

## Original Research Article

<https://doi.org/10.20546/ijcmas.2018.701.409>

## Human Anticancers and Antidiabetic Activities of the Cyanobacterium *Fischerella* sp. BS1-EG Isolated from River Nile, Egypt

Bassant E. Ahmed<sup>1</sup>, Mona H. Badawi<sup>1</sup>, Soha S. Mostafa<sup>2</sup> and Aziz M. Higazy<sup>1\*</sup>

<sup>1</sup>Department of Microbiology, Fac. Agric., Cairo University, Giza, Egypt

<sup>2</sup>Department of Microbiology, Inst. Soil, Water and Environment, ARC, Giza, Egypt

\*Corresponding author

### ABSTRACT

Cyanobacteria are known as a potential source of several metabolic compounds like phytohormones, phenols, antibiotics, anticancer, antiviral, anti-inflammatory as well as pharmaceuticals. These compounds are reported to be used in agriculture, biology and medicine. This study was performed to isolate *Fischerella* sp, from river Nile/ Egypt. Also, its potential to produce some bioactive compounds was evaluated. Results indicated that *Fischerella* BS1-EG isolate during this study has a considerable antifungal activity against *Aspergillus*, *Fusarium* and *Penicillium* sp. In general, the determined fungal activities by means of inhibition zone ranged between 8.5-16mm. Regarding the cell cytotoxicity of *Fischerella* BS1-EG on liver cancer (HepG-2), lung cancer (A549), colon cancer (HCT-116), breast cancer (MCF-7) data revealed that *Fischerella* BS1-EG crude extract exhibited a variable influence on all tested cell lines GC-MS analysis showed that 29 different compounds were detected and identified as fatty acids, alkaloids, phenols, amino acids, the most important 9 compounds were identified as anticancer, antimicrobial, anti-inflammatory agents. On the other hand, *Fischerella* BS1-EG proved to have anti hyperglycemia activity through inhibition of  $\alpha$ -glucosidase activity. These results may indicate that, for the first time, *Fischerella* BS1-EG is recorded to have different biological activities as anti-cancer as well as anti-hyperglycemia.

#### Keywords

Cyanobacteria,  
*Fischerella*, GC-MS, Anti-diabetic,  
Anti-cancer

#### Article Info

Accepted:  
26 December 2017  
Available Online:  
10 January 2018

### Introduction

Cyanobacteria, a promising photo auto trophic prokaryote, found in various freshwater and marine environments, is now well recognized as bio source of several pharmaceutical compounds. These compounds are necessary for treatment of different human diseases and disorders. In this respect, many species of cyanobacteria are known to have important role in treatment of various human diseases

e.g. antibacterial (Burja *et al.*, 2001), anti-HIV (Rajeev and Xu, 2004), anti-fungal (Burja *et al.*, 2001), anti-inflammatory (Shizuma, 2003), anti-oxidant and coenzyme (Plavisc *et al.*, 2004), and anti-diabetic (Priatni *et al.*, 2016). It is reported that, in general, cyanobacteria are still unexplored as natural source offering a large amount of chemicals for original compounds discovery and new drugs (Singh *et al.*, 2005). Traditional antibacterial and anticancer drugs producers

like Actinomycetes and Hyphomycetes have been in the focus of pharmaceutical research for decades. Since the discovery rate of interesting compounds in these classical source organisms is decreasing, it is time to turn to cyanobacteria and exploit their potential. In this respect, cyanobacteria are well known to produce anti-tumor, anti-cancer, anti-viral and anti-fungal compounds. Many of the pharmaceutically important compounds in cyanobacteria are peptides, including cyanobacterial toxins and important agents for anti-cancer drugs (Singh *et al.*, 2017). Several authors reported that *Fischerella* spp. can produce several compounds (Hagmann and Jüttner, 1996 and Ghasemi *et al.*, 2003) and some of these identified substances include fischerindole L (Park *et al.*, 1992), fischerellin A (Hagmann & Jüttner, 1996), ambiguine isonitriles A-F (Smitka *et al.*, 1992), ambigol A and B (Falch *et al.*, 1993), and tjipanazole D (Falch *et al.*, 1995).

However, this study was designed to isolate and purify *Fischerella* from river Nile, Giza, Egypt. Also, the pure culture was characterized and evaluated for its potential capacity to have antifungal, anticancer, anti-diabetic activities.

## Materials and Methods

### Enrichment culture of water samples for isolation of *Fischerella*

Two water samples were collected from intake site of drinking water station, Giza, Egypt. Liquid enrichment cultures were prepared from different water samples. Twenty five ml of water samples were aseptically added to 100 ml of Allen and Arnon broth (Allen and Arnon, 1955) and incubated at 30°C under continuous illumination, with Philips Fluorescent white lamps, at a relatively low light intensity (300 -400 lux).

### Purification and identification of *Fischerella* isolates

The isolated *Fischerella*, were successively subcultured several times on Allen and Arnon medium and incubated for 3 - 4 weeks at 30°C until the healthy and homogenous culture were obtained. All isolates were subjected to purification applying several successive transfers, single filament isolation and UV exposure (Higazy, 1985). After wet mount preparation, the *Fischerella* morphotypes such as filamentous nature, size, shape of vegetative cells, presence of heterocyst and akinetes as well as cell branching were identified and photographed using light microscope (Rippka *et al.*, 1979). In addition, pigment composition of all isolates was determined.

### Pigments contents

Total chlorophyll and total carotenoids were measured using spectrophotometer (Jenway, 6405 UV/vis) at (468 and 666 nm, respectively) according to Seely *et al.*, (1972). The total chlorophyll and total carotenoids concentrations were calculated with the following equations:

$$\text{Total chlorophyll (mg l}^{-1}\text{)} = \text{OD}_{666} \times D \times F$$

Where,  $E_{666}$ = the reading at 666 nm, D= volume of extract/volume of sample, F= 11.3 (factor to equal the reduction in absorbance).

$$\text{Total carotenoids (mg l}^{-1}\text{)} = \text{OD}_{468} \times D \times F$$

Where,  $E_{468}$ = the reading at 468 nm, D= volume of extract/volume of sample, F= 4.5 (factor to equal the reduction in absorbance).

Regarding Phycobiliproteins determination, cultures were sonicated for 40 seconds to break up filaments and release the water phycobiliproteins pigments, followed by

centrifugation at 8000 rpm to remove filament debris (Moares *et al.*, 2010). The optical density (OD) of the supernatant was measured at different wavelengths *e.g.* 562, 615 and 652 nm for phycoerythrin, phycocyanin and allophycocyanin, respectively. Phycobiliproteins concentration was calculated according to the following equations in  $\mu\text{g ml}^{-1}$  according to Bennett and Bogard (1973).

$$\text{Phycocyanin (PC)} = \text{OD}_{615} - 0.474(\text{OD}_{652}) / 5.34$$

$$\text{Allophycocyanin (APC)} = \text{OD}_{652} - 0.208(\text{OD}_{615}) / 5.09$$

$$\text{Phycoerythrin (PE)} = \text{OD}_{562} - 2.41(\text{PC}) - 0.849(\text{APC}) / 9.62$$

### Studying the antifungal activity

#### Preparation of microalgae extracts

At the stationary phase of growth, 30 days old, *Fischerella* culture of each species was harvested and dried in a hot air oven at 50°C over night. The dried biomass (5g) extracted with different solvent of aqueous, methanol, ethanol, acetone, chloroform, diethyl ether, ethyl acetate and hexane (HPLC grade). The extracts were sonicated for 20 min using ultrasonic microtip probe of 400 watt and centrifuged at 4500 rpm for 10 min. Supernatant was retained and the pellet was re-extracted as before three times. Combined supernatant was evaporated to dryness at 40°C using rotary evaporator. Dried extracts were stored in labeled sterile vials in a refrigerator till further use (Chauhan *et al.*, 2010).

#### Anti-fungal assay

Different fungal species were used for antifungal assay: *Aspergillus flavus* NRRL 3357, *A. ochraceus* ITAL 14, *A. carbonarius*

ITAL 204, *Fusarium verticelloides* ITEM 10027 and *Penicillium verrucosum* BFE 500. The fungal isolates were obtained from Applied Mycology Dept., Cranfield Univ., UK. The stock cultures were grown on potato dextrose agar slant at 30°C for 5 days and then kept in refrigerator till use.

#### Media used for anti-fungal assay

Potato dextrose agar, PDA medium (ATCC, 1984).

Yeast extract sucrose agar (YES medium) (Tsubouchi *et al.*, 1987).

#### Disc diffusion assay

The fungal strains were plated onto potato dextrose agar (PDA) and incubated for 5 days at 25°C. The spore suspension of each fungus was prepared in 0.01% Tween 80 solution. The fungal suspension was compared with the 0.5 McFarland standard, the turbidity of the inoculum suspension represented approximately  $2 \times 10^8$  cfu  $\text{ml}^{-1}$ . Similar to antibacterial test, sterilized filter paper discs (6 mm) were loaded with the extracts and dried completely under sterile conditions. Petri dishes of YES medium were inoculated with 50  $\mu\text{l}$  of each fungal culture and uniformly spread using sterile L- glass rod.

The extract loaded discs were placed on the seeded plates by using a sterile forceps. Negative control was prepared by using DMSO and the commercial fungicide Nystatin (1000 Unit  $\text{ml}^{-1}$ ) was used as a positive control. The inoculated plates were incubated at 30°C for 24 - 48 h. At the end of the period, antifungal activity was evaluated by measuring the zone of inhibition (mm) against the tested fungus (Medeiros *et al.*, 2011). All treatments consisted of three replicates and the averages of the experimental results were calculated.

### Anticancer assay

Cell cytotoxicity / viability of *Fischerella* extract were estimated on liver (HepG-2), lung (A549), Colon (HCT-116) and breast (MCF-7) cell lines applying neutral red uptake assay of Guillermo *et al.*, (2008). Results were obtained by measuring the OD of neutral red extract at 540nm in a microtiter plate reader spectrophotometer, using blanks which contain no cells as a reference.

### GC -MS analysis

At the stationary phase of growth, 30 days old, *Fischerella* culture was harvested and dried in a hot air oven at 50°C over night. The dried biomass (5g) extracted with solvent chloroform (HPC grade). The chemical composition of samples extract were performed using Trace GC Ultra-ISQ mass spectrometer (Thermo Scientific, Austin, TX, USA) with a direct capillary column TG-5MS (30 m x 0.25 mm x 0.25 µm film thickness). The column oven temperature was initially held at 50°C and then increased by 5°C /min to 180°C withhold 3 min then to 280°C by 10°C /min withhold 5min. The injector temperature was kept at 250°C. Helium was used as a carrier gas at a constant flow rate of 1 ml/min.

The solvent delay was 2 min and diluted samples of 1 µl were injected automatically using Auto sampler AS3000 coupled with GC in the split mode. EI mass spectra were collected at 70 eV ionization voltages over the range of m/z 40–650 in full scan mode.

The ion source and transfer line temperatures were set at 200 and 250°C respectively. The components were identified by comparison of their retention times and mass spectra with those of WILEY 09 and NIST 11 mass spectral database. The GC-MS experiments were performed in GC-MS lab., Atomic and

Molecular Physics Unit, Nuclear Research Center, Egyptian Atomic Energy Authority.

### α- Glucosidase inhibitory assay

The influence of *Fischerella* BS1-EG on α-glucosidase activity was determined according to the method of Kim *et al.*, (2005). The α-glucosidase was determined by measuring the yellow-colored paranitro phenol released from pNPG (the substrate solution p-nitrophenyl gluco pyranoside) at 405 nm. The results were expressed as percentage of the blank control.

Percentage of inhibition is calculated as follows:

$$\% \text{ Inhibition} = \frac{\text{abs control} - \text{abs extract}}{\text{abs control}} \times 100$$

### Results and Discussion

The enrichment culture of water samples indicated the considerable presence of different species of cyanobacteria, with relative abundance of *Fischerella*. Such *Fischerella* culture was subjected to purification and characterization studies. Results indicated that characters of all obtained culture of *Fischerella* are similar to that described by Rippka *et al.*, (1979).

Due to its rapid growth and recovery from UV treatment, as well as its healthy appearance, one isolate was selected and named *Fischerella* BS1-EG. The vegetative cells divide in more than plane to produce a mature trichome with the lateral branches. The heterocyst is terminal or lateral. Hormogonia composed from small cylindrical cells which enlarge and become rounded (Fig 1.). Concerning the ecological distribution of *Fischerella*, it is reported that it is mostly found in both terrestrial and aquatic environments (Uyeda *et al.*, 2016)

At the same time, data revealed that pigment composition of *Fischerella* BS1-EG culture was as follows:

4.06 and 0.70 mg g<sup>-1</sup> for total chlorophyll and total carotenoid, respectively. Also, it contains (mg g<sup>-1</sup>culture) 47.49, 58.86 and 32.37 of phycocyanin, allophycocyanin and phycoerthrin, in that order.

Concerning the antifungal activity of *Fischerella* BS1-EG culture against each of *Asperigillus flavus*, *A. ochraceus*, *A. carbonarius*, *Fusarium verticelloides*, *Penicillium verrucosum*, several solvents were used to extract all the compounds responsible for such activity. Results in Table (1) revealed that chloroform and aqueous solvents were the best in respect to extraction of antifungal compounds. For example, *Fischerella* BS1-EG extracts showed the highest fungal activities by means of inhibition averages zones using both chloroform and aqueous solvents ranged between 9.7-16.0 mm and 8.5-12.3 mm respectively.

Similarly, Devi and Mehta (2016) indicated that *Fischerella ambigua* extracts showed antifungal activities on different *Fusarium* species. They added that DCM: ISO extract (Dichloromethane: isopropanol) 1:1 of *F. ambigua* resulted in the maximum inhibition zones of 8.0 and 3.34 mm in *Fusarium undum* and *F. culmorum*, respectively. Also Becher and Juttner (2006) have found antifungal compounds such as hapalindol G and H from the extract of *Fischerella sp* which exhibited antifungal activities.

Concerning cell cytotoxicity of *Fischerella* BS1-EG on liver cancer (HepG-2), lung cancer (A549), Colon cancer (HCT-116) and breast cancer (MCF-7), data pointed out that *Fischerella* BS1-EG crude extract recorded a pronounced influence on all tested cell lines, The response of such cell lines toward

treatment with *Fischerella* BS1-EG extracts by means of viability percentage could be arranged as follows: on Liver cancer (HepG-2) > lung cancer (A549) > colon cancer (HCT-116) > breast cancer (MCF-7). This may indicate the anticancer effect of *Fischerella* on various cancer diseases. Similar findings were obtained by Acuna *et al.*, (2015) when they suggested that the indole alkaloids from *Fischerella ambigua* showed significant activity against Estrogen sensitive breast cancer cells.

In addition, the chemical composition of *Fischerella* BS1-EG extract was determined using trace GC Ultra-ICQ mass spectrometer (Fig.2). Also results in Table (3), showed that 29 different compounds were detected and identified as fatty acids, alkaloides, phenols and amino acids. In regard to their biological activities, the most important 9 compounds with relative percentage are presented In Table (4). Data indicated that such compounds have variable effects including, anti-tumor, anti-cancer, anti-inflammatory, anti-oxidant and anti-microbial activities. *e.g.* heptadecan, hexadecanoic acid, phytol, hexadecanoic acid methyl ester, 10-octadecanoic acid methyl ester, octadecanoic acid methyl ester, 1,4-benzenediol 2-(1,1-Dimethyle Thyl)-5-(2-Propenyl), 9- octodecanoic acid (Z), hexadecanoic acid ethyl ester and eicosan. Cyanobacteria and algae are the immense sources of several metabolites such as alkaloids, carbohydrates, flavonoids, pigments, phenols, steroids, vitamins which can be utilized in biotechnology and industrial fields (Guiheneuf *et al.*, 2016) as well as pharmacological areas including production of several bioactive metabolites that showed antibacterial (Melathi *et al.*, 2014).

Anti-cancer (Semary and Fouda, 2015), antifungal (Shaieb *et al.*, 2014), anti-viral (Abdo *et al.*, 2012) activities which led to remarkable interest in cyanobacterial and algal

secondary metabolites. Therefore and due to their high pharmaceutical value, a new point of view of exploiting cyanobacteria increased progressively.

During this study, different compounds were found in *Fischerella* BS1-EG extracts and identified by GC-MS. The most important compounds represented various bioactive metabolites with different biological activities. For example, eicosan (0.62%) was reported to have antibacterial, antitumor and cytotoxic effect (Belkhdar *et al.*, 2015). Devi and Mehta (2016), indicated that heptadecane (17.02%) was found in *F. ambigua* extract and it is known for its anticancer, antioxidant and

antimicrobial activities. In addition, it has been demonstrated that a little is known about the mechanisms by which olic acid could affect cell proliferation and cell death of the cancer cells. Therefore, further studies are required to fully clarify the pathway by which olic acid could reduce cancer risk, (Carillo *et al.*, 2012). However, Mericli *et al.*, (2017) showed that both olic acid (1.52% in this study) and palmitic acid (9.18% in this study) may have anticancer and anti-proliferative effects on colon cancer cells through signalling pathway and, therefore, they could be potential novel therapeutic agents.

**Table.1** Antifungal activity (inhibition zone in mm) of *Fischerella* Bg1/EG strain crude extracts applying different solvents

Fungi Culture	Applied Solvents				
	Hexane	Chloroform	DEE*	Methanol	Aqueous
<i>A. flavus</i>	8.3±0.57	9.8±0.58	8.0±1.00	8.5±1.80	8.5±0.50
<i>A. ochraceus</i>	7.7±0.76	9.7±0.29	8.8±0.28	7.5±0.50	11.2±1.25
<i>A. carbonarius</i>	13.5±1.32	16.0±0.50	13.2±1.04	13.5±1.80	12.2±1.53
<i>F. verticelloides</i>	14.7±1.75	10.3±0.76	9.5±0.50	11.0±1.5	10.3±1.04
<i>P. verrucosum</i>	8.2±1.15	9.7±0.29	9.3±1.04	7.8±0.76	12.3±1.75

\*DEE, diethyl ether

**Table.2** Anti-cancer activity as viability of human cell lines after treatment with *Fischerella* crude extract

Extract Concentration (µg/ml)	Viability% Cell line			
	Liver cancer (HepG-2)	Lung cancer (A549)	Colon cancer (HCT-116)	Breast cancer (MCF-7)
20	21.4	36.0	57.0	64.5
40	8.3	30.6	19.0	50.5
80	0.0	14.6	11.9	47.8
IC50 (µg/ml)	—	16.5	15.8	63.8

**Table.3** Compounds identified from GC-MS analysis of chloroform extract of *Fischerella* BS1-EG.

S. No.	Name of Compound	Molecular Formula	Molecular weight	RT	Area %
1.	Decane, 1,1' 1,1'-Oxybis	C20H42O	298	13.10	0.14
2.	Eicosan	C20H42	282	14.30	0.62
3.	Hexadecane	C16H34	226	15.66	0.81
4.	2-Decanal E	C10H18O	154	18.89	2.44
5.	1-Tetradecanol	C14H30O	214	19.13	0.91
6.	Pentacosane	C25H52	352	20.31	0.48
7.	Heptadecan	C17H36	240	20.52	17.02
8.	Heptadecane, 7-Methyl-	C18H38	254	21.35	13.92
9.	1-Hexadecanol, 2-Methyl-	C17H36O	256	20.78	1.02
10	7-Hexadecenal, (Z)-	C16H30O	238	22.73	1.61
11.	Docosane	C22H46	310	23.49	1.14
12.	1-Chlorooctadecane	C18H37Cl	288	24.23	0.54
13.	9,12,15-Octadeca Trienoic Acid, 2-(Acetyloxy)-1-[(Acetyloxy)Methyl]ETHYL ESTER, (Z,Z,Z)-	C25H40O6	436	25.37	0.21
14.	Dodecanoic Acid, 3-Hydroxy	C12H24O3	216	25.67	0.59
15.	2-Aminoethaneth Iol Hydrogen Sulfate (Ester)	C2H7NO3S2	157	25.78	0.24
16.	2,2-Dideutero Octadecanal	C18H34D2O	270	25.85	0.13
17	2,2,3,3,4,4 Hexadeutero Octadecanal	C18H30D6O	274	26.96	0.29
18.	Aspidospermidin 17-Ol 1-Acetyl-19,21-Epoxy-1 5,16-Dimethoxy-	C23H30N2O5	414	27.20	0.29
19.	9- Octodecanoic acid (Z)	C18H34O2	282	27.80	1.52
20.	Hexadecaonic Acid Methyl Ester.	C17H34O2	270	30.79	3.07
21.	Hexadecanoic Acid, Ethyl Este.	C18H36O2	298	31.49	0.86
22.	[1,1'-Bicyclopropyl]-2 Octanoic Acid	C21H38O2	322	32.35	0.21
23.	2'-Hexyl-, Methyl Ester 1,4-Benzenediol2-(1,1-DimethyleThyl)-5-(2-Propenyl).	C13H18O2	206	32.45	1.74
24.	OctadecanoicAcid, methylEster.	C19H38O2	298	34.47	1.77
25.	10-Octadecenoic acidMethyl Ester.	C19H36O2	296	34.81	2.6
26.	7-Methyl-Z-Tetradecen1-Ol Acetate.	C17H32O2	268	36.23	0.36
27.	Alanine,3-(Benzyloxy)-, L-	C10H13NO3	195	36.48	0.61
28.	Phytol.	C20H40O	296	37.45	8.02
29.	Hexadecanoic Acid .	C16H32O2	256	40.08	9.18

**Table.4** The most important identified compounds from GC-MS analysis of chloroform extract of *Fischerella*BS1-EG

No	Name of compound	Compound Nature	Biological Activity
1.	Eicosan	Aliphatic hydrocarbon	Anti-cancer activity against the human gastric cSGC-7901 cell line, Anti-bacterial, antitumor, antifungal, cytotoxic.
2.	Heptadecan	Aliphatic hydrocarbon	Anti-cancer, anti-bacterial, anti-oxidant.
3.	9- Octodecanoic acid (Z)	oleic acid (fatty acid)	Anti-gastric and breast cancer, anti-oxidant
4.	Hexadecaonic acid methyl ester	Palmitic acid methyl Ester	Anti-bacterial, anti-fungal, anti-oxidant, decrease blood cholesterol, anti-inflammatory.
5.	10-octadecenoic acid methyl ester	Unsaturated fatty acid, methyl ester	Anti-bacterial, anti-fungal, anti-oxidant, decrease blood cholesterol
6.	1,4-Benzenediol 2-(1,1-Dimethyl-2-Propenyl)-5-(2-Propenyl)-	Ibuprofen	Anti-inflammatory agent used in the therapy of rheumatism and arthritis, analgesic, antipyretic and platelet-inhibitors. Otherwise called as ibuprofen.
7.	Hexadecanoic acid ethyle ester	palmitic acid, ethyle eser	Antioxidant, Hypocholesterolemic, Nematicide, Pesticide, Antiandrogenic, flavor, Hemolytic 5 $\alpha$ reductase inhibitor.
8.	phytol	Diterpene	Can be used as a precursor for the manufacture of synthetic forms of vitamin E and vitamin K1 in ruminants, anti-bacterial, anti-cancer, cancer preventive, deuritic, anti-inflammatory.
9.	Hexadecanoic acid	palmitic acid	Anti-human leukemia, Antioxidant, Anti-inflammatory Antioxidant, Hypocholesterolemic nematicide, pesticide, anti androgenic, flavor hemolytic, 5- $\alpha$ reductase inhibitor, potent mosquito larvicide .

**Table.5** Total carbohydrates, exopolysaccharides (Eps) and anti-diabetic Activity of aqueous extract of *Fischerella* BS1-EG

Determination	<i>Fischerella</i> BS1-EG
Total carbohydrates %	32
EPS (g)	22
Inhibition of $\alpha$ -glucosidase % Water extract	7.56

**Fig.1** Light micrographs (a: 100 x, b: 600x) and liquid cultures (c and d) of 30 days old cultures of *Fischerella* Bs1- EG



(A)



(B)

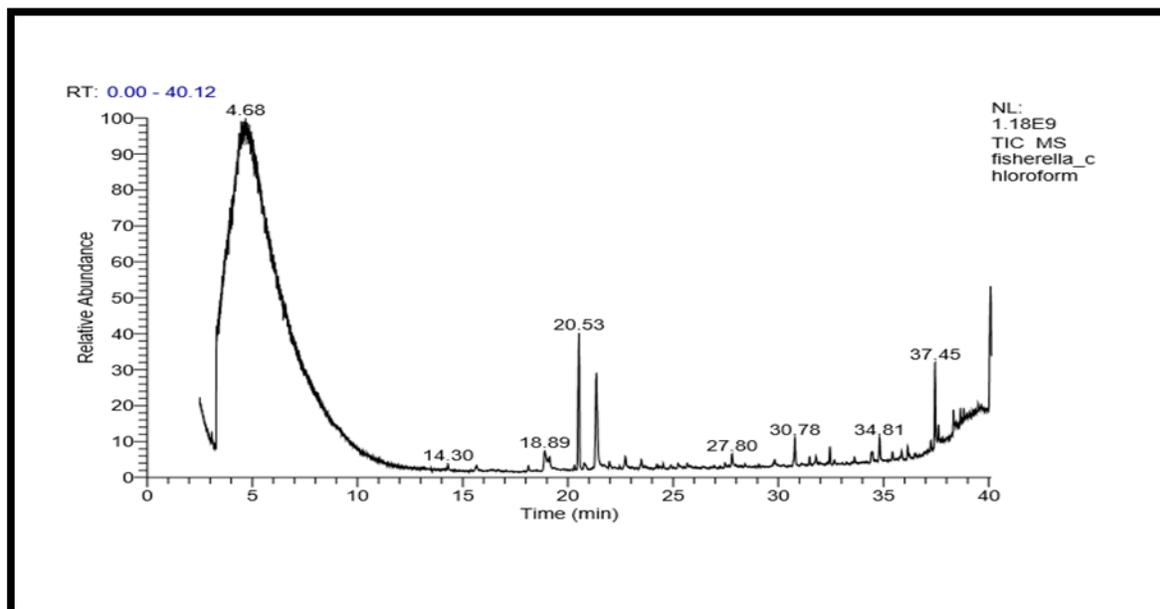


(C)



(D)

**Fig.2** Chromatogram of chloroform extract of *Fischerella* BS1-EG



At the same time, it is concluded from results of this study that *Fischerella* BS1-EG produced hexadecanoic acid (0.86%). This compound was also produced from ethanol extract of the aquatic plant *Eichornia crassipon* and proved to have anti-androgenic effect (Tyagi and Agarwal, 2017). Meanwhile, Gillat (2006) reported that anti-androgen are used in treatment of prostate cancer and prostate enlargement in male as well as treatment of acne, and polycystic ovary syndrome in females.

Meanwhile, phytol was detected in *Fischerella* BS1-EG extract (8.02%) and was reported to be used as a precursor for the manufacture of synthetic forms of vitamin E (Netscher, 2007) and Vitamin K (Daines *et al.*, 2003). Recently, phytol was found to act as anti-inflammatory anti-cancer (Tyagi and Agarwal, 2017) and improve immunological response against tumor in a very beginning stage of carcinogenesis (Singh *et al.*, 2017). Additionally, Data revealed that ibuprofen, 10-octadecanoic acid methyl ester and hexadecanoic acid methyl ester were detected

in *Fischerella* BS1-EG extracts with considerable concentration *i.e.* 1.74, 2.60 and 3.07 %. These compounds were previously reported to have anti-inflammatory, antioxidant, and antifungal activities (Belkhdar *et al.*, 2015).

On the other hand, anti-diabetic activity of *Fischerella*BS1-EG was estimated by analysis of inhibition percentage of  $\alpha$ -glucosidase activity. In this respect, data in Table (5) revealed that *Fischerella* BS1-EG culture had a potential activity on  $\alpha$ -glucosidase as inhibitor *e.g.* 7.56 % with total carbohydrates and EPS content of 32%, 22g in that order.

Results of this study revealed that *Fischerella* BS1-EG extract exhibited potential activity in alpha-glucosidase inhibition *i.e.* 7.5% indicating its anti-diabetic effect (Periatni *et al.*, 2016). It is well known that  $\alpha$ -glucosidase inhibitors are saccharides that act as competitive inhibitors of enzymes needed to digest carbohydrates specially  $\alpha$ -glucosidase enzyme formed in the brush border of small intestines. Since  $\alpha$ -glucosidase inhibitors

prevent the digestion of carbohydrates, such as starch and table sugar, it is therefore suggested that such inhibitors could be used to reduce the impact of carbohydrates on blood sugar and subsequently decrease the current blood glucose levels in diabetic patients (De Geeter *et al.*, 2014).

Several studies reported that anti-diabetic potential was reported by many plants (Kazeem *et al.*, 2013) and some marine cyanobacteria e.g. *Oscillatoria*, *Lyngbya*, *Phormidium* and *Synechococcus*. No previous studies were found concerning the anti-diabetic activity by any of *Fischerella sp.*

Therefore it could be concluded that results of this study is most likely the first report on the influence of *Fischerella sp* as a potential agent in the field of human anticancers and anti-diabetic treatment.

## References

- Abdo S. M., Mona H. H., Waleed M. E., Rawheya A. S. E. D., Gamila H. A. 2012. Antiviral activity of freshwater algae. *J. Appl. Pharm. Sci.* 2: 21–25.
- Acuña, M. U; Zi, T; Oriala, J. and de Blanco, E.J.C. 2015. Ambiguine I Isonitrile from *Fischerella ambigua* Induces Caspase-Independent Cell Death in MCF-7 Hormone Dependent Breast Cancer Cells. *nt J Cancer Res (Tortola)*.49(1): 1655–1662.
- Allen, M.B. and Arnon, D.I. 1955. Studies on nitrogen-fixing blue-green algae. I. Growth and nitrogen fixation by *Anabaena cylindrica* Lemm. *Plant Physiology*. 30: 366-372.
- ATCC 1984. American Type Culture Collection, 13<sup>th</sup> ed., USA, 517p.
- Becher PG, Juettner F. 2006 Insecticidal activity- a new bioactive property of the cyanobacterium *Fischerella*. *Polish J Ecol*; 54: 653-662.
- Belkhdar, G.; Benjouad, A. and Abd ennebi, E.H. 2015. Determination of some bioactive chemical constituents from *Thesium Humile Vahl*, *J.Matar. Environ.Sci.*, 6(10): 2778-2783.
- Bennett, A. and Bogard, L. 1973. Complementary chromatic adaptation in a filamentous blue-green alga. *J. Filament Biol.*, 58: 419-438.
- Burja, A.M., Banaigs, B., Abou-Mansour, E., Burgess, J.G. and Wright, P.C. 2001. Marine cyanobacteria: A prolific source of natural products. *Tetrahedron*, 57: 9347–9377.
- Carrillo, c; Cavia del M. and Alonso- torre, S.R. 2012. Antitumor effect of oleic Acid mechanisms of action. A review. *Nutr. Hosp.*, 27 (5): 1860-1865.
- Chauhan, A.; Chauhan, G.; Gupta, P.; Goyal, P. and Kaushik, P. (2010). *In vitro* antibacterial evaluation of *Anabaena sp.* against several clinically significant microflora and HPTLC analysis of its active crude extracts. *Indian J. Pharm.*, 42:105-107.
- Daines, Alison; Payne, Richard; Humphries, Mark; Abell, Andrew 2003. The Synthesis of Naturally Occurring Vitamin K and Vitamin K Analogues. *Current Organic Chemistry*, 7(16): 1625–34.
- De Geeter, M. and Williamson, B. 2016. Alternative agent in Type 1 Diabetes in Addition to Insulin Therapy: Metformin, Alpha-Glucosidase Inhibitors, pioglitazone, Glp-1 Agonists, Dpp-1V Inhibitors, and SGLT-2 Inhibitors, *Joarnal of pharmacy practice*, 29 (2): 144-159.
- Devi, K.M and Mehta, S. K. 2016. Antimicrobial activity and GC-MS analysis of fresh water Cyanobacterium, *Fischerella ambigua* *Wjpmr*, 2(5):199-208.
- Falch BS, König GM, Wright AD, Sticher O 1993. Ambigol A and B: New biological active polychlorinated

- aromatic compounds from the terrestrial blue-green alga *Fischerella ambigua*. *JOrg Chem* 58: 6570–6575.
- Falch BS, König GM, Wright AD, Sticher O, Angerhofer CK, Pezzuto JM, Bachmann H 1995. Biological activities of cyanobacteria: Evaluation of extracts and pure compounds. *Planta Med* 61: 321–328
- Gillatt, D. 2006. Androgen treatment in locally advanced prostate cancer: are they all the same?' *J.Cancer Res. Clin. Oncol.*, 1: S17-26.
- Guillermo Repetto, Ana del Peso & Jorge L Zurita, 2008. Neutral red uptake assay for the estimation of cell viability/cytotoxicity, *Nature Protocol*, 3(7), 1126-1131.
- Hagmann L, Jüttner F 1996. Fischerellin A, a novel photosystem-II-inhibiting allelochemical of the cyanobacterium *Fischerella muscicola* with antifungal and herbicide activity. *Tetrahedron Lett* 37: 6539–6542.
- Higazy, A.M. 1985. Asymbiotic N<sub>2</sub>- Fixation in Egyptian Aquatic Environment. Ph.D. Thesis, Fac. Agri., Cairo University, p123.
- Kazeem, M.I.; Adamson, J.O.; and Ogunwande, I.A. 2013. Modes of inhibition of  $\alpha$ - Amylase and  $\alpha$ -Glucosidase by Aqueous Extract of *Morinda Lucida* Benth leaf. *Biomed Research International*, volume 2013, ID: 527570:1-6.
- Kim, Y.M; Jeong, Y.K; Wang, M. H; Lee, W. Y. and Rhee, H.I. 2005. Inhibitory effect of pine extract on  $\alpha$ -glucosidase activity and postprandial hyperglucemia. *Nutrition*, 2 (6): 765-761.
- Kumar, P.P.; Kumaravel, S.; Lalitha, C. 2010. Screening of antioxidant activity, total phenolics and GC-MS study of *Vitex negundo*. *Afr. J. Biochem. Res.*, 4, 191–195.
- Malathi T., Babu M. R., Mounika T., Snehalatha D., Rao B. D. 2014. Screening of cyanobacteria strains for antibacterial activity. *Phykos.*, 44: 6–11.
- Mercili, F.; Becer, E.; Kabadayi, H.; Hanogalu, A.; Hanogalu, D.Y; Yauus, D.O; Ozek, T. and Vatansever, S. 2017. Fatty acid Composition and anticancer Activity In colon carcinoma cell lines of *Prunus dulcis* seed oil. *Pharmaceutical Biology*, 55 (1): 1239-1248.
- Moares, C.; Burkert, M. and Kalil, J. 2010. C-phycocyanin Extraction Process for Large-Scale Use. *J. Food Biochem.*, 34(1):133-138.
- Netscher, Thomas 2007. *Synthesis of Vitamin E"*. In: *Vitamin E. Vitamins & Hormones*. 76. (Litwack, Gerald, ed.) pp. 155–202. doi:10.1016/S0083- . ISBN978- 0-12-373592-8.
- Park A, Moore RE, Patterson GML. 1992. Fischerindole L, a new isonitrile from the terrestrial blue-green alga *Fischerella muscicola*. *Tetrahedron Lett.*, 33: 3257–3260.
- Plavsic, M., Terzic, S., Ahel, M. and van den Berg, C.M.G. 2004. Folic acid in coastal waters of the Adriatic Sea. *Mar. Freshw. Res.*, 53: 1245–1252.
- Priatni, S.; Budiwwati, T. A.; Ratnaningrum, D.; Kosasih, W.; Anderyani, R.; Susanti, H. and Susilaningih, D. 2016. Antidiabetic screening of some idonesian marine cyanobacteria collection. *Biodiversitas*, 17(2):642-646.
- Raghukumar, C., Viparty, V., David, J.J. and Chandramohan, D. 2001. Degradation of crude oil by marine cyanobacteria. *Appl. Microbiol. Biotechnol.*, 57: 433–436.
- Rajeev, K.J. and Xu, Z. 2004. Biomedical compounds from marine organisms. *Mar Drugs* 2, 123–146.
- Rippka, R.; Deruelles, J.; Waterbury, B.; Herdman, M. and Stanier, Y. 1979.

- Generic assignments, strain histories and properties of pure cultures of cyanobacteria. *J. Gen. Microbiol.*, 111:1-61.
- Seely, R.; Duncan, J. and Vidaver, E. 1972. Preparative and analytical extraction of pigments from brown algae with dimethyl sulfoxide. *Mar. Biol.*, 12: 184-188.
- Semary N. A. E., Fouda M. 2015. Anticancer activity of *Cyanotheca* sp. strain extracts from Egypt: first record. *Asian Pac. J. Trop. Biomed.* 5, 992-995. 10.1016/j.apjtb.2015.09.004.
- Shaieb F. A., Issa A. A., Meragaa A. 2014. Antimicrobial activity of crude extracts of cyanobacteria *Nostoc commune* and *Spirulina platensis*. *Arch. Biomed. Sci.* 2, 34-41.
- Shizuma, Y. 2003. Microalgal metabolites. *Curr. Opin. Microbiol.*, 6: 236-243.
- Singh, R; Parihar, P; Singh, M; Bajagwz, A; Kumar, J; Singh, S; Singh, P.V. and Prasad, S.M. 2017. Uncovering potential Applications of Cyanobacteria and Algal Medicine Current Status and Future Prospects. *Frontiers in Microbiology*, 8(article 515): 1-37.
- Singh, S., Kate, B.N. & Banerjee, U.C. 2005. Bioactive critical compounds from cyano-bacterial and microalgae: an overview. *Crit. Rev. Biotechnol.*, 25: 73-95.
- Smitka TA, Bonjouklian R, Doolin L, Jones ND, Deeter JB, Yoshida WY, Prinsep MR, Moore RE, Patterson GML, 1992: Ambiguine isonitriles, fungicidal hapalindole-type alkaloids from three genera of blue-green algae belonging to Stigonemataceae. *J Org. Chem.*, 57: 857-861.
- Tsubouchi, H.; Yamamoto, K.; Hisada, K.; Sakabe, Y. and Udagawa, S. 1987. Effect of roasting on ochratoxin A level in green coffee beans inoculated with *Aspergillus ochraceus*. *Mycopathologia*, 97: 111-115.
- Tyagi, T. and Agarwal, M. 2017. Phytochemical screening and GC-MS analysis of bioactive constituents in the ethanolic extract of *Pistia stratiotes* L. and *Eichhornia crassipes* (Mart.) Solms, *Journal of Pharmacognosy and Phytochemistry*, 6(1): 195-206
- Uyeda, Josef C., Luke J. Harmon, Carrine E. Blank 2016. Comprehensive Study of Cyanobacteria: Morphological and Ecological Evolutionary Dynamics through Deep Geologic Time. *Plos One*, 11(9): 1-32.

**How to cite this article:**

Bassant E. Ahmed, Mona H. Badawi, Soha S. Mostafa and Aziz M. Higazy. 2018. Human Anticancers and Antidiabetic Activities of the Cyanobacterium *Fischerella* sp. Isolated from River Nile, Egypt. *Int.J.Curr.Microbiol.App.Sci.* 7(01): 3473-3485.  
doi: <https://doi.org/10.20546/ijcmas.2018.701.409>