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In vitro Antioxidant and Antidiabetic Activities of *Spirulina platensis*: Insights into Enzymatic Inhibition and Insulin Gene Expression

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ABSTRACT

Background & Objective: Diabetes mellitus remains a global health challenge associated with oxidative stress and impaired insulin signaling. Natural compounds with dual antioxidant and enzyme-inhibitory potential are of great interest as complementary therapeutic agents. *Spirulina platensis*, a blue-green microalga rich in proteins, polyphenols, and phycocyanin, has been reported to exhibit diverse bioactivities. This study aimed to investigate the *in vitro* antioxidant and antidiabetic effects of *Spirulina platensis* extract, focusing on its enzymatic inhibition and modulation of insulin gene expression in pancreatic β\betaβ-cells.

Materials & Methods: Ethanolic extracts of *Spirulina platensis* were assessed for free-radical scavenging activity using DPPH and ABTS assays. The inhibitory activity against α\alphaα-amylase, α\alphaα-glucosidase, and protein tyrosine phosphatase-1B (PTP1B) was evaluated spectrophotometrically. Cytotoxicity and insulin secretion were analyzed in RIN-5F pancreatic β\betaβ-cells, followed by qPCR assessment of *INS I*, *INS II*, *IRS-I*, *IRS-II*, and *IRS-III* gene expression.

Results: The extract displayed strong, dose-dependent antioxidant activity ($p \leq 0.05p$ \le $0.05p \leq 0.05$) and significant inhibition of α\alphaα-amylase, α\alphaα-glucosidase, and PTP1B. No cytotoxicity was observed at concentrations below 100 μ\muμg/mL. Treatment with 20–60 μ\muμg/mL enhanced insulin secretion and markedly upregulated insulin-related gene expression in β\betaβ-cells.

Conclusion: *Spirulina platensis* demonstrates potent *in vitro* antioxidant and antidiabetic effects through enzymatic inhibition and the stimulation of insulin gene expression. These findings highlight *Spirulina* as a promising natural candidate for the development of safe, plant-based antidiabetic agents.

Keywords: *Spirulina platensis, antioxidant, antidiabetic, insulin, herbal drug*

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1. Introduction

Diabetes mellitus (DM) is a long-term metabolic condition marked by elevated blood sugar levels, which arise from either inadequate insulin production, insulin resistance, or a combination of both. The International Diabetes Federation has forecasted a 50% rise in the global population affected by diabetes (1,2). Persistent hyperglycemia is associated with oxidative stress, which plays a pivotal role in the pathogenesis and complications of diabetes, including neuropathy, retinopathy, nephropathy, and cardiovascular disease (3). Thus, agents capable of reducing oxidative stress and enhancing insulin function are of growing therapeutic interest. One promising strategy for managing diabetes involves the use of natural products that exhibit antioxidant activities (4).

Spirulina platensis, a blue-green microalga belonging to the Cyanobacteria phylum, is acknowledged as a functional food owing to its substantial nutritional value and bioactive content (5). It is rich in proteins, polyunsaturated fatty acids, vitamins, minerals, carotenoids, and phycobiliproteins—most notably C-phycocyanin, which exhibits potent antioxidant, anti-inflammatory, and immunomodulatory activities (5,6). While previous studies suggest that *Spirulina* may exert hypoglycemic effects in animal models (7-9), the underlying cellular and molecular mechanisms remain poorly understood.

The RIN-5F cell line is a rat insulinoma cell line that originates from pancreatic β-cells. These cells are widely used as an in vitro model for studying pancreatic β-cell function, insulin secretion, and the mechanisms involved in diabetes. Due to their ability to produce insulin and respond to glucose stimulation, RIN-5F cells are

commonly applied in research related to anti-diabetic compounds and the protective effects of natural products on β-cell dysfunction (10). Oxidative stress, together with excessive postprandial carbohydrate digestion mediated by digestive enzymes such as α-glucosidase, contributes to β-cell dysfunction and the progression of diabetes, thereby supporting the need for a multi-target therapeutic approach that combines antioxidant and enzyme-inhibitory strategies to preserve pancreatic β-cell function (11).

In the present study, we aimed to evaluate the *in vitro* antioxidant and antidiabetic potential of *Spirulina platensis*. Specifically, we assessed its free-radical scavenging capacity, its inhibitory effects on key carbohydrate-hydrolyzing enzymes (α\alphaα-amylase, α\alphaα-glucosidase, and PTP1B), and its modulation of insulin secretion and gene expression (*INS I, INS II, IRS-I, IRS-II,* and *IRS-III*) in RIN-5F cells. These findings may provide a mechanistic basis for the development of *Spirulina*-based nutraceuticals as safe and effective complementary therapies for diabetes management.

2. Materials and Methods

2.1 Chemicals and Reagents

All chemicals and reagents of analytical grade, such as DPPH (2,2-diphenyl-1-picrylhydrazyl), ABTS (2,2′-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid)), α-amylase, α-glucosidase, and p-nitrophenyl-α-D-glucopyranoside (pNPG), were sourced from Sigma-Aldrich (USA). Additionally, RPMI-1640 medium, fetal bovine serum (FBS), and various other materials for cell culture were procured from Gibco (USA).

2.2 Preparation of *Spirulina platensis* Extract

The *Spirulina* powder was commercially obtained from PepTina Company (Iran). The product was used as received without further modification. Dried *Spirulina platensis* powder (20 g) was suspended in 200 mL of 70% ethanol and stirred on a magnetic shaker for 24 hours. The mixture was centrifuged, filtered (Whatman No.1), and lyophilized using a freeze-dryer. Stock solutions were freshly prepared in cell culture medium before each experiment. The relatively high yield (24%, w/w) may be attributed to the efficient extraction of polar phytoconstituents using hydroalcoholic solvent.

2.3 Antioxidant Assays

2.3.1 DPPH Radical Scavenging Activity

The DPPH assay was conducted by combining 1 mL of extract (10–100 µg/mL) with 3 mL of a 100 µM DPPH solution in methanol. Following a 30-minute incubation period in the dark, the absorbance was recorded at 517 nm utilizing a UV–Vis spectrophotometer. β-Carotene served as the reference antioxidant.

2.3.2 ABTS Radical Scavenging Activity

The ABTS working solution was prepared by mixing 7 mM ABTS with 2.45 mM potassium persulfate and allowing the reaction to proceed in the dark overnight. Subsequently, 1 mL of the extract (10–100 µ\muµg/mL) was mixed with 3 mL of the diluted ABTS solution and incubated for 10 min in the dark. The absorbance was measured at 734 nm. Trolox served as the reference standard, and the results were expressed as Trolox equivalent antioxidant capacity (TEAC). The ABTS solution without the extract served as the negative control to determine the maximum radical absorbance, while a solvent blank (devoid of ABTS) was used to correct for background absorbance. The percentage of radical scavenging activity was determined using the following formula:

% Inhibition = [(A_control − A_sample) / A_control] × 100

2.4 Enzyme Inhibition Assays

2.4.1 α-Amylase Inhibition

Briefly, 125 µ\muµL of the extract was mixed with 125 µ\muµL of α\alphaα-amylase (3 U/mL) and incubated at 37 °C for 10 min. Subsequently, 125 µ\muµL of a 2% starch solution was added, and the mixture was incubated for an additional 30 min. The reaction was terminated by adding 250 µ\muµL of 3,5-dinitrosalicylic acid (DNS) reagent. The tubes were then heated in a boiling water bath for 15 min, allowed to cool to room temperature, and diluted with 1.5 mL of distilled water. The absorbance was recorded at 540 nm, with acarbose serving as the positive control.

2.4.2 α-Glucosidase Inhibition

The assay involved the combination of 20 µL of α-glucosidase enzyme with 60 µL of extract. After a 15-minute incubation period at 37°C, 50 µL of pNPG substrate was introduced. Following an additional 25 minutes of incubation, the reaction was terminated by the addition of 120 µL of Na_2CO_3, and the absorbance was measured at 405 nm. Acarbose served as the standard inhibitor (positive control), and the results were reported as a percentage of inhibition relative to the control. The enzyme solution devoid of sample acted as the negative control, indicating the maximum enzyme activity. A blank containing buffer in place of the enzyme was utilized to adjust for background absorbance. The percentage of α-glucosidase inhibition was determined using the equation provided:

% Inhibition = [(A_control − A_sample) / A_control] × 100

2.4.3 PTP1B Inhibition

The activity of protein tyrosine phosphatase 1B (PTP1B) was assessed using a commercial assay kit (Abcam, Cambridge, UK) in accordance with the manufacturer's instructions. Absorbance measurements were recorded at 540 nm, with ursolic acid serving as the positive control.

2.5 Cell Culture and Cytotoxicity Assay

The RIN-5F pancreatic β-cell line was maintained in RPMI-1640 medium enriched with 10% FBS and 1% antibiotics under standard conditions (37°C, 5% CO_2). For all experiments, cells from passages 5 to 8 were utilized to ensure consistency.

Cell viability was assessed using the MTT assay. A total of 2×10^5 cells per well were plated in 48-well plates, treated with varying concentrations of extracts (10–100 µg/mL) for 24 hours, and subsequently incubated with 0.5 mg/mL MTT for 4 hours. The resulting formazan crystals

were dissolved in DMSO, and the absorbance was recorded at 570 nm.

2.6 Insulin Secretion Assay

RIN-5F cells were incubated in Krebs–Ringer bicarbonate buffer (KRB) containing 4 or 20 mM glucose with or without *Spirulina* extract (20–60 µg/mL) for 1 hour. Supernatants were collected and centrifuged at 2,000 rpm for 5 minutes at 4°C. Insulin concentration was measured using a rat insulin ELISA kit (Abcam, UK).

2.7 Gene Expression Analysis

Total RNA was extracted from RIN-5F cells using an RNA isolation kit (Qiagen, Germany). RNA quality and quantity were assessed by spectrophotometry (A260/A280).

Complementary DNA (cDNA) was synthesized using a reverse transcription kit (Invitrogen, Carlsbad, CA, USA), and qPCR was performed using SYBR Green Master Mix (Applied Biosystems) on a real-time PCR system. Primers for INS I, INS II, IRS-I, IRS-II, and IRS-III were designed using Primer3 software and validated with GeneRunner. Expression levels were normalized to β-actin using the $2^{-}\Delta\Delta Ct$ method. The primer sequences for the target genes are presented in Table 1.

2.8 Statistical Analysis

All experiments were performed in triplicate, and the results are presented as mean ±\pm± standard error of the mean (SEM). Statistical analyses were conducted using SPSS software (version 16.0, SPSS Inc., Chicago, IL, USA).

The normality of the data distribution was evaluated using the Kolmogorov–Smirnov test, and the homogeneity of variances was assessed by Levene's test. Comparisons among groups were performed using one-way analysis of variance (ANOVA) followed by Tukey's post-hoc test for multiple comparisons. A p-value of ≤0.05\le 0.05≤0.05 was considered statistically significant.

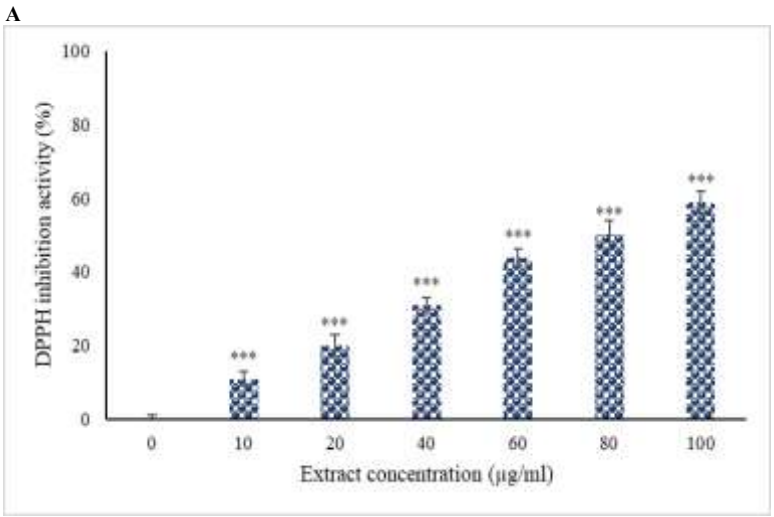
Table 1. Primer sequences used for gene expression analysis by quantitative real-time PCR (qPCR).

Target gene	Primer direction	Primer sequence (5′–3′)
INS I	Forward	CGTGGCTTCTTCTACACACCCA
INS I	Reverse	TGCAGCACTGATCCACAATGCC
INS II	Forward	CGTGGCTTCTTCTACACACCCA
INS II	Reverse	TCCAGTGCCAAGGTCTGAAGGT
IRS-I	Forward	AGTCTGTCGTCCAGTAGCACCA
IRS-I	Reverse	ACTGGAGCCATACTCATCCGAG
IRS-II	Forward	CCTGCCCCCTGCCAACACCT
IRS-II	Reverse	TGTGACATCCTGGTGATAAAGCC
IRS-III	Forward	GCAAGCATGGTACAGCGCCCT
IRS-III	Reverse	CCTTGGACCGCAGTGTCACAG

3. Result

3.1 Antioxidant Activity of *Spirulina platensis* Extract

The ethanolic extract of *Spirulina platensis* exhibited strong antioxidant activity in a concentration-dependent manner in both assays (Figure 1A and B). At concentrations ranging from 10 to 100 µ\muµg/mL, the extract showed a significant increase in free radical scavenging activity (p≤0.05p \le 0.05p≤0.05). At 100 µ\muµg/mL, *Spirulina* demonstrated 59.64±5.33%59.64 \pm 5.33\%59.64±5.33% inhibition in the DPPH assay and 63.12±6.66%63.12 \pm 6.66\%63.12±6.66% inhibition in the ABTS assay, which were comparable to the reference standard, β\betaβ-carotene. These findings indicate the presence of potent antioxidant compounds in *Spirulina*, likely attributable to its phycocyanin and polyphenolic constituents.



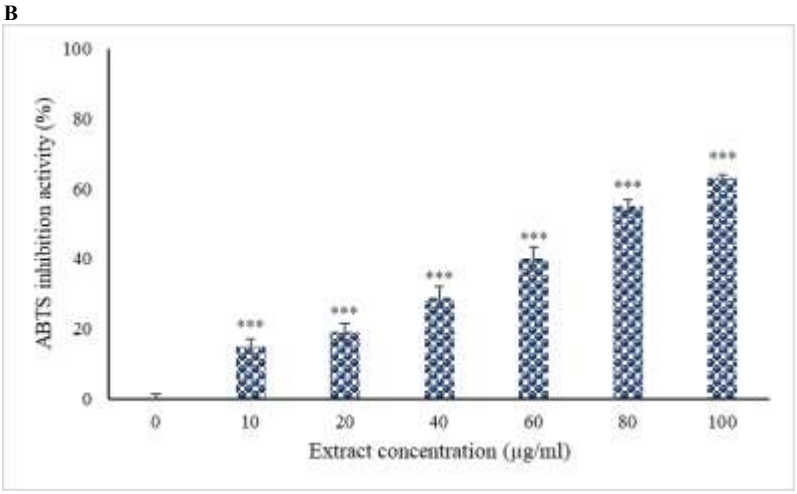
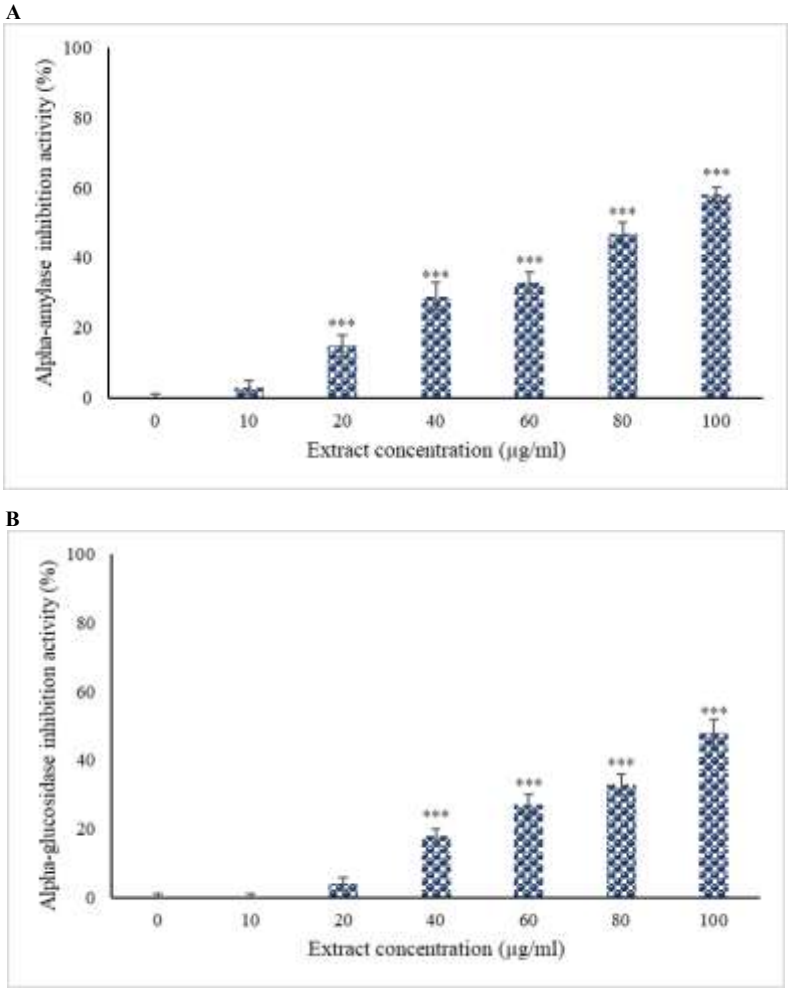


Figure 1. (A) DPPH and (B) ABTS radical scavenging activity of *Spirulina platensis* extract. *** indicates p ≤ 0.001. **(Prepared by Authors, 2026)**.

3.2 Inhibition of Carbohydrate-Hydrolyzing Enzymes

The extract significantly inhibited the activities of α\alphaα-amylase, α\alphaα-glucosidase, and protein tyrosine phosphatase 1B (PTP1B) (Figure 2A, B, and C). At 100 µ\muµg/mL, the inhibition rates were 58.6±3.1%58.6 \pm 3.1\%58.6±3.1% for α\alphaα-amylase, 48.2±2.8%48.2 \pm 2.8\%48.2±2.8% for α\alphaα-glucosidase, and 35.9±2.5%35.9 \pm 2.5\%35.9±2.5% for PTP1B, all of which were statistically significant compared with the control group (0 µ\muµg/mL) (p≤0.001p \le 0.001p≤0.001). The inhibitory potency of the extract approached that of acarbose for α\alphaα-amylase and α\alphaα-glucosidase, and ursolic acid for PTP1B.

These results suggest that *Spirulina platensis* may modulate glucose metabolism by simultaneously targeting multiple enzymes involved in carbohydrate digestion and insulin signaling.



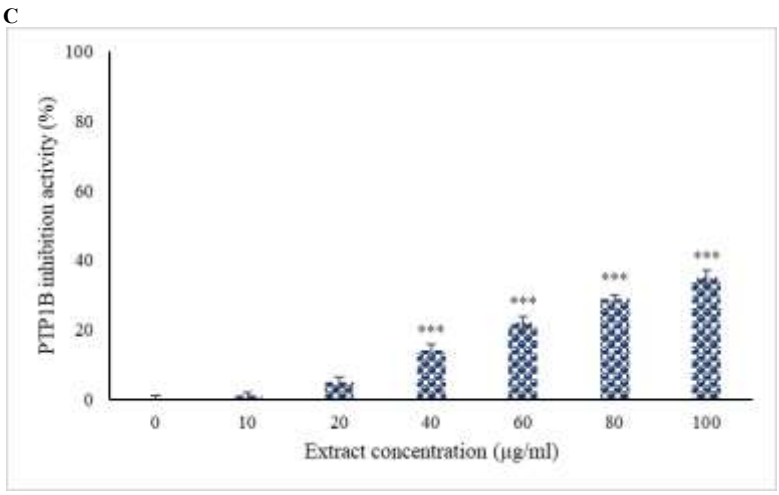


Figure 2. Inhibitory effects of *Spirulina platensis* extract on (A) α-amylase, (B) α-glucosidase, and (C) PTP1B enzyme activities. *** indicates p ≤ 0.001. (**Prepared by Authors, 2026**).

3.3 Cytotoxicity Assessment

The MTT assay revealed that the *Spirulina* extract did not exhibit cytotoxic effects on RIN-5F pancreatic β\betaβ-cells at concentrations below 100 µ\muµg/mL (p≥0.05p \ge 0.05p≥0.05; Figure 3A), indicating that the concentrations selected for subsequent functional assays were safe for *in vitro* analysis. This finding confirms the biocompatibility of the *Spirulina* extract for β\betaβ-cell studies and its potential for nutraceutical applications.

3.4 Effect on Insulin Secretion

Treatment with the *Spirulina platensis* extract significantly enhanced glucose-stimulated insulin secretion from RIN-5F cells (Figure 3B). At concentrations of 40 and 60 µ\muµg/mL, insulin secretion increased by 1.55- and 1.54-fold, respectively, compared with the control group (p≤0.05p \le 0.05p≤0.05). These results indicate that bioactive components in *Spirulina* may stimulate insulin release, potentially by activating intracellular signaling pathways associated with β\betaβ-cell function.

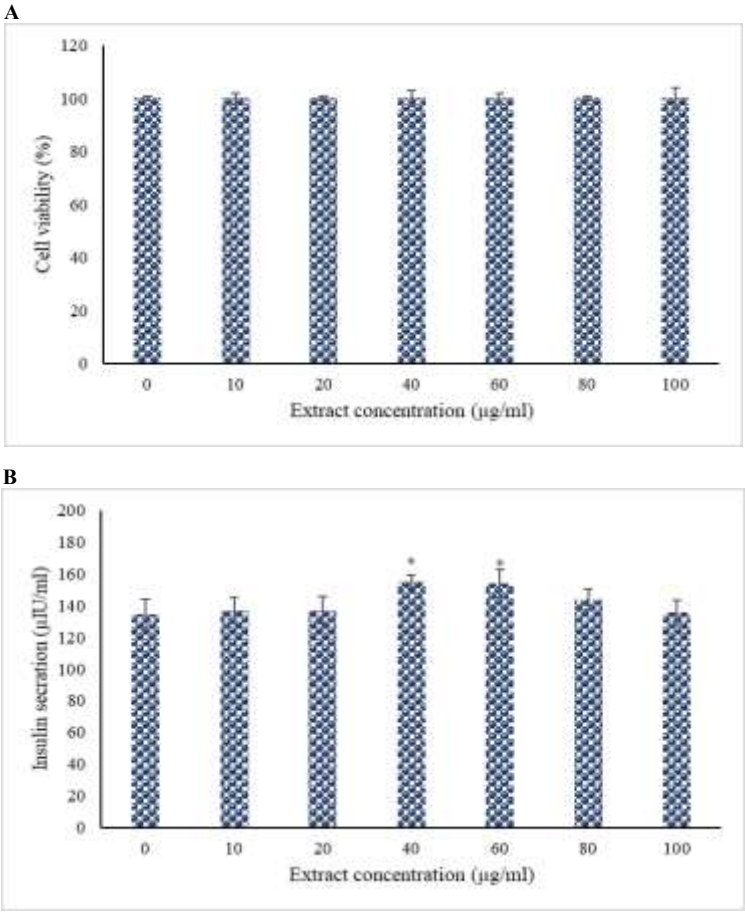


Figure 3. Effects of *Spirulina platensis* extract on (A) viability and (B) insulin secretion of RIN-F cells. * Indicates p ≤ 0.05. (**Prepared by Authors, 2026**).

3.5 Gene Expression Analysis

Quantitative PCR analysis demonstrated that the *Spirulina* extract significantly upregulated the expression of key insulin-related genes, including *INS I*, *INS II*, *IRS-I*, *IRS-II*, and *IRS-III* at 40 and 60 µ\muµg/mL (p≤0.001p \le 0.001p≤0.001; Figure 4). These transcriptional upregulations suggest that *Spirulina platensis* enhances insulin biosynthesis and intracellular signaling through the activation of critical genes involved in β\betaβ-cell function and glucose homeostasis.

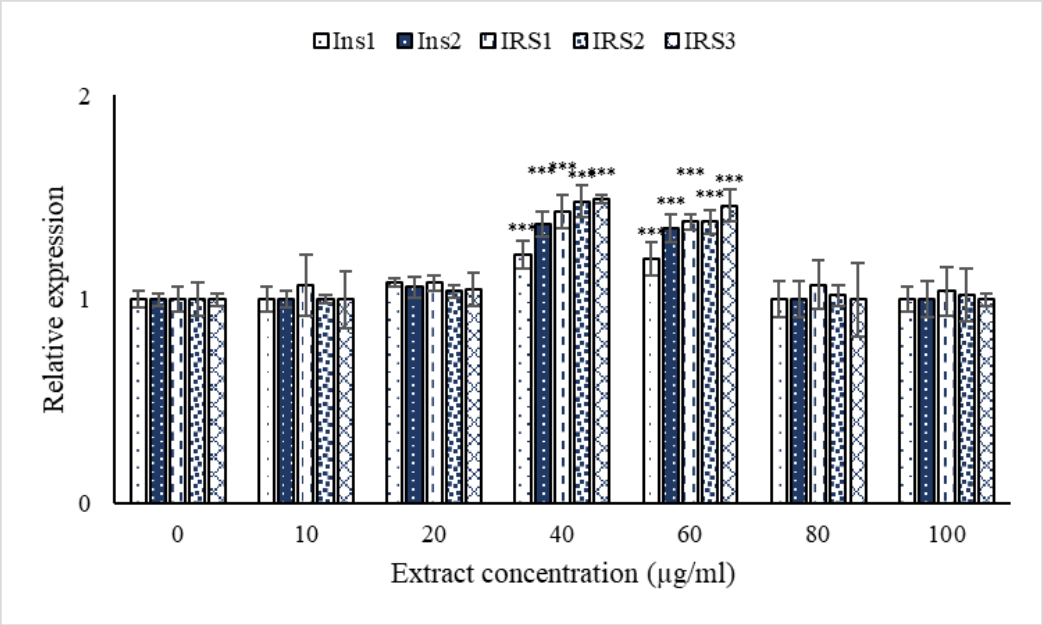


Figure 4. Relative expression levels of INS I, INS II, IRS-I, IRS-II, and IRS-III genes in RIN-5F cells treated with *Spirulina platensis* extract. *** indicates p ≤ 0.001. **(Prepared by Authors, 2026)**.

4. Discussion

The present study demonstrates that *Spirulina platensis* exhibits significant antioxidant and antidiabetic effects in vitro, supporting previous findings from in vivo investigations **(7-9)**. The extract's robust radical-scavenging activity (confirmed by the DPPH and ABTS assays) aligns with earlier reports attributing such efficacy in *Spirulina* to phycobiliproteins—notably C-phycocyanin—and diverse polyphenolic compounds **(12)**. Given the pivotal role of oxidative stress in β\betaβ-cell dysfunction and insulin resistance **(13)**, this potent antioxidant capacity likely underpins, at least in part, the antidiabetic potential of the algal extract. In line with mechanistic models, our findings of enzyme inhibition (α-amylase, α-glucosidase, and PTP1B) suggest multi-target action: by slowing carbohydrate digestion and enhancing insulin signal transduction. The involvement of PTP1B as a negative regulator of insulin signalling is well documented, and recent reviews highlight natural-product PTP1B inhibitors as promising diabetes interventions **(14)**. While direct evidence of *Spirulina* extract on PTP1B remains limited, the marine-derived bioactive molecule review identifies microalgal sources as potential PTP1B modulators **(15)**. Thus, our data contribute to a growing body of evidence positioning *Spirulina* as capable of modulating both digestive and intracellular glucose-metabolism pathways. Importantly, the extract enhanced insulin secretion from β-cells and upregulated expression of key insulin-related genes (INS I, INS II, IRS-I/II/III). This is consistent with prior work in which *Spirulina* extract protected pancreatic β-cells from cytokine-induced damage and supported insulin secretion **(16)**. Although gene expression of IRS family members has not been widely explored in *Spirulina* studies, our findings suggest that the extract may modulate β-cell function at the transcriptional level, possibly via antioxidant protection of β-cells. The observed upregulation of insulin-related genes may be mechanistically linked to the antioxidant properties of *Spirulina platensis* extract. Oxidative stress is known to impair pancreatic β-cell function by inducing reactive oxygen species ROS-mediated damage, which subsequently downregulates insulin gene expression and disrupts insulin signaling pathways. By scavenging free radicals and reducing intracellular ROS levels, the extract may help preserve β-cell integrity and enhance transcriptional activity of insulin-related genes. Furthermore, reduction in oxidative stress can modulate redox-sensitive signaling pathways such as PI3K/Akt and NF-κB, which are involved in insulin secretion and gene regulation. Therefore, the antioxidant capacity of *Spirulina* may indirectly contribute to improved insulin synthesis and signaling observed in this study. The absence of cytotoxicity below 100 µg/mL supports Spirulina's suitability for nutraceutical development. However, some limitations must be acknowledged. Firstly, our data derive from in vitro assays; in vivo pharmacokinetics, bioavailability and

safety remain to be established. Secondly, while we assessed enzyme inhibition and gene regulation, detailed molecular pathway analyses (e.g., PTP1B activity assay, protein phosphorylation states, insulin receptor activation) were not conducted. Furthermore, the dose–response in vivo and human translational relevance require further exploration. The study is limited by the absence of detailed phytochemical profiling, lack of in vivo validation, and no evaluation of potential synergistic effects among bioactive compounds.

5. Conclusion

The present study demonstrates that *Spirulina platensis* exhibits strong *in vitro* antioxidant and antidiabetic effects. The extract effectively scavenged free radicals, inhibited α\alphaα-amylase, α\alphaα-glucosidase, and PTP1B enzymes, enhanced insulin secretion, and upregulated the expression of key insulin-related genes in pancreatic β\betaβ-cells. These findings suggest that *Spirulina* may regulate glucose homeostasis and protect β\betaβ-cells from oxidative stress via multi-target mechanisms. Given its pronounced bioactivity and favorable safety profile (low cytotoxicity), *Spirulina platensis* represents a promising natural candidate for the development of safe nutraceutical or complementary therapies for diabetes management. Nevertheless, further *in vivo* and clinical investigations are warranted to validate its therapeutic efficacy and translational potential.

6. Declarations

6.1 Acknowledgments

We would like to express our sincere gratitude to Kermanshah University of Medical Sciences for its financial support.

6.2 Ethical Considerations

The study was approved by the Ethics Committee of Kermanshah University of Medical Sciences (Ethics Code: IR.KUMS.MED.REC.1403.232).

6.3 Authors' Contributions

“Conceptualization, resources, supervision, and funding acquisition, F. K-H.; methodology, investigation, M. P.; writing, I. R; editing the manuscript, A. G; validation, formal analysis and data curation, A. S-J.

6.4 Conflict of Interest

The authors declare no conflict of interest.

6.5 Fund or Financial Support

This research was funded by Kermanshah University of Medical Sciences, grant number 4030837. (Ethical code: IR.KUMS.MED.REC.1403.232)

6.6 Using Artificial Intelligence Tools (AI Tools)

Artificial Intelligence (AI) tools were used solely for language editing, proofreading, and improving the clarity and readability of the manuscript.
No AI tools were used to generate, fabricate, or modify research data, results, analyses, or scientific findings. All data were obtained and analyzed by the authors, who take full responsibility for the accuracy and integrity of the research.

References

1.American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabet Care. 2009;32 Suppl 1(Suppl 1):S62-7. [DOI:10.2337/dc09-S062] [PMID] [PMCID]

2. Li S, Wang J, Zhang B, Li X, Liu Y. Diabetes mellitus and cause-specific mortality: A population-based study. Diabetes Metab J. 2019;43(3):319-41 [DOI:10.4093/dmj.2018.0060] [PMID] [PMCID]

3. Caturano A, D'Angelo M, Mormone A, Russo V, Mollica MP, Salvatore T,et al. Oxidative stress in type 2 diabetes: Impacts from pathogenesis to lifestyle modifications. Curr Issues Mol Biol. 2023;45(8):6651-6666. [DOI:10.3390/cimb45080420] [PMID] [PMCID]

4. Vivó-Barrachina L, Rojas-Chacón MJ, Navarro-Salazar R, Belda-Sanchis V, Pérez-Murillo J, Peiró-Puig A,et al. The role of natural products on diabetes mellitus treatment: A systematic review of randomized controlled trials. Pharmaceutics. 2022;14(1):101. [DOI:10.3390/pharmaceutics14010101] [PMID] [PMCID]

5. Podgórska-Kryszczuk I. Spirulina-An invaluable source of macro- and micronutrients with broad biological activity and application potential. Molecules. 2024;29(22):5387. [DOI:10.3390/molecules29225387] [PMID] [PMCID]

6. Calella P, Cerullo G, Di Dio M, Liguori F, Di Onofrio V, Gallè F, et al. Antioxidant, anti-inflammatory and immunomodulatory effects of spirulina in exercise and sport: A systematic review. Front Nutr. 2022;9:1048258. [DOI:10.3389/fnut.2022.1048258] [PMID] [PMCID]

7. Xiaoyu He, Chang'e Wang, Yuxian Zhu, Xiaoqin Jiang, Yuyang Qiu, Fei Yin,et al. Spirulina compounds show hypoglycemic activity and intestinal flora regulation in type 2 diabetes mellitus mice. Algal Res. 2022; 66: 102791. [DOI:10.1016/j.algal.2022.102791]

8. Simon JP, Baskaran UL, Shallauddin KB, Ramalingam G, Evan Prince S. Evidence of antidiabetic activity of Spirulina fusiformis against

streptozotocin-induced diabetic Wistar albino rats. 3 Biotech. 2018;8(2):129. [DOI:10.1007/s13205-018-1156-8] [PMID] [PMCID]

9. Güldaş M, Ziyanok S, Şahan Y, Yıldız E, Gürbüz O. Antioxidant and anti-diabetic properties of spirulina platensis produced in turkey. Food Sci Technol.2021; 41(3): 615-25. [DOI:10.1590/fst.23920]

10. Potdar P, Kharat A, Sanap A, Kheur S, Bhonde R. Pancreatic β cell models for screening insulin secretagogues and cytotoxicity. J Appl Toxicol. 2025;45(1):89-106. [DOI:10.1002/jat.4658] [PMID]

11. Anastasiou IA, Eleftheriadou I, Tentolouris A, Koliaki C, Kosta OA, Tentolouris N. CDATA[The effect of oxidative stress and antioxidant therapies on pancreatic β-cell dysfunction: Results from in vitro and in vivo studies. Curr Med Chem. 2021;28(7):1328-46. [DOI:10.2174/0929867327666200526135642] [PMID]

12. El-Sakhawy M, Zahidul Iqbal M, Gabr G, Alqasem A, El-Sherbiny Ateya A, Ahmed F, et al.The mechanism of action of Spirulina as antidiabetic: a narrative review. Italian J Med. 2023; 17(2). [DOI:10.4081/itjm.2023.1639]

13. Eguchi N, Vaziri ND, Dafoe DC, Ichii H. The role of oxidative stress in pancreatic β cell dysfunction in diabetes. Int J Mol Sci. 2021;22(4):1509. [DOI:10.3390/ijms22041509] [PMID] [PMCID]

14. Liu Z, Gao H , Zhao Z , Huang M , Wang Sh ,Zhan J . Status of research on natural protein tyrosine phosphatase 1B inhibitors as potential antidiabetic agents: Update. Biomed Pharmacother. 2023;157:113990. [DOI:10.1016/j.biopha.2022.113990] [PMID]

15. Tamel Selvan K, Goon JA, Makpol S, Tan JK. Therapeutic potentials of microalgae and their bioactive compounds on diabetes mellitus. Marine Drugs. 2023; 21(9):462. [DOI:10.3390/md21090462] [PMID] [PMCID]

16. Lee J, Park A, Kim MJ, Lim HJ, Rha YA, Kang HG. Spirulina extract enhanced a protective effect in type 1 diabetes by anti-apoptosis and anti-ROS production. Nutrients. 2017;9(12):1363. [DOI:10.3390/nu9121363] [PMID] [PMCID]