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Antibacterial assay of cyanobacteria in *invitro* conditions and its valuable applications

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Abstract

Cyanobacteria are aquatic and photosynthetic they survive in fresh water ponds and sewage water. Since these cyanobacteria are quite small and unicellular, they often grow in large colonies more enough to see by naked eye. Cyanobacteria they produce bluish green colour pigments as they are phycocyanin, phycobiliproteins and carotenoids. It may surprise you to know that cyanobacteria are still around they are one of the largest and most important groups of bacteria on earth. The cyanobacterial ethanolic extracts of *Oscillatoria formosa, Oscillatoria subbrevis, Oscillatoria princeps, Oscillatoria sancta* and *Oscillatoria fischeri* showed effective antibacterial activity against pathogenic microorganisms like *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Clostridium perfringes*, *Salmonella typhi* and *Vibrio cholerae*. Cyanobacteria like *Oscillatoria curviceps*, *Lyngbya majuscula* and *Spirulina subsalsa* are rich source of bioactive compounds with antibacterial, antifungal, antialgal and antiviral properties. Some cyanobacteria like *Synechococcus elongatus* have ability to accumulate polyhydroxyalkanoates which may be used as bioplastics. In addition to these applications the Cyanobacteria are also useful in agricultural practices like *Nostoc commune* and *Anabaena aequalis* as biofertilizers. Some eukaryotic green algae like *Chlorella vulgaris, Botryococcus braunii* and *Schizochytrium limacinum* produce more oil content for ecofriendly production of more biodiesel.

Keywords: *Oscillatoria formosa; Clostridium perfringes*; Gram staining; Anti bacterial assay; Ciprofloxazin disc

1. Introduction

The freshwater ecosystem comprises both ponds and lakes in which freshwater ponds constitute a variety of plants, phytoplanktons, aquatic animals and prokaryotes [1]. The elements in freshwater ponds were mostly dependent on one another for their survival in the ecosystem [2-4]. The blue-green algae (cyanobacteria) were prevalent in freshwater ponds have capablity to perform nitrogenfixation and also secrete numerous biologically active substances, ultimately improving the productivity of the environment [5-6]. The cyanobacteria in the genera *Oscillatoria lyngbya* were often formed persistent and extensive blooms in the aquaculture ecosystem [7-8]. Usually, cyanobacteria grow in close association with the number of microorganisms, which include bacteria, fungi and protozoans [9-10]. Cyanobacteria play a vital role in converting atmospheric nitrogen into organic forms, such as nitrate or ammonia, and they also perform photosynthesis and ultimately release oxygen as a by product which other plants could utilize for growth and survival [11-12] and act as the food source for other organisms like zooplanktons, insects and snails [13]. Research showed that only very few species belonging to cyanobacteria were commercially available like *Spirulina platensis* [14-15].

Cyanobacteria, are ancient life forms on earth, and are one of the most studied organisms worldwide characterized them as usual prokaryotic microorganisms that can perform oxygenic photosynthesis [16-17]. They can also synthesize

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chlorophyll *a* similar to eukaryotic algae and plants, cyanobacteria use H_2O as an electron donor for the production of oxygen. The oldest fossil of cyanobacteria are dated approximately 3500 million years ago. The cyanobacteria blooms has given special consideration over worldwide because of it's highly effects on water environments by increasing input of nitrogen and phosphorus[18-19]. Cyanobacteria are still largely present in oceans and freshwaters. Most cyanobacteria live in water as phytoplankton. Cyanobacteria are often called "blue-green algae"and are named after the blue green pigment phycocyanin which together with chlorophyll a and other pigments, is used to capture light for photosynthesis.

Cyanobacteria were the first organisms capable of oxygenic photosynthesis and they are considered largely responsible for the rise in atmospheric O_2. The ribosomal RNA from cyanobacteria with DNA inside the chloroplasts of eukaryotes and revealed that all photosynthetic eukaryotes derived their photosynthetic capabilities from cyanobacteria through endosymbiosis [20]. Moreover, some organisms are producing toxins which also effect water quality. Cyanobacteria are light sensitive and can regulate their buoyancy that is essential property to float on the water surface. [21].

1.1. Antibacterial compounds of cyanobacteria

A huge number of bioactive compounds have been isolated and identified from many species of cyanobacteria have potential activity against different gram-positive and gram-negative bacteria such as *Pseudomonas aeruginosa, Staphylococcus aureus, Staphylococcus epidermidis, Enterococcus aerogenes, Salmonella typhi, Mycobacterium tuberculosis, Mycobacterium laprae, Vibrio cholarae, Bacillus subtilis, Bacillus cereus, Escherichia coli* and *Klebsiella pneumoniae*. Hormothamnions are cyclic undecapeptides, produced from marine cyanobacterium *Hormothamnion enteromorphoides*, shows activity against bacteria [22] and cyclic undecapeptides schizotrin form *Schizothrix sp.* [23]. The epilithic cyanobacterium *Nostoc spongiaeforme*. *Tenue* known for the production of a group of cyclic hexapeptide named as tenuecyclamides which also active against bacteria [24]. Muscoride A, anantibacterial oxazole peptide is isolated from freshwater *Nostoc muscorum* [25]. Malyngolides are a group of antibacterial compounds produced by marine cyanobacterium *Lyngbya majuscula* [26-27]. The freshwater cyanobacterium *Oscillatoria redeki* produced unsaturatedhydroxyl fatty acid α –dimorphenolic acid and coriolic acid which reduces thebacterial infections [28]. Noscomin, obtained from *Nostoc commune*, shows activity against *Bacillus cereus, Staphylococcus epidermididis* and *Escherichia coli* [29] carbomidocyclophanes are a group of compounds have potential against *Staphylococcus aureus* [30]; ambiguine 1 isonitrile from *Fishcerella sp*. active against *Escherichia coli ESS k-12, Staphylococcus albus* and *Bacillus subtilis* [31]; norbietane diterpenoid from *Microcoleus lacustris* active against *Staphylococcus aureus* [32]; phayokolide A produced by *Lyngbya sp*. shows activity against *Bacillus sp.* [33]and hapalindole T from *Fischerella sp.* active against *Staphylococcus aureus, Pseudomonas aeruginosa, Salmonella typhi* and *Escherichia coli.*

1.2. Antifungal compounds of cyanobacteria

Cyanobacteria are shows remarkable activity against various fungi and inhibit their growth and development. Antifungal potential was observed in a large number of cyanobacterial extracts [34].The cryptophycins comprises the largest class of cyanobacterial depsipeptides. Cryptophycin-1, an important member of cryptophycin class, was first isolated from *Nostoc ATCC53787* which exhibited antifungal properties [35-36]. Another compound, scytophycin, having antifungal potential was also reported from various species of cyanobacteria [37]. Scytophycins are highly cytotoxic metabolites. Ambigols are polychlorinated aromatic compound, isolated from terrestrial cyanobacterium *Fischerella ambigua*, having potent activity against several fungi [38] and other compound named parsiguine [39]. Cyanobacterium *Hapalosiphon fontinalis* produce a group of indole alkaloids, hapalolindoles, act as antifungal agent [40]. *Ambiguine isonitrils* are hapalolindole type alkaloids, with antifungal properties, produced by *Fischerella ambigua*, *Hapalosiphon hibernicus* and *Westiellopsis prolifica* [41].

1.3. Antialgal compounds of cyanobacteria

Several metabolites from cyanobacteria have isolated and identified as antialgal agent *i.e.* they inhibit the growth and development of different algal species. These metabolites are Galactosyldiacylglycerols from *Phormidium tenue* [42], Nostocin-A from *Nostoc spongiaeforme* [43], Cyanobacterin LU-1 from *Nostoc linckia* [44], Cyanobactericin from *Scytonema hoffmanii* [45],Fischerellin from *Fischerella muscicola* [46] and Aponin from *Gomphosphaeria aponia* [47].

1.4. Antiviral compounds of cyanobacteria

The capability to control the growth of cancer cell lines by natural products may lead to discovery of novel, highly effective anti-cancer drugs. Many cyanobacteria species collected from various sea shore and deep sea regions of the marine region has proved to be dominant source for production of different chemical classes of natural products with anti-proliferative, anti-tumor and anti-cancer properties. The first anticancer compound 'Tolytoxin' isolated by [48] from cyanobacteria. Tantazoles and mirabazoles are modified cytotoxic peptides of *Scytonema mirabile* [49]. Tantazoles

and mirabazoles are tumor selective cytotoxins but Tantazole-B and Didehydromirabazole A have potent activity against tumor [50]. *Hapalosiphonwel witschii* produce a novel cyclic depsipeptide 'hapalosin' have reverse Pglycoprotein- mediated multidrug resistance in tumor cell lines [51]. Cryptophycin-I is a microtubule depolymerising agent [52] which exhibits excellent activity against a wide range of solid tumors implanted in mice including drug resistance and multidrug resistance [53].Cryptophycin-I was isolated from *Nostoc sp. GSV224* in Moore's lab [54]. Its IC50 is 5PG/Ml for KB human nasopharyngeal cancer cell lines and3PG/Ml for LoVo human colorectal cancer cell lines. It has been observed that it is100-1000 times more potent than other antitumor drugs [54-55]. Curacin-A is a novel antimitotic and antiproliferative metabolite produced by *Lyngbya majuscula* [56]. Dolastatin-10 is a potent proliferative agent with an ED50 4.6×10^{-5} μg/ml. It binds to tubulin on the rhizoxinbindingsite and affects the assembly of microtubules in mitotic phase of cell cycle.Dolastatin-10 first isolated in fewer amounts from *Dolabella auricularia* but now, it has been proved that it is a cyanobacterial compound which later isolated from *Symploca sp.* [57]. Apratoxin-A is a cyclodepsipeptide which isolated from *Lyngbya sp.* showed activity against human tumor cell lines with IC50 ranging between 0.36 to 0.52 nm [58]. Tolyporphin is isolated from *Tolypothrix nodosa* has potential photosensitizing activity against tumor cells and 5000 time more efficient than the photodynamic treatment [59]. Somocystinamide-A is a product of marine species of *Lyngbya majuscula* which act as antitumor agent [60].

2. Material and methods

2.1. Blue green algae 11 broth

The algal culture grow in BG 11 broth at a ph 6.8,7.2 and 7.5 respectively. The auxenic cultures were obtained by repeated sub culturing under aseptic condition. The cultures were maintained under day light fluroscent tubes with 14 hrs of light and 10 hrs of dark cycle at room temperature.

2.2. Cyanobacteria sample collection and culture maintenance.

The water samples are collected from fresh stagnant water in many places of chennai, which is located in Tamil Nadu, India. The stagnant water samples were collected using teasing needles in sterilized bottles of 500 ml capacity. After the collection of samples, it was viewed in cavity slide using a trinocular microscope (Labomed Vision 2000 microscope) by wet mount method to identify the different species present in the fresh water ecosystem. This was followed by inoculating the culture in liquid BG-11 medium. The mixed culture was spread in agar plates containing BG-11 medium and the individual colonies were isolated. The mass culture of each colony was carried out by taking a loopful of distinct colonies from agar plates and transferring it to the conical flasks. This process was repeated until auxenic cultures were obtained.

2.3. Morphology and species identification of cyanobacteria

Morphological identification of cyanobacteria was accomplished by spreading an isolated pure culture on glass slides with the help of forceps. The cultures were covered with glass cover slips and their size, shape, color, and other features were observed under low (10×) and high power (100×) objective lens of the trinocular microscope (Labomed Vision 2000 Microscope). Numerous species of cyanobacteria present in fresh water ponds of Pudukkottai district were identified and confirmed using the book written by T.V. Desikachary [61] and also with the help of the "Manual of Freshwater Algae of Tamil Nadu" [62-63].

2.4. Gram staining technique of cyanobacteria.

A smear of cyanobacteria was made on a glass slide and thoroughly air-dried. In gram staining it was stained with 1 minute in crystal violet solution, 1 minute in iodine solution, 3-5 seconds in grams decolouriser finally stained with saffranin for 1 to $1\ ^{1/2}$ minutes. The glass slide was examined under 40 X magnification with direct illumination in a Dialux 20 microscope equipped with a 3 CCD Sony colour camera and connected to a PC showed gram negative result in this research study [64-65].

2.5. Preparation of cyanobacterial extract using souxlet apparatus.

The cyanobacterial cultures was bought from five different environmental stagnant water and purified by BG 11 broth around 40 days and obtained five different pure cultures *Oscillatoria formosa, Oscillatoria fischeri, Oscillatoria princeps, Oscillatoria subbrevis* and *Oscillatoria sancta* was dried for 21 days and finally converted into powder by using mixer blender. The extraction was performed by soaking the powdered cyanobacterial material in 99.9% ethanol solvent. The cyanobacterial extract was processed in souxlet apparatus at 25°C for 4 hours and filtered using Whatman No 4 filter paper. The collected ethanolic algal solvent extract was collected in 5 ml eppendorf tubes and stored in refrigerator at 4- 8°C for antibacterial studies.[66-67].

2.6. Antibacterial assay

The antibacterial activity test was done using the agar well diffusion method by using muller hinton agar media [68]. 0.1 ml of diluted inoculums (10^{-5} CFU ml-1) of the bacterial strains were swabbed on agar plates, and 5.0 mm size diameter wells on agar plates were made with a sterile cork borer (5.0 mm). Using a micropipette, 30 µl of five differerent pure cultures *Oscillatoria formosa, Oscillatoria fischeri, Oscillatoria princeps, Oscillatoria subbrevis* and *Oscillatoria sancta* ethanolic algal extract was added to the wells made on each plate. The plates were allowed to incubate at 37°C for 24 hrs. Antibacterial activity was measured by zone of inhibitions (mm) against the bacterial strains. controls were prepared using ethanol solvents. Ciprofloxazin (10 µg) antibiotic discs were used as a positive reference standard to determine the sensitivity of one strain from each bacterial species. The tests were performed in triplicate. The following antimicrobial index formula was used to compare the antimicrobial activity of the sample with the activity of the standard [69].

Antimicrobial Index = (Extract inhibition zone/Antibiotic inhibition zone) × 100

3. Results

Antibacterial assay of five different cyanobacterial extracts *Oscillatoria formosa*, *Oscillatoria fischeri*, *Oscillatoria princeps*, *Oscillatoria subbrevis* and *Oscillatoria sancta* against pathogenic microorganisms *Streptococcus pyogenes, Clostridium perfringes, Salmonella typhi, Vibrio cholerae* and *Shigella sonnei* is shown in Table 1. The cyanobacteria *Oscillatoria formosa* ethanolic extract 30 µl showed high activity against *Salmonella typhi* (19.46±0.18) least activity of (13.54±0.14) against *Streptococcus pneumoniae*. *Oscillatoria fischeri* ethanolic extract 30 µl showed high activity against Salmonella typhi (20.71±0.25) and least activity of (14.33±0.29) against *Streptococcus pyogenes*. *Oscillatoria princeps* ethanolic extract 30 µl showed high activity against vibrio cholerae of (21.08±0.36) least activity of (15.72±0.31) against *Clostridium perfringes*. *Oscillatoria subbrevis* ethanolic extract 30 µl showed high activity against *Vibrio cholerae* of (20.17±0.44) least activity of (13.43±0.35) against *Streptococcus pneumoniae*. *Oscillatoria sancta* ethanolic extract 30 µl showed high activity against *Salmonella typhi* of (20.29±0.08) least activity of (14.19±0.05) against *Clostridium perfringes*.

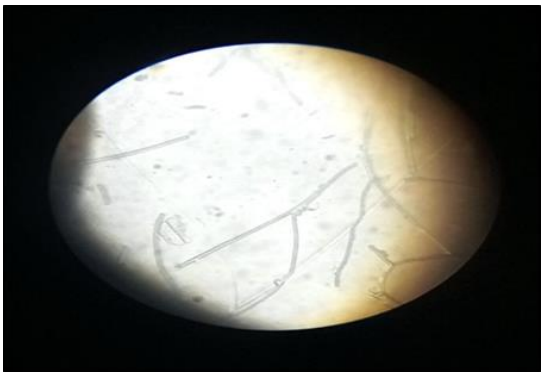

Figure 1 Original microscope picture of greenish filamentous cyanobacteria *Oscillatoria formosa* under 45 X objective

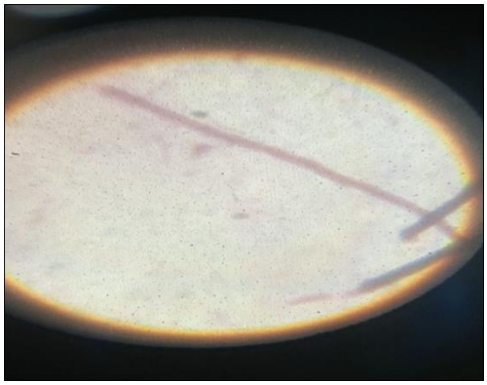

Figure 2 Original microscopic picture of cyanobacteria *Oscillatoria formosa* showed filamentous shaped gram negative pink colour under 100 X oil immersion objective

Table 1 Antibacterial assay of cyanobacteria

Microorganisms	*Oscillatoria formosa*	*Oscillatoria fischeri*	*Oscillatoria princeps*	*Oscillatoria subbrevis*	*Oscillatoria sancta*	Antibacterial agent
Streptococcus pyogenes	15.96 ±0.15[a]	14..33±0.29[a]	17.23±0.30[a]	18.42±0.40[a]	16.15±0.01[a]	23.91±1.00[a] Ciprofloxazin
Clostridium perfringes	17.83 ±0.17[b]	16.66±0.27[b]	15.72±0.31[b]	19.55±0.41[b]	14.19±0.05[b]	24.95±0.50[b] Ciprofloxazin
Streptococcus pneumoniae	13.54±0.14[a]	17.32±0.28[c]	19.11±0.33[a]	13.43±0.42[c]	18.21±0.07[a]	25.85±0.76[c] Ciprofloxazin
Salmonella typhi	19.46±0.18[a]	20.71±0.25[d]	16.05±0.35[a]	17.65±0.43[d]	20.29±0.08[a]	22.75±0.78[d] Ciprofloxazin
Vibrio cholerae	18.43±0.19[b]	19.85±0.26[e]	21.08±0.36[c]	20.17±0.44[e]	19.50±0.09[c]	24.69±0.79[e] Ciprofloxazin

The values are represented as the Mean ± SD of five cyanobacteria. These cyanobacteria have significant effect at 0.05 levels.

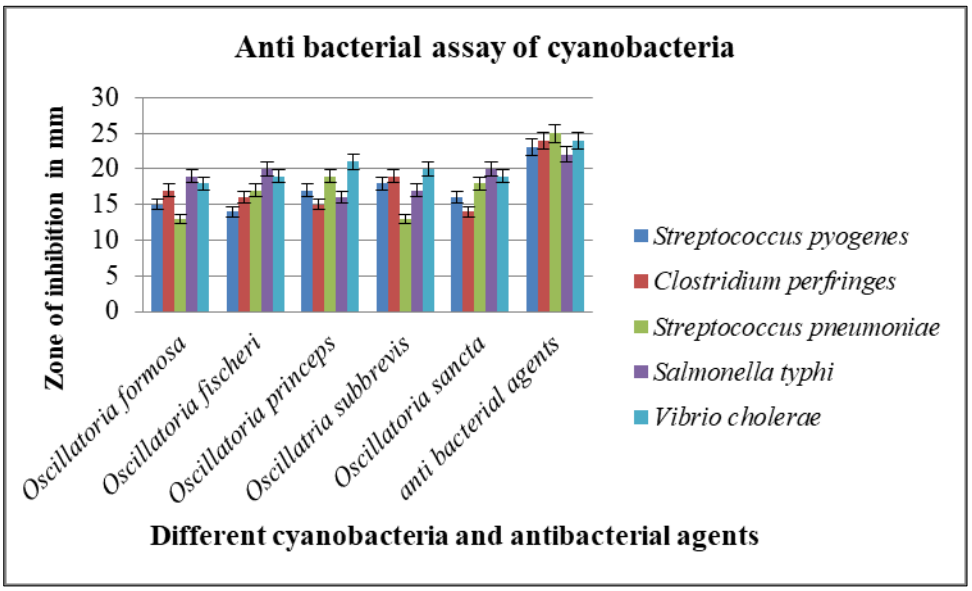

Figure 3 Inhibition of growth of selected highly pathogenic bacteria by different cyanobacteria

4. Discussion

The cyanobacteria such as *Oscillatoria formosa, Nostoc commune*, *Anabaena aequalis, Microcystis aeruginosa* and *Phormidium tenue* have been reported as the main cyanobacteria to showed high antibacterial activity. The production of highly active cyanotoxin produced by cyanobacteria during cell death as algal blooms in stagnant water which is a defence mechanism against other microorganisms like bacteria, fungi, viruses and eukaryotic microalgae present in same water. In this study the cyanobacteria belonging to genera *Oscillatoriaceae* isolated from different indian stagnant water were found to be active against pathogenic bacteria. A variety of solvents with different polarities, were used for the extraction of algal bioactive materials. In our research study we showed antibacterial activity is higher in cyanobacterial supernatants of ethanolic extracts. The results indicated that cyanobacterial ethanolic extracts of *Oscillatoria formosa, Oscillatoria princeps, Oscillatoria fischeri* and *Oscillatoria sancta* showed high activity against Gram positive bacteria and gram negative bacteria.

5. Conclusion

Cyanobacteria have been studied for their morphology and diversity but recently, cyanobacteria have gained a lot of attention because of their possible applications in various fields of microbiology. In this research work we have described the antibacterial activity of five different cyanobacteria belongs to the genus *Oscillatoriaceae*. Cyanobacteria has potential biologically active compounds against their antibacterial, antifungal, antialgal and antiviral activities. Several strains of cyanobacteria were found to accumulate polyhydroxyalkanoates, which can be used as a substitute for non biodegradable based plastics. Cyanobacteria are helpful in agricultural lands as biofertilizers. Some eukaryotic green algae produce more oil content for ecofriendly production of biodiesel.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare that they have no conflict of interest.

Statement of ethical approval

All laboratory procedures conducted in this research studies are highly pathogenic bacteria were in accordance with the ethical standards of the institutional research are comparable with ethical standards.

Statement of informed consent

The present research work does not have any studies conducted on animals / human subjects by any of the authors.

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