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Combined Effects of Exercise and Cinnamon Supplementation on Liver Fibrosis and Oxidative Stress in Women with Type 2 Diabetes Mellitus: A Double-Blind, Randomized Clinical Trial

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Abstract

Background: This double-blind, randomized clinical trial aimed to assess the effects of concurrent exercise and cinnamon supplementation on liver fibrosis (FIB-4 index) and oxidative stress in women with type 2 diabetes mellitus (T2DM).

Methods: Thirty women, aged 35-50 years, diagnosed with T2DM, were randomly assigned to one of four intervention groups: 1) Control (C), 2) Moderate-intensity aerobic exercise + resistance exercise (RME), 3) Cinnamon supplementation (Ci), and 4) Moderate-intensity aerobic exercise + resistance exercise + cinnamon supplementation (RMECi). Participants in the exercise groups performed a combined aerobic and resistance training program five times a week, targeting 400 kcal expenditure per day, while the supplementation groups consumed 1000 mg of cinnamon per day. Fasting blood samples were collected before and after the 8-week intervention to evaluate liver enzymes, FIB-4 index, and markers of oxidative stress (MDA, SOD, GPx, CAT). Statistical analyses, including paired t-tests and ANCOVA, were performed to determine the effects within and between groups.

Results: Results indicated significant reductions in FIB-4, MDA, ALT, and AST in the RME, Ci, and RMECi groups compared to the control group, with the RMECi group showing the most significant improvements. Additionally, antioxidant capacity, as indicated by SOD, GPx, and CAT levels, was enhanced in the intervention groups.

Conclusion: These findings suggest that the combination of exercise and cinnamon supplementation may have synergistic effects on improving liver function and reducing oxidative stress in women with T2DM.

Keywords: Diabetes Mellitus, Exercise, Cinnamon, Liver Fibrosis

Introduction

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Type 2 Diabetes Mellitus (T2DM) is linked to Metabolic Dysfunction-Associated Steatosis Liver Disease (MASLD), the leading cause of liver disease worldwide, particularly in T2DM patients (1). Given the increasing prevalence of MASLD in T2DM patients, identifying reliable and accessible diagnostic markers is crucial for timely intervention. Liver fibrosis typically develops as a result of persistent chronic liver injury, and it stands as one of the major long-term liver complications in individuals with T2DM (2). Previous studies have reported that elevated glucose or insulin levels increase collagen production and expression in liver cells, which plays a pivotal role in the development of liver fibrosis (3). However, liver fibrosis is an indirect marker, influenced by age and liver enzymes, which can change for reasons other than fibrosis modification. Liver biopsy is considered the gold standard for assessing liver fibrosis. However, it is an invasive procedure that causes patient discomfort, sampling variability, and potential complications (4). Among non-invasive approaches, the Fibrosis-4 (FIB-4) index is a widely used and validated method, particularly in T2DM patients, due to its simplicity, accessibility, and predictive value in detecting advanced fibrosis (5). While alternative markers and imaging techniques exist, FIB-4 remains an optimal choice in this study due to its ease of application in large-scale screenings and clinical settings. Additionally, the production of oxidants is recognized as the primary cause of liver injury in T2DM patients (6). Increased reactive oxygen species (ROS) and other oxidative stress markers disrupt normal liver cell function and likely contribute to the pathogenesis of liver fibrosis (7).

It appears that a combination of physical activity, a proper diet, and the use of natural substances, such as certain medicinal plants, are among the most effective approaches to improve T2DM management. While exercise's individual benefits are well-documented, the combined effects of aerobic and resistance training on liver fibrosis are less well-understood. Given the synergistic potential of combined exercise modalities, this study aims to assess whether concurrent aerobic and resistance training yields superior effects on liver fibrosis compared to either method alone. Both aerobic and resistance exercise are recognized as important interventions for improving T2DM and its associated complications (8). Aerobic exercise increases GLUT4, which enhances insulin sensitivity and glucose utilization, thereby improving glycemic control (9, 10). Resistance training also improves insulin function and metabolic regulation by promoting muscle growth and increasing the muscles' capacity to absorb glucose (10). Despite prior findings supporting the benefits of individual training modalities, whether their combination provides a cumulative or even synergistic effect remains unclear. Concurrent Exercise Training (CET), which includes both aerobic and resistance exercise, provides the benefits of both types of physical activity (11). This training method has demonstrated significant improvements in glycemic control, body composition, cardiorespiratory fitness (CRF), lipid profiles, inflammatory markers, and insulin sensitivity in this population (12). A study has shown that short-term concurrent exercise (aerobic-resistance) significantly improves liver steatosis and lipid indices, independent of weight loss, in patients with NAFLD (13).

On the other hand, due to the irreversible side effects of synthetic drugs, the use of medicinal plants is recommended for diabetic patients, as they generally have fewer side effects (14). However, while cinnamon supplementation has been shown to improve glycemic control in some studies, the effects of cinnamon supplementation on liver fibrosis, particularly in conjunction with exercise, remain underexplored**.** Cinnamon contains polyphenols such as catechins, procyanidins, cinnamic acid, and flavonoids (cinnamaldehyde and trans-cinnamaldehyde). Cinnamon interacts with hepatic glucose homeostasis by suppressing phosphoenolpyruvate carboxykinase (PEPCK) and glucose-6-phosphatase (G6Pase), which regulate gluconeogenesis (15). Existing studies indicate that cinnamon supplementation in T2DM patients reduces fasting glucose levels, HOMA-IR, total cholesterol (TC), LDL, and triglycerides (TG) (16). It has also been shown that cinnamon extract can modulate AST, ALP,

and ALT levels and significantly improve liver tissue structural lesions and correct HOMA-IR (17). However, some studies have suggested that cinnamon has no significant effect on blood glucose control, inflammation, or oxidative stress (18). Given the inconsistency in prior findings related to cinnamon's efficacy, this study will account for variables such as dosage, duration, and participant characteristics to provide a clearer understanding of its role in liver fibrosis.

Despite the well-documented individual benefits of exercise and cinnamon supplementation in managing T2DM, no study has yet examined their combined effects on liver fibrosis, particularly using FIB-4 as a marker. Understanding the interaction between these factors could provide valuable insights into improving health outcomes for women with T2DM. Thus, this study specifically hypothesizes that concurrent exercise training combined with cinnamon supplementation will produce a greater reduction in the FIB-4 index and oxidative stress markers compared to either intervention alone. By clarifying the potential synergistic effects of these interventions, this research aims to fill a critical gap in understanding integrative strategies for managing T2DM-related liver fibrosis.

Material and methods

In a double-blind clinical trial, 134 women with type 2 diabetes from Nowshahr city, aged between 35 and 50 years (41.73 ± 4.05), were purposefully selected in coordination with the Nowshahr Diabetes Association. The sampling among women with type 2 diabetes was done voluntarily, purposefully, and through availability. At the beginning of the study, the purpose of the research, benefits, and potential risks of participating were explained to the participants. The inclusion criteria for this study include: confirmation of Type 2 Diabetes (T2D) by a specialist doctor, the use of oral antidiabetic medications, an HbA1C level above 6.5, no foot ulcers, no diabetic eye complications (such as retinopathy), no cardiovascular diseases or peripheral nerve disorders, and consent to participate in the study. The exclusion criteria also encompass: not taking supplements or exercising, having an allergy to cinnamon, using other medicinal plants, a diagnosis of other underlying diseases during the study protocol (such as fatty liver, liver cirrhosis, or heart or respiratory failure), insulin use, concerns about the risks associated with exercising or taking supplements, and the absence of contact from the researcher for follow-up. After the initial screening via phone interviews and questionnaires, 30 participants were randomly assigned to one of four intervention groups:

1. Control (C)
2. Moderate-intensity aerobic exercise + resistance exercise (RME)
2. Cinnamon supplementation (Ci)
4. Moderate-intensity aerobic exercise + resistance exercise + cinnamon (RMECi)

In this study, subjects were selected using simple random sampling based on the random assignment method. After determining the sample size, the subjects were equally divided into 4 groups. Using the lottery method, the participants' names were written on separate pieces of paper and placed in a container. Then, their names were randomly drawn and assigned to the intervention or placebo groups accordingly.

Exercise Protocol

To estimate VO_2max, participants performed a 1-mile (1609 m) walk while wearing a heart rate monitor. VO_2max was calculated using the following formula (19):

VO2max (ml/min/kg) = 132.853 − (0.1692 × body mass in kg) − (0.3877 × age) + (6.315 × sex) − (3.2649 × time in min) − (0.1565 × HR)

Sex: man = 1, woman = 0; HR: Heart rate immediately after the end of walking.

The exercise program used in this study is shown in Table 2 and was performed five times a week by each group. Energy consumption was measured using the smart watches to measure 400 kcal from when the target intensity was reached (daily energy expenditure of 400 kcal per day by the ACSMs recommendation). After a 10-15-min warm-up under expert supervision, the participants ran on a treadmill at 50% VO2max in the RME group and 80% VO2max in the RVE group to reach a 200-kcal expenditure. Thereafter, total body resistance exercise (TRX) was performed. The TRX exercises comprised the use of resistance bands to perform various upper body, lower body, and abdominal exercises (Table 2). TRX was performed for a further 200-kcal expenditure (20). At the end, cooling Down was done for 10 minutes.

Table 1: Exercise program Details

Exercise Type		Exercise Program	Expenditure Calorie
Warming up		Stretching (10-15 min)	
Main exercise	**RME**	Treadmill (50% VO2max) + TRX	Resistance: 200 kcal Aerobic: 200 kcal
		TRX program—push up, standing row, Kneeling triceps extension, biceps curl, jump squat, lunge, leg curl, ab slide, reverse lying knee pull	
Cool down		Stretching (10 min)	

The TRX program included exercises such as push-ups, standing rows, kneeling triceps extensions, biceps curls, jump squats, lunges, leg curls, ab slides, and reverse lying knee pulls.

Cinnamon Consumption

Cinnamon bark was purchased and processed after approval from a certified herbalist. The bark was washed, dried, ground into powder, and encapsulated into 500 mg capsules. To maintain the double-blind nature of the study, placebo capsules were prepared and administered in the same manner as the cinnamon capsules, ensuring that the researchers remained unaware of which capsules were being administered. Participants in the supplementation groups consumed two capsules daily (1000 mg/day), one after breakfast and one after lunch (21). The researcher responsible for administering the supplement to the participants and study groups received it in a sealed container labeled with a unique code. The coding process was conducted exclusively by the principal investigator (PI), and the code remained inaccessible to all other personnel involved in the study.

Blood Sampling and Analysis

Blood samples were collected two days before and two days after the training period to minimize the acute effects of the final exercise session and supplementation. Samples were drawn from the antecubital vein after a 12-hour overnight fast. The FIB-4 index was calculated using the following formula:

$$[\text{Age} \times \text{AST (IU/L)}]/[\text{platelets } (\times 10^9) \times \sqrt{\text{ALT (IU/L)}}]$$

Statistical Analysis

The normality of the data was evaluated using the Shapiro-Wilk test. To account for baseline differences, ANCOVA was used with pre-test values as covariates. Paired t-tests were used to compare within-group differences (pre-test vs. post-test). For between-group comparisons, Analysis of Covariance (ANCOVA) was conducted, followed by Bonferroni post hoc tests to control for multiple comparisons. Statistical significance was set at $p<0.05$. All analyses were performed using SPSS version 23.

Results

Descriptive characteristics of the participants, along with statistical results for key variables, are presented in Table 2.

The results of the statistical analysis using ANOVA showed that at the beginning of the protocol, there were no significant differences between the groups in any of the studied indicators (weight, BMI, body fat, VO2max, glucose, insulin, AST, and ALT) ($p > 0.05$).

Table 2: Descriptive Characteristics of the Participants and Key Variables

Groups		C	RME	Ci	RMECi	Between-group p
Age (years)	**pre-test**	41.57±4.39	41.88±4.12	43.13±4.05	41.71±4.15	0.887
Height (M)	**pre-test**	1.57±0.03	1.59±0.03	1.56±0.11	1.62±0.05	0.455
Weight (kg)	**pre-test**	65.14±4.59	69.25±8.9	70.5±4.2	72.57±5.62	
	post-test	65.86±1.4	65±9[a]	67.38±4.5[ac]	67.43±4.35[a]	0.0001*
	Intragroup p	0.220	0.0001*	0.0001*	0.002*	
Body mass index	**pre-test**	26.27±2.27	27.17±2.92	29.17±5.45	27.5±1.8	
	post-test	26.56±1.2	25.48±2.89[a]	27.89±5.5[ab]	25.58±1.74[a]	0.0001*
	Intragroup p	0.230	0.0001[a]	0.0001*	0.002*	
Body fat (%)	**pre-test**	37.15±4.12	38.43±4.15	38.17±5.43	33.33±4.16	
	post-test	37.25±3.69	35.69±4.1[a]	35.36±6.17[a]	29.86±3.65[a]	0.003*
	Intragroup p	0.701	0.006*	0.001*	0.006*	
Vo2max (ml/kg/min)	**pre-test**	23.35±3.44	21.91±3.9	23.09±2.86	22.96±4.35	
	post-test	22.19±4.81	26.27±4.45[a]	23.58±2.82[b]	26.6±5.76[a]	0.0001*
	Intragroup p	0.218	0.003*	0.056	0.009*	
Glucose (mg/dL)	**pre-test**	186.86±44.82	189.25±26.8	190.13±34.39	181.57±31.98	
	post-test	188.71±41.41	158.5±20.88[ac]	159.38±23.87[ac]	130±21.65 [a]	0.0001*
	Intragroup p	0.353	0.001*	0.001*	0.0001*	
Insulin (μIU/mL)	**pre-test**	9.64±2.49	8.86±2.49	9.21±2.26	10.07±2.52	
	post-test	9.85±2.35	9.26±2.46	9.71±2.56	9.54±1.78	0.085
	Intragroup p	0.384	0.045*	0.046*	0.272	
AST (U/L)	**pre-test**	33±2.58	36.38±4.17	34.75±3.37	31.29±2.92	
	post-test	34.29±2.69[ac]	33±4.17[ac]	29.75±3.61[a]	20.71±1.97	0.0001*
	Intragroup p	0.012*	0.007*	0.0001*	0.0001*	
ALT (U/L)	**pre-test**	38.43±5.28	36.75±2.96	34.88±4.32	35.29±4.85	
	post-test	38.4±4.39 [ac]	32.88±4.22 [ac]	31.8±4.73 [a]	28.14±3.18	0.0001*
	Intragroup p	1.000	0.006*	0.017*	0.0001*	

* Difference with pre-test, a difference with C, b difference with RME, c difference with RMECi.

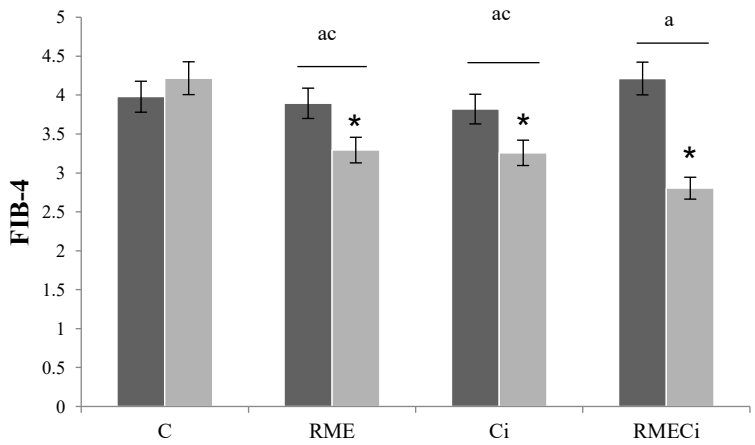

Figure 1. FIB-4 levels by dependent t and ANCOVA test (at p<0.05).
***Difference with pre-test, a difference with C, c difference with RMECi.**

C (Control), RME (Resistance and Moderate Aerobic Exercise), Ci (Cinnamon), RMECi (Resistance and Moderate Aerobic Exercise+Cinnamon).

Within-group comparisons revealed a significant reduction in FIB-4 levels in the RME (P = 0.002), Ci (P = 0.0001), and RMECi (P = 0.007) groups. Data analysis using covariance showed a significant difference in FIB-4 levels between the groups (P = 0.0001, F = 12.473). Post hoc Bonferroni tests revealed a significant reduction in FIB-4 levels in the RME (P = 0.015), Ci (P = 0.020), and RMECi (P = 0.0001) groups compared to the control group (C); RMECi also showed a greater reduction than RME (P = 0.040) and Ci (P = 0.031) (Figure 1).

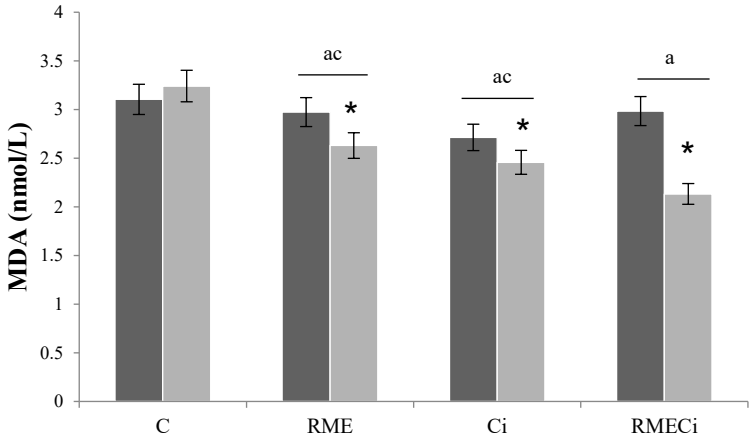

Figure 2. MDA levels by dependent t and ANCOVA test (at p<0.05).
***Difference with pre-test, a difference with C, c difference with RMECi.**
C (Control), RME (Resistance and Moderate Aerobic Exercise), Ci (Cinnamon), RMECi (Resistance and Moderate Aerobic Exercise+Cinnamon).

Furthermore, within-group comparisons showed a significant reduction in MDA levels in the RMECi group (P = 0.007). Covariance analysis indicated a significant difference in MDA levels between the groups (P = 0.0001, F = 11.255). Post hoc Bonferroni tests revealed a significant decrease in MDA levels in the RME (P = 0.031), Ci (P = 0.035), and RMECi (P = 0.0001) groups compared to the control group (C), with RMECi showing greater reduction than RME (P = 0.042) and Ci (P = 0.046) (Figure 2).

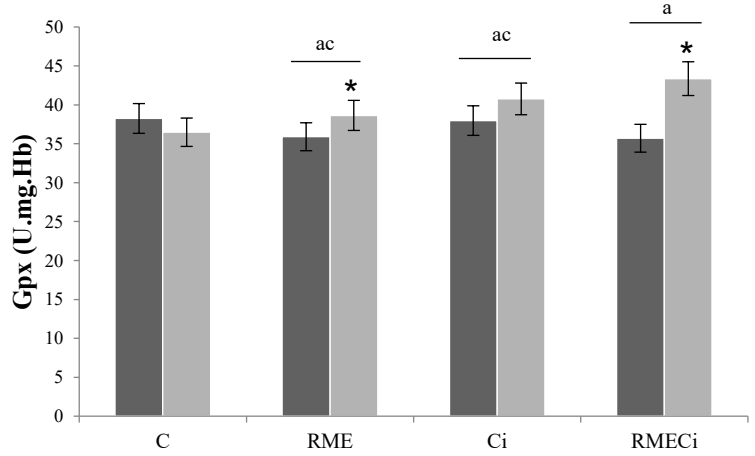

Figure 3. Gpx levels by dependent t and ANCOVA test (at p<0.05).
***Difference with pre-test, a difference with C, c difference with RMECi.**

C (Control), RME (Resistance and Moderate Aerobic Exercise), Ci (Cinnamon), RMECi (Resistance and Moderate Aerobic Exercise+Cinnamon).

Additionally, within-group comparisons indicated a significant increase in Gpx levels in the RME (P = 0.003) and RMECi (P = 0.002) groups. Covariance analysis revealed a significant difference in Gpx levels between the groups (P = 0.0001, F = 12.11). Post hoc Bonferroni tests showed a significant increase in Gpx levels in the RME (P = 0.037), Ci (P = 0.044), and RMECi (P = 0.0001) groups compared to the control group, with RMECi showing higher levels than RME (P = 0.018) and Ci (P = 0.016) (Figure 3).

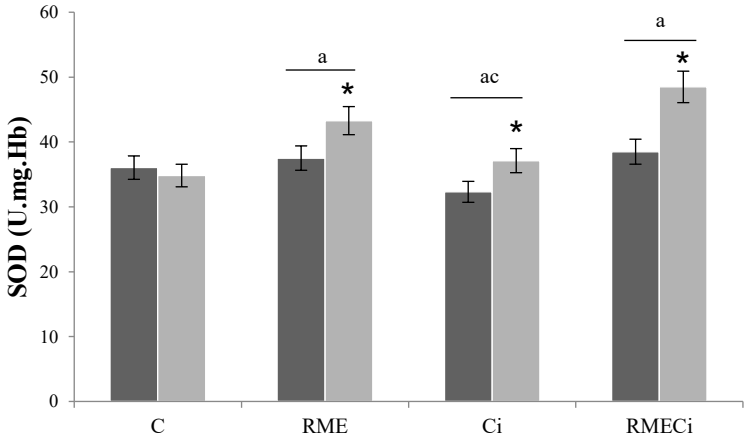

Figure 4. SOD levels by dependent t and ANCOVA test (at p<0.05).
***Difference with pre-test, a difference with C, c difference with RMECi.**
C (Control), RME (Resistance and Moderate Aerobic Exercise), Ci (Cinnamon), RMECi (Resistance and Moderate Aerobic Exercise+Cinnamon).

Within-group comparisons also showed a significant increase in SOD levels in the RME (P = 0.006), Ci (P = 0.014), and RMECi (P = 0.0001) groups. Covariance analysis indicated a significant difference in SOD levels between the groups (P = 0.0001, F = 11.875). Post hoc Bonferroni tests revealed a significant increase in SOD levels in the RME (P = 0.005), Ci (P = 0.044), and RMECi (P = 0.0001) groups compared to the control group, with RMECi showing higher levels than Ci (P = 0.032) (Figure 4).

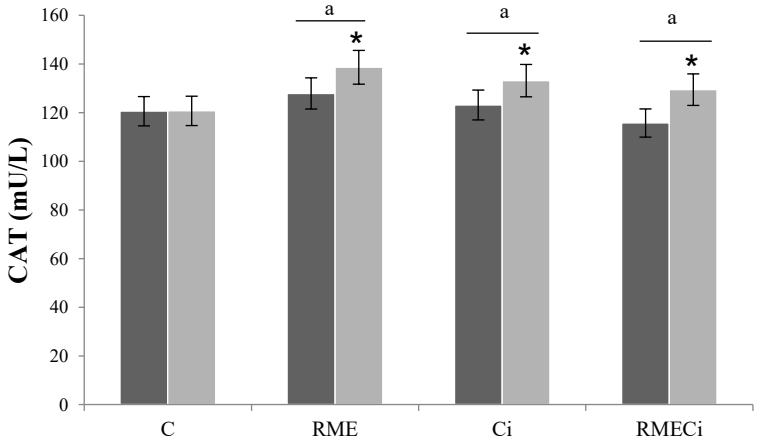

Figure 5. CAT levels by dependent t and ANCOVA test (at p<0.05).

***Difference with pre-test, a difference with C, c difference with RMECi.**
C (Control), RME (Resistance and Moderate Aerobic Exercise), Ci (Cinnamon), RMECi (Resistance and Moderate Aerobic Exercise+Cinnamon).

Finally, within-group comparisons showed a significant increase in CAT levels in the RME (P = 0.001), Ci (P = 0.011), and RMECi (P = 0.002) groups. Covariance analysis revealed a significant difference in CAT levels between the groups (P = 0.004, F = 5.674). Post hoc Bonferroni tests revealed a significant increase in CAT levels in the RME (P = 0.034), Ci (P = 0.047), and RMECi (P = 0.005) groups compared to the control group (Figure 5).

Discussion

This study investigated the effects of concurrent exercise and cinnamon supplementation on liver fibrosis index (FIB-4) and oxidative stress in women with Type 2 Diabetes (T2DM). The results indicated a significant reduction in FIB-4 levels in the RME, Ci, and RMECi groups compared to the control (C) group. The reduction was more pronounced in the RMECi group than in the RME and Ci groups. Similarly, ALT and AST levels significantly decreased in the RME, Ci, and RMECi groups compared to the C group, with the RMECi group showing a greater reduction than the RME and Ci groups.

Factors influencing liver fibrosis include age, insulin resistance, obesity, AST and ALT levels, and high circulating fat levels (22). In line with this study, a decrease in the FIB-4 indexes following exercise in individuals with diabetes has been confirmed by other studies (23). Asgari et al. (2025) showed that concurrent exercise (aerobic-resistance training) improves the harmful effects of steatotic liver disease in women by influencing liver enzymes and paraoxonase activity (24). Abbasi et al. (2025) also found that high-intensity interval training (HIIT) reduced ALT, AST, plasma fats, glucose, and HOMA-IR, leading to improvements in steatotic liver disease in obese adolescent girls (25). It seems that concurrent exercise can positively impact the Fatty Liver Index and Lipid Accumulation Index, providing beneficial effects on hepatic steatosis and lipid metabolism (13). However, some studies have shown that aerobic exercise does not significantly affect liver fibrosis, ALT, or AST. Houghton et al. (2017) found that, despite reductions in HTGC levels, visceral fat, and plasma triglycerides following 12 weeks of exercise, liver inflammation and fibrosis remained unchanged (26). Barani et al. (2014) reported that resistance and combined exercise had no significant effect on ALT and AST levels in women with fatty liver disease, though alkaline phosphatase (ALP) levels significantly decreased in the resistance exercise group (27).

The differences in the results may be due to variations in the study population, including gender, age, exercise protocols, and physical conditions of the participants. In the present study, the reduction in the FIB-4 index was attributed to the decrease in serum AST and ALT levels. Aerobic exercise inhibits AST and ALT activity by increasing HSP70 production. Furthermore, there is a negative relationship between insulin sensitivity and fat accumulation in liver tissue. Exercise inhibits liver fat synthesis and activates the AMP-activated protein kinase (AMPK) pathway by increasing fat oxidation. AMPK then prevents lipid synthesis in the liver by inactivating acetyl-CoA carboxylase, activating malonyl-CoA decarboxylase, and inhibiting lipogenic enzyme expression, including acetyl-CoA carboxylase and fatty acid synthase, thus preventing liver fibrosis (28). Another factor influencing liver enzyme changes is weight loss, which was observed in the experimental groups in this study. Weight loss, along with caloric restriction, leads to a reduction in liver TG content and hepatic gluconeogenesis, thereby decreasing AST and ALT levels (29). The significant reduction in ALT and AST due to exercise and diet may be attributed to increased tissue and hepatic insulin sensitivity, enhanced hepatic oxidation, inhibition of lipogenic enzymes, and consequently reduced liver fat (30). Although mechanisms involving AMPK, HSP70, and NO production are discussed, these pathways were not directly measured in this study. Therefore, their involvement remains

speculative and should be interpreted cautiously. Experimental studies measuring these molecular mechanisms directly are needed to confirm the precise pathways responsible for the observed changes in FIB-4 and oxidative stress markers.

Moreover, regular exercise has been shown to enhance the body's antioxidant capacity, potentially reducing cellular damage at the liver cell level (30). Another finding of the present study was the improvement in antioxidant capacity. In this study, MDA levels significantly decreased in the experimental groups, with the greatest reduction observed in the RMECi group. Additionally, Gpx, SOD, and CAT levels decreased in the experimental groups, with the RMECi group showing the best results. Naiji et al. (2022) reported that aerobic exercise in diabetic men led to a reduction in MDA and an increase in SOD, GPX, and CAT (23). Several mechanisms for the increased expression of SOD after exercise have been reported. It appears that increased NO production due to exercise influences cGMP, PKG, and p38 MAPK, leading to enhanced SOD expression (31). Notably, in this study, combined exercise may have impacted metabolic and physiological changes in the muscle and liver mitochondria. Aerobic exercise significantly increases blood flow and oxygen uptake by muscles while enhancing fat utilization for energy production and improving the volume of oxidative enzymes in mitochondria. This exercise also leads to a reduction in visceral fat (32). Resistance training increases protein synthesis, which can increase active muscle mass and mitochondrial oxidative metabolism, contributing to increased maximum oxygen uptake and lipolysis capacity (33). Both aerobic and resistance training also reduce pro-oxidant and pro-inflammatory proteins in liver cells. Along with these changes, oxidative enzymes that produce free radicals, such as MDA, are reduced, leading to increased expression of antioxidant enzymes like Gpx, SOD, and CAT.

Another result of this study was the significant reduction in FIB-4, MDA, and liver enzymes (ALT and AST) following cinnamon supplementation in women with diabetes. Additionally, antioxidant capacity improved following cinnamon consumption. Samadi et al. (2023) demonstrated an increase in total antioxidant capacity and a reduction in certain inflammatory markers after cinnamon supplementation (34). Miriranpour et al. (2020) also showed that cinnamon supplementation reduced advanced glycation end products and oxidized low-density lipoprotein (ox-LDL), while improving the activity of antioxidant enzymes, particularly catalase (35). Evidence suggests that cinnamon and its bioactive compounds, such as cinnamaldehyde, gallic acid, eugenol, and beta-caryophyllene, have antihyperglycemic, hypolipidemic, and antioxidant properties. Cinnamon's mechanisms of action may include facilitating glycogen synthesis in the liver, restoring pancreatic islet function, reducing gastric emptying rate, increasing glucose absorption, and enhancing insulin sensitivity in skeletal muscles and adipose tissue. Cinnamaldehyde, the main active compound in cinnamon, has been shown to regulate blood glucose through its effects on glycogen synthesis and inhibition of gluconeogenesis (36). Its role in insulin signaling and glucose transport has also been reported (36). Eugenol, another active compound, has antihyperglycemic, antioxidant, antibacterial, and anti-inflammatory properties and works by altering ghrelin secretion, food intake, and gastric emptying (36).

In this study, the combination of concurrent exercise and cinnamon showed better effects on the indices. One of the suitable interventions for treating T2DM is physical activity combined with the use of traditional, natural-origin medications that possess anti-fat and antioxidant properties. These can serve as beneficial complementary treatments, especially in prevention. The effect of combining exercise and herbal medicine was examined by Naiji et al. (2022), who showed that aerobic exercise combined with bitter cucumber reduced the FIB-4 index, liver enzymes, and oxidative stress in men with T2D (23). Fernández et al. (2022) also stated that a concurrent diet and exercise regimen was more effective than either intervention alone in improving liver enzymes and HOMA-IR (37). It seems that the combination of aerobic

exercise and herbal supplements, with their effects on fat mass, increases leptin and adiponectin, boosts mitochondrial biogenesis gene expression in the liver, and through their antioxidant effects, improves liver enzymes (38). In this study, the combination of concurrent exercise and cinnamon exhibited synergistic effects and had a better impact compared to each intervention alone. Therefore, it is recommended to use the combination of concurrent exercise and cinnamon for controlling and preventing liver-related diseases, particularly liver fibrosis.

Given potential confounders such as medication variability, dietary differences, and attrition bias, these results should be interpreted cautiously. Although efforts were made to control these factors, causality cannot be confirmed without further research involving larger samples and stricter controls. Limitations—including small sample size (N=30), single-center recruitment, purposive sampling, lack of detailed dietary control, medication variability, attrition bias, and no standardization of cinnamon's active compounds—may affect the validity and generalizability of findings. Current evidence on cinnamon's efficacy and safety is mixed and inconclusive. While some studies suggest benefits for glycemic and lipid control, especially in poorly controlled type 2 diabetes, variability in cinnamon types, doses, and study designs limit firm conclusions. Cinnamon is generally safe in typical amounts, but high doses or prolonged use—particularly of cassia cinnamon—may pose risks. Future research should focus on larger, multi-center trials with standardized cinnamon preparations, rigorous dietary monitoring, and controlled medication use to better assess cinnamon's therapeutic potential and safety.

Conclusion

The present study demonstrated that concurrent exercise and cinnamon supplementation may improve the FIB-4 index and antioxidant capacity in individuals with T2DM. However, given the lack of a direct statistical test for synergy and potential methodological limitations, further research is required to confirm the combined effects of exercise and cinnamon. The combination of concurrent exercise and cinnamon appears promising for liver health, but its use should be considered complementary rather than definitive.

Declarations

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Research Ethics Committee of the Islamic Azad University, Ayatollah Amoli Branch, with the code IR.IAU.AMOL.REC.1403.099 and was registered in the Clinical Trial Center under the number IRCT20140415017288N12.

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Authors' contributions

Concept/Design- A. Abdi/ A. Barari. Acquisition of Data-M. Ghasemi. Data Analysis/Interpretation- Kh. Jalali Dehkordi. Drafting of the manuscript- A. AbdI/M. Ghasemi. All authors approved the final version of the manuscript.

Conflicts of interest

The authors declare that they have no competing interests.

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