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Aerobic training and vitamin D supplementation effects on diabetes-related parameters in a rat model of type 2 diabetes

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Abstract

Background Diabetes mellitus (DM) is characterized by disturbances in glucose, lipid, and energy metabolism, including dyslipidemia and dysregulation of metabolic peptides like spexin; however, the effects of combined interventions, such as aerobic training and nutritional intervention, on these parameters are not fully elucidated. The objective of this study was to investigate the influences of aerobic training (AT) and vitamin D (Vit D) supplementation on the lipid profile and spexin levels in a model of rats with type 2 diabetes (T2D).

Methods A total of 56 male Wistar rats were divided into two groups: SHAM (non-diabetic control; $n=8$) and diabetic ($n=48$). The diabetic rats were further divided into six groups: AT with high doses of vitamin D (D + AT + HD; 10,000 IU/kg/week), AT with moderate doses of vitamin D (D + AT + MD; 5,000 IU/kg/week), high doses of vitamin D (D + HD; 10,000 IU/kg/week), moderate doses of vitamin D (D + MD; 5,000 IU/kg/week), AT receiving vehicle (sesame oil; D + AT + oil), and control (oil-receiving; D + C). To induce type 2 diabetes, rats were first fed a high-fat diet (HFD) for 2 weeks to induce obesity, followed by an intraperitoneal injection of 110 mg/kg nicotinamide and 55 mg/kg streptozotocin (STZ) dissolved in 0.1 M citrate buffer (pH 4.5). Blood samples were collected 48 h after the last training session under anesthesia for measuring spexin levels, and lipid profile parameters. Statistical analyses were performed using the paired t-test, one-way analysis of variance (ANOVA), and Tukey post hoc test.

Results Compared to the SHAM rats, there were significant increases in body weight, BMI, FI, and WC in the diabetic rats ($p<0.001$). Also, there was a significant decrease in body weight, BMI, FI, and WC of the diabetic groups who received interventions, especially in D + AT + HD (body weight: -11.07%, BMI: -10.25%, FI: -19.16%, WC: -16.54%). The lipid profiles were significantly improved, with the lowest total cholesterol (TC), triglycerides (TG), and low-density lipoprotein (LDL) levels and the highest high-density lipoprotein (HDL) levels being found in the D + AT + HD group compared with the D + C group ($p<0.05$). Moreover, the D + AT + HD group had elevated spexin levels compared with the other diabetic groups, which may play a metabolic role.

Conclusion AT and Vit D supplementation effectively normalized serum lipids and increased spexin levels in T2D rats. These findings suggest that AT and Vit D supplementation may serve as potential therapeutic strategies for managing T2D and its associated complications. Further studies are needed to elucidate the underlying mechanisms and to evaluate the long-term effects of these interventions in humans.

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Keywords Metabolic disorder, Exercise, Vitamin D, HOMA-IR

Introduction

Type 2 Diabetes (T2D) is a common and serious health condition with a global prevalence resulting in a high burden of global morbidity and mortality. As the epidemic continues to grow, it is crucial to find and mitigate effective treatments that will attain optimal glycemic and lipid control in patients suffering from this metabolic disease [1]. T2D poses a tremendous economic burden, and a substantial portion of healthcare expenditure is devoted to therapeutic and rehabilitative costs related to diabetes and its complications [2]. The role of specific non-pharmacological interventions on T2D management and its metabolic dysfunctions has been studied in recent years, particularly aerobic training (AT) [3] and vitamin D (Vit D) supplementation [4, 5]. AT, on the other hand, has been characterized as a beneficial approach for the management of T2D as it improves insulin sensitivity and lipid metabolism and induces weight loss [4, 6]. Similarly, vitamin D rich in fat originally recognized for its role in the mineralization of certain calcium phosphates in bones shows extra-skeletal effects, such as modulation of immune function, inflammation, insulin secretion, and cardiovascular protective properties [6, 7]. Vitamin D deficiency has been associated with chronic diseases, including diabetes metabolic syndrome, and cardiovascular diseases in observational studies [8]. Several clinical trials have investigated the potential advantages of Vit D supplementation in individuals with diabetes, showing evidence for an improvement in lipid profiles and inflammatory markers [9, 10]. However, studies investigating the effects of Vit D supplementation on metabolic-specific peptides such as spexin in diabetic patients are scarce [11].

A substantial problem in T2D patients is cardiovascular events, underlying dyslipidemia, and insulin resistance, and then high morbidity and mortality [12, 13]. Dyslipidemia (abnormal lipid levels) is known as a cardiovascular risk factor in T2D that needs to be managed carefully [14]. Despite consistent reports from observational studies about the beneficial effect of high Vit D on lipid profile, the results appear mixed when it comes to intervention studies, suggesting a need for further investigation [15, 16]. Recent studies have implicated the neuropeptide spexin in the regulation of both glucose and lipid metabolism [17, 18]. Altered levels of spexin in humans with T2D have been demonstrated in studies, suggesting the involvement of the peptide in T2D-related pathophysiology [19, 20]. Nevertheless, scarce literature is available regarding the effect of AT and Vit D on spexin levels in T2D. Most previous studies have evaluated the role of AT and Vit D on metabolic parameters such as insulin resistance and lipid profiles without concurrent evaluation of their combined influence on spexin levels. As a case in point, Cheshmazar et al. (2020) observed amelioration of lipid profiles and inflammatory markers but no impact on spexin levels as a result of Vit D supplementation in obese and overweight subjects [21]. Similarly, Khaledi et al. (2023) and Hoseini et al. (2023) showed that combined treatment with AT and Vit D improved glycemic control and was able to upregulate metabolic gene expression in T2D rats, but spexin was not the subject of these studies [6, 22]. Golpasandi et al. (2023) also emphasized the drawbacks of the combination of AT and Vit D in modulating the expression of autophagy signaling proteins in diabetic rats, but no role of spexin was discussed [23].

Due to the aforementioned limitations in the current literature, the current study was designed to evaluate the effects of AT and Vit D supplementation on spexin levels, and lipid profiles in T2D rats. AT and Vit D supplementation is hypothesized to enhance glycemic control, positively alter the lipid profile, and upregulate spexin levels, potentially contributing to T2D progression. This study is expected to explore the relationships between AT, Vit D, spexin levels, and metabolic outcomes, providing a foundation for further research to identify new therapeutic targets in the treatment of T2D.

Methods

Study design and participants

Male Wistar rats aged 10–12 weeks, with an initial weight range of 180–200 g, were obtained from the Laboratory Animal Care Center at the Medical Sciences University of Kermanshah. A total of 56 rats were used in this experimental study. After a 2-week adaptation period, the rats in the diabetic groups were fed a high-fat diet (HFD) for 2 weeks to induce obesity. The initial weights (180–200 g) and final weights after the HFD feeding period were recorded to confirm the development of obesity. Following this, type 2 diabetes was induced using nicotinamide and streptozotocin (STZ). The weights of the animals were also measured before and after the 8-week intervention period to assess the effects of the treatments. All rats were housed in clear polycarbonate cages in a controlled environment (12:12 h light/dark cycle; temperature 21 ± 2 °C; humidity 45–55%). They had free access to a standard diet and water [19, 20]. All the procedures were performed following the guidelines approved by the Ethics Committee of Razi University of Kermanshah (IR. RAZI. REC. 1401. 065) and in compliance with the ethical standards for laboratory animal studies. The rats were randomly assigned to two major groups: a

non-diabetic control (SHAM; $n = 8$) and a diabetic group (D; $n = 48$). The diabetic group was further divided into six subgroups: D + AT + HD: diabetic rats subjected to a high dose of Vitamin D (10,000 IU/week) and aerobic training (AT). D + AT + MD: Diabetic rats with a moderate dose of Vitamin D (5,000 IU/week) and aerobic training (AT). D + HD: Diabetic rats were administered a high dose of vitamin D (10,000 IU/week) and AT was not performed. D + MD: Diabetic rats treated with moderate-dose Vitamin D (5,000 IU/week) but without AT. D + AT + oil: Diabetic rats treated with vehicle (sesame oil) and aerobic training (AT). D + C: Diabetic control group treated with vehicle (sesame oil) in the absence of AT. The diabetic group consisted of 48 rats, estimated based on previous studies with a moderate effect size of 0.5, powerless of 0.8, a significance level of 0.05, an estimated standard deviation of 1.5, and a study design with seven groups and equal allocation ratios.

Diet and induction of diabetes

After a 2-week adaptation period to the new environment, the rats in the diabetic groups were fed a high-fat diet (HFD). The HFD contained 60% standard diet powder, 10% yeast powder, 5% sheep fat, 1% sodium chloride, 0.5% DL-methionine, and a balanced amount of vitamins and minerals according to the required nutritional standards (the composition was provided by Beh-Parvar Company). For 2 weeks, the animals were fed a high-fat diet (HFD) to induce obesity. After that, Diabetes was induced in the rats by intraperitoneal injection with 110 mg/kg nicotinamide and 55 mg/kg STZ in a 0.1 M citrate buffer (pH 4.5). Diabetes was diagnosed by measuring blood glucose levels (mg/dL) in the tail vein using a glucometer after 2 weeks [24, 25]. Rats with fasting blood glucose levels ≥ 250 mg/dL, measured after a 12-hour fasting period, were classified as diabetic and included in the study [26].

Vitamin D supplementation

In the study, Vitamin D supplementation was administered via subcutaneous injection once per week. The D + AT + HD and D + HD groups received a high dose of 10,000 IU/kg of Vitamin D supplement per week, while the D + AT + MD and D + MD groups received a moderate dose of 5,000 IU/kg of Vitamin D supplement per week. The selection of these doses was based on previous studies demonstrating their efficacy in improving metabolic parameters in rodent models of diabetes without inducing toxicity [27]. Specifically, high-dose Vitamin D (10,000 IU/kg/week) has been shown to enhance insulin sensitivity and reduce inflammation in diabetic rats, whereas moderate-dose Vitamin D (5,000 IU/kg/week) is effective in improving glycemic control and lipid profiles [22, 24]. Additionally, the rats obtained approximately 100 IU of Vitamin D from their standard diet, which aligns with the typical dietary intake levels for rodents. To ensure stability and proper absorption, vitamin D was administered via weekly subcutaneous injections mixed with sesame oil as the vehicle [28].

Aerobic training

The rats took part in aerobic training (AT) sessions for eight weeks, conducted five days a week. Each session included a five-minute warm-up and cool-down at a moderate speed, ranging from 5 to 10 m/min. The training started with a 15-minute session at a speed of 10 m/min and gradually progressed to a 30-minute session at a speed of 25 m/min. All AT sessions were performed on a treadmill set at a 0-degree incline. The running speed on the treadmill determined the intensity of the AT, with an average aerobic activity considered to be in the range of 20 to 25 m/min. This intensity level was estimated to be approximately 70–75% of the maximum oxygen consumption (Table 1) [29, 30].

Measurements

Body weight, Body Mass Index (BMI), Food Intake (FI), and Waist Circumference (WC) measurements were obtained weekly during the time frame of 8–10 AM. Body weight was measured using a Sartorius scale, body length was assessed using a tape measure from the nose to the anus, and BMI was computed accordingly. FI was determined by subtracting the weight of the uneaten food from the total amount initially provided [27].

Blood sampling and analysis

Blood samples were collected by anesthetizing the rats 48 h after the last training session with intraperitoneal injections of xylazine and ketamine. After achieving total anesthesia, the abdomen was dissected to allow access to the vena cava, and blood sampling. Afterward, the blood sample was centrifuged at 4,000 rpm for 10 min,

Table 1 Protocol progression across different weeks

Week	Acquaintance	1st	2nd	3rd	4th	5th	6th	7th	8th
Exercise duration (min)	5	15	15	20	20	25	25	30	30
Rolling speed (m/min)	10	10	10	15	15	20	20	25	25

and the serum was separated and used for subsequent analyses. Serum total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) concentrations were assessed through enzymatic colorimetric methods using commercial kits (Pars Azmoon, Tehran, Iran) on an automated analyzer (Abbott, Model Alcyon 300, USA). Serum spexin levels were also measured using a rat-specific ELISA kit (SPX; MyBioSource, USA) with a detection range of 15.63–1000 pg/mL and sensitivity of 5.7 pg/Ml (Table 2).

Statistical analysis

The data are reported as mean ± standard deviation (SD). The normality of the data distribution was evaluated using the Shapiro-Wilk test. Paired t-tests were utilized to analyze paired data for body weight, BMI, and FI. One-way analysis of variance (ANOVA) was conducted, followed by a Tukey test for comparing between groups. A significance level of $P < 0.05$ was considered statistically significant. The statistical analysis was carried out using SPSS version 26.

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Results

Body composition

The results revealed significant differences in body weight, BMI, food intake (FI), and waist circumference (WC) between the diabetic rats ($n = 48$) and the SHAM rats ($n = 8$) at baseline and after the 8-week intervention ($p < 0.001$). The SHAM group showed a 1.78% increase in body weight, a 1.66% increase in BMI, a 6.36% increase in FI, and a 6.51% increase in WC over the study period. In contrast, the D + AT + HD, D + AT + MD, D + AT + oil, D + HD, and D + MD groups exhibited significant reductions in these parameters compared to baseline ($p < 0.001$). Specifically, the D + AT + HD group demonstrated the most substantial reductions: an 11.07% decrease in body weight, a 10.25% decrease in BMI, a 19.16% decrease in FI, and a 16.54% decrease in WC. These findings highlight the effectiveness of the interventions in improving body composition in diabetic rats These findings highlight the effectiveness of the interventions in improving body composition in diabetic rats (Fig. 1).

Lipid profile

Significant differences were observed in the total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) levels between the diabetic and SHAM groups (Fig. 2). Among the diabetic groups, the D + AT + HD group exhibited the lowest TC (ES = 1.78, 95% CI: [-1.23, 3.34]), TG (ES = 1.65, 95% CI: [-2.23, 1.79]), and LDL levels (ES = 1.72, 95% CI: [-3.39, 2.57]), while the D + C group had the highest levels. HDL levels were significantly higher in the D + AT + HD group (ES = 1.85, 95% CI: [3.67, -2.45]) compared with the D + C group. The D + AT + HD, D + AT + MD, D + HD, D + MD, and D + AT + oil groups showed significantly lower TC, TG, and LDL levels and higher HDL levels compared with the D + C group ($p < 0.05$ for all). These findings highlight the beneficial effects of the interventions on lipid profiles in diabetic rats.

Spexin levels

Significant variations in spexin levels were observed among the diabetic groups (Fig. 3). The D + AT + HD group exhibited the highest spexin levels (ES = 1.92, 95% CI: [1.76, -2.27]), while the D + C group had the lowest. The D + AT + HD, D + AT + MD, D + HD, D + MD, and D + AT + oil groups all showed significantly higher spexin levels compared with the D + C group ($p < 0.05$). No significant differences were observed between the D + AT + MD group and the D + AT + oil or SHAM groups. These results emphasize the role of the interventions in modulating spexin levels in diabetic rats.

Discussion

The purpose of this study was to investigate the effect of aerobic training (AT) and different doses of vitamin D (Vit D) supplements on body composition, and lipid lipid-profiled spexin levels in rats with streptozotocin (STZ)-induced diabetes. The present findings reveal that the AT program with 8-week high or moderate doses of Vit D supplementation improved body composition, lipidemia parameters, and spexin concentrations with the most pronounced alterations D + AT + HD group. Conclusion: These findings indicate a possible synergistic effect between AT and Vit D, reinforcing their Niche therapeutic potential in the appropriate management of diabetes-associated metabolic dysregulations.

Table 2 Comparison of mean ± sd of body weight, FI, and BMI before and after intervention

Variables	D + AT + HD	D + AT + MD	D + HD	D + MD	D + AT + oil	D + C	SHAM
Body Weight (g)							
Before	316.87 ± 1.72	316.87 ± 1.72	308.75 ± 2.60	306 ± 2.50	313.87 ± 1.88	313.87 ± 1.88	224.12 ± 4.96
After	281.62 ± 2.06	286.62 ± 2.38	293.37 ± 2.55	295.62 ± 2.26	293.50 ± 2.20	293.50 ± 2.20	228.87 ± 5.27
Glucose (mmol/L)	272.12 ± 8.23	287.06 ± 16.45	285.23 ± 10.14	278.14 ± 8.10	265.25 ± 13.20	280.09 ± 16.11	118.06 ± 3.23

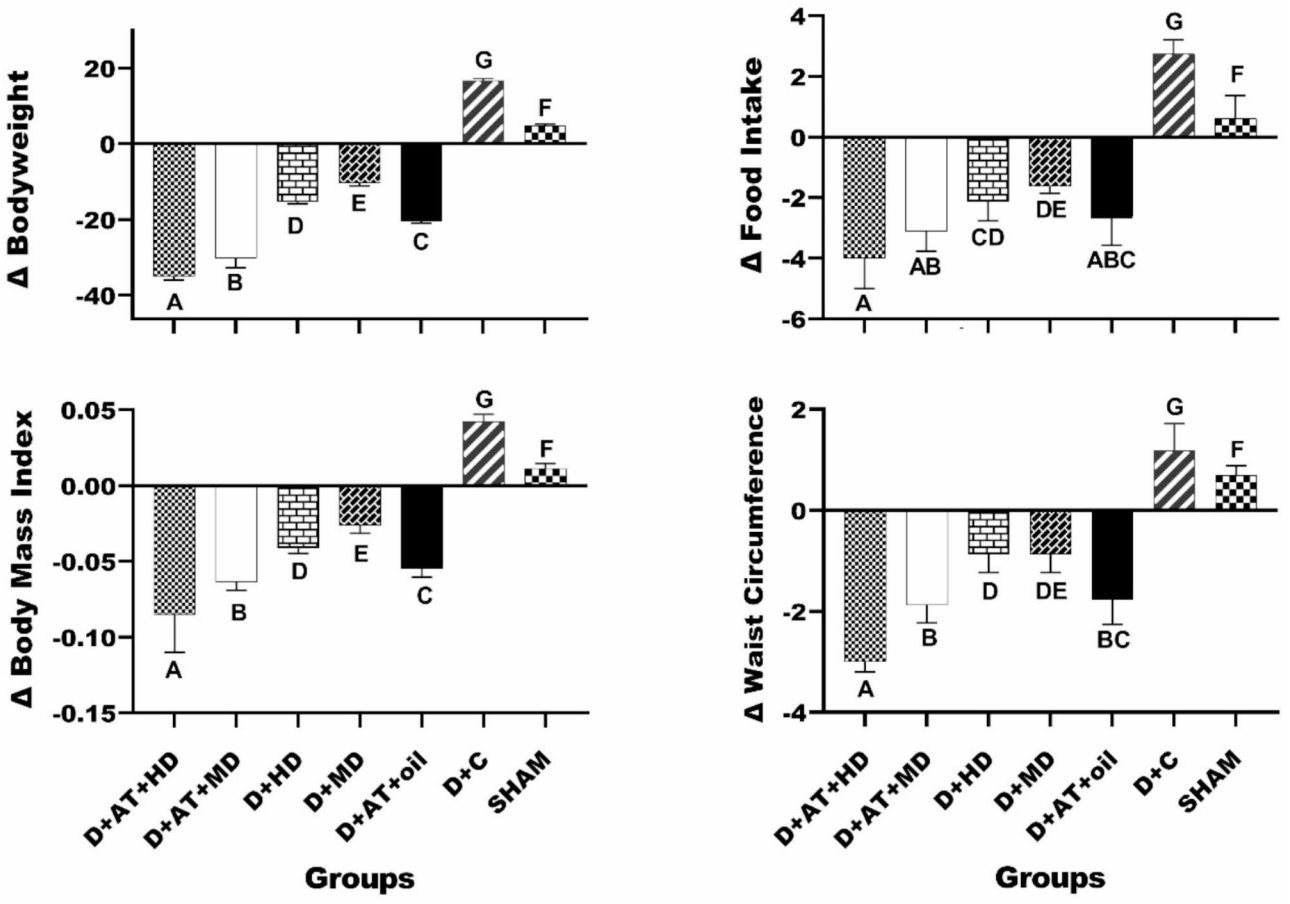

Fig. 1 Comparison changes of mean ± SD of body weight, BMI, FI and WC between groups
BMI: Body Mass Index; **FI**: Food Intake; **WC**: Waist Circumference; The mean values followed by different letters (A, B, C, D, E, F, and G) mean significantly different at the 0.05 level ($p<0.05$). The values followed by the same letter are not significantly different. Dissimilar letters represent a significant difference between the groups

Food intake and body composition

In comparison to the sedentary control group, AT and Vit D supplementation significantly reduced body weight, BMI, and food intake. These results are consistent with past studies demonstrating that AT and Vit D have independent effects on body weight and appetite regulation. For instance, Hoseini et al. (2017) found that AT decreased body weight and increased food intake in type-2 diabetic mice [27], while Khaledi et al. (2023) showed that Vit D supplementation showed similar effects on obese diabetic rats [6]. In detail, AT activates a pathway, AMP-activated protein kinase (AMPK), that increases fatty acid oxidation and energy expenditure, which is consistent with the observed reduction in body weight and body mass index (BMI) [31]. Moreover, AT might increase the secretion of satiety hormones like leptin and peptide YY, based on the fact that these hormones interfere with food intake [32]. Moreover, Vit D via its receptor (VDR) affects adipogenesis and appetite control, thereby providing further evidence of its contribution to body weight regulation [33]. Collectively, these data indicate that AT and Vit D exert a concerted effect on pathways that improve body composition and appetite control during diabetic conditions.

Lipid profile

Each of the treatment groups of AT and Vit D demonstrated statistically significant decreases in TC, TG, and LDL, but significant increases in HDL. Notably, the greatest improvements were seen in the D + AT + HD group, highlighting the synergy of adding AT to high-dose Vit D; this finding is in line with previous works such as Wang et al. (2017) [34], who found comparable hypolipidemic outcomes from AT in patients with dyslipidemia, Also, Vit D-induced changes in their lipid profile in ovariectomized rats were observed by Babaei et al. (2015) [33]. AT improves lipid metabolism by multiple mechanisms, including the activation of hormone-sensitive lipase (HSL) and adipose triglyceride lipase (ATGL), both of which stimulate lipolysis and the hydrolysis of stored triglycerides to free fatty acids (FFAs) [35]. These FFAs are then shuttled to the liver for β-oxidation, leading

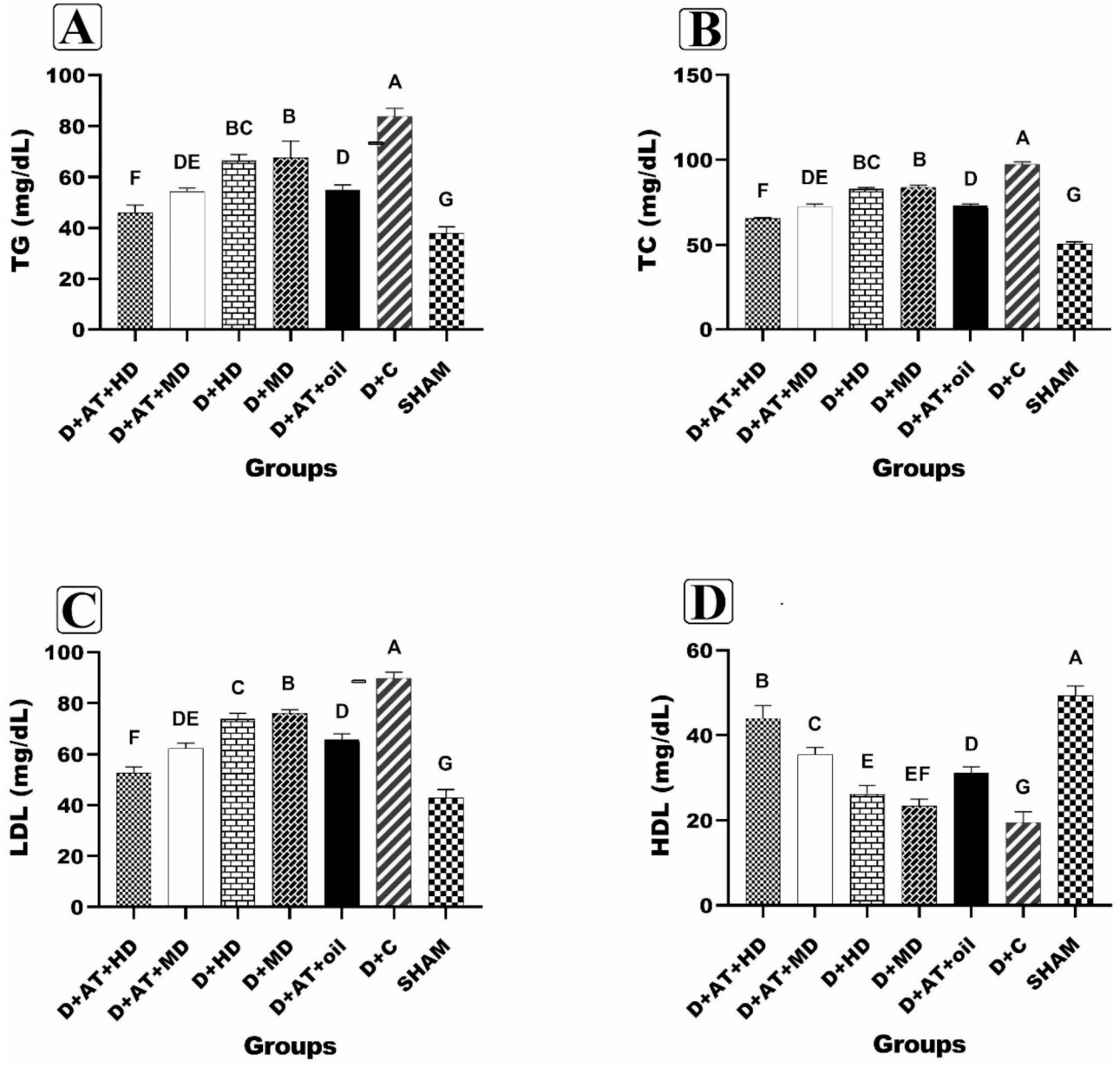

Fig. 2 Comparison between mean ± SD of lipid profiles between groups

D + AT + HD: Diabetic + Aerobic Training + High Dose of Vitamin D; **D + AT + MD**: Diabetic + Aerobic Training + Moderate Dose of Vitamin D; **HD**: Diabetic + High Dose of Vitamin D; **MD**: Diabetic + Moderate Dose of Vitamin D; **D + AT + oil**: Diabetic + Aerobic Training + Sesame Oil; **D + C**: Diabetic + Sesame Oil; **SHAM**: Non-Diabetic Control

Values were calculated using a One-Way analysis of variance followed by post hoc Tukey's test. The mean values followed by different letters (A, B, C, D, E, F, and G) mean significantly different at the 0.05 level ($p < 0.05$). The values followed by the same letter are not significantly different. Dissimilar letters represent a significant difference between the groups

to decreased hepatic TG production and elevation of HDL. AT also upregulates peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α), a central regulator of mitochondrial biogenesis and fatty acid oxidation [27, 35]. Clarifying the interrelationship of cholesterol metabolism and lipid metabolism in a general pattern, while elements of vitamin D–mediated stimuli via VDR include lipid metabolism by regulating the ATP-binding cassette transporter A1 (ABCA1), thereby affecting cholesterol excess and adjusting HDL levels via the ABCA1 pathway [36, 37]. Vit D downregulates sterol regulatory element-binding protein-1c (SREBP-1c), subsequently attenuating TG synthesis, and it enhances fatty acid oxidation through mechanisms consistent with PGC-1α upregulation [38]. These inter-relationships

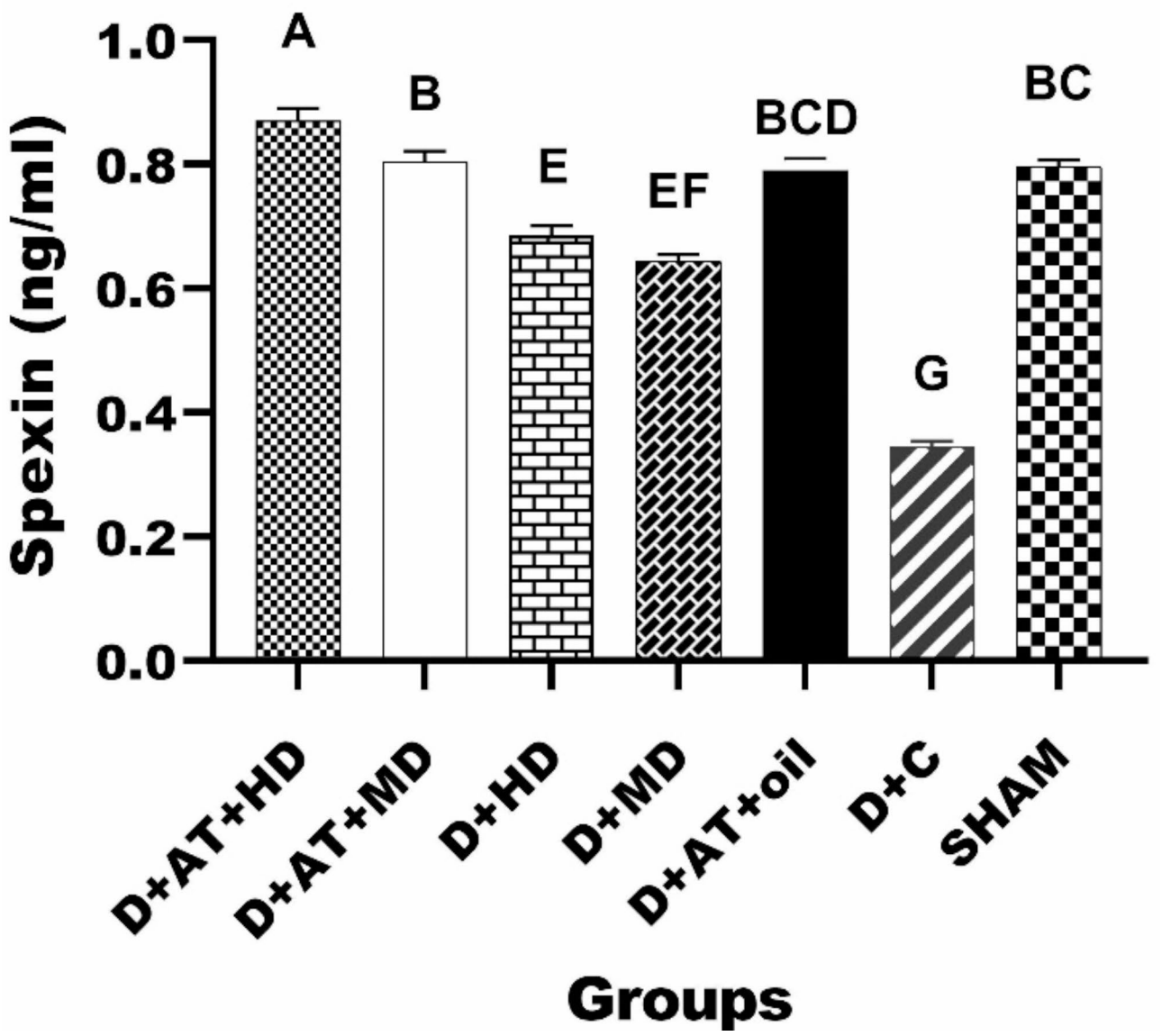

Fig. 3 Comparison between mean ± SD of spexin between groups

D + AT + HD: Diabetic + Aerobic Training + High Dose of Vitamin D; **D + AT + MD**: Diabetic + Aerobic Training + Moderate Dose of Vitamin D; **HD**: Diabetic + High Dose of Vitamin D; **MD**: Diabetic + Moderate Dose of Vitamin D; **D + AT + oil**: Diabetic + Aerobic Training + Sesame Oil; **D + C**: Diabetic + Sesame Oil; **SHAM**: Non-Diabetic Control

Values were calculated using a One-Way analysis of variance followed by post hoc Tukey's test. The mean values followed by different letters (A, B, C, D, E, F, and G) mean significantly different at the 0.05 level ($p < 0.05$). The values followed by the same letter are not significantly different. Dissimilar letters represent a significant difference between the groups

emphasize the synergistic effects of AT and Vit D in improving lipid components.

Spexin levels

A key and novel finding of this study was the significant elevation in spexin levels following both AT and Vit D supplementation, with the highest levels observed in the D + AT + HD group (AT combined with high-dose Vit D). Spexin, a peptide intricately involved in glucose homeostasis and metabolic regulation, appears to be modulated by these interventions through distinct yet interrelated pathways. The upregulation of spexin expression induced by AT may enhance glucose metabolism via key signaling pathways, including AMP-activated protein kinase (AMPK) and phosphoinositide 3-kinase/protein kinase B (PI3K/Akt), which are known to regulate energy balance and insulin sensitivity [35, 39]. Similarly, Vit D may promote spexin expression through its interaction with the vitamin D receptor (VDR), further supporting its role in metabolic regulation [40]. These findings are consistent with previous studies, such as Ceylan et al. (2020), which reported increased spexin levels following AT in healthy

individuals [41], and Sanli et al. (2021), which demonstrated Vit D-induced upregulation of spexin in diabetic mice [40].

The observed increase in spexin levels correlated with significant improvements in body composition (e.g., reductions in body weight, BMI, and waist circumference) and favorable changes in lipid profiles, including decreased TC, TG, and LDL, as well as increased HDL. These results suggest that spexin acts as a central mediator of the metabolic benefits induced by AT and Vit D, linking these interventions to improved glycemic control and lipid metabolism. These findings align with previous studies and suggest that spexin may play a central role in mediating the metabolic benefits of AT and Vit D supplementation. By exploring the relationships between AT, Vit D, and spexin upregulation, this study contributes to the current understanding of their therapeutic potential in type 2 diabetes (T2D) and identifies spexin as a promising target for future diabetes therapies. The synergistic effects of AT and high-dose Vit D on spexin levels highlight their combined utility in addressing metabolic dysregulation in T2D. However, further research is needed to fully elucidate the underlying mechanisms through which AT and Vit D modulate spexin expression and its downstream metabolic effects.

Novelty and clinical implications

This study adds to the growing evidence supporting the combined use of AT and Vit D as a competitive therapy for diabetes management. Although previous AT and Vit D studies have been conducted, we showed the potential for synergy between AT and Vit D in enhancing metabolic parameters. Furthermore, the finding of spexin as a central mediator of these effects is a new addition to the literature. However, our findings differed somewhat from those of previous studies on the scale of spexin upregulation. Such discrepancies can be attributed to differences in the experimental design, species, or duration of the intervention, and highlight the necessity for additional studies to elucidate these relationships.

Limitations

There are limitations to this study. To begin with, the utilization of STZ-induced diabetic rats as an animal model may restrict the direct translation of the findings to humans. Second, the sample size is small, which may affect the statistical power and gen realizability. Third, the 8-week time frame of this intervention is appropriate to evaluate the short-term consequences but does not consider the long-term consequences of supplementation of AT and Vit D. To overcome such limitations, future studies should include larger sample sizes, extended intervention periods, and human clinical trials to confirm these findings.

Conclusion

These findings show that AT, vitamin D supplementation, and their combination resulted in a remarkable increase in spexin levels and improved lipid profiles in a type 2 diabetic rat model. The combined intervention group (AT + vitamin D) showed the most pronounced effects, indicating a synergistic interaction between the two modalities. These results suggest that AT and vitamin D may have complementary modes of action in regulating metabolic health, but more studies are needed to more clearly define the underlying molecular pathways. Taken together, these data add to the increasing evidence that AT and vitamin D are promising therapeutic strategies for ameliorating the complications of type 2 diabetes.

Abbreviations

FI	Food intake
Vit D	Vitamin D
Akt	Protein kinase B
AT	Aerobic training
BMI	Body mass index
WC	Waist circumference
PI3K	Phosphatidylinositol 3-kinase
IRS-2	Insulin receptor substrate-2
AMPK	AMP-activated protein kinase

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13102-025-01125-2.

Supplementary Material 1

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Author contributions

Z.H. and N.B. were responsible for conceptualizing and designing the study, curating the data, managing the project, and conducting formal analysis. They also wrote the initial draft of the manuscript. R.H. contributed to the investigation and methodology, while N.B. provided resources for the study. All authors participated in the writing, reading, and approval of the final manuscript.

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Data availability

The datasets generated and analyzed during the current study are not publicly available due to ongoing data analysis but are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

All actions performed on the animals followed the Helsinki Guidelines and the guidelines of the Ethics Committee of the Razi University of Kermanshah (IR.RAZI.REC.1401.065 on 21/12/2022). The protocol followed the ARRIVE guidelines and the National Institutes of Health guidelines for the care and use of laboratory animals.

Consent for publication

Not applicable.

Competing interests
The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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