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Niromycin A: An Antialgal Substance Produced by *Streptomyces endus* N40

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Abstract: The antialgal activity of 107 *Actinomycete* isolates were isolated from different localities in El-Sharkia, El-Dakahliya and El-Meniya governorates. Egypt. Isolate No. 40 (isolated from Ekhtab. Aga, Dakahliya) was selected and identified as *Streptomyces endus* N40. The optimum culture conditions for the production of the antialgal metabolite were studied. It has been found that the optimum incubation temperature for the production of the antialgal metabolite from *Streptomyces endus* N40 was 28°C after incubation period (8 days) at pH 6.5. The most favorable carbon, nitrogen, phosphorus, microelement and vitamin sources were maltose (6 g L^{-1}), asparagine (1.486 g L^{-1}), K_2HPO_4 (I g L^{-1}), $FeSO_4.7H_2O$ (0.01 g L^{-1}) and (inositol) (0.01 mg L^{-1}), respectively. The maximum antialgal activity was obtained against *Anabaena* sp. *Anabaena flos-aqueae*, *Nostoc* sp. and *Anacystis nidulans.* The antialgal substance had extracted using xylene solvent Formulation and identification of the antialgal substance that produced by *Streptomyces endus* N40 was carrying out using IR, Mass, NMR spectra and elementary analysis and these results were emphasized that the molecular weight equal 279.33 KDa with chemical formula ($C_{15}H_{21}NO_4$) and identified as Niromycin A.

Key words: Streptomycetes, niromycin A, algal blooms, antibiotic, cyanobacteria

INTRODUCTION

Presently, the direct application of chemicals to control algal blooms harm and/or eventually disrupt the aquatic ecosystem by killing off beneficial plankton and even fish (McGuire *et al*., 1984; Reynolds, 1984; Sevrin-Reyssac and Pletikosic, 1990). Consistent with the panecological and environmental approaches to lake water conservation, many countries are currently seeking to develop suitable biological control agents (Imai *et al*., 1993; Kim *et al*., 2003; Manage *et al*., 2000; Boudjella *et al*., 2006; Volka and Furkert, 2006).

In particular, blooms of the cyanobacterium *Microcystis aeruginosa* Lemmermann f. *Aeruginosa* are widespread in eutrophic lakes and reservoirs throughout the world (Carmichael, 1992; Han *et al*., 2002; Hong *et al*., 2002; Choi *et al*., 2005) and may lead to the production of microcystin, a hepatotoxin that affects fish, birds, wild animals, livestock and humans. It is associated with allergies, irritation reactions, gastroenteritis, liver diseases and tumors (An and Carmichael, 1994; Bell and Codd, 1994; Dawson, 1998). Historically, these cyanobacterial (algal) blooms have also caused other problems, such as foul odors, decreased aesthetic value, deterioration of water quality and deoxygenation of water (Sigee *et al*., 1999). Also, *Oscillatoria rubescens* and *O. agardii* have been reported to produce hepatotoxins (Carpenter and Carmichael, 1995) and may be responsible for dermatitis or skin irritation when people are exposed to polluted water (Gorham and Carmichael, 1988). In addition, they produce unpleasant odors (Jüttner, 1976; Slater and Blok, 1983; Tsuchiya *et al*., 1992).

The search for new antibiotics continues to be of utmost importance in research programs around the world because of the increase of resistant pathogens and toxicity of some used antibiotics. Among

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microorganisms, actinomycetes are one of the most investigated groups particularly members of the genus *Streptomyces* from which, a large number of antibiotics was obtained and studied (Okami and Hotta, 1988). The vast majority of actinomycetes have originated from soil (Davies and Williams, 1970) and their isolation method deal almost exclusively with those suitable for *Streptomyces* species which grow rapidly on soil dilution plates. However, in recent years, the rate of discovery of new antibiotics in the genus *Streptomyces* was declining and isolation of other actinomycete genera, appeared to be necessary to assess the health hazard and to find novel strains producing commercially valuable antibiotics.

The genus *Streptomyces* has received considerable attention especially for its importance as a source of several secondary metabolites particularly antibiotics (Sanglier *et al*., 1993a; Young, 1993; Lazzarini *et al*., 2000; Habib *et al*., 2001; Kokare *et al*., 2004; Choi *et al*., 2005; Boudjella *et al*., 2006; Volk and Furkert, 2006). Some antibiotics have been found to use in therapy of plant and human diseases which are caused by bacteria, virus, amoeba and other fungi. This wide range of usefulness makes the substance producing actinomycetes are most important (Brooks *et al*., 1998; Castillo *et al*., 2003; Hammad, 2004; Sujatha *et al*., 2004). Fogg *et al*. (1973) reported that the metabolites of *Streptomycetes* have antimicrobial activities against cyanobacteria as *Anabaena cylindrical* and *Tolypothrix tenuis* and shriveling in the vegetative cells of *A. cylindrical* causes discoloration and complete lysis. The lytic activity explained the basis of the interaction; between the antibiotics and cell wall functional and or structural components which led to lytic appearance (Whyte *et al*., 1985). Gunnison and Alexander (1974) reported that the activity of cellulase or polygalacturonase enzymes producing *Streptomycete* (G4) against the cell wall of *Chlamydomonas reinhardtii* reached to 89 or 98% and *Ulothrix fimbrata* reached to 64 or 84%, respectively and attributed the lysis of *Cylindrospermum* sp.; to Streptomycete's lysozyme. In this study, we report the discovery of an antialgal actinomycetes active against *Anabaena* sp., *Anabaena flos-aqueae*, *Nostoc* sp. and *Anacystis nidulans* and also reported the antialgal features of this actinomycetes in regards to its activity at various algal and actinomycetal growth phases. We report also on the purification of lytic agent and the effect of the purified antibiotic on the tested alga.

MATERIALS AND METHODS

Strains and Media

Strain No. 40 was isolated on starch-nitrate agar medium from soil cultivated with pepper according to Waksman (1959). Experimental organism (Isolate No. 40) was classified by using ISP (International Streptomyces Project) according to Shirling and Gottlieb (1966) and Bergey's Mannual (1989) and identified as *Streptomyces endus* N40. *Anabaena* sp., *Anabaena flos-aqueae*, *Nostoc* sp. and *Anacystis nidulans* were taken from the algal lab. Faculty of Science, Zagazig University and cultivated on watanabe medium (Watanabe, 1951) and BG11 medium (Stanier *et al*., 1971). This study takes place in the Phycology and Water Research Lab, Faculty of Science, Zagazig University, during January 2005.

Assessment of Algal Lytic Actinomycete

Streptomyces endus N40 was streaked on agar plates and incubated for 8 days at 28°C. After detectable, the colonies of *Streptomyces endus* N40, the solid medium was cut into discs (5 mm) by using cork borer and placed on watanabe medium cultivated with cyanobacteria (*Anabaena* sp., *Anabaena flos-aqueae* and *Nostoc* sp.) according to Yamamoto (1978). After the elapse of incubation periods, the clear inhibition zones induced by *Streptomyces endus* N40 discs were measured by millimeter. With respect to the growth conditions of *Anacystis nidulans*, 0.1 mL of *Streptomyces endus* N40 suspension was seeded to the nutritive liquid medium of BGII, the initial optical density of algal

medium at zero time was calculated at 665 nm. Then all the flasks were incubated for 2 weeks under normal growth condition. The optical density (growth rate) was calculated every 2 days Uchida *et al*. (1998).

Separation of Lytic Agent Against Cyanobacteria

Optimization for the maximum production of lytic agent from *Streptomyces endus* N40 was carded out using different carbon, nitrogen, phosphorus, microelement and vitamin sources and take in consideration the best; pH value, incubation period and incubation temperature as previously mentioned. The best medium having (g L^{-1}); maltose 6 g; asparagine 1.486 g; K_2HPO_4 1 g; NaCl 0.5 g; $MgS0_4.7H_2O$, 0.5 g; $CaCO_3$ 3 g; $FeSO_4.5H_2O$, 0.01 g; vitamin Bio inositol), 0.01 mg and distilled water up to 1000 mL. After growing *Streptomyces endus* N40 on the optimum medium, the cultured broth (5 L) was centrifuged at 2000 rpm. And the resulting supernatant was dialyzed (cellulose bag method) against hypertonic sweet solution. Subsequently, the resulting residue was mixed with xylene (3 times). The organic layers were combined and concentrated under vacuum to about 50 mL using a rotary evaporator. To the concentrated layer, a non-polar organic solvent (petroleum ether 40-60) was added drop by drop untill yellowish crystalline substance appeared. The solid fraction was washed with ether and then dried in air. Continuous purification of substance using TLC (silica gel G54) was carried out. The major spots appeared at Rf = 0.7 was gathered and eluted with petroleum ether (40-60). The partially purified fractions were microanalyzed using IR, Mass and NMR spectra and elementary analysis for complete identification of substance.

RESULTS

Antagonistic Activity of Stereptomyces isolate on Tested Cyanobacteria

Clear inhibition zones represented in Table 1 and Fig. 1 revealed that the highly sensitive algal species to the block agar born actinomycete was detected against *Anabaena* sp. which gave a clear zone equal (26 mm) followed by *Nostoc* sp. which gave a clear zone equal (24 mm). While a clear zone of

Table 1: Inhibition zone (mm) of *Streptomyces endus* N40 against tested cyanobacteria

Tested algae	Diameter of discs = 5 mm Inhibition zones (mm)
Anabaena sp.	26
Anabaena flos-aqueae	22
Nostoc sp.	24

(I)- *Nostoc* sp. (II)- *Anahaena* sp. (III)- *Anabaena flos-aqueae*

Fig. 1: Inhibition zone (mm) of *Streptomyces endus* N40 against tested cyanobacteria

Anabaena flos-aaueae indicated 22 mm in a similar manner results in Table 2 showed chlorosis and complete lysis of *Anacystis nidualans* cells when treated with 1 mL *Streptomyces endus* N40 suspension. The maximum drop in algal growth is indicated after 10 days.

Optimization of the Environmental Conditions and Nutritional Requirements for Antialgal Substance Production by Streptomyces endus N40

The data recorded in Table 5-12 revealed that the highest biomass yield and antialgal substance production by *Streptomyces endus* N40 was achieved after incubation for 8 days at 28°C and pH 6.5 under shaking condition. Optimization for the maximum production of lytic agent from *Streptomyces endus* N40 was carried out using different carbon, nitrogen, phosphorus, microelement and vitamin sources. The best medium has (g L^{-1}): maltose 6 g; asparagine 1.486 g; K_2HPO_4 1 g; NaCI 0.5 g; $MgSO_4.7H_2O$ 0.5 g; $CaCO_3$ 3 g; $FeSO_4.5H_2O$ 0.01 g; vitamin Bio inositol), 0.01 mg and distilled water up to 1000 mL. These are agreement with the results obtained by (Naki *et al*., 2000; Ramadan, 2000; Toshio *et al*., 2000; Yutaka *el al*., 2001; Gupte and Kalkani, 2002; Ammar *et al*., 2003; Hammad, 2004; Ghaly *et al*., 2005).

Table 2: Antialgal activity induced by *Streptomyces endus* N40 in liquid media (inhibition expressed as a reduction in optical density at 665 nm)

	Absorbance reading at 665 nm					
Samples	Zero time	2nd day	4th day	6th day	8th day	10th day
Untreated alga	0.12	0.13	0.17	0.34	0.37	0.85
Treated alga	0.12	0.13	0.14	0.13	0.12	0.11

Untreated alga = *Anacystis alga*; Treated alga = *Anacystis nidulans alga* + *Streptomyces endus* N40

Table 3: The activity of different levels of Niromycin A on *Anacysfis nidulans*

	Absorbance reading at 665 nm								
Concentration of Niromycin A	Zero time	2nd day	4th day	6th day	8th day	10th day	12th day	14th day	16th day
Control	0.05	0.06	0.11	0.12	0.16	0.14	0.23	0.46	0.80
l0 μg mL^{-1}	0.19	0.30	0.62	0.44	0.45	0.44	0.31	0.26	0.33
20 μg mL^{-1}	0.13	0.28	0.60	0.40	0.42	0.42	0.20	0.21	0.24
30 μg nu^{-1}	0.10	0.20	0.54	0.38	0.34	0.29	0.18	0-20	0.21
40 μg mL^{-1}	0.05	0.16	0.29	0.28	0.28	0.20	0.16	0.19	0.20

Table 4: A comparative study of the characteristic properties of the tested substance in relation to reference substance (Niromycin A)

Chemical analysis	Niromycin A	Substance (under test)
C	64.49	64.50
H	7.58	7.58
N	5.01	5.01
O	22.91	22.91
Molecular weight	279.33	279.33
Formula	$C_{15}H_{21}NO_4$	$C_{15}H_{21}NO_4$

Table 5: Effect of the different incubation periods on the production of antialgal substance by *Streptomyces endus* N40

	Inhibition zone (mm) of {disc filter paper (5 mm)} broth extract		
Incubation period (day)	*Anabaena* sp.	*Anabaena flos-aquae*	*Nastoc* sp.
2	0	0	0
3	11	0	12
4	17	10	19
5	23	15	27
6	26	22	24
7	41	29	42
8	42	31	44
9	40	30	41
10	23	13	25
11	14	0	17
12	0	0	0

Table 6: Effect of different pH values on the production of antialgal substance by *Streptomyces endus* N40

	Inhibition zone (mm) of {disc filter paper (5 mm)} broth extract		
pH values	*Anabaena* sp.	*Anabaena flos-aquae*	*Nastoc* sp.
6	23	17	20
6.5	44	32	45
7	27	23	25
7.5	25	20	22
8	19	13	15

Table 7: Effect of different incubation temperature on the production of antialgal substance by *Streptomyces endus* N40

	Inhibition zone (mm) of {disc filter paper (5 mm)} broth extract		
Temperature	*Anabaena* sp.	*Anabaena flos-aquae*	*Nastoc* sp.
15	26	18	27
20	32	22	35
25	40	28	41
28	44	33	46
30	42	30	45
35	30	20	32
40	28	19	29
45	0	0	0

Table 8: Effect of different carbon sources on the production of antialgal substance by *Streptomyces endus* N40

	Inhibition zone (mm) of {disc filter paper (5 mm)} broth extract		
Carbon sources	*Anabaena* sp.	*Anabaena flos-aquae*	*Nastoc* sp.
Starch	37	32	35
D-glucose	29	20	21
D-fructose	32	25	28
D-galactose	22	18	19
Sucrose	22	13	15
Maltose	39	32	36
α-lactose	20	12	14

Table 9: Effect of different nitrogen sources on the production of antialgal substance by *Streptomyces endus* N40

	Inhibition zone (mm) of {disc filter paper (5 mm)} broth extract		
Nitrogen sources	*Anabaena* sp.	*Anabaena flos-aquae*	*Nastoc* sp.
Potassium nitrate	45	33	47
Peptone	43	30	45
Yeast extract	40	28	43
Beef extract	38	27	40
Asparagine	46	33	48
Sodium nitrate	31	23	33
Amm. Chloride	45	33	48
Amm. Nitrate	37	26	39
Amm. Sulphate	45	32	46

Table 10: Effect of different phosphorus sources on the production of antialgal substance by *Streptomyces endus* N40

	Inhibition zone (mm) of {disc filter paper (5 mm)} broth extract		
Phosphorus sources	*Anabaena* sp.	*Anabaena flos-aquae*	*Nastoc* sp.
K_2HPO_4	46	33	48
$(NH_4)_2HPO_4$	40	29	44
KH_2PO_4	42	31	46
Na_2HPO_4	39	29	42
NaH_2PO_4	44	33	48

Table 11: Effect of different microelements on the production of antialgal substance by *Streptomyces endus* N40

	Inhibition zone (mm) of {disc filter paper (5 mm)} broth extract		
Microelements	*Anabaena* sp.	*Anabaena flos-aquae*	*Nastoc* sp.
0.0	46	33	48
$FeSO_4$	46	35	49
$CuSO_4$	39	30	41
$MnCl_2$	45	34	48
Ni Cl_2	34	25	37
$ZnSO_4$	44	34	47
Na_3BO_3	41	32	43
$Na_2WO_4.2H_2O$	32	22	35
$COCl_2$	36	27	38
$(NH_4)_6MO_7O_{24}.4H_2O$	35	27	38

Table 12: Effect of different vitamins on the production of antialgal substance by *Streptomyces endus* N40

	Inhibition zone (mm) of {disc filter paper (5 mm)} broth extract		
Vitamins	*Anabaena* sp.	*Anabaena flos-aquae*	*Nastoc* sp.
0.0	46	35	49
Vitamin C	46	36	47
Vitamin A	42	31	43
Vitamin B_2	44	34	45
Vitamin B_6	43	32	43
Vitamin B_{10}	48	38	50
Vitamin B_{12}	46	36	48
Vitamin B-complex	47	37	49

Isolation and Purification of the Lytic Agent

Streptomyces endus N40 cultivated in 250 mL Erlenmeyer flask containing the optimized medium (100 mL) in each. After autoclaving, suspension of *Streptomyces endus* N40 was inoculated to the different flasks under aseptic condition. All the flasks were incubated at 28°C for 8 days. After the elapse of incubation period, the fermented flasks were collected and the spores of actinomycete as well as its hyphae were separated. The aliquot of fermented media were concentrated to 500 mL by dialysis method (cellulose bag), extracted by xylene at pH 7.0 (Ahmed *et al*., 2002) and the organic layer was collected and concentrated under vacuum by using rotary evaporator to dryness. The obtained residual fraction was purified by using thin layer chromatography, which manifested through ultraviolet lamp one spot at Rf = 0.7. The spots were collected by its elution and the physicochemical characteristics (IR, Mass spectrum, NMR spectrum and elementary analysis). (Williams and Fleming, 1987; Hayakawa *et al*., 1994; Stefani and Agodi, 2000) indicated that this substance is known as Niromycin A (Fig. 2-4). These microanalyses are carried in microanalysis center in Cairo University.

Identification of the Antialgal Substances Produced by Streptomyces endus N40

Taking into consideration the elementary analysis, IR, mass and NMR spectra and also on the basis of the recommended keys for the identification of antibiotics and in view of the comparative study of the recorded properties of the antibiotics, it could be stated that the substance extracted from *Streptomyces endus* N40 is named as Niromycin A (Table 4). The identification is carried out according to (Berdy, 1980a-c; Umezawa, 1977).

Elementary Analysis

The extracted substance from *Streptomyces endus* N40 was found to contain carbon (C = 64.5%), hydrogen (H = 7.58%), nitrogen (N = 5.01%) and oxygen (O = 22.91%).

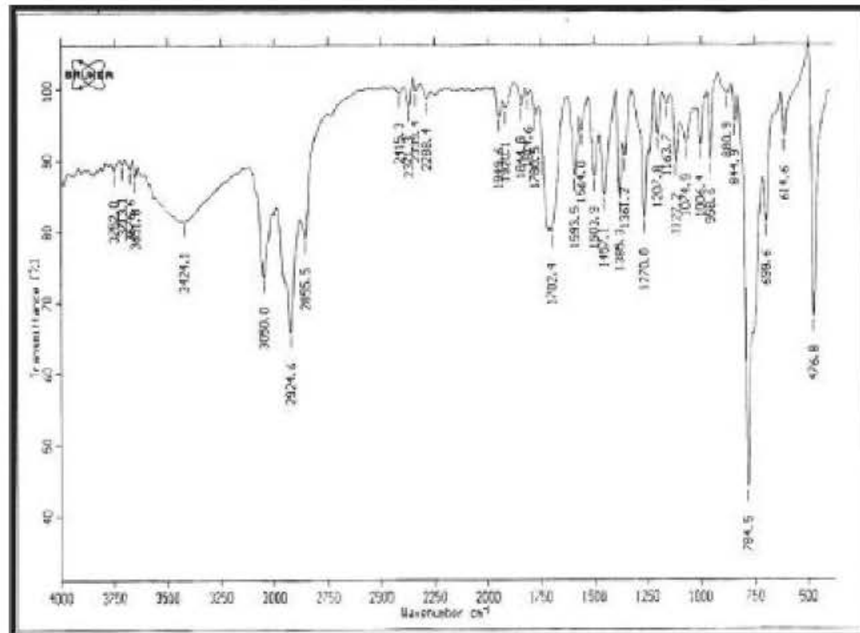


Fig. 2: Infra-red of *Streptomyces endus* N40 metabolite

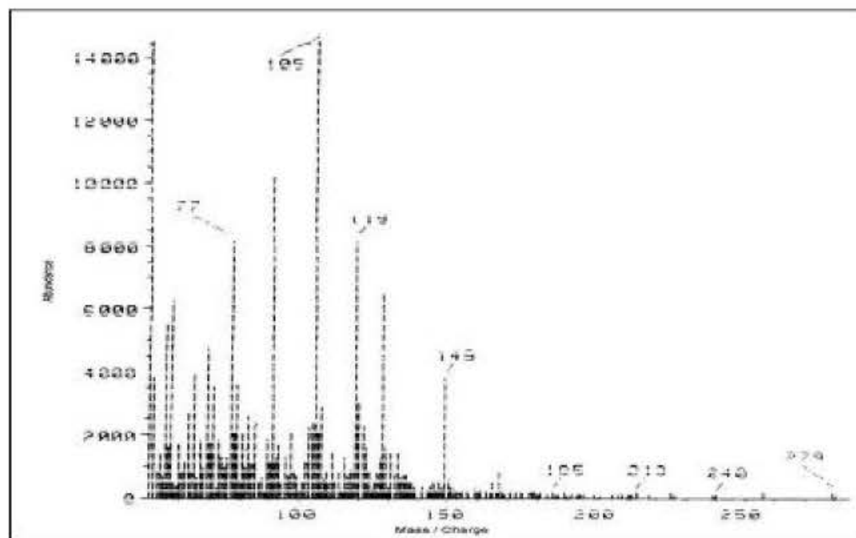


Fig. 3: Mass spectrum of *Streptomyces endus* N40 metabolite

Fig. 4: NMR spectrum of *Streptomyces endus* N40 metabolite

Infra-Red Spectrum (IR)

Besides the elementary analysis the identification of the compound was also confirmed by spectroscopic measurements. The infra-red spectrum of this compound showed an isopropanol band in the range of 1360 and 1385 cm^{-1}; aromatic ring in 1270,1122. 1006, 958. 784 cm^{-1}; CH-aliphatic in 2924. 2855 cm^{-1}; CH-aromatic in 3050 cm^{-1}; amidic carbonyl group in 1702 cm^{-1}; NH group in 3424 cm^{-1}; free OH group in 3651 cm^{-1} (Fig. 3).

Molecular Weight

The FD-MS spectrum showed the molecular peak at m/z 279.33 (Fig. 4).

Molecular Formula

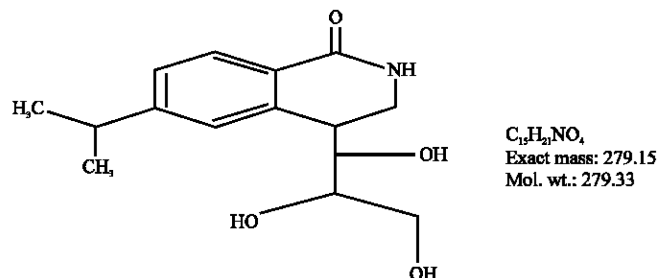
The molecular formula was determined on the basis of the results obtainedfrom the mass spectrometric and elementary analysis of the extracted compound as $C_{15}H_{21}NO_4$.

NMR Spectrum of the Antibiotic

The ^1H NMR of the antibiotics produced by *Streptomyces endus* N40 was investigated by Nuclear Magnetic Resonance (NMR). It could be deduced that the substance molecule is characterized by the following:

- Presence of two methyl groups (singlet at 1, 3).
- Presence of four protons of the sugar molecules (multiplete at 2.26-2.40).
- Presence of the carbon (C^2-H) (singlet at 5.04).
- Presence of the phenyl ring (multiplete at 7.48-7.64).
- Presence of the NH proton (singlet at 10.03).
- Presence of the free OH proton (singlet at 14.40).

Taking into consideration the elementary analysis, IR, mass and NMR spectra, the structure of the present substance could be suggested as follows:



All these results were applied according to spectroscopic methods in organic chemistry.

The Activity of Different Levels of Purified Antibiotic

The effect of different concentrations of the substance produced from *Streptomyces endus* N40 against *Anacystis nidulans* cyanobacterium is determined. The results in Table 3 showed the growth of algal species with addition of Niromycin A at different concentrations (10, 20, 30 or 40 μg mL^{-1}) to 50 mL liquid algal media. This growth calculated by colourimetric method at 665 nm after 14 and 16 days. Niromycin A inhibit the algal growth recording 43.5, 54.3, 56.5 or 58.7%, 14 days after incubation, respectively but the absorbance recorded 71.3, 73.8, 75 or 76.3%, respectively after 16 days incubation. The maximum inhibition of *Anacystis nidulans* recorded 76.3% with Niromycin A at a rate of 40 μ mL after 16 days.

DISCUSSION

Bacteria with antialgal activity against algae have been previously reported and the list includes *Pseudomonas* sp. (Kodani *et al*., 2002), *Alcaligenes denitrificans* (Manage *et al*., 2000) and *Streptomyces phaeofaciens* (Yamamoto *et al*., 1998). Indeed, several members of the genus *Streptomyces* have been previously reported as having cyanobacteria-killing activity (Safferman and Morris, 1962; Yamamoto *et al*., 1998). However, there is no report demonstrating the *in situ* application of antialgal bacteria against a cyanobacterial bloom. One of the major reasons is probably the unpredictability of the antialgal effects of bacteria on other members of the freshwater ecosystem (EPA, 2002).

Before application of an antialgal agent to freshwater systems, there should be information on (1) the antialgal activity against the target alga, (2) the effects on the other organisms in the freshwater ecosystem and (3) a forecast of the algal dynamics after the removal of the target alga (Choi *et al*., 2005). Here, the *Streptomyces endus* N40 release an algicidal substance and its concentration was time dependent. The maximum inhibitory effect was obtained after 10 days that equal 87% compared with its corresponding control. These results are in agreement with that of Safferman and Morris (1962) who found 213 cultures of soil isolated actinomycetes (out of 403 isolates) had inhibitory effects against the cyanobacteria (including species of *Anacystis*, *Fremyella*, *Lyngbya*. *Nostoc*. *Phormidium* and *Plectonema*). Also, Gromov *et al*. (1972) indicated that the *Flexibacter flexilis* var. *algavorum* lyses the cells of filamentous blue-green algae belonging to the genera *Anabaena*, *Phormidium* and *Nostoc*. On the other hand, Al-Tai (1982) found that the extra-cellular products of an actinomycete (AN6) were able to lyse cyanobacteria, fungi, bacteria and green algae. Thereafter, Whyte *et al*. (1985) indicated that the pure cultures of *Streptomyces achromogenes* were shown to lyse *Anabaena cylindrica* and *Tolypothrix lenuis*.

Yamamoto and Suzuki (1990) attributed that the lytic activity of Streprtomycetes under investigation secrete some lysozyme and protease which causing cell lysis of the toxic strain of

Microcystis aeruginosa. At the same time, Yamamoto *et al*. (1998) showed that *Streptomyces phaeofaciens* produced compounds causing extensive lysis of *Microcystis* cells. However, Sigee *et al*. (1999) found that formation of the lytic agent by *Streptomyces exfoliatus* occurs independently with the presence of cyanobacteria, the ability to destroy these organisms is probably due to the antagonist of actinomycetes. Hence, Choi *et al*. (2005) study the effects of the antialgal bacterium *S. neyagawaensis* on several dominant algae in the Paltang, Juam, Daechung Reservoir and Naktong River and found that *S. neyagawaensis* had an effect on *A. Xos-aquae* and *A. cylindrica* but not *A. macrospora* and *A. aynis*. It also affected strains within a species differently. For example, the antialgal activity was 38.8% on *M. aeruginosa* NIES-44 and 70.2% on *M. aeruginosa* NIES-298.

Also (Choi *et al*., 2005) reported that, there are two possible explanations: (1) the culture conditions utilized in this experiment were not suitable for bacterial growth and (2) *M. aeruginosa* exudates may suppress bacterial growth. The first explanation is based on the divergence between optimum culture conditions for the antialgal bacterium and the cyanobacterium. The bacterium did not grow well at pH 9 and 25°C. The second explanation is that the toxicity of microcystin, from *M. aeruginosa*, is known to inhibit growth of organisms such as cladocerans, copepods and mosquito larvae (Sathiyamoorthy and Shanmugasundaram, 1996; Singh *et al*., 2003).

In this study the purified antialgal substance was identified using the elementary analysis, IR, mass and NMR spectra and also on the basis of the recommended keys for the identification of antibiotics as Niromycin A. Niromycin A have an inhibitory effect on the algal growth and the maximum inhibition of *Anacystis nidulans* recorded 76.3% with Niromycin A at a rate of 40 μ mL after 16 days.

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