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**Impact of tomato and tomato-derived products on obesity and cardiometabolic health: a  
systemic review and meta-analysis.**

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## Abstract

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This article provides modest but biologically consistent evidences on the role of tomatoes and tomatoes-based products intake on several parameters linked to adiposity and obesity.

Tomatoes and tomato-based products are central components of the Mediterranean diet and have been associated with improved cardiometabolic health, but their effects on anthropometric parameters remain unclear. This review aimed to assess the potential effects of tomato-based interventions on obesity-related and cardiometabolic outcomes in individuals with overweight or obesity. We conducted a PRISMA-compliant systematic review and meta-analysis. Eligible studies included populations with a mean BMI  $\geq 25$  kg/m<sup>2</sup>, evaluated tomatoes, tomato-based products, or tomato extracts (excluding isolated lycopene) and reported at least one anthropometric outcome. Risk of bias was assessed using RoB 2 for randomized controlled trials (RCTs). Epidemiological and preclinical evidence was synthesized qualitatively. Forty-seven studies met inclusion criteria: 11 clinical trials RCTs, 5 epidemiological studies, and 31 preclinical studies. In RCTs, tomato-based interventions produced a small but significant reduction in waist circumference (MD -1.153 cm, 95% CI -2.27 to -0.04,  $p = 0.0432$ ), with no consistent effect on body weight or BMI. Meta-regression analyses indicated that supplementation type influenced blood pressure-related outcomes. Epidemiological studies consistently linked higher tomato intake to more favorable cardiometabolic profiles, whereas preclinical models showed reduced visceral adiposity, inflammation, and oxidative stress, together with improved glucose and lipid homeostasis. Tomato-based interventions confer modest but biologically consistent benefits, targeting visceral adiposity and cardiometabolic pathways rather than overall weight loss. The absence of a lycopene dose-response and the efficacy of lycopene-free matrices support a food-matrix synergy rather than lycopene as the primary bioactive. Combined clinical, epidemiological, and preclinical evidence suggests potential beneficial effects of tomatoes and tomato-based products on cardiometabolic health, which deserve further investigation. This review underscores the need to standardize tomato-derived interventions to improve comparability and strengthen the evidence.



**Keywords:** Tomato-based products; Lycopene; Obesity; Overweight; Body mass index; Body weight; Visceral adiposity; Anthropometric; Cardiometabolic health; Inflammation; Waist circumference.

## Introduction

The global rise in overweight and obesity is alarming: in 2022, an estimated 2.5 billion adults worldwide were overweight and 890 million were living with obesity, representing nearly 16% of the global adult population [1]. According to the World Health Organization (WHO), obesity is defined as an abnormal or excessive accumulation of body fat that may impair health, and is clinically diagnosed when the body mass index (BMI) is  $\geq 30$  kg/m<sup>2</sup>, while overweight corresponds to a BMI  $\geq 25$  kg/m<sup>2</sup>. Beyond this anthropometric definition, obesity is now recognized as a chronic multifactorial disease, resulting from a complex interaction among genetic, epigenetic, environmental, and nutritional factors. In addition to biological mechanisms, behavioral and environmental influences—such as sedentary lifestyles, high-calorie diets rich in ultra-processed foods, and insufficient physical activity—contribute substantially to its global spread [2,3]. Chronic obesity induces immune dysfunction and profound metabolic dysregulation, characterized by impaired glucose homeostasis leading to insulin resistance and by altered lipid metabolism resulting in dyslipidemia. These disturbances collectively increase the risk of cardiometabolic diseases, including type 2 diabetes mellitus (T2DM), hypertension, cardiovascular disease (CVD), and metabolic-associated fatty liver disease (MAFLD), as well as certain cancers, ultimately contributing to reduced quality of life, premature mortality, and escalating healthcare costs [4–7].

Given the multifactorial and inflammatory nature of obesity, nutritional strategies have emerged as fundamental approaches for both prevention and its management. Dietary patterns emphasizing whole, plant-based foods, rich in antioxidants and anti-inflammatory bioactives,



have demonstrated substantial benefits in modulating metabolic health. Among these, the Mediterranean diet—characterized by high consumption of fruits, vegetables, legumes, whole grains, olive oil, and moderate intake of fish and wine—has been consistently associated with reduced adiposity, improved insulin sensitivity, and lower incidence of cardiometabolic diseases [8–11]. Within this dietary framework, the tomato (*Solanum lycopersicum*) occupies a prominent place as one of the most globally consumed vegetables globally, both fresh and in processed forms such as sauces, pastes, and juices [12]. Tomatoes are a hallmark component of the Mediterranean diet and represent a major dietary source of carotenoids (particularly lycopene), vitamins (A, C and E), polyphenols, and other bioactive compounds with recognized antioxidant and anti-inflammatory properties [13,14].

The beneficial effects observed after tomato or tomato-product consumption have historically been largely attributed to lycopene [15–19]. This reductionist hypothesis, positioning lycopene as the principal “active ingredient” of tomatoes, has strongly shaped the design of clinical research over the past two decades. Early observational studies reported inverse associations between plasma lycopene or tomato intake and cardiovascular outcomes, reinforcing the assumption that lycopene alone mediated these benefits [20]. On this basis, numerous interventional trials were designed to test lycopene itself as a nutrient supplement, rather than tomatoes as a complex food and have administered isolated lycopene—typically in capsules or purified extracts, often at doses between 10 and 30 mg/day—to evaluate its effects on intermediate cardiometabolic endpoints. In parallel, several studies have employed lycopene-enriched or otherwise standardized tomato extracts to deliver controlled amounts of tomato-derived bioactive compounds [17,20]. Among these, Lyc-O-Mato<sup>®</sup> is a lipid-soluble tomato extract obtained from ripe tomatoes and standardized to contain approximately 6% lycopene, alongside other naturally occurring carotenoids (including phytoene, phytofluene, and β-



carotene) as well as small amounts of tocopherols and phytosterols, thereby preserving part of the native carotenoid matrix found in processed tomatoes [21–23]. This extract has been widely used in clinical and mechanistic studies as a model of lycopene-enriched tomato bioactives [24–27]. In contrast, Fruitflow<sup>®</sup> is a water-soluble, lycopene-free tomato extract standardized to three classes of hydrophilic compounds—nucleoside derivatives, phenolic conjugates (notably chlorogenic acid derivatives), and simple polyphenols such as rutin and caffeic acid. Its tightly controlled composition ensures reproducible bioactivity, and it is notable for being the first natural cardio-protective functional ingredient approved by the European Food Safety Authority (EFSA) [28]. Mechanistically, Fruitflow<sup>®</sup> exerts multiple effects, including inhibition of platelet activation, attenuation of oxidative stress through activation of Nrf2-dependent antioxidant pathways, and suppression of NF- $\kappa$ B-mediated inflammatory signaling. Collectively, these actions contribute to improved endothelial function and vascular homeostasis, supporting cardiometabolic health beyond the effects of individual compounds [29]. The demonstrated clinical efficacy of a lycopene-free tomato extract Fruitflow<sup>®</sup>—particularly on platelet aggregation and vascular fluidity—compared with the carotenoid-rich Lyc-O-Mato<sup>®</sup>, provides compelling evidence that the biological actions of tomatoes are not solely due to lycopene, but result from the synergistic interaction of multiple bioactives within the tomato matrix [30–35]. However, a second wave of research, clinical trials were designed to directly compare purified lycopene with whole-tomato preparations. In the cardiometabolic domain, Landrier *et al.* reported that, although both tomato-based products and lycopene have anti-inflammatory and anti-steatotic effects in experimental models, human trials show more consistent benefits from tomato-based products [17]. Similarly, Burton-Freeman and Sesso found that tomato-based products are more effective than lycopene supplements in improving oxidative stress, inflammation, and endothelial function, with comparable effects only on blood pressure [36]. Together with epidemiological evidence showing that high intakes of tomato

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products are associated with reduced cardiovascular disease (CVD) risk and mortality [20]. These findings support the concept of food synergy: tomato-related benefits arise from the combined actions of carotenoids, polyphenols, vitamins, minerals, and the lipid matrix rather than lycopene alone. The structural complexity of the tomato matrix modulates absorption, metabolism, and cellular signaling, producing biological effects that isolated lycopene cannot replicate. Accordingly, multiple clinical and experimental studies show greater improvements in antioxidant status, inflammation, and cardiometabolic markers with tomato-based products than with lycopene supplements [36–39]. Thus, while lycopene contributes significantly to the biological activity of tomatoes, accumulating evidence indicates that the tomato matrix itself exerts unique metabolic and immunomodulatory effects that cannot be reproduced by the isolated compound.

A growing number of studies have examined the health effects of tomatoes, tomato-based products, and lycopene, resulting in several systematic reviews and meta-analyses on cardiometabolic outcomes [20,40–45]. The 2021 umbrella review by Li *et al.* reported that higher dietary intake of tomatoes or lycopene, as well as higher circulating lycopene levels, is inversely associated with CVD, stroke, and all-cause mortality, and that across observational and interventional studies these exposures are also associated with a reduced risk of CVD, stroke, metabolic syndrome (MetS), and mortality [46]. Complementing these epidemiological insights, the recent systematic review and meta-analysis conducted by Zamani *et al.* in 2023 provided further clinical clarification by highlighting that tomato and lycopene consumption led to a significant reduction in malondialdehyde (MDA), a presumed marker of oxidative stress, but reported no consistent effect on body weight, BMI, lipid profile, blood pressure, or inflammatory markers [47]. Beyond overall cardiovascular risk, several systematic reviews have focused on cardiometabolic markers, including blood lipid profile, blood pressure, and



endothelial function [17,36]. The 2011 review by Burton-Freeman and Reimers provided one of the first comprehensive summaries of the physiological effects of tomato consumption, highlighting contributions to antioxidant defense, inflammatory modulation, and vascular function and emphasizing that these effects arise from the combined action of tomato carotenoids, vitamins, and phenolics rather than lycopene alone [13]. Building on this preliminary work, the 2014 review by Burton-Freeman and Sesso corroborated these findings, showing that diets rich in tomatoes and tomato-based products reliably improve endothelial function, reduce markers of oxidative stress, and attenuate inflammatory profiles [36]. These conclusions were reinforced by a 2017 systematic review and meta-analysis by Cheng *et al.*, which quantitatively demonstrated that tomato consumption produces significant reductions in low-density lipoprotein cholesterol (LDL-C) and systolic blood pressure (SBP), as well as an improvement in flow-mediated dilation, thus supporting the cardiometabolic benefits of tomato-based interventions [20]. Overall, existing studies indicate that tomatoes and tomato-based products generally have beneficial or neutral effects on key cardiometabolic parameters, but evidence specific to obesity remains limited. Although obesity is a major factor in cardiometabolic diseases, no systematic review or meta-analysis has directly examined the consequences of obesity. We therefore conducted a targeted systematic review and meta-analysis to evaluate the effects of tomatoes and tomato products in overweight or obese individuals on anthropometric parameters and obesity-related metabolic dysfunction, distinguishing these effects from those of isolated lycopene. This review provides an integrated synthesis of epidemiological, clinical and animal data on the impact of tomatoes and tomato-based products on obesity and associated metabolic disorders.



## Methods

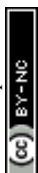
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### *Literature search*

A systematic search was conducted in PubMed according withto PRISMA recommendations. The full PubMed search string was: (((tomato) OR (Lyc-O-Mato) OR (Fruitflow)) AND ((obesity) OR (overweight) OR (type 2 diabetes) OR (metabolic syndrome) OR (cardiometabolic disease) OR (cardiovascular) OR (dyslipidemia) OR (oxidative stress) OR (high-fat diet)) NOT (review[Publication Type])). The search was performed independently by two researchers. The term “*tomato*” was used as the primary exposure keyword, as it appears systematically in all derivative expressions used in the literature. To ensure comprehensive retrieval of studies using standardized commercial tomato extracts, the terms “*Lyc-O-Mato*” and “*Fruitflow*” were also included. In addition to obesity-specific terms, more general keywords related to cardiac metabolism and inflammation were included to identify studies not listed under obesity-related headings, and the term “high-fat diet” was added to identify preclinical models of diet-induced obesity. No date restrictions were applied to allow inclusion of earlier foundational studies. Boolean operators were used to structure the search, reviews were excluded, and the last comprehensive search was performed on December 5, 2025.

### *Eligibility criteria*

To be eligible for further analysis, articles needed to (1) include a nutritional intervention involving tomatoes, tomato-based products (such as tomato juice, powder, paste, sauce, puree, or concentrated preparations), or tomato extracts (either laboratory-prepared or commercially standardized); (2) report at least one morphometric outcome, including body weight, BMI or waist circumference; (3) including a population with an average BMI greater than or equal to 25 kg/m<sup>2</sup>; and (4) constitute original peer-reviewed research, including clinical trials, observational studies, or animal intervention studies. Conversely, studies were excluded if (1)



the nutritional intervention relied solely on purified lycopene without any tomato-based products or tomato-derived extract; (2) no morphometric outcomes were reported; (3) the studied population in clinical trials had an average BMI lower than 25 kg/m<sup>2</sup> or the animal model was not suitable for diet-induced obesity, such as genetically induced obesity models; or (4) the publication did not qualify as original research, including reviews, meta-analyses, theses, editorials, commentaries, or conference abstracts.

### ***Data extraction, risk of bias assessment***

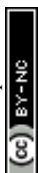
The extracted data included study and participant characteristics, duration, type, and dose of supplementation, control groups, measured outcomes, and significant results observed. Risk of bias was assessed for the primary outcomes (body weight, BMI, and waist circumference) with the Cochrane Risk of Bias 2 (RoB 2) tool for randomized controlled trials (RCTs), including parallel and cross-over designs [48]. Data extraction and risk-of-bias assessment were performed independently by two researchers.

### ***Assessment of publication bias***

Potential publication bias was evaluated using funnel plots and Egger's regression test. Because fewer than 10 studies were available for most outcomes (minimum of 7), these assessments were considered exploratory, in line with Cochrane guidance that funnel plot asymmetry tests are unreliable when fewer than 10 studies are included.

### ***Data synthesis***

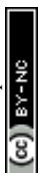
Quantitative synthesis focused on RCTs, while observational and preclinical studies were synthesized narratively. Meta-analysis was performed in RCTs comparing tomato-based intervention to an independent control group, and effect sizes were expressed as mean



differences (MD) in change from baseline between intervention and control groups, with 95% confidence intervals (CI). When standard deviations of change were not reported, they were derived from baseline and post-intervention values assuming a pre-post correlation coefficient of  $r = 0.50$ . Sensitivity analyses were performed using alternative correlation coefficients ( $r = 0.25$  and  $r = 0.75$ ) to assess the robustness of the results. Pooled effect estimates were obtained using random-effects models fitted by restricted maximum likelihood (REML). Primary outcomes were body weight, BMI, and waist circumference, selected as key anthropometric indicators of obesity and central adiposity with established cardiometabolic relevance. Forest plots were generated exclusively for these primary outcomes, whereas all other outcomes were summarized quantitatively in Table 2. Outcomes reported in fewer than two studies were not meta-analysed. Between-study heterogeneity was assessed using  $\tau^2$ ,  $I^2$ , and Cochran's Q test, and 95% prediction intervals were calculated. All analyses were conducted in R (4.5.1) using the *metafor* package, with statistical significance defined as a two-sided  $P < 0.05$ .

### Meta-regression analyses

Meta-regression analyses were conducted to investigate potential sources of between-study heterogeneity in anthropometric and cardiometabolic outcomes for RCTs of meta-analysis. Because the recommended minimum of ten studies per outcome for reliable meta-regression was not achieved, analyses were restricted to outcomes reported by at least seven studies and were undertaken on an exploratory basis to limit model instability and potential overfitting, consistent with Cochrane methodology. Both continuous (mean baseline BMI and daily lycopene intake) and categorical moderators (type of supplementation) were examined. Random-effects meta-regression models were fitted using REML. The continuous moderators were mean-centered prior to analysis. Associations with the continuous moderators were



evaluated using Wald tests of the regression coefficients, whereas between-group differences for the categorical moderator were assessed using the omnibus test of moderators (QM).

## Results

### *Search Results and Trial Flow*

A total of 2,802 records were identified through the PubMed database search. After removing duplicates, 2,800 unique records remained. Following title and abstract screening, 1,659 articles were excluded, and 297 full-text articles were assessed for eligibility. Of these, 250 were excluded for the following reasons: use of purified lycopene ( $n = 134$ ), absence of morphometric outcomes ( $n = 76$ ), unsuitable population ( $n = 25$ ), or non-original research ( $n = 15$ ). Ultimately, 47 studies met the inclusion criteria and were included in the systematic review and meta-analysis (**Figure 1**) [18,49–109]. Among these, 5 were observational epidemiological studies, 31 were animal model studies, and 11 were RCTs included in the meta-analysis.

### *Characteristics of randomized controlled interventional clinical studies*

Among the 11 clinical trials included (between 2000 and 2024), a total of 691 participants were included in these trials. Of these, 417 individuals (60.4 %) received a tomato or tomato-derived intervention (37.2 % men, 62.8 % women). Participants ranged from 18 to 83 years of age, with a mean age of 49.2 years. Most studies (81.8 %) recruited populations with average BMI values within the overweight range (25-30 kg/m<sup>2</sup>), and 18.2 % within the obesity range (**Table 1**). Across the intervention trials, tomato-based products were administered in diverse forms, with substantial variability in both dosage and lycopene content. The supplementation forms most frequently studied were tomato extract (33.3%), followed by fresh tomato (25.0%), tomato juice (16.7%) and combined tomato products (16.7%), with fewer studies using sofrito (8.3%) (**Supplementary Table S1**). Sofrito provided the highest lycopene density, with concentration



of 215.6 mg/kg for a daily dose of 100 g/d. Tomato juice also exhibited a high lycopene density (181.8 mg/L for 330 mL/d), followed by fresh tomatoes (55.5 mg/kg for 250.0 ± 50.0 g/d). Tomato extracts provided standardized doses, typically delivering 10-15 mg lycopene per capsule (or 0 mg for Fruitflow®), corresponding to a very high lycopene density relative to the administered mass. In terms of absolute lycopene intake, tomato juice provided the highest exposure (60.0 mg/d) over a mean duration of 3.5 weeks. Combined tomato-based products and sofrito yielded intermediate intakes (20.6 and 21.6 mg/d, respectively) over 12.5 and 6 weeks. Tomato extracts (10.0 ± 7.1 mg/d, for 8.6 weeks) and fresh tomatoes (250.0 ± 50.0 g/d, for 6.7 weeks) resulted in the lowest intake of lycopene.

### ***Risk of bias and study quality***

Overall, RCTs trials were judged to have predominantly low risk of bias across domains (45.4%), whereas several parallel RCTs showed some concerns (18.2%) or high risk of bias (36.4%), mainly related to the randomization process and deviations from intended interventions (**Supplementary Figure S1**). Visual inspection of funnel plots revealed no marked asymmetry (BMI, BW, SBP, DBP, TG, TC, LDL-C and HDL-C outcomes) (**Supplementary Figure S2**). Consistently, Egger's regression tests were not significant for all outcomes (all  $p > 0.1426$ ), providing no evidence of small-study effects or publication bias.

### ***Metabolic effects of tomato-based interventions: qualitative and quantitative evidence***

#### ***Effects of tomato-based interventions on anthropometric parameters***

Among 11 interventional trials, BMI (90.9%), body weight (72.7%), and waist circumference (63.6%) were the most frequently assessed anthropometric outcomes, whereas body fat mass (27.2%) and hip circumference (27.2%) were less commonly evaluated and other measures.



Only one study reported small but significant reductions in BMI ( $-0.27 \text{ kg/m}^2$ ) and body weight ( $-0.65 \text{ kg}$ ) following lycopene-free tomato extract (Fruitflow<sup>®</sup>) supplementation, and these reductions remained significant at the 15-day post-supplementation follow-up (**Table 1**) [54]. These effects were not associated with the longest intervention duration (45 days) and were not linked to lycopene intake, as observed in the absence of lycopene in this supplementation (**Supplementary Table S1**). In another study, anthropometric parameters decreased significantly after raw tomato supplementation versus control group, during 8 weeks, notably in waist circumference ( $-2.9 \pm 1.7 \text{ cm}$ ), hip circumference ( $-1.7 \pm 1.1 \text{ cm}$ ), and body fat mass ( $-0.8 \pm 1.3 \text{ kg}$  and  $-0.3 \pm 0.8 \%$ ) (**Table 1**) [52]. This reduction was not observed in the context of a long intervention duration or a high lycopene intake ( $11.0 \text{ mg lycopene /d}$ ) (**Supplementary Table S1**). Other anthropometric outcomes were unaffected.

Meta-analysis showed a significant reduction in waist circumference (MD  $-1.153 \text{ cm}$ , 95% CI  $-2.27$  to  $-0.04$ ,  $p = 0.0432$ , **Figure 2**). Although the study by Chen and Chien (2024) contributed the largest statistical weight (88.4%), effect estimates were consistent across studies, with no evidence of between-study heterogeneity ( $\tau^2 = 0.0$ ,  $I^2 = 0.0\%$ , Q-test  $p = 0.5833$ , **Figure 2**) [52]. Sensitivity analysis using different assumed pre-post correlation coefficients showed that the result remained statistically significant across all tested values of  $r$  ( $p = 0.0437$  for  $r = 0.25$ ,  $p = 0.0432$  for  $r = 0.50$ , and  $p = 0.0415$  for  $r = 0.75$ ; **Supplementary Table S2**), supporting the robustness of this finding. Supplementation was associated with a non-significant reduction in body weight (MD  $-0.659 \text{ kg}$ , 95% CI  $-1.94$  to  $0.63$ ,  $p = 0.3149$ , **Figure 3**). Heterogeneity was moderate to substantial ( $\tau^2 = 1.2$ ,  $I^2 = 37.9\%$ ), although the Q-test was not statistically significant ( $p = 0.1398$ ). No statistically significant pooled effects were observed for BMI (MD



-0.000 kg/m<sup>2</sup>, 95% CI -0.20 to 0.19,  $p = 0.9668$ , **Figure 4**), , with no evidence of between-study heterogeneity ( $\tau^2 = 0.0$ ,  $I^2 = 0.0\%$ , Q-test  $p = 0.9621$ ).

### *Effects of tomato-based interventions on cardiometabolic parameters*

Among the 9 studies assessing blood pressure, significant reductions were reported in approximately half of trials, mainly in high cardiometabolic risk populations (hypertensive or elevated cholesterol plasma). The largest decreases were observed with tomato extracts (Fruitflow<sup>®</sup> : -5.3 mmHg SBP and -3.0 mmHg DBP [54], and Lyc-O-Mato<sup>®</sup> : -11.0 mmHg SBP and -5.5 mmHg DBP [70]), whereas fresh tomato [52] produced only modest reductions. No consistent effects were observed in normotensive individuals. López-Yerena *et al.* reported a small but significant increase in diastolic blood pressure (DBP) with sofrito ( $+0.68 \pm 1.18$  mmHg,  $p = 0.0400$ ), likely attributable to its 2% sodium content [53]. The meta-analysis showed no significant effect of supplementation on these parameters (MD -2.894 mmHg, 95% CI -6.64 to 0.85,  $p = 0.1299$  for SBP and MD 0.077 mmHg, 95% CI -1.91 to 2.06,  $p = 0.9391$ , **Table 2**), but substantial heterogeneity was observed for SBP ( $\tau^2 = 0.0$ ,  $I^2 = 0.0\%$ , Q-test  $p = 0.9621$ ). Most trials evaluated lipid homeostasis parameters, with significant augmentations in total and high density lipoprotein-cholesterol (HDL-C) observed across different populations, including participants with hypercholesterolemia and healthy, suggesting that this parameter may be particularly sensitive to supplementation-induced changes (**Table 1**) [52,54,55,62]. In one study, raw tomato intake during 4 weeks, was associated with an increase HDL-C levels, with a positive association observed for both tomato intake ( $\beta = 5.79$ ) and adherence duration ( $\beta = 0.61$ ). The model showed a strong overall correlation ( $R = 0.83$ ), explaining 69% of the variance in HDL-C changes ( $R^2 = 0.69$ ), with high statistical significance ( $p < 0.0001$ ). The meta-analysis showed a non-significant trend toward an effect (MD 1.913 mg/dL, 95% CI -0.65



to 4.47,  $p = 0.1428$ , **Table 2**), with substantial between-study heterogeneity, although the  $I^2$  test for heterogeneity was not statistically significant ( $\tau^2 = 4.8$ ,  $I^2 = 45.5\%$ , Q-test  $p = 0.1266$ , **Table 2**), suggesting inconsistency in effect estimates across studies. Effects on triglycerides and total cholesterol were limited. Only one study reported reductions in triglycerides (-25.9 mg/dL) and total cholesterol (-6.1 mg/dL) (**Table 1**) [52], while the pooled meta-analysis did not show a statistically significant effect on either parameter (**Table 2**).

Glucose homeostasis outcomes were modest, with small reductions in fasting glucose reported mainly in metabolically at-risk populations (MetS or hypercholesterolemia) and limited. Chen and Chien reported that 8 weeks of raw tomato supplementation reduced fasting glucose by 5.2 mg/dL [52]. Similarly, Yu et al. showed that supplementation with lycopene-free tomato extract (Fruitflow<sup>®</sup>) led to a 5.4 mg/dL reduction in fasting glucose at the 15-day follow-up after a 45-day supplementation period [54]. No other parameters of glucose homeostasis, including insulin levels and insulin resistance indices, showed any effect in the included studies (**Table 1**) [52,66]. The most consistent oxidative stress-related effect was enhanced resistance of LDL particles to oxidation, evidenced by a longer copper ion-induced LDL oxidation lag time, suggesting reduced LDL susceptibility to oxidative modification [68], while endogenous antioxidant enzymes (SOD, CAT, GPx) remained largely unchanged [52,68]. Inflammatory markers showed heterogeneous but generally modest responses, with reductions in C-reactive protein (CRP) [54], observed in high-risk populations (hypercholesterolemia), alongside limited adipokine modulation. Selected studies also reported improvements in specialized cardiovascular endpoints, including reduced platelet aggregation with sofrito and modest changes in endothelial adhesion markers [53] (**Table 1**). Across all other outcomes assessed in



the quantitative meta-analysis, pooled estimates did not reach statistical significance (**Table 2**). Sensitivity analyses using alternative pre-post correlation coefficients confirmed the robustness of the findings, as  $p$ -values varied only minimally across the tested  $r$  values and the statistical interpretation of the results remained unchanged (**Supplementary Table S2**).

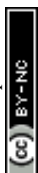
### ***Meta regression***

Owing to the limited number of studies (<10 per outcome), meta-regression analyses were restricted to outcomes with at least seven studies and should be interpreted cautiously. No significant associations were observed for anthropometric outcomes (**Supplementary Table S3**). For categorical moderator, significant differences across supplement types were observed for SBP (QM = 9.47,  $p = 0.0237$ , **Supplementary Figure S3 (A)**) and for DBP (QM = 8.62,  $p = 0.0349$ , **Supplementary Figure S3 (B)**), with a more pronounced overall decrease in this parameter for the supplementation with raw tomatoes. Additionally, mean change in triglycerides levels showed a positive trend toward association with mean baseline BMI as a continuous moderator ( $\beta = 5.94$ ,  $p = 0.0587$ , **Supplementary Figure S4**).

### ***Qualitative synthesis of epidemiologic and preclinical studies***

#### ***Qualitative synthesis of epidemiological studies***

5 epidemiological studies published between 2012 and 2023 were included with 2 reporting results from the same cohort and thus treated as a single study. These studies assessed associations between tomato consumption and anthropometric or cardiometabolic outcomes, encompassing a total of 52,275 participants (22.4% men, 77.6% women) (**Table S6**). Studies were conducted in adult with excess adiposity (mean BMI > 25 kg/m<sup>2</sup>), with a weighted mean BMI across studies of 26.9 kg/m<sup>2</sup>. Dietary intake was assessed using semi-quantitative food frequency questionnaires (FFQ) or repeated 24-h recalls, with tomato exposure defined as



whole tomato or total tomato-based product consumption. Participants were commonly categorized into low, moderate, and high tomato consumption groups, which were generally evenly distributed across cohorts, with comparable BMI values between intake categories. The majority of participants were free of major chronic disease at baseline (no CVD or cancer), while a substantial proportion represented populations at increased cardiometabolic risk. Large population-based cohorts accounted for the majority of participants (>95%), whereas smaller studies focused on specific subpopulations, including pregnant women (1.9%) individuals with MetS (0.1%), and HIV-positive women (0.9%).

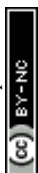
Among observational studies, 1 reported no association between tomato consumption and BMI or other anthropometric parameters [110], whereas another identified a non-linear (U-shaped) relationship across intake categories [111,112]. A prospective cohort study in pregnant women showed that higher tomato consumption was associated with lower odds of overweight/obesity (aOR = 0.50, 95% CI 0.30 to 0.84) and excessive gestational weight gain (aOR = 0.48; 95% CI 0.24–0.96) [113]. Among adults stratified by MetS status in 1 study, participants without MetS reported higher tomato intake than those with MetS ( $0.94 \pm 0.76$  vs.  $0.58 \pm 0.72$  portions/day). Tomato consumption was inversely correlated with both the number of MetS criteria fulfilled ( $r = -0.30$ , 95% CI -0.48 to -0.10) and MetS severity in overweight individuals ( $r = -0.47$ , 95% CI -0.71 to -0.12) [114]. Cardiometabolic parameters were assessed in 3 studies. Higher tomato intake was associated with lower blood pressure, total cholesterol, LDL-C cholesterol, fasting glucose, and insulin levels, as well as higher HDL-C. However, findings for triglycerides, LDL-C, and HDL-C were inconsistent across studies. Mortality outcomes were reported in 1 study, which showed lower all-cause, cardiovascular, stroke, and cancer mortality across increasing categories of tomato intake.



### *Qualitative synthesis of preclinical studies*

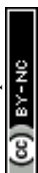
A total of 31 preclinical studies published between 1999 and 2024 investigated the effects of tomato-based interventions in experimental models of obesity or cardiometabolic dysfunction, with two publications reported distinct outcomes derived from the same animal cohorts and were therefore considered as single studies for synthesis. Most studies relied on rodent models. Overall, 55.1% used rats (mostly males), 27.6% mice, 6.9% hamsters, 3.5% *Drosophila melanogaster*, 3.5% gerbils, and 3.5% swine. Among studies, high-fat diet (HFD) models predominated, accounting for more than 62.1% of experimental designs. Other diet-induced models included high-sucrose diets (HSD), Western diets (WD), high-sugar-fat diets (HSF), and high-cholesterol diet (HCD) combined with HFD.

Tomato powder was the most frequently used form of supplementation, accounting for 41.4% of preclinical studies. It was typically incorporated into the diet at concentrations ranging from 3.0% to 41.7% (w/w), most commonly 5.0% (w/w), with intervention durations generally spanning 8-12 weeks (overall range: 4-24 weeks). Tomato extracts represented the second most common intervention (37.9%), followed by tomato juice (13.8%). Other formulations, including sofrito, tomato paste, and sauce, together accounted for the remaining 6.9% of studies. Among studies assessing body weight or body weight gain, tomato extract supplementation was associated with a reduction in these outcomes in 25.0% of studies. Tomato powder supplementation showed a positive effect in 57.1% of this studies, while extract was associated with reduced body weight in 42.9% of this studies. No significant effects on body weight outcomes were reported for sofrito, paste, or sauce-based interventions. Similarly, outcomes related to adipose tissue mass or adiposity indices were significantly improved in 43.8% of



studies. Among the studies reporting significant improvements, 57.1% investigated tomato extracts and 42.9% used tomato powder.

Overall, across all preclinical models of obesity and cardiometabolic dysfunction, tomato-based supplementation was consistently associated with improvements in cardiometabolic health, primarily through reductions in inflammation, oxidative stress, and hepatic lipid accumulation, whereas effects on circulating lipid levels were more variable. Improvements in glucose homeostasis (fasting glucose, insulin, and insulin resistance indices) were observed in a substantial proportion of studies, even in the absence of significant weight loss. Among studies assessing lipid homeostasis, 72.7% reported beneficial effects. Of these studies showing improvements, 50.0% investigated tomato powder supplementation, 37.5% investigated tomato extracts, and the remaining studies used tomato juice. Similarly, among studies assessing glucose homeostasis, 62.5% reported beneficial effects. Among these, 50.0% investigated tomato powder, 30.0% investigated tomato extracts, and the remaining studies evaluated tomato juice or tomato sauce. Studies assessing inflammatory and oxidative stress biomarkers reported positive effects in nearly all cases, regardless of the form of tomato-based supplementation (**Supplementary Table S5**).



## Discussion

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This systematic review and meta-analysis provides an integrated evaluation of clinical, epidemiological, and preclinical evidence on the effects of tomato and tomato-based interventions on obesity-related anthropometric and cardiometabolic outcomes. Collectively, the evidence indicates modest but biologically consistent effects in overweight or obese population. Epidemiological studies reinforce these conclusions by consistently associating higher tomato consumption with more favorable cardiometabolic profiles, while preclinical studies provide mechanistic insights and demonstrate effects on adiposity, inflammation, and metabolic regulation.

From an anthropometric perspective, pooled analyses revealed a small but statistically significant reduction in waist circumference in RCTs, whereas body weight and BMI did not show significant pooled effects. Sensitivity analyses confirmed the robustness and internal consistency of these findings despite their small magnitude. This divergence suggests that tomato-based interventions may preferentially influence abdominal fat distribution rather than overall body mass, a pattern consistent with epidemiological observations and preclinical data showing reductions in visceral adiposity without marked changes in total body weight. In animal models, particularly those using tomato powder or tomato extracts, reductions in visceral white adipose tissue mass and adiposity indices were frequently reported even in the absence of body weight loss, supporting the concept of adipose tissue remodeling rather than global weight reduction. Mechanistically, growing evidence indicates that tomato-derived bioactives can directly modulate adipose tissue biology. Preclinical studies show that these effects involve key pathways regulating adipocyte function, including modulation of PPAR $\gamma$  signaling and inhibition of NF- $\kappa$ B-mediated inflammation, contributing to reduced adipocyte hypertrophy and lipid accumulation [19,115,116]. While much of the evidence has focused on lycopene,



complementary mechanisms have been described for dietary polyphenols, notably through activation of thermogenic pathways, including increased brown adipose tissue (BAT) activity and induction of UCP1 and PGC-1 $\alpha$  expression, thereby enhancing energy expenditure and reducing adiposity [117]. Waist circumference is a sensitive marker of visceral adiposity and cardiometabolic risk, reflecting central fat distribution and ectopic lipid accumulation. In clinical weight-loss interventions, decreases of approximately 5-10 cm have been associated with  $\geq 10\%$  improvements in key cardiovascular risk markers, including total and LDL-C and DBP [118]. Importantly, population-based evidence shows that even modest waist circumference reductions ( $< 2$  cm) confer protection against incident MetS over long-term follow-up, whereas each 1-cm increase in waist circumference is associated with an approximately 10% higher risk [119]. Collectively, these data support the concept that even small reductions in waist circumference may yield significant metabolic benefits. The absence of consistent body weight or BMI reduction aligns with previous reviews and likely reflects the relatively short duration of most interventions and the fact that tomato-based strategies are not designed as weight-loss approaches. Instead, mechanistic evidence from preclinical studies indicates that tomato bioactives modulate adipose tissue function, including reduced adipocyte hypertrophy, and modulation of lipid-handling pathways (e.g., *PPAR $\gamma$* , *SREBP-1c*, *ACC*) [18,120,121]. In preclinical models, tomato extracts and tomato powder showed the highest proportion of studies reporting reductions in body weight gain and adiposity, whereas liquid or semi-solid products generally showed limited effects on anthropometric parameters but consistent metabolic benefits. Notably, higher lycopene content did not systematically translate into larger effects. Several studies reported substantial increases in circulating lycopene without corresponding anthropometric or metabolic improvements, and lycopene-free tomato extracts (e.g., Fruitflow®) produced comparable cardiometabolic effects [122]. Moreover, exploratory meta-regression analyses examining different supplementation types, sorted by lycopene



exposure levels, did not reveal any beneficial impact of higher lycopene intake. Although these findings are limited to a restricted set of parameters, they support the hypothesis that health effects are driven primarily by the food matrix of tomato products rather than by lycopene as an isolated nutrient. Both clinical and preclinical evidence indicate that the form of supplementation matters. Clinically, raw tomatoes generally tend to have more consistent cardiometabolic effects, with a marked impact specifically on blood pressure and plasma lipid levels. The strong association between sofrito and increased diastolic blood pressure can be explained by the presence of 2% sodium in its composition [53,123].

Cardiometabolic outcomes displayed a heterogeneous but coherent pattern. Qualitatively, improvements in lipid profile were more consistently observed in metabolically at-risk populations, whereas metabolically healthy individuals showed limited responsiveness. However, meta-regression analyses identified a positive association between baseline BMI and triglyceride response, indicating that the magnitude of the beneficial effect decreases with higher baseline adiposity. This response pattern indicates that individuals with low BMI show greater improvement in lipid metabolism than those who are overweight or obese. A similar pattern has been observed with other bioactive compounds, such as vitamin D, where overweight or obese individuals consistently show a reduced response to supplementation [124]. This may be explained by the fact that as excessive adiposity sets in, chronic inflammation, oxidative stress, and metabolic inflexibility increase, reducing the organism's metabolic responsiveness to nutritional modulation. Therefore, these results highlight the primarily preventive rather than therapeutic of tomato-based dietary supplements for metabolic health, with a greater impact observed before the onset of significant adiposity and metabolic impairment. Although not all studies assessed inflammatory or oxidative stress endpoints, the most consistent effects were observed on increased LDL oxidation lag time, suggesting



improved resistance of LDL particles to oxidation, and modest reductions in inflammatory markers such as CRP and adhesion molecules. Preclinical studies consistently demonstrated attenuation of oxidative stress pathways, reduced lipid peroxidation, and suppression of inflammatory signaling, providing mechanistic support for the clinical observations. These effects are biologically plausible and supported by known actions of tomato-derived compounds, including inhibition of NF- $\kappa$ B signaling, reduced expression of pro-inflammatory cytokines, improved redox balance, and enhanced resistance of lipoproteins to oxidative modification [13,15,17,36]. These mechanisms are further supported by human intervention studies showing that tomato-derived products act through bioavailability-driven cellular effects. Notably, supplementation with Lyc-o-Mato<sup>®</sup> increased plasma and lymphocyte carotenoids (lycopene, phytoene, phytofluene,  $\beta$ -carotene) and was associated with reduced oxidative stress-induced lymphocyte DNA damage, indicating improved cellular resistance to reactive species [125]. Similarly, dietary interventions with tomato-derived products were associated with reduced LDL oxidizability and lower urinary 8-iso-PGF2 $\alpha$ , reflecting decreased lipid peroxidation, likely mediated by carotenoid accumulation in membranes and lipoproteins with antioxidant activity [126]. Furthermore, these findings support the idea of a synergistic interaction between multiple tomato-derived bioactives, as human studies report concomitant increases in phytoene and phytofluene alongside lycopene. As shown in the human intervention study by Riso et al., tomato consumption also significantly increased intracellular vitamin C levels, a well-recognized antioxidant that can regenerate oxidized lipid-phase antioxidants and enhance overall cellular redox balance, thereby contributing to improved protection against oxidative damage [127]. Beyond these intracellular effects, vitamin C has been widely associated with cardioprotective properties, including improvement of endothelial function, reduction of oxidative stress, and limitation of LDL oxidation, all of which are key processes in the development of atherosclerosis [128]. Although tomato-derived compounds are often

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described as antioxidants, the classical oxidative stress hypothesis has been challenged by large-scale trials such as ATBC and Beta-Carotene and Retinol Efficacy Trial (CARET), which reported adverse effects of  $\beta$ -carotene supplementation in specific high-risk populations, notably smokers and asbestos-exposed individuals [129,130]. This highlights that antioxidant effects are context-dependent and may not systematically translate into clinical benefit, emphasizing the need for caution when interpreting oxidative stress-related outcomes.

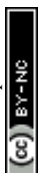
Across all available data, sex representation was unbalanced and varied depending on the type of study. Women were overrepresented in clinical trials ( $\approx 63\%$ ) and epidemiological studies ( $\approx 78\%$ ), while most preclinical experiments were conducted exclusively on male animals. Given the well-established sex differences in fat distribution, hormone regulation, lipid metabolism, inflammatory tone, and vascular function, men and women are likely to respond differently to tomato-based interventions. Sex hormones are known to modulate key pathways targeted by tomato bioactives, including adipogenesis, oxidative stress, and endothelial function [131,132]. Consequently, sex-dependent responses remain poorly characterized, limiting both the generalizability and mechanistic interpretation of the findings. Future studies should systematically include both sexes and be adequately powered to explore sex-specific effects, which is essential for a comprehensive understanding of the cardiometabolic impact of tomato-based interventions.

Overall, heterogeneity was low, supporting the reliability of the observed associations despite differences in population characteristics, baseline cardiometabolic risk, intervention form, dose, duration, and study design. Importantly, outcomes reaching statistical significance generally exhibited low or negligible heterogeneity, and sensitivity analyses supported the robustness of key findings. Nevertheless, several limitations must be acknowledged. Many clinical trials were



of short duration, included relatively small sample sizes, and were not specifically powered to detect changes in anthropometric outcomes. Considerable variability in tomato formulations, processing methods, and dosing further limits direct comparability across studies. Meta-regression analyses were exploratory due to the limited number of studies per outcome and should be considered hypothesis-generating rather than confirmatory. In addition, the underrepresentation of women and the predominance of male animals in preclinical research represent an important source of potential bias. Although dietary questionnaires were often used, these data were not consistently incorporated into the analyses. As a result, potential confounders (background diet, baseline tomato intake, intake of other antioxidant-rich foods, or lifestyle factors) may have influenced the observed effects. This highlights a well-recognized limitation in nutritional research, where isolating the independent impact of a single dietary component remains challenging due to the complexity of diet-lifestyle interactions. In particular, higher tomato consumption is often embedded within broader dietary patterns, such as the Mediterranean diet, characterized by high intake of plant-based foods and lower consumption of meat and processed products [133], making it difficult to separate the specific effects of tomatoes from overall dietary behaviors.

Overall, converging clinical, epidemiological, and preclinical data suggest that tomato-based interventions have modest beneficial effects in overweight or obese individuals, primarily targeting visceral adiposity and cardiometabolic pathways rather than inducing overt weight loss, with more apparent effects in individuals with high cardiometabolic risk. One of the main contributions of this review is to support that the effects of tomato-based interventions cannot be attributed to lycopene alone, as no association was observed between lycopene intake and the magnitude of anthropometric or cardiometabolic effects. Furthermore, comparable cardiometabolic and anthropometric effects were also observed with tomato matrices lacking



lycopene. These results contradict the assumption of a dominant role for isolated lycopene and instead highlight the importance of the tomato food matrix, supporting the concept of food synergy and reinforcing current paradigms that emphasize the benefits of whole foods and dietary habits rather than the isolated effect of nutrients. Overall, the data suggest that tomatoes and tomato-based products may have potential as a preventive nutritional approach in the context of overweight or obesity, particularly through their beneficial effect on waist circumference. Waist circumference is a clinically relevant marker of abdominal adiposity and cardiometabolic risk, and its reduction may therefore reflect an improvement in obesity-related risk profiles. Although modest, this effect is supported by established mechanisms and consistent with the extensive evidence linking plant-rich diets, such as the Mediterranean diet, with improved cardiometabolic health [134]. Future research should focus on long-term, sufficiently powered randomized trials using standardized interventions, clinically relevant endpoints, and sex-stratified analyses in order to better define the relevance of tomato-based interventions on cardiometabolic health.

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**Author contributions:** JFL and LS designed review, wrote paper and had primary responsibility for final content. LM participated to the writing and correction of the review. All authors have read and approved the final manuscript.



## References

- [1] Obesity and overweight. World Health Organ WHO 2025. <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight> (accessed November 10, 2025).
- [2] Swinburn BA, Sacks G, Hall KD, McPherson K, Finegood DT, Moodie ML, Gortmaker SL. The global obesity pandemic: shaped by global drivers and local environments. *The Lancet* 2011;378:804–14. [https://doi.org/10.1016/S0140-6736\(11\)60813-1](https://doi.org/10.1016/S0140-6736(11)60813-1).
- [3] Monteiro CA, Moubarac J-C, Cannon G, Ng SW, Popkin B. Ultra-processed products are becoming dominant in the global food system. *Obes Rev* 2013;14:21–8. <https://doi.org/10.1111/obr.12107>.
- [4] Valenzuela PL, Carrera-Bastos P, Castillo-García A, Lieberman DE, Santos-Lozano A, Lucia A. Obesity and the risk of cardiometabolic diseases. *Nat Rev Cardiol* 2023;20:475–94. <https://doi.org/10.1038/s41569-023-00847-5>.
- [5] Hruby A, Hu FB. The Epidemiology of Obesity: A Big Picture. *PharmacoEconomics* 2015;33:673–89. <https://doi.org/10.1007/s40273-014-0243-x>.
- [6] Blüher M. Obesity: global epidemiology and pathogenesis. *Nat Rev Endocrinol* 2019;15:288–98. <https://doi.org/10.1038/s41574-019-0176-8>.
- [7] The GBD 2015 Obesity Collaborators. Health Effects of Overweight and Obesity in 195 Countries over 25 Years. *N Engl J Med* 2017;377:13–27. <https://doi.org/10.1056/NEJMoa1614362>.
- [8] Estruch R, Ros E, Salas-Salvadó J, Covas M-I, Corella D, Arós F, Gómez-Gracia E, Ruiz-Gutiérrez V, Fiol M, Lapetra J, Lamuela-Raventos RM, Serra-Majem L, Pintó X, Basora J, Muñoz MA, Sorlí JV, Martínez JA, Fitó M, Gea A, Hernán MA, Martínez-González MA. Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. *N Engl J Med* 2018;378. <https://doi.org/10.1056/NEJMoa1800389>.
- [9] Schwingshackl L, Hoffmann G. Mediterranean dietary pattern, inflammation and endothelial function: A systematic review and meta-analysis of intervention trials. *Nutr Metab Cardiovasc Dis* 2014;24:929–39. <https://doi.org/10.1016/j.numecd.2014.03.003>.
- [10] Buckland G, Bach A, Serra-Majem L. Obesity and the Mediterranean diet: a systematic review of observational and intervention studies. *Obes Rev* 2008;9:582–93. <https://doi.org/10.1111/j.1467-789X.2008.00503.x>.
- [11] Davis C, Bryan J, Hodgson J, Murphy K. Definition of the Mediterranean Diet; A Literature Review 2015;7:9139–53. <https://doi.org/10.3390/nu7115459>.
- [12] FAOSTAT Analytical Brief. Agricultural production statistics 2010–2023. Food and Agriculture Organization of the United Nations (FAO); 2024.
- [13] Burton-Freeman B, Reimers K. Tomato Consumption and Health: Emerging Benefits. *Am J Lifestyle Med* 2011;5:182–91. <https://doi.org/10.1177/1559827610387488>.
- [14] Rao A, Rao L. Carotenoids and human health. *Pharmacol Res* 2007;55:207–16. <https://doi.org/10.1016/j.phrs.2007.01.012>.
- [15] Landrier J-F, Tourniaire F, Fenni S, Desmarchelier C, Borel P. Tomatoes and lycopene : inflammatory modulator effects. *Tomatoes Lycopene Hum. Nutr. Health Prev. Chronic Dis.*, CRC Press, Boca Raton. Florida (USA); 2017, p. np.
- [16] Sani L, Astier J, Ould-Ali D, Borel P, Landrier J-F. Tomato Puree Enrichment in a High-Fat Meal Reduces Postprandial Plasma and Adipose Tissue Inflammation Biomarkers in



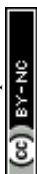
- Healthy Male Adults: A Crossover Randomized Controlled Trial. *Mol Nutr Food Res* 2025;69:e70115. <https://doi.org/10.1002/mnfr.70115>.
- [17] Landrier J-F, Breniere T, Sani L, Desmarchelier C, Mounien L, Borel P. Effect of tomato, tomato-derived products and lycopene on metabolic inflammation: from epidemiological data to molecular mechanisms. *Nutr Res Rev* 2025;38:95–111. <https://doi.org/10.1017/S095442242300029X>.
- [18] Fenni S, Hammou H, Astier J, Bonnet L, Karkeni E, Couturier C, Tourniaire F, Landrier J-F. Lycopene and tomato powder supplementation similarly inhibit high-fat diet induced obesity, inflammatory response, and associated metabolic disorders. *Mol Nutr Food Res* 2017;61:1601083. <https://doi.org/10.1002/mnfr.201601083>.
- [19] Gouranton E, Thabuis C, Riollet C, Malezet-Desmoulins C, El Yazidi C, Amiot MJ, Borel P, Landrier JF. Lycopene inhibits proinflammatory cytokine and chemokine expression in adipose tissue. *J Nutr Biochem* 2011;22:642–8. <https://doi.org/10.1016/j.jnutbio.2010.04.016>.
- [20] Cheng HM, Koutsidis G, Lodge JK, Ashor AW, Siervo M, Lara J. Lycopene and tomato and risk of cardiovascular diseases: A systematic review and meta-analysis of epidemiological evidence. *Crit Rev Food Sci Nutr* 2019;59:141–58. <https://doi.org/10.1080/10408398.2017.1362630>.
- [21] Rath S, Olempska-Ber Z, Kuznesof PM. Lycopene extract from tomato Chemical and Technical Assessment (CTA) 2009.
- [22] Lycopene extract from tomato. Food and Agriculture Organization of the United Nations (FAO); 2009.
- [23] LycoRed Natural Products Industries Ltd. Application for the Evaluation of Lyc-O-Mato lycopene oleoresin from tomatoes under European Regulation (EC) No. 258/97 for extension of food use. European Commission / Novel Food Application; 2004.
- [24] Neuman I, Nahum H, Ben-Amotz A. Reduction of exercise-induced asthma oxidative stress by lycopene, a natural antioxidant. *Allergy* 2000;55:1184–9. <https://doi.org/10.1034/j.1398-9995.2000.00748.x>.
- [25] Aust O, Stahl W, Sies H, Tronnier H, Heinrich U. Supplementation with Tomato-Based Products Increases Lycopene, Phytofluene, and Phytoene Levels in Human Serum and Protects Against UV-light-induced Erythema. *Int J Vitam Nutr Res* 2005;75:54–60. <https://doi.org/10.1024/0300-9831.75.1.54>.
- [26] Riso P, Visioli F, Grande S, Guarnieri S, Gardana C, Simonetti P, Porrini M. Effect of a Tomato-Based Drink on Markers of Inflammation, Immunomodulation, and Oxidative Stress. *J Agric Food Chem* 2006;54:2563–6. <https://doi.org/10.1021/jf053033c>.
- [27] Bunker CH, McDonald AC, Evans RW, de la Rosa N, Boumosleh JM, Patrick AL. A Randomized Trial of Lycopene Supplementation in Tobago Men with High Prostate Cancer Risk. *Nutr Cancer* 2007;57:130–7. <https://doi.org/10.1080/01635580701274046>.
- [28] O’Kennedy N, Raederstorff D, Duttaroy AK. Fruitflow®: the first European Food Safety Authority-approved natural cardio-protective functional ingredient. *Eur J Nutr* 2017;56:461–82. <https://doi.org/10.1007/s00394-016-1265-2>.
- [29] Dey A, N Keerthi, Banerjee A, Duss R, Pathak S, Duttaroy AK. Hallmarks of Aging and the Bioactive Compounds of Fruitflow ® , a Water-Soluble Tomato Concentrate 2025. <https://doi.org/10.20944/preprints202509.0316.v2>.



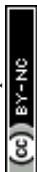
- [30] O’Kennedy N, Duss R, Duttaroy AK. Dietary Antiplatelets: A New Perspective on the Health Benefits of the Water-Soluble Tomato Concentrate Fruitflow®. *Nutrients* 2021;13:2184. <https://doi.org/10.3390/nu13072184>.
- [31] Das RK, Datta T, Biswas D, Duss R, O’Kennedy N, Duttaroy AK. Evaluation of the equivalence of different intakes of Fruitflow in affecting platelet aggregation and thrombin generation capacity in a randomized, double-blinded pilot study in male subjects. *BMC Nutr* 2021;7:80. <https://doi.org/10.1186/s40795-021-00485-5>.
- [32] Uddin M, Biswas D, Ghosh A, O’Kennedy N, Duttaroy AK. Consumption of Fruitflow® lowers blood pressure in pre-hypertensive males: a randomised, placebo controlled, double blind, cross-over study. *Int J Food Sci Nutr* 2018;69:494–502. <https://doi.org/10.1080/09637486.2017.1376621>.
- [33] Chen H, Zhang S, Wang H, Bao L, Wu W, Qi R. Fruitflow inhibits platelet function by suppressing Akt/GSK3 $\beta$ , Syk/PLC $\gamma$ 2 and p38 MAPK phosphorylation in collagen-stimulated platelets. *BMC Complement Med Ther* 2022;22:75. <https://doi.org/10.1186/s12906-022-03558-5>.
- [34] Chen H, Zhang S, Wang H, He R, Zhang X, Qi R. Effect of fruitflow on platelet function: A randomized placebo-controlled clinical trial in middle-aged and elderly subjects. *J Funct Foods* 2022;99:105315. <https://doi.org/10.1016/j.jff.2022.105315>.
- [35] O’Kennedy N, Crosbie L, Song H-J, Zhang X, Horgan G, Duttaroy AK. A randomised controlled trial comparing a dietary antiplatelet, the water-soluble tomato extract Fruitflow, with 75 mg aspirin in healthy subjects. *Eur J Clin Nutr* 2017;71:723–30. <https://doi.org/10.1038/ejcn.2016.222>.
- [36] Burton-Freeman BM, Sesso HD. Whole Food versus Supplement: Comparing the Clinical Evidence of Tomato Intake and Lycopene Supplementation on Cardiovascular Risk Factors. *Adv Nutr* 2014;5:457–85. <https://doi.org/10.3945/an.114.005231>.
- [37] Aguilera JM. The food matrix: implications in processing, nutrition and health. *Crit Rev Food Sci Nutr* 2019;59:3612–29. <https://doi.org/10.1080/10408398.2018.1502743>.
- [38] Tapsell LC, Neale EP, Satija A, Hu FB. Foods, Nutrients, and Dietary Patterns: Interconnections and Implications for Dietary Guidelines. *Adv Nutr* 2016;7:445–54. <https://doi.org/10.3945/an.115.011718>.
- [39] Jacobs DR, Tapsell LC. Food synergy: the key to a healthy diet. *Proc Nutr Soc* 2013;72:200–6. <https://doi.org/10.1017/S0029665112003011>.
- [40] Senkus KE, Tan L, Crowe-White KM. Lycopene and Metabolic Syndrome: A Systematic Review of the Literature. *Adv Nutr* 2019;10:19–29. <https://doi.org/10.1093/advances/nmy069>.
- [41] Tierney AC, Rumble CE, Billings LM, George ES. Effect of Dietary and Supplemental Lycopene on Cardiovascular Risk Factors: A Systematic Review and Meta-Analysis. *Adv Nutr* 2020;11:1453–88. <https://doi.org/10.1093/advances/nmaa069>.
- [42] Nam Y, Hwang I-G, Jang H-H. Role of lycopene from tomato on cardiovascular risk: an umbrella review of systematic reviews and meta-analyses of intervention studies. *Food Funct* 2026;17:622–30. <https://doi.org/10.1039/D5FO04213E>.
- [43] Mordente A, Guantario B, Meucci E, Silvestrini A, Lombardi E, E. Martorana G, Giardina B, Bohm V. Lycopene and Cardiovascular Diseases: An Update. *Curr Med Chem* 2011;18:1146–63. <https://doi.org/10.2174/092986711795029717>.
- [44] Petyaev IM. Lycopene Deficiency in Ageing and Cardiovascular Disease. *Oxid Med Cell Longev* 2016;2016:3218605. <https://doi.org/10.1155/2016/3218605>.



- [45] Story EN, Kopec RE, Schwartz SJ, Harris GK. An Update on the Health Effects of Tomato Lycopene. *Annu Rev Food Sci Technol* 2010;1:189–210. <https://doi.org/10.1146/annurev.food.102308.124120>.
- [46] Li N, Wu X, Zhuang W, Xia L, Chen Y, Wu C, Rao Z, Du L, Zhao R, Yi M, Wan Q, Zhou Y. Tomato and lycopene and multiple health outcomes: Umbrella review. *Food Chem* 2021;343:128396. <https://doi.org/10.1016/j.foodchem.2020.128396>.
- [47] Zamani M, Nia FB, Ghaedi K, Mohammadpour S, Amirani N, Goudarzi K, Kolbadi KSH, Ghanavati M, Ashtary-larky D. The Effects of Lycopene and Tomato Consumption on Cardiovascular Risk Factors in Adults: A Grade Assessment Systematic Review and Meta-analysis. *Curr Pharm Des* n.d.;29:1671–700. <https://doi.org/10.2174/1381612829666230726112510>.
- [48] Higgins JPT, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L, Sterne JAC, Cochrane Bias Methods Group, Cochrane Statistical Methods Group. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011;343:d5928–d5928. <https://doi.org/10.1136/bmj.d5928>.
- [49] Boileau TW-M, Boileau AC, Erdman JW. Bioavailability of all-trans and cis-Isomers of Lycopene. *Exp Biol Med* 2002;227:914–9. <https://doi.org/10.1177/153537020222701012>.
- [50] Wang Y, Ausman LM, Greenberg AS, Russell RM, Wang X-D. Dietary lycopene and tomato extract supplementations inhibit nonalcoholic steatohepatitis-promoted hepatocarcinogenesis in rats. *Int J Cancer* 2010;126:1788–96. <https://doi.org/10.1002/ijc.24689>.
- [51] Abete I, Perez-Cornago A, Navas-Carretero S, Bondia-Pons I, Zulet MA, Martinez JA. A regular lycopene enriched tomato sauce consumption influences antioxidant status of healthy young-subjects: A crossover study. *J Funct Foods* 2013;5:28–35. <https://doi.org/10.1016/j.jff.2012.07.007>.
- [52] Chen C-Y, Chien Y-W. Fresh Tomato (*Lycopersicon esculentum* Mill.) in the Diet Improves the Features of the Metabolic Syndrome: A Randomized Study in Postmenopausal Women. *Biology* 2024;13:588. <https://doi.org/10.3390/biology13080588>.
- [53] López-Yerena A, Padro T, De Santisteban Villaplana V, Muñoz-García N, Pérez A, Vilahur G, Badimon L. Vascular and Platelet Effects of Tomato Soffritto Intake in Overweight and Obese Subjects. *Nutrients* 2023;15:5084. <https://doi.org/10.3390/nu15245084>.
- [54] Yu Y, Wu Y, Xie L, Chang C. The effect of water-soluble tomato concentrate on elevated serum cholesterol in the middle-aged and elderly Chinese individuals. *Front Nutr* 2024;11:1410420. <https://doi.org/10.3389/fnut.2024.1410420>.
- [55] Yang T-H, Chen YC, Ou T-H, Chien Y-W. Dietary supplement of tomato can accelerate urinary aMT6s level and improve sleep quality in obese postmenopausal women. *Clin Nutr* 2020;39:291–7. <https://doi.org/10.1016/j.clnu.2019.02.009>.
- [56] Pourahmadi Z, Mahboob S, Saedisomeolia A, Reykandeh MT. The Effect of Tomato Juice Consumption on Antioxidant Status in Overweight and Obese Females. *Women Health* 2015;55:795–804. <https://doi.org/10.1080/03630242.2015.1050546>.
- [57] Ferro Y, Mazza E, Angotti E, Pujia R, Mirarchi A, Salvati MA, Terracciano R, Savino R, Romeo S, Scuteri A, Mare R, Costanzo FS, Pujia A, Montalcini T. Effect of a novel functional tomato sauce (OsteoCol) from vine-ripened tomatoes on serum lipids in individuals with common hypercholesterolemia: tomato sauce and hypercholesterolemia. *J Transl Med* 2021;19:19. <https://doi.org/10.1186/s12967-020-02676-3>.



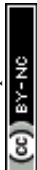
- [58] Li Y-F, Chang Y-Y, Huang H-C, Wu Y-C, Yang M-D, Chao P-M. Tomato juice supplementation in young women reduces inflammatory adipokine levels independently of body fat reduction. *Nutrition* 2015;31:691–6. <https://doi.org/10.1016/j.nut.2014.11.008>.
- [59] Hirose A, Terauchi M, Tamura M, Akiyoshi M, Owa Y, Kato K, Kubota T. Tomato juice intake increases resting energy expenditure and improves hypertriglyceridemia in middle-aged women: an open-label, single-arm study. *Nutr J* 2015;14:34. <https://doi.org/10.1186/s12937-015-0021-4>.
- [60] Llanos AA, Peng J, Pennell ML, Krok JL, Vitolins MZ, Degraffinreid CR, Paskett ED. Effects of Tomato and Soy on Serum Adipokine Concentrations in Postmenopausal Women at Increased Breast Cancer Risk: A Cross-Over Dietary Intervention Trial. *J Clin Endocrinol Metab* 2014;99:625–32. <https://doi.org/10.1210/jc.2013-3222>.
- [61] Vinha AF, Barreira SVP, Costa ASG, Alves RC, Oliveira MBPP. Pre-meal tomato (*Lycopersicon esculentum*) intake can have anti-obesity effects in young women? *Int J Food Sci Nutr* 2014;65:1019–26. <https://doi.org/10.3109/09637486.2014.950206>.
- [62] Cuevas-Ramos D, Almeda-Valdés P, Chávez-Manzanera E, Meza-Arana CE, Brito-Córdova G, Roopa Mehta R, Oscar Pérez-Méndez O, Francisco J. Gómez-Pérez F. Effect of tomato consumption on high-density lipoprotein cholesterol level: a randomized, single-blinded, controlled clinical trial. *Diabetes Metab Syndr Obes Targets Ther* 2013:263. <https://doi.org/10.2147/DMSO.S48858>.
- [63] Odai T, Terauchi M, Okamoto D, Hirose A, Miyasaka N. Unsalted tomato juice intake improves blood pressure and serum low-density lipoprotein cholesterol level in local Japanese residents at risk of cardiovascular disease. *Food Sci Nutr* 2019;7:2271–9. <https://doi.org/10.1002/fsn3.1066>.
- [64] Nishimura M, Tominaga N, Ishikawa-Takano Y, Maeda-Yamamoto M, Nishihira J. Effect of 12-Week Daily Intake of the High-Lycopene Tomato (*Solanum Lycopersicum*), a Variety Named “PR-7”, on Lipid Metabolism: A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study. *Nutrients* 2019;11:1177. <https://doi.org/10.3390/nu11051177>.
- [65] Ried K, Frank OR, Stocks NP. Dark chocolate or tomato extract for prehypertension: a randomised controlled trial. *BMC Complement Altern Med* 2009;9:22. <https://doi.org/10.1186/1472-6882-9-22>.
- [66] Thies F, Masson LF, Rudd A, Vaughan N, Tsang C, Brittenden J, Simpson WG, Duthie S, Horgan GW, Duthie G. Effect of a tomato-rich diet on markers of cardiovascular disease risk in moderately overweight, disease-free, middle-aged adults: a randomized controlled trial. *Am J Clin Nutr* 2012;95:1013–22. <https://doi.org/10.3945/ajcn.111.026286>.
- [67] Shidfar F, Froghifar N, Vafa M, Rajab A, Hosseini S, Shidfar S, Gohari M. The effects of tomato consumption on serum glucose, apolipoprotein B, apolipoprotein A-I, homocysteine and blood pressure in type 2 diabetic patients. *Int J Food Sci Nutr* 2011;62:289–94. <https://doi.org/10.3109/09637486.2010.529072>.
- [68] Upritchard JE, Sutherland WH, Mann JI. Effect of supplementation with tomato juice, vitamin E, and vitamin C on LDL oxidation and products of inflammatory activity in type 2 diabetes. *Diabetes Care* 2000;23:733–8. <https://doi.org/10.2337/diacare.23.6.733>.
- [69] García-Alonso FJ, Jorge-Vidal V, Ros G, Periago MJ. Effect of consumption of tomato juice enriched with n-3 polyunsaturated fatty acids on the lipid profile, antioxidant biomarker status, and cardiovascular disease risk in healthy women. *Eur J Nutr* 2012;51:415–24. <https://doi.org/10.1007/s00394-011-0225-0>.



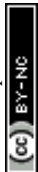
- [70] Engelhard YN, Gazer B, Paran E. Natural antioxidants from tomato extract reduce blood pressure in patients with grade-1 hypertension: A double-blind, placebo-controlled pilot study. *Am Heart J* 2006;151:100.e6-100.e1. <https://doi.org/10.1016/j.ahj.2005.05.008>.
- [71] Breniere T, Bournot L, Sicard F, Astier J, Fanciullino A-L, Riva C, Borel P, Bertin N, Landrier J-F. Tomato genotype but not crop water deficit matters for tomato health benefits in diet-induced obesity of C57BL/6JRj male mice. *Food Res Int* 2024;188:114512. <https://doi.org/10.1016/j.foodres.2024.114512>.
- [72] Di Majo D, Ricciardi N, Moncada A, Allegra M, Frinchi M, Di Liberto V, Pitonzo R, Rappa F, Saiano F, Vetrano F, Miceli A, Giglia G, Ferraro G, Sardo P, Gambino G. Golden Tomato Juice Enhances Hepatic PPAR- $\alpha$  Expression, Mitigates Metabolic Dysfunctions and Influences Redox Balance in a High-Fat-Diet Rat Model. *Antioxidants* 2024;13:1324. <https://doi.org/10.3390/antiox13111324>.
- [73] Luis Heriberto VM, Patrick MS, Elihu CP, Bravo G, Julian ACD. Whole tomato lipidic extract improved sperm quality in obese rats induced by a high-carbohydrate diet. *Andrology* 2025;13:955–67. <https://doi.org/10.1111/andr.13736>.
- [74] Gambino G, Giglia G, Allegra M, Di Liberto V, Zummo FP, Rappa F, Restivo I, Vetrano F, Saiano F, Palazzolo E, Avellone G, Ferraro G, Sardo P, Di Majo D. “Golden” Tomato Consumption Ameliorates Metabolic Syndrome: A Focus on the Redox Balance in the High-Fat-Diet-Fed Rat. *Antioxidants* 2023;12:1121. <https://doi.org/10.3390/antiox12051121>.
- [75] Kayode OT, Afolabi OA, Ajayi GO. Antioxidant and antilipidemic action of ketogenic diet and tomato powder mix in high sugar and fat fed Harwich fruit flies. *Heliyon* 2023;9. <https://doi.org/10.1016/j.heliyon.2023.e20411>.
- [76] Pipitone RM, Zito R, Gambino G, Di Maria G, Javed A, Lupo G, Giglia G, Sardo P, Ferraro G, Rappa F, Carlisi D, Di Majo D, Grimaudo S. Red and golden tomato administration improves fat diet-induced hepatic steatosis in rats by modulating HNF4 $\alpha$ , Lepr, and GK expression. *Front Nutr* 2023;10:1221013. <https://doi.org/10.3389/fnut.2023.1221013>.
- [77] Rinaldi de Alvarenga JF, Garcia-Aloy M, Ulaszewska M, Zagmutt S, Perez-Montero M, Vrhovsek U, Lamuela-Raventós RM, Rodriguez-Rodriguez R. Integrated Metabolomics, Lipidomics, and Genomics Reveal the Presence of a New Biomarker, Butanediol Glucuronide, Associated with the Activation of Liver Ketogenesis and Lipid Oxidation by Tomato-Based Sofrito in Obese Rats. *Antioxidants* 2022;11:2165. <https://doi.org/10.3390/antiox11112165>.
- [78] Ferron AJT, Aldini G, Francisqueti-Ferron FV, Silva CCVDA, Bazan SGZ, Garcia JL, Campos DHSD, Ghiraldeli L, Kitawara KAH, Altomare A, Correa CR, Moreto F, Ferreira ALA. Protective Effect of Tomato-Oleoresin Supplementation on Oxidative Injury Recoveries Cardiac Function by Improving  $\beta$ -Adrenergic Response in a Diet-Obesity Induced Model. *Antioxidants* 2019;8:368. <https://doi.org/10.3390/antiox8090368>.
- [79] Ferron AJT, Francisqueti-Ferron FV, Vágula de Almeida Silva CC, Bazan SGZ, Dijon Henrique Salomé de Campos, Jéssica Leite Garcia, Luciana Ghiraldeli, Igor Otávio Minatel, Camila Renata Correa, Fernando Moreto, Ana Lucia Anjos Ferreira. Tomato-Oleoresin Anti-Inflammatory Effect Recovers Obesity-Induced Cardiac Dysfunction by Modulating Myocardial Calcium Handling. *Cell Physiol Biochem* 2020;54:1013–25. <https://doi.org/10.33594/000000284>.



- [80] Jesuz VA de, Campos M de BE, Souza VR de, Bede TP, Moraes BPT de, Silva AR, Albuquerque CFG de, Azeredo VB de, Teodoro AJ. Lycopene and Tomato Sauce Improve Hepatic and Cardiac Cell Biomarkers in Rats. *J Med Food* 2019.
- [81] Róvero Costa M, Leite Garcia J, Cristina Vágula de Almeida Silva C, Junio Togneri Ferron A, Valentini Francisqueti-Ferron F, Kurokawa Hasimoto F, Schmitt Gregolin C, Henrique Salomé de Campos D, Roberto de Andrade C, dos Anjos Ferreira AL, Renata Corrêa C, Moreto F. Lycopene Modulates Pathophysiological Processes of Non-Alcoholic Fatty Liver Disease in Obese Rats. *Antioxidants* 2019;8:276. <https://doi.org/10.3390/antiox8080276>.
- [82] Elvira-Torales LI, Navarro-González I, González-Barrio R, Martín-Pozuelo G, Doménech G, Seva J, García-Alonso J, Periago-Castón MJ. Tomato Juice Supplementation Influences the Gene Expression Related to Steatosis in Rats. *Nutrients* 2018;10:1215. <https://doi.org/10.3390/nu10091215>.
- [83] Li C, Liu C, Fu M, Hu K, Aizawa K, Takahashi S, Hiroyuki S, Cheng J, Von Lintig J, Wang X. Tomato Powder Inhibits Hepatic Steatosis and Inflammation Potentially Through Restoring SIRT1 Activity and Adiponectin Function Independent of Carotenoid Cleavage Enzymes in Mice. *Mol Nutr Food Res* 2018;62:1700738. <https://doi.org/10.1002/mnfr.201700738>.
- [84] Mohri S, Takahashi H, Sakai M, Takahashi S, Waki N, Aizawa K, Suganuma H, Ara T, Matsumura Y, Shibata D, Goto T, Kawada T. Wide-range screening of anti-inflammatory compounds in tomato using LC-MS and elucidating the mechanism of their functions. *PLOS ONE* 2018;13:e0191203. <https://doi.org/10.1371/journal.pone.0191203>.
- [85] Xia H, Liu C, Li C-C, Fu M, Takahashi S, Hu K-Q, Aizawa K, Hiroyuki S, Wu G, Zhao L, Wang X-D. Dietary Tomato Powder Inhibits High-Fat Diet–Promoted Hepatocellular Carcinoma with Alteration of Gut Microbiota in Mice Lacking Carotenoid Cleavage Enzymes. *Cancer Prev Res (Phila Pa)* 2018;11:797–810. <https://doi.org/10.1158/1940-6207.CAPR-18-0188>.
- [86] Rodriguez-Rodriguez R, Jiménez-Altayó F, Alsina L, Onetti Y, Rinaldi de Alvarenga JF, Claro C, Ogalla E, Casals N, Lamuela-Raventos RM. Mediterranean tomato-based sofrito protects against vascular alterations in obese Zucker rats by preserving NO bioavailability. *Mol Nutr Food Res* 2017;61:1601010. <https://doi.org/10.1002/mnfr.201601010>.
- [87] Sandoval V, Rodríguez-Rodríguez R, Martínez-Garza Ú, Rosell-Cardona C, Lamuela-Raventós RM, Marrero PF, Haro D, Relat J. Mediterranean Tomato-Based *Sofrito* Sauce Improves Fibroblast Growth Factor 21 (FGF21) Signaling in White Adipose Tissue of Obese ZUCKER Rats. *Mol Nutr Food Res* 2018;62:1700606. <https://doi.org/10.1002/mnfr.201700606>.
- [88] García-Alonso FJ, González-Barrio R, Martín-Pozuelo G, Hidalgo N, Navarro-González I, Masuero D, Soini E, Vrhovsek U, Periago MJ. A study of the prebiotic-like effects of tomato juice consumption in rats with diet-induced non-alcoholic fatty liver disease (NAFLD). *Food Funct* 2017;8:3542–52. <https://doi.org/10.1039/C7FO00393E>.
- [89] Aborehab NM, El Bishbishy MH, Waly NE. Resistin mediates tomato and broccoli extract effects on glucose homeostasis in high fat diet-induced obesity in rats. *BMC Complement Altern Med* 2016;16:225. <https://doi.org/10.1186/s12906-016-1203-0>.
- [90] Bajerska J, Chmurzynska A, Mildner-Szkudlarz S, Drzymala-Czyż S. Effect of rye bread enriched with tomato pomace on fat absorption and lipid metabolism in rats fed a high-fat diet. *J Sci Food Agric* 2015;95:1918–24. <https://doi.org/10.1002/jsfa.6899>.



- [91] Lee L-C, Wei L, Huang W-C, Hsu Y-J, Chen Y-M, Huang C-C. Hypolipidemic Effect of Tomato Juice in Hamsters in High Cholesterol Diet-Induced Hyperlipidemia. *Nutrients* 2015;7:10525–37. <https://doi.org/10.3390/nu7125552>.
- [92] Zidani S, Benakmoum A, Ammouche A, Benali Y, Bouhadeb A, Abbeddou S. Effect of dry tomato peel supplementation on glucose tolerance, insulin resistance, and hepatic markers in mice fed high-saturated-fat/high-cholesterol diets. *J Nutr Biochem* 2017;40:164–71. <https://doi.org/10.1016/j.jnutbio.2016.11.001>.
- [93] Smith BW, Miller RJ, Wilund KR, O'Brien WD, Erdman JW. Effects of Tomato and Soy Germ on Lipid Bioaccumulation and Atherosclerosis in ApoE<sup>-/-</sup> Mice. *J Food Sci* 2015;80. <https://doi.org/10.1111/1750-3841.12968>.
- [94] Vilahur G, Cubedo J, Padró T, Casaní L, Mendieta G, González A, Badimon L. Intake of cooked tomato sauce preserves coronary endothelial function and improves apolipoprotein A-I and apolipoprotein J protein profile in high-density lipoproteins. *Transl Res* 2015;166:44–56. <https://doi.org/10.1016/j.trsl.2014.11.004>.
- [95] Pierine DT, Navarro MEL, Minatel IO, Luvizotto RAM, Nascimento AF, Ferreira ALA, Yeum K-J, Corrêa CR. Lycopene supplementation reduces TNF- $\alpha$  via RAGE in the kidney of obese rats. *Nutr Diabetes* 2014;4:e142. <https://doi.org/10.1038/nutd.2014.39>.
- [96] Luvizotto R, Nascimento A, Miranda N, Wang X-D, Ferreira A. Lycopene-rich tomato oleoresin modulates plasma adiponectin concentration and mRNA levels of adiponectin, SIRT1, and FoxO1 in adipose tissue of obese rats. *Hum Exp Toxicol* 2015;34:612–9. <https://doi.org/10.1177/0960327114551395>.
- [97] Bernal C, Martín-Pozuelo G, Lozano AB, Sevilla Á, García-Alonso J, Canovas M, Periago MJ. Lipid biomarkers and metabolic effects of lycopene from tomato juice on liver of rats with induced hepatic steatosis. *J Nutr Biochem* 2013;24:1870–81. <https://doi.org/10.1016/j.jnutbio.2013.05.003>.
- [98] Martín-Pozuelo G, Navarro-González I, González-Barrio R, Santaella M, García-Alonso J, Hidalgo N, Gómez-Gallego C, Ros G, Periago MJ. The effect of tomato juice supplementation on biomarkers and gene expression related to lipid metabolism in rats with induced hepatic steatosis. *Eur J Nutr* 2015;54:933–44. <https://doi.org/10.1007/s00394-014-0770-4>.
- [99] Choi K-M, Lee Y-S, Shin D-M, Lee S, Yoo K-S, Lee MK, Lee J-H, Kim SY, Lee Y-M, Hong J-T, Yun Y-P, Yoo H-S. Green tomato extract attenuates high-fat-diet-induced obesity through activation of the AMPK pathway in C57BL/6 mice. *J Nutr Biochem* 2013;24:335–42. <https://doi.org/10.1016/j.jnutbio.2012.06.018>.
- [100] Choi S-K, Seo J-S. Lycopene supplementation suppresses oxidative stress induced by a high fat diet in gerbils. *Nutr Res Pract* 2013;7:26–33. <https://doi.org/10.4162/nrp.2013.7.1.26>.
- [101] Luvizotto RDAM, Nascimento AF, Imaizumi E, Pierine DT, Conde SJ, Correa CR, Yeum K-J, Ferreira ALA. Lycopene supplementation modulates plasma concentrations and epididymal adipose tissue mRNA of leptin, resistin and *IL-6* in diet-induced obese rats. *Br J Nutr* 2013;110:1803–9. <https://doi.org/10.1017/S0007114513001256>.
- [102] Melendez-Martinez AJ, Nascimento AF, Wang Y, Liu C, Mao Y, Wang X-D. Effect of tomato extract supplementation against high-fat diet-induced hepatic lesions. *HepatoBiliary Surg Nutr* 2013;2.
- [103] Shao D, Bartley GE, Yokoyama W, Pan Z, Zhang H, Zhang A. Plasma and hepatic cholesterol-lowering effects of tomato pomace, tomato seed oil and defatted tomato seed in



- hamsters fed with high-fat diets. *Food Chem* 2013;139:589–96. <https://doi.org/10.1016/j.foodchem.2013.01.043>.
- [104] Ibrahim HS, Ahmed LA, El-din MME. The Functional Role of Some Tomato Products on Lipid Profile and Liver Function in Adult Rats. *J Med Food* 2008;11:551–9. <https://doi.org/10.1089/jmf.2007.0517>.
- [105] Hsu Y-M, Lai C-H, Chang C-Y, Fan C-T, Chen C-T, Wu C-H. Characterizing the Lipid-Lowering Effects and Antioxidant Mechanisms of Tomato Paste. *Biosci Biotechnol Biochem* 2008;72:677–85. <https://doi.org/10.1271/bbb.70402>.
- [106] Suganuma H, Inakuma T. Protective Effect of Dietary Tomato against Endothelial Dysfunction in Hypercholesterolemic Mice. *Biosci Biotechnol Biochem* 1999;63:78–82. <https://doi.org/10.1271/bbb.63.78>.
- [107] Femia AP, Caderni G, Ianni M, Salvadori M, Schijlen E, Collins G, Bovy A, Dolara P. Effect of diets fortified with tomatoes or onions with variable quercetin-glycoside content on azoxymethane-induced aberrant crypt foci in the colon of rats. *Eur J Nutr* 2003;42:346–52. <https://doi.org/10.1007/s00394-003-0431-5>.
- [108] Bobek P, Ozdín L, Hromadová M. The effect of dried tomato, grape and apple pomace on the cholesterol metabolism and antioxidative enzymatic system in rats with hypercholesterolemia. *Nahr Food* 1998;42:317–20. [https://doi.org/10.1002/\(SICI\)1521-3803\(199810\)42:05%3C317::AID-FOOD317%3E3.0.CO;2-Y](https://doi.org/10.1002/(SICI)1521-3803(199810)42:05%3C317::AID-FOOD317%3E3.0.CO;2-Y).
- [109] Das S, Otani H, Maulik N, Das DK. Lycopene, tomatoes, and coronary heart disease. *Free Radic Res* 2005;39:449–55. <https://doi.org/10.1080/10715760500053685>.
- [110] Sesso HD, Wang L, Ridker PM, Buring JE. Tomato-Based Food Products Are Related to Clinically Modest Improvements in Selected Coronary Biomarkers in Women. *J Nutr* 2012;142:326–33. <https://doi.org/10.3945/jn.111.150631>.
- [111] Mazidi M, Ferns GA, Banach M. A high consumption of tomato and lycopene is associated with a lower risk of cancer mortality: results from a multi-ethnic cohort. *Public Health Nutr* 2020;23:1569–75. <https://doi.org/10.1017/S1368980019003227>.
- [112] Mazidi M, Katsiki N, George ES, Banach M. Tomato and lycopene consumption is inversely associated with total and cause-specific mortality: a population-based cohort study, on behalf of the International Lipid Expert Panel (ILEP). *Br J Nutr* 2020;124:1303–10. <https://doi.org/10.1017/S0007114519002150>.
- [113] Madlala HP, Steyn NP, Kalk E, Davies M-A, Nyemba D, Malaba TR, Mehta U, Petro G, Boule A, Myer L. Association between food intake and obesity in pregnant women living with and without HIV in Cape Town, South Africa: a prospective cohort study. *BMC Public Health* 2021;21:1504. <https://doi.org/10.1186/s12889-021-11566-2>.
- [114] Popiolek-Kalisz J. The Relationship between Dietary Flavonols Intake and Metabolic Syndrome in Polish Adults. *Nutrients* 2023;15:854. <https://doi.org/10.3390/nu15040854>.
- [115] Marcotorchino J, Romier B, Gouranton E, Riollet C, Gleize B, Malezet-Desmoulin C, Landrier J. Lycopene attenuates LPS -induced TNF- $\alpha$  secretion in macrophages and inflammatory markers in adipocytes exposed to macrophage-conditioned media. *Mol Nutr Food Res* 2012;56:725–32. <https://doi.org/10.1002/mnfr.201100623>.
- [116] Hung C-F, Huang T-F, Chen B-H, Shieh J-M, Wu P-H, Wu W-B. Lycopene inhibits TNF- $\alpha$ -induced endothelial ICAM-1 expression and monocyte-endothelial adhesion. *Eur J Pharmacol* 2008;586:275–82. <https://doi.org/10.1016/j.ejphar.2008.03.001>.



- [117] Flori L, Piragine E, Spezzini J, Citi V, Calderone V, Martelli A. Influence of Polyphenols on Adipose Tissue: Sirtuins as Pivotal Players in the Browning Process. *Int J Mol Sci* 2023;24. <https://doi.org/10.3390/ijms24119276>.
- [118] Han TS, Richmond P, Avenell A, Lean MEJ. Waist circumference reduction and cardiovascular benefits during weight loss in women. *Int J Obes* 1997;21:127–34. <https://doi.org/10.1038/sj.ijo.0800377>.
- [119] Hosseinpanah F, Barzin M, Mirmiran P, Azizi F. Effect of changes in waist circumference on metabolic syndrome over a 6.6-year follow-up in Tehran. *Eur J Clin Nutr* 2010;64:879–86. <https://doi.org/10.1038/ejcn.2010.79>.
- [120] Gouranton E, Aydemir G, Reynaud E, Marcotorchino J, Malezet C, Caris-Veyrat C, Blomhoff R, Landrier JF, Rühl R. Apo-10'-lycopenoic acid impacts adipose tissue biology via the retinoic acid receptors. *Biochim Biophys Acta BBA - Mol Cell Biol Lipids* 2011;1811:1105–14. <https://doi.org/10.1016/j.bbalip.2011.09.002>.
- [121] Mounien L, Tourniaire F, Landrier J-F. Anti-Obesity Effect of Carotenoids: Direct Impact on Adipose Tissue and Adipose Tissue-Driven Indirect Effects. *Nutrients* 2019;11:1562. <https://doi.org/10.3390/nu11071562>.
- [122] Das D, Jothimani G, Banerjee A, Duttaroy AK, Pathak S. The cardioprotective effects of Fruitflow® against Doxorubicin-induced toxicity in rat cardiomyoblast cells H9c2 (2–1) and high-fat diet-induced dyslipidemia and pathological alteration in cardiac tissue of Wistar Albino rats. *Biomed Pharmacother* 2024;180:117607. <https://doi.org/10.1016/j.biopha.2024.117607>.
- [123] Farquhar WB, Edwards DG, Jurkovic CT, Weintraub WS. Dietary Sodium and Health. *JACC* 2015;65:1042–50. <https://doi.org/10.1016/j.jacc.2014.12.039>.
- [124] De Oliveira LF, De Azevedo LG, Da Mota Santana J, De Sales LPC, Pereira-Santos M. Obesity and overweight decreases the effect of vitamin D supplementation in adults: systematic review and meta-analysis of randomized controlled trials. *Rev Endocr Metab Disord* 2020;21:67–76. <https://doi.org/10.1007/s11154-019-09527-7>.
- [125] Porrini M, Riso P, Brusamolino A, Berti C, Et. A. Daily intake of a formulated tomato drink affects carotenoid plasma and lymphocyte concentrations and improves cellular antioxidant protection. *Br J Nutr* 2005. <https://doi.org/10.1079/bjn20041315>.
- [126] Visioli F, Riso P, Grande S, Galli C, Et. A. Protective activity of tomato products on in vivo markers of lipid oxidation. *Eur J Nutr* 2003. <https://doi.org/10.1007/s00394-003-0415-5>.
- [127] Riso P, Visioli F, Erba D, Testolin G, Porrini M. Lycopene and vitamin C concentrations increase in plasma and lymphocytes after tomato intake. Effects on cellular antioxidant protection. *Eur J Clin Nutr* 2004. <https://doi.org/10.1038/sj.ejcn.1601974>.
- [128] Ashor AW, Lara J, Mathers JC, Siervo M. Effect of vitamin C on endothelial function in health and disease: A systematic review and meta-analysis of randomised controlled trials. *Atherosclerosis* 2014;235:9–20. <https://doi.org/10.1016/j.atherosclerosis.2014.04.004>.
- [129] Omenn GS, Goodman GE, Thornquist MD, Balmes J, Cullen MR, Glass A, Keogh JP, Meyskens FL, Valanis B, Williams JH, Barnhart S, Hammar S. Effects of a Combination of Beta Carotene and Vitamin A on Lung Cancer and Cardiovascular Disease. *N Engl J Med* 1996;334:1150–5. <https://doi.org/10.1056/NEJM199605023341802>.
- [130] The Effect of Vitamin E and Beta Carotene on the Incidence of Lung Cancer and Other Cancers in Male Smokers | *New England Journal of Medicine*. *N Engl J Med* 1994;330.



- [131] Mauvais-Jarvis F. Sex differences in metabolic homeostasis, diabetes, and obesity. *Biol Sex Differ* 2015;6:14. <https://doi.org/10.1186/s13293-015-0033-y>.
- [132] Karastergiou K, Smith SR, Greenberg AS, Fried SK. Sex differences in human adipose tissues – the biology of pear shape. *Biol Sex Differ* 2012;3:13. <https://doi.org/10.1186/2042-6410-3-13>.
- [133] Panagiotakos DB, Pitsavos C, Stefanadis C. Dietary patterns: A Mediterranean diet score and its relation to clinical and biological markers of cardiovascular disease risk. *Nutr Metab Cardiovasc Dis* 2006;16:559–68. <https://doi.org/10.1016/j.numecd.2005.08.006>.
- [134] Estruch R, Ros E, Salas-Salvadó J, Covas M-I, Corella D, Arós F, Gómez-Gracia E, Ruiz-Gutiérrez V, Fiol M, Lapetra J, Lamuela-Raventos RM, Serra-Majem L, Pintó X, Basora J, Muñoz MA, Sorlí JV, Martínez JA, Fitó M, Gea A, Hernán MA, Martínez-González MA. Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. *N Engl J Med* 2018;378. <https://doi.org/10.1056/NEJMoa1800389>.
- [135] Park E, Stacewicz-Sapuntzakis M, Sharifi R, Wu Z, Freeman VL, Bowen PE. Diet adherence dynamics and physiological responses to a tomato product whole-food intervention in African–American men. *Br J Nutr* 2013;109:2219–30. <https://doi.org/10.1017/S0007114512004436>.



**Table 1.** Clinical trials investigating the effects of tomato and tomato-based product supplementation on anthropometrics parameters and metabolic dysfunction parameters associated with obesity.

Study	Study design <sup>1</sup>	Study population	Average BMI of population	Number of subjects <sup>2</sup>	Duration <sup>3</sup>	Form of tomato	Tomato dosage	Outcomes	Main results <sup>4</sup>
<b>Chen C-Y. and Chien Y-M., 2024 [52]</b>	Two-arm RCT, OL  <b>Control:</b> iso-caloric and macronutrients diet with sprouts and restricted tomatoes and tomato-based products	Women with MetS or moderate hypercholesterolemia (45-70y)	26.4 kg/m <sup>2</sup>	<b>53 ♀</b> I: 30 ♀ C: 23 ♀	<b>8w</b>	<b>Raw tomato</b>	<b>200g/d</b>	<i>BW, BMI, BFM, WC, HC, BP, TG, TC, LDL-C, HDL-C serum, FBG, Insulin, HOMA-IR and QUICKI indexes and IL-6 plasma</i>	↓ BFM, WC and HC ↓ SBP ↓ TC and TG serum ↑ HDL-C serum ↓ FBG plasma
<b>Yu Y. et al., 2024 [54]</b>	Two-arm RCT, DB  <b>Control:</b> 300 mg placebo tablets and sugar-coated, with the same excipients as Fruitflow (microcrystalline cellulose, lactose, and magnesium stearate)	Adults with elevated TC levels (35-65y)	25.1 kg/m <sup>2</sup>	<b>60 (11 ♂, 49 ♀)</b> I: 30 (5 ♂, 25 ♀) C: 30 (6 ♂, 24 ♀)	<b>45d</b> (follow-up for over 15d)	<b>Tomato extract (Fruitflow®)</b>	<b>1 tablet/d (150mg extract)</b>	<i>BW, BMI, BFM, BP, TG, TC, LDL-C, HDL-C, FGB, CRP, Hcy serum</i>	↓ BW and BMI* (and after 15d follow-up for BMI) ↓ SBP and DBP* ↑ HDL-C serum* ↓ FBG serum (after 15d follow-up) ↓ CRP serum (after 15d follow-up) ↓ Hcy serum* (and after 15d follow-up)
<b>López-Yerena A. et al., 2023 [53]</b>	Two-arm RCT cross-over, OL  <b>Control:</b> Habitual diet without tomato or tomato-based products	Overweight or obese adults (27-60y)	31.1 kg/m <sup>2</sup>	<b>40 (27 ♂, 13 ♀)</b>	<b>6w</b> (2w WO)	<b>Soffritto</b>	<b>100g/d</b>	<i>BW, BMI, WC, WHR, BP, TG, TC, LDL-C, HDL-C, LDL-C/HDL-C ratio, FBG, AST, ALT, GGT, Urea, Uric acids, Creatinine, TP, Endothelial function and Platelet aggregation</i>	↑ DBP ↓ Platelet aggregation
<b>Yang T.H. et al., 2020 [55]</b>	Two-arm RCT, OL  <b>Control:</b> 1500kcal diet (iso-macronutrients), with 5 servings of vegetables/d	Overweight or obese adults (57-61y)	27.0 kg/m <sup>2</sup>	<b>36 ♀</b> I: 20 ♀ C: 16 ♀	<b>8w</b>	<b>Raw beefsteak tomato</b>	<b>250g/d</b>	<i>BW, BMI, BFM, WC, HC, WHR, BMR, BP, TG, TC, LDL-C, HDL-C, CRP, AST and ALT levels</i>	↑ TC, LDL-C and HDL-C serum*
<b>Pourahma di Z. et al., 2015</b>	Two-arm RCT, DB  <b>Control:</b> 330mL water/d	Overweight or obese students	28.3 kg/m <sup>2</sup>	<b>75 ♀</b> I: 40 ♀ C: 35 ♀	<b>20d</b>	<b>Tomato juice</b>	<b>330mL/d</b>	<i>BW, BMI, SOD, CAT, GSH-Px and TAC levels</i>	NS





[56]		non-smokers (20-30y)							
<b>Cuevas-Ramos D. et al., 2013 [62]</b>	Two-arm RCT, SB  Control: 300g raw cucumber/d	Healthy adults (18-65y)	27.1 kg/m <sup>2</sup>	<b>50</b> <b>(9 ♂, 41 ♀)</b> I: 26 (4 ♂, 22 ♀) C: 24 (5 ♂, 19 ♀)	<b>4w</b> (after 2w of isocaloric diet)	<b>Raw tomato</b>	<b>300g/d</b> (≈2 tomatoes)	<i>BMI, WC, HC WHR, TG, TC, LDL-C and HDL-C serum</i>	↑ HDL-C serum* ↑ HDL-C serum with tomato intake (β = 5.79) and adherence days (β = 0.61) (R=0.83, R <sup>2</sup> =0.69, p<0.0001)
<b>Park E. et al., 2012 [135]</b>	Two-arm RCT, OL  Control: Other fruit-based products (apple or grape juice, canned fruit and boxes of raisins)	Adults at elevated risk for prostate cancer (51-83y)	29.7 kg/m <sup>2</sup>	<b>33 ♂</b> I: 21 ♂ C: 12 ♂	<b>3m</b>	<b>Tomato products</b>	<b>≥ 1serving/d</b>	<i>BW, BP and TC plasma</i>	NS
<b>Thies F. et al., 2012 [66]</b>	Triple-arm RCT, SB  Control: Low-tomato control diet (<10mg LYC/w)	Healthy adults (40-65y)	26.8 kg/m <sup>2</sup>	<b>225</b> <b>(93 ♂, 132 ♀)</b> I "Tomato": 81 (35 ♂, 46 ♀) I "Extract": 68 (28 ♂, 40 ♀) C: 76 (30 ♂, 46 ♀)	<b>12w</b> (after 4w of control diet)	<b>Tomato products or extract tomato</b> (Holland and Barret)	<b>Equivalent to ≈32.3-50.1mg LYC/d</b> (Tomato) or <b>1capsule/d</b> (Extract)	<i>BW, BMI, WC, BP, TG, TC, LDL-C, HDL-C, ApoA-I, ApoB-100, FBG, Insulin, HOMA-IR and QUICKI indexes, CRP, IL-6, ICAM-1 and Ox-LDL serum</i>	NS
<b>Ried K. et al., 2009 [65]</b>	Three-arm RCT, DB  Control: 1 placebo capsule/d with soy oil (matched o tomato extract capsules by colour, odour and size)	Adults prehypertensive (22-73y)	26.2 kg/m <sup>2</sup>	<b>36</b> <b>(19 ♂, 17 ♀)</b> I "Tomato": 15 (7 ♂, 8 ♀) C: 10 (5 ♂, 5 ♀)	<b>8w</b>	<b>Tomato extract</b>	<b>1 capsule/d (250mg extract)</b>	<i>BW, BMI, WC, BP</i>	NS
<b>Engelhard Y.N. et al., 2006 [70]</b>	Single-arm, RCT cross-over, SB  Control: 1 placebo capsule/d (identical looking) (4 weeks)	Adults with hypertension grade 1 (30-70y)	29.5 kg/m <sup>2</sup>	<b>31</b> <b>(18 ♂, 13 ♀)</b>	<b>8w</b> (after 4w of placebo period)	<b>Tomato extract</b> (Lyc-o-Mato®)	<b>1 capsule/d (250mg)</b>	<i>BMI, WC, BP, TG, TC, LDL-C, HLD-C, ApoA-I, ApoB-100, FBG, TBARS and GPx activities, Urea, Uric acids, Creatinine and Hcy serum</i>	↓ SBP and DBP
<b>Upritchard J.E. et al., 2000 [68]</b>	Four-arm RCT, OL  Control: Placebo gelatin capsule with starch (8 weeks)	Adults with well-controlled type 2 diabetes (<75y)	30.9 kg/m <sup>2</sup>	<b>52</b> <b>(32 ♂, 20 ♀)</b> I "Tomato": 15 (10 ♂, 5 ♀) C: 76 (30 ♂, 46 ♀)	<b>4w</b> (after 4w of placebo period)	<b>Tomato juice</b>	<b>500mL/d</b>	<i>BMI, BP, TC, FBG, CRP, ICAM-1 and VCAM-1 plasma</i>	↑ LDL oxidation lag time by copper ions (in Tomato group)*

**ApoA-I:** Apolipoprotein A-I, **ApoB:** Apolipoprotein B, **AST:** Aspartate aminotransferase, **aMT6s:** 6-sulfatoxymelatonin, **ALT:** Alanine aminotransferase, **BFM:** Body fat mass, **BMI:** Body mass index, **BMR:** Basal metabolic rate, **BP:** Blood pressure, **CAT:** Catalase, **CRP:** C-reactive protein, **DBP:** Diastolic blood pressure, **FBG:** Fasting blood glucose, **FRAP:** Ferric reducing antioxidant power, **GGT:** G-glutamyl transferase, **GPx:** Glutathione peroxidase, **GSH:** Reduced glutathione, **HADS:** Hospital Anxiety and Depression Scale, **HC:** Hip circumference, **Hcy:** Homocystein, **HDL-C:** High-density lipoprotein cholesterol, **HOMA-IR:** Homeostatic model assessment of insulin resistance, **HR:** Heart rate, **ICAM-1:** Intercellular adhesion molecule-1, **IL-6:** Interleukin-6, **LDL-C:** Low-density lipoprotein cholesterol, **MCP-1:** Monocyte chemoattractant protein-1, **MDA:** Malondialdehyde, **MetS:** Metabolic syndrome, **QUICKI:** Quantitative insulin sensitivity check index, **REE:** Resting energy expenditure, **SBP:** Systolic blood pressure, **SOD:** Superoxide dismutase, **TAC:** Total antioxidant capacity, **TBARS:** Thiobarbituric acid reactive substances, **TC:** Total cholesterol, **TG:** Triglycerides, **TP:** Total protein, **VCAM-1:** Vascular cell adhesion molecule-1, **WC:** Waist circumference, **WHR:** Waist-to-hip ratio, **WO:** Wash-out.

<sup>1</sup> Study design abbreviations: **RCT**, Randomized controlled trial. Blinding: **OL**, Open-label; **SB**, Single-blind; **DB**, Double-blind.

<sup>2</sup> Number subjects abbreviations: **C**, Number of subjects in the control group; **I**, Number of subjects in the intervention group. **♂**, Males; **♀**, Females.

<sup>3</sup> Duration abbreviations: **d**, Days; **w**, Weeks; **m**, Months.

<sup>4</sup> The results presented indicate values that differ significantly from the control group. When significance is observed relative to baseline, this is indicated by an asterisk \*.



**Table 2.** Primary meta-analysis of randomized controlled trials assessing the effects of tomato and tomato-based product interventions on anthropometric and cardiometabolic outcomes

Description	Description		Pooled effect estimates			Heterogeneity			Prediction interval
	N of studies	N of subjects	MD	95% CI	P-value (Effect)	Tau <sup>2</sup>	I <sup>2</sup> (%)	P-value (Q-test)	
<b>Anthropometric parameters</b>									
BW (kg)	7	362	-0.659	[-1.94; 0.63]	0.31	1.2	37.9	0.13	[-3.14; 1.83]
BMI (kg/m <sup>2</sup> )	8	441	-0.004	[-0.20; 0.19]	0.96	0.0	0.0	0.96	[-0.25; 0.24]
BFM (%)	3	149	-0.069	[-0.72; 0.59]	0.83	0.0	0.0	0.90	[-0.72; 0.59]
BFM (kg)	2	89	-0.282	[-0.91; 0.34]	0.37	0.0	0.0	0.82	[-0.91; 0.34]
HC (cm)	3	139	-0.193	[-1.01; 0.62]	0.64	0.0	0.0	0.97	[-1.01; 0.62]
WC (cm)	5	242	-1.153	[-2.27; -0.04]	<b>0.04</b>	0.0	0.0	0.58	[-2.27; -0.04]
WHR	4	219	-0.005	[-0.02; 0.01]	0.63	0.0	0.0	0.96	[-0.02; 0.01]
<b>Blood pressure</b>									
SBP (mmHg)	8	549	-2.894	[-6.64; 0.85]	0.12	14.1	56.7	<b>0.01</b>	[-11.15; 5.37]
DBP (mmHg)	8	549	0.077	[-1.91; 2.06]	0.93	2.9	38.4	0.16	[-3.82; 3.98]
<b>Lipid homeostasis</b>									
TG (mg/dL)	7	502	0.181	[-11.23; 11.59]	0.97	70.3	31.8	0.19	[-19.82; 20.18]
TC (mg/dL)	8	535	1.881	[-3.11; 6.87]	0.46	0.0	0.0	0.35	[-3.11; 6.87]
LDL-C (mg/dL)	8	562	0.234	[-3.98; 4.45]	0.91	0.0	0.0	0.56	[-3.98; 4.45]
HDL-C (mg/dL)	7	502	1.913	[-0.65; 4.47]	0.14	4.8	45.5	0.12	[-3.09; 6.91]
ApoA-I (mg/dL)	3	287	-0.785	[-6.75; 5.18]	0.79	0.0	0.0	0.79	[-6.75; 5.18]
ApoB-100 (mg/dL)	3	287	-3.309	[-8.22; 1.61]	0.18	0.0	0.0	0.82	[-8.22; 1.61]
<b>Glucose homeostasis</b>									
FBG (mg/dL)	5	420	0.592	[-1.21; 2.39]	0.51	0.0	0.0	0.25	[-1.21; 2.39]
Insulin (μU/mL)	3	278	0.447	[-1.50; 2.40]	0.65	1.9	65.7	0.07	[-2.90; 3.80]
QUICKI	3	278	0.135	[-0.11; 0.38]	0.28	0.0	92.8	<b>&lt;0.0001</b>	[-0.35; 0.62]
<b>Inflammatory and oxidative stress biomarkers</b>									
CRP (mg/dL)	3	257	3.855	[-3.88; 11.59]	0.32	25.9	50.8	0.13	[-8.77; 16.48]
IL-6 (pg/L)	2	225	-0.094	[-0.34; 0.15]	0.44	0.0	0.0	0.78	[-0.34; 0.15]
Ox-LDL (mmol/L)	2	225	0.204	[-6.83; 7.24]	0.95	0.0	0.0	0.84	[-6.83; 7.24]
<b>Renal function</b>									
Creatinine (mg/dL)	2	142	0.015	[-0.01; 0.04]	0.23	0.0	0.0	0.61	[-0.01; 0.04]
Urea (mg/dL)	2	142	0.352	[-2.14; 2.85]	0.78	0.0	0.0	0.83	[-2.14; 2.85]
Uric acid (mg/dL)	2	142	-0.154	[-0.49; 0.18]	0.36	0.0	0.0	0.72	[-0.49; 0.18]

Pooled mean differences (MD; ΔI-ΔC) with 95% confidence intervals (CI) were calculated using random-effects models (REML).

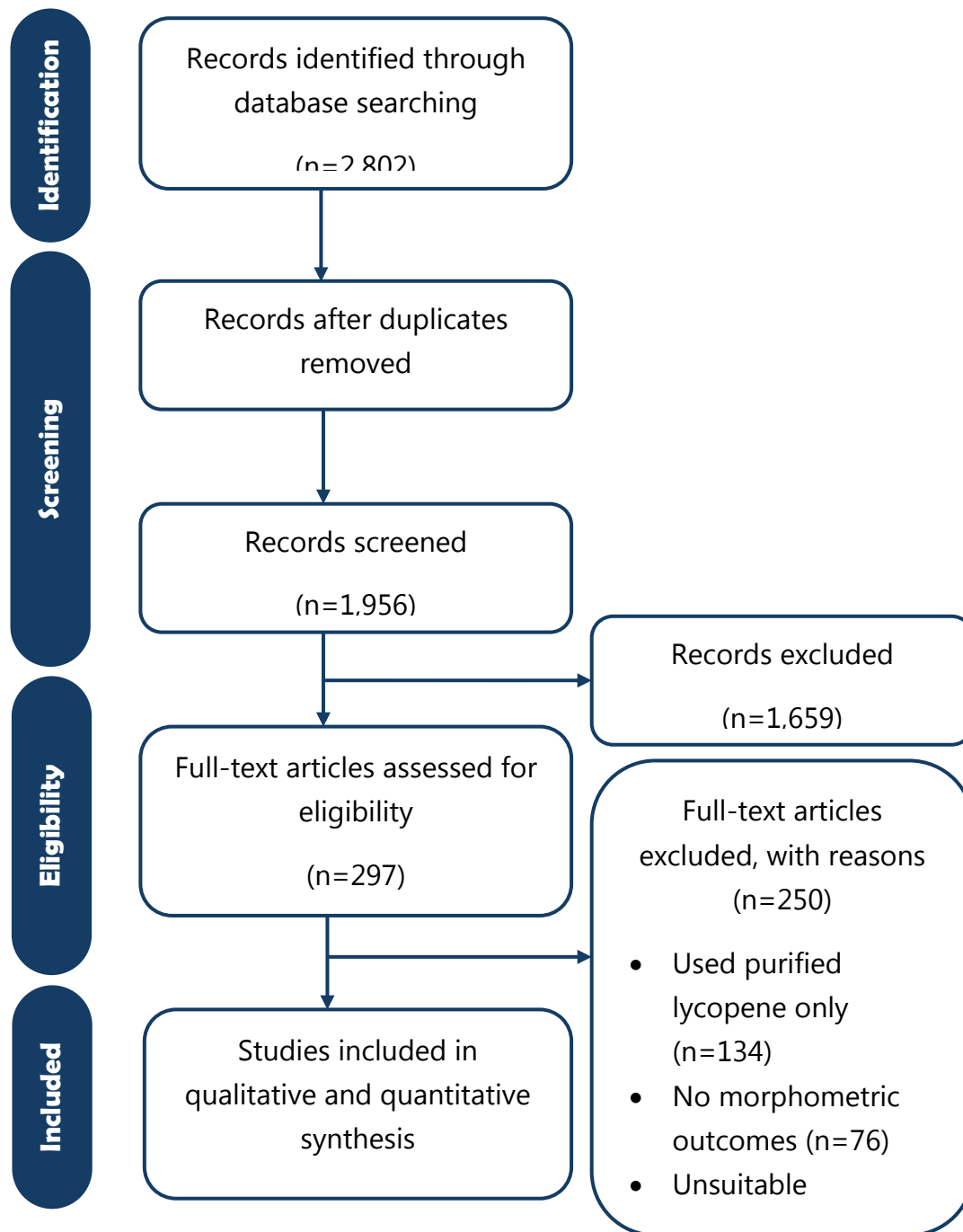
When change-score standard deviations were not reported, they were derived from pre- and post-intervention standard deviations assuming a within-group correlation coefficient ( $r$ ) of 0.5; sensitivity analyses using  $r = 0.25$  and  $r = 0.75$  showed consistent results.

Heterogeneity was assessed using  $\tau^2$ ,  $I^2$ , and Cochran's Q test. Prediction intervals indicate the expected range of true effects in future

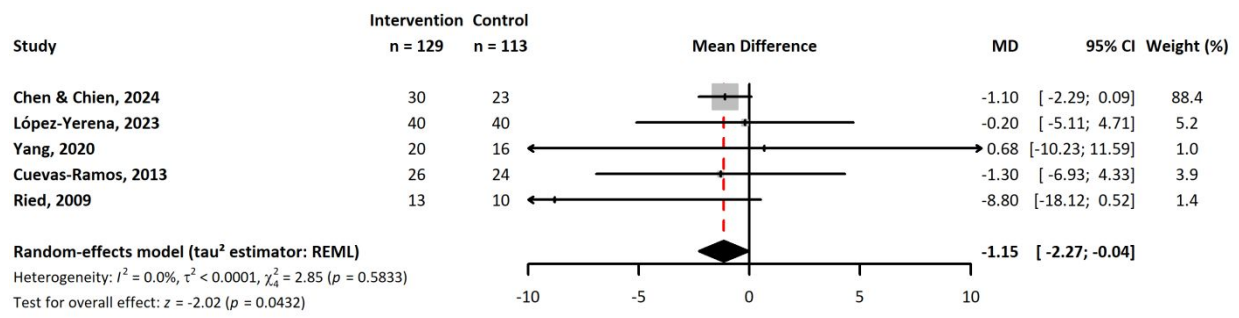


studies. Outcomes reported by fewer than two studies were not pooled. **ApoA-I**: Apolipoprotein A-I, **ApoB**: Apolipoprotein B, **BFM**: Body fat mass, **BMI**: Body mass index, **BW**: Body weight, **CRP**: C reactive protein, **DBP**: Diastolic blood pressure, **FBG**: Fasting blood glucose, **HC**: Hip circumference, **HDL-C**: High-density lipoprotein cholesterol, **IL**: Interleukin, **LDL-C**: Low-density lipoprotein cholesterol, **Ox-LDL**: Oxidized low-density lipoprotein, **QUICKI**: Quantitative insulin sensitivity check index, **SBP**: Systolic blood pressure, **TC**: Total cholesterol, **TG**: Triglycerides, **WC**: Waist circumference, **WHR**: Waist-to-hip ratio.



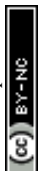
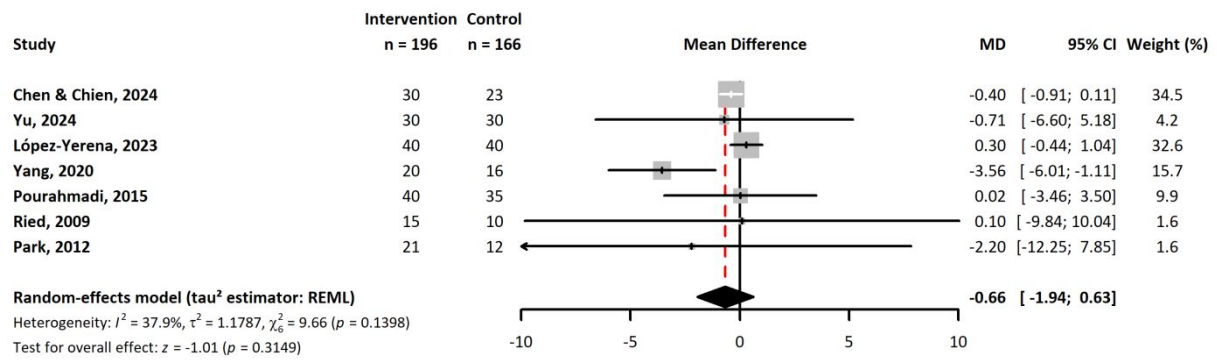
**Figure 1.** PRISMA 2009 Flow diagram of study selection.View Article Online  
DOI: 10.1039/D6FO00495D

**Figure 2.** Forest plots of the effect of tomato supplementation on waist circumference View Article Online  
DOI: 10.1039/D6FO00495D



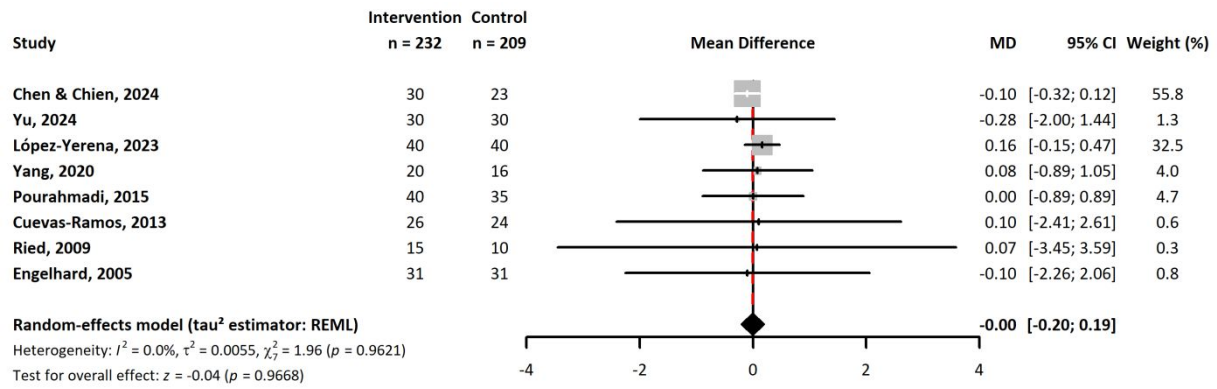
**Figure 3.** Forest plots of the effect of tomato supplementation on body weight

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**Figure 4.** Forest plots of the effect of tomato supplementation on body mass index

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### Data availability statement

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No primary research results, software or code have been included and no new data were generated or analysed as part of this review

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