Strength training and chromium picolinate supplementation do not reduce adiposity or improve muscle morphology in obese rats

El entrenamiento de fuerza y la suplementación con picolinato de cromo no reducen la adiposidad ni mejoran la morfología muscular en ratas obesas

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Abstract

Introduction: Obesity induces metabolic dysfunctions, such as insulin resistance and dyslipidemia, which negatively affect skeletal muscle remodeling and function. Strength training (ST) is an effective intervention to combat these changes, improving glycemic control, reducing adiposity, and increasing muscle mass. Chromium picolinate (CrPic), a nutritional supplement proposed to improve insulin signaling and protein synthesis, has been commercially promoted as a strategy to improve body composition. Although some mechanistic studies suggest beneficial effects of CrPic, there is limited evidence on its efficacy, particularly in combination with ST. Furthermore, the integrative impact of this association on skeletal muscle morphology and metabolic parameters in obesity remains unclear.
Objective: To investigate the effects of strength training combined with CrPic supplementation on skeletal muscle morphology, adiposity, lipid profile, and glucose tolerance in obese rats.
Methodology: We employed a 22-week experimental protocol, which was divided into three stages: (1) obesity induction, (2) obesity maintenance, and (3) ST protocol and/or CrPic intervention. We submitted rats to ST three times per week and administered CrPic daily via orogastric gavage.
Result: ST combined with CrPic supplementation did not promote a reduction in adiposity or in comorbities such as glucose intolerance and insulin resistance. In relation to biochemical parameters, rats that underwent ST combined with CrPic supplementation had a higher high-density lipoprotein concentration, suggesting a positive effect of ST. ST and CrPic did not promote morphological alterations in skeletal muscles.
Conclusion: ST in combination with CrPic supplementation is not an efficient tool to reduce adiposity and increase muscle mass.

Keywords

Chromium picolinate; hypercaloric diets; rats; strength training; obesity.

Resumen

Introducción: La obesidad ocasiona disfunciones metabólicas, como resistencia a la insulina y dislipidemia, que perjudican la remodelación y función del músculo esquelético. El entrenamiento de fuerza contrarresta estos efectos al mejorar el control glucémico, reducir la adiposidad y aumentar la masa muscular. El picolinato de cromo (CrPic), suplemento para optimizar la señalización de insulina y la síntesis proteica, se promociona para mejorar la composición corporal. Aunque estudios mecanicistas apuntan a beneficios de CrPic, la evidencia sobre su eficacia es limitada, sobre todo en combinación con entrenamiento de fuerza. El impacto conjunto de esta asociación en la morfología muscular y los parámetros metabólicos en obesidad no se ha definido.
Objetivo: Investigar los efectos del entrenamiento de fuerza con suplementación de CrPic sobre morfología del músculo esquelético, adiposidad, perfil lipídico y tolerancia a la glucosa en ratas obesas.
Metodología: Protocolo de 22 semanas en tres fases: inducción de obesidad, mantenimiento y fase de intervención con entrenamiento de fuerza y/o CrPic. Las ratas realizaron entrenamiento de fuerza tres veces por semana y recibieron CrPic por sonda orogástrica.
Resultados: La combinación de entrenamiento y CrPic no redujo adiposidad ni mejoró intolerancia a la glucosa o resistencia a la insulina. En bioquímica, el grupo con entrenamiento y CrPic mostró mayor HDLc, indicando efecto positivo atribuible al entrenamiento de fuerza. Ni el entrenamiento ni CrPic causaron cambios morfológicos en músculos esqueléticos.
Conclusión: En este modelo, el entrenamiento de fuerza con CrPic no es eficaz para reducir adiposidad ni aumentar masa muscular.

Palabras clave

Picolinato de cromo; dietas hipercalóricas; ratas; entrenamiento de fuerza; obesidad.

Introduction

Obesity is considered a chronic metabolic disease that is influenced by intrinsic and extrinsic factors; it is considered a risk factor for several medical complications (McPherson et al., 2019; Moreno-Fernández et al., 2018). This disease is associated with skeletal muscle reduction and increases in visceral fat pads, which can act to potentiate metabolic disorders (Mazurkiewicz et al., 2024; Mityukova et al., 2023; Zamboni et al., 2008). Muscle and adipose tissues are strongly interrelated from a pathogenic point of view. Indeed, sarcopenia can aggravate obesity and vice versa (Zamboni et al., 2008). In addition to musculoskeletal impairments, obesity is characterized by profound metabolic alterations, including increased adiposity, dyslipidemia, insulin resistance, and elevated blood pressure, which collectively exacerbate cardiovascular risk and metabolic inefficiency (Wilson et al., 2002; Fox et al., 2007; Gregolin et al., 2024). These systemic changes are intrinsically linked to muscle tissue homeostasis and function, as insulin signaling and lipid metabolism directly affect protein synthesis, energy balance, and muscle remodeling (Li et al., 2023). Therefore, the evaluation of these metabolic markers is essential to fully understand the physiological context in which muscle adaptations occur in obesity.

A reduction in muscle mass induces a 2%-3% decrease in the basal metabolic rate per decade after 20 years of age and a 4% decline per decade after 50 years of age (C.-H. Kim et al., 2000; Zoico et al., 2004).

Several studies have shown that strength training (ST) improves glycemic control, increases skeletal muscle strength and volume, and exerts positive changes in body composition (Lee et al., 2017; Mei et al., 2024; Santos et al., 2024). ST is recommended to promote greater energy expenditure, resulting in changes in body composition and reducing obesity-related risks (Contreiro et al., 2020; Guedes, Pieri, Luciano, Marques, Guglielmo, & Souza, 2019; H. J. Kim et al., 2022). Researchers have shown that ST decreases adipose tissue and increases skeletal muscle tissue and ameliorates the inflammatory condition triggered by obesity (Contreiro et al., 2020; Guedes, Pieri, Luciano, Marques, Guglielmo, & Souza, 2019; ìtalo Lourenço, 2020). In this regard, several studies have proposed different dietary supplements, which can be an alternative or adjunctive treatment option for many overweight individuals who wish to lose weight, promising to reduce adiposity more quickly and effectively than other strategies (Anton et al., 2008; Mautone Gomes et al., 2023).

Chromium picolinate (CrPic) is a synthetic compound formed by chelating trivalent chromium with picolinic acid, a tryptophan-derived metabolite that enhances its gastrointestinal absorption (DiSilvestro, 2007). Initially recognized for its role as an insulin cofactor, CrPic has been shown to improve glucose tolerance and carbohydrate metabolism (Mertz, 1969; Vincent, 2000; Tian, 2013), as well as to increase amino acid uptake and stimulate protein synthesis (Clarkson, 1997), which has led to its commercial promotion as a supplement with potential benefits in weight management (Tian, 2013). Mechanistic studies have demonstrated that CrPic can positively modulate insulin signaling pathways in skeletal muscle and adipose tissue. In obese, insulin-resistant rats, CrPic increased IRS-1 phosphorylation and PI3K activity, while reducing PTP1B expression and activity, thus enhancing intracellular insulin signaling (Wang et al., 2009). Similar molecular effects were observed in pigs supplemented with nano-CrPic, which upregulated PI3K, AKT, UCP3 and IL-15 expression in muscle and increased adiponectin while decreasing SOCS3 in adipose tissue, indicating improved insulin sensitivity and possible impacts on muscle hypertrophy and fat reduction (Hung et al., 2020). Additionally, in rats fed a high-fat diet, CrPic combined with biotin reduced HOMA-IR, plasma insulin, total cholesterol, and triglycerides, and modulated hepatic and cerebral expression of PPAR-γ, IRS-1 and NF-κB, further supporting its potential role in improving metabolic efficiency and body composition (Orhan et al., 2019).

However, there is no scientific evidence that this supplement reduces body mass in people with obesity and animal models of obesity (Gomes et al., 2005; Wang et al., 2009). Nevertheless, only a few studies have evaluated the combination between ST and CrPic supplementation, as well as whether this combination could potentiate a reduction in body mass and increase in muscle mass in obesity (Clancy, 1994; Yazaki et al., 2010).

Considering that metabolic parameters such as insulin sensitivity, lipid profile, and adiposity levels can influence skeletal muscle remodeling and hypertrophy capacity, these variables were included in the present study as complementary outcomes to provide a more integrative understanding of the physiological effects of strength training and chromium picolinate supplementation in obese rats.

Thus, the aim of this study was to investigate the effects of strength training combined with chromium picolinate supplementation on skeletal muscle morphology, adiposity, lipid profile, and glucose tolerance in obese rats. It was hypothesized that ST in combination with CrPic supplementation increases skeletal muscle mass and, consequently, reduces adipose tissue.

Method

Animals and Experimental Protocol

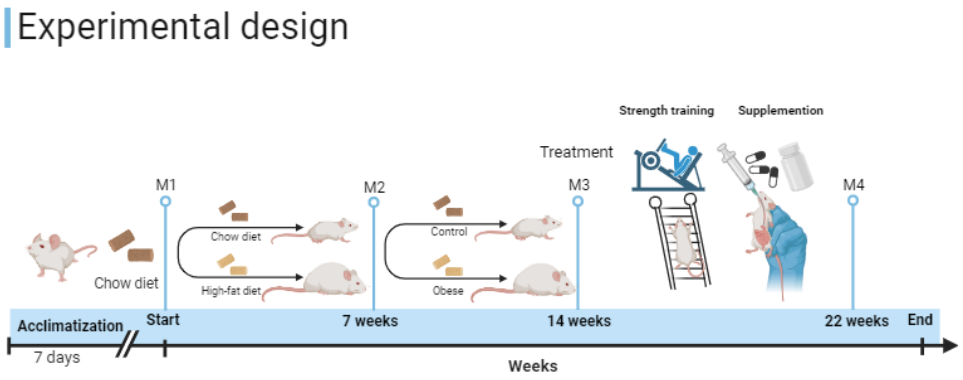
Seventy-three male Wistar rats aged 30 days were obtained from the Animal Facility of the Federal University of Espírito Santo (Espírito Santo, Brazil). The experimental procedures were performed by the Guide for the Care and Use of Laboratory Animals published by the US National Institutes of Health. This study was approved by the Animal Use Ethics Committee of the Federal University of Espírito Santo, under protocol 25/2017.

Experimental Design

Initially, during a brief acclimatization period (7 days), rats were individually housed in wire bottom cages on a 12/12 dark/light cycle with controlled temperature (24 ± 2°C) and humidity. (55 ± 5%). They had free access to the standard rodent chow (Agroceres®, Rio Claro, São Paulo, Brazil), which results in a heterogeneous distribution of body weight gain in these animals. After acclimatization for 7 days, the rats were randomly distributed into two groups: (1) control, fed a normocaloric diet (C, n = 11); and (2) obese, fed a high-fat diet (HFD) (Ob, n = 42). The C group was given standard rodent chow with 12.3% of the calories from fat, 57.9% from carbohydrates, and 29.8% from protein (Agroceres®, Rio Claro, São Paulo, Brazil). The Ob group received an HFD with 37.6% of the calories from fat, 44.6% from carbohydrates, and 17.8% from protein. All animals had free access to water and rat chow (40 g/day); after 24 hours the amount of food not ingested was measured.

The 22-week experimental protocol was divided into three stages, as shown in Figure 1: (1) induction of obesity (7 weeks), (2) maintenance of obesity (7 weeks), and (3) ST protocol and/or CrPic supplementation (8 weeks). The onset of obesity was determined according to previous studies carried out by our laboratory (Cordeiro, 2022; Lima-Leopoldo et al., 2014). At week 14, obese rats were distributed according to the absence or presence of CrPic supplementation and ST: obese (Ob; n = 10), obese subjected to CrPic supplementation (ObCr-Pic; n = 11), obese subjected to ST (ObST; n = 11), and obese subjected to ST and CrPic supplementation (ObSTCrPic; n = 10) (Figure 1). Because the aim was to evaluate only the effect of CrPic supplementation and/or ST in obese rats, the results from group C are not presented.

Figure 1. Schematic representation of the 22-week experimental protocol. Initially, animals were distributed into two groups: control (C; rats fed a normocaloric diet; n = 11) and obese (Ob; rats fed a high-fat diet; n = 42). After 7 weeks (obesity induction), the body weight of C and Ob rats was significantly different, and this time point was considered the onset of obesity. Obesity was maintained for 7 weeks. Then the obese rats were redistributed in obese (Ob), obese subjected to supplementation with chromium picolinate (ObCrPic), obese subjected to strength trainingg (ObST), and obese subjected to strength training and chromium picolinate supplementation (ObSTCrPic).



Food Consumption, Caloric Intake, and Feed Efficiency

Feed efficiency (FE; %) was calculated as [the total weight gain of the animals (g) / the total caloric intake (kcal)] × 100 [8]. Calorie intake (CI) was calculated with the following formula: weekly food consumption (FC) × the caloric value of each diet (g × kcal).

Nutritional Profile

The nutritional profile was determined by analyzing body weight (BW) and BF. The adiposity index (AI) was determined according to previous studies carried out by our laboratory (Cordeiro, 2022; Lima-Leopoldo et al., 2014a).

ST Protocol

Familiarization. At week 14, all groups were familiarized as described previously [12,34]. Familiarization of the ObST and ObSTCrPic groups with the load apparatus proceeded gradually by allowing the rats to climb for 3 non-consecutive days without any weight prior to the ST protocol. Specifically, the rats were stimulated to perform three complete climbs on the ladder, with a 60-second rest interval between climbs. After the familiarization period, the animals performed the initial and final maximum load carrying test (MLCT) as described previously (Hornberger, 2004; Melo et al., 2020). The absolute (g) and relative loads (%) were analyzed, and to compare between MLCT, the change (Δ) in force was calculated by using the formula (expressed as a percentage): [(final MLCT – initial MLCT) × 100] / initial MLCT (Neto et al., 2016a).

Progression of the ST Protocol. The rats were subjected to ST three times a week for 8 weeks. The protocol consisted of four climbs (series) of stairs with 50%, 75%, 90%, and 100% intensity of the pre-established MLCT. After performing the four series, the animals were subjected to a fifth series with 30 g added to the load to follow the evolution of the force and to adjust the maximum load. The recovery interval between sets was 60 seconds (Leite et al., 2013; Speretta et al., 2012).

CrPic Supplementation

The ObCrPic and ObSTCrPic groups were treated daily with CrPic solution by orogastric gavage (80 mg/kg/day CrPic; Chromax® chromium picolinate, Nutition 21, Inc., Saddle Brook, NY, USA) for 8 weeks. The supplement was administered so that the average daily consumption per rat was 8 µg/kg of mineral chromium per day (equivalent to 560 µg of chromium for a 70 kg adult human) (Komorowski, 2012). The CrPic dose was adjusted weekly according to the change in BW to maintain a constant CrPic dose throughout the study.

Euthanasia

At the conclusion of the experimental protocol (22 weeks), following an 6-hour fasting period, the animals were anesthetized and sedated with ketamine (70 mg/kg/i.p) and xylazine (10 mg/kg/i.p). In cases where animals still exhibited signs of nociceptive reflex after anesthetic induction, an anesthetic overdose (lethal dose) was administered, consisting of three times the doses of ketamine hydrochloride and xylazine hydrochloride used during the animal's anesthetic induction. Following euthanasia, the animals underwent a median thoracotomy to collect blood and tissue samples.

Comorbidities Associated with Obesity

After 22 weeks, systolic blood pressure (SBP) was measured indirectly by using the tail plethysmography method (Pfeffer et al., 1971). In addition, all rats were fasted for 4-6 hours prior to the glucose tolerance test as described previously (Pfeffer et al., 1971). For lipid and hormonal profile analysis, blood samples were collected in Falcon tubes and centrifuged at 10,000 rpm for 10 minutes and then stored at -80ºC. The insulin was determined by enzyme-linked immunosorbent assay (ELISA) using specific kits (Linco Research Inc, St. Louis, MO, USA). Serum concentrations of triglycerides (TG), total cholesterol, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) were determined by using specific kits (Bioclin®, Brazil) and analyzed with the BS-200 automated biochemical apparatus.

Measurement of the Skeletal Muscle Water Content

After removing the gastrocnemius, biceps, and tibialis muscles, wet weight (WW) and dry weight (DW) were determined before and after drying the samples at 60°C for 48 hours. Water content (%H2O) was estimated by using the following formula: %H2O = [(WW – DW) / WW] × 100.

Skeletal Muscle and Adipose Tissue Histology

The gastrocnemius, tibialis anterior, and biceps brachii muscles from the left hindlimb were removed and fixed. Tissue sections (5 µm thick) were transferred to slides and stained with hematoxylin and eosin (HE). Images were captured with a camera attached to an optical microscope (Eclipse 400, Nikon) at 40× magnification. One-hundred cells per animal were evaluated to calculate the cross-sectional area with Image J Pro-Plus® (National Institutes of Health, Bethesda, MD, USA). The weight of skeletal muscles was normalized by the tibia length to evaluate skeletal muscle hypertrophy.

Adipose tissue was fixed for 24 hours in 4% paraformaldehyde with 0.1 M phosphate buffer (pH 7.4). After dehydration in ethanol and clearing in xylol, the tissue was embedded in paraffin to form blocks. Sections (5 µm thick) were obtained using a LEICA RM2125 microtome (LEICA Biosystems Inc., Buffalo Grove, IL, USA) and stained with HE. Five fields of retroperitoneal and visceral fat were analyzed, from which 16 adipocytes were quantified, resulting in a total of 80 adipocytes used to calculate the cell area (µm2). Sample selection was performed randomly, and histological processing and morphometric analyses were carried out by an independent investigator blinded to the experimental groups. This approach characterizes a double-blind procedure, ensuring the reliability and impartiality of data collection and analysis.

Statistical Analysis

All data were tested for normality using the Shapiro–Wilk test. Variables are presented as mean ± standard deviation (SD). Comparisons between two independent groups (e.g., Control vs. Obese) were performed using Student's t test for independent samples. For comparisons involving more than two groups or time × group interactions, two-way analysis of variance (ANOVA) or two-way repeated measures ANOVA was used, followed by Tukey or Bonferroni post hoc tests, as appropriate. Statistical significance was set at $p < 0.05$. All statistical analyses and graphical representations were performed using GraphPad Prism version 8.0 (GraphPad Software, San Diego, CA, USA).

Results

Characterization of Obesity

Figure 2 illustrates the evolution of BW from weeks 1 to 14. There was no significant difference in BW between the C and Ob groups until week 4, when the Ob group was significantly heavier than the C group. We characterized this time as the onset of obesity. The Ob group remained significantly heavier than the C group up to week 14.

Figure 2. Evolution of body weight over 14 weeks; week 4 was the onset of obesity. The experimental groups are control (C, n = 11) and obese (Ob, n = 42). The data are presented as the mean ± standard deviation and were analyzed with two-way repeated measures ANOVA followed by the *post hoc* Bonferroni test (*p < 0.05).

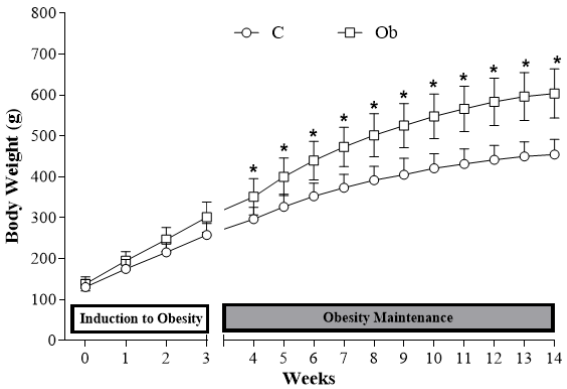


Table 1 shows the general characteristics of the periods of induction and maintenance of obesity in the C and Ob groups. The Ob group had significantly higher final BW (32.75%), weight gain (43.83%), caloric intake, and feed efficiency compared with the C group. However, food consumption was reduced in the Ob group compared with the C group.

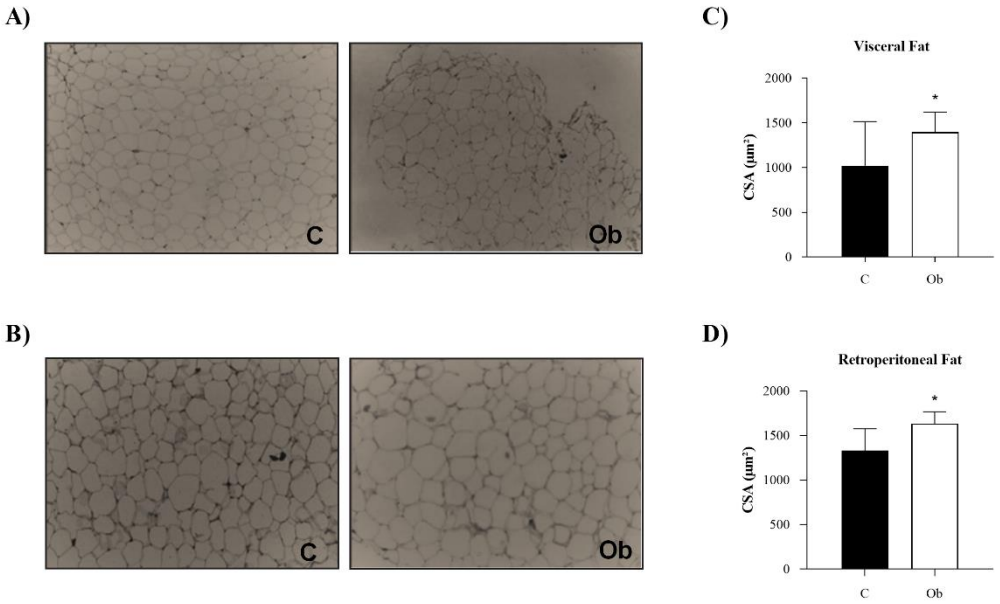
Table 1. General characteristics of the periods of induction and maintenance of obesity

		Experimental groups
Variables	C (n = 11)	Ob (n = 42)
IBW (g)	130 ± 18	138 ± 17
FBW (g)	455 ± 37	604 ± 60*
BWG (g)	324 ± 32	466 ± 55*
FC (g/day)	25.8 ± 0.8	17.7 ± 0.9*
CI (g × kcal/day)	75.4 ± 2.4	81.4 ± 4.1*
FE (%)	4.39 ± 0.41	5.85 ± 0.77*

The experimental groups are control (C, n = 11) and obese (Ob, n = 42). IBW = initial body weight; FBW = final body weight; BWG = body weight gain; FC = food consumption; CI = caloric intake; FE = feed efficiency. The data are presented as the mean ± standard deviation and were analyzed with Student's t test for independent samples (*p < 0.05).

The cross-sectional areas of visceral and retroperitoneal fat cells at the end of the 22-week experiment are summarized in Figure 3. The Ob group presented significantly larger cross-sectional areas in these fat deposits compared with the C group, emphasizing the effectiveness of an HFD in the development of obesity.

Figure 3. The effect of obesity on the size of the visceral and retroperitoneal adipocyte of Wistar rats after 22 weeks. Representative histological images of visceral (A) and retroperitoneal (B) fat pads stained with hematoxylin and eosin. The cross-sectional areas (CSA) of visceral (C) and retroperitoneal fat (D) adipocytes. The scale bar is 50 µm. The experimental groups are control (C; n = 6) and obese (Ob; n = 5). The data are presented as the mean ± standard deviation and were analyzed with Student's t test for independent samples (*p < 0.05).



ST and CrPic Supplementation in Obesity

Figure 4 shows the evolution of BW from weeks 15 to 22 after redistributing the obese rats into the treatment groups. There was no significant difference in BW between the Ob, ObCrPic, ObST and ObST-CrPic groups over the treatment period. Note that the C group is only presented in the graph as a reference; it was not considered in the statistical analyses.

Figure 4. Evolution of body weight during the 8 weeks of strength training and/or chromium picolinate supplementation. The experimental groups are control (C, n = 11), sedentary obese (Ob, n = 10), obese subjected to chromium picolinate supplementation (ObCrPic, n = 11), obese subjected to strength training (ObST, n = 11), and obese subjected to strength training and chromium picolinate supplementation (ObSTCrPic, n = 10). The data are presented as the mean ± standard deviation and were analyzed with two-way ANOVA followed by the *post hoc* Tukey test.

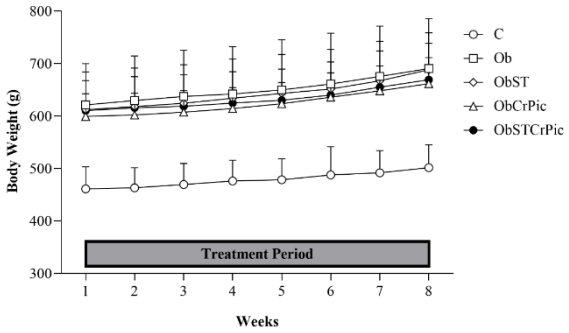


Table 2 shows the general characteristics of the experimental groups after treatment from weeks 8 to 15. There was no significant difference between the groups regarding the evaluated adiposity and nutritional parameters.

Table 2. General characteristics of rats subjected to strength training and/or chromium picolinate supplementation.

	Experimental groups			
Variables	Ob	ObCrPic	ObST	ObSTCrPic
IBW (g)	621 ± 79	599 ± 43	612 ± 72	610 ± 57
FBW (g)	690 ± 95	661 ± 50	688 ± 71	669 ± 70
BW gain (g)	69 ± 29	62 ± 19	76 ± 17	59 ± 34
Epididimal fat pad (g)	13.4 ± 3.9	11.4 ± 5.2	12.7 ± 3.6	12.4 ± 2.4
Retroperitoneal fat pad (g)	34.1 ± 9.7	33.9 ± 12.2	36.9 ± 9.0	31.3 ± 5.1
Visceral fat pad (g)	18.5 ± 5.6	17.0 ± 5.8	18.9 ± 4.1	17.0 ± 6.0
BF (g)	66.0 ± 17.9	62.3 ± 20.9	68.5 ± 1.3	60.7 ± 12.2
AI (%)	9.44 ± 1.73	9.36 ± 2.86	9.89 ± 1.45	9.03 ± 1.09
FC (g/day)	17.2 ± 0.3	17.1± 0.5	17.0 ± 0.7	16.7 ± 0.4
CI (g x Kcal/day)	78.7 ± 1.5	78.3 ± 2.2	77.8 ± 3.0	76.5 ± 1.7
FE (%)	1.57 ± 0.66	1.43 ± 0.43	1.74 ± 0.37	1.37 ± 0.80

The data are presented as the mean ± standard deviation and were analyzed with two-way ANOVA followed by the *post hoc* Tukey test. The experimental groups are sedentary obese (Ob, n = 10), obese subjected to chromium picolinate supplementation (ObCrPic, n = 11), obese subjected to strength training (ObST, n = 11), and obese subject to strength training and chromium picolinate supplementation (ObSTCrPic, n = 10). IBW = initial body weight; FBW = final body weight; BWG = body weight gain; BF = body fat; AI = adiposity index; FC = food consumption; CI = caloric intake; FE = feed efficiency.

There were no significant differences in the absolute and relative training loads between the groups in the initial MLCT (pre-training), but the maximum workload capacity of the groups subjected to ST (i.e., ObST vs. Ob and ObSTCrPic vs. ObCrPic) was increased throughout the training period (Figure 5A and B). In addition, the maximum carrying load capacity increased significantly in the ObST and ObSTCrPic groups compared with the Ob and ObCrPic groups (27% and 25%, respectively) (Figure 5A). Regarding the relative load carried, the groups subjected to ST presented higher values than the sedentary groups (Figure 5B). Furthermore, Δ Force was elevated in the ObST and ObSTCrPic groups compared with the Ob and ObCrPic groups (Figure 5C). There was no difference between the ObST and ObSTCrPic groups.

Figure 5. Strength performance of the groups in the initial maximum load carrying test (IMCLT) and the final maximum load carrying test (FMCLT). The experimental groups are sedentary obese (Ob, n = 9), sedentary obese subjected to chromium picolinate supplementation (Ob-CrPic, n = 10), obese subjected to strength training (ObST, n = 10), and obese subjectedto strength training and chromium picolinate supplementation (ObSTCrPic, n = 11). The data are presented as the mean ± standard deviation and were analyzed with ANOVA followed by the *post hoc* Tukey test (*p < 0.05 vs. Ob; #p < 0.05 vs. ObCrPic; &IMCLT vs. FMCLT).

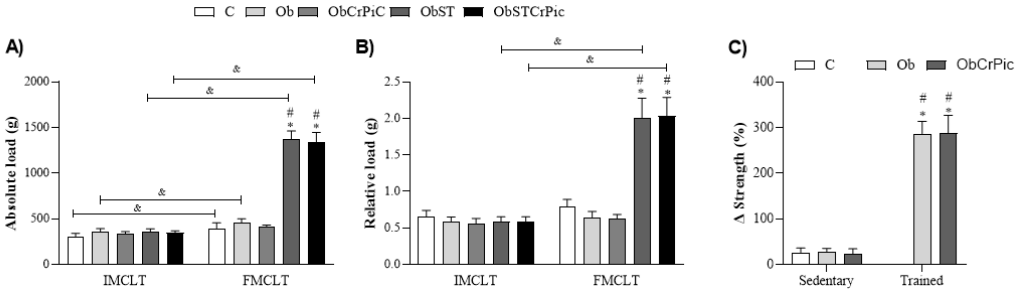


Table 3 shows the lipid profile data for the experimental groups. The ObSTCrPic group had a higher HDL concentration compared to the Ob and ObCrPic groups. When comparing only the ObSTCrPic group with the ObCrPic group, it can be suggested that ST has a positive effect.

Table 3. Biochemical profile.

	Experimental groups			
Variables	Ob	ObCrPic	ObST	ObSTCrPic
TG (mg/dL)	19.5 ± 7.3	24.1 ± 5.1	22.4 ± 9.4	20.0 ± 9.9
T-Chol (mg/dL)	60.8 ± 11.7	66.5 ± 12.0	62.7 ± 6.0	67.2 ± 4.7
LDL (mg/dL)	6.0 ± 2.0	6.9 ± 3.0	6.8 ± 1.7	6.2 ± 0.7
HDL (mg/dL)	18.7 ± 3.4	19.8 ± 3.5	22.0 ± 1.0	23.2 ± 1.7*#

TG: triglycerides; T-Chol: total cholesterol; LDL: low-density lipoprotein; HDL: high-density lipoprotein: Ob (n=5); ObCrPic (n=6); ObST (n=6) and ObSTCrPic (n=6). The data are presented as the mean ± standard deviation and were analyzed with two-way ANOVA followed by the *post hoc* Tukey test (*p < 0.05 vs. Ob; #p < 0.05 vs. ObCrPic).

Figure 6 shows the data for systolic blood pressure (Figure 6A), glucose tolerance test (Figure 6B), and area under the glycemic curve (Figure 6C) in the different experimental groups. No significant differences in systolic blood pressure were observed between the groups (p > 0.05). In the glucose tolerance test, all treated groups (ObCrPic, ObST, and ObSTCrPic) showed profiles similar to the Ob group, with no statistically significant differences in blood glucose levels at the different time points evaluated. Consequently, the analysis of the area under the curve (AUC) also revealed no differences between the groups, indicating that neither chromium picolinate nor physical training, alone or in combination, promoted significant changes in the glycemic response during the test.

Figure 6. Comorbidities associated with obesity. The experimental groups are sedentary obese (Ob, n = 10), obese subjected to chromium picolinate supplementation (ObCrPic, n = 11), obese subjected to strength training (ObST, n = 11), and obese subjected to strength training and chromium picolinate supplementation (ObSTCrPic, n = 10). AUC: area under the glucose curve; SBP: systolic blood pressure; The data are presented as the mean ± standard deviation and were analyzed with two-way ANOVA followed by the *post hoc* Tukey test (&p < 0.05 vs. C).

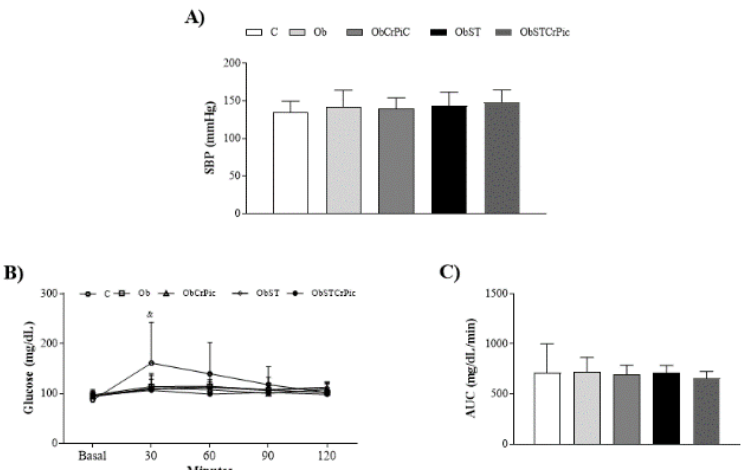


Table 4 shows the water content of the gastrocnemius, tibialis, and biceps brachii muscles at the end of the 22-week experimental protocol. The ObSTCrPic group had a lower water content in the biceps brachii compared with the ObCrPic group. For the tibialis and gastrocnemius, there were no significant differences between the groups.

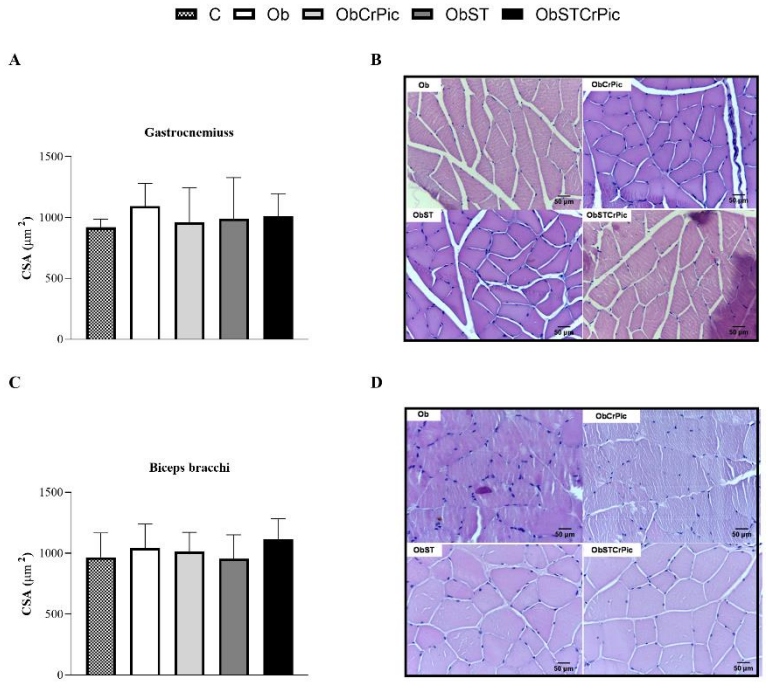
Table 4. Morphometric parameters and water content in skeletal muscles.

	Experimental groups			
Variables	Ob	ObCrPic	ObST	ObSTCrPic
Gastrocnemius (%)	74.3 ± 2.6	74.6 ± 1.0	74.0 ± 0.6	74.6 ± 2.2
Tibialis (%)	73.0 ± 2.0	74.7 ± 2.0	74.4 ± 1.7	76.5 ± 6.1
Biceps brachii (%)	74.8 ± 2.1	77.2 ± 2.4	76.3 ± 2.8	73.3 ± 3.9#
Gastrocnemius/tíbia (g/cm)	0.59 ± 0.05	0.60 ± 0.07	0.59 ± 0.06	0.60 ± 0.04
Tibialis/tíbia (g/cm)	0.22 ± 0.02	0.23 ± 0.05	0.21 ± 0.07	0.23 ± 0.02
Biceps brachii/tíbia (g/cm)	0.07 ± 0.01	0.08 ± 0.02	0.08 ± 0.01	0.08 ± 0.01

The experimental groups are sedentary obese (Ob, n = 10), obese subjected to chromium picolinate supplementation (ObCrPic, n=11), obese subjected to strength training (ObST, n = 11), and obese subjected to strength training and chromium picolinate supplementation (ObSTCrPic, n = 10). The data are presented as the mean ± standard deviation and were analyzed with two-way ANOVA followed by the *post hoc* Tukey test (#p < 0.05 *vs.* ObCrPic).

Figure 7 illustrates the morphology of the gastrocnemius, tibialis, and biceps brachii muscles. There were no significant differences between the groups.

Figure 7. Histological sections of the gastrocnemius (A), tibialis (B), and biceps brachii (C) muscles. The cellular cross-sectional area (CSA) of the gastrocnemius (D), tibialis €, and biceps brachii (F) muscles. The experimental groups are sedentary obese (Ob, n = 7), obese subjected to chromium picolinate supplementation (ObCrPic, n = 7), obese subjected to strength training (ObST, n = 7), and obese subjected to strength training and chromium picolinate supplementation (ObSTCrPic, n = 7). The data are presented as the mean ± standard deviation and were analyzed with two-way ANOVA followed by the *post hoc* Tukey test.



Discussion

We investigated the influence of ST and CrPic supplementation on the skeletal muscle morphology of obese rats. Despite the fact that the ST protocol increased strength, it was not able to modify body composition and promote skeletal muscle hypertrophy in obese rats. In addition, ST combined with CrPic supplementation was not an efficient tool to reduce body fat and increase muscle strength.

Our experimental design included the induction and maintenance of obesity. The onset of obesity at week 8, based on a significant difference in BW, is in agreement with other studies that also found a significant difference in BW in a HFD-induced obesity model in the first weeks of the protocol (Cordeiro,

2022; Francisqueti et al., 2017; Lima-Leopoldo et al., 2014b). Moreover, the higher caloric intake consumed by the obese group maintained the elevated BW and obesity throughout the experiment(Cordeiro, 2022; Lima-Leopoldo et al., 2014). The FE also accounts for the elevated BW and adiposity observed in the rats fed an HFD (Cardoso et al., 2023; Dankel et al., 2021; Iossa et al., 2000). These findings are associated with the high obesogenic effect of this diet, which leads to a reduction in the rate of lipid oxidation as opposed to an excessive intake of fats, favoring lipogenesis, increasing the oxidation of proteins, and contributing to reduce energy expenditure (Cardoso et al., 2023; Dankel et al., 2021; Iossa et al., 2000).

In disagreement with our initial hypothesis, this study did not show a reduction in body fat with isolated ST. Several hypotheses can explain why ST did not reduce BW and body fat. The first is related to the fact that ST was not able to develop a negative energy balance in these animals. This conclusion is supported by the unchanged food consumption, caloric intake, and feed efficiency, as well as the absence of significant reductions in body weight, adiposity index, and fat deposit weight. Thus, for there to be significant weight loss, it is essential to associate physical exercise with a low-calorie diet. Therefore, it seems that only the caloric expenditure resulting from physical exercise is not enough to reduce body fat (Damiani et al., 2020; Laurindo et al., 2021).

In addition to submitting obese rats to ST, we investigated the effect of CrPic alone or combined with ST on body parameters. Chromium increases glucose uptake based on increased insulin sensitivity. In a previous study, the authors emphasized that insulin sensitivity is dependent on the level of chromium supplementatio, which stimulates the insulin receptor tyrosine kinase activity in the plasma membrane, triggering intracellular signaling reactions with the objective of stimulating the translocation of glucose transporters (GLUT) (Gomes et al., 2005). In the current study, we administered 1 mg/kg/day of CrPic for 8 weeks via orogastric gavage, adjusting the dose each week based on the change in BW. However, researchers have emphasized that dosages between 200 and 1000 µg/day in a short period of time do not produce positive effects regarding the loss of fat and lean mass gain (Dong et al., 2007; Staniek et al., 2013) . The effects related to insulin sensitivity are postulated to be triggered with doses equivalent to 1,000 µg/day (Cefalu, 2002). Studies evaluating the effect of CrPic (1 mg/kg/day) found no effect on glucose and sensitivity to insulin action (Staniek et al., 2013; Wang et al., 2009). Thus, the administration of low doses of CrPic within a short treatment period may be the reason for the absence of positive effects on body composition. The main difference between this study and other CrPic supplementation protocols is the methodology to ensure actual consumption: While other studies (Dong et al., 2007; Staniek et al., 2013) provided CrPic ad libitum in water, we opted for administration via orogastric gavage.

Evidence has shown that physical exercise is not only an important factor in reducing BW, but also as a significant stimulator of anti-inflammatory responses, and, consequently, reduces the risks of associated chronic diseases such as type 2 diabetes, hypertension, and atherosclerosis (Effting et al., 2022; Guedes et al., 2019). Atherosclerotic plaques are normally formed by disturbances in the metabolism of lipoproteins and lipids, which are risk factors for cerebrovascular and coronary artery diseases (Fraga et al., 2017; Liang et al., 2021). As physical exercise participates in the elimination of cholesterol, HDL is considered antiatherogenic (Effting et al., 2022; Guedes et al., 2019). In the present study, ST was demonstrated to significantly elevate HDL levels in rats, an effect observed independently of CrPic. This outcome aligns with the findings of Albarello et al. (2017), who illustrated that ST elicits an increase in HDL levels, while leaving body composition and biochemical parameters of total cholesterol, triglycerides, low-density lipoprotein, and glucose unaffected. These findings underscore the potential of ST to positively influence lipid profiles, particularly with regard to HDL augmentation, thus potentially contributing to the prevention of cardiovascular diseases.

ST and CrPic supplementation had no effects on skeletal muscle morphology in obese rats: There were no significant differences in the weights and cross-sectional areas of the muscles after the ST protocol. These results are consistent with previous studies that also did not find significant changes after ST with a vertical ladder apparatus (Chi et al., 2020; Neto et al., 2016).

Multiple factors can contribute to the divergence between our results and literature. For example, Nascimento, (2017) found a 45% increase in the cross-sectional area of the triceps brachii in animals trained using a ladder apparatus. Researchers have used several ST protocols that vary regarding the training frequency, volume, and intensity relative to the animal's weight and/or strength performance (Chi et al., 2020; Í. Lourenço et al., 2020; Neto et al., 2016). The staircase training model has previously been

considered inefficient in the literature. Hornberger Jr. & Farrar, (2004) examined its effects on various muscles including the soleus, plantaris, flexor hallucis longus (FHL), gastrocnemius, and quadriceps femoris. Their findings indicated that only the FHL muscle experienced significant effects from the training. However, these results have been recently challenged, with suggestions that the measures used might not effectively reflect the true impact of the training (Í. Lourenço et al., 2020). In contrast, Tibana et al. (2017) demonstrated that although resistance training does not lead to increased muscle mass, it is effective in inducing significant growth in the average cross-sectional area of muscle fibers and enhancing the load-bearing capacity of rodents.

Our study also assessed the impact of the Staircase Training (ST) protocol on strength performance. Rats subjected to ST were able to carry progressively larger loads over time, indicating strength gains. While some studies have reported that excess adipose tissue can impair functional capacity (Dlamini & Khathi, 2024; Li et al., 2025; Sheptulina et al., 2023), studies evaluating ST with a vertical ladder device have noted improved functional performance under obese conditions (H. J. Kim et al., 2022; Lim et al., 2022; Tang et al., 2016). The CrPic did not enhance ST-induced strength gains, highlighting the positive effect of ST alone.

It is well-established that resistance training leads to a series of neural and muscular adaptations (Damas et al., 2018; Krutki et al., 2017). Although a single session of resistance training increases protein synthesis, significant changes in muscle size are not typically observed in the early weeks of regular exercise (Krause Neto et al., 2024; Otis et al., 2005). Strength gains, particularly in the initial phases, are primarily attributed to neural adaptations and improvements, such as increased motor unit recruitment, better rate coding, synchronization, and double discharges (Damas et al., 2018; Krutki et al., 2017; Schoenfeld, 2020).

The current study employed an ST protocol of only 8 weeks, which may not have provided sufficient time for muscle adaptations, including increases in muscle mass and cross-sectional area of the gastrocnemius and biceps brachii muscles. Previous research has shown that ST protocols can increase strength without corresponding changes in muscle mass (Carbone et al., 2017; Perilhão et al., 2020). Additionally, studies suggest that the ST stimulus was potent enough to remodel the neuromuscular junction structure, indicating that the effect cannot be attributed to muscle fiber hypertrophy or fiber-type conversion (Arabzadeh et al., 2022; Deschenes et al., 2000; Krause Neto et al., 2024).

In addition, obesity can damage skeletal muscles, and there may be capillary refraction, which impairs the function of tissue because it no longer receives oxygen and nutrients (Paavonsalo et al., 2020). Another explanation may be related to the fact that obesity has negative consequences on postprandial myofibrillar protein synthesis of protein-rich foods (Beals et al., 2018). The interaction between ST and nutrition on the stimulation of myofibrillar protein synthesis rates is decreased in adults with obesity compared with adults with a normal weight (Beals et al., 2018). For this reason, we suggest that the low rate of protein synthesis may be one of the reasons why obese rats did not exhibit skeletal muscle hypertrophy.

In the current study, no significant differences were found in the cross-sectional areas and weights of skeletal muscles in the CrPic-treated groups. This result contradicts the assumption that CrPic is a dietary supplement that can positively influence muscle mass gain, promoting greater stimulation of amino acid uptake and consequently increasing protein synthesis (Clarkson, 1997). However, taken together, scientific evidence regarding its efficacy in this aspect is limited, with varied methodologies and conflicting results (Lukaski et al., 2007; Pittler et al., 2003). Furthermore, a review study (Tian et al., 2013) concluded that the effects of CrPic on body composition and muscle mass gain are minimal and inconsistent.

Thus, the evidence does not provide support for the benefits of CrPic, showing mixed or inconclusive results regarding its efficacy in improving body composition (Marmett & Nunes, 2016; Pittler et al., 2003), lipid metabolism (Deschenes et al., 2000), insulin sensitivity (Staniek et al., 2013; Wang et al., 2009), or muscle mass gain (Pittler et al., 2003). Moreover, there is not robust knowledge regarding the safety and toxicity of high doses of the supplement (Tian et al., 2013). Therefore, more high-quality research and well-designed studies are needed to accurately determine the efficacy of chromium picolinate as a supplement for muscle mass gain, especially in the condition of obesity.

Limitations

Despite the relevance of the findings, this study presents some limitations that must be acknowledged. First, the duration of the resistance training protocol (eight weeks) may have been insufficient to induce significant morphological adaptations in skeletal muscle, particularly in the context of obesity—a condition that inherently impairs protein synthesis and the anabolic environment necessary for muscle hypertrophy. Previous studies have shown that more pronounced structural adaptations in muscle tissue typically require longer intervention periods.

Another important limitation relates to the chromium picolinate supplementation dose (1 mg/kg/day), which, according to existing literature, may not be adequate to promote meaningful metabolic changes, especially over a short duration. Additionally, the supplementation period may have been too brief to elicit consistent effects on body composition and muscle morphology. Future studies with extended intervention durations, higher supplementation doses, and additional nutritional control are warranted to confirm and expand upon the present findings.

Conclusions

In summary, the ST protocol was effective in improving strength performance in obese rats. However, neither ST alone nor in combination with chromium picolinate (CrPic) supplementation was sufficient to induce significant changes in body composition or skeletal muscle morphology. The lack of hypertrophic response may be related to the short duration of the training period, the physiological impairments associated with obesity, and the low dose and short-term administration of CrPic. These findings highlight the complexity of promoting morphological and metabolic adaptations in skeletal muscle under conditions of diet-induced obesity and suggest that more prolonged interventions or combined strategies may be necessary to achieve these outcomes.

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