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REVIEW ARTICLE

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Validation of protocol for the treatment of obesity by the ketogenic diet, vitamin D and metabolic activators: a systematic umbrella review

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Abstract

Introduction: Obesity remains a major health risk worldwide, with a burden of comorbidities and mortality of up to 2.8 million people per year. However, implementing appropriate dietary regimens for weight reduction can potentially mitigate the epidemic of obesity and its comorbidities. Among these regimens, vitamin D, ketogenic diet, L-carnitine, morosil®, inositol, taurine, and coenzyme Q10 stand out. **Objective:** To present the main clinical studies, meta-analyses, consensuses, and guidelines to support the efficacy and safety of the treatment protocol for obesity and its comorbidities. **Methods:** The PRISMA Platform systematic review rules were followed. The search was conducted from January to February 2025 in the Web of Science, Scopus, Embase, PubMed, Science Direct, Scielo, and Google Scholar databases. The quality of the studies was based on the GRADE instrument, and the risk of bias was analyzed according to the Cochrane instrument. **Results and Conclusion:** A total of 153 articles were found, and 54 articles were evaluated in full, and 34 were included in this systematic review. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 16 studies with a high risk of bias and 26 studies that did not meet GRADE and AMSTAR-2. Most studies showed homogeneity in their results, with X^2=87.8% >50%. It was concluded that the main clinical studies, meta-analyses, consensuses, and guidelines published to date indicate promising results to support the efficacy and safety of the treatment protocol for obesity and its comorbidities, with the most solid results being presented by studies of vitamin D, ketogenic diet, and L-carnitine. The studies revealed that morosyl, inositol, taurine, coenzyme Q10, and chromium picolinate present better results in treating obesity when associated with other metabolic activators. Therefore, the proposal of the present treatment protocol can be validated by the associated use of these compounds in the treatment of patients with obesity.

Keywords: Obesity. Comorbidities. Ketogenic diet. Vitamin D. Metabolic activators. Protocol.

Highlight - Protocol

This study was developed to scientifically consolidate the obesity treatment protocol, as presented in the protocol below:

- **1st stage:** Based on clinical studies, guidelines, and consensus, perform vitamin D correction (establish a vitamin D correction standard, that is, what amount of vitamin D to inject into the muscle according to the patient's deficiency).
- **2nd stage:** Administer the ketogenic diet to patients with obesity.
- **3rd stage:** Application once a week to the muscle of "morosil®, L-carnitine, inositol, taurine, coenzyme Q10, and chromium picolinate"
- After 10 weeks, follow up the protocol by changing the ketogenic diet to a low-carb diet and continuing to inject into the muscle every two weeks.

Introduction

Obesity remains a major health risk worldwide, with a burden of comorbidities and a mortality rate of up to 2.8 million people per year. This widespread problem is closely linked to the development of chronic diseases, including diabetes, hypertension, and heart disease, all of which are predominantly associated with an unhealthy lifestyle and poor dietary habits. However, implementing appropriate dietary regimens for weight reduction can potentially mitigate the obesity epidemic to some extent. Among such regimens, the very low-carbohydrate, high-fat ketogenic diet has emerged as a highly effective approach for rapid weight loss **[1,2]**.

In addition, hypovitaminosis D is highly prevalent and constitutes a public health problem worldwide. It can affect more than 90% of individuals, depending on the population studied. Bioactive compounds derived from natural foods and plants have been widely used to prevent and manage metabolic disorders such as obesity, type 2 diabetes, insulin resistance, non-alcoholic fatty liver disease (NAFLD), and cardiovascular diseases (CVD) due to their diverse health benefits.1 Furthermore, a 2008 World Health Organization report revealed that up to 80% of diabetic patients rely on natural products for the treatment of their condition.2 Therefore, the consumption of bioactive compounds in foods is an effective strategy to reduce the risks of metabolic diseases **[3,4]**.

Since excessive reactive oxygen species (ROS) production causes mitochondrial defects, the antioxidant properties of bioactive dietary compounds may be suitable targets for improving mitochondrial function. Dietary antioxidants, such as resveratrol, quercetin, coenzyme Q10, curcumin, and astaxanthin, are abundant in grapes and berries, vegetables and fruits, turmeric (Curcuma longa Linn.), salmon, and shrimp, respectively **[5]**.

Furthermore, these bioactives have demonstrated beneficial health effects, including antioxidant and anti-inflammatory effects that can reduce mitochondrial oxidative damage. In particular, they are known to improve mitochondrial dysfunction and mitigate obesity-associated metabolic diseases. Therefore, it is crucial to identify bioactive dietary components and natural products capable of maintaining mitochondrial integrity and function to prevent obesity-associated metabolic diseases. This review summarizes the current knowledge on some selected bioactive components that can preserve mitochondrial homeostasis, thus offering potential preventive and therapeutic avenues for mitochondria-related metabolic disorders **[5]**.

The ketogenic diet (KD) has gained clinical attention for its potential benefits in weight loss and metabolic syndrome. By mimicking fasting through carbohydrate restriction, KD shifts energy utilization to ketone bodies (KB) instead of glucose. Despite promising results, the effects on different weight loss indicators remain controversial, with challenges in monitoring adherence patterns, optimal macronutrient composition, potential risks, and long-term sustainability. This article aims to review the different weight loss outcomes of KD interventions for obesity, monitored by KB (adherence indicator) **[6]**.

Current literature on KD interventions for weight loss in obesity shows reductions in different outcomes, including body weight, body mass index, waist circumference, visceral adipose tissue, fat mass, and body fat percentage. Small reductions in lean body mass and skeletal muscle mass were observed without resistance training. There was variability in adherence (KB markers), carbohydrate intake (7-27% of daily energy), diet duration (28 days to 12 months), and frequency of follow-up (weekly to biannual). The ketogenic diet, particularly accompanied by exercise, positively influenced appetite regulation. Ketogenic diet interventions improve weight-related outcomes in participants with obesity but present challenges in reducing lean body mass without resistance training and in adherence variability. Standardizing methodologies, refining interventions and suitability for subpopulations, defining KB markers, and defining clinical relevance are essential to optimize the efficacy of the ketogenic diet **[7]**.

Also, the KD is a high-fat, low-carbohydrate eating approach that aims to facilitate weight loss, improve mental clarity, and increase energy levels. By significantly reducing carbohydrate intake and increasing fat and protein intake, this diet induces a metabolic state called ketosis, in which the body uses fat as its primary fuel source instead of carbohydrates. The main goal of the ketogenic diet is to decrease total body fat and improve metabolic health. Recent research indicates potential benefits in reducing the risk of certain diseases, including type 2 diabetes, hyperlipidemia, heart disease, and cancer **[8]**.

The effect of supplementation with a Moro juice extract (Morosil(®) was assessed. The results showed that the intake of Moro juice extract was able to induce a significant reduction in body mass index **[9]**. Some studies have reported the use of myo-inositol alone or in combination with other metabolic agents in the treatment of obesity and its comorbidities. In addition, it has been shown that taurine regulates and improves metabolic health, contributing to the treatment of overweight or obese patients **[10]**. Treatment with coenzyme Q10 points to the reconfiguration of mitochondrial metabolism, which is intrinsically linked to metabolic diseases and promotes tumor growth,

especially in patients with obesity **[11]**.

Given this, the present study consolidates the treatment protocol for obesity and its comorbidities, presenting the main clinical studies, meta-analyses, consensuses, and guidelines to support the efficacy and safety of the protocol.

Methods

Study Design

This study followed the international systematic review model, following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) rules. Available at: http://www.prisma-statement.org/?AspxAutoDetectCookieSupport=1. Accessed on: 01/21/2025. The AMSTAR 2 (Assessing the methodological quality of systematic reviews) methodological quality standards were also followed. Available at: https://amstar.ca/. Accessed on: 01/21/2025.

Search Strategy and Search Sources

The literature search process was carried out from January to February 2025 and developed based on Web of Science, Scopus, Embase, PubMed, Lilacs, Ebsco, Scielo, and Google Scholar, covering scientific articles from various periods to the present day. The following descriptors (DeCS/MeSH Terms) were used: *Obesity. Comorbidities. Ketogenic diet. Vitamin D. Metabolic activators. Protocol*, and using the Boolean "and" between the MeSH terms and "or" between the historical findings.

Study Quality and Risk of Bias

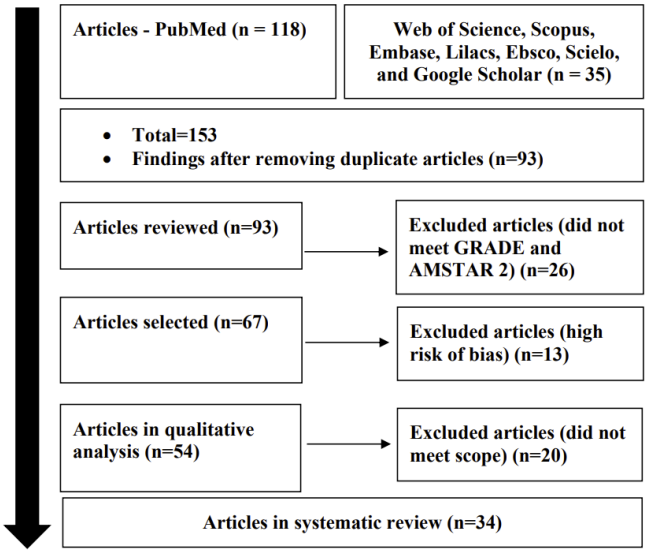
The quality was classified as high, moderate, low, or very low regarding the risk of bias, clarity of comparisons, precision, and consistency of analyses. The most evident emphasis was on systematic review articles or meta-analyses of randomized clinical trials, followed by randomized clinical trials. The low quality of evidence was attributed to case reports, editorials, and brief communications, according to the GRADE instrument. The risk of bias was analyzed according to the Cochrane instrument by analyzing the Funnel Plot graph (Sample size versus Effect size), using Cohen's test (d).

Results and Discussion

Summary of Findings

A total of 153 articles were found that were submitted to eligibility analysis, and 34 final studies were selected to compose the results of this systematic review. The studies listed were of medium to high quality (Figure 1), considering the level of scientific evidence of studies such as meta-analysis, consensus, randomized clinical trials, prospective, and observational. Biases did not compromise the scientific basis of the studies. According to the GRADE instrument, most studies presented homogeneity in their results, with X^2=87.8%>50%. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 13 studies with high risk of bias and 26 studies that did not meet GRADE.

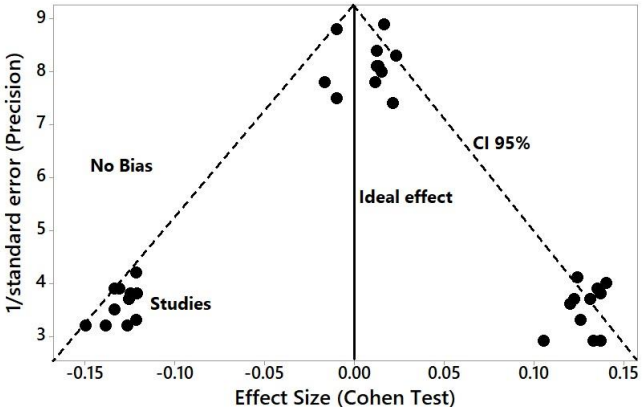
Figure 1. Screening of the articles.



Source: Own authorship.

Figure 2 presents the results of the risk of bias of the studies using the Funnel Plot, showing the calculation of the Effect Size (Magnitude of the difference) using Cohen's Test (d). Precision (sample size) was determined indirectly by the inverse of the standard error (1/Standard Error). This graph had a symmetrical behavior, not suggesting a significant risk of bias, both among studies with small sample sizes (lower precision) at the base of the graph and in studies with large sample sizes at the top.

Figure 2. The symmetrical funnel plot does not suggest a risk of bias among the studies with small sample sizes, which are shown at the bottom of the graph. High confidence and high recommendation studies are shown above the graph (n= 34 studies).



Source: Own authorship.

Major Scientific Studies – Support for the Obesity Treatment Protocol

Vitamin D

By the 2024 Vitamin D Consensus as well as the Central and Eastern European Expert Consensus Statement, assays used to determine serum 25-hydroxyvitamin D (25(OH)D) concentration, which remains a critical and controversial issue for defining vitamin D status, were reviewed. Definitions of nutritional status (i.e., sufficiency, insufficiency, and deficiency) were also reviewed. New areas were reviewed, including vitamin D cutoff values and how they should be defined in the context of specific diseases, sources of vitamin D, and risk factors associated with vitamin D deficiency. Non-skeletal aspects related to vitamin D, including the reproductive system, neurology, chronic kidney disease, and falls, were also discussed **[12,13]**.

The aforementioned consensuses evaluated a randomized clinical trial comparing 3 different dosing regimens in vitamin D deficient participants with similar total cumulative doses at the end of the study (D3 daily 10,000 IU for 8 weeks, then 1,000 IU for 4 weeks; 50,000 IU weekly for 12 weeks; and 100,000 IU every 2 weeks for 12 weeks), the group receiving daily supplementation was the fastest to achieve sufficiency (<2 weeks, although they received a higher cumulative dose in the first 8 weeks when compared to the other 2 arms) and achieved the highest serum 25(OH)D levels. Daily administration was associated with higher systemic exposure to 25(OH)D (larger area under the curve, +23% and +27% compared with weekly and biweekly administration, respectively), even when corrected for cumulative dose. The higher 25(OH)D exposure in daily regimens may be due to lower activation of the 24-hydroxylase enzyme (CYP24A1) **[14]**.

In a RCT in lactating women comparing the effect of bolus (150,000 IU) versus daily dosing of vitamin D3 (5,000 IU) on vitamin D3 catabolism, a single high-dose bolus of vitamin D led to higher 24,25(OH)2D3 production, relative to the 25(OH)D3 value, than daily vitamin D supplementation, with this effect persisting for at least 28 days after supplementation. The greater therapeutic potential of daily regimens compared with other regimens may be less relevant at lower doses (≤2,000 IU) **[15]**. Furthermore, two studies comparing 2000 IU/day vs 50,000 IU/month and 800 IU/day vs 5600 IU/month found no statistically significant differences in the 2 areas under the curves **[15,16]**.

Studies show that daily administration of cholecalciferol may be the most efficient and beneficial strategy for increasing serum 25(OH)D, with extraskeletal benefits of cholecalciferol supplementation, especially in pathological conditions such as obesity, according to Table 1 **[12,13]**.

Table 1. Important recommendations from 25 (OH) D.

✓ **Obesity and Bariatric Surgery**	**Dose Recommended**
✓ **Obese people have lower vitamin D than non-obese people;**	**30 < 25(OH)D(ng/mL) < 70**
✓ **Bariatric surgery as an aggravating factor;**	
✓ **Secondary hyperparathyroidism**	

Source: References 12 and 13.

The authors Zotarelli Filho et al. (2021) **[17]** conducted a literature review of randomized clinical studies, meta-analyses, and international consensuses. For patients with obesity, serum vitamin D levels should be between 30 and 70 ng/mL. Several current clinical studies and meta-analyses have demonstrated significant results with vitamin D supplementation in cardiovascular complications, diabetes, cancer, autoimmune diseases, cognitive function, among others, with doses above 30 ng/mL, reaching up to 70 ng/mL and maintaining the serum level at 50 ng/mL, regardless of the route of delivery (oral, parenteral, or muscular) of vitamin D.

A cross-sectional clinical study showed that obese children with below-ideal vitamin D levels were 3.35 times more likely to have damage to intestinal integrity. Overweight/obesity and fructose intake were associated with inflammation (elevated calprotectin) **[18]**. Furthermore, an observational cohort study compared vitamin D levels in patients 2 years after bariatric surgery (Roux-en-Y gastric bypass/RYGB and sleeve gastrectomy/SG) with a very low energy diet (VLED). 971 individuals eligible for surgical, RYGB (n = 388), SG (n = 201), and medical (n = 382) treatment in routine care were consecutively enrolled between 2015 and 2017. Vitamin D deficiency (S-25(OH)D < 25 mmol/L) was found in 5.2% of individuals with obesity at baseline versus 1.7% of the general population. Surgical intervention for obesity followed by vitamin D supplementation was not associated with a higher risk of vitamin D deficiency, regardless of the type of surgery, compared with individuals undergoing medical treatment. However, individuals living with obesity and seeking weight loss treatment are more likely to have deficient vitamin D levels compared with the general population **[19]**.

It was also observed that serum 25-hydroxyvitamin D levels were associated with obesity among North

American adolescents, and a cross-sectional study explored the mediating impact of homeostasis model assessment of insulin resistance (HOMA-IR) on this association. A total of 2,696 adolescents were eligible for inclusion, and the mean age of all adolescents was 15.4 years. Overall, the percentage of general and central obesity was 38.0% and 38.6%, respectively. Deficient or insufficient 25-hydroxyvitamin D concentrations were associated with a significant risk of general and central obesity among North American adolescents, and approximately 30% and 50%, respectively, of these associations were mediated by HOMA-IR **[20]**.

Another cross-sectional study examined the association between vitamin D levels and insulin resistance in non-diabetic obesity. A total of 3,887 individuals were included in this study. Serum vitamin D level was significantly lower in obese participants with insulin resistance than in participants without insulin resistance. Linear regression models showed that vitamin D level was inversely associated with HOMA-IR in obesity after adjustment for covariates **[21]**.

A systematic review and meta-analysis of randomized controlled trials analyzed the effects of vitamin D supplementation on parameters of the Metabolic Syndrome in patients with obesity or type 2 diabetes. Vitamin D supplementation had no effect on any of the analyzed outcomes (fasting blood glucose and insulinemia, glycated hemoglobin, HOMA index, systolic and diastolic blood pressure, weight, waist circumference, total cholesterol, LDL and HDL, and triglycerides). However, subgroup analyses indicated that the use of vitamin D up to 2000 IU per day reduced fasting blood glucose and glycated hemoglobin of participants. In addition, the intervention reduced diastolic blood pressure only in participants with vitamin D deficiency **[22]**.

Ketogenic Diet

A meta-analysis study suggested a common protocol for the ketogenic diet (KD) and its effectiveness in controlling weight and weight-related comorbidities, as well as possible side effects. Of the 645 articles retrieved, 15 studies met the inclusion criteria and were reviewed, revealing four main findings. First, KD was shown to result in significant short-, medium-, and long-term weight loss, as well as improvements in body composition parameters, as well as glycemic and lipid profiles. Second, when compared with other weight loss interventions of the same duration, KD demonstrated a significant effect on reducing body weight, fat mass, waist circumference, total cholesterol, and triglyceridemia, as well as improving insulin resistance. Third, although KD also resulted in significant reductions in glycemia, HbA1c, and LDL cholesterol, these changes were similar to those obtained with other weight loss interventions **[23]**.

A cohort study evaluated the time it took for the KD and Mediterranean (MD) diets to achieve a 5% loss of initial body weight. A total of 268 individuals with obesity or overweight were randomized into two arms, MD and KD, for a maximum period of 3 months or until they reached 5% body weight loss. This result was achieved after one month of KD and 3 months of MD. Both diets were effective in terms of BW ($p < 0.0001$) and FM loss ($p < 0.0001$). These two nutritional protocols are effective in improving anthropometric parameters and body composition, but take different periods to reach the goal **[24]**.

Despite this, the authors Merovci et al. (2024) **[25]** conducted a randomized clinical trial demonstrating that in the absence of weight loss, a low-carbohydrate ketogenic diet has no beneficial effect on glucose tolerance, insulin sensitivity, or other metabolic parameters.

Even so, the authors Luong et al. (2024) **[26]** developed a study with 11 obese individuals who underwent a randomized crossover trial with two 3-week interventions: 1) a KD and 2) a standard diet. The KD enabled a weight loss of 2.2 kg and increased insulin-stimulated glucose disposal. In addition, the KD decreased the suppression of insulin-mediated lipolysis, reducing insulin resistance in skeletal muscle in obese individuals.

Morosil®

The authors Cardile V, Graziano AC, Venditti (2015) **[27]** conducted a clinical study, evidencing the effect of supplementation with a Moro juice extract (Morosil(®), 400 mg/day) was evaluated in healthy overweight human volunteers for 12 weeks. The results showed that the intake of Moro juice extract was able to induce a significant reduction in body mass index (BMI) after 4 weeks of treatment. Furthermore, in individuals treated with Moro extract, body weight, BMI, waist, and hip circumference were significantly different from the placebo group.

A study investigated in vitro the antioxidant and anti-adipogenic activities of Morosil® (anthocyanin, a class of polyphenolic compounds). The results showed that Morosil® exerts antioxidant and anti-adipogenic activities during adipocyte differentiation from 3T3-L1 preadipocytes **[28]**.

L-Carnitine

Authors Hamedi-Kalajahi et al. (2025) **[29]** conducted a meta-analysis of placebo-controlled clinical trials to evaluate the effect of L-carnitine on

anthropometric indices. A total of 16,352 participants were included. The duration of the interventions ranged from 8 to 30 weeks, with L-carnitine dosages ranging from 150 to 4000 mg/day. The combined results of the eight meta-analyses indicated that L-carnitine supplementation can significantly reduce weight. Furthermore, a meta-analysis study analyzed the effect of L-carnitine supplementation on weight and body composition, including as many randomized controlled trials as possible and conducting a dose-response analysis for the first time. The meta-analysis of high-quality randomized controlled trials confirmed only the effect on body weight. A non-linear dose-response association was observed between L-carnitine supplementation and body weight reduction, suggesting that an intake of 2000 mg/day of L-carnitine per day provides the maximal effect in adults. This association was not observed for BMI, waist length, and body fat percentage **[30]**.

Authors Fallah and Mahdavi (2025) **[31]** designed a randomized controlled, double-blind clinical study to evaluate the effects of combined supplementation of L-carnitine + multispecies/multistrain synbiotic compared to monotherapy with L-carnitine on atherogenic indices, body composition, visceral obesity and appetite sensations in 46 metabolically healthy women with obesity, randomly assigned to co-supplementation groups (L-carnitine tartrate (2×500 mg/dL) + synbiotic (one capsule/day)) or monotherapy (L-carnitine tartrate (2×500 mg/dL) + maltodextrin (one capsule/day)) for 8 weeks. Combined supplementation of L-carnitine + synbiotics was more efficient in improving atherogenic indices as markers of cardiovascular risk, body composition, visceral obesity, and appetite sensations in metabolically healthy women with obesity.

A recent retrospective study (2025) **[32]** evaluated the effects of a combination of L-carnitine, L-arginine, L-cysteine, and myo-inositol on metabolic and reproductive parameters in overweight/obese patients. This was followed by 12 weeks of daily oral supplemental treatment with L-carnitine (500 mg), acetyl-L-carnitine (250 mg), L-arginine (500 mg), L-cysteine (100 mg), and myo-inositol (1 g). Administration of a combination of L-carnitine, L-arginine, L-cysteine, and myo-inositol improved plasma gonadotropin levels and insulin sensitivity in overweight/obese patients and restored hepatic insulin clearance.

Inositol

Authors Antoniotti et al. (2025) **[33]** evaluated, through a randomized, placebocontrolled, double-blind clinical study, the efficacy of the combined administration of myo-inositol and zinc, a mineral involved in the insulin pathway, in patients with pediatric obesity and insulin resistance, based on HOMA-IR, glucose-insulin metabolism, and lipid profile. Materials and methods. A total of 56 patients (10-18 years old, Tanner stage ≥ 3) with obesity and insulin resistance were randomized to receive myo-inositol (2000 mg), zinc gluconate (5 mg) and galacto-oligosaccharides (GOS) of plant origin (1000 mg) (TRT) or placebo (PLC) containing only GOS of plant origin (1000 mg). After 3 months of supplementation with myo-inositol and zinc, beneficial effects were observed on the lipid profile and in the management of obesity complications. Furthermore, a randomized clinical trial compared the effects of α-lipoic acid (ALA), myo-inositol (MI), and propolis supplementation on metabolic parameters and liver function in obese patients with non-alcoholic fatty liver disease. 92 obese patients with non-alcoholic fatty liver disease were randomly allocated into groups for 8 weeks. Dietary recommendations for weight loss accompanied by MI and subsequent ALA supplementation improved metabolic parameters and hepatic steatosis **[34]**.

Taurine

Authors Sun et al. (2024) **[35]** conducted a meta-analysis study on the effects of long-term taurine supplementation on blood lipids, blood glucose, and insulin sensitivity in overweight or obese adults. The final number of studies that met the inclusion criteria was 9 randomized trials. The overall analysis showed that taurine supplementation significantly decreased fasting triglyceride and insulin levels. In subgroup analysis, long-term taurine intake led to improved BMI in overweight adults. However, improvements in HbA1c and HOMA-IR were observed only in obese participants after taurine supplementation. Furthermore, long-term intake of 3g of taurine significantly improved HbA1c levels.

A meta-analysis conducted by authors Guan and Miao (2020) **[36]** evaluated the effects of taurine supplementation on liver markers and, secondarily, also explored anthropometric measurements. Taurine dosage ranged from 0.5 to 6 g/d for 15 days to 6 months. The pooled effect sizes suggested a significant effect of taurine administration on systolic blood pressure (weighted mean difference), diastolic blood pressure, total cholesterol, and triglycerides. However, no effect was observed on fasting blood glucose, as well as on body mass index and body weight in patients with liver dysregulation.

A randomized study investigated the effects of taurine supplementation in conjunction with exercise on markers of oxidative and inflammatory stress in plasma and subcutaneous white adipose tissue of obese

women. 16 obese women were randomized into two groups: taurine supplementation group (Tau, n = 8) and taurine supplementation + exercise group (Tau + Exe, n = 8). The intervention consisted of daily taurine supplementation (3g) and exercise training for 8 weeks. Taurine supplementation, in conjunction with exercise, modulated the levels of inflammatory markers in plasma and white adipose tissue subcutaneous fat and improved the plasticity of subcutaneous white adipose tissue in women with obesity **[37]**.

Another randomized clinical trial evaluated taurine supplementation and a dietinduced weight loss intervention on body composition and some biochemical indices in women with obesity. Participants were randomly divided into intervention (standard weight loss group + Tau cap 3 g/day for 8 weeks, n=20) and control (standard weight loss group + placebo cap for 8 weeks, n=18) groups. To achieve weight loss, all participants received an individualized diet that included a 30% reduction in total energy intake. The results showed that taurine supplementation together with a weight loss diet, may be more effective in improving lipid profile and metabolic risk factors compared to a weight loss diet alone **[38]**.

Coenzyme Q10

Authors Jiang et al. (2024) **[39]** demonstrated that oral treatment with coenzyme Q10, an inhibitor of mitochondrial transcription (IMT), shifts metabolism toward fatty acid oxidation, normalizes body weight, reverses hepatosteatosis, and restores normal glucose tolerance. This metabolic reprogramming caused by reduced mtDNA expression in the liver provides a principle for the drug treatment of obesity and obesity-related pathologies.

A population-based cohort study by Liang et al. (2025) **[40]** observed trends in coenzyme Q10 supplement use among adults and explored its associations with all-cause mortality, cardiovascular disease (CVD), and obesity. A prospective cohort study used data from the National Health and Nutrition Examination Survey (1999-2018). During a mean of 9.8 years of follow-up, 5237 deaths were identified, including 1428 deaths due to CVD. In the multivariable model, coenzyme Q10 supplement use was not associated with all-cause mortality and CVD mortality. Subgroup analyses suggested that coenzyme Q10 supplement use was associated with lower all-cause mortality in participants with obesity.

A meta-analysis showed that coenzyme Q10 supplementation significantly decreased serum C-reactive protein (CRP) and malondialdehyde, while increasing total antioxidant capacity and serum superoxide dismutase (SOD) activity. However, coenzyme Q10 supplementation did not significantly reduce tumor necrosis factor alpha (TNF-α) and interleukin-6 (IL-6) levels. Based on weighted mean difference analysis, CoQ10 supplementation significantly reduced TNF-α, IL-6, and CRP levels **[41]**.

The authors Ghavami et al. (2020) **[42]** investigated the efficacy of coenzyme Q10 supplementation on body weight, body mass index (BMI), and waist circumference (WC) through a meta-analysis of randomized clinical trials. It was observed that CoQ10 supplementation did not show significant results on body weight, BMI and WC. However, better designed studies are still needed to confirm these findings.

Chromium Picolinate

Chromium picolinate (CrP) has been shown to improve body composition by maintaining lean body mass **[43]**. CrP is recommended in the medical literature for reducing body weight. A systematic review of randomized clinical trials evaluated the effects of CrP supplementation in 622 overweight or obese participants versus placebo. At all CrP doses investigated (200 µg, 400 µg, 500 µg, 1000 µg), we observed an effect on body weight in favor of CrP of debatable clinical relevance after 12 to 16 weeks of treatment: mean difference (MD) -1.1 kg (95% CI -1.7 to -0.4). No firm evidence and no dose gradient could be established when comparing different doses of CrP with placebo for various measures of weight loss (body weight, body mass index, percentage of body fat composition, change in waist circumference). There were two serious adverse events and study withdrawal in participants taking 1000 µg of CrP, and one serious adverse event in an individual taking 400 µg of CrP **[44]**.

Authors Vajdi et al. (2024) **[45]** performed a meta-analysis to investigate the associations between chromium supplementation and body composition in patients with T2DM. Randomized controlled trials reporting the effects of chromium supplementation on body composition, such as body weight (BW), body mass index (BMI), fat mass (FM), and waist circumference (WC), in patients with T2DM were used. The results showed that chromium supplementation had no significant effect on FM (SMD = -0.43%; 95% CI -0.94, 0.09), BMI (SMD: 0.09 kg/m², 95% CI: -0.03, 0.20), WC (SMD: -0.47 cm, 95% CI: -1.10, 0.16) and WC (SMD: -0.26 kg, 95% CI: -0.69, 0.16). However, subgroup analysis revealed that chromium intake decreased FM in individuals aged ≥ 55 years, and when chromium picolinate was used as an intervention. Furthermore, there was a non-linear association between chromium supplementation dose and WC.

Limitations

There is a lack of randomized clinical studies, especially for metabolic activators such as morosil®, L-carnitine, inositol, taurine, coenzyme Q10, and chromium picolinate, to corroborate the efficacy of these compounds, as well as for the future production of a guideline through the construction of a meta-analysis study. In addition, the scientific literature does not present the best route (oral, parenteral, or muscular) and safe dosage of administration of these compounds, as well as whether the administration should be daily or in bolus.

Conclusion

It was concluded that the main clinical studies, meta-analyses, consensuses, and guidelines published to date indicate promising results to support the efficacy and safety of the treatment protocol for obesity and its comorbidities, with the most solid results being presented by studies of vitamin D, ketogenic diet, and L-carnitine. Studies have shown that morosil®, inositol, taurine, coenzyme Q10, and chromium picolinate present better results in the treatment of obesity when associated with other metabolic activators. Therefore, the proposal of the present treatment protocol can be validated by the associated use of these compounds in the treatment of patients with obesity.

CRediT

Author contributions: **conceptualization, data curation, formal Analysis, investigation, methodology, project administration, supervision, writing - original draft, and writing-review & editing-** Arthur Jorge Macedo Moises.

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Informed Consent

Not applicable.

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Data Sharing Statement

No additional data are available.

Conflict of Interest

The authors declare no conflict of interest.

Similarity Check

It was applied by Ithenticate®.

Application of Artificial Intelligence (AI)

Not applicable.

Peer Review Process

It was performed.

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