NEXT-GENERATION ALGAE

VOLUME II: APPLICATIONS IN MEDICINE AND THE PHARMACEUTICAL INDUSTRY

Edited By

Charles Oluwaseun Adetunji

Julius Kola Oloke

Naveen Dwivedi

Sabeela Beevi Ummalyma

Shubha Dwivedi

Daniel Ingo Hefft

Juliana Bunmi Adetunji

Scrivener Publishing

WILEY

Next-Generation Algae

Scrivener Publishing
100 Cummings Center, Suite 541J
Beverly, MA 01915-6106

Publishers at Scrivener
Martin Scrivener (martin@scrivenerpublishing.com)
Phillip Carmical (pcarmical@scrivenerpublishing.com)

Next-Generation Algae

Volume II: Applications in Medicine and the Pharmaceutical Industry

Edited by

Charles Oluwaseun Adetunji

Julius Kola Oloke

Naveen Dwivedi

Sabeela Beevi Ummalyma

Shubha Dwivedi

Daniel Ingo Hefft

and

Juliana Bunmi Adetunji

Scrivener Publishing

WILEY

This edition first published 2023 by John Wiley & Sons, Inc., 111 River Street, Hoboken, NJ 07030, USA and Scrivener Publishing LLC, 100 Cummings Center, Suite 541J, Beverly, MA 01915, USA
© 2023 Scrivener Publishing LLC
For more information about Scrivener publications please visit www.scrivenerpublishing.com.

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise, except as permitted by law. Advice on how to obtain permission to reuse material from this title is available at http://www.wiley.com/go/permissions.

Wiley Global Headquarters
111 River Street, Hoboken, NJ 07030, USA

For details of our global editorial offices, customer services, and more information about Wiley products visit us at www.wiley.com.

Limit of Liability/Disclaimer of Warranty
While the publisher and authors have used their best efforts in preparing this work, they make no representations or warranties with respect to the accuracy or completeness of the contents of this work and specifically disclaim all warranties, including without limitation any implied warranties of merchantability or fitness for a particular purpose. No warranty may be created or extended by sales representatives, written sales materials, or promotional statements for this work. The fact that an organization, website, or product is referred to in this work as a citation and/or potential source of further information does not mean that the publisher and authors endorse the information or services the organization, website, or product may provide or recommendations it may make. This work is sold with the understanding that the publisher is not engaged in rendering professional services. The advice and strategies contained herein may not be suitable for your situation. You should consult with a specialist where appropriate. Neither the publisher nor authors shall be liable for any loss of profit or any other commercial damages, including but not limited to special, incidental, consequential, or other damages. Further, readers should be aware that websites listed in this work may have changed or disappeared between when this work was written and when it is read.

Library of Congress Cataloging-in-Publication Data

ISBN 978-1-119-85728-0

Cover image: Pixabay.Com
Cover design by Russell Richardson

Set in size of 11pt and Minion Pro by Manila Typesetting Company, Makati, Philippines

Printed in the USA

10 9 8 7 6 5 4 3 2 1

Contents

Preface

The application of both micro and macroalgae has been recognized as a next-generation biotechnological tool with the potential to mitigate various challenges faced by humankind globally, particularly in catering to the needs of an ever-increasing population. This companion volume includes valuable information on nanoparticle synthesis derived from algae and microalgae, as well as their diverse uses and applications in the production of products for pathogen diagnostics, pharmacological properties, and different drugs/medicines for human health. Algae has numerous medical attributes that could serve as a permanent replacement to all the challenges associated with synthetic drugs, such as high level of resistance, low effectiveness, and high cost. In recent years, there has been a significant shift in focus toward the application of algae, owing to its numerous applications in several sectors. Algae is a valuable resource for not only energy and food, but also conservation, environmental bioremediation, pharmacologically active substances, agriculture, new industrially important bio-products, and nutraceuticals.

This book explains how the application of algae could help to resolve diverse human health challenges through the use of nutritional supplements, therapeutic proteins, vaccines, and algae-derived drugs. It also provides great detail about the biological activities of some natural drugs derived from algae, such as anticancer, antimicrobial, antiviral, antiulcer, antiinflamatory, antihyperlipidermia, antithrombic agents, anticoagulants, cardioverscular, antitumour, immunomdularory, and various antibiotics. Also, it describes the use of algae-derived antioxidants in the management of several health concerns such as inflammations, chronic disorders, and cardiovascular diseases.

This second volume places special emphasis on the discovery of novel and biologically active compounds from algae. It covers a wide range of applications, including the use of astaxanthin and carotenoids derived from algae for the production of nutraceuticals, pharmaceuticals, additives, food supplements, and feed. The book also discusses the production of polyunsaturated fatty acids (PUFAs) and its biomedical applications, recent advancements in the research of sulfated polysaccharides from algal origin, and its antiulcer bioactivities. Other topics include the application of algae in wound healing, the use of nanotechnology for the bioengineering of useful metabolites derived from algae and their multifaceted applications, and the production of single-cell proteins and pigments with high relevance in industry. This book targets a diverse audience, including global leaders, industrialists, pharmaceutical and food industry professionals, innovators, policy makers, educators, researchers, and undergraduate and postgraduate students in various interdisciplinary fields such as medicine, pharmaceuticals, and biotechnology. The information contained in this book will be invaluable to anyone seeking to explore the potential applications of algae in various fields and to discover new biologically active compounds derived from algae for use in medicine, pharmaceuticals, and other related industries.

I want to express my deepest appreciation to all the contributors who have dedicated their time and efforts to make this book a success. Furthermore, I want thank my coeditors for their effort and dedication during this project. Moreover, I wish to gratefully acknowledge the suggestions, help, and support of Martin Scrivener and others from Scrivener Publishing.

Charles Oluwaseun Adetunji
(Ph.D, AAS affiliate MNYA; MBSN; MNSM, MNBGN)
Dean Faculty of Science, Edo State University, Uzairue, Nigeria
March 2023

1

Discovery of Novel and Biologically Active Compounds from Algae

M. Singh[1*], N. Gupta[2], P. Gupta[3], Doli[1], P. Mishra[1] and A. Yadav[1]

[1]Faculty of Pharmacy, RBS Engineering Technical Campus, Bichpuri, Agra, India
[2]Faculty of Engineering & Technology, RBS Engineering Technical Campus, Bichpuri, Agra, India
[3]Department of Chemistry, Faculty of Engineering and Technology, SRM Institute of Science and Technology, Modinagar, Ghaziabad, Uttar Pradesh, India

Abstract

The identification of new therapeutically active constituents from algae is generating growing attention due to the unique makeup of these organisms and the potential for widespread industrial use of these constituents. Recent study has concentrated on algae, which have a novel biochemical proclivity and a diverse variety of possible commercial uses, as a provider of novel biologically active constituents. The growing number of researchers are becoming interested in identifying novel physiologically active chemicals from algae, owing to its unique composition and the potential for vast commercial uses. It is very essential to identify the organisms of those species that produce bioactive secondary metabolites that could be a potential source for new drug development. A variety of constituents, such as carbohydrates, minerals, oil, proteins along with polyunsaturated fatty acids, are found in algae preparations. Additionally, biologically active constituents such as antioxidants (tocopherols or vitamin E), vitamin C and pigments (like phycobilins, carotenoids and chlorophylls) are found in algae preparations. These biologically active compounds possess different therapeutic properties, such as antimicrobial (antibacterial, antiviral, antifungal), antineoplastic, antioxidative and anti-inflammatory properties. They also have the potential to be used as food by humans. Algae have been discovered to be a significant source of physiologically active chemicals that may be used in a variety of goods for animals, plants, cosmetics, and medicines, among other things.

**Corresponding author*: monikaa6@gmail.com

Charles Oluwaseun Adetunji, Julius Kola Oloke, Naveen Dwivedi, Sabeela Beevi Ummalyma, Shubha Dwivedi, Daniel Ingo Hefft and Juliana Bunmi Adetunji (eds.) Next-Generation Algae: Volume II: Applications in Medicine and the Pharmaceutical Industry, (1–40) © 2023 Scrivener Publishing LLC

Keywords**:** Algae, biologically active compounds, therapeutic activities

1.1 Introduction

Water occupies almost 70% of Earth's surface. Therefore, it is a tremendous resource for the identification of novel/unique compounds with potential therapeutic uses. Over the last several decades, a vast variety of new chemicals obtained from marine creatures with pharmaceutically therapeutic benefits have been discovered. Because of this, marine resources are considered a promising source of new therapeutically active chemicals not only for the creation of active pharmaceutical ingredients but also for the development of food items [1].

The marine environment has a diverse range of fauna (sea hares, fishes, soft corals, sponges, nudibranchs, tunicates, sea slugs, bryozoans, echinoderms, shells, along with prawns) and flora (microorganisms such as micro/macroalgae, cyano- and actinobacteria, bacteria, fungi, halophytes). Among the most remarkable characteristics of marine life is the close connection that exists between different groups of creatures in order to enable them to adapt to the harsh and tough ocean circumstances that are significantly different than those that exist in a given ecosystem [2]. Phytoplankton (microalgae) have received tremendous interest nowadays because they are seen as a continuous raw material for producing a range of bioactive constituents. There are many different types of compounds that could be utilized in nutraceuticals, pharmaceuticals and as ingredients in some products like cosmetics. Some of these include terpenoids, amino acids, phycobiliproteins [3], fatty acids, chlorophylls, steroids, phenolic compounds, halogenated ketones, vitamins, and carotenes [4]. Photosynthetic microorganisms are known as cyanobacteria. They are Gram-negative and abundantly distributed throughout the environment. In various types of industries, including biofuel, nutrition, agriculture, and medicines, etc., they have a huge spectrum of biotechnological applications to offer [5].

Micro- and macroalgae (seaweeds), which make up the majority of marine algae, have possible potential use in different areas of biomedicine and marine pharmacology. Nowadays, tissue culture technologies are an up-and-coming area. As significant marine biological resources, algae are abundant on shallow, coastal, and backwater substrates and may be found in great quantities in shallow, coastal, and backwater habitats. It has also been discovered that algae may grow on a variety of solid objects such as rocks and stones as well as on dead corals, pebbles, and other small objects.

A surprising amount of agar is produced by algae in intertidal and shallow water, with a total production of about 6000 tonnes of total agar yield. Investigations have demonstrated that unrefined and refined compounds generated from marine algae showed significant antimicrobial action *in vitro* against a broad range of both Gram-negative as well as Gram-positive pathogenic microorganisms and also showed *in vivo* activity [6]. In addition to being interesting as research targets, because of their potential therapeutic qualities, the natural significant bioactive chemicals derived from microalgae are anticipated to be commercialized in the next several years [3].

In the aquatic environment, marine algae, including dinoflagellates (unicellular along with biflagellate organisms) and phytoplankton, are symbiotic in corals, seaweeds, and sea anemones, among other things. A wide variety of seaweeds are divided into four groups: Chlorophyta (means green algae), Rhodophyta (means Red algae), Phaeophyta (means Brown algae), and Cyanobacteria (certain filamentous Blue-green algae) [1]. Neoplasm (cancer, carcinoma or malignancy), diabetes, metabolic syndrome, obesity, chronic stress, stroke, immunological diseases and chronic respiratory sickness are all contributing to an increase in global morbidity and death. Dietary modification along with lifestyle modification are currently suggested as potential approaches to preventing or treating various ailments [3]. Furthermore, foods containing bioactive constituents may have the ability to behave as necessary nutrients. Antibiotics were formerly considered to be "magic bullets," but by picking certain bacteria for treatment, they might end up becoming a contributing factor to the spread of illness [7].

1.2 Microalgae-Derived Natural Products

Microalgae are microorganisms of only one cell in size that flourish in salt water. It also thrives in freshwater environments. Their diameter or length ranges from 3 to 10 millimeters, and they are available in a variety of forms and sizes. Microalgae include both bacterial and eukaryotic species, and the term "microalgae" applies to both [8]. Cyanobacteria are structurally comparable to bacteria in terms of their composition. They are classified as microalgae, however, because of the presence of chlorophyll and other photosynthesis-related compounds in their composition. Known as green algae due to the fact that they have the same quantities of chlorophyll-a and chlorophyll-b as green plants [9, 10], they have been studied extensively.

Microalgae produce biocompounds by utilizing light energy along with inorganic nutrients (nitrogen, phosphorus, carbon dioxide, and other elements) and are classified as autotrophic microorganisms. They include nutrients of great nutritional value, such as proteins, lipids, carbohydrates, polymers, and pigments, as well as medicinal properties. In recent research, it has been shown that microalgae may create a vast variety of chemical constituents (compounds) with diversified biological functions, including phycobilins, polysaccharides, polyunsaturated fatty acids, proteins, sterols, carotenoids, and vitamins, among other substances [10].

Phaeophyta, i.e., brown algae, are a well-known commercialized alginate source due to their brown color. Alginates are straight, long chains of amino acids. They consist of residues of the amino acids. Alginates are usually observed in toothpastes and ice creams, where they are employed as thickening agents, foam stabilizers, and preservatives. When taken orally, a low-density agonic acid gel formed from alginate salts operate as a "raft" that floats over the stomach content, similar to corresponding gelatine. As a result, stomach acid is prevented from refluxing into the esophagus. Therefore, sodium/magnesium salts of agonic acid are included in variety of compound antacid formulations, such as Favicon (Reckitt & Coleman) or Alicen (Rorer), among others [11]. There are wide variety of applications of algae, from biofuel production, in particular bioethanol, macro- and microalgae fermentation, to enzyme extraction in the paper, textile, and detergent industries, and laboratory applications [12].

Bioactive constituents are substances that are physiologically active in the human body and have functional characteristics in the body. Many biologically active compounds that have the possibility of being used as useful components are being developed and manufactured, including polyphenols, phycocyanins, fatty acids, carotenoids, and other polyunsaturated compounds.

1.3 Bioprospecting for New Algae

Numerous new compounds were found in marine algae during the previous six decades, and a vast variety of these chemicals have been shown to have intriguing biological activities [13]. When it comes to the isolation of new species, there are numerous obstacles to overcome; the dearth of information regarding the metabolite demands of growth genus, pH, need for consumption of certain nutrients (e.g., sulphate, nitrogen sources, and phosphorus), and other growth parameters, like crop density and temperature, among others. It is critical to understand the chemical interactions between strains that have not been thoroughly described or novel strains in order to maximize their production [3]. In 2009, Ou *et al.* [14] found that clinical studies are useful for concentrating efforts on extracting protective bioactive substances with specific therapeutic properties using various pharmacological models. The method of developing novel molecules as therapies, from preclinical validation through FDA clearance, is lengthy, laborious, and costly. A bioactive molecule with high therapeutic promise requires preclinical investigations, human clinical trials [14, 15], along with regulatory process permission from the FDA following post-trial for commercialization and marketing in the contemporary environment [15]. Keep in mind that not all of the medicines included in the database have been authorized by the Food and Drug Administration (FDA), but they are all recognized only after evaluation of biological action. In many other countries, medications are permitted for clinical use; however, in the United States, none of them have been approved. Animal and human clinical trials are conducted in order to evaluate the therapeutic property of the isolated constituents in various periods of development, using a variety of pharmacological models to do so [3]. Over 18,000 bioactive compounds have been identified to date. Despite this, only six drugs derived from marine sources have been clinically authorized and commercialized. Moreover, only a few algal isolates have been acknowledged clinically. Brentuximab vedotin, marketed under the trade name Adcetris, is, for instance, an antibody-drug combination made from bioactive molecules [16] derived from an algal source used to treat non-Hodgkin lymphoma [17]. Fucoidan extracts have anti-aging action on the human body in clinical double-blind trials [18]. Interestingly, the first antiviral algal component found from Eucheume/Chondrus, a red edible alga, is iota-carrageenan (Carragelose). Numerous derivatives of dolastatin have been developed and are being clinically investigated in EMA tests and by the FDA [19]. These derivatives names are glembatumumab vedotin, depatuxizumab mafodotin, and pinatuzumab vedotin. It has been revealed in clinical studies that EPA, coupled with DHA, are essential amino acids from marine macroalgae that have clinical use [20]. As feed additives and immunological boosters, Ocean Feed™ from macroalgae and Tasco™ from *A. nodosum* were already on the market [21].

There have been several well-publicized incidents in the UK of livestock and other animals being poisoned as a result of cyanobacteria contamination in their drinking water. *Anabaena flosaquae* is a plant that produces the alkaloid named anatoxin-a, which is a neurotoxin that depolarizes neuromuscular blocking and has both nicotinic and muscarinic action [5, 22].

1.4 Therapeutically Essential Natural Products

Marine organisms, which include both animals and plants, are the richest sources of bioactive constituents, which have a diverse variety of pharmacological actions, including free radical scavenging, anticancer, neuroprotective, analgesic, antimicrobial, and immunomodulatory properties, among other activities. Underwater drugs provide an alternate source for meeting the growing need for safe, effective, and low-cost medications, which is increasing in tandem with the world population's dramatic rise. In developed nations, the disease of neoplasm (cancer) is among the most prevalent causes of mortality, whereas communicable infections are the main cause of mortality in impoverished (developing) nations. Despite the significant advances in neoplasm or tumor therapy that have occurred over the past three decades, there is still a pressing need for novel medicines in the field of cancer biology, particularly in the relatively untapped field of marine anticancer chemicals, to combat cancer [2].

Chlorella and *Spirulina* are the most common microalgae species found on the market, and they dominate the whole market. The first is a green microalga that includes microalgae and also macroalgae, part of the broad phylum of Chlorophyta [12].

Polyketides, alkaloids, cyanopeptides, isoprenoids and other metabolites are among the cyanobacterial natural products classified according to their metabolic origins. While much of the research was focused on toxicity, many studies also have revealed that cyanobacteria create chemicals of considerable pharmaceutical and biotechnological importance. Forty percent (40%) of lipopeptides, others are less than 10% (e.g., fatty acids, amino acids, amides, and macrolides) make up cyanobacterial compounds. Therefore, Cyanobacteria activity is dominated by lip peptides such as cytotoxic (41%), antitumor (13%), antiviral (4%), and antibiotics (12%). The remaining 18% of cyanobacterial activity includes antimalarial, antimitotic, and immunosuppressive agents, herbicides, antifeedant, and multi-drug resistance reversing agents, among others [23].

Various types of Blue-green algae are available in the market as organic algae nutraceuticals, as well as a source of pharmacologically important substances. Examples of such species are *Spirulina, Chlorella* and *Aphanizomenon flos-aquae*. *Spirulina* sp. is a kind of blue-green algae that is found in the ocean. Lipids, chlorophyll, protein, carotenoids, minerals, vitamins, and vibrant colors are all rich in this plant's composition. Moreover, they might contain helpful probiotic components [24]. As well as other carotenoids, minerals (including Ca and Fe) and B vitamins (including B12), *Spirulina* sp. is a wonderful abundant source of potassium, calcium, magnesium, iron, selenium and zinc. As an added bonus, important component fatty acid is beneficial in potentiating hair and skin growth, regulating metabolism and maintaining bone health. It also ensures proper functioning of reproductive system. Numerous minerals and vitamins have powerful antioxidant activities that assist in the elimination of toxins from the environment and the prevention of diseases. Cyanobacteria have recently attracted the public's curiosity due to their high concentrations of bioactive chemicals and their potential as dietary supplements. They also serve as a model for organisms belonging to some very promising categories of organisms in terms of the production of bioactive chemicals. Scientific evidence demonstrating bioactive chemicals produced from blue-green algae may show therapeutic promise in the treatment of illness and health issues in both human clinical trials and animal clinical studies [1].

Agars as well as carrageenan are generated from species of red algae. Both the agents are utilized as gelling, thickening, and emulsifying agents, and are the most significant products obtained from red algal species. Agar is also utilized as a microbiological culture medium, and agarose, which is a component of nutrient agar used for microbial growth, is also utilized in electrophoresis, immunodiffusion, and gel chromatography, among other applications. It's also used as a hydrogel in the surgical dressing by Geistlich, which is another use. A carrageenan implant is a substance used in the pharmaceutical industry to induce inflammation in models for animal testing. It may be utilized to evaluate prospective anti-inflammatory and anti-arthritis medicines to produce edema. According to Blunden and Gordon [11], the gastrointestinal system of primates does not absorb high molecular weight carrageenans, and as a result, they are believed to be acceptable additions for human consumption, given that the molecular weight is tightly controlled.

1.5 Screening for Bioactive Constituents

Multidisciplinary approaches are needed for the determination of bioactive constituents. The advancement of analytical and molecular methods is a critical ongoing process that is required as a precondition for the targeting of novel products by means of high-throughput strategies. Public and private interest has been growing over the last few decades, along with their investments in marine biotechnology, which has further increased the possibility of generating information and collecting huge amounts of data to elaborate a better understanding of different cellular processes and mechanism of biological actions. Furthermore, marine biotechnology tends to utilize genomics, transcriptomics, proteomics, metabolomics, metagenomics, and metatranscriptomics, etc. [25], in conjunction with heterologous expression or genetic engineering to identify potential bioactive species and increase the required constituents/substances production [26].

A "test first" approach or an "isolate first" method is used in the screening process of natural goods, respectively. Natural bioactive components have been discovered using both approaches, and a recent trend has been to advocate the use of a fusion method, in which extracted or fractioned extracts are evaluated for the presence of biologically active elements. Bioassays are only utilized when the extracts demonstrate a high level of biological activity [27]. In order to isolate or identify fractions of extracts for chemical characterization, a number of techniques might be utilized. One of these techniques is liquid chromatography–mass spectrometry (LC-MS) and another is nuclear magnetic resonance (NMR). If novel constituents are identified, they should be refined as well as evaluated utilizing biological tests. Ideally, those tests should be reliable, repeatable, quick, cost-effective, simple to run, and sensitive, and should also be reproducible [3].

Microorganisms play an increasingly significant role in modern life, since they have evolved into essential components of a number of human life functions, such as digestion and food assimilation, among others. They also focus on human well-being by providing diversified foods, chemicals, and medications. Many microbiological pathogens, including fungi, protozoa, viruses, and bacteria, are responsible for serious illnesses despite the fact that effective management strategies are available. Bacteria and fungi are responsible for the spoilage of food goods [6]. De Vera *et al.* carried out experiments on more than 30 marine microalgae strains (haptophytas, dinoflagellates, chlorophyta, and heterokontophytas) in order to obtain extracts for evaluation of biological activity. As part of their research, they chose a number of intriguing samples for additional investigation of marine bioactive compounds. The unialgal isolates were kindly provided by the Oceanographic Center of Vigo. The available strains were cultured in the lab environment to determine their viability. Cell-free culture medium extract and biomass extract (two types) were produced from each strain. In order to get knowledge about antibacterial, antiproliferative, and anticancer (apoptotic) characteristics, these two extracts were further analyzed in order to get information on these qualities [28].

As per the current scenario on the non-selective and unsystematic widespread use of antibiotics as antimicrobial agents, a new generation of antibiotic-resistant and genetically modified microorganisms has emerged, posing a serious threat to the treatment of infectious diseases. The negative consequences and side effects of frequently used antibiotics, as well as the increasing prevalence of infectious diseases, have fueled the pursuit of novel antimicrobial agents from diversified sources from the marine environment [6].

1.6 Extraction Methods

Various methods or techniques can be utilized to separate potential therapeutically or biologically active constituents from different varieties of algal biomass. Various extracting agents were utilized to extract soluble constituents derived from the microalgae matrix. The simplest approach is to separate algal powder using water or organic solvents for large-scale samples, with the latter being the preferred method. The extraction rates vary from 8 to 30% of the dry algal yield under these conditions [29].

New types of extraction methods, like enzymolysis and extraction aided by a microwave, have, however, recently emerged. The first has impressive impacts, with high catalytic effectiveness characteristics, high specificities, mild reactive and maximum efficiency [30]. Moreover, there were several advantages to using the latter technique, including shorter processing times, the use of less solvents, greater extraction rates, and the production of better low-cost products [31, 32]. Complementary to the investigation of soluble chemicals, cell-binding compounds (CBCs) that are attached to the cell wall and cannot be easily isolated by applying the conventional methods of isolation with aqueous solvents, are also being investigated.

This could also limit the study of marine-derived active components and their potential industrial applications. Of interest is the enzyme digestion of algae, which produces high biological yields compared to water and organic extracts [33], and which exhibits improved biological activity. Michalak and Chojnacka reviewed an examination on the use of enzyme assistants using seaweed as an alternate approach for increasing the recovery of industrially valuable chemicals from the sea [30].

Recent extraction methods extract biologically active constituents without causing any loss of that activity. These are supercritical fluid extraction (SFE), ultrasound-assisted extraction (UAE), and microwave-assisted extraction (MAE). Among others, enzyme-assisted extraction (EAE) and pressurized liquid extraction (PLE) also have the advantage of extracting therapeutically active constituents. Moreover, this type of extraction method is distinguished by a larger yield of extraction, a shorter processing time, and, as a result, is more environmentally friendly as compared to previous extraction methods. The extraction of soxhlets, as well as liquid–liquid extraction along with solid–liquid extraction, are all examples of traditional extraction methods (SLE) [34]. Their primary disadvantage is the use of a huge quantity of solvents (many of which are hazardous) and the large amount of time needed for isolation [35].

Starting a decade ago, there seemed to be a substantial rise in the use of alternative techniques to replace traditional methods largely due to the numerous advantages of new extraction techniques. As per number of authors, new green technologies (e.g., higher yields) are superior to extraction by organic solvents, which incorporates the release of solvents. These solvents could be potentially hazardous for the environment and can also cause hydrothermal stress to extracts in terms of functional properties. The degradation of thermally labile compounds may also result from the high-temperature processing [36]. For instance, in the matter of the SFE utilization with carbon dioxide, the yield of the lipid removal was higher than in the case of Soxhlet solvent.

Because of the numerous advantages of new extraction techniques, it has been noticed that they have increasingly been used to replace old approaches in recent years. The superiority of new green technologies (e.g., better yield) over extraction techniques by organic solvent has been demonstrated by numerous authors. As a result of hydrothermal stress, organic solvent extraction entails the release of potentially toxic solvents into the surrounding environment. The functional characteristics of the extracts were severely harmed as a result of the release of potentially hazardous solvents. High-temperature processing can cause the deterioration of components that are thermally labile as well as the degradation of other constituents [36]. For example, when utilizing SFE with CO_2, the amount of lipid extracted from *Sargassum hemiphyllum* was greater than when using the Soxhlet solvent extraction technique with chloroform/methanol [37]. Tierney *et al.* discovered in their research that PLE was more efficient than standard SLE in the extraction of polyphenols using a water:acetone (20:80) mixture [38]. Denery *et al.* also had a parallel observation that compared to conventional solvent extraction techniques, PLE displayed more or equivalent carotenoids extraction abilities from *Haematococcus pluvialis* as well as *Dunaliella salina* [39]. Pasquet *et al.* examined extraction of pigment from two marine microalgae using two different approaches (one is cold and hot soaking and another is ultrasound-assisted extraction). Due to its high rate, uniform heating, reproducibility, and higher separation rates, MAE has been selected as the most effective pigment extraction technique [40]. Authors investigated the emerging green technologies (such as MAE, SFE and PLE) being more capable of replacing traditional organic solvent extractions. Extraction with SFE is one of the most widely utilized methods of extraction on an analytic and preparatory scale nowadays [41]. Aim of this chapter is to show the unique qualities of biologically active constituents and their wide applications obtained from algal biomass. The utilization of extracts from various algae is widely described in different areas of food, nutraceuticals and fuel manufacturing. It also explains the application in agriculture (plants and animal products) and cosmetics of algal extracts.

New extraction techniques are widely used in several industries for obtaining algal extracts such as SFE, UAE, MAE, PLE, EAE, etc. These techniques protect against degradation of the bioactive constituents isolated from algae. Algae's unique properties allow for a wide range of applications to be developed. They contain a high concentration of kilo grains (such as eicosapentaenoic acid, docosahexaenoic acid, β-linoleic acid) and in components such as polyunsaturated fatty acids (PUFAs) protein, minerals, carbohydrates, fats, oil, (e.g., docosahexaenoic acid, eicosapentaenoic acid along with γ-linoleic acid), in addition to the amount of bioactive constituents. These bioactive constituents are polyphenols, carotenoids, terpenoids, and tocopherols, which have antiviral, antibacterial, antifungal, antioxidative, anti-inflammatory, and antitumor activities. For plants, animals and human beings, algal extracts generated in solvent-free conditions or algal extracts obtained from minimal use of solvents are safe. These all are used in modern agriculture for three different categories:

- Animals (feed additives),
- Plants (bioregulators, biostimulants, fertilizers), and
- Humans (food, cosmetics, pharmaceuticals) [31, 42].

1.7 Biosynthesis and Biological Activities

Due to the influence of time-course and cohabitation on biological substances, biochemical pathways have been developed to the point where many microalgal lines now assemble a large number of distinct compounds. Despite the fact that secondary plant metabolites are more comprehensive than algae-derived metabolites, the diversity of secondary algal-derived metabolites is orders of magnitude more than that of soil plants [5, 3]. Bioactive substances are additional nutritional components found in small

Table 1.1 Algae and cyanobacterial constituents with potential biological action.

Name of microalgae	**Bioactive compounds**	**Biological action**	**Reference**
Arthrospira platensis (also known as *Spirulina platensis*)	PUFAs (n-3) fatty acids, oleic acid, linolenic acid, (vitamin E), phytol, palmitoleic acid, sulfated polysaccharide	Antiviral action	[46–49]
Botryococcus braunii	Carotenoids, linear alkadienes	Antioxidant action	[50, 51]
Caulerpa racemosa	Polyphenols	Antioxidant action	[52]
Chlorella ellipsoidea	Zeaxanthin, violaxanthin	Anti-inflammatory action, anticancer action	[53, 54]
Chlorella minutissima	Eicosapentaenoic acid (EPA)	Antioxidant action, cholinesterases inhibitory action	[48]
Chlorella protothecoides	Zeaxanthin, canthaxanthin, lutein	Anti-inflammatory action, antifungal action	[55–57]
Chlorella pyrenoidosa	Sulfated polysaccharide, lutein	Antiproliferative action	[49]
Chlorella sp.	Carotenoids poly-unsaturated fatty acids, sulfated polysaccharides, sterols	Immunostimulant action, antitumor action, antioxidant action	[49, 53, 58, 59]
Chlorella vulgaris	Canthaxanthin, peptide, astaxanthin, oleic acid	Antioxidant action and antitumor action	[48, 53]
Chlorella zofingiensis	Lutein, astaxanthin	Anti-inflammatory action	[60, 61]

(Continued)