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Evaluation of Anticancer Activities of *Spirulina platensis* ethanolic extract on Lung cancer cells

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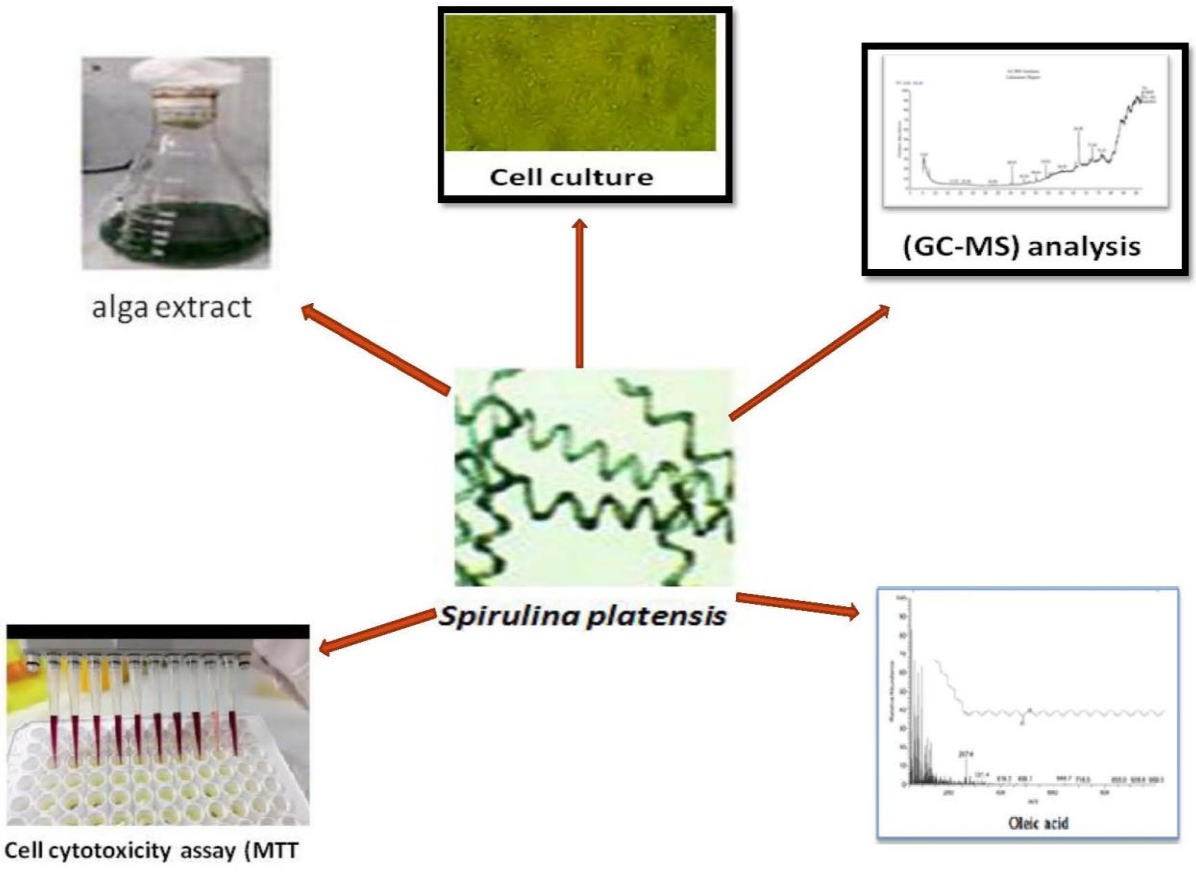
ABSTRACT

Lung cancer is one of the leading causes of cancer-related mortality globally, necessitating the search for novel, natural therapeutic agents. The study evaluated the anticancer potential of an ethanolic extract of *Spirulina platensis* collected from alkaline soils in Wadi Hagul, Egypt. The biomass was cultured using Zarrouk's medium, and the ethanolic extract was prepared by cold maceration. The cytotoxic effect of the extract against A549 human lung carcinoma cells was assessed using the MTT assay. Results revealed a dose-dependent cytotoxic response, with an IC_{50} value of 78.72 ± 1.06 µg/mL. Morphological observations confirmed apoptotic changes at higher concentrations. Gas chromatography–mass spectrometry (GC-MS) analysis identified 41 bioactive compounds, with oleic acid eicosyl ester (54.8%) and prostaglandin A2-biotin (53.2%) being the major constituents. These compounds are known for their anti-inflammatory, antioxidant, and antiproliferative effects. The findings suggest that *S. platensis* ethanolic extract exerts significant anticancer effects through bioactive compound-mediated mechanisms, supporting its potential as a promising candidate for pharmaceutical applications targeting lung cancer.

Graphical abstract



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1. Introduction

Cancer is defined as the unchecked proliferation of cells, resulting from disruptions in the regulatory systems that control normal cell division. It continues to be one of the leading causes of death globally, accounting for nearly 10 million fatalities in 2020—approximately one out of every six deaths worldwide [1]. Among various cancers, lung cancer stands out as one of the most common forms, ranking third among men and fourth among women [2], with its occurrence predominantly in older individuals.

Microalgae are a valuable source of diverse bioactive compounds, including proteins, minerals, polysaccharides, steroids, fatty acids, carotenoids, halogenated substances, and peptides. Many of these compounds exhibit potent biological effects, especially anticancer activities. These molecules can engage with specific cellular targets, disrupting cell proliferation or inducing programmed cell death (apoptosis) through the activation of key intracellular pathways [3]. Notably, blue-green algae have gained attention for their potential role in maintaining and enhancing respiratory health [4, 5].

Spirulina, blue-green algae, is one of the Earth's oldest known forms of life. *Spirulina* grows best in very alkaline environments, although it may flourish across a wide variety of pH values [6]. Additionally, *Spirulina* can be found in soil, while it's more commonly associated with aquatic environments like lakes and ponds, it also thrives in moist soils and can be a beneficial addition to soil ecosystems [7].

Conventional treatments like chemotherapy and radiotherapy often have significant side effects and limitations while natural compounds have emerged as valuable sources for anticancer drug development, with nearly 60% of current anticancer drugs derived from natural origins [8].

Spirulina platensis, is renowned for its rich nutritional profile and biologically active components. It contains high levels of proteins, essential amino acids, minerals, essential fatty acids, vitamins, and fat-soluble antioxidants such as vitamin E and carotenoids [9, 10]. Additionally, *Spirulina* is abundant in functional compounds with recognized antioxidant and anti-inflammatory properties, including phenolic phytochemicals [11, 12] and the phycobiliprotein known as C-phycocyanin [13]. Antioxidants play a critical role in neutralizing or preventing the harmful effects of reactive oxygen species. The biological effects of algal-derived compounds are closely tied to their specific chemical composition and structure. Fucoidan a compound from algae has been reported to suppress lung cancer progression by slowing tumor growth, promoting cancer cell apoptosis, and enhancing the efficacy of chemotherapy drugs through synergistic interactions [14]. Blue-green algae, particularly *Spirulina*, are a promising source of natural anticancer agents due to their high antioxidant content. These bioactive compounds contribute to various therapeutic effects, including cancer suppression, immune system enhancement, and protection against oxidative stress–related diseases such as diabetes and inflammation [6]. On the other hand [15] demonstrated the immunomodulatory and cytotoxic effects of *Spirulina*-based extracts against several cancer cell lines, including A549.

Moreover, lipid metabolic reprogramming which includes fatty acid uptake, synthesis, oxidation, and structural modification is crucial for meeting the energetic demands, membrane remodeling, and signaling functions that facilitate cancer cell survival and proliferation [16, 17].

In light of these findings, the present study aims to investigate the anticancer potential of crude *Spirulina platensis* extract against the human lung cancer A549 cell line.

2. Materials and Methods

2.1. Collection of alga and preparation of extract

Spirulina platensis alga was collected in March 2025 from the rhizosphere (root zone) of *Pulicaria undulata* plants growing near olive trees in a cultivated area of Wadi Hagul, Suez Governorate, Egypt specifically at the entrance of the valley near the Ain Sokhna district. The soil in this area was alkaline in nature. Pure cultures were cultivated using Zarrouk medium, following the method outlined by [18], under continuous agitation at 30 ± 2 °C and pH 10. The cultures were maintained under alternating light and dark cycles (16/8 hours), with manual shaking twice daily. After cultivation, the algal biomass was harvested, and the supernatant was discarded. The collected S. platensis cells were preserved by freezing at –20 °C until further use.

To prepare the aqueous extract, 50 grams of dried algae were immersed in 200 mL of aqueous ethanol and left to soak for 72 hours. Following this, the mixture was allowed to settle for an additional 24 hours before being centrifuged for 20 minutes. The supernatant was then processed using a rotary evaporator to remove the solvents, and the remaining residue was stored at 4 °C for subsequent analysis.

2.2. Cell culture

Human lung carcinoma A549 cells were supplemented from the VACSERA, Nasr City, Pharmaceutical, the cells were maintained in accordance with the manufacturer's instructions. For cell culture, the cells were grown in a medium containing 10% fetal bovine serum (FBS), 100 µg/mL streptomycin and 100 µg/mL penicillin.

2.3. Cell Morphology Assay

The morphological changes of cells were observed under a microscope (Primovert, Zeiss, Gottingen, Germany).

2.4. Cell cytotoxicity assay (MTT)

Viability of cancer cell lines was examined by MTT assay. According to [19] the cells were cultured in a 96-well plate with tested therapeutics for 24 hours at 37°C. Then the cells were incubated for 2 hrs with the new medium containing MTT (5mg/ml in PBS) (BIO BASIC CANADA INC). Incubate (37^{O}C, 5% CO_2) for 4 hours to allow the MTT to be metabolized. Read optical density at 560nm and subtract background at

620nm. Optical density should be directly correlated with cell quantity.

2.5. Gas chromatography-mass spectrometry (GC-MS) analysis

The analyses of crude extract was performed using Trace GC1310-ISQ mass spectrometer (thermo Scientific, Austin, TX, USA) at the regional center for Mycology and Biotechnology (RCMB) at Al-Azhar University with a direct capillary column TG-5MS (30 m x 0.25 mm x 0.25µm film thickness). The components were identified by comparison of their retention times and mass spectra with those of WILEY09 and NIST 11 mass spectral database. All previous analysis was determined at the Regional Center for Mycology and Biotechnology (RCMB) at Al- Azhar University.

2.6. Statistical Analysis

Results were expressed as mean ± standard error (SE). The obtained data were analyzed using the one-way analysis of variance (ANOVA) and Tukey's post-hoc test. The difference considered statically significant at $P \leq 0.05$.

3. Result and Dissection

3.1. Morphological Changes of Treated Cells

Figure 1 illustrates the impact of varying concentrations of crude *Spirulina platensis* extract on A549 lung cancer cell lines, ranging from 31.25 to 1000 µg/mL. At the lowest concentration tested (31.25 µg/mL), no notable alterations were observed in either cell viability or morphology of the A549 cells ($P > 0.05$). In contrast, at 125 µg/mL, subtle modifications began to appear on the cell surface and within the cytoskeleton, which could be correlated with changes in cell viability. At concentrations of 250 and 500 µg/mL, more pronounced effects were evident, including cell shrinkage, rounding of the cells, reduced adhesion to the culture surface, and a noticeable decline in cell number. The highest tested dose, 1000 µg/mL, induced a significant increase in necrotic activity ($P < 0.05$), suggesting severe cytotoxicity at this level.

These findings align with earlier research by [20], which reported that crude microalgal extracts exhibit potent antioxidant and cell-repairing effects in vitro on A549 human lung adenocarcinoma cells and effectively suppressed colony formation at a concentration of 5 µg/µL. Furthermore, the study by [21] demonstrated that crude *S. platensis* extract exerts considerable influence on the lung cancer cell cycle, particularly by arresting cells in the G2 phase. This prevents progression into the M phase, thereby halting cancer cell proliferation, with the antioxidant effect being concentration-dependent.

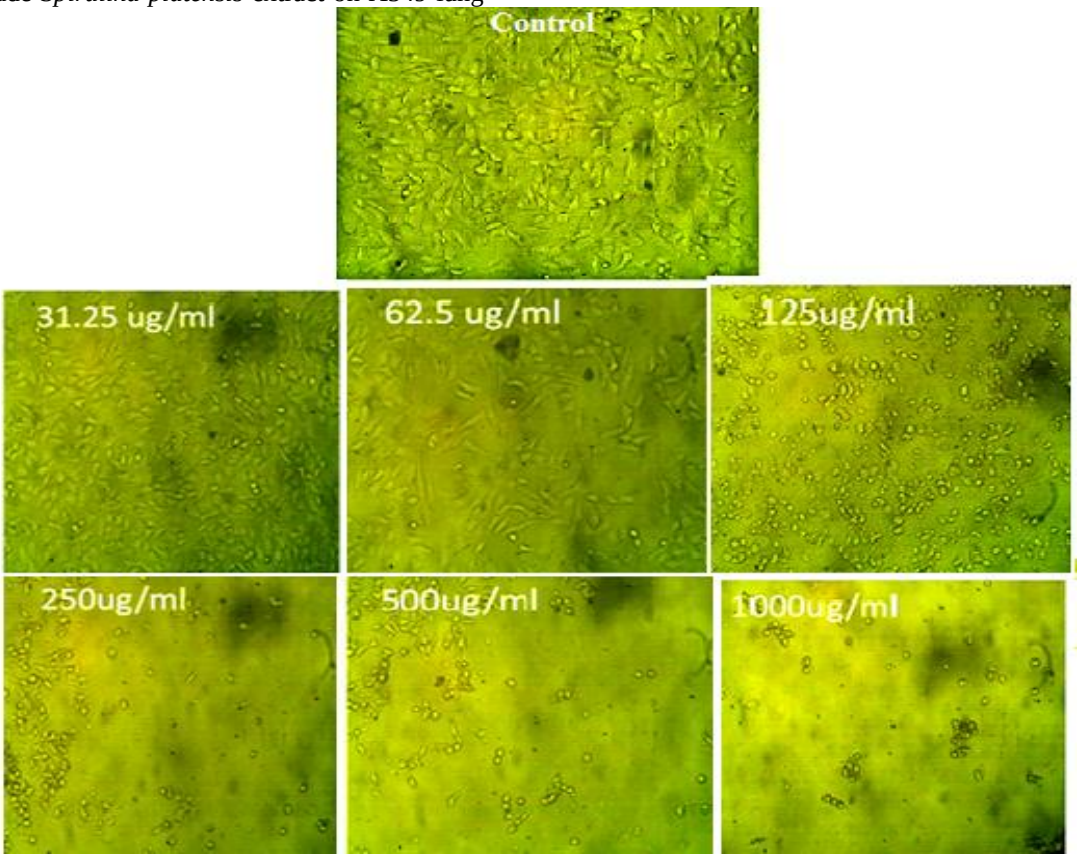

Fig. 1. Morphological changes in A549 lung cancer cells after 24-hour treatment with different concentrations of Spirulina platensis ethanolic extract.(A) Control: Cells show normal morphology.(B) 31.25 µg/mL: No visible morphological changes.(C) 62.5 µg/mL: Slight cell rounding.(D) 125 µg/mL: Early signs of shrinkage and detachment appear.(E) 250 µg/mL: More pronounced shrinkage and cell detachment.(F) 500 µg/mL: Significant rounding, loss of adhesion, and reduced cell number. (G) 1000 µg/mL: Severe cytotoxicity and necrosis with extensive cell damage.

3.2. Cytotoxicity

Lung cancer cells (A549) were exposed to *Spirulina platensis* extract at concentrations of 31.25, 62.5, 125, 250, 500, and 1000 µg/mL, and cell viability was assessed after 24 hours using the MTT assay (as shown in Table 1 and Fig. 2). The cytotoxic effect of the extract on A549 cells demonstrated a clear dose-dependent pattern. As the concentration of the extract increased, cell viability progressively declined. Notably, the extract exhibited a 100% reduction in viability at the highest tested concentration of 1000 µg/mL (Fig. 2). The half-maximal inhibitory concentration (IC50) of the extract was calculated to be 78.72 ± 1.06 µg/mL for the A549 cell line.

Table 1. Effect of different concentration of *S. platensis* extract on Viability and Toxicity on A549 lung cancer cells post 24 h using MTT assay.

Concen. Of algal extract µg/ml	**O.D**	**Viability %**	**Toxicity %**	**IC50 ± SD** µg/ml
0	0.563	100	0	-
1000	0.0186	3.31	96.68	78.72 ± 1.06
500	0.0216	3.84	96.151	
250	0.029	5.15	94.849	
125	0.0926	16.45	83.540	
62.5	0.279	49.67	50.32	
31.25	0.5623	99.881	0.118	

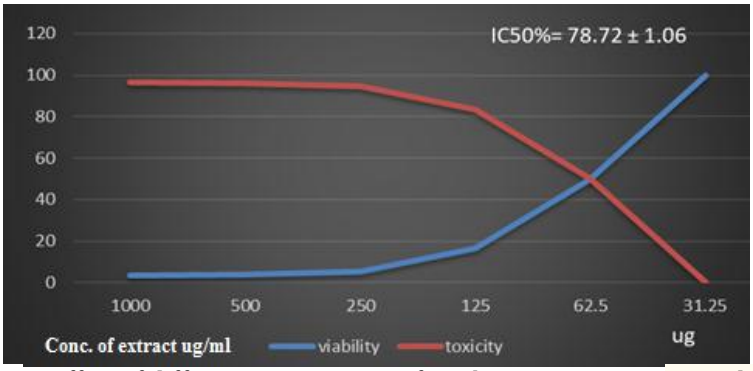

Fig. 2. Effect of different concentration of *S. platensis* extract on A549 lung cancer cells post 24 hrs using MTT assay

This trend is consistent with findings reported by [21], who observed an IC50 of 129.5 µg/mL for *S. platensis* extract on A549 cells using MTT analysis. In that study, the greatest reduction in cell viability occurred at 500 µg/mL, and a clear inverse relationship was established—meaning that as the concentration of the algal extract increased, the viability of A549 cells decreased accordingly.

3.3. Phytocomponents identified in the crude extract of *S. platensis* by GC-MS

The GC-MS analysis of *Spirulina platensis* identified 41 prominent compounds, as detailed in Table 2 and illustrated in Fig. 3. The GC-MS results included the probability percentages for each detected compound, indicating the most likely bioactive constituents. The highly probable compounds were confirmed through their spectral profiles and are depicted in Fig. 3.

Among the major unsaturated fatty acids detected in the *S. platensis* extract were oleic acid (54.8%), prostaglandin A2-biotin (53.2%), 2-hydroxy-3-[(9E)-9-octadecenoyloxy] (52.18%), ethyl acetate (31.38%), 9-octadecenoic acid (Z) (29.47%), and heptadecane (27.5%), as presented in Fig. 4.

According to Table 2, Oleic acid Eicosyl ester was identified as the most abundant compound in the extract, comprising 54.8% of the total composition. This monounsaturated fatty acid, while not essential, is well-known for its potent anti-inflammatory effects, particularly in autoimmune disorders, as well as its protective action against breast cancer [22].

Monounsaturated fatty acids (PUFAs) like oleic acid (OA) are considered crucial for both nutrition and therapeutic applications due to their wide-ranging health benefits [23]. OA, an omega-9 fatty acid, has exhibited strong cytotoxic and apoptosis-inducing effects in several cancer cell types [24, 25]. Furthermore, it has been shown to improve the performance of chemotherapeutic agents such as tamoxifen, paclitaxel, and trastuzumab in drug-resistant cancer cells [26]. In addition, OA has demonstrated considerable anti-proliferative effects on liver, lung, prostate, and tongue cancer cells [27, 28].

Furthermore, one of the most prominent compounds identified in the *Spirulina platensis* extract was prosta-

glandins (PGs), making up 53.2% of the total composition. PGs are widely recognized for their involvement in cancer development, with prostaglandin E2 (PGE2) frequently associated with tumor promotion [29]. According to [30], administration of Prostaglandin A2-biotin (PSP) led to a significant reduction in both tumor size and weight in mice bearing lung cancer. The biological functions of PGs are closely tied to their physicochemical properties, which are, in turn, influenced by the algal species responsible for their production [31]. A recent 2025 study also emphasized the anti-inflammatory and tumor-suppressive effects of PGD2 and its signaling mechanisms in lung adenocarcinoma (LUAD) [32].

In addition, the *S. platensis* crude extract was found to contain a high concentration of glycosides, particularly 2-Hydroxy-3-[(9E)-9-octadecenoyloxy], accounting for 52.18%. Current research indicates that cardiac glycosides (CGs) exhibit potent anticancer and antiviral properties. Their primary mechanism of action involves inhibition of the Na^+/K^+-ATPase pump, which leads to a reduction in intracellular potassium and an increase in sodium and calcium levels [33].

Another important finding was the prevalence of three fatty acid methyl esters: 9-octadecenoic acid (Z)-, 9-hexadecenyl ester (Z), and 9-octadecenoic acid, 2-hydroxy-1-(hydroxymethyl) ethyl ester. Among them, hexadecanoic acid is notable for its anti-inflammatory activity through the inhibition of phospholipase A2 [34]. Additionally, 9,12-octadecadienoic acid methyl ester has demonstrated both anti-inflammatory and liver-protective properties [35], while 9-octadecenoic acid is known for its antioxidant potential and its role in combating cancer [36].

4. Conclusion

Spirulina platensis serves as an abundant reservoir of crucial bioactive constituents, encompassing antioxidants, essential minerals, and a complete spectrum of amino acids and fatty acids. The findings of this study reveal that the ethanol extract of *S. platensis* exerts pro-apoptotic effects and plays a role in suppressing the proliferation of A549 lung cancer cells by boosting oxidative stress within the cells. Nonetheless, additional research is necessary to isolate, purify, and characterize these active compounds and to thoroughly investigate their underlying mechanisms of action before they can be explored as candidates for pharmaceutical development.

Table 2. Phyto-constituents profile for the ethanol extract of *S. platensis* using GC-MS analysis

NO.	Compound	RT	Peak area (%)	Mol. W.	Mol. Formula
1	2-Hydroxy-3-[(9E)-9 Octadecenoyloxy]	39.55	52.18	620	$C_{39}H_{72}O_5$
2	Acetic acid Ethyl Ester	5.32	31.38	88	$C_4H_8O_2$
3	9-Octadecenoic acid (Z)	39.55	29.47	282	$C_{18}H_{34}O_2$
4	Heptadecane	40.52	27.5	240	$C_{17}H_{36}$
5	9-Octadecenoic acid,1,2,3propanetriyl ester	65.36	26.91	884	$C_{57}H_{104}O_6$
6	Hexadecenoic acid,2- Hydroxy -1- (Hydroxy methyl) Ethyl ester	66.91	23.76	330	$C_{19}H_{38}O_4$
7	Octadecenoic acid,2- Hydroxy -1- (Hydroxy methyl) Ethyl ester	72.41	13	358	$C_{21}H_{42}O_4$
8	9-Octadecenoic acid (Z)-,9-Hexadecenyl Ester, (Z)-	8.54	9.82	504	$C_{34}H_{64}O_2$
9	9-Hexadecenoic acid, 9 Octadecenylester, (Z,Z)-	69.72	9.3	504	$C_{34}H_{64}O_2$
10	9-Octadecenoic acid(Z)-, oxiranylm ethylester	46.66	9.15	338	$C_{21}H_{38}O_3$
11	Acetic acid, Butyl Ester	5.04	8.5	116	$C_6H_{12}O_2$
12	Hexadecanic acid, Ethyl Ester	50.02	8.24	284	$C_{18}H_{36}O_2$
13	Glycerol 1-Palmitate	66.91	7.92	330	$C_{19}H_{38}O_4$
14	2-Ethyl-1-Hexyl Propionate	7. 58	6	186	$C_{11}H_{22}O_2$
15	2-Hexadecen-1-OL,3,7,11,15-Tetramethyl	53.92	4.86	296	$C_{20}H_{40}O$
16	Dideuterooctadecanal	36.82	3.55	270	$C_{18}H_{34}D_2O$
17	4H-1-Benzopyran-4-One,2-(3,4DihdroxyPhenyl)-6,8-DI-á-D-Glucopyranosyl-5,7Dihdroxy-	65.05	3.33	610	$C_{27}H_{30}O_{16}$
18	Hexadecenoic acid,(2-PHENYL-1,3-Dioxola N-4-Methyl ester	67.2	2.56	418	$C_{26}H_{42}O_4$

19	3-Amino-4-[(1-Benzyl-2methoxy-2-Oxoethyl) Amino]-4- Oxobutanoic Acid	7. 58	2.52	294	$C_{14}H_{18}N_2O5$
20	Hexadecenoic acid, 2, 3 Dihdroxypropyl ester	48.15	2.06	330	$C_{19}H_{38}O_4$
21	3,5,9-Trioxa-5-phosphaheptacos-18-e1aminium,4-hydroxy-N,N,N-trimethyl-10-oxo-7	10.68	2	785	$C_{44}H_{84}NO_8P$
22	Ethanaminum,2-[2,3-BIS[(1-Oxo-9-Octadecenyl) Oxy] Propoxy] hydroxyphophoiny]	10.68	2.77	785	$C_{44}H_{84}NO_8P$
23	Dotriacontane	32.83	1.99	450	$C_{32}H_{66}$
24	Oleic acid Eicosyl ester	78.5	54.8	562	C38 H 74 O_2
25	9-Octadecenoic acid	55.19	1.57	282	$C_{18}H_{34}O_2$
26	9,12 .15-_Octadecenoic acid2.3 bis [(Trimethylsi-lyl) Oxy] -propyl] ester	50.31	1.44	500	$C_{27}H_{56}O_4Si_2$
27	Prostaglandin A2-biotin	82.09	53.2	644	$C_{35}H_{56}N_4O5S$
28	(Epoxyethano)-1H-Indolizino[8,1CD]Carbazol-7-OL,6-Acetyl , Octahydro-8,9-Dimethoxy-	45.2	1.19	414	$C_{23}H_{30}N_2O_5$
29	2,2,3,3,4,4Hexadeuterooctadecanal	32.83	1.1	274	$C_{18}H_{30}D_{6O}$
30	Strychane, 1-acetyl-20à-hydroxy-16-methylene-	8. 51	1.07	338	$C_{21}H_{26}N_2O_2$
31	1,3,5-Triazine-2,4-Diamine,6-Chloro-N-Ethyl-	36.82	0.73	173	$C_5H_8ClN_5$
32	1H-Purin-6 Amine, [(2Fluorophenyl Methyl]	50.31	0.59	243	$C_{12}H_{10}FN_5$
33	E)-13-Docosenoic acid	46.66	0.58	338	$C_{22}H_{42}O_2$
34	Octadecynoic acid	46.66	0.58	280	$C_{18}H_{32}O_2$
35	PSI.,PSI.Carotene, Tetrahydro-1,1'-Dimethoxy-	10.68	0.5	600	$C_{42}H_{64}O_2$
36	2-(3-Acetoxy-4, 4,10,13,14-Pentamethyl- (Pro-ponic acid)	39.75	0.46	430	$C_{27}H_{42}O_4$
37	9- Octadecenoic acid,2 hdroxy-1-(hdroxy Methyl) ethylester	76.92	0.44	356	$C_{21}H_{40}O_4$
38	2,4-Di-tert-butylphenol	34.01	0.42	206	$C_{14}H_{22}O$
39	Estra-1,3,5(10)-trien-17á-ol	47.83	0.28	256	$C_{18}H_{24}O$
40	Oleyl oleate	92	0.27	532	$C_{36}H_{68}O_2$
41	Oleic acid	93	27.11	282	C18H34 O_2

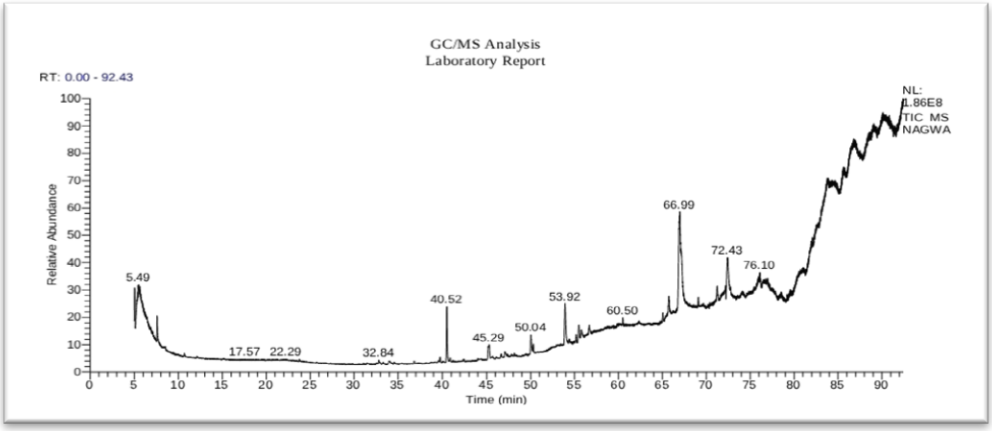

Fig. 3. GC – MS with ethanol extract of *Spirulina platensis*

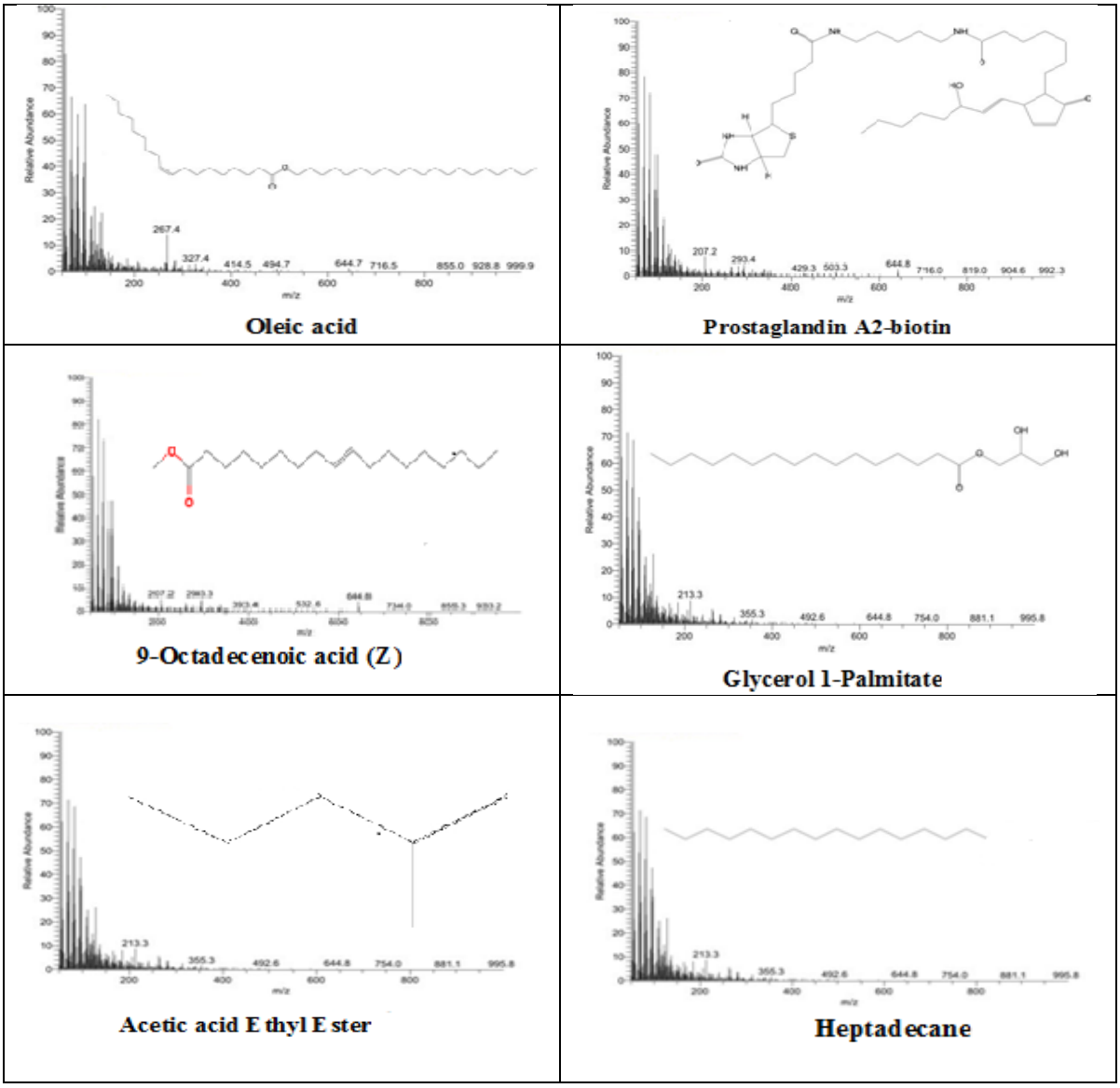

Fig. 4. GC – MS for fatty acids compounds with ethanol extract of *Spirulina platensis*

References

1. U. Anand, A. Dey, A.K.S. Chandel, R. Sanyal, A. Mishra, D.K. Pandey, V. De Falco, A. Upadhyay, R. Kandimalla, A. Chaudhary, J.K. Dhanjal, S. Dewanjee, J. Vallamkondu, J.M. Pérez de la Lastra, Cancer chemotherapy and beyond: current status, drug candidates, associated risks and progress in targeted therapeutics, Genes Dis. 10(4) (2022) 1367–1401. https://doi.org/10.1016/j.gendis.2022.02.007.
2. A. Czerwonka, K. Kaławaj, A. Sławińska-Brych, M.K. Lemieszek, M. Bartnik, K.K. Wojtanowski, B. Zdzisińska, W. Rzeski, Anticancer effect of the water extracts of a commercial Spirulina (Arthrospira platensis) product on the human lung cancer A549 cell line, Biomed. Pharmacother. 106 (2018) 292–302. https://doi.org/10.1016/j.biopha.2018.06.116.
3. J.W. Blunt, B.R. Copp, R.A. Keyzers, M.H.G. Munro, M.R. Prinsep, Marine natural products, Nat. Prod. Rep. 32 (2015) 116–211. https://doi.org/10.1039/C5NP00156K.
4. M. Ismail, M.F. Hossain, A.R. Tanu, H.U. Shekhar, Effect of spirulina intervention on oxidative stress, antioxidant status, and lipid profile in chronic obstructive pulmonary disease patients, Biomed. Res. Int. 2015 (2015) 486120. https://doi.org/10.1155/2015/486120.
5. M.F. McCarty, J.H. O'Keefe, J.J. DiNicolantonio, Carvedilol and Spirulina may provide important health protection to smokers and other nicotine addicts: a call for pertinent research, Mo. Med. 112(1) (2015) 72–75. PMCID: PMC6170079.
6. N.K. AlFadhly, N. Alhelfi, A.B. Altemimi, D.K. Verma, F. Cacciola, A. Narayanankutty. Trends and Technological Advancements in the Possible Food Applications of *Spirulina* and Their Health Benefits: A Review. Molecules. 27 (2022) 5584. https://doi.org/10.3390/molecules27175584
7. E. Myung, H. Kim, N. Choi, K. Cho, *The biochar derived from Spirulina platensis for the adsorption of Pb and Zn and enhancing the soil physicochemical properties*. Chemosphere 364 (2024) 143203.

https://doi.org/10.1016/j.chemosphere.2024.143203
8. E.A. El-Fayoumy, S.M.M. Shanab, H.S. Gaballa, M.A. Tantawy, E.A. Shalaby, Evaluation of antioxidant and anticancer activity of crude extract and different fractions of Chlorella vulgaris axenic culture grown under various concentrations of copper ions, BMC Complement. Med. Ther. 21 (2021) 51. https://doi.org/10.1186/s12906-020-03194-x.
9. J. Simpore, F. Kabore, F. Zongo, D. Dansou, A. Bere, S. Pignatelli, D.M. Biondi, G. Ruberto, S. Musumeci, Nutrition rehabilitation of undernourished children utilizing spiruline and misola, Nutr. J. 5 (2006) 3. https://doi.org/10.1186/1475-2891-5-3.
10. M.M. Abdel-Daim, Pharmacodynamic interaction of Spirulina platensis with erythromycin in Egyptian Baladi bucks (Capra hircus), Small Rumin. Res. 120(2–3) (2014) 234–241. https://doi.org/10.1016/j.smallrumres.2014.05.013.
11. L. Machu, L. Misurcova, J.V. Ambrozova, Phenolic content and antioxidant capacity in algal food products, Molecules 20(1) (2015) 1118–1133. https://doi.org/10.3390/molecules20011118.
12. G.S. Jensen, V.L. Attridge, J.L. Beaman, J. Guthrie, A. Ehmann, K.F. Benson, Antioxidant and anti-inflammatory properties of an aqueous cyanophyta extract derived from Arthrospira platensis: contribution to bioactivities by the non-phycocyanin aqueous fraction, J. Med. Food 18(5) (2015) 535–541. https://doi.org/10.1089/jmf.2014.0083.
13. J. Riss, K. Décordé, T. Sutra, J.C. Baccou, N. Jouy, J.P. Brune, H. Oréal, J.P. Cristol, J.M. Rouanet, Phycobiliprotein C-phycocyanin from Spirulina platensis is powerfully responsible for reducing oxidative stress and NADPH oxidase expression induced by an atherogenic diet in hamsters, J. Agric. Food Chem. 55(19) (2007) 7962–7967. https://doi.org/10.1021/jf070529g.
14. F. Atashrazm, R.M. Lowenthal, G.M. Woods, A.F. Holloway, J.L. Dickinson, Fucoidan and cancer: a multifunctional molecule with anti-tumor potential, Mar. Drugs 13(4) (2015) 2327–2346. https://doi.org/10.3390/md13042327.
15. A. Czerwonka, K. Kaławaj, A. Sławińska-Brych, M.K. Lemieszek, M. Bartnik, K.K. Wojtanowski, B. Zdzisińska, W. Rzeski, *Anticancer effect of the water extract of a commercial Spirulina (Arthrospira platensis) product on the human lung cancer A549 cell line*. Biomed. Pharmacother. 106(2018) 292–302. https://doi.org/10.1016/j.biopha.2018.06.116.
16. E. Tajvidi, N. Nahavandizadeh, M. Pournaderi, A. Zargar Pourrashid, F. Bossaghzadeh, Z. Khoshnood, Study the antioxidant effects of blue-green algae Spirulina extract on ROS and MDA production in human lung cancer cells, Biochem. Biophys. Rep. 28 (2021) 101139. https://doi.org/10.1016/j.bbrep.2021.101139
17. R.J. DeBerardinis, N.S. Chandel, Fundamentals of cancer metabolism, Sci. Adv. 2(5) (2016) e1600200. https://doi.org/10.1126/sciadv.1600200.
18. I. Martinez-Reyes, N.S. Chandel, Cancer metabolism: looking forward, Nat. Rev. Cancer 21(10) (2021) 669–680. https://doi.org/10.1038/s41568-021-00378-6.
19. C. Zarrouk, Contribution à l'étude d'une cyanobactérie: Influence de divers facteurs physiques et chimiques sur la croissance et la photosynthèse de Spirulina maxima (Setchell et Gardner) Geitler, PhD Thesis, University of Paris, Paris, 1966, 85 pp.
20. T.F. Slater, B. Sawyer, U. Strauli, The determination of the points of coupling of tetrazolium salts with the respiratory chain has provoked several investigations, Biochim. Biophys. Acta 77 (1963) 383–393.
21. S.P. Somasekharan, A. El-Naggar, P.H. Sorensen, Y. Wang, H. Cheng, An aqueous extract of marine microalgae exhibits antimetastatic activity through preferential killing of suspended cancer cells and anticolony forming activity, Evid. Based Complement. Alternat. Med. 2016 (2016) 9730654. https://doi.org/10.1155/2016/9730654.
22. H. Sales-Campos, P. Reis de Souza, P.B. Crema, J. Santana da Silva, C.C. Ribeiro, An overview of the modulatory effects of oleic acid in health and disease, Mini-Rev. Med. Chem. 13(2) (2013) 201–210.
23. S.M. Grundy, What is the desirable ratio of saturated, polyunsaturated, and monounsaturated fatty acids in the diet?, Am. J. Clin. Nutr. 66(4 Suppl) (1997) 988S–990S. https://doi.org/10.1093/ajcn/66.4.988S.
24. J.H. Lim, Z. Gehart-Hines, J.E. Dominy, Y. Lee, S. Kim, M. Tabata, Y.K. Xiang, P. Puigserver, Oleic acid stimulates complete oxidation of fatty acids through protein kinase A-dependent activation of SIRT1–PGC1α complex, J. Biol. Chem. 288(10) (2013) 7117–7126. https://doi.org/10.1074/jbc.M112.415729.
25. A. Saeed, S. Abotaleb, N. Alam, A. ElMehalawy, S. Gheda, In vitro assessment of antimicrobial, antioxidant and anticancer activities of some marine macroalgae, Egypt. J. Bot. 60(1) (2020) 81–96. https://doi.org/10.21608/ejbo.2019.11363.1303.
26. T.H. Kim, S.C. Kwon, J.N. Kim, J.H. Yoon, S.G. Cho, Ginseng seed oil inhibits the growth of estrogen receptor-positive breast cancer cells, Anticancer Res. 40(8) (2020) 4529–4535. https://doi.org/10.21873/anticanres.14458.
27. L. Jiang, W. Wang, Q. He, Y. Wu, Z. Lu, J. Sun, Z. Liu, Y. Shao, A. Wang, Oleic acid induces apoptosis and autophagy in the treatment of tongue squamous cell carcinomas, Sci. Rep. 7 (2017) 11277. https://doi.org/10.1038/s41598-017-11842-5.
28. K. Yamagata, E. Uzu, Y. Yoshigai, C. Kato, M. Tagami, Oleic acid and oleoylethanolamide decrease interferon-γ-induced expression of PD-L1 and induce apoptosis in human lung carcinoma cells, Eur. J. Pharmacol. 903 (2021) 174116. https://doi.org/10.1016/j.ejphar.2021.174116.
29. A. Santiso, A. Heinemann, J. Kargl, Prostaglandin E2 in the tumor microenvironment, a convoluted affair mediated by EP receptors 2 and 4, Pharmacol. Rev. 76 (2024) 388–413. https://doi.org/10.1124/pharmrev.123.000901.

30. Y. Lu, B. Peng, Y. Lin, Q. Lin, X. Xia, S. Zhong, L. Luo, R. Huang, Spirulina polysaccharide induces the metabolic shifts and gut microbiota change of lung cancer in mice, Curr. Res. Food Sci. 5 (2022) 1313–1319. https://doi.org/10.1016/j.crfs.2022.08.010.
31. Y. Kang, Z.J. Wang, D. Xie, X. Sun, W. Yang, X. Zhao, N. Xu, Characterization and potential anti-tumor activity of polysaccharide from Gracilariopsis lemaneiformis, Mar. Drugs 15 (2017) 100. https://doi.org/10.3390/md15040100.
32. Q. Liu, H. Chen, D. Tang, H. Zhang, S. Chen, Y. Meng, B. Zheng, F. Liu, J. Zhou, W. Zhang, Biological and prognostic insights into the prostaglandin D2 signaling axis in lung adenocarcinoma, Front. Pharmacol. 16 (2025) 1562261. https://doi.org/10.3389/fphar.2025.1562261.
33. R. Dhanasekhar, K. Ranjith, D. Bhowmik, A. Vasco, P. Ghosh, Anticancer and antiviral properties of cardiac glycosides: a review to explore the mechanism of actions, Molecules 25(16) (2020) 3596. https://doi.org/10.3390/molecules25163596.
34. V. Aparna, K.V. Dileep, P.K. Mandal, P. Karthe, C. Sadasivan, M. Haridas, Anti-inflammatory property of n-hexadecanoic acid: structural evidence and kinetic assessment, Chem. Biol. Drug Des. 80(3) (2012) 434–439. https://doi.org/10.1111/j.1747-0285.2012.01418.x.
35. M. Sermakkani, V. Thangapandian, GC-MS analysis of Cassia italica leaf methanol extract, Asian J. Pharm. Clin. Res. 5(2) (2012) 90–94.
36. J.I. Wilsy, D.A. Beschi, M.R. Appavoo, J.I. Wilsy, GC-MS analysis, collected from Kavalkinaru area, Tirunelveli District, Tamil Nadu, India, Eur. J. Mol. Clin. Med. 7 (2021) 4287–4292.