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The Interactive effect of High Intensity Interval training and nanocurcumin consumption on regulating glucose metabolism in obese and overweight women

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Abstract

Aim: The aim of the present study was to investigate the effect of high-intensity interval training (HIIT) and nanocurcumin consumption on the regulation of glucose metabolism in obese and overweight women.

Method: Forty obese and overweight women (BMI=31.09 ± 2.77) were divided into five groups of 8: high-intensity interval training (HIIT), nanocurcumin (NanoC), HIIT + NanoC, placebo (Pl), and control. The HIIT training groups ran for eight weeks, three sessions per week, at an intensity of 80% of maximum heart rate (HRmax). The nanocurcumin groups received 80 mg of it daily for eight weeks. HbA1c, fasting glucose, insulin resistance index (HOMA-IR), and time to exhaustion (TTE) were measured before and after the intervention and analyzed using two-way analysis of variance (ANOVA).

Results: The results showed that glucose and HOMA-IR levels were significantly different between the study groups ($p<0.001$). The greatest reduction in serum glucose (14.72%) and HOMA-IR (47.54%) was observed in the HIIT+NanoC group compared to the NanoC and PL groups ($p<0.001$, for all comparisons). Also, HbA1c levels in the HIIT+NanoC group had the greatest significant reduction compared to both the HIIT ($p=0.001$) and NanoC ($p=0.001$) groups. In addition, TTE in the HIIT+NanoC group was significantly increased compared to the NanoC, HIIT, and Pl groups($p<0.001$).

Conclusion: HIIT training and nanocurcumin supplementation as non-pharmacological interventions had beneficial effects on glucose control, especially on insulin resistance in obese and overweight women. The combination of these two interventions as well as HIIT training had greater effects on improving glucose metabolism than nanocurcumin consumption alone.

Keywords: HIIT, nano-curcumin, obesity, glucose metabolism, insulin resistance.

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1. Introduction

Obesity and overweight have increasingly emerged as one of the major public health concerns in recent decades and are recognized as key risk factors for the development of insulin resistance, type 2 diabetes, and other metabolic disorders (1). An increase in fat mass, particularly in the visceral region, is associated with unfavorable alterations in adipokine secretion, heightened systemic inflammation, and disruption of glucose homeostasis, ultimately leading to reduced insulin sensitivity (2). Therefore, identifying effective approaches to improve glucose metabolism in overweight and obese women is of particular importance.

High-intensity interval training (HIIT) has garnered significant research attention in recent years as a novel and efficient exercise modality, owing to its time-saving nature and substantial metabolic effects (3). Studies have demonstrated that HIIT can improve insulin sensitivity and peripheral glucose uptake by increasing oxidative enzyme activity, enhancing muscular mitochondrial capacity, and stimulating related signaling pathways, such as GLUT-4 (4, 5). Furthermore, compared to moderate-intensity continuous training (MICT), HIIT is capable of inducing similar or even greater changes in glucose metabolism indices with a lower total exercise volume (6, 7).

On the other hand, the use of natural compounds possessing antioxidant and anti-inflammatory properties has gained attention as a complementary strategy to counteract metabolic disturbances (8). Curcumin, the active constituent of turmeric, has demonstrated proven effects in reducing oxidative stress, inhibiting inflammatory pathways (such as NF-κB), and improving pancreatic beta-cell function (9). However, the low bioavailability of curcumin in its conventional form has limited its therapeutic efficacy. Consequently, the utilization of novel formulations, such as nano-curcumin—which offers enhanced absorption and stability—has been proposed as a potential strategy to augment the effectiveness of this compound in human studies (10).

Recent studies have indicated that nano-curcumin supplementation may reduce fasting blood glucose levels, HbA1c, and insulin resistance indices (HOMA-IR) in diabetic patients and individuals at risk (11). Fakhri et al. (2020) demonstrated in a study that curcumin supplementation, in conjunction with exercise training, may exert beneficial effects in strengthening the antioxidant system and preventing lipid peroxidation in overweight individuals (12). Similarly, Qarakhannlou et al. (2025) showed in another study that HIIT, combined with curcumin supplementation, has a greater impact on reducing obesity in women, suggesting that curcumin and HIIT may be considered as a therapeutic approach to mitigate the adverse outcomes of obesity (13).

Despite the separate evidence supporting the beneficial effects of HIIT and nano-curcumin consumption on glucose metabolism, few studies have investigated the combined effects of these two interventions (12). The potential mechanism of curcumin's action on glucose metabolism is primarily through the reduction of insulin resistance. This occurs via the inhibition of key inflammatory pathways such as NF-κB, the reduction of oxidative stress, and the activation of the AMPK pathway, which plays a crucial role in glucose uptake. The nano-formulation of curcumin, by enhancing bioavailability, further augments these effects (14).

Given that HIIT can act through the stimulation of muscle-dependent metabolic pathways and nano-curcumin can function by reducing inflammation and oxidative stress (15), it is anticipated that the simultaneous implementation of these two strategies may exert synergistic effects in improving glycemic regulation and enhancing insulin sensitivity.

Therefore, the primary research question of this study is whether combining high-intensity interval training with nano-curcumin supplementation can exert a greater effect on improving glucose metabolism in obese and overweight women than either intervention alone. Addressing this question may provide valuable scientific evidence for designing multifaceted interventions aimed at preventing or controlling type 2 diabetes in high-risk populations.

2. Methods

2.1. Participants

This study was a quasi-experimental investigation employing a pretest-posttest design with a control group. The target population comprised adult women aged 30–40 years who were overweight or obese and residing in Marivan County, with a body mass index (BMI) of 25 kg/m² or higher, and who met the initial requirements for participation in exercise training and supplementation.

This population included healthy women (without diagnosed and medically treated diabetes) or women with mild to moderate metabolic disorders that were controlled on an outpatient basis, provided that they met the inclusion and exclusion criteria. The inclusion criteria were as follows: women aged 30–40 years, BMI greater than 25, no diagnosis of type 1 or type 2 diabetes under pharmacological treatment, no regular participation in a structured exercise program exceeding two sessions per week during the three months prior to the study, willingness to cooperate and signing the informed consent form, and no chronic use of curcumin supplements or medications affecting glucose metabolism during the previous three months.

To determine the required sample size, G*Power software version 3.1 was used. Given the study design as a clinical trial with five groups and pretest-posttest measurements, a two-way ANOVA was considered in order to examine the main effect of group, the effect of time, and the group × time interaction effect on glucose metabolism variables. The parameters used for sample size calculation included a significance level of α=0.05\alpha = 0.05α=0.05, statistical power of 0.80 (an 80% probability of detecting a true effect), and a medium effect size (f=0.25f = 0.25f=0.25). The exclusion criteria were as follows: pregnancy or lactation, serious cardiac disease, uncontrolled hypertension (e.g., blood pressure greater than 160/100 mmHg), or any medical condition preventing participation in HIIT; acute or advanced hepatic or renal disorders (ALT/AST more than three times the normal range); use of glucose-lowering medications (such as metformin or insulin) or other agents known to substantially alter glucose metabolism; a history of severe allergy to curcumin/turmeric; participation in another clinical study or use of dietary supplements affecting glucose within the previous three months.

Ultimately, 40 participants were purposively selected based on the inclusion criteria and then randomly allocated, using block randomization via the website org.randomizer.www, into five groups (n = 8 per group): HIIT, nano-curcumin (NanoC), NanoC + HIIT, placebo, and control.

Recruitment was conducted through public health announcements, posters displayed at healthcare centers, social networks, and referrals from local clinics. Initial applicants were screened by telephone/online and then, during an in-person session, were accepted or excluded based on BMI assessment, a brief clinical examination, baseline fasting glucose tests, HbA1c, liver enzymes, and medical history.

All stages of the study were carried out in accordance with the ethical principles governing human research, and the study protocol was approved by the Ethics Committee of the Research Institute of Islamic Azad University, Sanandaj Branch, under approval code IR.IAU.SDJ.REC.1404.036. Prior to enrollment, participants read and signed the informed consent form. They were informed about the study objectives, procedures, potential benefits and risks, and their right to withdraw from the study at any time. In addition, the confidentiality of personal information and laboratory data was fully guaranteed, and all results were reported only in an aggregated and anonymous manner.

Before the commencement of the interventions, all participants attended an orientation session on the study and the HIIT protocol in order to become familiar with the execution of the exercises, the intensity and timing of each session, and the use of equipment. At this stage, general health status, medical history, medications, and lifestyle habits were assessed to ensure that the participants were eligible to take part in the training program and supplementation.

The initial assessment included baseline metabolic and physiological measurements, namely body weight, height, and body mass index (BMI); waist circumference and waist-to-hip ratio; resting blood pressure and heart rate; and blood sampling for the determination of fasting glucose, HbA1c, serum insulin, and the HOMA-IR index. Blood sampling was performed after 10 to 12 hours of overnight fasting between 8:00 and 9:00 a.m., in a seated position, from the antecubital vein using a sterile disposable syringe. On average, 5 mL of venous blood was collected and transferred into anticoagulant-free tubes for serum preparation.

The collected blood samples were centrifuged at 3000 rpm for 10 minutes to separate the serum. The separated serum was then transferred into Eppendorf tubes and stored at −80◦C until analysis. Fasting glucose concentration was measured using an enzymatic method with a kit supplied by Pars Azmoon, Iran, and analyzed using an automated biochemical analyzer (Hitachi 704, Japan). Serum insulin concentration was determined by ELISA using a kit from Monobind, USA, and an ELISA reader (Stat Fax 303, USA).

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The Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) was calculated using the following formula:

HOMA-IR= (Fasting Insulin (µIU/mL) ×Fasting Glucose(mmol/L))/22.5

In addition, HbA1c was measured using a kit from Biosystems, Spain, and an autoanalyzer (BA-400, Spain). Internal and external quality control procedures were performed regularly for all biochemical assays to ensure the accuracy and reliability of the results. All analyses were conducted in a certified laboratory under the supervision of qualified specialists.

Table 2. Descriptive and anthropometric characteristics of the subjects.

Group/ Variables	Age (year)	Height (cm)	Weight (kg)		BMI (kg/m^2)		body fat (%)	
			Pre- test	Post- test	Pre- test	Post- test	Pre- test	Post- test
Control	35.38 ± 4.27	165.67 ± 4.14	86.61 ± 5.27	87.14 ± 5.38	31.48 ± 2.17	32.30 ± 2.15	36.56 ± 2.18	36.64 ± 2.43
Nano-C	34.25 ± 2.65	166.16 ± 5.16	87.49 ± 6.16	86 ± 5.47	31.86 ± 2.45	31.27 ± 2.72	37.41 ± 2.27	37.57 ± 2.39
HIIT	36.25 ± 4.28	165.62 ± 4.72	85.23 ± 7.20	82.34 ± 6.51	31.25 ± 2.27	30.14 ± 3.41	38.33 ± 3.10	±37.23$^{†¥§*}$ 3.06
HIIT+NanoC	34.50 ± 3.58	166.39 ± 5.44	84.19 ± 4.69	79.18 ± 4.69	30.42 ± 2.54	29.15 ± 3.36	38.49 ± 3.01	±36.67$^{†¥§*}$ 3.32
Placebo	36.39 ± 2.91	165 ± 6.10	86.13 ± 5.18	87.08 ± 6.23	31.66 ± 2.33	31.64 ± 2.52	37.73 ± 2.36	37.52 ± 2.84

(*): Significant compared to pre-test. (§): Significant compared to control group. (¥): Significant compared to placebo group. (†): Significant compared to nanocurcumin supplement group.

2.2. Training protocol

The HIIT and HIIT+NanoC groups performed a high-intensity interval training protocol for 8 weeks, with 3 sessions per week. Each training session consisted of 5 minutes of warm-up (light jogging and dynamic stretching), 20–25 minutes of the main exercise bout, and 5 minutes of cool-down (slow walking and static stretching). The main exercise phase included repeated cycles of 1 minute of high-intensity activity (85–90% of maximum heart rate) followed by 2 minutes of active recovery (40–50% of maximum heart rate). Exercise intensity was monitored and controlled using a heart rate monitor (Polar, Finland). To maintain the prescribed intensity, running speed or cycling resistance was adjusted according to each participant's capacity. Predicted maximum heart rate was calculated using the formula HRmax=220−Age. Exercise intensity was progressively increased over the 8-week period; for example, fewer cycles were performed in the first weeks and gradually increased by week 8.

Table 1. HIIT Training Protocol

Week	Number, duration, and intensity of high-intensity bouts	Number, duration, and intensity of active recovery bouts
1	4 bouts of 1 min at 80% HRmax	4 bouts of 4 min at 60% HRmax
2	5 bouts of 1 min at 80% HRmax	5 bouts of 3 min at 60% HRmax
3	6 bouts of 1 min at 80% HRmax	6 bouts of 2 min at 60% HRmax
4	7 bouts of 1 min at 80% HRmax	7 bouts of 1 min at 60% HRmax
5	8 bouts of 1 min at 80% HRmax	8 bouts of 1 min at 60% HRmax
6	9 bouts of 1 min at 80% HRmax	9 bouts of 1 min at 60% HRmax
7	10 bouts of 1 min at 80% HRmax	10 bouts of 1 min at 60% HRmax
8	10 bouts of 1 min at 80% HRmax	10 bouts of 1 min at 60% HRmax

2.3. Supplementation protocol

The NanoCurcumin and NanoC+HIIT groups received 80 mg of nano-curcumin supplementation daily, administered in capsule form. The nano-curcumin formulation, produced as curcumin nanoparticles by the Knowledge-Based Nanodaru Company, Iran, was used for 8 weeks. In the placebo group, participants received placebo capsules for the same period. The nano-curcumin capsules contained 80 mg of curcumin in nanosized particles with high bioavailability and were designed to be visually identical to the placebo capsules in terms of color, odor, and shape to ensure participant blinding. The placebo capsules contained microcrystalline cellulose powder and did not include any active ingredient. Participants were instructed to take one capsule in the morning and one capsule at night, and they were asked to take the supplement regularly and report any adverse effects. Both the supplement and placebo were provided free of charge.

2.4. Intervation

The intervention lasted for 8 weeks, and no exercise or supplementation intervention was provided to participants in the control group. Throughout the study period, all participants were asked to maintain their usual diet and avoid any major changes in lifestyle. General recommendations regarding the importance of a balanced diet and maintaining normal physical activity were provided to all participants. Adherence to the exercise protocol and supplement intake was regularly recorded and monitored. For training sessions, attendance was documented, and for supplementation, participants were asked to mark daily supplement intake on a designated form and return the remaining capsules at the end of the study so that compliance could be assessed.

2.5. Statistical analysis

Descriptive statistics, including mean and standard deviation (SD), were used to summarize demographic data and primary study variables. The normality of data distribution was assessed using the Kolmogorov-Smirnov test. To compare baseline differences among groups, a one-way analysis of variance (One-way ANOVA) was performed; in cases where significant differences were detected, Tukey's Honestly Significant Difference (HSD) post-hoc test was employed for pairwise comparisons. To analyze the effects of the intervention on glucose metabolism variables over time and between groups, a 5 × 2 repeated measures ANOVA (five groups and two time points) was utilized. In the event of a significant group × time interaction effect, post-hoc LSD (Least Significant Difference) for between-group comparisons and paired t-tests for within-group comparisons were conducted to further investigate the differences.

All statistical analyses were performed using SPSS software (version 25), and the level of statistical significance was set at $P<0.05$. Prior to conducting the repeated measures ANOVA, the assumptions of homogeneity of variance and sphericity were verified using Levene's test and Mauchly's test, respectively. In instances where the assumption of sphericity was violated, the Greenhouse-Geisser correction was applied to adjust the results.

3. Results

3.1. Participants' characteristics and compliance

A total of 40 overweight and obese women participated in this study and were equally distributed into five groups of eight participants each. All participants completed the study protocol, with no attrition or dropouts reported. The baseline demographic characteristics of the participants, including age, height, weight, and BMI, are presented in Table 1. As shown in Table 1, no significant differences were observed in the baseline demographic variables between the groups ($P>0.05$), indicating that the groups were homogeneous regarding these characteristics.

Glucose

The repeated measures ANOVA results for fasting glucose revealed a significant main effect of time ($F=31.25$, $P<0.001$), a significant main effect of group ($F=18.73$, $P<0.001$), and a significant group × time interaction effect ($F=12.89$, $P<0.001$). These findings indicate that fasting glucose levels changed throughout the study period, and these changes varied significantly between the intervention groups. In other words, the interventions applied to the groups induced significant alterations in fasting glucose levels.

Post-hoc and Synergistic Effect

Post-hoc analyses demonstrated that fasting glucose levels decreased significantly after 8 weeks in the HIIT, NanoCurcumin, and NanoC+HIIT groups ($P<0.01P < 0.01$). Conversely, no significant changes were observed in the placebo and control groups ($P>0.05$). Furthermore, between-group comparisons following the intervention revealed that the NanoC+HIIT group exhibited a significantly greater reduction in fasting glucose levels compared to the HIIT and NanoCurcumin-only groups ($P<0.05P < 0.05$). These results suggest a synergistic effect of combining HIIT with NanoCurcumin in improving fasting glucose levels.

Fasting Insulin

Regarding fasting insulin levels, the repeated measures ANOVA revealed a significant main effect of time ($F=28.50$, $P<0.001$), a significant main effect of group ($F=15.67$, $P<0.001$), and a significant group × time interaction effect ($F=10.21$, $P<0.001$). These findings indicate that fasting insulin concentrations underwent significant fluctuations throughout the study period, and these longitudinal changes varied significantly across the experimental groups.

Post-Hoc Insulin

Post-hoc analyses demonstrated that fasting insulin levels were significantly reduced after 8 weeks in the HIIT, NanoCurcumin, and NanoC+HIIT groups ($P<0.01$); however, no significant alterations were observed in the placebo and control groups ($P>0.05$). Furthermore, between-group comparisons following the intervention revealed that the NanoC+HIIT group exhibited a significantly greater reduction in fasting insulin compared to both the HIIT and NanoCurcumin-only groups ($P<0.05P < 0.05P<0.05$). This finding further corroborates the synergistic effect of combining HIIT with NanoCurcumin in enhancing insulin sensitivity.

HOMA-IR

The analysis of HOMA-IR results followed a similar pattern. A significant main effect of time ($F=29.87$,

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P<0.001), a significant main effect of group (F=17.05, P<0.001), and a significant group × time interaction effect (F=11.54, P<0.001) were observed for HOMA-IR. These results clearly demonstrate that the implemented interventions induced substantial alterations in the homeostatic model assessment of insulin resistance.

Table 3. Descriptive and anthropometric characteristics of the subjects.

Group / Variable		Control	NanoC	HIIT	NanoC+HIIT	Placebo
Weight	Pre-Test	86.61 ± 5.27	87.49 ± 6.16	85.23 ± 7.20	84.19 ± 4.69	86.13 ± 5.18
	Post-Test	87.14 ± 5.38	86 ± 5.47	82.34 ± 6.51	79.18 ± 4.69	87.08 ± 6.23
Glucose (mg/dL)	Pre-Test	118.5 ± 4.75	116.87 ± 8.21	114.75 ± 6.11	114.62 ± 4.68	114.62 ± 6.07
	Post-Test	123 ± 5.55	111.12 ± 2.47*	110.12± 5.51¥§*	97.75± 4.83¥§*	116 ± 5.90
Insulin (µIU/mL)	Pre-Test	20.62 ± 3.20	19.5 ± 2.87	19.12 ± 3.44	18.5 ± 2.44	22.12 ± 2.41
	Post-Test	22.12 ± 2.94*	18.12 ± 2.47*	16.62 ± 3.15	14.62 ± 1.92¥*	22.5 ± 2.29
HOMA-IR	Pre-Test	6.05 ± 1.97	5.58 ± 2.54	5.41 ± 1.72	5.23 ± 1.56	6.26 ± 2.24
	Post-Test	6.71± 2.24	4.97 ± 2.23¥§*	4.10± 2.18†¥§*	3.52± 2.37†¥§*	6.44 ± 2.09

(*) Significant difference compared with the pre-test; (§) significant difference compared with the Control group; (¥) significant difference compared with the Placebo group; (†) significant difference compared with the Nano-curcumin supplementation group.

Post-hoc HOMA-IR

Post-hoc testing indicated that HOMA-IR indices were significantly diminished in the HIIT, NanoCurcumin, and NanoC+HIIT groups after 8 weeks (P<0.01), whereas no significant changes occurred in the placebo and control groups (P>0.05). Inter-group comparisons post-intervention confirmed that the NanoC+HIIT group achieved a more pronounced reduction in HOMA-IR relative to the HIIT and NanoCurcumin groups (P<0.05). This reinforces the synergistic impact of these two interventions on mitigating insulin resistance.

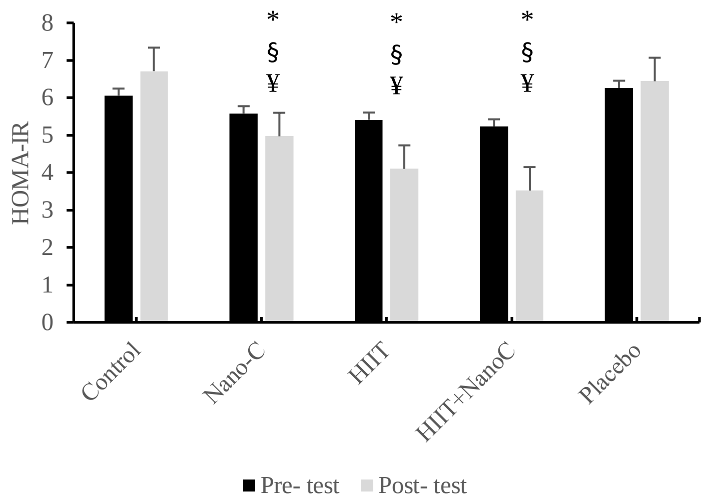

Figure 1. Effect of High Intensity Interval training and nanocurcumin consumption on HOMA-IR in obese and overweight women. (*): Significant compared to pre-test. (§): Significant compared to control group. (¥): Significant compared to placebo group. (†): Significant compared to nanocurcumin supplement group.

HbA1c

Regarding HbA1c levels, the repeated measures ANOVA results showed a significant main effect of time (F=25.10, P<0.001), a significant main effect of group (F=13.98, P<0.001), and a significant group × time interaction effect (F=9.87, P<0.001). These results suggest that HbA1c levels underwent significant changes during the study, with these variations being significantly different among the groups.

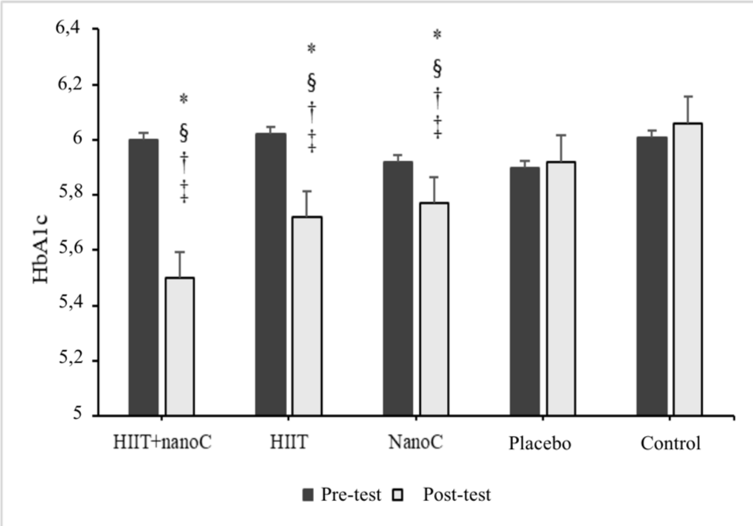

Figure 2. Changes in HbA1c levels at pre-test and post-test in the study groups. (*) Significant difference compared with the pre-test; (§) significant difference compared with the NanoC group; (†) significant difference compared with the Placebo group; (‡) significant difference compared with the Control group (p = 0.05).

Weight, BMI, and Body Fat %

The results indicated that weight, BMI, and body fat percentage exhibited significant effects of both time and group. Regarding body weight, there were significant main effects of time (P=0.001), group (P=0.001), and a significant time× group interaction (P=0.006). The HIIT group demonstrated a weight reduction of 5.51% compared to the control group (P=0.001), 5.44%5.44\%5.44% compared to the placebo group (P=0.001), and 4.26% compared to the nanocurcumin supplementation group (P=0.001). The NanoC+HIIT group achieved a weight reduction of 9.13%9.13\%9.13% relative to the control (P=0.001), 9.07%relative to the placebo (P=0.001), and 7.93% relative to the nanocurcumin group (P=0.003); however, no significant difference was observed between the HIIT and NanoC+HIIT groups (P=0.07).

In terms of BMI, both the effect of time (P=0.003) and the time ×\times× group interaction (P=0.002) were significant. The HIIT group showed a BMI reduction of 5.90% compared to the control (P=0.003), 4.74% compared to the placebo (P=0.047), and 4.48% compared to the nanocurcumin group (P=0.048). The NanoC+HIIT group exhibited BMI reductions of 9.98% compared to the control, 7.87% compared to the placebo, and 6.78% compared to the nanocurcumin group (all P=0.001); nonetheless, the difference between the HIIT and NanoC+HIIT groups was not statistically significant (P=0.13).

Regarding body fat percentage, the effects of time (P=0.001), group (P=0.001), and time ×\times× group interaction (P=0.004) were all significant. The HIIT group showed reductions of 3.75% relative to the control and 3.44%relative to the placebo; however, no significant differences were observed when compared to the nanocurcumin group (P=0.069) or the NanoC+HIIT group (P=0.11).

Serum Glucose, Insulin, and HOMA-IR

The Synergistic Effect of HIIT and Nanocurcumin Supplementation on Glycemic Levels in Obese Women

The results revealed significant main effects for time (P=0.001), group (P=0.001), and the times× group interaction (P=0.008) for serum glucose levels. Similarly, for the HOMA-IR index, significant effects were observed for time (P=0.001), group (P=0.001), and the time× group interaction (P=0.001).

Regarding mean serum glucose levels, compared to baseline, the NanoC, HIIT, and NanoC+HIIT groups showed reductions of 4.92%, 12.75%, and 14.72%, respectively, while the placebo group exhibited a 3.80% increase. Furthermore, the HIIT and NanoC+HIIT groups showed significantly greater reductions compared to the NanoC group, with decreases of 9.90% and 12.03% respectively (P=0.001).

For the HOMA-IR index, the NanoC, HIIT, and NanoC+HIIT groups demonstrated reductions of 25.93%, 38.90%, and 47.54%, respectively (all P=0.001). The most pronounced reduction was observed in the NanoC+HIIT group (P=0.001). Compared to the NanoC group, the HIIT and NanoC+HIIT groups showed reductions of 17.51% and 29.18%, respectively (P=0.001), although no significant difference was found between the HIIT and NanoC+HIIT groups (see Table 3).

HbA1c and Insulin Analysis
The Synergistic Effect of HIIT and Nanocurcumin on HbA1c and Insulin Levels

The results indicated that the effect of time on HbA1c levels was significant; overall HbA1c values decreased from pre-intervention to post-intervention regardless of the group (paired t-test: t=3.16, P=0.003), a decrease primarily driven by the intervention groups. The effect of the group was also significant (two-way ANOVA: F=5.20, df=4, P=0.001), with the HIIT and NanoC+HIIT groups exhibiting lower HbA1c levels. An additional analysis of the change in HbA1c (ΔHbA1c=pre−post) revealed significant inter-group differences (F=5.016, df=4, P=0.002), where intervention groups experienced more substantial reductions. Moreover, a significant time× group interaction was observed (F=4.904, df=4, P=0.001), with the NanoC+HIIT group demonstrating the greatest reduction, whereas the control group showed no significant change.
According to the data in Table 3, the combination of HIIT and nanocurcumin supplementation resulted in the most significant reduction in serum insulin levels (43.5%). This reduction is not only significant compared to the control group (which showed a 31.6% increase), but it is also substantially greater than the effects of either intervention alone (HIIT: 29% reduction; Nanocurcumin: 13% reduction). This finding highlights a potent synergistic effect between exercise and this supplement in improving insulin sensitivity.

TTE

In the present study, TTE was evaluated in five groups including HIIT, NanoC, NanoC+HIIT, placebo, and control during two phases: pre test and post test. The results showed that the interaction effect of time and group for TTE was significant (P<0.001). The greatest increase in TTE was observed in the NanoC+HIIT group (approximately a 3 minute increase compared with the pre test), followed by the HIIT group and then the NanoC group. In contrast, the changes observed in the placebo and control groups were minimal and not statistically significant.
Regarding time to exhaustion (TTE), the group effect was independently significant (P<0.001), whereas the effect of time alone was not significant (P=0.845).

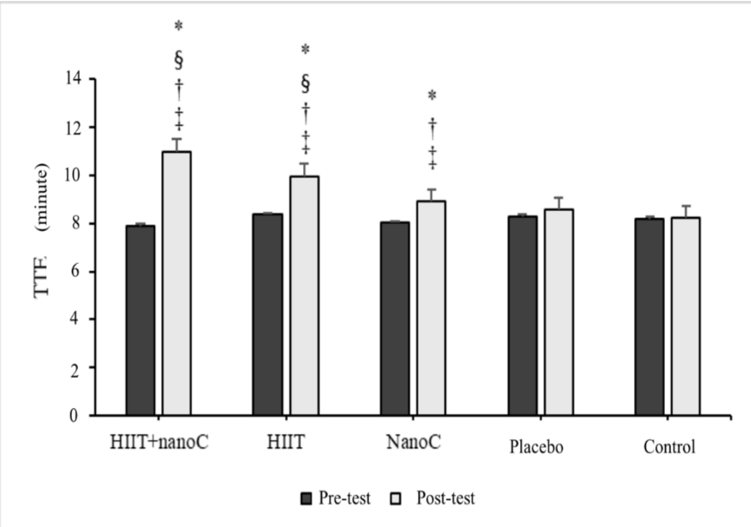

Figure 3. Changes in the TTE index at pre-test and post-test in the study groups. (*) Significant difference compared with the pre-test; (§) significant difference compared with the NanoC group; (†) significant difference compared with the Placebo group; (‡) significant difference compared with the Control group (p = 0.05)

4. Discussion

In the present study, the investigation of the effects of HIIT training, nanocurcumin supplementation, and their combination on serum glucose indices, HOMA IR, HbA1c, and TTE in obese or overweight women showed that all three interventions had significant effects on these variables. Previous studies clearly demonstrate that HIIT can improve insulin sensitivity and reduce serum glucose and HOMA IR (17,18) In addition, curcumin (especially in nano form) has often been reported as an anti-inflammatory and antioxidant compound that can improve metabolic function (15,19,20). The findings of one study showed that the combination of high intensity interval training with curcumin supplementation, as a noninvasive method, can produce positive and considerable effects in improving indices associated with type 2 diabetes (19). In another study, it was reported that 12 week supplementation with 80 mg per day of nanomicellar curcumin was able to improve MDA, TAC, and adiponectin levels, but it had no significant effect on hs CRP and NF ϰB within or between the groups (21). Fakhri and colleagues also reported in their study that curcumin supplementation combined with exercise training may have beneficial effects in strengthening the antioxidant system and preventing lipid peroxidation in overweight individuals (15).

The results of combining the two interventions (HIIT training and nanocurcumin) are to some extent consistent with the findings of studies that have examined the synergistic effects of curcumin and exercise (22). Many of these studies indicate that the combined effect of curcumin and exercise enhances the metabolic response. Naghizadeh reported in his study that the combination of high intensity interval training and curcumin consumption had a greater effect on improving glucose status and lipid profile in men with type 2 diabetes and hyperlipidemia compared with each intervention alone (22). Babaii and colleagues also showed in their study that the combination of high intensity interval training with curcumin supplementation, as a noninvasive approach, can produce positive and considerable effects in improving indices associated with type 2 diabetes (23).

However, some studies have reported smaller reductions or even different results following curcumin supplementation or HIIT training, which may be due to several differences (24,25). Among these factors are differences in the characteristics of the studied population, such as gender, baseline physical activity level, or health status (such as the presence of diabetes), variations related to the dose and form of curcumin consumption (nano form compared with the conventional form, amount, and duration of supplementation), differences in the intensity or duration of HIIT protocols, and the use of various measurement methods including different biological markers or short term assessments. In addition, shorter follow up periods or the absence of long term follow up in some studies may be another reason for the inconsistency of the results.

The anti-inflammatory and antioxidant properties of curcumin are primarily attributed to its ability to scavenge free radicals and inhibit pro-inflammatory pathways, such as nuclear factor-kappa B (NF-ϰB) and signal transducer and activator of transcription 3 (STAT3) (26,27). By suppressing these inflammatory mediators, curcumin can reduce oxidative stress and improve endothelial function, which are crucial for enhancing insulin sensitivity and mitigating the complications of metabolic syndrome. Furthermore, studies have suggested that curcumin may improve insulin signaling by activating AMP-activated protein kinase (AMPK) and enhancing glucose uptake in peripheral tissues (28). The nanoformulation of curcumin, as used in this study, offers enhanced bioavailability and absorption compared to conventional curcumin, potentially leading to more pronounced therapeutic effects.

High-intensity interval training (HIIT) is well-established to improve cardiorespiratory fitness, enhance mitochondrial function, and increase glucose transporter type 4 (GLUT4) expression in skeletal muscle (29,30). These adaptations collectively contribute to improved glucose disposal and insulin sensitivity. HIIT has also been shown to reduce visceral adipose tissue, a key contributor to metabolic dysfunction, and to modulate the release of myokines, which are signaling proteins produced by muscle that can exert beneficial effects on glucose metabolism and inflammation (31). The combination of HIIT with nanocurcumin may, therefore, offer synergistic benefits by simultaneously targeting inflammation, oxidative stress, and insulin signaling pathways, leading to a more comprehensive improvement in metabolic health.

The synergistic effect observed between HIIT and nanocurcumin supplementation in this study likely arises from the complementary mechanisms of action of these two interventions. While HIIT directly improves insulin signaling and energy expenditure, nanocurcumin provides potent anti-inflammatory and antioxidant support, protecting against exercise-induced oxidative stress and further enhancing insulin sensitivity. This dual action could lead to greater reductions in glucose levels, HOMA-IR, and HbA1c, as well as greater improvements in TTE, than either intervention alone. The enhanced bioavailability of the nanoform of curcumin may amplify these synergistic effects, ensuring that a sufficient concentration of curcumin reaches target tissues to exert its beneficial actions.

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Our findings align with previous research highlighting the efficacy of HIIT and curcumin in managing metabolic dysfunction (17,19,22). For instance, Naghizadeh et al. (22) reported similar synergistic effects of combined HIIT and curcumin on glucose and lipid profiles in men with type 2 diabetes. However, the present study uniquely utilized a nanomicellar formulation of curcumin and investigated its combined effects with HIIT in overweight/obese women, providing valuable insights into the potential of this specific intervention strategy in a relevant clinical population. The observed improvements in TTE also corroborate other studies showing enhanced exercise capacity following HIIT (29).

Despite the promising results, this study has several limitations. Firstly, the relatively short duration of the intervention (8 weeks) may not be sufficient to observe the long-term effects of the combined therapy. Secondly, while the nanoformulation of curcumin enhances bioavailability, individual responses can still vary. Thirdly, the study population, while relevant, consisted of overweight/obese women, and the findings may not be generalizable to other populations, such as men or individuals with different metabolic health statuses. Future research should aim to explore the long-term efficacy and generalizability of this combined intervention strategy across diverse demographic groups and to elucidate the precise molecular mechanisms underlying the observed synergistic effects.

5. Conclusion

Overall, the results of the present study demonstrate that the combination of HIIT and nanocurcumin acts synergistically, producing the greatest improvements in blood glucose control, reduction of HOMA-IR, reduction of HbA1c, and increase in TTE in obese women. These findings highlight the importance of implementing multi-modal interventions (exercise + supplementation) in the management of metabolic disorders.

6. Highlights

The findings of the present study showed that HIIT training and nanocurcumin supplementation can have beneficial effects on improving glucose metabolism as well as insulin resistance in obese women. Furthermore, the interactive (synergistic) effect of these two interventions produces more pronounced effects in improving glucose metabolism.

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Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

Authors' Contributions

Khalid Mohammadzadeh Salamat: Research design, supervision of data collection, interpretation of results, and writing and revising the article.

Tarifeh Babaii: Execution of the research protocol, data collection, statistical analysis of results, and designing the initial draft of the article.

Zaher Etemad: Assistance in interpreting results and reviewing and approving the initial and final versions of the article.

Supplementary Materials

This article does not contain Supplementary Materials.

Data Availability Statement

We have full control over all primary data and we are agreeing to allow the journal to review their data if requested.

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