proceedings of the National Seminar on Harmful/ Beneficial Insects of Agricultural Importance with Special Reference to the Nuisance Pest Luprops tristis in Rubber Plantations,* 86–91.

Rajivgandhi, G. N., Ramachandran, G., Maruthupandy, M., Manoharan, N., Alharbi, N. S., Kadaikunnan, S., Khaled, J. M., et al., (2020). Anti-oxidant, anti-bacterial and anti-biofilm activity of biosynthesized silver nanoparticles using *Gracilaria corticata* against biofilm producing *K. pneumoniae. Colloids and Surfaces A: Physicochemical and Engineering Aspects, 600,* 124830.

Ramaswamy, V., Cresence, V. M., Rejitha, J. S., Lekshmi, M. U., Dharsana, K. S., Prasad, S. P., & Vijila, H. M., (2007). *Listeria* – review of epidemiology and pathogenesis. *J. Microbiol. Immunol. Infect., 40,* 4–13.

Rathore, S. S., Chaudhary, D. R., Boricha, G. N., Ghosh, A., Bhatt, B. P., Zodape, S. T., & Patolia, J. S., (2009). Effect of seaweed extract on the growth, yield and nutrient uptake of soybean (*Glycine max*) under rainfed conditions. *S. Afr. J. Bot., 75,* 351–355.

Rengasamy, K. R., Kulkarni, M. G., Stirk, W. A., & Van, S. J., (2015a). Eckol – a new plant growth stimulant from the brown seaweed *Ecklonia maxima*. *J. Appl. Phycol., 27,* 581–587.

Rengasamy, K. R., Kulkarni, M. G., Stirk, W. A., & Van, S. J., (2014). Advances in algal drug research with emphasis on enzyme inhibitors. *Biotechnol. Adv., 32,* 1364–1381.

Rengasamy, K. R., Kulkarni, M. G., Stirk, W. A., & Van, S. J., (2015b). Eckol improves growth, enzyme activities, and secondary metabolite content in maize (*Zea mays* cv. Border King). *J. Plant Growth Regul., 34,* 410–416.

Riad, N., Zahi, M. R., Trovato, E., Bouzidi, N., Daghbouche, Y., Utczás, M., Mondello, L., & El Hattab, M., (2020). Chemical screening and antibacterial activity of essential oil and volatile fraction of *Dictyopteris polypodioides*. *Microchemical Journal, 152,* 104415.

Roberts, L., (2020). Global polio eradication falters in the final stretch. *Science, 367*, 14, 15.

Rodrigues, D., Alves, C., Horta, A., Pinteus, S., Silva, J., Culioli, G., Thomas, O. P., & Pedrosa, R., (2015b). Antitumor and antimicrobial potential of bromoditerpenes isolated from the red alga *Sphaerococcus coronopifolius*. *Marine Drugs, 13,* 713–726.

Rodrigues, D., Freitas, A. C., Pereira, L., Rocha-Santos, T. A., Vasconcelos, M. W., Roriz, M., Rodríguez-Alcalá, L. M., et al., (2015a). Chemical composition of red, brown and green macroalgae from Buarcos bay in central west coast of Portugal. *Food Chemistry, 183,* 197–207.

Rodriguez-Amaya, D. B., (2016). Natural food pigments and colorants. *Curr. Opin. Food Sci., 7,* 20–26.

Rosa, G. P., Tavares, W. R., Sousa, P. M. C., Pagès, A. K., Seca, A. M. L., & Pinto, D. C. G. A., (2020). Seaweed secondary metabolites with beneficial health effects: An overview of successes *in vivo* studies and clinical trials. *Marine Drugs, 18*, 8.

Rosaline, X. D., Sakthivelkumar, S., Rajendran, K., & Janarthanan, S., (2012). Screening of selected marine algae from the coastal Tamil Nadu, South India for antibacterial activity. *Asian Pacific Journal Tropical of Biomedicine, 2*, S140–S146.

Roseline, T. A., Murugan, M., Sudhakar, M. P., & Arunkumar, K., (2019). Nanopesticidal potential of silver nanocomposites synthesized from the aqueous extracts of Red Seaweeds. *Environmental Technology and Innovation, 13,* 82–93.

Rouphael, Y., De Micco, V., Arena, C., Raimondi, G., Colla, G., & De Pascale, S., (2017). Effect of *Ecklonia maxima* seaweed extract on yield, mineral composition, gas exchange, and leaf anatomy of zucchini squash grown under saline conditions. *J. Appl. Phycol., 29,* 459–470.

Rupérez, P., Gómez-Ordòñez, E., & Jiménez-Escrig, A., (2013). Biological activity of algal sulfated and non-sulfated polysaccharides. In: Hernandez-Ledesma, B., & Herrero, M., (eds.), *Bioactive Compounds from Marine Foods: Plant and Animal Sources* (pp. 219–247). John Wiley and Sons.

Saha, M., Goecke, F., & Bhadury, P., (2018). Algal natural compounds and extracts as antifoulants. *J. Appl. Phycol., 30,* 1859–1874.

Saha, M., Rempt, M., Gebser, B., Grueneberg, J., Pohnert, G., & Weinberger, F., (2012). Biofouling dimethylsulphopropionate (DMSP) and proline from the surface of the brown alga *Fucus vesiculosus* inhibit bacterial attachment. *Biofouling, 28,* 593–604.

Sahayaraj, K., Rajesh, S., Asha, A., & Rathi, J. M., (2012). Marine algae for the cotton pest and disease management. *Proceedings of International Conference on Agricultural Science and Engineering, Nigeria, 1,* 49–62.

Samarakoon, K., & Jeon, Y. J., (2012). Bio-functionalities of proteins derived from marine algae: A review. *Food Res. Int., 48,* 948–960.

Sangha, J. S., Khan, W., Ji, X., Zhang, J., Mills, A. A. S., Critchley, A. T., & Prithiviraj, B., (2011). Carrageenans, sulfated polysaccharides of Red Seaweeds, differentially affect *Arabidopsis thaliana* resistance to *Trichoplusia ni* (Cabbage Looper). *PLoS One, 6,* e26834.

Sanjeewa, K. K. A., Kim, E. A., Son, K. T., & Jeon, Y. J., (2016). Bioactive properties and potentials cosmeceutical applications of phlorotannins isolated from brown seaweeds: A review. *J. Photochem. Photobiol. B Biol., 162,* 100–105.

Sanniyasi, E., Venkatasubramanian, G., Anbalagan, M. M., Raj, P. P., & Gopal, R. K., (2019). *In vitro* anti-HIV-1 activity of the bioactive compound extracted and purified from two different marine macroalgae (seaweeds) (*Dictyota bartayesiana* J.V.Lamouroux and *Turbinaria decurrens* Bory). *Scientific Reports, 9,* 12185.

Sathya, R., Kanaga, N., Sankar, P., & Jeeva, S., (2017). Antioxidant properties of phlorotannins from brown seaweed *Cystoseira trinodis* (Forsskal) C. Agardh. *Arabian Journal of Chemistry, 10*(Suppl 2), S2608–S2614.

Schmidt, R. E., Ervin, E. H., & Zhang, X., (2003). Questions and answers about biostimulants. *Golf Course Manag., 71,* 91–94.

Schrader, K. K., (2003). *Natural Algicides for the Control of Cyanobacterial-Related Off-Flavor in Catfish Aquaculture.* American Chemical Society: Washington, DC, USA.

Seca, A., & Pinto, D., (2018). Overview on the antihypertensive and anti-obesity effects of secondary metabolites from seaweeds. *Marine Drugs, 16*, 237.

Senthilkumar, K., Manivasagan, P., Venkatesan, J., & Kim, S. K., (2013). Brown seaweed fucoidan: Biological activity and apoptosis, growth signaling mechanism in cancer. *Int. J. Biol. Macromol., 60,* 366–374.

Senthilkumar, K., Ramajayam, G., Venkatesan, J., Kim, S. K., & Ahn, B. C., (2017). Biomedical applications of fucoidan, seaweed polysaccharides. In: *Seaweed Polysaccharides* (pp. 269–281).

Shah, M. T., Zodape, S. T., Chaudhary, D. R., Eswaran, K., & Chikara, J., (2013). Seaweed sap as an alternative liquid fertilizer for yield and quality improvement of wheat. *J. Plant Nutr., 36,* 192–200.

Sharma, B. R., Kim, H. J., Kim, M. S., Park, C. M., & Rhyu, D. Y., (2017). *Caulerpa okamurae* extract inhibits adipogenesis in 3T3-L1 adipocytes and prevents high-fat diet-induced obesity in C57BL/6 mice. *Nutrition Research, 47,* 44–52.

Sharma, S., Chen, C., Khatri, K., Rathore, M. S., & Pandey, S. P., (2019). *Gracilaria dura* extract confers drought tolerance in wheat by modulating abscisic acid homeostasis. *Plant Physiol. Biochem., 136,* 143–154.

Shi, Q., Wang, A., Lu, Z., Qin, C., Hu, J., & Yin, J., (2017). Overview on the antiviral activities and mechanisms of marine polysaccharides from seaweeds. *Carbohydr. Res., 453, 454*, 1–9.

Shukla, P. S., Shotton, K., Norman, E., Neily, W., Critchley, A. T., & Prithiviraj, B., (2018). Seaweed extract improve drought tolerance of soybean by regulating stress-response genes. *AoB Plants, 10*(1), plx051.

Silva, L. D., Bahcevandziev, K., & Pereira, L., (2019). Production of bio-fertilizer from *Ascophyllum nodosum* and *Sargassum muticum* (Phaeophyceae). *Journal of Oceanology and Limnology, 37*, 918–927.

Sim, S. Y., Shin, Y. E., & Kim, H. K., (2019). Fucoidan from *Undaria pinnatifida* has anti-diabetic effects by stimulation of glucose uptake and reduction of basal lipolysis in 3T3-L1 adipocytes. *Nutrition Research, 65,* 54–62.

Souza, B. W., Cerqueira, M. A., Martins, J. T., Quintas, M. A., Ferreira, A. C., Teixeira, J. A., & Vicente, A. A., (2011). Antioxidant potential of two Red Seaweeds from the Brazilian coasts. *J. Agric. Food Chem., 59,* 5589–5594.

Stadnik, M. J., & Freitas, M. B., (2014). Algal polysaccharides as source of plant resistance inducers. *Trop. Plant Pathol., 39,* 111–118.

Steevensz, A. J., MacKinnon, S. L., Hankinson, R., Craft, C., Connan, S., Stengel, D. B., & Melanson, J. E., (2012). Profiling phlorotannins in brown macroalgae by liquid chromatography high resolution mass spectrometry. *Phytochem. Anal., 23*, 547–553.

Stirk, W. A., Tarkowská, D., Turečová, V., Strnad, M., & Van, S. J., (2014). Abscisic acid, gibberellins and brassinosteroids in Kelpak, a commercial seaweed extract made from *Ecklonia maxima*. *J. Appl. Phycol., 26,* 561–567.

Sudatti, D. B., Fujii, M. T., Rodrigues, S. V., Turra, A., & Pereira, R. C., (2018). Prompt induction of chemical defenses in the Red Seaweed *Laurencia dendroidea*: The role of herbivory and epibiosis. *J. Sea Res., 138,* 48–55.

Suganya, A. M., Sanjivkumar, M., Chandran, M. N., Palavesam, A., & Immanuel, G., (2016). Pharmacological importance of sulfated polysaccharide carrageenan from Red

Seaweed *Kappaphycus alvarezii* in comparison with commercial carrageenan. *Biomed. Pharmacother., 84,* 1300–1312.

Suganya, S., Ishwarya, R., Jayakumar, R., Govindarajan, M., Alharbi, N. S., Kadaikunnan, S., Khaled, J. M., et al., (2019). New insecticides and antimicrobials derived from *Sargassum wightii* and *Halimeda gracillis* seaweeds: Toxicity against mosquito vectors and antibiofilm activity against microbial pathogens. *South African Journal of Botany, 125,* 466–480.

Sugiura, Y., Usui, M., Katsuzaki, H., Imai, K., Kakinuma, M., Amano, H., & Miyata, M., (2018). Orally administered phlorotannins from *Eisenia arborea* suppress chemical mediator release and cyclooxygenase-2 signaling to alleviate mouse ear swelling. *Marine Drugs, 16*, 267.

Sujitha, V., Murugan, K., Dinesh, D., Pandiyan, A., Aruliah, R., Hwang, J. S., Kalimuthu, K., et al., (2017). Green-synthesized CdS nano-pesticides: Toxicity on young instars of malaria vectors and impact on enzymatic activities of the non-target mud crab *Scylla serrata. Aquatic Toxicology, 188,* 100–108.

Sun, Y. Y., Xing, J. Z., Zhang, J. S., Zhou, W. J., & Pu, Y. F., (2018a). Sesquiterpenoids with antialgal activity against the common red tide microalgae from marine macroalga *Porphyra yezoensis*. *Environ. Sci. Pollut. Res., 25*, 7844–7859.

Sun, Y., Dong, S., Zhou, W., Guo, L., Guo, G. L., & Zhang, X., (2019). A comprehensive review of secondary metabolites with antialgal activity from marine macroalgae against red tide microalgae. *J. Coast. Res., 93*(S1), 475–488.

Sun, Y., Wang, H., Guo, G., Pu, Y., Yan, B., & Wang, C., (2016). Isolation, purification, and identification of antialgal substances in green alga *Ulva prolifera* for antialgal activity against the common harmful red tide microalgae. *Environ. Sci. Pollut. Res., 23,* 1449–1459.

Sun, Y., Zhou, W., Wang, H., Guo, G., Sua, Z., & Pu, Y., (2018b). Antialgal compounds with antialgal activity against the common red tide microalgae from a green algae *Ulva pertusa*. *Ecotoxicology and Environmental Safety, 157,* 61–66.

Susanto, E., Fahmi, A. S., Hosokawa, M., & Miyashita, K., (2019). Variation in lipid components from 15 species of tropical and temperate seaweeds. *Marine Drugs, 17*, 630.

Suutari, M., Majaneva, M., Fewer, D. P., Voirin, B., Aiello, A., Friedl, T., Chiarello, A. G., & Blomster, J., (2010). Molecular evidence for a diverse green algal community growing in the hair of sloths and a specific association with *Trichophilus welckeri* (Chlorophyta, Ulvophyceae). *BMC Evolutionary Biology, 10*, 86.

Tabarsa, M., Rezaei, M., Ramezanpour, Z., & Waaland, J. R., (2012). Chemical compositions of the marine algae *Gracilaria salicornia* (Rhodophyta) and *Ulva lactuca* (Chlorophyta) as a potential food source. *J. Sci. Food Agric., 92,* 2500–2506.

Tanna, B., & Mishra, A., (2019). Nutraceutical potential of seaweed polysaccharides: Structure, bioactivity, safety, and toxicity. *Compr. Rev. Food Sci. Food Saf., 18,* 817–831.

Tanna, B., Choudhary, B., & Mishra, A., (2018). Metabolite profiling, antioxidant, scavenging and anti-proliferative activities of selected tropical green seaweeds reveal the nutraceutical potential of *Caulerpa* spp. *Algal Research, 36*, 96–105.

Tapiero, H., Townsend, D. M., & Tew, K. D., (2004). The role of carotenoids in the prevention of human pathologies. *Biomed. Pharmacother., 58,* 100–110.

Torres, M. D., Flórez-Fernández, N., & Domínguez, H., (2019). Integral utilization of Red Seaweed for bioactive production. *Marine Drugs, 19,* 314.

Umavandhana, R., & Jayanthi, S., (2018). Phytochemical screening and free radical scavenging activity on some selected seaweeds from Gulf of Mannar, India. *Res. J. Pharm. Tech., 11*, 3385–3388.

Umezawa, T., Oguri, Y., Matsuura, H., Yamazaki, S., Suzuki, M., Yoshimura, E., Furuta, T., et al., (2014). Omaezallene from red alga *Laurencia* sp.: Structure elucidation, total synthesis, and antifouling activity. *Angew. Chem. Int. Ed., 53*, 3909–3912.

Vaikundamoorthy, R., Krishnamoorthy, V., Vilwanathan, R., & Rajendran, R., (2018). Structural characterization and anticancer activity (MCF7 and MDA-MB-231) of polysaccharides fractionated from brown seaweed *Sargassum wightii*. *Int. J. Biol. Macromol., 111,* 1229–1237.

Vasantharaja, R., Abraham, L. S., Inbakandan, R. D., Thirugnanasambandam, R., Senthilvelana, T., Ayesha, J. S. K., & Prakash, P., (2019). Influence of seaweed extracts on growth, phytochemical contents and antioxidant capacity of cowpea (*Vigna unguiculata* L. Walp). *Biocatalysis and Agricultural Biotechnology, 17*, 589–594.

Venkatesan, M., Arumugam, V., Pugalendi, R., Ramachandran, K., Sengodan, K., Vijayan, S. R., Sundaresan, U., et al., (2019). Antioxidant, anticoagulant and mosquitocidal properties of water soluble polysaccharides (WSPs) from Indian seaweeds. *Process Biochemistry, 84,* 196–204.

Vera, J., Castro, J., Gonzalez, A., & Moenne, A., (2011). Seaweed polysaccharides and derived oligosaccharides stimulate defense responses and protection against pathogens in plants. *Marine Drugs, 9,* 2514–2525.

Vishchuk, O. S., Ermakova, S. P., & Zvyagintseva, T. N., (2011). Sulfated polysaccharides from brown seaweeds *Saccharina japonica* and *Undaria pinnatifida*: Isolation, structural characteristics, and antitumor activity. *Carbohydr. Res., 346,* 2769–2776.

Vishchuk, O. S., Ermakova, S. P., & Zvyagintseva, T. N., (2013). The fucoidans from brown algae of Far-Eastern seas: Anti-tumor activity and structure-function relationship. *Food Chem., 141*, 1211–1217.

Wahl, M., (1989). Marine epibiosis. I. Fouling and antifouling: Some basic aspects. *Mar. Ecol. Prog. Ser., 58,* 175–189.

Wally, O. S. D., Critchley, A. T., Hiltz, D., Craigie, J. S., Han, X., Zaharia, L. I., Abrams, S. R., & Prithiviraj, B., (2013). Regulation of phytohormone biosynthesis and accumulation in *Arabidopsis* following treatment with commercial extract from the marine macroalgae *Ascophyllum nodosum*. *J. Plant Growth Regul., 32,* 324–339.

Wang, B. G., Gloer, J. B., Ji, N. Y., & Zhao, J. C., (2013). Halogenated organic molecules of Rhodomelaceae origin: Chemistry and biology. *Chem. Rev., 113,* 3632–3685.

Wang, H. M. D., Li, X. C., Lee, D. J., & Chang, J. S., (2017a). Potential biomedical applications of marine algae. *Bioresour. Technol., 244,* 1407–1415.

Wang, L., Wang, X., Wu, H., & Liu, R., (2014). Overview on biological activities and molecular characteristics of sulfated polysaccharides from marine green algae in recent years. *Marine Drugs, 12,* 4984–5020.

Wang, R., Feng, L., Tang, X., Wang, J., & Dong, S., (2012). Allelopathic growth inhibition of *Heterosigma akashiwo* by the three *Ulva* species (*Ulva pertusa, Ulva linza, Enteromorpha intestinalis*) under laboratory conditions. *Acta Oceanol. Sin., 31,* 138–144.

Wang, R., Xiao, H., Wang, Y., Zhou, W., & Tang, X., (2007a). Effects of three macroalgae, *Ulva linza* (Chlorophyta), *Corallina pilulifera* (Rhodophyta) and *Sargassum thunbergii* (Phaeophyta) on the growth of the red tide microalga *Prorocentrum donghaiense* under laboratory conditions. *J. Sea Res., 58,* 189–197.

Wang, S., Wang, W., Hou, L., Qin, L., He, M., Li, W., & Mao, W., (2020). A sulfated glucuronorhamnan from the green seaweed *Monostroma nitidum*: Characteristics of its structure and antiviral activity. *Carbohydr. Polym., 227,* 115280.

Wang, Y., Xiang, L., Wang, S., Wang, X., Chen, X., & Mao, Z., (2017b). Effects of seaweed fertilizer on the *Malus hupehensis* Rehd. seedlings growth and soil microbial numbers under continue cropping. *Acta Ecol. Sin., 37,* 180–186.

Wang, Y., Yu, Z., Song, X., Tang, X., & Zhang, S., (2007b). Effects of macroalgae *Ulva pertusa* (Chlorophyta) and *Gracilaria lemaneiformis* (Rhodophyta) on growth of four species of bloom-forming dinoflagellates. *Aquatic Botany, 86,* 139–147.

Wang, Z. J., Xub, W., Liang, J. W., Wang, C. S., & Kang, Y., (2017c). Effect of fucoidan on B16 murine melanoma cell melanin formation and apoptosis. *Afr. J. Tradit. Complement Altern. Med., 14,* 149–155.

Wei, R., Lee, M. S., Lee, B., Oh, C. W., Choi, C. G., & Kim, H. R., (2016). Isolation and identification of anti-inflammatory compounds from ethyl acetate fraction of *Ecklonia stolonifera* and their anti-inflammatory action. *J. Appl. Phycol., 28,* 3535–3545.

Wells, M. L., Potin, P., Craigie, J. S., Raven, J. A., Merchant, S. S., Helliwell, K. E., Smith, A. G., et al., (2017). Algae as nutritional and functional food sources: Revisiting our understanding. *J. Appl. Phycol., 29,* 949–982.

West, J., Calumpong, H. P., & Martin, G., (2017). Seaweeds. In: *United Nations the First Global Integrated Marine Assessment* (pp. 223–228). Cambridge University Press.

Wielgosz-Collin, G., Kendel, M., & Couzinet-Mossion, A., (2016). Lipids, fatty acids, glycolipids, and phospholipids. In: Fleurence, J., & Levine, I., (eds.), *Seaweed in Health and Disease Prevention* (pp. 185–221). San Diego: Academic Press.

Wijesekara, I., & Kim, S. K., (2015). Application of marine algae derived nutraceuticals in the food industry. In: Kim, S. K., & Chojnacka, K., (eds.), *Marine Algae Extracts: Processes, Products and Applications* (pp. 627–638). Weinheim: Wiley-VCH Verlag GmbH and Co.

Wong, K., & Cheung, P. C., (2000). Nutritional evaluation of some subtropical red and green seaweeds: Part I – proximate composition, amino acid profiles and some physico-chemical properties. *Food Chemistry, 71,* 475–482.

Yamasaki-Miyamoto, Y., Yamasaki, M., Tachibana, H., & Yamada, K., (2009). Fucoidan induces apoptosis through activation of caspase-8 on human breast cancer MCF-7 cells. *J. Agric. Food Chem., 57,* 8677–8682.

Yan, M. D., Lin, H. Y., & Hwang, P. A., (2019). The anti-tumor activity of brown seaweed oligo-fucoidan via lncRNA expression modulation in HepG2 cells. *Cytotechnology, 71*, 363–374.

Yang, C., Lai, S., Chen, Y., Liu, D., Liu, B., Ai, C., Wan, X. Z., et al., (2019b). Anti-diabetic effect of oligosaccharides from seaweed *Sargassum confusum* via JNK-IRS1/PI3K signaling pathways and regulation of gut microbiota. *Food and Chemical Toxicology, 131,* 110562.

Yang, H. W., Fernando, K. H. N., Oh, J. Y., Li, X., Jeon, Y. J., & Ryu, B. M., (2019a). Anti-obesity and anti-diabetic effects of *Ishige okamurae. Marine Drugs, 17*, 202.

Ye, C., & Zhang, M., (2013). Allelopathic effect of macroalga *Gracilaria tenuistipitata* (Rhodophyta) on the photosynthetic apparatus of red-tide causing microalga *Prorocentrum micans*. *IERI Procedia, 5,* 209–215.

Ying-Ying, S., Hui, W., Gan-Lin, G., Yin-Fang, P., Bin-Lun, Y., & Chang-Hai, W., (2015). Green alga *Ulva pertusa* – a new source of bioactive compounds with antialgal activity. *Environ. Sci. Pollut. Res., 22,* 10351–10359.

Yoshie-Stark, Y., Hsieh, Y. P., & Suzuki, T., (2003). Distribution of flavonoids and related compounds from seaweeds in Japan. *Journal – Tokyo University of Fisheries, 89,* 1–6.

Yu, R. X., Yu, R. T., & Liu, Z., (2018). Inhibition of two gastric cancer cell lines induced by fucoxanthin involves down regulation of Mcl-1 and STAT3. *Human Cell, 31*, 50–63.

Yu, X. Q., He, W. F., Liu, D. Q., Feng, M. T., Fang, Y., Wang, B., Feng, L. H., Guo, Y. W., & Mao, S. C., (2014). A seco-laurane sesquiterpene and related laurane derivatives from the red alga *Laurencia okamurai* Yamada. *Phytochemistry, 103*, 162–170.

Yusuf, R., Kristiansen, P., & Warwick, N., (2012). Potential effect of plant growth regulators on two seaweed products. *Acta Hortic., 958,* 133–138.

Zerrif, S. E. A., El Ghazi, N., Douma, M., El Khalloufi, F., & Oudra, B., (2018). Potential uses of seaweed bioactive compounds for harmful microalgae blooms control: Algicidal effects and algal growth inhibition of *Phormidium* sp. (freshwater toxic cyanobacteria). *Smetox. J., 1,* 59–62.

Zerrifi, A. S., Tazart, Z., El Khalloufi, F., Oudra, B., Campos, A., & Vasconcelos, V., (2019). Potential control of toxic cyanobacteria blooms with Moroccan seaweed extracts. *Environmental Science and Pollution Research, 26*, 15218–15228.

Zerrifi, S. E. A., El Khalloufi, F., Oudra, B., & Vasconcelos, V., (2018). Seaweed bioactive compounds against pathogens and microalgae: Potential uses on pharmacology and harmful algae bloom control. *Marine Drugs, 16*, 55.

Zha, S., Kuwano, K., Shibahara, T., & Ishibashi, F., (2020). Algicidal hydroxylated C18 unsaturated fatty acids from the red alga *Tricleocarpa jejuensis*: Identification, synthesis and biological activity. *Fitoterapia, 145,* 104639.

Zhao, C., Yang, C., Liu, B., Lin, L., Sarker, S. D., Nahar, L., Yu, H., et al., (2018). Bioactive compounds from marine macroalgae and their hypoglycemic benefits. *Trends Food Sci. Technol., 72,* 1–12.

Zhao, G., Zhao, J., Peng, L., Zou, L., Wang, J., Zhong, L., & Xiang, D., (2012). Effects of yeast polysaccharide on growth and flavonoid accumulation in *Fagopyrum tataricum* sprout cultures. *Molecules, 17*, 11335–11345.

Zhao, L., Feng, C., Wu, K., Chen, W., Chen, Y., Hao, X., & Wu, Y., (2017). Advances and prospects in biogenic substances against plant virus: A review. *Pest. Biochem. Physiol., 135*, 15–26.

Zorofchian, M. S., Karimian, H., Khanabdali, R., Razavi, M., Firoozinia, M., Zandi, K., & Abdul, K. H., (2014). Anticancer and antitumor potential of fucoidan and fucoxanthin, two main metabolites isolated from brown algae. *The Sci. World J., 3,* 768323.

Zou, P., Lu, X., Zhao, H., Yuan, Y., Meng, L., Zhang, C., & Li, Y., (2019). Polysaccharides derived from the brown algae *Lessonia nigrescens* enhance salt stress tolerance to wheat seedlings by enhancing the antioxidant system and modulating intracellular ion concentration. *Front. Plant Sci., 10,* 48.

Zubia, M., Robledo, D., & Freile-Pelegrin, Y., (2007). Antioxidant activities in tropical marine macroalgae from the Yucatan Peninsula, Mexico. *J. Appl. Phycol., 19,* 449–458.

CHAPTER 1

Introduction to Plant Responses to Environmental Stress

PREETHA BHADRA[1], SAGAR MAITRA[2*], and MASINA SAIRAM[2]

[1]Department of Biotechnology, M.S. Swaminathan School of Agriculture, Centurion University of Technology and Management, Odisha 761211, India

[2]Department of Agronomy and Agroforestry, M.S. Swaminathan School of Agriculture, Centurion University of Technology and Management, Odisha 761211, India

[*]Corresponding author. E-mail: sagar.maitra@cutm.ac.in

ABSTRACT

Anthropogenic activities contribute to different environmental stresses, such as water scarcity or excess water, salinity, high and low temperatures, heavy metal pollution, and solar radiation which cause considerable damages in plants. Inhibited growth of plants and decreased crop productivity have led to global food insecurity. Plant response to these environmental pressures can be visualized in the form of physiological and molecular mechanisms. Photosynthesis and carbon assimilation are affected in crops that are influenced generally by environmental disturbances. The downregulation of Calvin–Benson–Bassham cycle is influenced by stomatal conductance, CO_2 diffusion through stomata, diminished activity of ribulose bisphosphate carboxylase/oxygenase action, which thus diminishes the CO_2 concentration, subsequently bringing about decreased biomass and crop productivity. Other responses involve the combination of stress hormones, for example,

---

Photosynthesis and Respiratory Cycles during Environmental Stress Response in Plants. Aryadeep Roychoudhury (Ed.)

abscisic acid regulates stomatal movement, and the formation of reactive oxygen species causing oxidative damage. There is an intricate organization of collaboration among metabolites and enzymes that regulate plant adaptations to diverse stresses. This chapter focuses on the major abiotic stresses adversely affecting plant growth, productivity, and survival.

1.1 INTRODUCTION

Plant environment, physiology, and natural chemistry have been evaluated widely since time immemorial (Zargar et al., 2015; Zhang et al., 2015). Changes in ecological conditions may be characterized, based on the reactions that a living cell goes through, by restricting certain activities in presence of any challenge (Yadav et al., 2004; Wang et al., 2012; Zhang et al., 2013). For straightforwardness, we characterize a restricting variable as one that decides the pace of development or biochemical response, and that an adjustment in its level can bring about an adjustment of the plant metabolic activities. Stresses are consequently characterized as ecological disorders that outcome awkwardness in metabolism and require biochemical as well as metabolic changes (Eckardt and Pell, 1995; Tournaire et al., 2003; Velikova et al., 2005; Iglesias-Ferna´ndez and Matilla, 2016; Shahid et al., 2017). Schematically, the grouping of occasions related to the reaction of living cells to a natural variation might be portrayed as follows: (1) environmental change, (2) sensing mechanism, (3) adaptation, and (4) new steady state. Plants in an open field face combined vagaries in the natural environment. The progressions occur in two diverse time scales, namely, circadian cycle, which senses light and temperature in a 24 h cycle; and occasional cycle that fluctuates as per the environmental conditions and geological area of the specific environment where the green development occurs (Chatterjee et al., 2017; Dizengremel et al., 2012). In thick algal societies, another cycle is forced by the concentrated blending framework that basically brings about a light-dim cycle, which varies as far as part of seconds when contrasted with the hours or months in the other two cycles. Microalgae have surely evolved different systems for detecting and adapting to variations in their conditions. Such adjustments are intended to balance productively the retention of excitation energy along with the creation of diminishing force (NADPH) and compound energy (ATP) for supporting cellular development. Failure to perform this is due to overexcitation of the photosynthetic apparatus that may bring about the production of reactive oxygen species prompting oxidative damages (Baker, 1996; Carmo-Silva et al. 2010; Brauer et al., 2016).

Proper functioning of chloroplast includes communications with other cell organelles, trade of metabolites, support of phytohormones, reactive oxygen species (ROS), and serious cross-talk with the core (anterograde and retrograde flagging). Chloroplasts, both during biogenesis and senescence, react to the natural variations by adjusting with proper alterations. Plastids have a plastid-encoded RNA polymerase (PEP) and phage-type RNA polymerase (NEP). Numerous TOC receptors empower the activity of various import pathways with various substrate inclinations. These may take part in the separation of plastids. As of late, advancement in chloroplast development is managed by the rebuilding of the protein import apparatus. A RING-type ubiquitin E3 ligase has been identified, targeting the parts of the plastid protein import hardware. Plastid improvement is under the immediate control of the ubiquitin-proteasome framework.

The Calvin–Benson–Bassham (CBB) cycle is dedicated to CO_2 assimilation and sugar production in oxyphototrophs. Phosphoribulokinase (PRK) is a fundamental catalyst of the CBB cycle, catalyzing ATP-mediated transformation of ribulose-5-phosphate (Ru5P) to ribulose-1,5-bisphosphate. The oxyphototrophic PRK is redox-controlled and can be additionally managed by the reversible relationship with both glyceraldehyde-3-phosphate dehydrogenase (GAPDH) and oxidized chloroplast protein CP12. The subsequent GAPDH/CP12/PRK complex is focal in the regulation of the CBB cycle (Jordan et al., 1996; James et al., 2006; Hancock et al., 2014; Gupta et al., 2018). Environmental stresses faced by plants may be characterized as the state when abiotic factors disturb the plants to accomplish their growth, development, and regenerative processes. Abiotic stress influences the development, photosynthesis, and other vital activities of plants. Accordingly, an outline related to the impact of environmental burdens on the Calvin cycle of photosynthesis as well as connected proteins is introduced in this chapter. Under challenging situations, plants try to adjust by hindering metabolic exercises, particularly biosynthesis, that influences general development and yield (Lawlor and Tezara, 2009; Osakabe and Osakabe, 2012; Mustafa and Komatsu, 2016).

1.2 WATER STRESS

Environmental pattern is rapidly changing because of increasing earth temperature, and therefore, crop development is confronted with genuine ecological burdens like dry spell, salinity, temperature, UV, ozone (O_3), and flooding (Fig. 1.1). Flooding pressure is one of the significant concerns brought about by sudden precipitation within a short span of time. Excess water pressure in the farming area may create waterlogging or submergence stress. Waterlogging is brought about by the abundance of water in cultivating regions, so that the entire root region as well as certain portions of shoot is inundated, while submergence implies to the situation when an entire plant is covered with water (Parry et al., 2008; Qureshi et al., 2013). The excess soil moisture stress is because of poor seepage and concentrated water system. Considering the losses due to excess water stress, many harvest raisers have zeroed in on the advancement of flood lenient assortments or recognizable proof of flood-tolerant crops and cultivars (Fig. 1.1). Along these lines, a few flooding resilience assortments or promotions have been created, while then again, explicit hereditary and biochemical systems have additionally been recognized in rice and other crops (Schnarrenberger et al., 1995; Reddy et al., 2004; Yan et al., 2006).

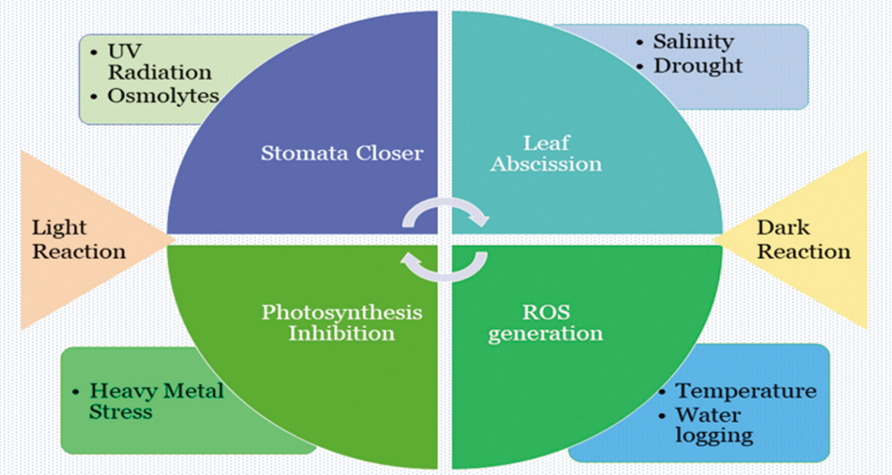


FIGURE 1.1 Different forms of abiotic stress.

1.2.1 *MORPHOLOGICAL RESPONSE*

Under submerged conditions, plants face oxygen insufficiency and react morphologically to maximize oxygen uptake. Aerenchyma tissue may develop in the root cortical cells that provide oxygen ceaselessly from shoot to roots. Besides, plants undergo morphological changes in roots to endure such pressure (Vu et al., 1984; Zeng et al., 2008). The unusual roots are invigorated by prior root primordia situated at the shoot region. Roots, situated at the soil surface, are stretched out in woody and herbaceous species. Shoot parts likewise show some morphological changes as in *Rumex palustris* during flooding pressure. The increments in the petiole length and leaf regions over the water level are other such responses. Shoots also undergo hypertrophy that resembles white elastic tissue, which are normally noticeable in stems, close to water surfaces. Hypertrophic tissues are auxiliary aerenchyma and are outside the phellogens. The principal job of hypertrophic tissues in the shoot is the improvement of oxygen development in plant tissues to create energy through mitochondrial activity.

1.2.2 WATERLOGGING TOLERANCE STRATEGY

Waterlogging in a crop field is characterized by the submergence of plant parts. Under such circumstance, excess moisture condition in the rhizosphere is very common. Under submergence, the majority of the shoots is presented to air in different crops such as maize, wheat, and soybean, and hence is presented to water stagnation because of excess rainfall (Ruelland et al., 2009; Ueda et al., 2015; Sharma et al., 2017). Waterlogging stress instigates genuine yield loss, relying upon the crop development stage (reproductive stage showed more yield loss than vegetative stage). To endure waterlogging, plants bring about morphological or metabolic changes. In the case of soybean, unusual rooting occurs as compared to shoot formation that is near the water surface during waterlogging.

1.3 SALT STRESS

Productivity of all crops is affected by high salt levels; yet, it contrasts extraordinarily among species and among cultivars. The formative developmental phase of plant and the external factors likewise adjust plant reactions against salinity. The abundance of salt not only impacts growth and developmental processes such as poor seed germination, plant height, root length, and yield output but also affects the food web as a whole. This occurs because of salt-incited oxidative damage and reduced photosynthesis rate. In spite of the adverse effects, plants can endure and complete the crop cycle in high salinity conditions (Kim et al., 2005; Lee et al., 2007; Mutava et al., 2015) due to the evolution of organic, synthetic, and physiological systems. Among the salt tolerance systems, salt overly sensitive pathways, hyperosmotic sensors, and Na and K carriers are the mainstream regulators. In addition, osmoregulation and hormonal variations have been recognized as natural salinity resilience mechanism of plants. Rhizospheric colonization of the growth-promoting rhizobacteria (PGPR) can also improve plant resilience against salinity. Generating transgenic salt-tolerant plants is another effective approach, which however has limitation because salt tolerance is a multigenic trait (Denman et al., 2007; Fernandez et al., 2012; Hu et al., 2015).

1.4 HEAVY METAL STRESS

The presence of heavy metals in farmlands causes various abnormalities in the developmental processes of plants and affects distinct biochemical and physiological cycles. Among the various metals, Mo, Cu, Co, Mn, Ni, Zn, and Fe are needed in minor quantities by plants and are viewed as fundamental micronutrients. Some of them act as cofactors for a few essential metabolic enzymes; however, when present in excess, they exert a destructive effect on plants. Arsenic (As), cadmium (Cd), chromium (Cr), and lead (Pb) are nonessential to plants and are regarded as insignificant elements (Fig. 1.2).

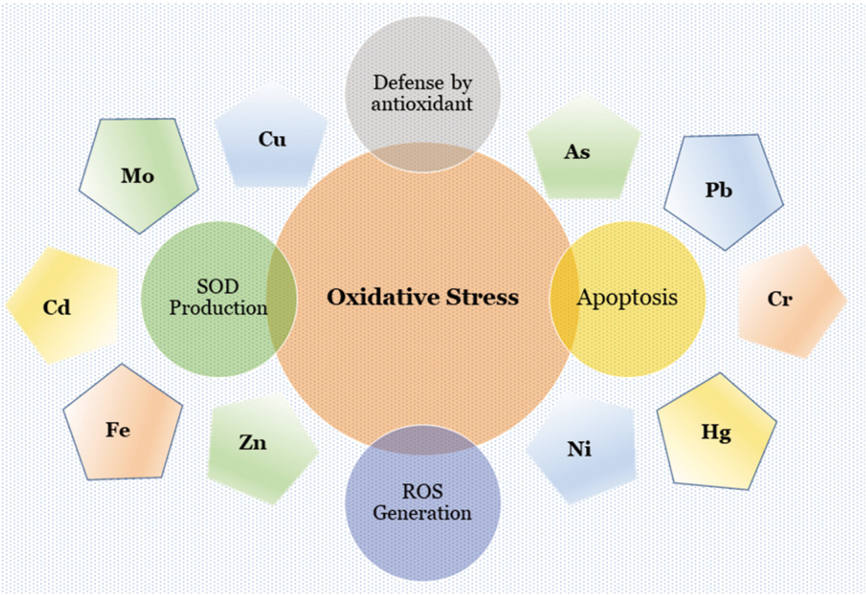


FIGURE 1.2 Heavy metals causing plant stress.

1.5 RADIATION STRESS

During the previous few decades, pulverization of timberlands and burning of petroleum derivatives prompted the aggravation of carbon dioxide, chlorofluorocarbons, methane, nitrous oxide, and such greenhouse gases, which enhance solar radiation to arrive on the earth (Xiong et al., 2006; Chakrabarty et al., 2009; Tripathi et al., 2016). This active radiation is retained and reradiated by the above ozone-depleting harmful substances, causing global warming and creating an enhancement in temperature on earth surface. Further, the amount of ozone-depleting substances is as yet expanding and causing climatic aberrations. Environmental change contemplates are vital in farming and natural science. Reactions of the plants to different ecological disturbances are represented by complex subatomic and biochemical sign transduction measures, coordinating to regulating resilience in plants. Stress conditions created by radiation include (UV-B) irradiance, which induces a varied cluster of plant reactions including variations in developmental rates and productivity. Different reports have shown the harming impact of UV-B to DNA, proteins, and lipids, causing ROS accumulation by perturbing the decrease of NADPH formation during photosynthetic electron transport chain. The induction of various phenolic compounds (stilbenes and flavonoids) and vitamin D is stimulated by UV-B (Pankovic et al., 1999; Feller et al., 2008; Cechin et al., 2018) as defense mechanism.

1.6 CONCLUSION AND FUTURE PERSPECTIVES

Plants are consistently affected by different ecological burdens that incorporate abiotic and biotic factors. Stresses due to abiotic factors are common in the present scenario of climate change because of a few anthropogenic factors like contamination, global warming, and depletion of ozone. It was seen that up to 70% of the yield efficiency is influenced by natural elements (Asada, 1994). The physiological activities of plants inclusive of unequivocal reactions are likewise being upset under stress situations. So, to fulfill the developing need for food around the world, viable, novel, and strong methodologies ought to be adopted. The application of phytohormones could be an intelligent game plan, which can improve the yield. The phytohormones are incredible endogenous substances for fitting functional reactions in plants. Further investigations in the field of proteomics, transcriptomics, metabolomics, and novel cell imaging procedures would upgrade our comprehension of photosynthetic mechanism under abiotic stresses. The different strides in RuBisCO debasement, and the enzyme regulations associated with photosynthetic cycles still need to be clarified under environmental stresses. Nanotechnology is also regarded as one of the encouraging ways to deal with the improvement of environmental stress resilience. Nanoparticle application has been found to improve abiotic stress resistance by lowering ROS as well as improving photosynthesis. However, positive or adverse consequences of nanoparticles largely rely on various factors, namely, their size, surface charge, etc. Future research should further explore beneficial outcomes of nanoparticles on different physiological regulations like osmolyte synthesis, and maintaining ionic homeostasis under abiotic stresses.

KEYWORDS

- **environmental stress**
- **antioxidants**
- **plant responses**
- **reactive oxygen species**
- **oxidative damages**

REFERENCES

Asada, K. Mechanisms for Scavenging Reactive Molecules Generated in Chloroplasts under Light Stress. In *Photoinhibition of Photosynthesis: From Molecular Mechanisms to the Field*; Baker, N. R.; Bowyer, J. R.; Bios Scientific Publishers Ltd: Oxford, **1994,** pp 129–142.

Armada, E.; Rolda´n, A.; Azcon, R. Differential Activity of Autochthonous Bacteria in Controlling Drought Stress in Native Lavandula and Salvia Plants Species under Drought Conditions in Natural Arid Soil. *Microb. Ecol.* **2014,** *67,* 410420.

Ashraf, M.; Harris, P. J. C. Photosynthesis under Stressful Environments: An Overview. *Photosynthetica* **2013**, *51*, 163190.

Asner, G. P.; Alencar, A. Drought Impacts on the Amazon Forest: The Remote Sensing Perspective. *New Phytol*. **2010,** *187* (3), 569578.

Atkin, O. K.; Macherel, D. The Crucial Role of Plant Mitochondria in Orchestrating Drought Tolerance. *Ann. Bot*. **2009,** *103*, 581597.

Baker, N. R. Photoinhibition of Photosynthesis. In *Light as an Energy Source and Information Carrier in Plant Physiology*; Jennings, P. R., Zucchelli, F., Ghetti, F., Colombetti, G.; NATO ASI Series, Series A: Life Science, Vol. 287; Plenum Press: New York, 1996.

Bahrami-Rad, S.; Hajiboland, R. Effect of Potassium Application in Drought-Stressed Tobacco (*Nicotiana rustica* L.) Plants: Comparison of Root with Foliar Application. *Ann. Agric. Sci.* **2017,** *62*, 121130.

Balestrini, R.; Lumini, E.; Borriello, R.; Bianciotto, V. Plant-Soil Biota Interactions. In *Soil Microbiology, Ecology and Biochemistry*; 2015; p 311338.

Bartels, D.; Sunkar, R. Drought and Salt Tolerance in Plants. *CRC Crit. Rev. Plant Sci*. **2005,** *24*, 2358.

Brauer, M.; Freedman, G.; Frostad, J.; van Donkelaar, A.; Martin, R. V.; Dentener, F. Ambient Air Pollution Exposure Estimation for the Global Burden of Disease 2013. *Environ. Sci. Technol*. **2016,** *50*, 7988.

Carmo-Silva, A. E.; Keys, A. J.; Andralojc, P. J.; Powers, S. J.; Arrabac¸a, M. C.; Parry, M. A. J. Rubisco Activities, Properties, and Regulation in Three Different C4 Grasses under Drought. *J. Exp. Bot.* **2010,** *61* (9), 23552366.

Cechin, I.; Gonzalez, G. C.; Corniani, N.; Terezinha de, F. F. The Sensitivity of Sunflower (*Helianthus annuus* L.) Plants to UV-B Radiation Is Altered by Nitrogen Status. *Cieˆncia Rural, Santa Maria* **2018,** *48* (02), e20170369.

Chakrabarty, D.; Trivedi, P. K.; Misra, P.; Tiwari, M.; Shri, M.; Shukla, D. Comparative Transcriptome Analysis of Arsenate and Arsenite Stresses in Rice Seedlings. *Chemosphere* **2009,** *74*, 688702.

Chatterjee, S.; Sharma, S.; Gupta, D. K. Arsenic and Its Effect on Major Crop Plants: Stationary Awareness to Paradigm with Special Reference to Rice Crop. In *Arsenic Contamination in the Environment: The Issues and Solutions*; Gupta, D. K., Chatterjee, S., Eds.; Springer International Publishing AG, 2017; pp 123143. https://doi.org/10.1007/978-3-319-54356-7-6.

Denman, K. L.; Brasseur, G.; Chidthaisong, A.; Ciais, P.; Cox, P. M.; Dickinson, R. E. Couplings between Changes in the Climate System and Biogeochemistry. In *Climate Change 2007: The Physical Science Basis. Contribution of Working Group I to the Fourth Assessment Report of the Intergovernmental Panel on Climate Change*; Solomon, S., Qin, D., Manning, M., Chen, Z., Marquis, M., Averyt, K. B., Tignor, M., Miller, H. L., Eds.; Cambridge University Press: Cambridge, 2007; pp 499–587.

Dizengremel, P.; Vaultier, M. N.; Thiec, D. L.; Cabane, M.; Bagard, M.; Ge´rant, D. Phosphoenolpyruvate Is at the Crossroads of Leaf Metabolic Responses to Ozone Stress. *New Phytol*. **2012,** *195*, 512–517.

Duman, F.; Ozturk, F.; Aydin, Z. Biological Responses of Duckweed (*Lemna minor* L.) Exposed to the Inorganic Arsenic Species As(III) and As(V): Effects of Concentration and Duration of Exposure. *Ecotoxicology*. **2010,** *19*, 983–993.

Eckardt, N.; Pell, E. Oxidative Modification of Rubisco from Potato Foliage in Response to Ozone. *Plant Physiol. Biochem*. **1995,** *33*, 273–282.

Faller, P.; Kienzler, K.; Krieger-Liszkay, A. Mechanism of Cd21 Toxicity: Cd21 Inhibits Photoactivation of Photosystem II by Competitive Binding to the Essential Ca21 Site. *Biochim. Biophys. Acta. Bioenerg*. **2005,** *1706*, 158–164.

Fang, Y.; Xiong, L. General Mechanisms of Drought Response and Their Application in Drought Resistance Improvement in Plants. *Cell. Mol. Life Sci*. **2015,** *72*, 673–689.

Feller, U.; Anders, I.; Demirevska, K. Degradation of Rubisco and Other Chloroplast Proteins under Abiotic Stress. *Gen. Appl. Plant Physiol.* **2008,** *34*, 5–18.

Fernandez-Garcia, N.; Romojaro, F.; Olmos, E.; Estrella, E.; Bolarin, M. C.; Flores, F. B. Understanding the Mechanisms of Chilling Injury in Bell Pepper Fruits Using the Proteomic Approach. *J. Proteomics* **2012,** *75*, 5463–5478.

Finnegan, P. M.; Chen, W. Arsenic Toxicity: The Effects on Plant Metabolism. *Front. Physiol.* 2012, 3 (182). https://doi.org/10.3389/fphys.2012.00182.

Gupta, D. K.; Chatterjee, S., Eds. *Arsenic Contamination in the Environment: The Issues and Solutions*; Springer International Publishing: AG Switzerland, 2007. https://doi.org/10.1007/978-3-319-54356-7.

Gupta, B. K.; Sahoo, K. K.; Ghosh, A.; Tripathi, A. K.; Anwar, K.; Das, P. Manipulation of Glyoxalase Pathway Confers Tolerance to Multiple Stresses in Rice. *Plant Cell Environ.* **2018,** *41* (5), 1186–1200. https://doi.org/10.1111/pce.12968.

Hancock, R. D.; Morris, W. L.; Ducreux, L. J.; Morris, J. A.; Usman, M.; Verrall, S. R. Physiological, Biochemical and Molecular Responses of the Potato (*Solanum tuberosum* L.) Plant to Moderately Elevated Temperature. *Plant Cell Environ.* **2014,** *37*, 439–450.

Hu, X.; Wu, L.; Zhao, F.; Zhang, D.; Li, N.; Zhu, G. Phosphoproteomic Analysis of the Response of Maize Leaves to Drought, Heat and Their Combination Stress. *Front. Plant Sci.* **2015,** *6*, 1–21.

Iglesias-Ferna´ndez, R.; Matilla, A. J. Flooding Stress and O2-shortage in Plants. In *Water Stress and Crop Plants: A Sustainable Approach*; Ahmad, P., Ed., Vol. 1; About Wiley Online Library Chapter 41; 2016. https://doi.org/10.1002/9781119054450.ch41.

James, R. A.; Munns, R.; von Caemmerer, S.; Trejo, C.; Miller, C.; Condon, T. A. G. Photosynthetic Capacity Is Related to the Cellular and Subcellular Partitioning of Naþ, Kþ and Cl- in Salt-Affected Barley and Durum Wheat. *Plant Cell Environ.* **2006,** *29*, 2185–2197.

Jordan, B. R.; He, J.; Chow, W. S.; Anderson, J. M. Changes in mRNA Levels and Polypeptide Subunits of Ribulose- 1, 5-Bisphosphate Carboxylase in Response to Supplemental UV-B Radiation. *Plant Cell Environ.* **1996,** *15*, 91–98.

Kim, S. Y.; Lim, J. H.; Park, M. R.; Kim, Y. J.; Park, T.; Seo, Y. W. Enhanced Antioxidant Enzymes Are Associated with Reduced Hydrogen Peroxide in Barley Roots under Saline Stress. *J. Biochem. Mol. Biol.* **2005,** *38*, 218–224.

Kosova, K.; Vitamvas, P.; Prasil, I. T.; Renaut, J. Plant Proteome Changes under Abiotic Stress—Contribution of Proteomics Studies to Understanding Plant Stress Response. *J. Proteome* **2011,** *74*, 1301–1322.

Lawlor, D. W. Limitations to Photosynthesis in Water-Stressed Leaves: Stomatal vs. Metabolism and the Role of ATP. *Ann. Bot.* **2002,** *89*, 871–885.

Lawlor, D. W.; Tezara, W. Causes of Decreased Photosynthetic Rate and Metabolic Capacity in Water Deficient Leaf Cells: A Critical Evaluation of Mechanisms and Integration of Processes. *Ann. Bot.* **2009,** *103*, 561–579.

Lee, D. G.; Ahsan, N.; Lee, S. H.; Kang, K. Y.; Bahk, J. D.; Lee, I. J. A Proteomic Approach in Analyzing Heat-Responsive Proteins in Rice Leaves. *Proteomics* **2007,** *7*, 3369–3383.

Mustafa, G.; Komatsu, S. Toxicity of Heavy Metals and Metal-Containing Nanoparticles on Plants. *Biochim. Biophys. Acta.* **2016,** *1864*, 932–944.

Mutava, R. N.; Prince, S. J. K.; Syed, N. H.; Song, L.; Valliyodan, B.; Chen, W. Understanding Abiotic Stress Tolerance Mechanisms in Soybean: A Comparative Evaluation of Soybean Response to Drought and Flooding Stress. *Plant Physiol. Biochem.* **2015,** *86*, 109–120.

Nouri, M. Z.; Moumeni, A.; Komatsu, S. Abiotic Stresses: Insight Into Gene Regulation and Protein Expression in Photosynthetic Pathways of Plants. *Int. J. Mol. Sci.* **2015,** *16*, 20392–20416.

Osakabe, K.; Osakabe, Y. Plant Light Stress. In *Encyclopaedia of Life Sciences*; Robinson, S. A., Ed.; Nature Publishing Group: London, 2012.

Pankovic, D.; Sakac, Z.; Kevresan, S.; Plesnicar, M. Acclimation to Long-Term Water Deficit in the Leaves of Two Sunflower Hybrids: Photosynthesis, Electron Transport and Carbon Metabolism. *J. Exp. Bot.* **1999,** *50*, 127–138.

Parry, M. A. J.; Keys, A. J.; Madgwick, P. J.; Carmo-Silva, A. E.; Andralojc, P. J. Rubisco Regulation: A Role for Inhibitors Centre. *J. Exp. Bot.* **2008,** *59*, 1569–1580.

Pell, E. J.; Landry, L. G.; Eckardt, N. A.; Click, R. E. Effects of Gaseous Air Pollutants on Ribulose Bisphosphate Carboxylase/Oxygenase: Effects and Implications. In *Plant Response to the Gaseous Environment: Molecular, Metabolic and Physiological Aspects*; Alscher, R. G., Wellburn, A. R., Eds.; Chapman and Hall: London, 1994; pp 239–254.

Qureshi, M. I.; Abdin, M. Z.; Ahmad, J.; Iqbal, M. Effect of Long-Term Salinity on Cellular Antioxidants, Compatible Solute and Fatty Acid Profile of Sweet Annie (*Artemisia annua* L.). *Phytochemistry*. **2013,** *95*, 215–223.

Reddy, A. R.; Chaitanya, K. V.; Vivekanandan, M. Drought-Induced Responses of Photosynthesis and Antioxidant Metabolism in Higher Plants. *J. Plant Physiol.* **2004,** *161*, 1189–1202.

Rı´o Segade, S.; Vilanova, M.; Giacosa, S.; Perrone, I.; Chitarra, W.; Pollon, M. Ozone Improves the Aromatic Fingerprint of White Grapes. *Sci. Rep.* **2017,** *24*, 16301. https://doi.org/10.1038/s41598-017-16529-5.

Ruelland, E.; Vaultier, M. N.; Zachowski, A.; Hurry, V. Cold Signalling and Cold Acclimation in Plants. In *Advances in Botanical Research*; Jean-Claude, K., Michel, D., Eds., vol. 49. Academic Press, 2009; pp 35–150.

Schnarrenberger, C.; Flechner, A.; Martin, W. Enzymatic Evidence Indicating a Complete Oxidative Pentose Phosphate in the Chloroplasts and an Incomplete Pathway in the Cytosol of Spinach Leaves. *Plant Physiol.* **1995,** *108*, 609–614.

Shahid, M.; Shamshad, S.; Rafiq, M.; Khalid, S.; Bibi, I.; Niazi, N. K. Chromium Speciation, Bioavailability, Uptake, Toxicity and Detoxification in Soil-Plant System: A Review. *Chemosphere* **2017,** *178*, 513–533.

Sharma, S.; Chatterjee, S.; Kataria, S.; Joshi, J.; Datta, S.; Vairale, M. G. A Review on Responses of Plants to UV-B Radiation Related Stress. In *UV-B Radiation: From Environmental Stressor to Regulator of Plant Growth*; Singh, V. P., Singh, S., Prasad, S. M., Parihar, P., Eds.; John Wiley Sons: New York, 2017; pp 75–97. https://doi.org/10.1002/9781119143611, Ch. 5.

Tournaire-Roux, C.; Sutka, M.; Javot, H.; Gout, E.; Gerbeau, P.; Luu, D. T. Cytosolic pH Regulates Root Water Transport during Anoxic Stress through Gating of Aquaporins. *Nature*. **2003,** *425*, 393–397.

Tripathi, A. K.; Pareek, A.; Singla-Pareek, S. L. A NAP-Family Histone Chaperone Functions in Abiotic Stress Response and Adaptation. *Plant Physiol.* **2016,** *171*, 2854–2868.

Ueda, Y.; Siddique, S.; Frei, M. A Novel Gene, Ozone-Responsive Apoplasticprotein1, Enhances Cell Death in Ozone Stress in Rice. *Plant Physiol.* **2015,** *169*, 873–889.

Velikova, V.; Tsonev, T.; Pinelli, P.; Alessio, G. A.; Loreto, F. Localized Ozone Fumigation System for Studying Ozone Effects on Photosynthesis, Respiration, Electron Transport

Rate and Isoprene Emission in Field-Grown Mediterranean Oak Species. *Tree Physiol.* **2005,** *25*, 1523–1532.

Vu, C. V.; Allen, L. H.; Garrard, L. A. Effects of UV-B Radiation (280–320 nm) on Ribulose-1, 5 Bisphosphate Carboxylase in Pea and Soybean. *Environ. Exp. Bot.* **1984,** *24*, 131–143.

Wang, H. B.; Xie, F.; Yao, Y. Z.; Zhao, B.; Xiao, Q. Q.; Pan, Y. H. The Effects of Arsenic and Induced-Phytoextraction Methods on Photosynthesis in Pteris Species with Different Arsenic-Accumulating Abilities. *Environ. Exp. Bot.* **2012,** *75*, 298–306.

Xin, Z.; Browse, J. Cold Comfort Farm: The Acclimation of Plants to Freezing Temperatures. *Plant Cell Environ.* **2000,** *23*, 893–902.

Xiong, Z.; Zhao, F.; Li, M. Lead toxicity in Brassica pekinensis Rupr.: effect on nitrate assimilation and growth. *Environ. Toxicol.***2006,** *21* (2), 147–153.

Yadav, R. S.; Hash, C. T.; Bidinger, F. R.; Devos, K. M.; Howarth, C. J. Genomic Regions Associated with Grain Yield and Aspects of Post Flowering Drought Tolerance in Pearl Millet across Environments and Tester Background. *Euphytica.* **2004,** *136*, 265–277.

Yan, S. P.; Zhang, Q. Y.; Tang, Z. C.; Su, W. A.; Sun, W. N. Comparative Proteomic Analysis Provides New Insights Into Chilling Stress Responses in Rice. *Mol. Cell. Proteomics.* **2006,** *5*, 484–496.

Zargar, S. M.; Kurata, R.; Inaba, S.; Oikawa, A.; Fukui, R.; Ogata, Y. Quantitative Proteomics of Arabidopsis Shoot Microsomal Proteins Reveals a Cross-Talk Between Excess Zn and Iron Deficiency. *Proteomics.* **2015,** *15*, 1196–1201.

Zeng, Z. Z.; Wei, J.; Wei, R. H.; Zhu, X. Q. Investigation of Frost Bitten Sugarcane in Liujiang County. In *Proceedings of Annual Meeting of Guangxi Society of Sugarcane Technologists*; 2008; pp 189–192.

Zhang, L.; Zhang, L.; Sun, J.; Zhang, Z.; Ren, H.; Sui, X. Rubisco Gene Expression and Photosynthetic Characteristics of Cucumber Seedlings in Response to Water Deficit. *Sci. Hortic.* **2013,** *161*, 81–87.

Zhang, B. Q.; Yang, L. T.; Li, Y. R Physiological and Biochemical Characteristics Related to Cold Resistance in Sugarcane. *Sugar Tech.* **2015,** *17*, 49–58.

CHAPTER 4

Microalgae: A Valuable Source of Natural Colorants for Commercial Applications

CHIDAMBARAM KULANDAISAMY VENIL,[1]
MATHESWARAN YAAMINI,[1] and LAURENT DUFOSSÉ[2]

[1] *Department of Biotechnology, Anna University, Regional Campus, Coimbatore – 641046, Tamil Nadu, India*

[2] *Université de la Réunion, CHEMBIOPRO Chimie et Biotechnologie des Produits Naturels, ESIROI Département Agroalimentaire, Sainte-Clotilde F – 97490, Ile de La Réunion, Indian Ocean, France*

ABSTRACT

The harmful effects of synthetic colorants have created an increased awareness among the stakeholders towards natural colorants, especially for applications in the fields of medicine, food, and cosmetics. Such indulgence of the stakeholders has led to the exploration of natural resources like plants, bacteria, algae, etc., for producing natural/organic colorants/products. Of these natural sources, microalgae are one of the valuable and recognized natural sources for producing vitamins, proteins, pigments, fuels, medicines, etc.; and currently, such products are gradually reaching the global markets. Microalgae produce a broad spectrum of attractive coloring pigments like chlorophylls, carotenoids, zeaxanthin, lutein, etc. These algal pigments are eco-friendly and harmless potential compounds to be applied as natural colorants in food, nutraceuticals, cosmetics, and pharma industries. Producing pigments from algae has many advantages,

---

Microalgal Biotechnology: Bioprospecting Microalgae for Functional Metabolites towards Commercial and Sustainable Applications. Jeyabalan Sangeetha, PhD, Svetlana Codreanu, PhD, & Devarajan Thangadurai, PhD (Eds.)

such as easy extraction, enhanced yields and cheaper production with no seasonal variations. This chapter discusses on the classes of algal pigments, cultivation of algae, factors affecting pigment production and metabolic engineering. In addition, the possible applications of these colorants in food, cosmetics, and health care industries are highlighted too.

4.1 INTRODUCTION

Microalgae, being unicellular or filamentous microbes, are an extremely diverse grouping of simple, plant-like organisms capable of, producing glowing eco-friendly colors (Begum et al., 2016). Globally there is a surging need for natural colorants owing to the positive awareness that has been created among the stakeholders, customers, etc., for safe and biodegradable colorants. By the way, the exploration and exploitation of algae for natural colorants has opened up many exciting possibilities for producing eco-friendly and renewable stable coloring materials. Apart from their coloring properties, they have also many prospective health benefits to humans and animals. Most of the algal metabolites, especially pigments are possessing antiaging, antioxidant, and neuroprotective properties which facilitate them fitting to be utilized in nutraceutical, human make-ups, healthcare, etc. Algal pigments like β-carotene from *Arthrospira* and *Dunaliella* are commercially available as nutritional supplements and they have gained acceptance globally (Koyande et al., 2019). Moreover, algae are being the prospective natural sources to be screened for novel metabolites for various kinds of applications.

Microalgae are extraordinary organisms that can thrive even in extreme environments with the required amount of light and humidity (Kiesenhofer and Fluch, 2018). Owing to their enormous potential for the production of valuable natural products, further researches are emerging in the field of microalgae. Algal pigments are explicitly precious commercial natural dyes, antioxidants, and vitamins in the food and cosmetic industry. Mainly vital pigments like chlorophylls, carotenoids, and phycobiliproteins (PBPs) have extensive broad scope of appliances in diagnostics, biomedical investigation, therapeutics, colorings in make-up products, dairy products, and other foodstuffs; and they are also getting a significant organic identity owing to their non-toxic and non-carcinogenic nature (Sathasivam and Ki, 2018).

In biotechnological point of view, microalgae are incredible sources for pigments because they produce a wide spectrum of colors and various molecules, including chlorophylls (green), carotenoids (red, orange, and yellow) and PBPs (red and blue) (Mulders et al., 2014). Regardless of having all these outstanding advantages, currently microalgae are commercially exploited only for three types of pigments, namely β-carotene (*Dunaliella salina*), astaxanthin (*Haematococcus pluvialis*) and phycocyanin (PC) (*Arthrospira platensis*) (Camacho et al., 2019).

This chapter appraises and emphasizes on the significance of microalgae producing pigments and their possible utilization in food, pharmaceutical, and cosmetics industries for the improvement of health and well-being of humans.

4.2 SWOT ANALYSIS OF ALGAL PIGMENTS

The SWOT (strength, weakness, opportunities, and threats) analysis of algal pigments is represented in Figure 4.1.

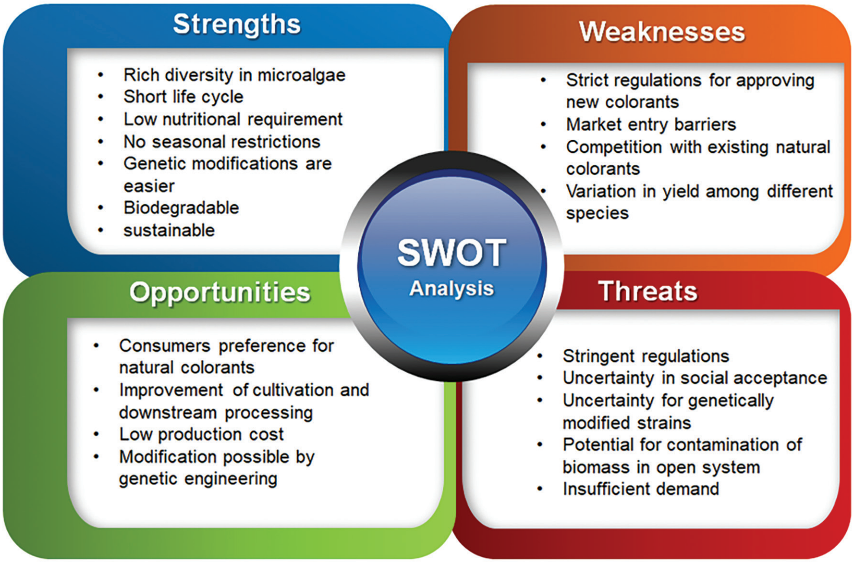


FIGURE 4.1 SWOT (Strength, weakness, opportunities, and threats) analysis of algal pigments.

4.2.1 STRENGTH

Algae produce various shades of coloring pigments without seasonal variations and are continually attracting the interests of multiple markets including food, nutraceuticals, and cosmetics industry. There is a broad opportunity for generating huge markets by the development of optimized microalgal cultivation system and thereby producing valuable algal compounds. Applying of hydrolysates from agricultural residues for microalgal growth is one of the cost-effective methods for algal cultivation. The carbon sources from sweet sorghum, cassava, molasses, rice straw, etc., can be exploited as the low-cost substrates for microalgal cultivation (Gao et al., 2010; Lu et al., 2010; Li et al., 2011; Yan et al., 2011). Current trends for products derived from algae have opened up many new opportunities for the research and development of novel algal products to meet the emerging market needs.

4.2.2 WEAKNESS

The microalgal cultivation is a challenging endeavor as it is a labor intensive one and consists of expensive processes. Further, distinguishing between natural and synthetic pigments is a hard one because of the chirality in isomers. Therefore, it is very easy for the adulterated products to get entry into the market falsely claiming them as organic products. Firm set of laws and slow-moving legislation only may obstruct the route of adulterated products to bazaar, and this factor would slowly open the way to develop new algal products (Novoveska et al., 2019). Moreover, the commercial applicability of algal pigments has also to be checked for their toxicity and quality to get the regulatory endorsement before entering the market.

4.2.3 OPPORTUNITIES

Consumers' preference towards natural pigments increases the need for natural colorants. Exploring potent pigment producing algae may lead to the identification of novel and rare strains. The commercialization of food-grade algal pigments is increasing because of the biotechnological advancement and low capital investment, and this trend is supporting the growth of algal pigment markets globally. The large share of this global pigment market is mainly attributed to the consumer demand for plant-derived alternatives, strict regulation against the use of synthetic colorants and the eco-friendly harmless properties of algal pigments such as high nutritional value, non-toxicity, and their biodegradability.

4.2.4 THREATS

The major threat is the stringent regulations and competition from the already existing commercial natural colorants. Also there is a possibility of contamination when cultured in an open system.

4.3 CLASSES OF ALGAL PIGMENTS

There are three main types of photosynthetic pigments like chlorophylls, carotenoids (carotenes and xanthophylls) and phycobilins in algae. The pigments, chlorophylls, and carotenoids are fat-soluble and phycobilins are water-soluble (Figure 4.2).

4.3.1 CHLOROPHYLLS

Three different types of chlorophylls are there, namely chlorophyll a, b, and c. The chlorophyll particle is the porphyrin containing tetrapyrrole rings. Phorbin is made by the adding of iso-cyclic ring to pyrrole rings. Every pyrrole ring comprises 1 nitrogen and 4 carbon atoms. The central hole contains nitrogen atoms, in which Mg^{2+} metal ions can combine. The formyl group in the second ring of chlorophyll b is interchanged by methyl group in chlorophyll a (Scheer et al., 2004). Because of these structural variations, chlorophyll a has a maximum wavelength at 660–665 nm, with blue-green pigments and chlorophyll b has a maximum wavelength at 642–652 with green-yellow pigments. Owing to the exposure of chlorophyll molecules to heat, light, oxygen, and weak acids, many degraded products are formed (Cubas et al., 2008).

Chlorella contains two key types of chlorophylls (a, b), up to 4.5% of dry weight, and so it may be mainly the smart creation material when developed under most favorable conditions (Cuaresma et al., 2011; Miazek and Ledakowicz, 2013). Alternatively, it has been construed that chlorophyll in microalgal biomass is condensed drastically under stress circumstances (Markou and Nerantzis, 2013).

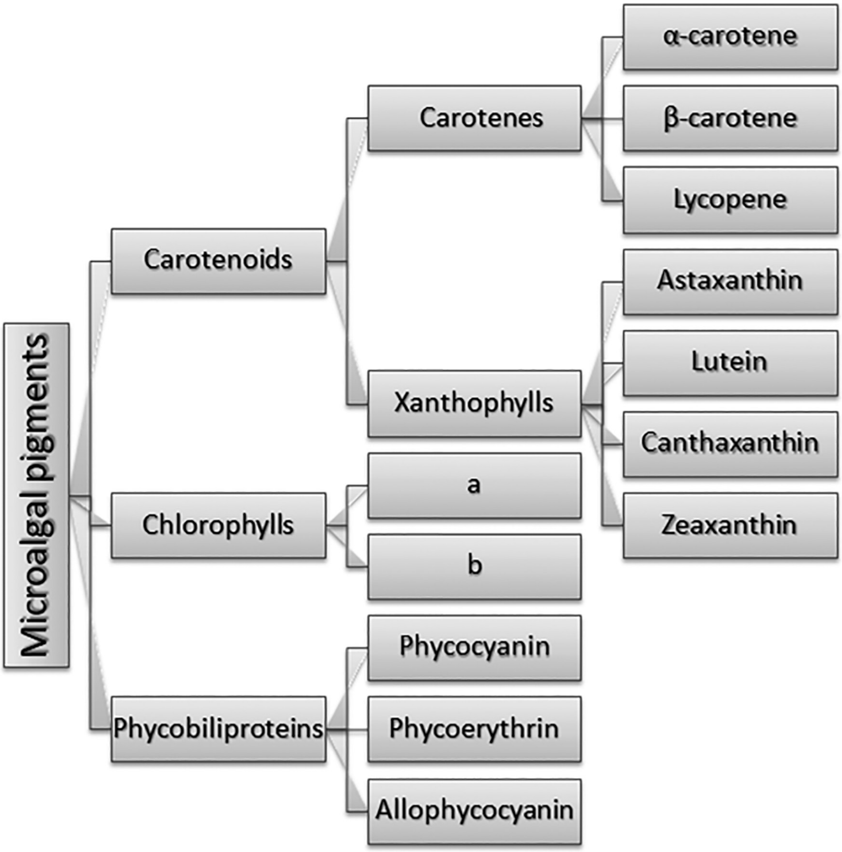


FIGURE 4.2 Natural pigments from microalgae.

4.3.2 CAROTENOIDS

Carotenoids are terpenoid pigments derived from 40 carbon polyene chain. It has light absorption characteristics that are crucial for photosynthesis. Carotenoids may have cyclical groups and oxygen possessing performing groups. The hydrocarbon carotenoids are considered as carotenes whereas the oxygenated derivatives are xanthophylls with oxygen being replaced by hydroxyl groups. β-carotene is produced by unicellular algae *Dunaliella salina* under stressed conditions. It is a mixture of 2 stereoisomers, all-trans, and 9-cis in equal amounts with health promoting properties (Del-Campo et al., 2007). The pro-vitamin A is high in β-carotene because every molecule produces 2 molecules of retinol (Christaki et al., 2013). The microalgal pigments possess solid antioxidant activity and intervene in the harmful effects of free radicals by defending the lipophilic part from lipid peroxidation (Lordan et al., 2011; Pangestuti and Kim, 2011). β-carotene acts as a pro-oxidant in the lipid peroxidation process when there is high oxygen pressure and thereby enhances the carotenoid production (Stahl and Sies, 2003).

The freshwater microalgae, *Haematococcus pluvialis* has a high level of astaxanthin, and it is mainly used as coloring compounds in aquaculture; moreover, it has strong antioxidant activity (Daubrawa et al., 2005). Astaxanthin has promising health benefits and aid in curing various diseases like cancer, metabolic syndrome, cardiovascular diseases (CDVs) and it also enhances the immune system by protecting the skin from radiation (Yuan et al., 2011). *H. pluvialis* has four phases and in the aplanospores phase, the astaxanthin is accumulated which is prompted under stress conditions like pH, salinity, temperatures, nutrient depletion, etc. (Li et al., 2017). The mass production of astaxanthin from *H. pluvialis* is carried out by 2-stage batch culture. In the first stage, biomass production occurs, whereas in the second stage, the cultures are stressed to induce astaxanthin production.

Microalgae can synthesize high amount of carotenoids like astaxanthin, β-carotene, canthaxanthin, and echinenone under unfavorable conditions (Singh et al., 2019). *Botryococcus braunii*, *Chlorella* sp., *Chlorococcum* sp., *Coelastrella striolata*, *Haematococcus pluvialis*, *Dunaliella salina*, *Nanochloropsis* sp., *Scenedesmus* sp., and *Arthrospira platensis* are well-known for the production of β-carotene, lutein, canthaxanthin, astaxanthin, and fucoxanthin (Ambati et al., 2018).

The combination of algal β-carotene isomers has a higher accumulation of more than 10 times in comparison with synthetic carotenoids. Carotenoids, like β-carotene, lutein, zeaxanthin, and fucoxanthin involve in photosynthesis process like chlorophylls and absorb blue, violet, and green light of the visible spectrum and thereby reflect yellow, orange, and red colors (Naruka et al., 2019). Gunerken et al. (2015) states that algal carotenoids are given more importance but their commercial use is quite little owing to their high extraction and purification cost.

4.3.3 PHYCOBILINS

PBPs are creative of apoproteins (α and β subunits) and covalently related to prosthetic groups, phycobilins. The two preserved subunits, α and β form a αβ monomer and aggregates to form αβ trimers and αβ hexamers. They are sunlight harvesting pigments found normally in Cyanophyceae and Cryptophyceae. Based on the amino acid sequences and spectroscopic analysis, they are divided into red (phycoerythrin (PE)), blue (phycocyanin) and allophycocyanin (APC). PC, APC, and PE, are consisting of different non-covalently connected subunits with molecular weight of about 16,000–20,000 Daltons, 15,500–17,500 Daltons, and 20,000–22,000 Daltons, respectively. Their constitution varies with species and environmental settings (Chu, 2012). They are used in various fields like markers for electrophoresis, isoelectric focusing, flow cytometry, etc., because of their fluorescent properties and they also have antioxidant properties (Raposo et al., 2013).

It can defuse the reactive oxygen species (ROS) because of their chemical structures and chelating nature (Rodriguez-Sanchez et al., 2012). PBPs are produced commercially from two well-known species: PC from *Arthrospira* sp. and PE from *Porphyridium* sp. (Rodriguez-Sanchez et al., 2012; Borowitzka, 2013). These protein-bound exclusive pigments are found in microalgae and are degraded under stress environments like phosphorus, nitrogen, and sulfur starvation (Eriksen, 2008; Hifney et al., 2013).

PBPs are formed by bonding protein with phycobilins and chromophores. They are colored pigments and found in red algae and cyanobacteria. *Arthrospira platensis* and *Aphanizomenon flos-aquae* are the major sources of phycobiliprotein. They are commercially used as organic dyes in make-ups and in pharmaceutical industries owing to their antioxidant, anti-inflammatory, neuroprotective, and hepatoprotective properties. The volume of global market of PC averages around 5–10 million USD. The commercial producers of PBPs are from the cyanobacteria *Arthrospira* and rhodophyte *Porphyridium*.

4.4 CULTIVATION OF MICROALGAE FOR PIGMENT PRODUCTION

The cultivation methods of microalgae are the main restricting factors for producing microalgae pigments at the industrial level, and developing low-cost cultivation methods for their economical production of pigments is indispensable. There are different modes of cultivation of microalgae: photoautotrophic, heterotrophic, mixotrophic, and photoheterotrophic. In autotrophic cultivation, the microalgae produce raw compounds in daylight to process inert carbon source, CO_2 (Khan et al., 2018). The open pond system is the ancient method for autotrophic cultivation and due to its high susceptibility to contamination and fluctuations in temperature, the open pond system is inappropriate for industrial scale level production.

The heterotrophic cultivation method is depending on the metabolism of organic compounds that afford carbon source and they can grow under dark conditions. This kind of cultivation is a proven method for cell growth and considerably decreasing the cultivation cost. Glucose is used as the main source for this type of cultivation, and it is possible that low-cost alternatives could be explored for use in the heterotrophic method of cultivation. Algae like *Arthrospira*, *Dunaliella*, and *Chlorella* were effectively cultivated for single-cell protein and pigment production (Mata et al., 2010). For the production of pharmaceutical products, closed photobioreactors are preferred for maintenance of pure cultures. The heterotrophic microalgae should be cultivated in conventional bioreactors without light. Bumbak et al. (2011) have testified that the cultivation of heterotrophic microalgae is an encouraging method in the active fermentation set-up for bacteria. The main rewards of cultivating microalgae in heterotrophic conditions are: (i) microalgae are potential to grow even in lack of light; (ii) their cell density increases; (iii) they could be cultivated in industrial-scale fermenters; and (iv) they could be cultivated at reduced cost.

The primary xanthophyll pigment, lutein is produced by microalgal species akin to *Muriellopsis* sp., *Scenedesmus* sp., *Dunaliella* sp. and *Chlorella* sp. at high concentrations. Lutein protects the eye from oxidative damage by blue light and lutein intake decrease the age-linked macular deterioration (Hu et al., 2018). Glucose is the preferred cheap source for heterotrophic cultivation of microalgae *C. protothecoides* and *C. pyrenoidosa* for lutein production. Glycerol has been used for the cultivation of *Scenedesmus* sp. for lutein production (Yen et al., 2011).

Astaxanthin from *H. pluvialis* has antioxidant activity 90 times more than that of synthetic astaxanthin without any toxicity (Régnier et al., 2015). Natural astaxanthin from microalgae are derived mainly from green algae *Haematococcus pluvialis* (Li et al., 2011), and later

Chlorella zofingensis (Liu et al., 2014) and *Chlorococcum* have been testified for their capability to produce astaxanthin. Astaxanthin from *H. pluvialis* has got the sanction of FDA to be used as human dietetic complement, while other sources are mainly utilized as aquaculture feed.

Heterotrophic growth of *H. pluvialis* in dark could assimilate acetate and hence the inclusion of acetate in the medium enhances the astaxanthin production. Ferrous ions enhance the astaxanthin accumulation and when added with acetate, astaxanthin production was greater (Zhang et al., 2016). The astaxanthin production in *H. pluvialis* increases with increasing concentrations of NaCl in the growth medium. Liu et al. (2014) reported that cultivation of *H. pluvialis* is a challenging task due to its slow growth and bacterial contamination in open cultivation system. The addition of glucose, fructose, and sucrose as carbon sources can be considered as an alternative for the heterotrophic cultivation of *Chlorella zofingensis* for astaxanthin production (Liu et al., 2012).

PC has been used as coloring agents in chewing gums, candies, jellies, and dairy products (Sekar and Chandramohan, 2008). The development of PC producing *Arthrospira platensis* is a challenging one in autotrophic cultivation and hence heterotrophic method is preferable. The strain is cultured utilizing glucose as a carbon source for producing PC. The unicellular red alga, *Galdieria sulphuraria*, is a capable strain for heterotrophic PC production. *G. sulphuraria* is a polyextremophilic algae and it can be grown in the dark condition at very low pH. It grows utilizing sugar and sugar alcohols as carbon sources under heterotrophic and mixotrophic conditions (Jain et al., 2014).

Dunaliella salina is cultured in open ponds with high salinity for viable production of β-carotene (Spolaore et al., 2006). This strain *Dunaliella* sp. can grow under heterotrophic conditions utilizing glucose and acetate as the carbon source. There are reports that photoheterotrophic cultivation of *D. salina* for β-carotene with acetate and mixotrophic cultivation with glucose favors carotene production (Mojaat et al., 2008; Morowvat and Ghasemi, 2016). Nevertheless, these were not followed more because of their low growth prospective and low β-carotene production of *D. salina* under sub optimal mixotrophic cultivation. Thus, the major carotenoids lutein, astaxanthin, and PC could be extracted economically and beneficially from heterotrophically cultivated microalgae.

4.5 FACTORS AFFECTING PIGMENT PRODUCTION

The light, temperature, and nutritional requirements are important factors for the growth of microalgae and its pigments.

4.5.1 ENVIRONMENTAL FACTORS

Light and temperature play the vital role in microalgal cultivation. Light is the most important factor for restricting the microalgae growth. Different spectral properties of light influence the comparative pigment composition and act as photomorphogenic signals in microalgae (Kagawa and Suetsugu, 2007). Pisal and Lele (2005) have testified that light intensity plays a major role in the enhanced production of carotenoids from *D. salina*. The duration of light and its' intensity directly influence the growth of algae and photosynthesis. Microalgae require light for photochemical phase to produce adenosine triphosphate (ATP), nicotinamide adenine dinucleotide phosphate-oxidase (NADPH) and require dark to produce required molecules for the growth (Cheirsilp and Torpee, 2012). Al-Qasmi (2012) revealed that the increase in light duration is directly proportional to the increase in cultured microalgae. Light intensity performs a significant part by dominating the pigment build up in algal cells. β-carotene increased sharply with light intensity at higher irradiation (11.2 μmol/m^2/sec). Astaxanthin production in *H. pluvialis* is higher under light intensity of 546 μmol/m^2/sec (Imamoglu et al., 2009). The light intensity greatly influences the culture concentration, cell ripeness and pigment yield. The white light strength for chlorophyll synthesis and PC is higher in *S. fussiformis* (Madhyastha and Vatsala, 2007).

The relationship between temperature and algal growth rate increases exponentially until the optimum temperature is reached. Microalgae can grow in a wide temperature range between 5°C and 40°C. The effect of temperature on the growth of microalgae demonstrated that the growth rate was highest in the temperature range of 27–31°C (Kitaya et al., 2005). The carotenoid production enhances in the blue green microalgae when cultured in higher temperature (Garcia-Gonzalez et al., 2005). The phycobiliprotein from *Anabaena* sp. was higher in the optimum temperature of 30°C whereas the optimum temperature for *S. platensis*, *Anabaena* sp., *Nostoc* sp. was 25, 35 and 36°C, respectively (Hemlata and Fatma, 2009). Bocanegra et al.

(2004) have assessed that the production of astaxanthin from *H. pluvialis* is higher at the optimum temperature of 28°C. Sanchez et al. (2008) found that 55 and 60°C were the extreme temperatures for carotenoid production from *C. vulgaris* and *Nannochloropsis gaditana* correspondingly.

The microalgae have a pH range in which growth is optimal depending on chemical equilibrium and are more accustomed to assimilate. Wang et al. (2010) has reported that the optimal pH range for the growth is between 7 and 9. The phycobiliprotein from the blue-green microalgae, *S. platensis* was enhanced at pH 8 whereas phycobiliprotein from the *Nostoc* sp. was enhanced at pH 9 (Hemlata and Fatma, 2009). Chauhan and Pathak (2010) reported that the chlorophyll production from *S. platensis* was achieved at pH 9. The optimum production of carotenoids from *Scenedesmus almeriensis* was at pH 8 whereas for *Chlorococcum citriforme* and *Neospongiococcus gelatinosum* the optimum production was at pH 7 (Campo et al., 2000).

4.5.2 NUTRIENTS

Nitrogen is essential for the life as it is the central element of protein and an inherent material and it is plentiful in microalgae following carbon, oxygen, and hydrogen (Benavente-Valdes et al., 2016). When microalgal cells grow and divide, they need a supply of nitrogen. Under limited nitrogen supply, the photosynthesis process may continue and the resultant compounds give the minimum amount of pigments. The chlorophyll a and b production from *Chlorella minutissima* increased when nitrogen was added to the medium (Ordog et al., 2012). All through the nitrogen starvation, the microalgae stop splitting as nitrogen is the basic requirements for cell metabolism. Chlorophyll production by *S. platensis* increases with the boost in nitrogen intensity in the culture medium. The phycobiliprotein by *Anabaena* was high in nitrogen free media whereas PBPs by the *Fischerella* sp. was higher in nitrogen supplemented media (Soltani et al., 2007). Nitrogen in the medium increases the pigment production and this strategy can be used for large-scale cultivation.

Phosphorous, the major element in the cell plays an important role in producing ATP for nucleic acid metabolism. Qu et al. (2008) have reported that phosphate assimilation by *Chlorella pyrenoidosa* in biomass production was observed under different culture conditions. The use of phosphorous deprivation as medium constitution reduces process costs in large scale cultivation both in the open and closed systems.

4.6 METABOLIC ENGINEERING

The metabolic pathways can be exploited to develop the pigment substance of microalgae that can be either through upregulation/downregulation of enzymes responsible for pigment synthesis and the formation of metabolic sink (Mulders et al., 2014). The regulation of enzymes can stimulate the synthesis of pigments and thereby increasing the production of the desired pigments. Rosenberg et al. (2008) reports that over expressing enzymes are openly liable for the end production of targeted pigments and this can be used for concurrent boosting of various pigment production. The main challenge linked with the overproduction of pigments is storage space and transportation. For overproduction of microalgal pigments, the application of metabolic engineering procedures like enzyme expression seems to be advantageous. Further research is mandatory to develop the present metabolic engineering strategies for pigment production in microalgae.

Factors like light, temperature, nutrients, etc., influence the algal pigment production. The upregulation of *psy* gene in *Chlorella zogengiensis* under nitrogen limitation resulted in a 4-fold increase in astaxanthin production (Mao et al., 2018). Couso et al. (2012) have reported that exposure of *C. reinhardtii* to high light intensity triggered the expression levels of *psy* and *pds* and increased the chlorophyll production by 2 and 4 folds respectively. The genetic analysis revealed that *Lcyβ* mRNA and the level of carotenoids were increased in *D. salina* under various conditions like light intensity and nutrition (Ramos et al., 2008). The gene *chyB* responsible for zeaxanthin production in *C. reinhardtii* is also upregulated by the light. The production of lutein from *C. reinhardtii* is mediated through 2 cytochrome P450 dependent hydroxylases and under light stress, *cyp97a5* and *cyp97c3* encoding the hydroxylases are up regulated and thereby increasing the lutein production (Couso et al., 2012).

4.7 APPLICATIONS OF ALGAL PIGMENTS

4.7.1 FOOD COLORANTS

Phycobilins are utilized as organic dyes in foodstuff and cosmetic industry. In food products, they are used as colorants in fermented dairy products, ice creams, milkshakes, etc. (Sekar and Chandramohan, 2008). The microalgae like *Arthrospira platensis Chlorella* sp. *Dunaliella terticola, Dunaliella salina*, *Aphanizomenon flos-aquae* are reported to contain nutritional value with high protein content (Soletto et al., 2005). Microalgae, *Arthrospira* sp., *Chlorella* sp., *Nitzchia* sp., *Navicula* sp., *Crypthecodinium* sp., are also sources of food for many animals and are used as feed for marine and earthly animals. Sathasivam et al. (2019) reports that of late microalgae are getting prominence in health-food supermarkets and *Chlorella* and *Arthrospira* are dominating the algal market.

β-carotene is utilized as a pro-vitamin A (retinol) and also it has a main role in the making of healthy foods (Krinsky and Johnson, 2005; Spolaore et al., 2006). β-carotene from *Dunaliella* is utilized to draw the attention of the consumers as foodstuff colorants to increase the look of margarine, cheese, fruit juices, baked goods, dairy products, canned foods, and confectionary. Adding up, β-carotene is also used as a colorant and a pioneer of vitamin A in pet foods (Cantrell et al., 2003). β-carotene from microalgae is most widely used as foodstuff coloring agents in pasta, fruit juices, soft drinks, confectionery, margarine, dairy products, and salad dressings (Christaki et al., 2011, 2013; Guedes et al., 2011). PC, a blue pigment is susceptible to high temperatures and light and it could be used in several foodstuff produce like chewing gums, candies, dairy products, jellies, ice creams, and beverages; Its' color is steady in dried up provisions (Dufossé, 2009; Gouveia, 2014). PE, a red pigment can be utilized for the pigmentation of confectionaries, gelative desserts, and milk produce. Microalgal pigments can be used to enhance the yellowish color of egg yolk and chicken hide thereby improving the appearance of pet foods (Figure 4.3) (Spolaore et al., 2006; Mata et al., 2010; Guedes et al., 2011; Skjanes et al., 2013).

4.7.2 HEALTH BENEFITS OF ALGAL PIGMENTS

4.7.2.1 ANTIOXIDANT ACTIVITY

The microalgal pigments like fucoxanthin, phycoerythrobilin, chlorophyll, and their derivatives comprise potential antioxidant activity. The antioxidant activity of these pigments depends on their structural features (porphyrin ring, phythyl chain and conjugated double bonds). Chlorophyll exhibits antioxidant activity and its' porphyrin ring plays a vital role for its activity. Chlorophyll derivatives which are deficient in Mg^{2+} and phytyl chain possess more antioxidant activity compared to chlorophyll. Chlorophyll derivatives from *Enteromorpha prolifera* have strong antioxidant activity (Pangestuti and Kim, 2011).

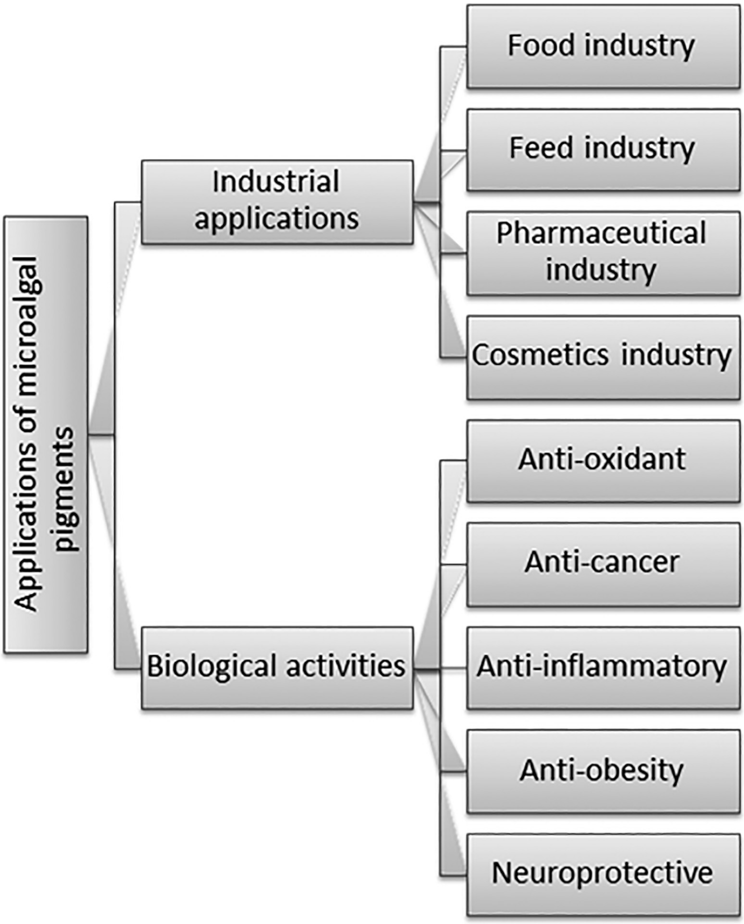


FIGURE 4.3 Applications of natural pigments from microalgae.

Fucoxanthin from *Hijikia fusiformis*, *Undaria pinnatifida* and *Odontella aurita* has major antioxidant activity. Many studies testify that the number of hydroxyl groups on fucoxanthin is linked to the effects of ROS suppression (Yang et al., 2019). β-carotene from *Dunaliella* stimulates antioxidant enzymes like catalase, superoxide dismutase (SOD), peroxidase, and antilipid peroxidase. The algal carotenoids like β-carotene from *Arthrospira platensis*, astaxanthin from *Haematococcus pluvialis*, lutein from *Botryococcus braunii* have significant antioxidant activities by substantially increasing the SOD, peroxidase, and catalase (Cezare-Gomes et al., 2019).

Phycoerythrobilin from *Porphyra* and PBPs from the *Lyngbya* sp. have tough antioxidant activity. The antioxidant properties of PBPs in *Arthrospira* have excellent dietary applications. PC derivatives from *Aphanizomenon flos-aquae* (AFA) is a powerful antioxidant and used against oxidative damage (Benedetti et al., 2004). Because of the stronger antioxidant activity, astaxanthin acts as a super vitamin E and is 10 times higher than β-carotene and 500 times more effective than α-tocoferol (Begum et al., 2016).

4.7.2.2 ANTICANCER ACTIVITY

The cancer cells in humans are stimulated by free radicals and the natural anticancer drugs have got positive impact in the healing of cancer. The algal pigments have radical scavenging activity and they can be applied to indirectly reduce the cancer development. Lutein, β-carotene and chlorophyll a from *Porphyra tenera* showed antimutagenic activity in *Salmonella typhimurium*. Siphonaxanthin from *Codium fragile* is an effective evolution inhibitor against HL-60 cells, better than fucoxanthin. The structure of fucoxanthin have epoxide and allenic bond whereas siphonaxanthin does not have these functional group but have additional hydroxyl group. Fucoxanthin exerts antitumor activity through apoptotic induction (Kotake et al., 2005). Antiproliferative activity of fucoxanthin, fucoxanthinol, β-carotene and astaxanthin evaluated, established that fucoxanthin and fucoxanthinol have notable antiproliferative effects on human T-cell leukemia virus *in vitro* (Ishikawa et al., 2008). Hosokawa et al. (2010) have assessed that fucoxanthin decreases the viability of human colon cancer cell lines and stimulate apoptosis in a dosage and time related manner. Fucoxanthin inhibits the increase of human colon cancer cell lines by induction of cell cycle arrest at G0/G1 phase (Das et al., 2005). Fucoxanthin has significant antiproliferative effects on human urinary bladder cancer cell line by stirring up apoptosis and it was characterized by morphological changes.

PC has significant anticancer properties opposed to human melanoma and human breast adenocarcinoma. It promotes the manifestation of CD59 protein in HeLa cells and has antineoplastic effects on colon carcinogenesis (Jiang et al., 2017). PC contains an anti-cancerous effect by dipping the tumor necrosis factor (TNF-alpha) in the blood serum of mice treated with endotoxin, and it also exhibited neuroprotective effects in the rat cerebella granule cell cultures. Shih et al. (2003) have testified that APC inhibits enterovirus 71-induced cytopathic effects, viral sign development, and viral-induced apoptosis. β-carotene from *Dunaliella* sp. comprises of 40% 9-cis and 50% all-trans stereoisomers that play a decisive role in reducing the incidence of numerous varieties of cancer and degenerative diseases (Begum et al., 2016). *Dunaliella* sp. contains xanthophylls that showed enhanced anti-cancerous activity and upper bioactivity (Roodenburg et al., 2000). β-carotene can induce the immune system and could be involved in curing more than 60 dreadful diseases including cancer, coronary heart diseases, premature aging and arthritis (Mattson, 2004).

4.7.2.3 ANTI-INFLAMMATORY ACTIVITY

The microalgal pigments have promising anti-inflammatory activities that are mainly due to the modulation of macrophage function. Pheophytin α from *E. prolifera* have buried 12-*o*-tetradecanoylphorbol-13-acetate-induced superoxide radicals. Fucoxanthin possesses anti-inflammatory properties both *in vitro* and *in vivo* in response to bacterial lipopolysaccharides (LPSs). The anti-inflammatory properties of fucoxanthin are similar to the commercially available anti-inflammatory steroidal drugs. The inhibition of nuclear factor-kB (NF-kB) and phosphorylation of mitogen activated protein kinases are responsible for the anti-inflammatory properties of fucoxanthin. PC reduces allergic inflammatory response by suppressing antigen-specific IgE antibody (Nemoto-Kawamura et al., 2004). PC is effective in the treatment of acute lung injury by inhibiting inflammatory response and apoptosis in lung tissue (Leung et al., 2013). Phycocyanobilin, are found in blue-green algae and contain potential anti-inflammatory effects.

4.7.2.4 ANTI-OBESITY ACTIVITY

Obesity is one of the greatest health challenges in several modern and developing countries. Wang et al. (2008) have reported that excess growth of adipose tissue from adipocyte hypertrophy and the addition of new adipocytes from precursor cells and regulation of adipogenesis seems to be the best strategy to treat obesity. Fucoxanthin from *U. pinnatifida* inhibits the differentiation of 3T3-L1 preadipocytes into adipocytes. Okada et al. (2008) reported that carotenoids with keto group, expoxy group, hydroxy-carotenoid did not show inhibitory outcome on adipocyte differentiation, whereas the healing with fucoxanthin and neoxanthin has noteworthy anti-obesity effect. The natural pigment, fucoxanthin from marine algae can be used as slimming supplements and medicines in the prevention and management of obesity. Siphonaxanthin, a green algal pigment lowers the lipid accumulation in KK-Ay mice and also lowers the expression of key adipogenesis genes *Cebpa*, *Pparg*, *Fabp4* and *Scd1* (Li et al., 2015). PC stimulates antiobesity effect which might be due to the hypocholesterolemic action. PC inhibits pancreatic lipase resulting in the inhibition of intestinal absorption of dietary fat which can lower serum cholesterol, total cholesterol, triglyceride, and low-density lipids (Pangestuti and Kim, 2011).

4.7.2.5 NEUROPROTECTIVE ACTIVITY

Neurodegenerative diseases surpass cancer and are the next most reason of casualty among elders. Fucoxanthin from *H. fusiformis* inhibited N-myc expression and cell cycle progression of GOTO cells, human neuroblastoma cell line. Khodesevich and Monyer (2010) have found that fucoxanthin reduced cell damage in cortical neurons during hypoxia and oxygen reperfusion. Astaxanthin is a first-rate candidate for testing Alzheimer’s diseases and other neurological diseases. Astaxanthin mediated neuroprotection in subarachnoid hemorrhage is credited to the downregulation of augmented nuclear factor kappa B activity and the expression of inflammatory cytokines and intercellular adhesion molecule 1 (Grimmig et al., 2017). PC showed protecting role against hippocampus neuronal cell death and enhanced locomotive behavior in Mongolian Gerbil (Penton-Rol et al., 2011). The neuroprotective activity of PC is accredited towards its antioxidant, anti-inflammatory, and immunomodulatory properties (Wu et al., 2016).

4.7.3 SKIN CARE BENEFITS OF ALGAL PIGMENTS

Microalgal extracts are commonly used in the countenance and skincare products for refreshing, antiaging, anti-irritant, etc. They are also utilized as sun protectants and hair care stuff. Protein rich extort from *Arthrospira* plays an essential role in early skin aging, tightening the skin and *Chlorella vulgaris* stimulates collagen synthesis in skin and supports tissue regeneration and wrinkle reduction. A product has been launched from *Nannochloropsis oculata* with exceptional skin contraction properties and *D. salina* induce cell propagation and optimistically manipulate the energy metabolism of skin. Astaxanthin from *H. pluvialis* exhibited enhanced improvements in skin wrinkles, skin texture, moisture content, etc. (Tominaga et al., 2012). Astaxanthin plays an important role in protecting against photooxidative damage (Camera et al., 2009). Algal pigments showed considerable antioxidant effect and they play a potential role in restricting aging due to the creation of free radicals in the cells. These pigments, particularly are vibrant dyes even at very low levels (parts per million), and possess significant utilities in the pharmaceutical industry (fluorescence-based indicators, biochemical tracers in immune assays) and in the cosmetic industry (skin cream to stimulate collagen synthesis).

4.8 FUTURE PERSPECTIVES AND CONCLUSIONS

For the past about six or seven decades, the world is consuming a lot of non-degradable materials produced from plastics, and discharge them in the environment after their wear and tear. This has caused irreparable damage to the environment and ecology. Confronting with such environmental damages finding alternative eco-friendly, harmless, and degradable materials were imperative to maintain our environment in a sustainable manner. Awareness created in this respect has turned the attention of the stakeholders towards the production of degradable products from natural sources. By the way production of natural colorants from plants, microbes, and algae for application in food, medicine, cosmetic, textile, etc., has emerged and progressed considerably. Among them algae have a major stake and a better prospective natural resource in producing degradable natural products like coloring pigments, etc.

Microalgae have now emerged as a major prospective natural resource for producing pigments such as carotenoids, chlorophylls, and PBPs for commercial applications in the food, pharma, and cosmetics industry. These pigments have proved their incredible capabilities of coloring foods, antioxidant, anticancer, anti-obesity, anti-inflammatory, and neuroprotective activities along with skincare benefits. Yet exploitation of pigment producing algae from unexplored niches would be a fruitful venture to unravel novel high-yielding pigment producers and other metabolites. Metabolic engineering allows manipulating microalgae to have high growth for biomass and pigment production. The exploitation of microalgae for natural colorants can increase the profitability and health benefits overcoming sustainability challenges. Nevertheless, the bottlenecks, like high production costs and low yields, stability of the pigments, etc., need to be addressed before microalgae can be moved from niche markets to large-scale use. The future of algal pigments is bright, colorful, and ecologically sustainable.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGMENTS

Dr. C.K. Venil thanks the UGC for awarding the Dr. D.S. Kothari Postdoctoral Fellowship (BL/17-18/0479). Also, the authors thank Anna University, Regional Campus – Coimbatore for providing necessary facilities to carry out the project work. Professor Laurent Dufossé deeply thanks the Conseil Régional de La Réunion, Réunion Island, Indian Ocean, for continuous financial support of research activities dedicated to microbial pigments. This work was supported and funded by the University Grants Commission (UGC), New Delhi under the Dr. D.S. Kothari Post-doctoral Fellowship (BL/17-18/0479) dated 25th September 2018.

KEYWORDS

- **biomass production**
- **cultivation**
- **factors**
- **food colorants**
- **health benefits**
- **microalgae**
- **pigments**
- **skincare**

REFERENCES

Al-Qasmi, M., (2012). A review of effect of light on microalgae growth. *Proceedings of the World Congress on Engineering, 1*, 3–8.

Ambati, R. R., Gogisetty, D., Aswathanarayana, R. G., et al., (2018). Industrial potential of carotenoid pigments from microalgae: Currents trends and future prospects. *Critical Reviews in Food Science and Nutrition, 59*, 1880–1882.

Begum, H., Yusoff, F. M., Banerjee, S., Khatoon, H., & Shariff, M., (2016). Availability and utilization of pigments from microalgae. *Critical Reviews in Food Science and Technology, 56*, 2209–2222.

Benavente-Valdés, J. R., Aguilar, C., Contreras-Esquivel, J. C., Méndez-Zavala, A., & Montañez, J., (2016). Strategies to enhance the production of photosynthetic pigments and lipids in *Chlorophycae* species. *Biotechnology Reports, 10*, 117–125.

Benedetti, S., Benvenuti, F., & Pagliarani, S., (2004). Antioxidant properties of a novel phycocyanin extract from the blue-green alga *Aphanizomenon flos-aquae*. *Life Science, 75*, 2353–2362.

Bocanegra, D. A. R., Guerrero, L. I., Martinez, J. F., & Tomasini, C. A., (2004). Influence of environmental and nutritional factors in the production of astaxanthin from *Haematococcus pluvialis*. *Bioresource Technology, 92*(2), 209–214.

Borowitzka, M. A., (2013). High-value products from microalgae – their development and commercialization. *Journal of Applied Phycology, 25*, 743–756.

Bumbak, F., Cook, S., Zachleder, V., Hauser, S., & Kovar, K., (2011). Best practices in heterotrophic high cell density microalgal processes: Achievements, potential and possible limitations. *Applied Microbiology and Biotechnology, 91*, 31–46.

Camacho, F., Macedo, A., & Malcata, F., (2019). Potential industrial applications and commercialization of microalgae in the functional food and feed industries: A short review. *Marine Drugs, 17*(6), 312.

Camera, E., Mastrofrancesco, A., Fabbri, C., et al., (2009). Astaxanthin, canthaxanthin and beta-carotene differently affect UV-A-induced oxidative damage and expression of oxidative stress-responsive enzymes. *Experimental Dermatology, 18*, 222–231.

Campo, D. J. A., Moreno, J., Rodriguez, H., Vargas, M. A., Rivas, J., & Guerrero, M. G., (2000). Carotenoid content of chlorophycean microalgae: Factors determining lutein accumulation in *Muriellopsis* sp. (*Chlorophyta*). *Journal of Biotechnology, 76*, 51–59.

Cantrell, A., McGarvey, D. J., Trustcott, G., Rancan, F., & Bohm, F., (2003). Singlet oxygen quenching by dietary carotenoids in a model membrane environment. *Archives of Biochemistry and Biophysics, 412*, 47–54.

Cezare-Gomes, E. A., Mejia-da-Silva, L. D., Pérez-Mora, L. S., et al., (2019). Potential of microalgae carotenoids for industrial application. *Applied Biochemistry and Biotechnology, 188*, 602–634.

Chauhan, U. K., & Pathak, N., (2010). Effect of different conditions on the production of chlorophyll by *Spirulina platensis*. *Journal of Algal Biomass Utilization, 1*, 89–99.

Cheirsilp, B., & Torpee, S., (2012). Enhanced growth and lipid production of microalgae under mixotrophic culture condition: Effect of light intensity, glucose concentration and fed-batch cultivation. *Bioresource Technology, 110*, 510–516.

Christaki, E., Bonos, E., Giannenas, I., & Florou-Paneri, P., (2013). Functional properties of carotenoids originating from algae. *Journal of the Science of Food and Agriculture, 93*, 5–11.

Christaki, E., Florou-Paneri, P., & Bonos, E., (2011). Microalgae: A novel ingredient in nutrition. *International Journal of Food Science and Nutrition, 62*, 794–799.

Chu, W. L., (2012). Biotechnological applications of microalgae. *International Journal of Medical Science and Education, 6*, 24–37.

Couso, I., Vila, M., Vigara, J., et al., (2012). Synthesis of carotenoids and regulation of the carotenoid biosynthesis pathway in response to high light stress in the unicellular microalga *Chlamydomonas reinhardtii*. *European Journal of Phycology, 47*(3), 223–232.

Cuaresma, M., Janssen, M., Vilchez, C., & Wijffels, R. H., (2011). Horizontal or vertical photobioreactors? How to improve microalgae photosynthetic efficiency. *Bioresource Technology, 102*, 5129–5137.

Cubas, C., Gloria, L. M., & Gonzalez, M., (2008). Optimization of the extraction of chlorophylls in green beans (*Phaseolus vulgaris* L.) by N,N-dimethylformamide using response surface methodology. *Journal of Food Composition and Analysis, 21*, 125–133.

Das, S. K., Hashimoto, T., Shimizu, K., et al., (2005). Fucoxanthin induces cell cycle arrest at G0/G1 phase in human colon carcinoma cells through up-regulation of p21WAF1/Cip1. *Biochim. Biophys. Acta, 1726*(3), 328-335.

Daubrawa, F., Sies, H., & Stahl, W., (2005). Astaxanthin diminishes gap junctional intercellular communication in primary human fibroblasts. *Journal of Nutrition, 135*, 2507–2511.

Del Campo, A. J., Garcia-Gonzalez, M., & Guerrero, M. G., (2007). Outdoor cultivation of microalgae for carotenoid production: Current state and perspectives. *Applied Microbiology and Biotechnology, 74*, 1163–1174.

Dufossé, L., (2009). Microbial and microalgal carotenoids as colorants and supplements. In: Britton, G., Liaaen-Jensen, S., & Pfander, H., (eds.), *Carotenoids, Nutrition and Health* (Vol. 5). Birkhauser Verlag, Basel, Switzerland.

Eriksen, N. T., (2008). Production of phycocyaninda pigment with applications in biology, biotechnology, foods and medicine. *Applied Microbiology and Biotechnology, 80*, 1–14.

Gao, C., Zhai, Y., Ding, Y., & Wu, Q., (2010). Application of sweet sorghum for biodiesel production by heterotrophic microalga *Chlorella protothecoides*. *Applied Energy, 87*, 756–761.

Garcia-Gonzalez, M., Moreno, J., Manzano, J. C., Florencio, F. J., & Guerrero, M. G., (2005). Production of *Dunaliella salina* biomass rich in 9-cis-β-carotene and lutein in a closed tubular photobioreactor. *Journal of Biotechnology, 115*, 81–90.

Gouveia, L., (2014). From tiny microalgae to huge biorefineries. *Oceanography, 2*, 120.

Grimmig, B., Kim, S. H., Nash, K., Bickford, P. C., & Douglas, S. R., (2017). Neuroprotective mechanisms of astaxanthin: A potential therapeutic role in preserving cognitive function in age and neurodegeneration. *GeroScience, 39*(1), 19–32.

Guedes, A. C., Amaro, H. M., & Malcata, F. X., (2011). Microalgae as sources of carotenoids. *Marine Drugs, 9*, 625–644.

Gunerken, E., D'Hondt, E., Eppink, M. H. M., Garcia-Gonzalez, L., Elst, K., & Wijffels, R. H., (2015). Cell disruption for microalgae biorefineries. *Biotechnology Advances, 33*, 243–260.

Hemlata, & Fatma, T., (2009). Screening of Cyanobacteria for phycobiliproteins and effect of different environmental stress on its yield. *Bull. Environ. Contam. Toxicol., 83*, 509.

Hifney, A. F., Issa, A. A., & Fawzy, M. A., (2013). Abiotic stress-induced production of β-carotene, allophycocyanin and total lipids in *Spirulina* sp. *Journal of Biology and Earth Science, 3*, 54–64.

Hosokawa, M., Miyashita, T., Emi, S., Tsukui, T., Beppu, F., Okada, T., & Miyashita, K., (2010). Fucoxanthin regulates adipocytokine mRNA expression in white adipose tissue of diabetic/obese KK-Ay mice. *Archives of Biochemistry and Biophysics, 504*, 17–25.

Hu, J., Nagarajan, D., Zhang, Q., Chang, J. S., & Lee, D. J., (2018). Heterotrophic cultivation of microalgae for pigment production: A review. *Biotechnology Advances, 36*, 54–67.

Imamoglu, E., Dalay, M. C., & Sukan, F. V., (2009). Influences of different stress media and high light intensities on accumulation of astaxanthin in the green alga *Haematococcus pluvialis*. *New Biotechnology, 26*, 199–204.

Ishikawa, C., Tafuku, S., Kadekaru, T., Sawada, S., Tomita, M., Okudaira, T., Nakazato, Tet al., (2008). Antiadult T cell leukemia effects of brown algae fucoxanthin and its deacetylated product, fucoxanthinol. *International Journal of Cancer, 123*, 2702–2712.

Jain, K., Krause, K., Grewe, F., Nelson, G. F., Weber, A. P., Christensen, A. C., & Mower, J. P., (2014). Extreme features of the *Galdieria sulphuraria* organellar genomes: A consequence of polyextremophily? *Genome Biology and Evolution, 7*(1), 367–380.

Jiang, L., Wang, Y., Yin, Q., Liu, G., Liu, H., Huang, Y., & Li, B., (2017). Phycocyanin: A potential drug for cancer treatment. *Journal of Cancer, 8*(17), 3416–3429.

Kagawa, T., & Suetsugu, N., (2007). Photometrical analysis with photosensory domains of photoreceptors in green algae. *FEBS Letters, 581*, 368–374.

Khan, M. I., Shin, J. H., & Kim, J. D., (2018). The promising future of microalgae: Current status, challenges and optimization of a sustainable and renewable industry for biofuels, feed and other products. *Microbial Cell Factory, 17*, 36.

Khodosevich, K., & Monyer, H., (2010). Signaling involved in neurite outgrowth of postnatally born subventricular zone neurons *in vitro*. *BMC Neuroscience, 11*, 18.

Kiesenhofer, D. P., & Fluch, S., (2018). The promises of microalgae – still a long way to go. *FEMS Microbiology Letters, 35*, 257.

Kitaya, Y., Azuma, H., & Kiyota, M., (2005). Effects of temperature, CO_2/O_2 concentrations and light intensity on cellular multiplication of microalgae, *Euglena gracilis*. *Advances in Space Research, 35*(9), 1584–1588.

Kotake, N. E., Asai, A., & Nagao, A., (2005). Neoxanthin and fucoxanthin induce apoptosis in PC-3 human prostate cancer cells. *Cancer Letters, 220*, 75–84.

Koyande, A. K., Chew, K. W., Rambabu, K., Tao, Y., Chu, D. T., & Show, P. L., (2019). Microalgae: A potential alternative to health supplementation for humans. *Food Science and Human Wellness, 8*, 1–24.

Krinsky, N. I., & Johnson, E. J., (2005). Carotenoid actions and their relation to health and disease. *Molecular Aspects of Medicine, 26*, 459–416.

Leung, P. O., Lee, H. H., Kung, Y. C., Tsai, M. F., & Chou, T. C., (2013). Therapeutic effect of c-phycocyanin extracted from blue-green algae in a rat model of acute lung injury induced by lipopolysaccharide. *Evidence-Based Complementary and Alternative Medicine*, 916590.

Li, J., Zhu, D. L., Niu, J., Shen, S. D., & Wang, G., (2011). An economic assessment of astaxanthin production by large-scale cultivation of *Haematococcus pluvialis*. *Biotechnology Advances, 29*, 568–574.

Li, K., Cheng, J., Ye, Q., He, Y., Zhou, J., & Cen, K., (2017). *In vivo* kinetics of lipids and astaxanthin evolution in *Haematococcus pluvialis* mutant under 15% CO_2 using Raman microspectroscopy. *Bioresource Technology, 244*(2), 1439–1444.

Li, P., Miao, X., R., & Zhong, J., (2011). *In situ* biodiesel production from fast-growing and high oil content *Chlorella pyrenoidosa* in rice straw hydrolysate. *Journal of Biomedicine and Biotechnology, 2011*, 141201.

Li, Z. S., Noda, K., Fujita, E., Manabe, Y., Hirata, T., & Sugawara, T., (2015). The green algal carotenoid siphonaxanthin inhibits adipogenesis in 3t3-l1 preadipocytes and the accumulation of lipids in white adipose tissue of KK-Ay mice. *The Journal of Nutrition, 145*(3), 490–498.

Liu, J., Huang, J., Jiang, Y., & Chen, F., (2012). Molasses-based growth and production of oil and astaxanthin by *Chlorella zofingiensis*. *Bioresource Technology, 107*, 393–398.

Liu, J., Sun, Z., Gerken, H., Liu, Z., Jiang, Y., & Chen, F., (2014). *Chlorella zofingiensis* as an alternative microalgal producer of astaxanthin: Biology and industrial potential. *Marine Drugs, 12*(6), 3487–3515.

Lordan, S., Paul, R. R., & Stanton, C., (2011). Marine bioactives as functional food ingredients: Potential to reduce the incidence of chronic diseases. *Marine Drugs, 9*, 1056–1100.

Lu, Y., Zhai, Y., Liu, M., &. Wu, Q., (2010). Biodiesel production from algal oil using cassava (*Manihot esculenta* Crantz) as feedstock. *Journal of Applied Phycology, 22*, 573–578.

Madhyastha, H. K., & Vatsala, T. M., (2007). Pigment production in *Spirulina fussiformis* in different photophysical conditions. *Biomolecular Engineering, 24*, 301–305.

Mao, X., Wu, T., Sun, D., Zhang, Z., & Chen, F., (2018). Differential responses of the green microalga *Chlorella zofingiensis* to the starvation of various nutrients for oil and astaxanthin production. *Bioresource Technology, 249*, 791–798.

Markou, G., & Nerantzis, E., (2013). Microalgae for high-value compounds and biofuels production: A review with focus on cultivation under stress conditions. *Biotechnology Advances, 31*, 1532–1542.

Mata, T. M., Martins, A. A., & Caetano, N. S., (2010). Microalgae for biodiesel production and other applications: A review. *Renewable and Sustainable Energy Reviews, 14*, 217–232.

Mattson, M. P., (2004). Pathways towards and away from Alzheimer's disease. *Nature, 430*, 631–639.

Miazek, K., & Ledakowicz, S., (2013). Chlorophyll extraction from leaves, needles and microalgae: A kinetic approach. *International Journal of Agricultural and Biological Engineering, 6*, 107–115.

Mojaat, M., Pruvost, J., Foucault, A., & Legrand, F. J., (2008). Effect of organic carbon sources and Fe^{2+} ions on growth and β-carotene accumulation by *Dunaliella salina*. *Biochemical Engineering Journal, 39*(1), 177–184.

Morowvat, M. H., & Ghasemi, Y., (2016). Culture medium optimization for enhanced β-carotene and biomass production by *Dunaliella salina* in mixotrophic culture. *Biocatalysis and Agricultural Biotechnology, 7*, 217–223.

Mulders, K. J. M., Lamers, P. P., Martens, D. E., & Wijffels, R. H., (2014). Phototrophic pigment production with microalgae: Biological constraints and opportunities. *Journal of Phycology, 50*(2), 229–242.

Naruka, M., Khadka, M., Upadhayay, S., & Kumar, S., (2019). Potential applications of microalgae in bioproduct production: A review. *Octa Journal of Biosciences, 7*(1), 1–5.

Nemoto-Kawamura, C., Hirahashi, T., Nagai, T., Yamada, H., Katoh, T., & Hayashi, O., (2004). Phycocyanin enhances secretary IgA antibody response and suppresses allergic IgE antibody response in mice immunized with antigen-entrapped biodegradable microparticles. *Journal of Nutritional Science and Vitaminology, 50*(2), 129-136.

Novoveska, L., Ross, M. E., Stanley, M. S., Pradelles, R., Wasiolek, V., & Sassi, J. F., (2019). Microalgal carotenoids: A review of production, current markets, regulations and future directions. *Marine Drugs, 17*, 640.

Okada, T., Nakai, M., Maeda, H., Hosokawa, M., Sashima, T., & Miyashita, K., (2008). Suppressive effect of neoxanthin on the differentiation of 3T3-L1 adipose cells. *Journal of Oleo Science, 57*, 345–351.

Ördög, V., Stirk, W., Bálint, P., Staden, J., & Lovász, C., (2012). Changes in lipid, protein and pigment concentrations in nitrogen-stressed *Chlorella minutissima* cultures. *Journal of Applied Phycology, 24*, 907–914.

Pangestuti, R., & Kim, S. K., (2011). Biological activities and health benefit effects of natural pigments derived from marine algae. *Journal of Functional Foods, 3*, 255–266.

Pentón-Rol, G., Martínez-Sánchez, G., Cervantes-Llanos, M., et al., (2011). C-Phycocyanin ameliorates experimental autoimmune encephalomyelitis and induces regulatory T cells. *International Immunopharmacology, 11*(1), 29–38.

Pisal, D. S., & Lele, S. S., (2005). Carotenoid production from microalgae, *Dunaliella salina*. *Indian Journal of Biotechnology, 4*, 476–483.

Qu, C., Wu, Z., & Shi, X., (2008). Phosphate assimilation by *Chlorella* and adjustment of phosphate concentration in basal medium for its cultivation. *Biotechnology Letters, 30,* 1735.

Ramos, A., Coesel, S., Marques, A., Rodrigues, M., et al., (2008). Isolation and characterization of a stress-inducible *Dunaliella salina* Lcy- β gene encoding a functional lycopene β-cyclase. *Applied Microbiology and Biotechnology, 79*(5), 819.

Raposo, M. F., De Morais, R. M., & Bernardo De, M. A. M., (2013). Bioactivity and applications of sulphated polysaccharides from marine microalgae. *Marine Drugs, 11*(1), 233–252.

Régnier, P., Bastias, J., Rodriguez-Ruiz, V., et al., (2015). Astaxanthin from *Haematococcus pluvialis* prevents oxidative stress on human endothelial cells without toxicity. *Marine Drugs, 13*(5), 2857-2874.

Rodriguez-Sanchez, R., Ortiz-Butron, R., Blas-Valdivia, V., Hernandez-Garcia, A., & Cano-Europa, E., (2012). Phycobiliproteins or C-phycocyanin of *Arthrospira* (*Spirulina*) *maxima* protect against $HgCl_2$-caused oxidative stress and renal damage. *Food Chemistry, 135*, 2359–2365.

Roodenburg, A. J., Leenen, R., Van, H. H. K. H., Weststrate, J. A., & Tijburg, L. B., (2000). Amount of fat in the diet affects the bioavailability of lutein esters but not of alpha-carotene, beta-carotene, and vitamin E in humans. *American Journal of Clinical Nutrition, 71*, 1187–1193.

Rosenberg, J. N., Oyler, G. A., Wilkinson, L., & Betenbaugh, M. J., (2008). A green light for engineered algae: Redirecting metabolism to fuel a biotechnology revolution. *Current Opinion in Biotechnology, 19*(5), 430–436.

Sánchez, J. F., Feranadez, J. M., Acién, F. G., Rueda, A., Pérez-Parra, J., & Molina, E., (2008). Influence of culture conditions on the productivity and lutein content of the new strain *Scenedesmus almeriensis*. *Process Biochemistry, 43*, 398–405.

Sathasivam, R., & Ki, J. S., (2018). A review of the biological activities of microalgal carotenoids and their potential use in healthcare and cosmetic industries. *Marine Drugs, 16*, 26.

Sathasivam, R., Radhakrishnan, R., Hashem, A., & Abd, A. E. F., (2019). Microalgae metabolites: A rich source for food and medicine. *Saudi Journal of Biological Sciences, 26*, 709–722.

Scheer, H., William, J. L., & Lane, M. D., (2004). Chlorophylls and carotenoids. In: Lennarz, W., & Lane, M., (eds.), *Encyclopedia of Biological Chemistry*. Academic Press, New York.

Sekar, S., & Chandramohan, M., (2008). Phycobiliproteins as a commodity: Trends in applied research, patents and commercialization. *Journal of Applied Phycology, 20*, 113–136.

Shih, S. R., Tsai, K. N., & Li, Y. S., (2003). Inhibition of enterovirus 71-induced apoptosis by allophycocyanin isolated from a blue-green alga *Spirulina platensis*. *Journal of Medical Virology, 70*, 119–125.

Singh, D. P., Khattar, J. S., Rajput, A., Chaudhary, R., & Singh, R., (2019). High production of carotenoids by the green microalga *Asterarcys quadricellulare* PUMCC5 under optimized conditions. *PLoS One, 14*(9), e0221930.

Skjanes, K., Rebours, C., & Lindblad, P., (2013). Potential for green microalgae to produce hydrogen, pharmaceuticals and other high value products in a combined process. *Critical Reviews in Biotechnology, 33*, 172–215.

Soletto, D., Binaghi, L., Lodi, A., Carvalho, J. C. M., & Converti, A., (2005). Batch and fed-batch cultivations of *Spirulina platensis* using ammonium sulphate and urea as nitrogen sources. *Aquaculture, 243*, 217–224.

Soltani, N., Khavari-Nejad, R. A., Yazdi, M. T., & Shokravi, S., (2007). Growth and some metabolic features of cyanobacterium *Fischerella* sp. FS18 in different combined nitrogen sources. *Journal of Science Islamic Republic of Iran, 18*, 123–128.

Spolaore, P., Joannis-Cassan, C., Duran, E., & Isambert, A., (2006). Commercial applications of microalgae. *Journal of Bioscience and Bioengineering, 101*, 87–96.

Stahl, W., & Sies, H., (2003). Antioxidant activity of carotenoids. *Molecular Aspects of Medicine, 24*, 345–351.

Tominaga, K., Hongo, N., Karato, M., & Yamashita, E., (2012). Cosmetic benefits of astaxanthin on humans subjects. *Acta Biochimica Polonica, 59*(1), 43.

Wang, C., Li, H., Wang, Q., & Wei, P., (2010). Effect of pH on growth and lipid content of *Chlorella vulgaris* cultured in biogas slurry. *Chinese Journal of Biotechnology, 26*, 1074–1079.

Wang, T., Wang, Y., & Kontani, Y., (2008). Evodiamine improves diet-induced obesity in a uncoupling protein-1-independent manner: Involvement of antiadipogenic mechanism and extracellularly regulated kinase/mitogen-activated protein kinase signaling. *Endocrinology, 149*, 358–366.

Wu, Q., Liu, L., Miron, A., Klimova, B., Wan, D., & Kuca, K., (2016). The antioxidant, immunomodulatory, and anti-inflammatory activities of spirulina: An overview. *Archives of Toxicology, 90*, 1817–1840.

Yan, D., Lu, Y., Chen, Y. F., & Wu, Q., (2011). Waste molasses alone displaces glucose-based medium for microalgal fermentation towards cost-saving biodiesel production. *Bioresource Technology, 102*, 6487–6493.

Yang, G., Jin, L., Zheng, D., et al., (2019). Fucoxanthin alleviates oxidative stress through Akt/Sirt1/$FoxO_3\alpha$ signaling to inhibit HG-induced renal fibrosis in GMCs. *Marine Drugs, 17*, 702.

Yen, H. W., Sun, C. H., & Ma, T. W., (2011). The comparison of lutein production by *Scenesdesmus* sp. in the autotrophic and the mixotrophic cultivation. *Applied Biochemistry and Biotechnology, 164*, 353–361.

Yuan, J. P., Peng, J., Yin, K., & Wang, J. H., (2011). Potential health-promoting effects of astaxanthin: A high-value carotenoid mostly from microalgae. *Molecular Nutrition and Food Research, 55*, 150–165.

Zhang, Z., Wang, B., Hu, Q., Sommerfeld, M., Li, Y., & Han, D., (2016). A new paradigm for producing astaxanthin from the unicellular green algae *Haematococcus pluvialis*. *Biotechnology and Bioengineering*, *113*(10), 2088–2099.