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**RESEARCH ARTICLE**

# Invitro Antimicrobial Activity of *Oscillatoria angustissima*

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## *Abstract*

Cyanobacteria and eukaryotic algae occur in fresh water marine and terrestrial habitats. A number of cyanobacteria and microalgae produce various biologically active compounds. These include antibiotics in which laboratory tests inhibited bacteria and fungi that incite diseases of human. In general, isolation of bioactive compounds from cyanobacteria is done with two objectives. One is to discover new compounds for pharmaceutical, agricultural or bio-control application. The other is to better understand the interactions of individual organism within their natural communities. For each of these purpose there is needed to screen new cultureable organism.

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## Introduction

Cyanobacteria are an assemblage of Gram-Negative eubacteria. They are structurally diverse and widely distributed throughout the world and are later known as blue green algae. Cyanobacteria are characterized by their capacity to perform biological nitrogen fixation and oxygenic photosynthesis. Cyanobacteria are very resistant to extreme environmental conditions. They are assuming increasing importance in frontier areas of biotechnology. The typical anabiosis and rapid restoration of activity under favorable conditions are characteristic of them (Pankratova *et al.,* 1987). The several classes of marine and macro-algae have been identified over the last few decades and their chemical constitution and pharmacological activity have been studied in detail (Umemura *et al*., 2003, Takamatsu *et al*., 2003, and Mayer *et al.,* 2003).

Cyanobacteria are prokaryotic organisms capable of oxygenic photosynthesis. They appeared to be a rich source of many useful products and are known to produce a number of bioactive compounds (Carmichael *et al.,* 2001; Codd *et al.,* 1997) and also source of many useful natural products which are used as feed and fertilizer. During the last few decades, cyanobacteria have been described as potentially important source for vitamins, fuels, fine chemicals and many other pharmaceutical products. To date, more than 10,000 marine derived compounds have been isolated and this is coming from less than 1% of the total marine biodiversity. The range of marine organisms tapped for their natural products production include sponges, tunicales, bryozoans, nudibranchs and gorgonians of these microorganisms. One particular group that is emerging as a source of important bioactive compounds is the marine blue-green algae or cyanobacteria for antibiotics and other pharmacologically active compounds has received over increasing interest as a potential source for new drugs (Fish and Codd *et al.,* 1994; Borowitzka *et al.,* 1995). Cyanobacteria from local habitats seem to be a source of potential new bioactive substances that could contribute to reduction of the number of bacteria, fungi, viruses and other microorganisms.

Algal organisms are rich source of structurally novel and biologically active metabolites. Secondary or primary metabolites produced by these organisms may be potential bioactive compounds of interest in the pharmaceutical industry.

Cyanobacteria and eukaryotic algae occur in fresh water, marine and terrestrial soil habitats. A number of cyanobacteria and microalgae produce various biologically active compounds. These include antibiotics which in laboratory tests inhibited bacteria and fungi that in cite diseases of humans.

In general, isolation of bioactive compounds from cyanobacteria is done with two objectives. One is to discover new compounds for pharmaceutical,

agricultural or bio control application. The other is to better understand the interactions of individual organisms within their natural communities. For each of these purposes there is a need to screen new culturable organisms. Microalgae such as *Ochrmonas sp*., *Prymnesium parvum* and a number of blue green algae produce toxins that may have potential pharmaceutical applications.

Various strains of cyanobacteria are known to produce intracellular and extracellular metabolites with diverse biological activities such as anti-algal, antibacterial, antifungal and antiviral activity. Nitrogen fixing strains produce compounds with different activity spectra and different molecular weights but their chemical structures have not been established (Katircioglu *et al*., 2006). Marine organisms are a rich source of structurally novel and biologically active metabolites (Borowitzka MA *et al.,* 992). Secondary or primary metabolites produced by these organisms may be potential bioactive compounds of interest in the pharmaceutical industry. Many bioactive and pharmacologically active substances have been isolated from algae. Extracts of marine algae were reported to exhibit antibacterial activity. Many authors had found antibacterial activities of microalgae. Cyanobacteria and eukaryotic microalgae produce various biologically active compounds. These include antibodies, which in laboratory tests, inhibited bacteria and fungi that incite diseases of humans (Kulik *et al.,* 1995). Tropical waters and along the South West Coast of India, the *Trichodesmenium sp*., is largely confined to the surface and occurs in various intensity, almost every year from February to May along West Coast of India. Decaying blooms of *Trichodesmenium sp*., may lead to anoxic conditions and mortality as has been reported for Orysters in India. *Trichodesmenium sp*., has also been described as non-toxic or sometimes toxic to a range of organisms.

Cyanobacteria are a very old group of organisms and represent relies of the oldest photoautotrophic vegetation in the world that occurs in fresh water, marine and terrestrial habitats. Cyanobacteria have drawn much attention as prospective and rich sources of biologically active constituents and have been identified as one of the most promising groups of organisms to be able of producing bioactive compounds. Cyanobacteria are known to produce metabolites with diverse biological activities such as antibacterial, antifungal, antiviral, anticancer, anti-plasmodial, algicide, anti-platelet aggregation and immunosuppressive activities.

Screening of cyanobacteria for antibiotics and other pharmacologically active compounds has received ever increasing interest as a potential source for new drugs. Cyanobacteria from local habitats seem to be a source of potential new active substances that could contribute to reduction of the number of bacteria, fungi, viruses and other microorganisms.

Cyanobacteria of cran have not yet been studied for antimicrobial activity and little work has been done to screen. Cyanobacteria isolated from paddy fields with regard to their production of bioactive compounds. In order to find the potential of cyanobacteria for production of antibacterial and antifungal compounds in rice fields of north of cran 150 strains of heterocystous cyanobacteria were isolated and their potency were studied. The results are presented in this paper (Flores E *et al*.,1986).

The search for plants with antimicrobial activity has gained increasing importance in recent times, due to growing worldwide concern about the alarming increase in the rate of infection by antibiotic resistant microorganisms. Although extremely effective antibiotics are able to induce resistance in bacteria, for 480 years bacterial resistance has been the main factor responsible from the increase of morbidity, mortality and health care costs of bacterial infections. The defense mechanism against antibiotics is widely present in bacteria (eg : *Pseudomonas, Klebsiella, Enterobacter, Acinetobacter, Salmonella, Staphylococcus, Enterococcus* and *Streptococcus*) and became a world health problem. However, there has been a rising interest of researchers for natural products from plants for the discovery of new antimicrobial and antioxidant agents in the last three decades. Several algal species contain natural bioactive compounds that act as potent antimicrobial agents. For example, *Spirulina* species have some valuable antiviral and antioxidant compounds (Davis, P.H. *et al*., 1982).

Cyanobacteria are the Gram-Negative photosynthetic prokaryotes found in almost all the ecological habitats. They are morphologically, physiologically and metabolically very diverse group and have been the thrust area for investigation since long. However, increasing trend of identifying of biological resources for the production of bioactive molecules prompted scientific community to screen cyanobacteria in recent past.

Cyanobacteria produce metabolites with diverse biological functions such as antibacterial, antifungal, antiviral, anticancer or cytotoxic, anti-plasmodial, anti-platelet aggregation and immunosuppressive. Literature survey revealed that *Nostoc communes, Cytonema hofmanni, Hapalosiphon fontinalis, Anabaena spp., Nostoc spongiaeforme, Microcystis aeruginosa, Synechocystis* and *Synechococcus, Phormidium sp.,* and *Fischerella sp.,* are documented for the

production of antimicrobial agents. Owing to the above facts, this group of organisms warrants extensive screening for the production of various bioactive compounds.

It was observed during survey of literature that most of the screening efforts have been done using mesophilic cyanobacteria and no reports exists so far on thermotolerant or thermophilic genera except one. Therefore, present study was almost to screen thermophilic cyanobacterial cultures isolated from Soldhar and Ringigad thermal springs (Tapoban geothermal field, Chamoli, Uttarakhand) for the production of antibacterial components (Fish,S.A *et al.,* and Codel,G.A *et al.,* 1994).

Researchers studying marine cyanobacteria in order to find novel natural products are finding containing an abundance of potent bioactive compounds with promising anticancer, antibiotic and anti-inflammatory activity. Marine algae are among the largest producers of biomass in the marine environment. They also produce a wide variety of chemically active metabolites, potentially to protect themselves against other organisms. These active metabolites also known as biogenic compounds produced by several species of marine, macro and micro algae which have antibacterial, anti-algal, anti-macro fouling and antifungal properties. Many of the metabolites are novel structures that represent unique biosynthetic pathways. Some of the most promising compounds function in target cells as tubilin polymerization inhibitors (compounds that inhibit the formation of cellular microtubules during the process of mitosis), actin polymerization inhibitors (compounds that inhibit development of actin filaments in cells) and neurotoxins. Numerous promising compounds have been identified in the cyanobacterium *Lyngbya majuscule* (mermaid's hair or fireweed). This filamentous cyanobacterium can be found in tropical and subtropical marine and estuarine environments around the world. Some strains cause swimmer's itch (see William Gerwick's power point presentation, Introduction of drug discovery from marine organisms "11.Resources power point Gerwick" on this CD).

Medicinal plants are natural resources yielding valuable herbal products which are often in the treatment of various ailments. For this purpose, the use of plant extracts in traditional medicine has been going on from ancient times. Herbalism and folk medicine, both ancient and modern have been the source of much useful therapy. During the last 20 years renewed interest has emerged to help developing safer antimicrobial drugs from the natural sources. Presumably due to the increasing development of drug resistance to human pathogenic organisms as well as the appearance of undesirable side effects of certain antibiotics and the emergence of previously uncommon infections.

*Scoparia dulcis* L., commonly known as sweet broom weed is a perennial herb widely distributed in tropical and subtropical regions. In these regions, fresh or dried *S. dulcis* plants have been traditionally used as remedies for stomach troubles, hypertension, diabetes, bronchitis and as analgesic and antipyretic agents. In view of its high reputation and wide publicity but also intensified research efforts by researchers. More recently, a number of the speculated medicinal values of *S. dulcis* have been validated by scientific research.

Secondary metabolites from marine organisms are an important source of biomolecules for drug discovery and development (Cragg *et al.,* 2004). Since its inception in the 1950's, a myriad of novel marine derived compounds with unique carbon skeleton never been reported from terrestrial source, have been identified. A number of these natural products posses potent biological properties and currently are either in preclinical or clinical testing for the treatment of various human ailments (Cragg *et al.,* 2004).

Cyanobacteria are an ancient group of photosynthetic prokaryotic organisms and are thought to be the first organism to be carried out oxygenic photosynthesis. These organisms can inhibit a range of habitats including fresh water marine and soil environments as well as extreme habitats such as hot spring waters and arctic and Antarctic environments. Under eutrophic conditions, these organisms are able to form intense blooms. The bloom forming process can be caused by increased levels of nutrients like P and V. cyanobacteria have a number of special features and besides their ability for dinitrogen fixation. Many of them have long been recognized as producers of a wide array of secondary metabolites which allow the group to dominate under systems of high herbivory and extreme nutrient and light conditions (Fig.1) (Sompong, U. *et al*., 2005).

Cyanobacteria (also known as blue-green algae due to the presence of certain pigments) are among the oldest phototrophic prokaryotic organisms. The search for cyanobacteria with antimicrobial activity has gained importance in recent years due to growing worldwide concern about an alarming increase in the emergence of antibiotic resistance and further increase in the rate of infections by these antibiotic-resistant microorganisms. Various strains of cyanobacteria are known to produce intracellular and extracellular metabolites with diverse biological activities such as antibacterial and antifungal. The aim of study reported here was to investigate the antibacterial activity of various organic extracts and spent medium

of *Anabaena sp*., against the bacteria of clinical significance.

The ocean which is called the mother of origin of life is also the source of structurally unique natural products that are mainly accumulated in living organism. Several of these compound show pharmacological activities and are helpful for the invention and discovery of bioactive compound. Primarily for deadly diseases like cancer, acquire immunodeficiency syndrome, etc. The lives saving drugs are mainly found abundantly in microorganisms such as algae, invertebrates and vertebrates. Modern technologies have opened vast areas of research for the extraction of biomedical compounds from ocean and seas to treat the deadly disease.

Screening of cyanobacteria for antibiotics and pharmaceutically active compounds has received ever increasing attention for sometimes. The bioactive molecules isolated show a broad spectrum of biological activities including toxins, antibiotics, fungicides and algaecides (Borowitzka *et al.*, 1995). The importance of cyanobacteria as a potential drug resource is evident by launching of the cyanomyces project in Europe, anticipated to generate novel therapeutic substances by combining genes from actinomyces and cyanobacteria.

## Material and Methods

### Collection and Isolation of Cyanobacterial Culture

Cyanobacterial mats were obtained from Microbial Germplasm Culture Collection Unit, Sri Gowri Biotech Research Academy, Thanjavur. The cyanobacterial cultures were isolated by using spread plate method in ASN III medium.

### Identification

After isolation, the individual colony was picked up from the plates and observed under Nikon microscope (oil immersion 100 X) after wet mount preparation. The cyanobacterial morphotypes such as filamentous nature, size, shape of vegetative cells and akinetes were identified and photographed under Nikon digital microscope (Japan). Identification of cyanobacterial isolates were carried out by using the taxonomic publication of Desikaehary *et al.*, 1959). The identification cultures were mass cultivated in the ASN III broth medium.

### Mass Cultivation of Cyanobacteria

Each cyanobacterium was cultured in a 250ml flask containing 150ml of ASN III medium without shaking for 30 days. The incubation temperature was 28±2°C and illumination was provided at 3000lux with a white continuous light. As more culture was required to obtain extraction was done by having them left under 3000lux light intensity and 8hrs under darkness. Algae were harvested approximately after a good mat formation.

### Microbial Cultures Used for Antimicrobial Assay

Bacterial cultures namely *Salmonella typhi, Enterobacter aerogenes, Staphylococcus aureus* were obtained from Sri Gowri Biotech Academy, Thanjavur. Pure inoculums were prepared from the above cultures and maintained for further studies.

### Microbial Inoculums Preparation

A young microbial inoculums/culture was prepared and used for the experiment. The Nutrient Broth (NB) were prepared, poured into tubes and sterilized. The pure microbial cultures were inoculated in the tubes using inoculation needle or loop. Then the bacterial tubes were incubated at 37°C for 24-48 hours.

### Preparation of Solvent Extract from Cyanobacteria

The cyanobacteria were extracted with methanol, acetone, water as per the method of Perez et al., 1990. The dried cyanobacterial cultures were freeze dried before extraction. Following this, the culture was thawed by keeping it in room temperature for 10min and the water content formed was removed using filter paper. Water extracts were made by responding 50mg of freeze dried cyanobacterial material in 3ml of distilled water. After careful mixing, the sample was kept at room temperature for 30min. The suspension was centrifuged at 2500rpm for 6min. The supernatant was drawn with a pipette and 100µl of the aqueous extract was transferred to each well and air dried before using organic extracts were made from cyanobacteria using methanol and ethyl acetate. The pre-weighed cyanobacterial cultures were crushed using mortar and pestle. The sample was mixed and was then left with the extraction fluid for 10min. The sample was centrifuged at 2500rpm for 6min and the supernatant was transferred to a clean 2ml eppendorf tube. The solvent was evaporated to dryness.

### Media for Antimicrobial Activity

**Composition of Nutrient Agar Medium**

| | | |
|---|---|---|
| Peptone | : | 5gm |
| Beef extract | : | 3gm |
| Sodium chloride | : | 5gm |
| Agar | : | 15gm |
| Distilled water | : | 1000ml |

**Composition of Potato Dextrose Medium**

| | | |
|---|---|---|
| Potato | : | 200gm |
| Dextrose | : | 20gm |
| Agar | : | 18gm |
| Distilled water | : | 1000ml |

**Preparation of Medium**

**Nutrient Agar Medium**

The ingredients (Peptone-5g; Beef extract-3g; NaCl-15g) were weighed and taken in a conical flask containing 1000ml distilled water. Then pH of the medium was adjusted to 6.8 using the pH meter by the addition of either acid or alkali. The flask were sterilized in an autoclave at 121°C for 15lbs pressure for 15min and allowed to cool.

**Potato Dextrose Agar Medium**

The ingredients (Potato-200g; Dextrose-20g; Agar-18g) were weighed and taken in a conical flask containing 1000ml distilled water. The pH of the medium was adjusted to 5.6 using a pH meter by the addition of either acid or alkali. The flask were sterilized by using autoclave at 15lbs pressure for 15min and allowed to cool.

**Antimicrobial Activity (Perez *et al*., 1990)**

The antimicrobial activity of *Oscillatoria subuliformis* were performed by agar well diffusion method described by Perez et al., 1990. The antimicrobial activities of the *O. subuliformis* were tested against the selected bacterial and fungal strains. The sterilized nutrient agar and potato dextrose agar medium was poured into each sterile petriplates and allowed to solidify. By using a sterile cotton swabs, fresh bacterial and fungal culture with known population count was spread over the plates by following spread plate technique. A well was cut on the media and was filled with known quality of solvent extracts of *O. subuliformis*. Then the plates were incubated for 24hrs at 37°C for bacteria and 48hrs at 27°C for fungi. After the incubation period, the results were observed and the diameter of inhibition zone around each isolates was measured.

**Antibiotic Sensitivity Test on Microbes (Positive Control)**

The antibiotic sensitivity test using standard antibiotics (penicillin, ampicillin, tetracycline for bacteria and fluconazole, griseofulvin, amphotrisin for fungi) were analyzed by following the method of Bauer *et al*., 1996.

The sterilized nutrient agar and potato dextrose agar medium was poured into each sterile petriplates and allowed to solidify. By using a sterile cotton swabs, a fresh bacterial and fungal culture with known population count spread over the plates by following spread plate technique. Then the selected standard antibiotic discs namely ampicillin, griseoflavin were placed on the bacterial and fungal culture plates. Then the plates were incubated for 24hrs at 37°C for bacteria and 27°C for 48hrs for fungi. After the incubation period, the results were observed and the diameter of the inhibition zone was measured around the isolates.

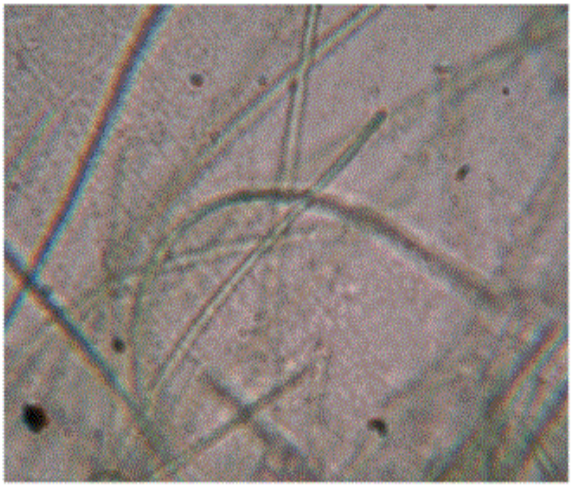
**Antimicrobial Effects of Solvents (Negative Control)**

The antimicrobial activity of methanol, acetone and water solvents was tested against the selected bacterial and fungal strains. The sterilized nutrient agar and potato dextrose agar medium was poured into each petriplates and allowed to solidify. By using a sterile cotton swabs, a fresh bacterial and fungal cultures with known population count was spread over the plates by following spread plate technique.

Then the plates were incubated for 24hrs for fungi. After the incubation period, the results were observed and the diameter of the inhibition zone was measured around the isolates.

## Results

In the present investigation, the antimicrobial activity of cyanobacteria were collected from at Sri Gowri Biotech Research Academy, Thanjavur (Dt.) brought into the laboratory for further process. The antimicrobial activity of two extracts of cyanobacteria, culture-A and culture-B were also comparatively analyzed against standard antibiotics by antibiotic sensitivity test. (Plate-1).



*Oscillatoria amphibia*

**1. Antibacterial Activity of Cyanobacteria**

The antibacterial activity of cyanobacteria, culture-A and culture-B was assessed using the agar well diffusion method by measuring the diameter of growth inhibition zones and its subsequent was tabulated (Table- 1.1 & 1.2). The results indicate that the extracts of cyanobacteria had an excellent activity against tested bacterial pathogens followed by ethanol, petroleum ether and distilled

water. The maximum zone of inhibition was observed against *Salmonella typhi* in methanol [-], acetone [-], water [-], *Enterobacter* in methanol [-], acetone [-], water [-] and *Staphylococcus aureus* in methanol 15, acetone [-], water [-]. It was examined from the available data that cyanobacteria-A showed significantly higher rate of sensitivity various extracts when compared cyanobacteria-B. The maximum zone of inhibition was observed against all bacterial pathogens.

**2. Antifungal Activity of Cyanobacteria**

The antifungal activity of cyanobacteria, culture-A and culture-B was assessed using the agar well diffusion method by measuring the diameter of growth inhibition zones and its subsequent was tabulated. (Table. 2.1 & 2.2). The results indicate that the extracts of cyanobacteria had an excellent activity against tested bacterial pathogens followed by methanol, acetone and water. The maximum zone of inhibition was observed against *Penicillium granules* in methanol 10mm, acetone 12mm, water [-], *Aspergillus flavus* in methanol 5mm, acetone [-], water [-]. It was examined from the available data that cyanobacteria culture-A showed significantly higher rate of sensitivity various extracts when compared cyanobacteria culture-B. The maximum zones of inhibition were observed against all fungal pathogens.

**3. Antibiotic Sensitivity Test (Positive Control)**

All the test bacterial isolates showed high sensitivity against antibiotic tested organisms such as *Salmonella typhi*, *Enterobacter* and *Staphylococcus aureus*. The results were given in (Table.3& Fig.3). When compared with the antibiotics namely ampicillin and griseofulvin, extracts of cyanobacteria culture-A and culture-B showed a lesser antibacterial activity.

**4. Effects of Solvents (Negative Control)**

The results of control experiments (solvents) showed no antibacterial activity against the all pathogens. (Table.4 & Fig.4).

**1. Antibacterial Activity of Cyanobacteria**

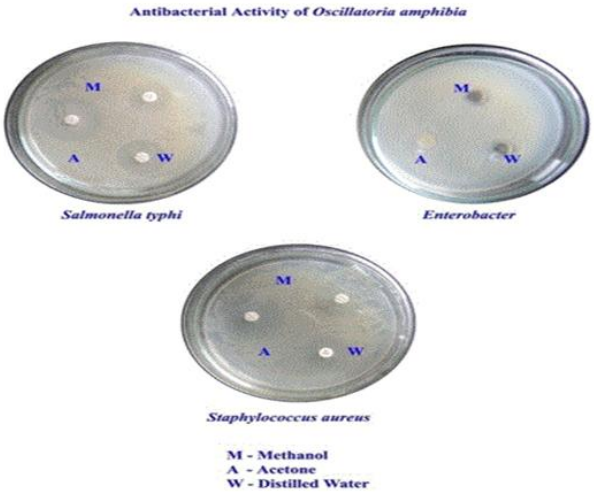
**Table- 1.1**

| Name of Cyanobacterial Culture | Name of the organism | Methanol | Acetone | Water |
|---|---|---|---|---|
| *Oscillatoria Angustissima* | *Salmonella typhi* | 5mm | 4mm | - |
| *Oscillatoria Angustissima* | *Enterobacter* | 6mm | 5mm | - |
| *Oscillatoria Angustissima* | *Staphylococcus aureus* | 8mm | 6mm | - |

**Table- 1.2**

| Name of Cyanobacterial Culture | Name of the organism | Methanol | Acetone | Water |
|---|---|---|---|---|
| *Lyngbya Aestuarii* | *Salmonella typhi* | 7mm | 7mm | - |
| *Lyngbya Aestuarii* | *Enterobacter* | 6mm | 6mm | - |
| *Lyngbya Aestuarii* | *Staphylococcus aureus* | 10mm | 10mm | - |

**Figure- 1**




## 2. Antifungal Activity of Cyanobacteria

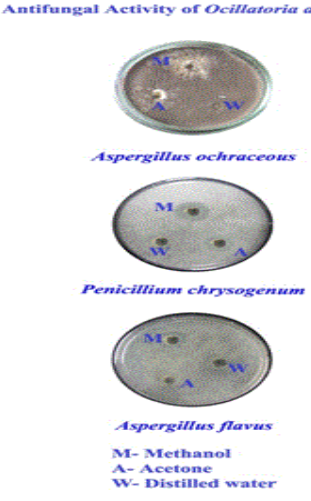
**Table- 2.1**

| Name of Cyanobacterial Culture | Name of the organism | Methanol | Acetone | Water |
|---|---|---|---|---|
| *Oscillatoria Angustissima* | *Penicillium granules* | 4mm | 3mm | - |
| *Oscillatoria Angustissima* | *Aspergillus flavus* | 3mm | 3mm | - |
| *Oscillatoria Angustissima* | *Acremonium* | 3mm | - | - |

**Table- 2.2**

| Name of Cyanobacterial Culture | Name of the organism | Methanol | Acetone | Water |
|---|---|---|---|---|
| *Lyngbya Aestuarii* | *Penicillium granules* | 4mm | 3mm | - |
| *Lyngbya Aestuarii* | *Aspergillus flavus* | 3mm | 2mm | - |
| *Lyngbya Aestuarii* | *Acremonium* | 3mm | 2mm | - |

**Figure -2**

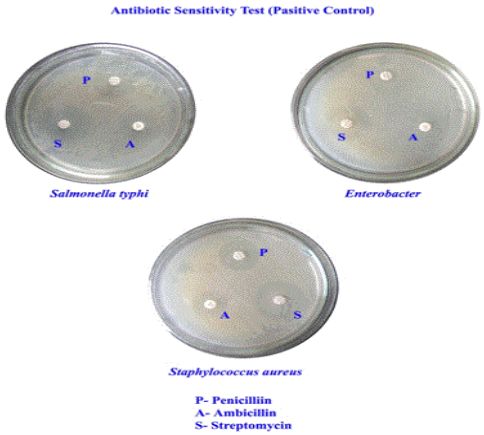


**3. Antibiotic Sensitivity Test (Positive Control)**

**Table- 3**

| Name of Cyanobacterial Culture | Name of the organism | Fluconozal |
|---|---|---|
| *Oscillatoria Angustissima* | *Penicillium* | 11mm |
| *Oscillatoria Angustissima* | *Aspergillus flavus* | 10mm |
| *Oscillatoria Angustissima* | *Acremonium* | 12mm |

**Figure- 3**

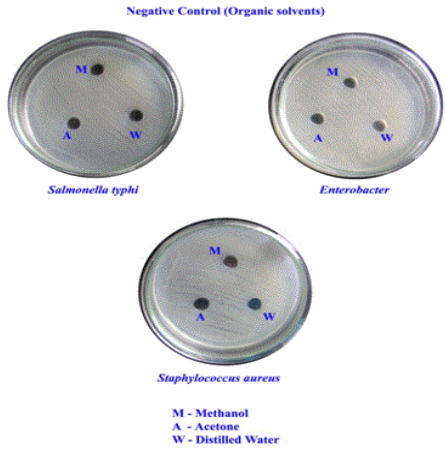



**4. Effects of Solvents (Negative Control)**

**Table- 4**

| Name of Cyanobacterial Culture | Name of the organism | Methanol | Acetone | Water |
|---|---|---|---|---|
| *Lyngbya Aestuarii* | *Penicillium* | - | - | - |
| *Lyngbya Aestuarii* | *Aspergillus flavus* | - | - | - |
| *Lyngbya Aestuarii* | *Acremonium* | - | - | - |

**Figure- 4**



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