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Original Research Article

Green Synthesis of Selenium Nanoparticles Using *Arthrospira platensis* Biomass and Their Anti-Hyperglycemic Effect: An *In Vivo* Research in Mice

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ABSTRACT

Diabetes mellitus, a chronic metabolic disorder marked by persistent hyperglycemia, often requires multifaceted therapeutic approaches. Although *Arthrospira platensis* exhibits antihyperglycemic properties, its bioactive compounds have limited bioavailability. This study synthesized selenium-functionalized *A. platensis* nanoparticles (Se-APNPs) using Na_2SeO_3 and evaluated their effects in diabetic mice. *Arthrospira platensis* powdered (raw material) (AP-P), Se-APNPs (10% and 20% v/v), infused AP-P (10% v/v), and glibenclamide were tested following diabetes induction via alloxan. The 10% Se-APNPs significantly lowered fasting glucose (84 mg/dL), outperforming glibenclamide, while infused AP-P showed superior wound healing (94.5%), comparable to the drug (96.6%). Growth performance was optimal in the 10% Se-APNP group, but higher concentrations indicated potential testicular toxicity. These findings highlight Se-APNPs as a promising approach for glycemic regulation and metabolic improvement, with infused AP-P excelling in wound repair. Dose optimization is crucial for maximizing efficacy and minimizing toxicity.

Keywords: *Arthrospira platensis*, Bioactive Compounds, Diabetes Mellitus, Selenium Nanoparticles, Wound Healing.

Introduction

Diabetes mellitus (DM) is a condition characterized by elevated blood glucose levels due to inadequate insulin secretion, insulin action, or both. It has emerged as a global health burden, contributing to approximately 5.1 million deaths annually.[1,2,3] As of October 2023, approximately 537 million people worldwide are living with diabetes, while 316 million people are at high risk due to impaired glucose tolerance, as reported by the International Diabetes Federation (IDF). In 2019, roughly 463 million people aged 20 to 79 were affected, and this number is projected to increase to 578 million by 2030 and rise another one-third by 2040.[4,5] The standard pharmacological therapy for diabetes commonly involves glibenclamide, a sulfonylurea. However, its long-term administration may cause side effects, including gastrointestinal problems and central nervous system (CNS) disruptions.[6] *Arthrospira platensis* (blue-green alga), a filamentous cyanobacterium, contains proteins, polysaccharides, pigments, vitamins, and other bioactive compounds known for antihyperlipidemic, antioxidant, and antihypertensive effects.[7,8] Hatami, Ghalishourani[9] reported that *A. platensis* extract exhibits anti-hyperglycemic activity by stimulating pancreatic *β*-cells' insulin production and reducing pancreatic lipase activity via glycolipid Hb2. Antioxidant compounds, such as *β*-carotene and phycocyanin, promote insulin secretion.[10]

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Arthrospira platensis additionally inhibits *α*-amylase, an enzyme responsible for carbohydrate digestion, with an inhibition rate of 62%.[11] Although this rate is lower than that of glibenclamide (73%), its limitation may be attributed to the incomplete digestion and absorption of bioactive compounds in raw form.[12] Nanotechnology provides a promising approach to enhance the therapeutic efficacy and bioavailability by improving the *in vivo* performance of biomolecules through nanoscale modification.[13]

The biomedical application of *A. platensis* in nanoparticle-based systems has been well documented, particularly in the synthesis of silver nanoparticles (AgNPs).[14] Although AgNPs derived from *A. platensis* demonstrate therapeutic potential, their anti-hyperglycemic benefits remain underexplored. Moreover, AgNPs may pose cytotoxic risks due to nonspecific distribution.[15] Therefore, the development of *A. platensis*-based nanoparticles with improved biocompatibility, higher bioavailability, and reduced toxicity is essential to ensure safety in anti-hyperglycemic applications. Selenium nanoparticles exhibit potent hypoglycemic effects[13] and offer a balanced profile of efficacy and toxicity, demonstrating vigorous biological activity, high bioavailability, and low toxicity when formulated through nanotechnology.[16] As a result, the use of selenium-functionalized *A. platensis* nanoparticles (Se-APNPs) as an anti-hyperglycemic agent might present a promising therapeutic strategy.

This research aimed to synthesize Se-APNPs and to evaluate their therapeutic potential in diabetic mice by assessing glycemic control, wound healing, growth performance, and testicular health. The study directly compared Se-APNPs with the A. platensis-powdered (AP-P) and AP-P infusion to determine effectiveness in metabolic regulation and wound repair. The findings highlight Se-APNPs as a dual-function nanobiotechnological intervention for diabetes management, emphasizing the importance of dose optimization to achieve therapeutic benefits while preventing toxicity.

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Materials and Methods

Alga preparation

Arthrospira platensis was cultured in 500 mL culture jars containing 100 mL of seawater, maintained at 27±2°C under continuous illumination for approximately 15 hours daily at 3,000 lux. The culture volume was gradually increased by adding seawater as the growth medium.[17] Biomass powdering followed the procedure of Gheda, Abo-Shady[18], in which *A. platensis* biomass was centrifuged at 5000 rpm for 15 minutes and rinsed with sterile distilled water during the second centrifugation cycle. The biomass was then dried in a 50°C oven for three days before being made into AP-P using a manual mortar and pestle.

Gas Chromatography-Mass Spectrometry (GC-MS) analysis and preparation of AP-P infusion

GC-MS analysis was performed using a 7890B GC system coupled with a 5977A mass spectrometer and equipped with a DB-5MS column (30 m × 0.25 mm × 0.25 μm). An ionization energy of 75 eV was used for compound fragmentation, and mass spectra were analyzed using flame ionization detection.[19] For infusion preparation, 10 g of AP-P was mixed with 100 mL of distilled water and heated to 90°C for 15 minutes with periodic stirring. The warm mixture was filtered through flannel cloth to obtain 100 mL of AP-P infusion.[20]

Synthesis of Arthrospira platensis nanoparticles with Na_2SeO_3 (Se-APNPs)

A 10 mM sodium selenite (Na_2SeO_3) solution was incorporated into AP at 10% and 20% (w/v). The mixture was incubated at room temperature under constant light and agitation. A visible colour change in the suspension indicated nanoparticle formation. The samples were then homogenized for 20 minutes at 15,000 rpm and freeze-dried to obtain Se-APNP powder.[21]

Liquid Chromatography-High-Resolution Mass Spectrometry (LC-HRMS) of Se-APNPs

The LC-HRMS analysis was performed using a Thermo Scientific Dionex Ultimate 3000 RSLCnano UHPLC system and a Thermo Scientific Q Exactive High-Resolution Mass Spectrometer. Approximately 0.1 mg of the sample was diluted in ethanol, vortex-mixed, and filtered through a 0.2 μm filter. A 5 μL aliquot of the filtrate was then injected for analysis.[22]

Scanning Electron Microscopy (SEM) analysis of Se-APNPs

Scanning electron microscopy (SEM) analysis was performed using a TESCAN MIRA instrument at accelerating voltages ranging from 0 to 15 kV. Before measurement, samples were filtered and dried. Micrographs were captured at magnifications of 50 k and 100 k to examine nanoparticle morphology and size distribution.[21]

Preparation for test animals

Thirty-five male white mice (20 g to 30 g) aged 3 to 4 months were obtained from the Animal Research Facility of the University of Muhammadiyah Malang, Indonesia. They were acclimatized to the laboratory environment for 7 days under controlled housing conditions (22 to 25 °C, 50 to 60% humidity, and a 12-h light/dark cycle) with easy access to standard feed and drinking water *ad libitum*.[23] Prior to treatment, all mice were fasted for 18 hours and weighed to determine the precise alloxan dosage; initial (baseline) blood samples were also collected via the lateral tail vein.[20] Diabetes was induced by administering alloxan monohydrate (150 mg/kg Body Weight) as a single intraperitoneal (IP) injection. Successful diabetes induction was confirmed 72 hours post-induction by measuring fasting blood glucose (FBG) from the lateral tail vein using a glucometer. Only mice exhibiting an FBG level were selected for inclusion in the subsequent treatment phase.[24]

Ethical approval

This research received ethical clearance (approval No. E.5.a/214/KEPKUMM/VII/2024; issued on 31/7/2024) from the Animal Care and Use Committee, Faculty of Medicine, University of Muhammadiyah Malang, East Java, Indonesia.

Experimental design

The laboratory-based experiment was carried out at the Pharmacology Laboratory, Faculty of Health Sciences, Universitas Muhammadiyah Malang, from May to July 2024. Data collection was performed through face-to-face sessions, while adhering to strict health protocols. A completely randomized design comprising six treatment groups with four replications each was applied as follows.[6,23,25,26]

Group 0:	Normal mice without intervention were fed with standard feed.
Group 1:	Diabetic mice were administered glibenclamide (0.6 mg/kg body weight).
Group 2:	Diabetic mice were administered AP-P (10% v/v).
Group 3:	Diabetic mice were administered AP-P infusion (10% v/v).
Group 4:	Diabetic mice were administered Se-APNPs (10% v/v).
Group 5:	Diabetic mice were administered Se-APNPs (20% v/v).

Parameter analysis

Blood samples were collected from the tail vein at 0, 1, 2, 3, 6, 12, and 24 hours. Glucose levels were measured using the Fine test glucometer. All treatments were administered over 15 days, during which fasting blood glucose was measured on days 0, 3, 7, 11, and 15.[25] Body weight was recorded at the start and end of the experiment using an analytical balance. Growth performance was evaluated based on changes in body weight.[27] Relative testis weight was calculated by dividing testis weight (g) by body weight (g) and multiplying by 100.[28] For wound-healing assessment, a full-thickness square wound (0.5 cm × 0.5 cm) was created on the thoracolumbar region after shaving and disinfecting the skin. Wound contraction percentages were calculated on days 1, 3, and 7 using Equation (1).[29]

$$\% \text{ wound contraction} = \frac{(\text{Wound area at day 0} - \text{Wound area at day n}) \times 100\%}{\text{Wound area at day 0}} \quad (1)$$

Statistical Analysis

A one-way Analysis of Variance (ANOVA) was utilised to examine the experimental results. At the same time, multiple comparisons were performed using the Duncan test to identify significant differences in treatment effects on Statistic 26. The results are presented as mean ± standard deviation (SD), which shows notable differences between groups at each time point ($p < 0.05$).

Results and Discussion

Scanning Electron Microscopy (SEM) Image of Se-APNPs

SEM observations revealed that the Se-APNPs exhibited heterogeneous particle sizes ranging from 40 to 500 nm (

Figure ***1***). The predominantly spherical morphology suggests successful selenium functionalization, which may enhance the particles' bioavailability and interaction with biological systems. The polydisperse size distribution indicates a non-uniform nucleation and growth pattern during synthesis. These findings are consistent with previous studies that have used SEM to confirm nanoparticle formation and characterize the surface morphology of biosynthesized selenium nanoparticles.[30,31,32,33] Although SEM provides valuable morphological information, it is limited in accurately determining nanoparticle size distributions in colloidal systems.[32] This study, therefore, considers SEM as supportive evidence of nanoparticle formation. To obtain a more comprehensive characterization, future research should integrate additional analytical techniques such as dynamic light scattering (DLS) or transmission electron microscopy (TEM). The observed structural integrity and dispersion of Se-APNPs

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further support their potential to improve bioavailability and therapeutic efficacy in managing metabolic disorders, including diabetes.

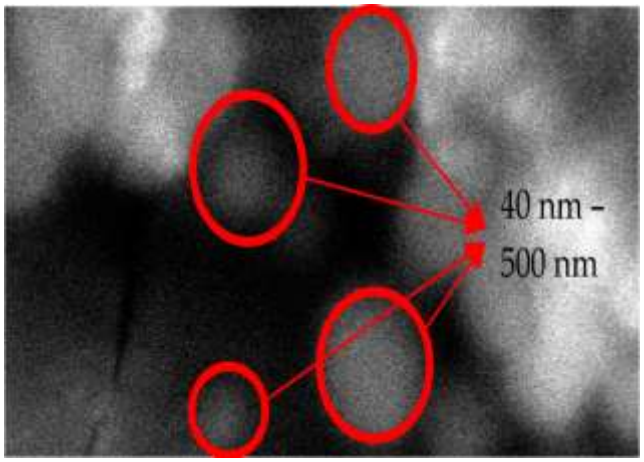

Figure 1: SEM micrograph illustrating the surface morphology and size distribution of Se-APNPs. The nanoparticles appear predominantly spherical with a heterogeneous size range between approximately 40 nm and 500 nm, confirming successful nanoparticle formation

GC-MS Analysis and Metabolite Identification of AP-P

The total ion chromatogram presents a detailed chemical profile of *A. platensis*, reflecting the retention times and relative abundance of its constituents (Figure 2). The dominant peak within 30 minutes indicates the presence of a major bioactive compound at high concentration. GC-MS analysis identified a broad spectrum of metabolites, including terpenoids, fatty acids, hydrocarbons, and oxygenated derivatives, many of which are associated with anti-diabetic activity (Table 1). These metabolites contribute to glucose homeostasis through multiple mechanisms, such as enhancing insulin sensitivity and reducing oxidative stress, which are key drivers of hyperglycemia. Fatty acids and their derivatives modulate insulin signaling and lipid metabolism, while oxidative stress-mitigating compounds help prevent β-cell damage.[34,35] Notably, the high levels of heptadecane (62.79%) suggest that this strain of *A. platensis* may serve as a valuable source of metabolic regulators.[36,37] Phytol (10.22%) and neophytadiene (11.11%) are also noteworthy for their glucose-regulating and lipid-lowering properties.[38,39,40] The presence of hexadecanoic acid esters supports their potential as natural α-amylase and α-glucosidase inhibitors, analogous to the mechanism of acarbose.[41,42] Collectively, these findings reinforce the role of AP-P as a promising candidate for diabetes management.

LCHRMS Analysis and Metabolite Identification of Se-APNPs

LCHRMS metabolomic profiling revealed that Se-APNPs contains diverse bioactive compounds associated with metabolic regulation, antioxidant defense, and anti-hyperglycemic potential (Figure 3). The identified metabolites include amino acids, bioactive molecules, and lipid-based constituents (Selenium nanoparticles are known to reduce oxidative stress and enhance insulin receptor sensitivity, thereby attenuating hyperglycemia-induced tissue damage.[43,44]). Selenium nanoparticles are known to reduce oxidative stress and enhance insulin receptor sensitivity, thereby attenuating hyperglycemia-induced tissue damage.[43,44] Among the amino acids detected, L-valine, L-phenylalanine, L-histidine, and L-glutamic acid are involved in insulin secretion, β-cells protection, neurotransmission, and glucose utilization.[45,46,47,48] The presence of D- and L-proline suggests potential involvement in collagen synthesis and cellular adaptation.[49,50] Additionally, acetophenone and nicotinic acid derivatives in Se-APNPs are associated with enhanced glucose uptake and lipid metabolism.[51,52] Choline and stearamide further contribute to improving insulin sensitivity and lipid regulation.[53,54] Finally, the presence of TEMPO (2,2,6,6-tetramethyl-1-piperidinyl) highlights an antioxidant component that may counteract oxidative stress.[55] Although selenium was not detected throughout the whole analysis, its functionalization of the nanoparticles plausibly improves bioactivity.

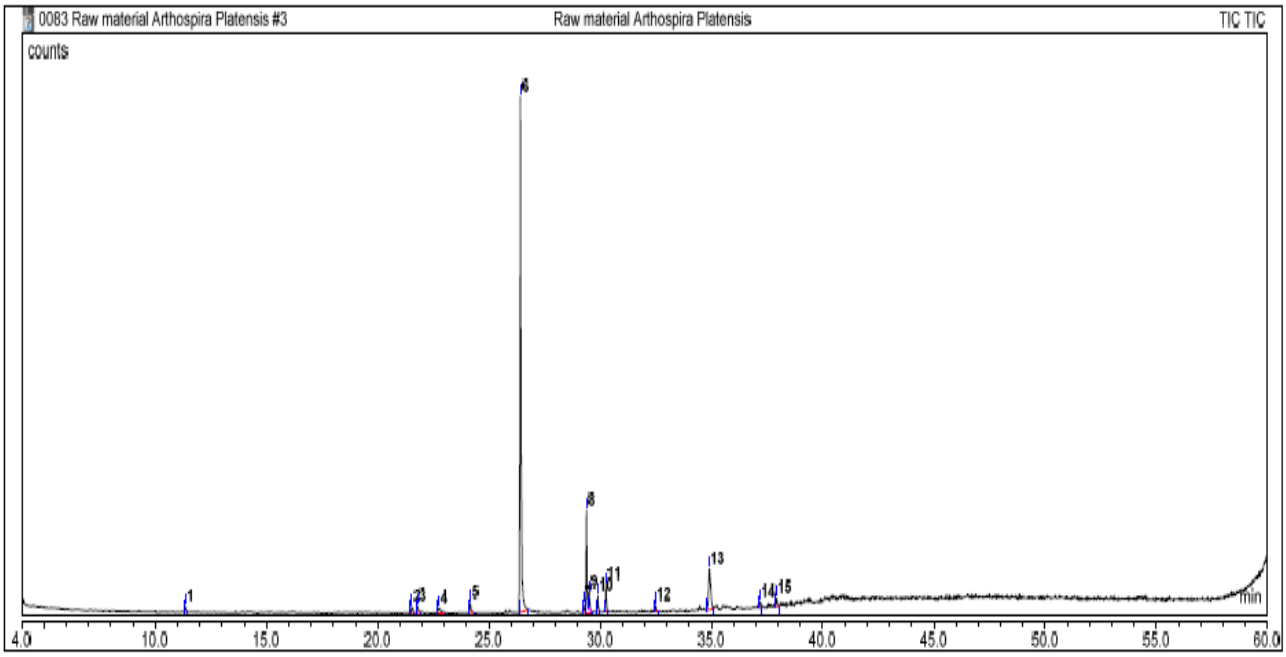

Figure 2: Total Ion Chromatogram (TIC) of *A. platensis* Raw Material Analyzed by GC-MS

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Table 1: Identified Compounds in RMAP by GC-MS Analysis

No.	Retention Time (min)	Compound Name	Molecular Formula	Molecular Weight (g/mol)	Relative Area (%)
1	11.35	Cyclohexanol, 2,4-dimethyl-	$C_8H_{16}O$	128	0.76
2	21.53	3-Buten-2-one, 4-(2,6,6-trimethyl-1-cyclohexen-1-yl)-	$C_{13}H_{20}O$	192	0.88
3	21.79	Dodecane, 2,6,11-trimethyl-	$C_{15}H_{32}$	212	0.89
4	22.76	2(4H)-Benzofuranone, 5,6,7,7a-tetrahydro-4,4,7a-trimethyl-	$C_{11}H_{16}O_2$	180	1.70
5	24.16	Hexadecane	$C_{16}H_{34}$	226	1.41
6	26.42	Heptadecane	$C_{17}H_{36}$	240	62.79
7	29.25	1-Hexadecanol, 2-methyl-	$C_{17}H_{36}O$	256	0.84
8	29.39	Neophytadiene	$C_{20}H_{38}$	278	11.11
9	29.51	2-Hexadecene, 3,7,11,15-tetramethyl-	$C_{20}H_{40}$	280	1.80
10	29.90	Neophytadiene	$C_{20}H_{38}$	278	1.73
11	30.25	3,7,11,15-Tetramethyl-2-hexadecen-1-ol	$C_{20}H_{40}O$	296	2.95
12	32.49	Hexadecanoic acid, ethyl ester	$C_{18}H_{36}O_2$	284	1.00
13	34.91	Phytol	$C_{20}H_{40}O$	296	10.22
14	37.20	Hexadecanoic acid, 1-(hydroxymethyl)-1,2-ethanediyl ester	$C_{35}H_{68}O_5$	568	0.77
15	37.93	Hexadecanoic acid, 1-(hydroxymethyl)-1,2-ethanediyl ester	$C_{35}H_{68}O_5$	568	1.15

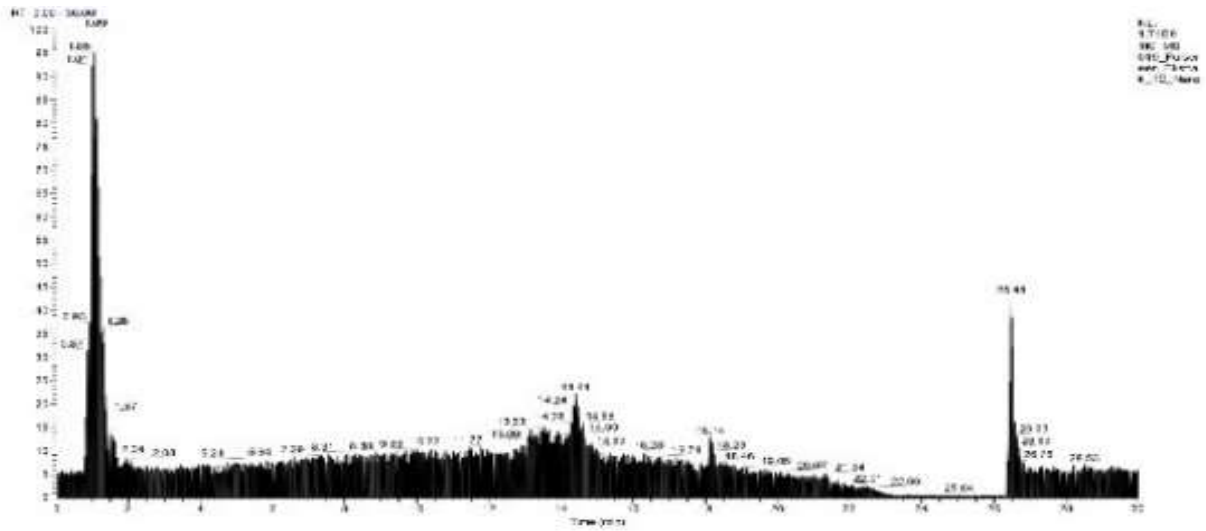

Figure 3: Metabolite Profile of Se-APNPs Identified by LCHRMS

Functionalization improves the targeted delivery of these metabolites, strengthening their therapeutic potential against metabolic disorders, especially diabetes mellitus. Future studies should include *in vivo* validation, pharmacokinetic assessment, and mechanistic analysis to clarify their disease-modulating actions.

Blood sugar level analysis

Over the 15-day monitoring period, blood glucose profiles showed significant differences ($p < 0.05$) among the treatment groups (Figure 4). The negative control group showed no significant reduction in glucose levels, confirming sustained hyperglycemia. In contrast, glibenclamide administration produced a transient decrease that peaked on day 3, followed by irregular fluctuations, indicating unstable glycemic control. Both AP-P and its infusion demonstrated measurable antihyperglycemic effects, significantly reducing glucose to 96 mg/dL and 104.5 mg/dL, respectively, indicating its potential role in glycemic control. The most significant decrease was observed in the groups that received Se-APNPs treatment. The 10% nanoparticle formulation (Group 4) decreased glucose considerably from 200.5 mg/dL to 84 mg/dL, whereas one of the 20% formulations (Group 5) reduced it from 195 mg/dL to 93 mg/dL. Based on those findings, nanoparticle formulations showed superior efficacy compared with the raw and

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infusion forms, likely due to enhanced bioavailability and selenium synergy.

Table 2: Metabolite Profile of Se-APNPs Identified by LCHRMS

No	Compound Name	Molecular Formula	Calculated MW	RT (min)	Area (Max.)	mzCloud Best Match (%)
1	L-Norleucine	$C_6H_{13}NO_2$	131.09415	1.087	5.43E+09	99.6
2	Acetophenone	C_8H_8O	120.05694	1.053	4.24E+09	81.7
3	L-Phenylalanine	$C_9H_{11}NO_2$	165.07825	1.148	7.77E+08	99.6
4	L-Valine	$C_5H_{11}NO_2$	117.07869	0.975	5.65E+08	99.7
5	L-Phenylalanine	$C_9H_{11}NO_2$	165.07825	0.959	5.27E+08	99.5
6	D-Leucineamide	$C_6H_{14}N_2O$	130.11007	1.03	4.59E+08	96.9
7	L-Norleucine	$C_6H_{13}NO_2$	131.09415	1.574	4.45E+08	99.8
8	Choline	$C_5H_{13}NO$	103.09921	1.15	3.96E+08	94
9	Prolinamide	$C_5H_{10}N_2O$	114.07887	1.051	3.78E+08	95.2
10	D-(+)-Proline	$C_5H_9NO_2$	115.06289	1.109	3.51E+08	99.5
11	D-(-)-Proline	$C_5H_9NO_2$	115.06295	1.163	3.47E+08	99.2
12	DL-Alanine	$C_3H_7NO_2$	89.04758	0.98	2.93E+08	72.3
13	L-Phenylalanine	$C_9H_{11}NO_2$	165.07825	1.985	2.31E+08	99.6
14	Histamine	$C_5H_9N_3$	111.07945	1.11	2.25E+08	98.7
15	Hypoxanthine	$C_5H_4N_4O$	136.03789	0.902	1.51E+08	99.8
16	L-Phenylalanine	$C_9H_{11}NO_2$	165.07825	1.629	1.42E+08	99.6
17	L-Pyroglutamic Acid	$C_5H_7NO_3$	129.04207	0.852	1.58E+08	99.5
18	L-Histidine	$C_6H_9N_3O_2$	155.06874	1.114	9.59E+07	98.5
19	Uracil	$C_4H_4N_2O_2$	112.02698	0.849	8.25E+07	99.5
20	Acetophenone	C_8H_8O	120.05694	1.583	8.05E+07	81.2
21	Dibenzylamine	$C_{14}H_{15}N$	197.11951	1.077	4.50E+07	86.9
22	Dibenzylamine	$C_{14}H_{15}N$	197.11951	7.334	4.12E+07	99.3
23	L-Pyroglutamic Acid	$C_5H_7NO_3$	129.04207	1.13	3.54E+07	67
24	2,5-Dimethylpyrazine	$C_6H_8N_2$	108.06842	1.061	3.36E+07	78.2
25	2,2,6,6-Tetramethyl-1-piperidinol (TEMPO)	$C_9H_{19}NO$	157.14615	11.792	2.95E+07	89
26	L-Glutamic Acid	$C_5H_9NO_4$	147.05258	0.964	2.88E+07	99.5
27	Bis(4-ethylbenzylidene)sorbitol	$C_{24}H_{30}O_6$	414.20232	14.701	2.80E+07	99.5
28	N-Acetyltyramine	$C_{10}H_{13}NO_2$	179.09387	0.855	2.76E+07	95.8
29	L-Glutamic Acid	$C_5H_9NO_4$	147.05258	1.163	2.66E+07	77.8
30	DL-Tryptophan	$C_{11}H_{12}N_2O_2$	204.08913	1.131	2.55E+07	90.1
31	DL-Tryptophan	$C_{11}H_{12}N_2O_2$	204.08913	0.978	2.30E+07	98.8
32	Stearamide	$C_{18}H_{37}NO$	283.26389	24.213	2.27E+07	97.9
33	Thymine	$C_5H_6N_2O_2$	126.04252	0.852	2.24E+07	95.7
34	Dodecylamine	$C_{12}H_{27}N$	185.21358	14.849	2.20E+07	84.3
35	N-Acetyl-L-leucine	$C_8H_{15}NO_3$	173.10451	0.858	2.17E+07	90.7
36	Choline	$C_5H_{13}NO$	103.09947	26.385	1.46E+07	95.7
37	Nicotinic Acid 1-Oxide	$C_6H_5NO_3$	139.02632	0.854	1.36E+07	98.8

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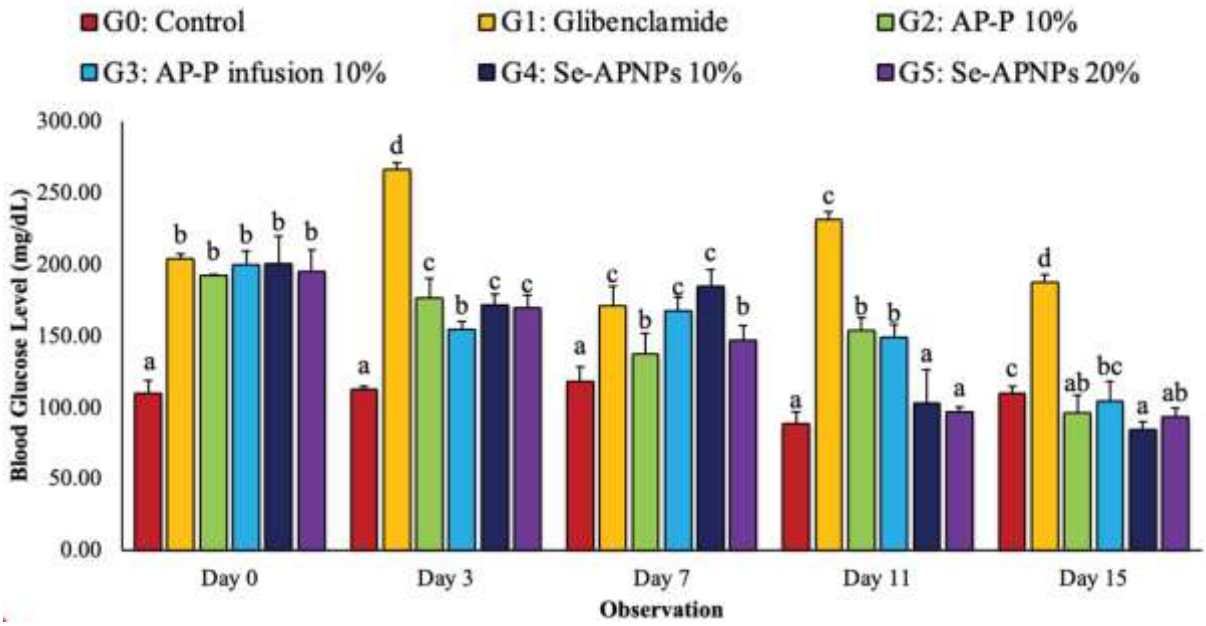

Figure 4: Average blood glucose levels of diabetic mice treated with *A. platensis* formulations and Se-APNPs over 15 days. Different letters (a–d) denote significant differences ($p < 0.05$, one-way ANOVA + Duncan test).

The 20% Se-APNPs exhibited the most substantial hypoglycemic effect, outperforming glibenclamide and other *A. platensis* forms. Their sustained glucose-lowering action highlights their promise as an alternative therapy for diabetes. Previous studies have shown that *A. platensis* reduced blood glucose by improving insulin sensitivity, which is consistent with the glucose reductions observed in Groups 2 and 3 of this study.[56,57] However, Se-APNPs (Groups 4 and 5) produced even greater hypoglycemic effects, in line with Karas, Alexeree[58], who noted enhanced antidiabetic bioactivity in selenium-enriched compounds. Moreover, Ebokaiwe, Okori[59] and Lin, Suzuki[60] demonstrated that selenium nanoparticles (SeNPs) improved glucose metabolism by reducing oxidative stress and promoting insulin secretion. These reports align with the present observation that Se-APNP significantly reduced glucose levels (84 mg/dL and 93 mg/dL), surpassing the effect of standard therapies. A dose-dependent response similar to this study was also reported by Wang, Wang[61], who observed stronger hypoglycemic effects at higher SeNP concentrations. Overall, this study suggests that Se-APNPs function as a more potent antidiabetic agent than either SeNPs or *A. platensis* alone, owing to synergistic interactions between selenium and *A. platensis* bioactive compounds. Compared with glibenclamide, Se-APNPs provided superior glucose control with a lower risk of hypoglycemia. Consistent with Sen, Balaraman[62], who emphasized the safety of natural antioxidant-based therapies, Se-APNPs represent a promising next-generation antidiabetic candidate warranting further investigation for long-term efficacy and mechanistic pathways.

Testis index changes in mice

Arthrospira platensis, Se-functionalized nanoparticles, and glibenclamide exerted differential testicular health ($p < 0.05$) in diabetic mice (Figure 5). The diabetic control group exhibited marked testicular atrophy, whereas glibenclamide (0.39 g) offered the most significant protection. Raw (0.22 g) and infused (0.23 g) *A. platensis* moderately restored testis weight. Meanwhile, Se-APNPs demonstrated a dose-dependent pattern: the 10% formulation (0.18 g) yielded mild benefits, whereas the 20% formulation (0.16 g) reduced testis weight, suggesting potential toxicity at higher concentrations. These findings were consistent with relative testis index values, further emphasizing the importance of optimizing selenium dosage

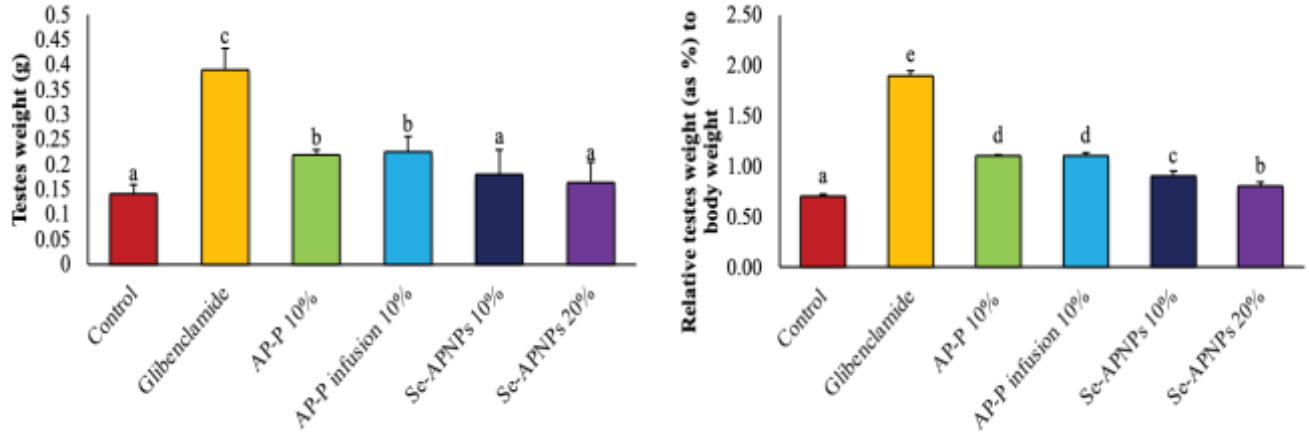

Figure 5: Effect of various *A. platensis* formulas and/or Glibenclamide on the absolute weight of testes (left) and the comparative weight of testes of control (right) and induced diabetic mice. $p < 0.05$ is considered significant.

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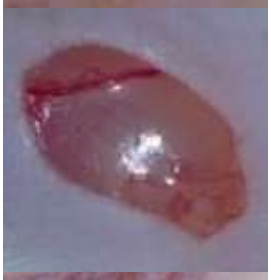
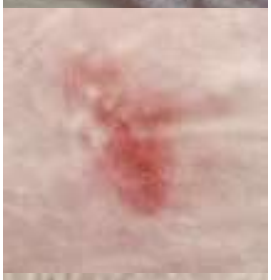
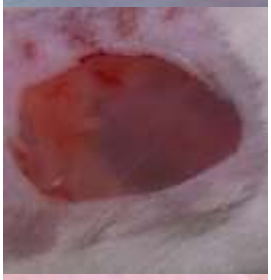
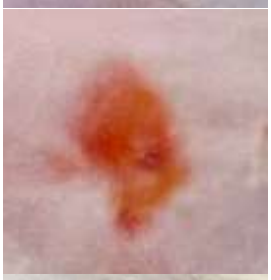
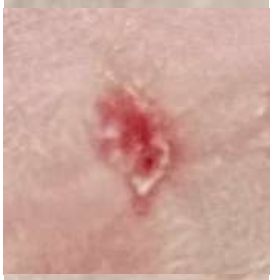
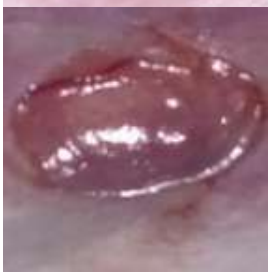
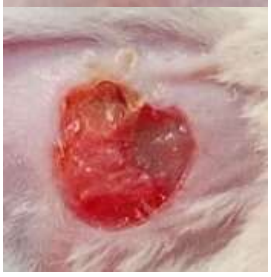
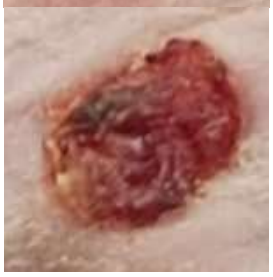
Previous studies have established that diabetes impairs testicular function primarily through oxidative stress and metabolic dysfunction.[63,64] The protective effects of *A. platensis* supplementation are attributed to its antioxidant compounds, which mitigate diabetes-induced reproductive damage.[65,66] Selenium nanoparticle–based therapies align with existing evidence demonstrating that selenium enhances testicular function at moderate doses but may provoke oxidative damage and toxicity when administered excessively.[67,68] Therefore, selenium dosing must be carefully calibrated to maximize therapeutic benefit and minimize reproductive toxicity in diabetic management.

Would healing

The dataset evaluates wound-healing progression over 1, 3, and 7 days across different treatment groups (Table 3). Glibenclamide (G1) and Infused AP-P 10% (G3) demonstrated the highest wound-healing efficacy, achieving healing rates of 96.60% and 94.52%, respectively, by Day 7 ($p < 0.05$; Figure 6).

Table 3: Effect of various treatments on wound healing progression over 7 days.

Treatment	Day 1	Day 3	Day 7
Group 0			
Group 1 (Glibenclamide)			
Group 2 (AP-P 10%)			
Group 3 (AP-P infusion 10%)			
Group 4 (Se-APNPs 10%)			

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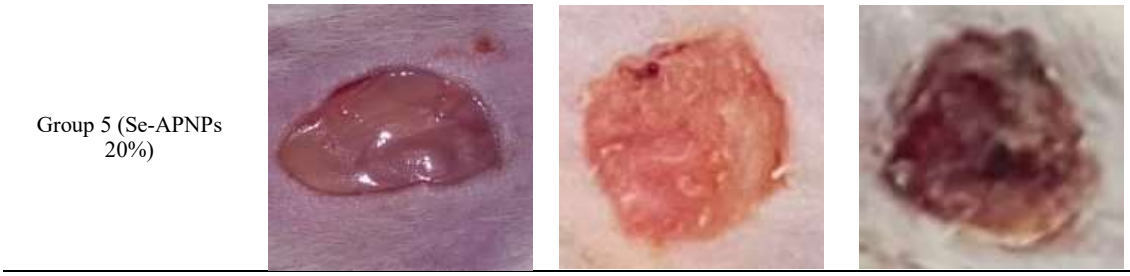

Values represent the percentage of wound contraction measured on Days 1, 3, and 7. Wound areas were recorded using standardized digital imaging, and the percentage of healing was calculated using formula (1). Data are presented as mean values from four replicates per treatment group.

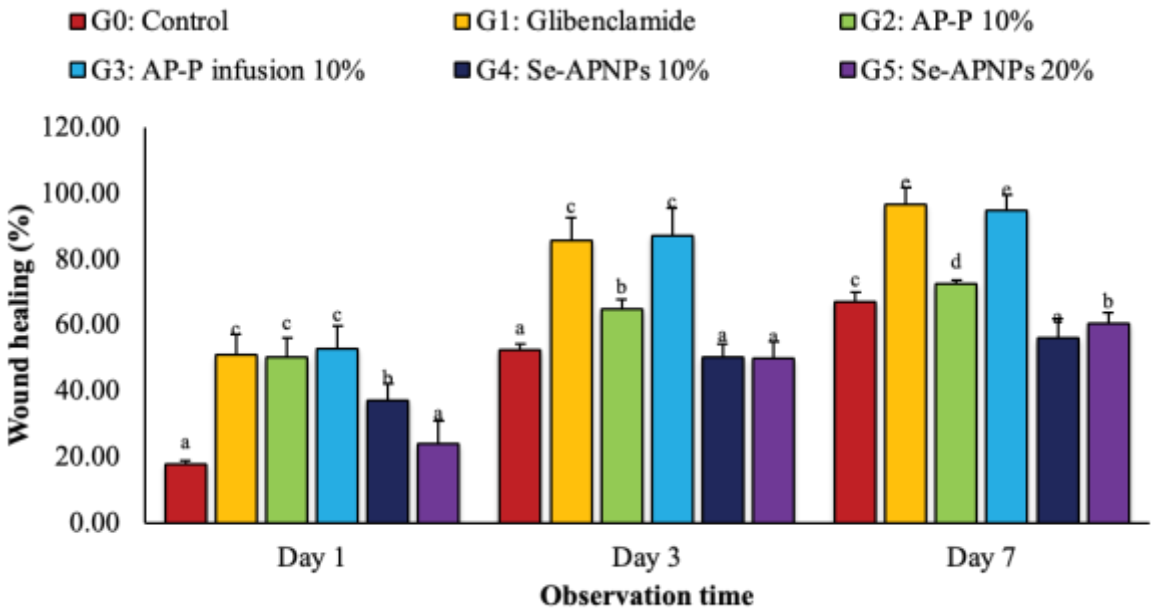

Figure 6: Wound healing percentage in diabetic mice treated with *A. platensis* formulations and Se-APNPs over a 15-day period. Different letters (a–d) denote significant differences ($p < 0.05$, one-way ANOVA + Duncan test).

These findings indicate that both treatments effectively accelerated tissue repair. Their efficacy might result from stimulation of collagen synthesis and granulation tissue formation, driven by proliferative and anti-inflammatory mechanisms.[69,70] The bioactive constituents of infused AP-P, such as neophytadiene, phytol, and TSC (Table 1), further contribute to healing by enhancing fibroblast proliferation, antioxidant defense, and inflammatory modulation.[71,72,73] In contrast, AP-P 10% (G2) showed moderate healing throughout the observation period, whereas the untreated control group (G0) consistently had a lower closure rate, confirming the need for therapeutic intervention. This result proved that the extraction process during infusion likely increases the availability of active compounds, explaining why infused AP-P (G3) outperformed raw AP-P (G2). Previous studies support this assumption, as red algae extracts have been shown to enhance epithelial regeneration and collagen deposition in both *in vitro* and *in vivo* wound models.[74,75,76] Surprisingly, the Se-APNPs (G4 and G5) showed the slowest and least complete healing responses. The wound-healing process appeared to be dose-dependent, indicating that an optimal selenium level is required to achieve compatibility and therapeutic efficacy. Although Day 7 healing rates were lower in G4 and G5, previous literature shows that selenium nanoparticles can enhance antioxidant defense, keratinocyte migration, and neovascularization when appropriately formulated.[77,78,79] Without optimization, however, their regenerative capacity might not be fully realized. Factors such as nanoparticle concentration, particle size, and delivery method likely need refinement to maximize the therapeutic potential of Se-APNPs in wound-healing applications. Overall, these findings highlight that AP-P infusion provides the most balanced combination of efficacy and safety, while Se-APNPs require formulation optimization to fully harness their wound-repair potential.

Growth rate analysis

The growth rate data revealed apparent differences ($p < 0.05$) in body weight progression among treatment groups over the 15-day period (Figure 7). The negative control group (Group 0) exhibited minimal growth change, increasing only from 20.00 g to 21.33 g, confirming that untreated diabetic mice were unable to achieve normal growth. The glibenclamide group (G1) displayed a rapid increase in body weight, peaking at 25.00 g on Day 7, but subsequently declined to 23.00 g, suggesting temporary metabolic recovery followed by instability. Among the *A. platensis*-treated groups, Group 2 (AP-P 10%) showed a steady increase in body weight, reaching 26.00 g, indicating sustained metabolic improvement. In contrast, infused AP-P 10% (G3) triggered a sharp early rise to 27.50 g on Day 3, followed by a decline to 22.50 g, implying a strong short-term effect but limited long-term metabolic stability or reduced efficiency once antioxidant compounds were metabolized. The most favorable growth performance was recorded in the Se-APNPs 10% (G4), which demonstrated continuous weight gain from 20.50 g to 30.00 g. This pattern reflects enhanced metabolic activity, nutrient utilization, and overall physiological recovery. Conversely, Se-APNPs 20% (G5) produced negligible growth (20.50 g to 21.00 g), indicating that excessive selenium exposure may impair metabolism or suppress growth.

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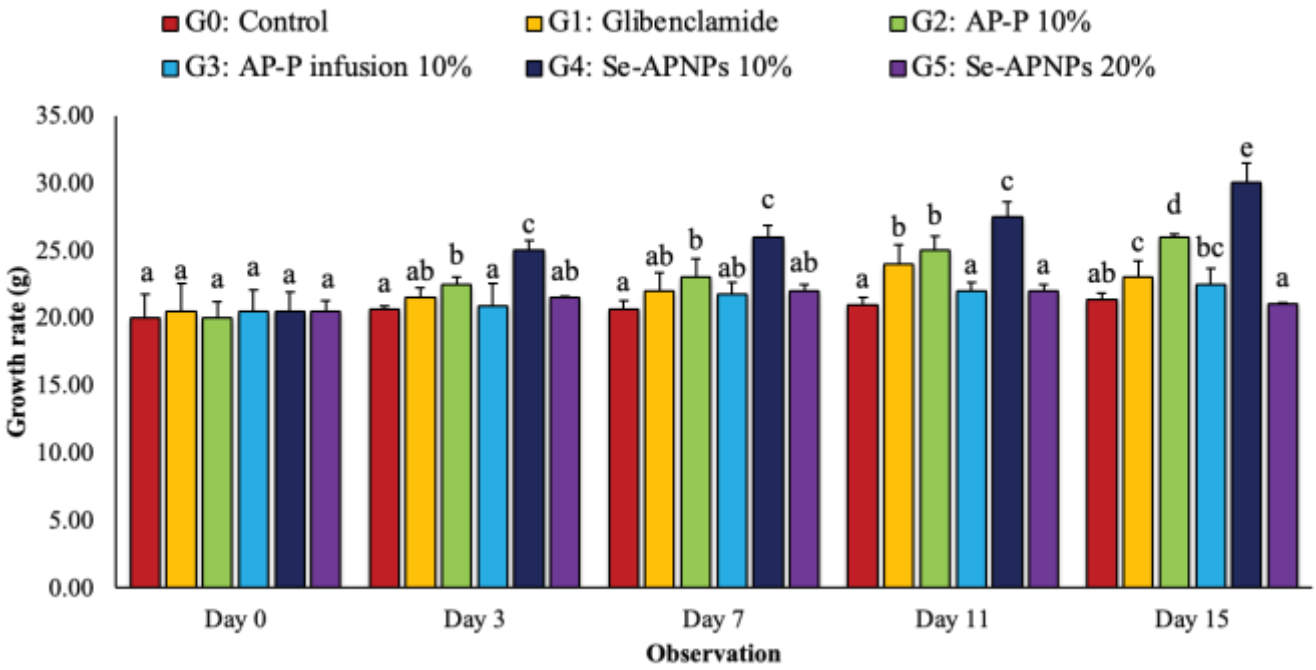

Figure 7: Body weight changes of diabetic mice treated with *A. platensis* formulations and Se-APNPs over 15 days. Different letters (a–d) denote significant differences ($p < 0.05$, one-way ANOVA + Duncan test).

Selenium nanoparticles (SeNPs) have been shown to improve mitochondrial efficiency and glucose metabolism,[43,83] although dose-dependent responses have been reported, where high selenium concentrations induce oxidative stress rather than provide additional benefit.[84] The temporary weight gain seen in the glibenclamide group (G1) aligns with earlier evidence describing transient glibenclamide-induced weight gain resulting from altered insulin dynamics and compensatory metabolism.[85,86] Overall, Group 4 (Se-APNPs 10%) demonstrated the most effective growth performance, likely due to optimal selenium bioavailability and metabolic support. The reduced performance of Group 5 (Se-APNPs 20%) highlights a threshold effect in selenium dosage, while raw and infused *A. platensis* (G2 and G3) provided beneficial but inconsistent outcomes. These results reinforce the potential of selenium-functionalized nanoparticle supplementation as a sustainable alternative for improving metabolic health in diabetes.

Conclusion

Diabetic mice displayed complementary yet distinct therapeutic responses to raw *A. platensis* biomass and selenium-functionalized nanoparticles (Se-APNPs). The 10% Se-APNP formulation exhibited the most pronounced antihyperglycemic response, reducing fasting blood glucose to 84 mg/dL and outperforming the standard antidiabetic drug glibenclamide. Raw AP-P or AP-P infusion showed a wound-healing efficiency of 94.5%, comparable to that of glibenclamide (96.6%). The 10% Se-APNP group also performed, showing improved growth. However, at higher concentrations (20%), the efficacy was reduced, and potential testicular toxicity occurred. Overall, *A. platensis* can be formulated for diabetes management, where SeAPNPs regulate the glycemic and metabolic activities, while the infused AP-P serves as an alternative approach in wound healing. Optimal doses should be determined to ensure therapeutic safety and efficacy. Further studies should assess the chronic toxicity of Se-APNPs and clarify their molecular mechanisms. Combined pharmacokinetic, histopathological, and clinical analyses will enhance understanding and support their translation into sustainable nanobiotechnological therapies for diabetes and metabolic diseases.

Conflict of interest

The authors declare no conflicts of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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