Mini Review Article
Volume 7:7, 2021

Journal of Antimicrobial Agents

ISSN: 2472-1212 Open Access

Antimicrobial Agents from Microalgae as Potential Source for Treatment of *Mycobacterium Tuberculosis*: A Short Review

Inam Ullah*

Department of Genetics, Hazara University, Garden Campus, Mansehra, Pakistan

Abstract

Tuberculosis is dreadful disease which cause millions of deaths worldwide each year. The emergence of multidrug resistant strains makes situation ever worse. The search for new drugs used for therapies is enhanced which results in the discovery of some bioactive agents from micro algae which manifest antibacterial activities against these multidrug resistant strains. Many bioactive compounds like unsaturated fatty acids, phenols, polysaccharides, terpenes, lipids, sterols and phenolic compounds have been extracted from different microalgae e.g. *I. galbana, C. friebergensis*, *C. marina*, *T. gracilis* using different solvents like ethanol, chloroform, hexane crude extracts, n-butanol, methane and water have shown to present anti-mycobacterial activities. Present studies show that unsaturated fatty acids show antibacterial activity against multidrug resistance mycobacterium tuberculosis and can be used as alternative to ancient drugs for treatment of tuberculosis.

Keywords: Multiple drug resistance • Antimicrobial activity • Bioactive compounds • Solvent extraction

Introduction

Tuberculosis TB, acquired immune deficiency syndrome AIDS and malaria are most very significant epidemiological diseases worldwide. TB is systemic very chronic disease which effects lungs and the main causative agent of TB is Mycobacterium tuberculosis. In 2015 it was hypothesized that one third of the world population was infected with mycobacterium tuberculosis and 10% of them were caught tuberculosis. In Mexico approximately 15,000 new cases and 2,000 deaths have been reported annually. The ancient drugs used for the treatment of TB are the combination of different anti tuberculosis drugs which are given over 9-12 months for surety so that mycobacterium is completely eliminated. However this extended period of medication can result in the development of drug resistant strains of mycobacterium. Specific pathogenic diseases which become multi drug resistant can be treated using alternative drugs. However the use of alternative drugs for multidrug resistant Mycobacterium is not applied because these drugs shows less effectiveness, more toxicity and are very much expensive. Therefore the search for new drugs which are less toxic, most effective and less costly were inevitable. Microalgae and cyanobacteria are cosmopolitan microorganism because they can be found in various aquatic environments like high temp, high salt conditions, in frozen lakes.

Microalgae produce various metabolic compounds to survive in these harsh environments. These metabolic products are shown to have various antibacterial, antifungal, antiviral activities which can be used in the development of various drugs in pharmaceutical industries. Different studies have conducted to estimate the antimicrobial and anti-mycobacterial activity of different algal compounds. The two diatoms *Skeletonema costatum* and *Chaetoceros pseudocurvisetus* have shown anti-mycobacterial activities only when they are cultured in phosphate starvation conditions. The chemical properties of bioactive compounds showed that they are associated with chlorophyll and lipid breakdown. The anti-mycobacterial activity has also been found in methanolic extracts of cyanobacteria for genus *Oscillatoria*, *Spirulina*, *Anabaena*, *Scytonema*, and *Hapalisiphon*. Furthermore anthraquinone derivatives of Eucapsia sp. Have also shown anti-mycobacterial activities. Two new compounds Carbamidocyclofanes form cyanobacteria Nostoc sp. have been described for their anti-mycobacterial activity. The hexanic extracts of cyanobacteria *Mycrocystis aeruginosa* have also shown activity against mycobacterium tuberculosis, M. terrae, and M. chelonae and M. kansasii. Their cytotoxicity is based on the microcystins content which monocyclic hepta-peptide toxins which show its activity as inhibitor or act as protein phosphatase.

***Address to correspondence:** Inam Ullah, Department of Genetics, Hazara University, Garden Campus, Mansehra, Pakistan, Tel: 3247265065; E-mail: inam18618@gmail.com*

Received: 06 October, 2021; **Accepted:** 20 October, 2021; **Published:** 27 October, 2021

Bioactive Compounds from Algae

In food, pharmaceuticals, cosmetics, biomedical industries algae are beneficial source of bioactive agents. Many bioactive agents from algae have antibacterial, antiviral and antifungal effects. Microalgae living in different conditions like fresh water, salt waters, and high temperatures produced different kinds of primary and secondary metabolites that are used and antimicrobial agents [1].

Polysaccharides

The cell wall of microalgae contain many polysaccharides including alginic acid, alginates, fucoidans and other derivatives. These polymeric compounds consist of chains of monosaccharaides linked through glycosidic bonds. Some sulphated galactans of red algae contain disaccharides as repeating units in the backbone. For example in *Isochrysis galbana* the carbohydrate is approximately 13% of the dry mass. Mono-sugars compositions in *Isochrysis* is 2.07% fucose, 2.50% rhamnose, 2.72% arabinose, 8.49% xylose, 15.7% mannose, 32.73% galactose, and 35.79% glucose. The first isolated intracellular and extracellular polysaccharides from *Isocrysis galbana* is highly branched chain of hetero polysaccharide contain (1→3) (1→6) glucan. Glucan contain linear chain of (1→6)-linked β glucopyranose consist backbone of the structure. Every residue is substituted by glycopyranose at position 3, which in turn may be substituted at C-6 by a single glycopyranose or by rather short (up to tetra saccharide) oligosaccharide chains. The strength of bioactive compounds from microalgae showing antimicrobial activities may depends on their distribution, molecular mass, their charge, density, sulphate content in microalgae containing sulphur in their polysaccharide structure, and on structural and conformational aspects of algae. Mover over oligosaccharides can also induce some response against viral, fungal, and bacterial infections in plants [2].

Lipids

Microalgae contain lipids as 0.12% to 6.73% as their dry mass which are mainly composed of different lipids including phospholipids, glycolipids, and some nonpolar glycerol lipids.

- Poly-phospholipids located in the extracellular membrane of chloroplast and interpret for 10-20% of the total phospholipids present in the microalgae. N-6 fatty acids are also present in high quantity in algae. Other phospholipids present in algae are mainly oleic acid, palmitic acid, and eicosapentanoic acids. In green algae major phospholipid is phospharidylglycerol, red algae contain phosphatidylcholine, and brown algae contain phosphatidylcholine and phophatidylethanolamine as major phospholipids in their cells.
- Glycolipids are situated in photosynthetic films and they are major component of algal lipids. The main component of these glycolipids is n-3 polyunsaturated fats. There are three main types of glycolipids present in microalgae which are mono-galactosyl-diacylglycerides, di-galactosyl-diacylglycerides, and sulfo-quinovosyl-diacylgl-ycerides.
- The most common neutral lipid present in microalgae is triacylglycerol whose concentration ranges from 1-90% in different microalgae. It is also main energy storage compound [3].

Unsaturated-Fatty Acids

These are long aliphatic hydrocarbon chains containing carboxylic group at one end containing one or more double bonds in their aliphatic hydrocarbon chain. These can be classified as monounsaturated fatty acids or polyunsaturated fatty acids. They can also be classified on the basis of position of double bond in aliphatic chain e.g. n-3 or n-6 unsaturated fatty acids. Green algae mainly contain C18 unsaturated fatty acids e.g. Alpha-linolenic, stearidonic, and linolenic acids. Red algae contain C20 unsaturated fatty acids e.g. arachidonic and eicosapentaenoic acids. While brown algae contain both C18 and C20 unsaturated fatty acids. The oxygenation of polyunsaturated fatty acid e.g. C16, C18, C20, C22 polyunsaturated fatty acids results in Oxylipins which have capability to show resistant under abiotic and biotic stresses like pathogenic microbes and herbivores [4].

Sterols

Sterols are underlying segments of cell layer involve in controlling the cell viscosity and penetration of different molecules. They are composed of four rings structures containing hydroxyl group at carbon 3 and two methyl groups at carbon 18 and 19 and side chain at carbon no. 17. Microalgae contain cholesterol, fucosterol, isofucosterol and clioansterol as major sterols. Sterols have antimicrobial activity because they can cause changes in cell wall of the bacterium resulting in its destruction.

Peak no	Compound	Retention time	Molar mass (Da)	Abundance (%)
1	Unidentified	107.35	428	3.1
2	Unidentified	107.39	428	5.5
3	Cholest-5-en-24-1, 3-(acetyloxy)-, 3 beta-ol	107.44	426	11.2
4	Ergost-5-en-3 beta-ol	112.22	400	16.2
5	(24R)-methylergost-5-en-3 beta-ol	112.64	400	3.6
6	5 beta-ergosta-7-en-3 beta-ol	113.22	400	2.9
7	ergosta-5,7-dien-3 beta-ol	114.09	398	6.3
8	ergosta-5,22(E)-dien-3 beta-ol	115.2	398	2.6
9	24-oxocholesterol acetate	115.28	386	18.9
10	5 beta-ergosta-7,22(z)-dien-3 beta-ol	115.39	398	5.3
11	24-methylcholesta-5,22-dien-3 beta-ol	115.45	398	9.4

12	ergosta-4,7,22-trien-3 beta-ol	117.07	396	4.1
13	ergosta-5,7,22(E)-trien-3 beta-ol	117.84	396	4.9
14	24-methylcholest-5-en-3 beta-ol	118.74	396	6.3

Table 1. Natural sterols isolated from *Isochrysis galbana*.

Phenolic compounds

These are products of secondary metabolism which do not participate straightly in process like cell growth, photosynthesis etc. They mainly composed of aromatic ring containing one or more hydroxyl groups and their antibacterial activity is associated with changes in permeability of microbial cell wall, disappearance of macromolecules inside cells, or interfere with cell membrane structure or cell integrity resulting in cell death. Synthetically, structures going from straightforward phenolic atoms to more complex molecules with polymeric structure with a wide scope of sub-atomic sizes ranges from 126-650 K Da have been portrayed. Polymeric phenolic compounds can be separated into phloroglucinols and phloroprotanins. Phloroglucinols consists of a sweet smelling phenolic ring which contain three hydroxyl groups. Phlorotannins are oligomeric or polymeric compounds containing phloroglucinol with additional hydroxyl and halogen groups. Phloroprotannins can be further divided into six classes based on the linkage present in them. For example phlorethols containing aryl-ether linkage, fucols with aryl-aryl bond, fucophlotherols containing ether or phenyl linkage, eckols with dibenzo dioxin bonding, fuhalols containing ortho-para-masterminded ether spans consisting of one additional hydroxyl group, and carmalols containing dibenzo dioxin moiety. Green algae mostly contain straight forward phenols like hydroxylcinnamic, benzoic acids and their derivatives and flavonoids. While brown algae has high concentration of phenolic compounds than red and green algae. Furthermore brown algae contain phenols like phloroglucinol, eckol, and dieckol which show some antimicrobial activities.

Terpenes

Terpenes are one of the significant groups of metabolic compounds created mainly by algae living in marine environment. Synthetically they are gotten from forerunner isoentenypl pyrophosphate containing five carbon atoms in its structure. They are further classified into hemiterpenes containing 5C atoms, monoterpenes 10C atoms, sesquiterpenes 15C atoms, diterpenes 20C atoms, sesterpenes 25C atoms, triterpenes 30C atoms and polyterpenes containing more than 30 carbon atoms. A few terpenes were segregated from ocean algae for example diterpene neophytadiene, the sesquiterpenes cartilagineol, obtusol and elatol and the diterpene aldehyde halitunal manifest some activities against specific viruses. The dolstane ditrerpenes e.g. 4-hydroxy-9, 14-dihydroxydolasta-1, 15, 17-diene and 4, 7, 14-trihydroxydolasta-1, 15, 8-diene, the diterpenoid halimediatrial and halimedalactone, the antimicrobial cyclopropane containing sesquiterpene cycloeudesmol, the sesquiterpenoid puupehenone and its subordinates also manifest antiviral activities. The sesquiterpene-elatol can be used as antifouling agents. The capisterones that are triterpenes sulphate esters manifest some antifungal activities.

Antimicrobial Activity of Algal Agents against *Mycobacterium Tuberculosis*

Mycobacterium tuberculosis is multidrug resistant strain of mycobacterium cause tuberculosis in humans. Millions of people die each year from tuberculosis. The use of ancient antibiotics has become limited against these bacteria as they develop resistance against ancient antibiotics by causing some mutations in their DNA. Therefore development of new drugs for the treatment of antibiotic resistant strains of bacteria has become vital. Microalgae are good source of many antibacterial agents which can destroy these resistant strains of mycobacterium. The activity of antibacterial agents from different alga *I. galbana*, *N. occulata*, *D. inorta*, *C. friebergensis*, *C. marina*, *T. gracilis*, *P. lutheri*, *C. salina*, *C. vulgaris*, *D. saline*, *C. calcitrans*, *Platymonas spp*, *S. salina*, *N. salina*, *C. ovalis*, were obtained from central Marine Fisheries Research Institute (CMFRI) at Tuticorin, South Indian were observed against mycobacterium tuberculosis. The bioactive compounds were extracted by using five different polar and nonpolar solvents. Ethanol, n-butanol, chloroform, methanol and water were used for the extraction of bioactive compounds from microalgae [5].

The percentage contribution in inhibition of different mycobacterium tuberculosis isolates showed that *Isochrysis galbana* contain showed maximum 50% inhibition of mycobacterium tuberculosis isolates. The percentage contribution of different solvent in the extraction of bioactive compounds from *Isochrysis galbana* showed that methanol, chloroform, and n-butanol showed maximum extraction of 33%, 50%, 17% among other solvents used for the extraction of bioactive compounds from *I. galbana*. The next major algae involved in inhibition of mycobacterium strain was *T. gracilis* which showed 40% inhibition of total isolates of mycobacterium tuberculosis. The percentage contribution of solvents involved in extraction of bioactive compounds form *T. gracilis* showed that methanol and chloroform showed maximum extraction of bioactive compounds from *T. gracilis* than any other solvent used in extraction. The third major algae which showed inhibition of mycobacterium isolates were *C. friebergensis* which showed 20% inhibition of mycobacterium isolate. The best solvent which results in maximum extraction of bioactive compounds from *C. friebergensis* was chloroform.

The minimum inhibitory concentration of Isochrysis galbana against mycobacterium tuberculosis isolate found to be 50-60 micro gram, the minimum inhibitory concentration of T. gracilis was found to be 70-80 micro gram and of *C. friebergensis* was 80-90 micro gram. The active compounds that were involve in the inhibition of mycobacterium were sterols, fixed oils and fats etc. Further showed that thirteen unsaturated sterols were present in *I. galbana*. These unsaturated fatty acids have effect on the inhibition of multidrug resistance mycobacterium tuberculosis and can be used in place of conventional antibiotics.

Assessment of anti-mycobacterial activity of algal compounds while using hexane crude extract as extraction solvent

The antimicrobial activity of six different strains of microalgae A. marina, Rhodomonas, I. galbana, P. cruentum, C. Mexicana, and N. palea were observed using hexane crude as extraction solvent. All the hexane crude extracts of six alga strains showed inhibition of mycobacterium isolates. The hexane crude extracts of P. cruentum, C. Mexicana, and I. galbana showed the inhibition of mycobacterium growth with efficiency 99.4%, 98.4%, and 98.3% respectively which is approximately similar with the synthetic antibiotic isoniazid (99.4%) used for the treatment of mycobacterium tuberculosis infections.

The inhibition capacity of remaining algal A. marina (81.3%), Rhodomonas spp. (89.3%), and N. palea (95.4%) extracts were found to be 80-90% for mycobacterium tuberculosis. The lowest Minimum Inhibitory Concentration (MIC) of hexane crude extract was found to be of I. galbana which is 50 micro g/ml. the Minimum Inhibitory Concentration (MIC) of isoniazid was 0.06 micro g/ml.

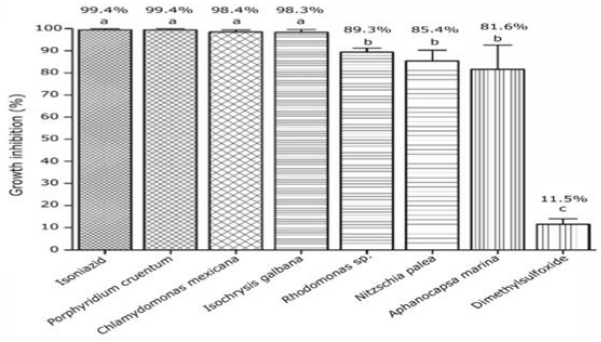

Figure 1. Percentage inhibition of hexane crude algal extracts.

Discussion

The difference in growth pattern and biomass may be associated with the adaptability of each strain to the culture conditions for different microalgae. When unfavorable conditions occur algae usually do not promote cell growth but produce various secondary metabolites which may have antibacterial activity. Methanol, ethanol, dichloromethane, hexane, and chloroform are most commonly used solvent for extraction of bioactive metabolites from algae. Many authors suggest that crude extracts with MIC less than 100 can be studied as potential agent against mycobacterium. *I. galbana* showed maximum activity against mycobacterium isolates.

Conclusion

These algae contain unsaturated fatty acids, terpenes, sterols, which may contribute to their anti-mycobacterial actions. Therefore these unsaturated fatty acids can be used in the control of mycobacterium as they have effect on multidrug resistant bacteria mycobacterium tuberculosis.

References

1. Prakash, S, Sasikala S L, Huxley V, and Aldous J. "Isolation and Identification of MDR-Mycobacterium Tuberculosis and Screening of Partially Characterised Antimycobacterial Compounds from Chosen Marine Micro Algae." Asian Paci J Trop Med 3 (2010): 655-661.
2. Sotgiu, Giovanni, and Migliori Giovanni Battista. "Facing Multi-Drug Resistant Tuberculosis." Pulm Pharmacol Therap 32 (2015): 144-148.
3. Powers, J H "Antimicrobial Drug Development-The Past, the Present, and the Future." *Clin Microbiol Infect 10 (2004): 23-31.*
4. Ramos, Daniela Fernandes, Matthiensen Alexandre, Colvara Wilson, and Souza de Votto Ana Paula, et al. "Antimycobacterial and Cytotoxicity Activity of Microcystins." J Venom Anim Toxins Include Trop Dis 21 (2015): 1-7.
5. Bhadury, Punyasloke, and Wright Phillip C. "Exploitation of Marine Algae: Biogenic Compounds for Potential Antifouling Applications." Planta 219 (2004): 561-578.
6.

How to cite this article: Ullah, Inam . "Antimicrobial Agents from Microalgae as Potential Source for Treatment of Mycobacterium Tuberculosis: A Short Review." *J Antimicro Agent* 7 (2021) : 250