CHAPTER 6

Marine Algal Sources for Treating Bacterial Diseases

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Contents

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Abstract

Microorganisms are the causative agents for various types of diseases in humans, animals, and plants. The invention of antibiotics against the bacterial diseases in the early twentieth century improved the heath conditions of the humans, but it resulted in the development of variable drug/multidrug-resistant strains which are now posing great challenge to cure the diseases. The need for searching novel bioactive compounds having potential therapeutic value resulted in exploration of oceans. Screening diverse fauna and flora in oceans opened new avenues for the development of novel therapeutic agents such as sesquiterpenes, phlorotannins, bromoditerpenes, halogenated furanones, and algal lectin which show effect on a wide range of Gram-negative and positive bacteria. Hence these bioactive compounds can be used as broad spectrum antibiotics, antibacterial, and antifouling agents.

I. INTRODUCTION

The encounter between the humans and the infectious agents is known from the ancient times. There are various types of infectious agents like bacteria, virus, and fungi which cause various types of diseases in humans, and the outcome of the disease symptoms varies from disease causing agents (Nelson and Williams, 2001; Nene, 2007). Humans have produced various types of treatments/remedies for different types of bacterial diseases from ancient times by using variety of practices like Ayurveda depending upon the availability of the natural resources in those countries (Gopal *et al*., 2008; Kerr and Kerr, 1999).

Irrational use of antibiotics from biological sources or by chemical synthesis for treating different bacterial diseases resulted in the development of the drug/multidrug-resistant strains, posing great challenge to cure the bacterial diseases. Considering novel mechanisms of action, drug resistance, toxicity, production, and cost-affectivity, various researchers from different parts of the globe turned their eyes on the diverse marine fauna and flora having potential therapeutic values. The cutting edge technological developments in science helped the researchers to discover the untapped antimicrobial potentials of marine algal sources in the development of novel antibiotic compounds (Hornsey and Hide, 1974; Morse *et al*., 1979; Troxler and Lester, 1967).

This chapter is focused on the marine algal sources for treating bacterial diseases, and emphasis would be on marine algae and their extracts/bioactive compounds treating various types of bacterial diseases.

II. MARINE ALGAL SOURCES AS THERAPEUTICS

Marine alga has rich biodiversity potential; can serve various requirements as food, natural sources, bioactive compounds for treatment/remedies for various types of bacterial diseases like tuberculosis, multidrug-resistant bacteria, viral infections like HIV, Herpes viruses, fungal infections, protozoan infection like malaria; and is also helpful against helminthis diseases, cancer; immunogenic, cardiovascular, neurological, and other diverse mechanisms and functions of these bioactive compounds need to be explored (Bernam *et al*., 2004; Chang *et al*., 2003; Fennell *et al*., 2003; Luescher-matti, 2003; Maskey *et al*., 2004; Mayer *et al*., 1999; Venkateshwar Goud *et al*., 2003; Zhu *et al*., 2004).

III. TYPES OF MARINE ALGAE USED FOR ANTIBACTERIAL SCREENING

Macroalgae are generally classified into Phaeophyta (brown algae), Rhodophyta (red algae), and chlorophyta (green algae) based on the photosynthetic pigmentation on their cellular composition.

A. Phaeophyta (brown algae)

Brown algae are the largest group of marine algal species found in oceans. The number of identified species is increasing with the large-scale screening and isolation of the novel therapeutic compounds. The exact number of species in the oceans is not known but it is expected to be several thousands, its pigmentation varies from yellow brown to dark brown and produces huge amounts of protective mucous (Ginsburg, 2003; Stegenga *et al*., 1997).

B. Rhodophyta (red algae)

Rhodophyta, second largest, most primitive group of macroalgae present in more diverse environments, is compared to the other types of marine algae. It produces various types of antibacterial products but the numbers of antibacterial products from these species are low when compared to the brown algae (Ginsburg, 2003; Stegenga *et al*., 1997).

C. Chlorophyta (green algae)

Chlorophyta (green algae) are present in lower ratios when compared to the Phaeophyta and Rhodophyta. The pigmentation of these species varies from yellowish green to dark green in color. These species are very closely

related to the terrestrial plants, and this algae exhibit few structural and chemical properties which can have an impact in the development of novel antibiotics (Ginsburg *et al*., 2000; Stegenga *et al*., 1997). Marine algae are vulnerable to the various types of biological and physiological agents, and in response to these, marine algae produce different types of bioactive secondary metabolites which provide protection from the biological and physical agents (Donia and Hamann, 2003; Haefner, 2003). Few bioactive compounds from the marine algae strongly deter the growth of the surrounding bacteria, and these active compounds have shown their effect on various human pathogens (Vairappan, 2003; König *et al*., 2000).

IV. BIOACTIVE COMPOUNDS OF MARINE ALGAE

A. Sesquiterpenes

Bioactive sesquiterpenes isolated from red algae species *Laurencia rigida*; *Laurencia luzonesis* yielded deschloroelatol, elatol, luzonenone, luzofuran, 3,4-epoxypalisadin, 1,2-dehydro-3,4-epoxypalisadin B, and 15-hydroxy-palisadin; and a new diterpene former has shown antibacterial action on *Bacillus megaterium* and also possess antifungal action (König *et al*., 2000; Kuniyoshi *et al*., 2005).

B. Phlorotannins

Crude extracts, purified diverse phlorotannins (phloroglucinol, eckol, phlorofucofuroeckol A, dieckol and 8.8′-beckol) extracted from brown algae, *Ecklonia kurome* tested on multiresistant *Staphylococcus aureus* and foodborne pathogens exhibited the antibacterial activity on Gram-positive bacteria, *S. aureus*, *B. Cereus* and Gram-negative bacteria *C. jejuni*, *E. coli*, *S. Enteritidis*, *S. typhimurium*, *V. parahaemolyticus* (Nagayama *et al*., 2002). Antibacterial mechanism of action of phlorotannins is not precisely known but one study supports that it may be due to the interaction of phlorotannins with the bacterial proteins and enzymes which will result in the bactericidal action. The toxicity of phlorotannins was evaluated by the studies on the mice and it found to be safe without causing toxicity to the animals, moreover in some parts of Japan, it is consumed as food so that this can be used as food supplement or drug for the treatment (Gopal *et al*., 2008; Schulz *et al*., 1992).

C. Bromoditerpenes

Two bromoditerpenes sphaerolabdadiene-3,14-diol and bromosphaer-one isolated from the marine red algae *Sphaerococcus coronopifolius* from the Atlantic ocean, sea coast of Morocco, exhibited antibacterial

action against Gram-positive organism *S. aureus* and antimalarial activity against the chloroquine-resistant plasmodium falsciparum; the exact mechanism of bactericidal action is not discovered (Etahiri *et al*., 2001).

Diethyl ether extracts of seaweeds *Cystoseira mediterranea*, *Enteromorpha linza*, *Ulva rigida*, *Gracilaria gracilis*, and *Ectocarpus siliculosus* are isolated from the Urla coast (Turkey showed effective results against all test organisms such as *Candida* sp., *Enterococcus faecalis*, *S. aureus*, *Streptococcus epidermidis*, *Pseudomonas aeruginosa*, and *Escherichia coli*). Fresh weights of algal extracted using the diethyl ether showed the strong broad spectrum antibiotic activity against the tested bacterial strains; moreover they have shown the more activity against the Gram positive, which was more when compared to the Gram-negative bacteria (Tuney *et al*., 2006).

D. Halogenated furanones

Halogenated compounds elatol extracted from the marine red algae *Laurencia majuscule* elatol has shown activity against the human pathogenic bacteria species *Staphylococcus epidermis*, *Klebsiella pneumonia*, and *Salmonella*, whereas iso-obtusol shown action on *K. pneumonia* and *Salmonella species* (Vairappan, 2003). Halogenated furanone isolated from the marine algae *Delisea pulchra* has shown broad spectrum antibiotic action against the bacterial bio film formation, quorum sensing (QS), and swarming, but the molecular mechanism is completely not elucidated. Studies on action of halogenated furanones on biosynthetic pathway AI-2, which is found in most of the Gram-positive and Gram-negative bacteria and will covalently modify the LuxS enzyme (*S*-ribosylhomocysteine lyase, EC 4.4.1.21) which produces autoinducers-2 (AI-2), thereby showing action on bacterial QS; therefore, these furanones can be used for clearing the bacterial films on the ponds and lakes (Zang *et al*., 2009).

E. Algal lectins

Lectins are the substances extensively distributed in the plants, animals, and marine algae. They are proteinaceous in nature having the capacity of attaching distinctive carbohydrates for producing unique biological properties like aggregation of erythrocytes, algae, yeast, and bacteria. Study conducted on the marine algal lectins belonging to eight Rhodophyta, three chlorophyta, and two phaeophyta species on four vibrio bacterial species (*V. neresis* and *V. pelagius*, *Eucheuma serra*, and *Galaxaura marginata*) strongly inhibited *V. vulnificus* (fish pathogen) but were inactive against the other two *vibrios*. Aqueous Ethanol and saline

extracts of red algae *E. serra* and *Pterocladia capillacea* have shown strong action at lowest concentrations on the *V. Vulnificus*. The strong antimicrobial action of marine algal lectins toward fish pathogenic bacteria *V. Vulnificus* can be used as the antibiotics in the aquacultures (Liao *et al.*, 2003).

V. MARINE ALGAE AGAINST HUMAN PATHOGENIC DRUG/ MULTIDRUG-RESISTANT STRAINS

Various workers used different types of solvents like acetone, ethyl alcohol, chloroform, ethyl, methanol, acetic acid, and benzene for the extraction of bioactive compounds from the marine algal sources; method of extraction and solvents play an important role in varying degrees of antibacterial activity against the Gram-positive and Gram-negative bacterial strains (Rosell and Srivastava, 1987; Sastry and Rao, 1994; Zheng *et al.*, 2001). Screening 151 marine algal species for antibacterial properties on five bacterial species found that the antibiotic production of the algal species varies with the seasons and also varies within the morphological similar species. The changes in the antibiotic production of the several species are also fluctuated due to the seasonal changes (Hornsey and Hide, 1974). Marine seaweeds *Ulva fasciata* (green algae) and *Hypnea musciformis* (red algae) isolated from the southeast and southwest coast of India showed antibacterial activities. Green algae *U. Fasciata* exhibited broad spectrum antibiotic inhibited *B. cereus*, *E. coli*, *B. Subtilis*, *A. hydrophila*, *V. fischeri*, and shrimp pathogen *V. harveyi* at incubation temperatures 20° and 30° (Selvin and Lipton, 2004).

The methanol extracts of seaweeds isolated from Gulf of Mannar, India, exhibited differential activity on multidrug-resistance bacterial strains *E. coli*, *K. pneumoniae*, *P. aeruginosa*, and *S. Aureus*, *Padina tetrastromatica*, of human urinary tract infections. *Stocheospermum marginatum* shown strong action against nonmultidrug-resistance bacterial strains. *Grateloupia lithophila* has shown effect on both multidrug-resistant and nonmultidrug-resistant strains, *Caulerpa* sp., *Gracilaria corticata*, and *Valoniopsis pachynema* exhibited weak activity (Manikandan *et al.*, 2011). Methanolic extracts of 26 marine seaweeds isolated from Morocco, Mediterranean coast are tested against the three Gram-positive *E. faecalis* (ATCC-29212), *E. faecalis* (ATCC-29213) and two Gram-negative bacteria *E. coli*, *Klebseila*, *Pneumonia* all the tested seaweeds shown the activity against the bacteria. Few types of seaweed exhibited the strong activity and few have shown moderate activity. The seaweed *H. musciformis* shown the broad spectrum antibiotic activity with zone of inhibition ranged from 10 to 35 mm (Rhimou *et al.*, 2010). Study

conducted on 32 marine algal isolates from Karachi, Pakistan showed the promising results against Gram-positive and Gram-negative bacteria, human, animal, plant pathogens, and common pests. *Codium shameelii* and *Iyengaria stellata* have shown the action against the three Gram-positive bacteria; *Colpomenia sinuosa* on three Gram-negative/positive bacteria; *Cystoseira indica* on two Gram-positive/negative bacteria; *Sargassum ilicifolium* shown action against two Gram-negative bacteria. In Rhodophyta, *Botryocladia leptopoda* has shown action against two Gram-positive and three Gram-negative bacteria, *Champia compressa* has shown action only on two Gram-negative bacteria (Muhammad and Shameel, 2004). Crude methanol extracts of *Saragassum cinereum* (brown algae) antibacterial activity against the *staphylococcus aureus*, *P. aeruginosa*, *Salmonella typhi*, *Streptococcus*, and *Klebsiella* species has shown the high activity against them which indicates the potential use in medical application (Divya *et al.*, 2011).

Several species of marine brown algae *Plocamium telfairiae*, *Gelidium amansii*, *Plocamium* sp., *P. Hamatum*, *Lessonia nigrescens Bory*, *Sargassum ringgoldianum* have shown antimycobacterial activity (Table 6.1; Collins and Franzblau, 1997; Ikekawa *et al.*, 1968; Kamimoto, 1956; König *et al.*, 1999).

VI. MARINE ALGAE IN CONTROLLING BIOFILM/ ANTIFOULING BACTERIA

Marine algae are susceptible for various types of disease from the surrounding bacteria; in order to protect from these, they developed the defense mechanisms to combat the bacterial diseases by producing the various secondary metabolites like halogenated furanones, these secondary metabolites are generally found on the surface of the algae. *Delisea pulchra* (red algae) has shown the antifouling action (Dworjanyn and Steinberg, 1999; Givskov *et al.*, 1996). However, *Bonnemaisonia hamifera* (macroalgae) also shown the greater antifouling action against nine diverse strains from five varied bacterial groups (Nylund *et al.*, 2005; Smyrniotopoulos *et al.*, 2003). The compounds isolated from the green algae *Caulerpa prolifera* have shown the antifouling activity against antifouling bacteria and microalgae *Phaeodactylum tricornutum* (Smyrniotopoulos *et al.*, 2003). Antifouling action of the halogenated furanones can be used for treating the aquatic systems. However, the higher concentrations ranging from 1 to 50 μM are toxic to various higher organisms like rainbow trout and artemia (Defoirdt *et al.*, 2004; Rasch *et al.*, 2004, 2007). The exact mechanism of action of these algal metabolites is inexplicable (Table 6.2).

TABLE 6.1 Antibacterial activity of marine algae against human pathogenic bacteria

Source	Bioactive compounds	Activity
Laurencia rigida	Sesquiterpenes	Antibacterial
Ecklonia Kurome	Phlorotannins	Antibacterial
Sphaerococcus coronopifolius	Bromoditerpenes	Antibacterial
Laurencia majuscule	Halogenated compounds	Antibacterial
Ulva fasciata	Methanol extract	Broad spectrum
Cladophora glomerata	Methanol extract	Multidrug resistant bacteria
Hypnea musciformis	Methanol extract	Broad spectrum
Codium shameelii (chlorophyta)	Methanol extract	Gram positive
Iyengaria stellata (Phaeophyta)	Methanol extract	Gram positive
Sargassum ilicifolium	Methanol extract	Gram negative
Saragassum cinereum (brown algae)	Methanol extract	Broad spectrum
Botryocladia leptopoda (Rhodophyta)	Methanol extract	Broad spectrum
Ecklonia Kurome	Phloroglucinol, eckol, phlorofucofuroeckol A, dieckol and 8.8′-beckol	Antibacterial
Laurencia majuscula	Elatol, iso-obtusol	Antibacterial
Grateloupia lithophila	Methanol extracts	Multidrug resistance/ nonmultidrug resistance
Cystoseira mediterranea, *Enteromorpha linza*, *Ulva rigida*, *Gracilaria gracilis*	Diethyl ether	Broad spectrum antibacterial activity
Plocamium telfairiae, *Gelidium amansii*, and *G. Capillaries*	Organic extracts	Antimycobacterial
Plocamium sp., *P. hamatum*	Monoterpenes	Antimycobacterial
Lessonia nigrescens Bory	Phytosterol saringosterol	Antimycobacterial
Sargassum ringgoldianum	Saringosterol	

TABLE 6.2 Antifouling activity of marine algae

Source	Bioactive compounds	Activity
Delisea pulchra (red algae)	Halogenated furanones	Antifouling
Caulepra prolifera (green algae)	Sesquiterpenoids	Antifouling
Bonnemaisonia hamifera (macroalgae)	Halogenated furanones	Antifouling

VII. ALGAL SOURCES FOR TREATING FISH BACTERIAL DISEASE

Commercial aquaculturing production is badly affected by several bacterial and viral infections (Muroga, 2001). Antibiotics are frequently used for treating the bacterial diseases, which not only pose risk of developing drug resistance against these antibiotics but also transfer of the drug-resistance genes to the human pathogenic bacteria which may have huge impact on health of human beings (Guglielmetti *et al*., 2009; Verschuere *et al*., 2000).

Use of chemical disinfectants on bacterial diseases in aquaculture has shown toxic effects on environment and to higher animals (Planas and Cunha, 1999; Subasinghe *et al*., 2000). The search for the novel mechanisms and therapeutics from the oceans has begun to cure the bacterial diseases. QS is one of the universal mechanism by which the bacterial cells communicate with each other depending upon the presence or absence of the signaling molecules in the surrounding environment. Aquatic organisms like microalgae, macroalgae, and invertebrates have the potential mechanism to disturb the QS mechanism by degradation of signals through enzymatic or chemical inactivation against the antagonist organism, and this action varies from organism to organism. This mode of action of marine algae can be useful in controlling the pathogenic bacteria (Defoirdt *et al*., 2004; Schauder and Bassler, 2001; Wang *et al*., 2008; Waters and Bassler, 2005).

QS using the microalgae is not completely understood, but this method of curing bacterial diseases is practiced; this technique is also known as green water technique, which was observed in the freshwater species (Palmer *et al*., 2007). Green water technique is used for controlling the bacterial infections in the aquafarming which makes use of the addition of diverse algal species mixture to the aquafarming. The exact positive mechanism of action of these algae is not well reported but it may be due to involvement of combined factors like nutritive values, stimulatory

TABLE 6.3 Antibacterial activity of marine algae against fish bacterial diseases

Source	Bioactive compounds	Activity
Cladophora glomerata	Methanol extract	Antibacterial
E. serra	Lectins	Antibacterial
Pterocladia capillacea	Lectins	Antibacterial

factors, improvement of abiotics, and inhibitory results in rapid development of the aquacultures. Bacterial QS was observed in the freshwater species (Kellam and Walker, 1989; Muller-Feuga, 2000; Reitan *et al*., 1997; Tinh *et al*., 2008).

Yuvaraj *et al*. (2011) studied antibacterial effects of *Cladophora glomerata* (green seaweed) of crude and purified extract on multidrug-resistant bacteria *Acinetobacter baumannii,* a human pathogen and the various fish pathogens like *Vibrio fischeri*, *V. Vulnificus*, *V. Anguillarum*, *V. parahaemolyticus*, *E. coli*, and *B. Cereus.* Second, third, and fifth fractions of *C. glomerata* exhibited good antibacterial activity against fish pathogens *V. fischeri*, *V. Vulnificus* and human pathogen *A. baumannii*, respectively. The result presumes that the long-chain hydrocarbons may act as potential bioactive substance and can be exploited in pharmaceutical preparations (Yuvaraj *et al*., 2011). Lectins isolated from the red algae are effective in controlling the fish pathogenic bacteria *V. Vulnificus* (Liao *et al*., 2003) (Table 6.3).

VIII. CONCLUSION

For thousands of years, man was dependent upon the nature for various purposes and he used nature's ability for the treatment and remedies against different human diseases. The latest improvements in the science and technology explored the untapped potentials of marine resources. The marine algal bioactive sources from Phaeophyta, Rhodophyta, and Chlorophyta will provide potential drugs for treating drug/multidrug-resistant bacterial diseases of human as well as aquaculture can have profound effect on the health and economic status of nations.

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