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REVIEW

The effects of quinoa seed supplementation on cardiovascular risk factors: A systematic review and meta-analysis of controlled clinical trials

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This meta-analysis was designed to determine the effect of quinoa seed on cardiovascular disease (CVD) risk factors in adults. PubMed, Scopus, ISI Web of Science, and Cochrane library were searched electronically from their inception to February 2020 to identify eligible RCTs. We calculated the pooled estimates of weighted mean differences (WMDs) and their 95% confidence intervals (CIs) by using random-effects models. Five eligible RCTs representing 206 subjects were enrolled. The pooled result showed that quinoa seed supplementation significantly lowered the body weight (WMD: −1.26 kg, 95% CI: −2.35, −0.18, p = .02), waist circumference (WC) (WMD: −1.15 cm, 95% CI: −2.08, −0.21, p = .01), fat mass (FM) (WMD: −0.59%, 95% CI: −1.14, −0.03, p = .03), insulin serum level (WMD: −0.86 pmol/L, 95% CI: −13.38, −1.59, p = .01), triglyceride (TG) (WMD: −7.20 mg/dl, 95% CI: −9.52, −4.87, p < .001), total cholesterol (TC) (WMD: −6.86 mg/dl, 95% CI: −10.64, −3.08, p < .001), and low density lipoprotein (LDL) (WMD: −3.08 mg/dl, 95% CI: −5.13, −1.03, p = .003) levels. However, no significant changes were seen in other markers (p > .05). The current evidence suggests that quinoa seed might be utilized as a possible new effective and safe supplementary option to better prevent and control CVD in humans.

KEYWORDS

glycemic control, lipid profile, meta-analysis, quinoa seed, systematic review

1 | INTRODUCTION

Cardiovascular disease (CVD) continues to be a major cause of adult death, and places a substantial burden on the health care systems and economies worldwide (Wilkins et al., 2017). Several risk factors for CVD can be modified by lifestyle changes (Association, 2017; Pourmasoumi, Hadi, Najafgholizadeh, Joukar, & Mansour-Ghanaei, 2020). Increased consumption of fruit and vegetables could therefore prevent CVD, as they are rich in dietary fiber, vitamins, mineral, and flavonoids (Alissa & Ferns, 2017; Hadi, Pourmasoumi, Najafgholizadeh, Kafeshani, & Sahebkar, 2019). Furthermore, certain phytochemicals, especially polyphenols may have beneficial health effects against CVD (Alissa & Ferns, 2017; Hasani et al., 2019; Zheng et al., 2017). Recently, using natural products with different beneficial characteristics attracted huge attention regarding the management of CVD (Cicero et al., 2017; Ebrahimi et al., 2019; Heinrich et al., 2020; Pahlavani et al., 2019; Rasad, Entezari, Ghadiri, Mahaki, & Pahlavani, 2018; Sahebkar et al., 2016; Williamson, Liu, & Izzo, 2020).

Quinoa (*Chenopodium quinoa*) is a flowering plant in the amaranth family; the seeds are rich in protein, dietary fiber, B vitamins, and minerals in amounts greater than in many grains. As well, significant amounts of essential fatty acids such as linoleic and a-linolenic, and

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high concentrations of antioxidants such as a- and g-tocopherol can be detected from the selected seeds (Filho et al., 2017). The main producers of this herb include Peru and Bolivia; although its cultivation has spread to more than 70 countries, even Europeans (Sezgin & Sanlier, 2019).

In recent years, this "pseudocereal" has attracted researcher's attention, especially for clinical interventions. Yao et al., in a cellular investigation, assessed the effects of quinoa saponins (QS) on the differentiation of 3 T3-L1 preadipocytes. They observed that QS reduced intracellular triglycerides (TG) and expression of peroxisome proliferator-activated receptor γ (PPARγ), and sterol regulatory element-binding protein-1c (SREBP-1c), so it was considered as adipose tissue mass modulatory factor (Yao et al., 2015). Animal studies were also conducted in this area. Noratto et al. revealed that mice fed with quinoa have lower levels of total cholesterol (TC), low-density lipoprotein (LDL), oxidized LDL, and higher serum insulin, compared to the control group (Noratto, Murphy, & Chew, 2019). Such results were detected from human subjects. In a 12-week intervention with a dose of 50 g/day quinoa, Navarro-Perez et al. reported that serum TG was lowered from 1.14 to 0.72 mmol/L, whereas they did not show any significant reduction for other lipid profile and anthropometric indices (Navarro-Perez, Radcliffe, Tierney, & Jois, 2017). Furthermore, a 4-week intervention was carried out in postmenopausal women analyzing the effect of quinoa flake consumption on lipid profiles and oxidative stress markers. The positive results were observed for TG, TC, and LDL (De Carvalho et al., 2014). Anyway, the limited number of studies that investigated the issue have shown relatively controversial results.

The main aim of the present study, therefore, was to collect and reanalyze the related clinical trials' data, and reach a conclusion about the effectiveness of quinoa seed supplementation on glycemic control, lipid profile, and anthropometric indices in adults.

2 | METHODS

This systematic review and meta-analysis was performed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines (Moher, Liberati, Tetzlaff, & Altman, 2009) and the PICOS model for the definition of the inclusion criteria: P (Population): "adults," I (Intervention): "impact of the of quinoa supplementation," C (Comparators): "same conditions with control or placebo," O (Outcome): "insulin, fasting blood glucose (FBG), TG, TC, LDL, high-density lipoprotein (HDL), body weight, body mass index (BMI), waist circumference (WC), and fat mass (FM)", and S (study design): "randomized controlled trials."

2.1 | Search strategy

For this meta-analysis, we performed a search of PubMed (http://www.ncbi.nlm.nih.gov/pubmed), Scopus (http://www.scopus.com), ISI Web of Science (http://www.webofscience.com), and Cochrane library (http://www.cochranelibrary.com) databases from their inception to February 2020 to identify clinical trials that examined the effects of quinoa seed supplementation on cardiovascular risk factors in adults. No language restriction was considered while searching the mentioned databases. A search strategy was performed with the use of exploded Medical Subject Heading (MeSH) terms and corresponding key words. Briefly, we used the following format of search terms: (*Chenopodium quinoa*s OR Quinoas OR Quinoa) AND (Glycosylated Hemoglobin A OR Insulin Resistance OR Insulin OR Glucose OR Glucose Intolerance OR Fasting Blood Sugar OR Waist Circumference OR Body Mass Index OR Total Cholesterol OR Triglycerides OR High-Density Lipoprotein Cholesterol OR Low-Density Lipoprotein Cholesterol OR Lipid Profile). Reference lists of identified publications were also hand searched to identify other studies potentially eligible for inclusion.

2.2 | Study selection

Two researchers (S.A. and V.M.) assessed articles independently for eligibility. The decision to include studies was hierarchical and was made initially on the basis of screening the studies' titles and abstracts, and if a decision was not reached at this stage, then the full-text of the article was evaluated to make such a judgment. The full text of the selected articles was independently assessed by the same researchers. Studies were in our analysis if they met the following criteria: (a) study was a randomized controlled trail (RCT) in human with either a parallel or crossover design; (b) participants needed to have specifically ingested the quinoa seed intervention; (c) trials used a suitable control group, that is, the only difference between the control and treatment groups was quinoa seed; and (d) studies had to assess at least one primary outcomes (i.e., anthropometric indices [body weight, BMI, WC, FM], lipid profile [TC, LDL, HDL, TG], and glycemic markers [insulin, FBG]). Exclusion criteria were as follows: studies that included children, adolescence, pregnant or lactating women, trials with follow-up less than 2 weeks; and publications with duplicate data. Any disagreement was resolved by consensus or consultation with the other coauthors.

2.3 | Data extraction

Details on study characteristics (first author's last name, year of publication, study design, country, sample size, and follow-up duration) participant characteristics (age, sex, and health status), specification of interventions (amount of quinoa seed), type of comparison group, and outcomes, were independently extracted by the reviewers (S.A. and V.M.) using a standardized form. All missing data were requested from the original investigators via email. Any disagreements in abstracted data between the reviewers were adjudicated by a third author (A.Gh.).

2.4 | Quality assessment

The methodological quality of the included studies was assessed independently by two authors (S.A. and V.M.) using the Cochrane Collaboration tool (Higgins et al., 2011), where the following domains are included: selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias. Each item was scored as a low, unclear, or high risk of bias. Finally, the overall quality of the studies was categorized into weak, fair, or good, if <3, 3, or ≥4 domains were rated as low risk, respectively.

2.5 | Statistical analysis

This meta-analysis was performed using STATA software (version 11.0; Stata Corporation). The weighted mean differences (WMD) and standard deviation (SD) of relevant variables were collected in similar units, to estimate the pooled effects. In the case that net changes were not directly reported in intervention and control groups, WMD was calculated by the minus of the post-intervention data from the baseline value. Also, the SD of changes was estimated by [SD = SEM × sqrt (n); n = number of subjects] where standard error of mean (SEM) was reported. The SD of the mean difference was calculated using the following formula: SD = square root [(SD pre-treatment)^2 + (SD post-treatment)^2 − (2 × R × SD pre-treatment × SD post-treatment)] (Follmann, Elliott, Suh, & Cutler, 1992). To ensure the meta-analysis was not sensitive to the selected correlation coefficient (R = 0.5), all analyses were repeated using correlation coefficients of 0.2 and 0.8. To account for the potential heterogeneity in study designs we employed a random effects models. The degree of heterogeneity was quantified using the I-squared (I^2) statistic, and I^2 values of 25, 50, and 75 were considered as low, moderate, and high estimates, respectively. Sensitivity analysis is also conducted to detect the influence of a single study on the overall estimate via eliminating

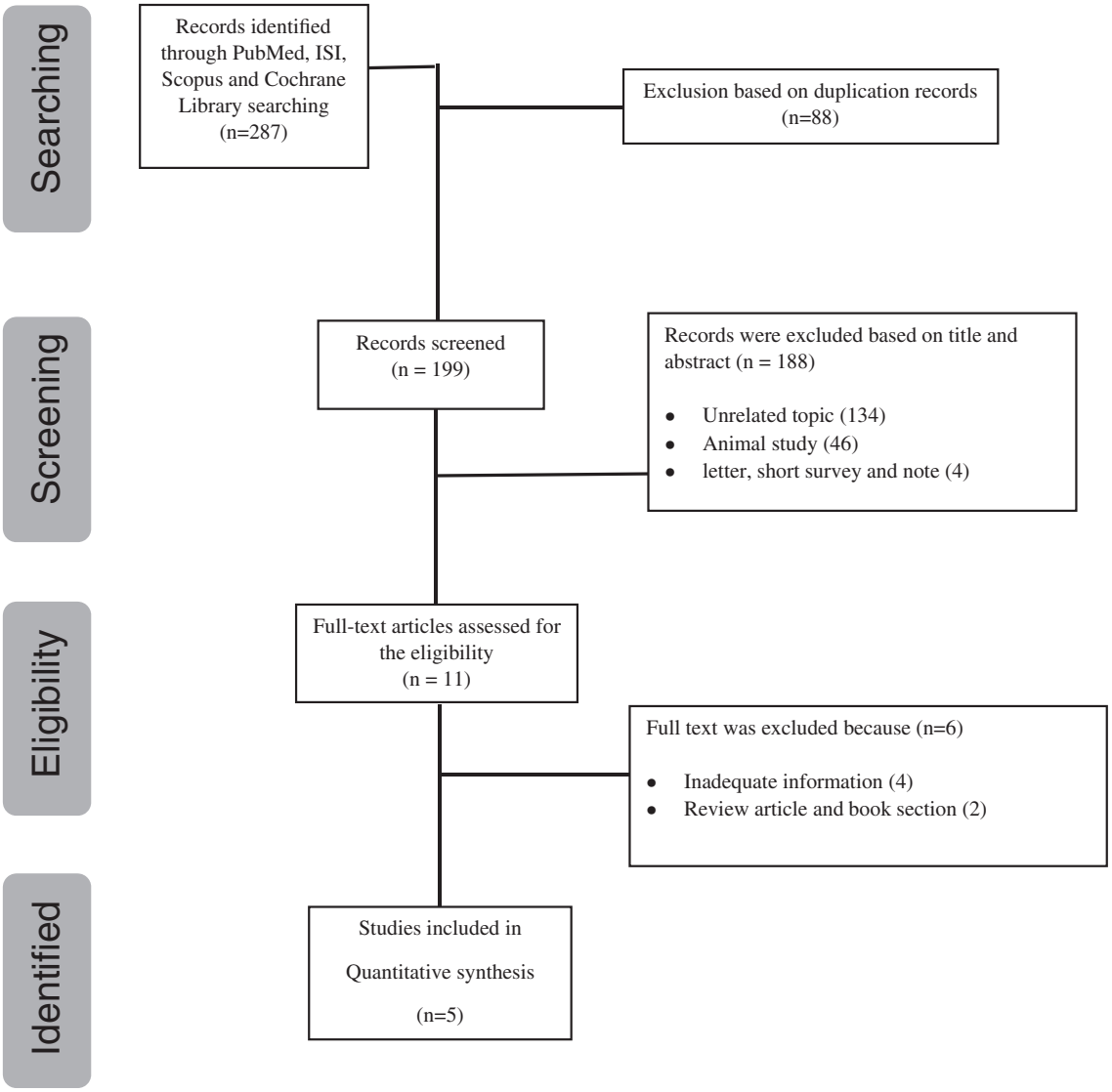

FIGURE 1 PRISMA flow diagram of study selection process

TABLE 1 Characteristics of the five included trials

Author publication year	Location	Design	Intervention			Gender	Intervention/control	Daily dose, g	Duration (week)	Patient features	Outcomes
			Number	Mean (range) age	Mean BMI (kg/m^2)						
Abellán Ruiz et al., 2017	Peru	RP	19	59.5	27	M/F	Processed quinoa/ placebo	20	4	Pre-diabetics	BMI, FBG
Anusha, Hymavathi, Vijayalakshmi, Reddy, & Robert, 2018	India	RC	10	(20–50)	(18–27)	M/F	*Chenopodium quinoa* wild/foxtail millet	65	4.5	Pre-diabetics	TG, TC, LDL, HDL
De Carvalho et al., 2014	Brazil	RP	18	61	29.5	F	Quinoa flakes/ corn flakes	25	4	Postmenopausal women	Weight, BMI, WC, FBG, TG, TC, LDL, HDL
Li et al., 2018	UK	RC	28	51.5	27.7	M	Quinoa-enriched bread/ refined wheat bread	20	4	Healthy overweight	Weight, BMI, FM, FBG, insulin, TG, TC, LDL, HDL
Navarro-Perez et al., 2017	Australia	RP	16	35	32.8	M/F	Chenopodium quinoa/ control	25	12	Overweight and obese	Weight, BMI, WC, FM, FBG, insulin, TG, TC, LDL, HDL
Navarro-Perez et al., 2017	Australia	RP	18	40	31.4	M/F	Chenopodium quinoa/ control	50	12	Overweight and obese	Weight, BMI, WC, FM, FBG, insulin, TG, TC, LDL, HDL

Abbreviations: BMI, body mass index; F, female; FBG, fasting blood glucose; HDL; high-density lipoprotein; LDL, low-density lipoprotein; M, male; RC randomized cross-over; RP, randomized parallel; TC, total cholesterol; TG, triglyceride; WC, waist circumference.

one study and repeating the analysis. Publication bias was evaluated via the Egger's regression asymmetry test. *p*-values <.05 were considered statistically significant.

3 | RESULTS

3.1 | Study selection

Out of 287 provided articles in initial search, 88 duplicated studies excluded. After screened for title and abstract evaluation of unduplicated studies: 188 unrelated studies discarded due to primary evaluation of inclusion criteria: Unrelated title (*n* = 134), animal study (*n* = 46), letter, short survey, and note (*n* = 4). Consequently, 11 studies remained and after full text scrutinized six studies were excluded: (a) review and book section (*n* = 2), (b) studies that enough information was not stated in them (*n* = 4). Finally, five trials met all inclusion criteria. The PRISMA flow diagram of search process is depicted in Figure 1.

3.2 | Study characteristics

Characteristics of included studies are abstracted in Table 1. In total, 206 participants were recruited. Included studies were published between 2013 and 2018. The follow-up period ranged between 4 weeks and 12 weeks. The sample size of the included studies ranged from 10 to 28 participants. Three studies were parallel (Abellán Ruiz et al., 2017; De Carvalho et al., 2014; Navarro-Perez et al., 2017) and two studies were cross over (Anusha et al., 2018; Mann et al., 2018) randomized clinical trial. Selected studies enrolled subjects with prediabetes (Abellán Ruiz et al., 2017; Anusha et al., 2018), healthy overweight and obese subjects (Mann et al., 2018; Navarro-Perez et al., 2017), and postmenopausal women (De Carvalho et al., 2014). included studies carried out in different countries such UK (Mann et al., 2018), India (Anusha et al., 2018), Brazil (De Carvalho et al., 2014), Australia (Navarro-Perez et al., 2017) and Peru (Abellán Ruiz et al., 2017). Some studies enrolled only males (Mann et al., 2018) and females (De Carvalho et al., 2014) and the rest of included studies involved both genders (Abellán Ruiz et al., 2017; Navarro-Perez et al., 2017; Anusha et al., 2018). In addition, studies performed in subjects with different baseline BMI and age ranged from 18 to 32.8 kg/m^2 and 20 to 61 year, respectively. Quinoa seed as the intervention was used with doses from 20.0 to 65.0 g, in addition, refined wheat bread (Mann et al., 2018), foxtail millet (Anusha et al., 2018), corn flakes (De Carvalho et al., 2014), or placebo (Abellán Ruiz et al., 2017) were chosen as the control regimen in these studies. However, one study received no intervention as a control group (Navarro-Perez et al., 2017). Most studies reported a good level of compliance.

3.3 | Quality assessment

Among five studies included in the systematic review, four were categorized as good quality (Abellán Ruiz et al., 2017; De Carvalho et al., 2014; Li et al., 2018; Navarro-Perez et al., 2017), and one was low quality (Anusha et al., 2018). The details of quality assessment according to the domains used by the Cochrane Collaborations tool are provided in Table 2.

3.4 | Effect of quinoa supplementation on anthropometric indices

The results of analysis indicated that quinoa supplementation had not any significant effect on BMI (WMD: −0.31 kg/m^2, 95% CI: −0.91, 0.29, p = .31) (I^2 = 0.0%, p = .91). On the other hand, it was found that quinoa supplementation had a significant effect on body weight loss (WMD: −1.26 kg, 95% CI: −2.35, −0.18, p = 0.02) (I^2 = 0.0%, p = .87),

TABLE 2 Quality assessment of included studies

Author (year)	Sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective Outcome reporting	Other potential threats to validity	Overall quality
Abellán Ruiz et al., 2017	U	L	L	L	L	L	U	Good
Anusha et al., 2018	U	U	H	H	L	L	U	Weak
De Carvalho et al., 2014	U	L	L	L	L	L	U	Good
Li et al., 2018	L	L	H	U	L	L	U	Good
Navarro-Perez et al., 2017	L	L	U	L	L	L	U	Good

Abbreviations: H, high risk of bias; L, low risk of bias; U, unknown risk of bias.

TABLE 3 The effects of quinoa on anthropometric measurements, glycemic control, and serum lipids

Variables	Number of effect sizes	Weighted mean difference	CI 95%	*p*-value	Heterogeneity	
					I^2 (%)	*p*-value heterogeneity
BMI	5	−0.31	−0.91, 0.29	.31	0.0	.91
Body weight	4	−1.26	−2.35, −0.18	.02	0.0	.87
WC	3	−1.15	−2.08, −0.21	.01	0.0	.50
FM	3	−0.59	−1.14, −0.03	.03	28.8	.24
FBG	5	−0.86	−1.97, 0.26	.13	0.0	.56
Insulin	3	−7.48	−13.38, −1.59	.01	83.6	.002
TG	5	−7.20	−9.52, −4.87	<.001	96.9	<.001
TC	5	−6.86	−10.64, −3.08	<.001	89.0	<.001
LDL	5	−3.08	−5.13, −1.03	.003	93.0	<.001
HDL	5	−0.36	−1.12, 0.40	.35	90.0	<.001

Abbreviations: BMI, body mass index; FBG, fasting plasma glucose; FM, fat mass; HbA1C: hemoglobin A1C; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglycerides; WC, waist circumference.

WC (WMD: −1.15 cm, 95% CI: −2.08, −0.21, p = .01) (I^2 = 0.0%, p = .50) and FM (WMD: −0.59%, 95% CI: −1.14, −0.03, p = .03) (I^2 = 28.8%, p = .24) (Table 3) (Figure S1). We could not perform subgroup analysis due to lack of sufficient study.

3.5 | Effect of quinoa supplementation on glycemic control

Overall estimate of effect size demonstrated a significant reduction in insulin serum level (WMD: −7.48 pmol/L, 95% CI: −13.38, −1.59, p = .01) with considerable between-study heterogeneity (I^2 = 83.6%, p = .002). However, quinoa supplementation had not any significant effect on FBG (WMD: −0.86 mg/dl, 95% CI: −1.97, 0.26, p = .13) level. Although, there was not between-study heterogeneity (I^2 = 0.0%, p = .56) (Table 3) (Figure S1). We could not perform subgroup analysis due to lack of sufficient study.

3.6 | Effect of quinoa supplementation on serum lipids

Overall, five clinical trials (90 intervention and 71 control subjects) investigated the effect of quinoa supplementation on concentrations of lipid ingredients. After pooled effect size significant decreasing effect was observed on TG (WMD: −7.20 mg/dl, 95% CI: −9.52, −4.87, p < .001) (I^2 = 96.9%, p < .001), TC (WMD: −6.86 mg/dl, 95% CI: −10.64, −3.08, p < .001) (I^2 = 89.0%, p < .001) and LDL (WMD: −3.08 mg/dl, 95% CI: −5.13, −1.03, p = .003) (I^2 = 93.0%, p < .001) levels. However, quinoa supplementation had not statistically significant effect on HDL (WMD: −0.36 mg/dl, 95% CI: −1.12, 0.40, p = .35) (I^2 = 90.0%, p < .001) level (Table 3) (Figure S1). We could not perform subgroup analysis due to lack of sufficient study.

3.7 | Sensitivity analysis

Sensitivity analysis showed that Navarro-Perez et al. (Navarro-Perez et al., 2017) influenced on overall effect of quinoa on body weight (WMD: −1.27 kg, 95% CI: −2.61, 0.06), WC (WMD: −0.57 cm, 95% CI: −2.01, 0.86), FM (WMD: −0.16%, 95% CI: −0.91, 0.59), FBG (WMD: −1.45 mg/dl, 95% CI: −2.91, −0.00), insulin (WMD: −1.19 pmol/L, 95% CI: −8.34, 5.94), and HDL (WMD: −1.10 mg/dl, 95% CI: −1.89, −0.30). In addition, Anusha et al. (Anusha et al., 2018) influenced on overall effect of quinoa on TC (WMD: 1.46 mg/dl, 95% CI: −3.44, 6.38), and LDL (WMD: 12.95 mg/dl, 95% CI: 7.64, 18.25).

3.8 | Publication bias

Based on Egger's regression test, There was no evidence of publication bias for studies examining the effect of quinoa supplementation on BMI (p = .85), WC (p = .19), FM (p = .72), FBG (p = .95), insulin (p = .566), TG (p = .88), TC (p = .31), LDL (p = .17), and (p = .43). However, there were significant publication bias for body weight (p = .02).

4 | DISCUSSION

In the present systematic review and meta-analysis, five controlled trial with six intervention arms, were included. Our findings suggest that quinoa supplementation significantly affects body weight loss, WC, and FM, without any significant effect on BMI. We also found significantly lower serum insulin, as well as serum TG, TC, and LDL levels, in individuals randomized to quinoa intervention. However, quinoa supplementation did not affect serum HDL and FBG concentrations, significantly. No evidence of a substantial publication bias was seen for all variables except body weight. In addition, the sensitivity analysis results show that the exclusion of Navarro-Perez et al. and

Anusha et al. studies can influence the significance of our pooled effect size for body weight, WC, FM, FBG, insulin, HDL, TC, and LDL. These results may be due to the small number of included studies.

Quinoa is a pseudo grain, with exceptional nutritional value, and a gluten-free alternative for celiac patients. It has a high biological value protein, similar to animal proteins, with an extraordinary balance of essential amino acids, especially lysine and sulfur-containing amino acids, which are deficient in many other grains (Bastidas, Roura, Rizzolo, Massanés, & Gomis, 2016). Also, quinoa is rich in essential fatty acids and dietary fibers, has a low glycemic index and contains considerable amounts of vitamins, minerals, and various phytochemicals, including betalains, phytosterols, phytoecdysteroids, polyphenols, saponins, and carotenoids (Escribano et al., 2017; Vilcacundo & Hernández-Ledesma, 2017). Regarding these bioactive compounds, quinoa has been found to hold high antioxidant and free radical scavenging activities (Pasko et al., 2010; Paśko et al., 2009; Simnadis, Tapsell, & Beck, 2015).

Based on our results, quinoa supplementation favorably affects anthropometric measures and body weight loss, except BMI status. The lack of any significant effect of quinoa on BMI, should be interpreted with caution, due to the limited number of studies included. Phytoecdysteroids, mainly 20-hydroxyecdysone, have been introduced as the major contributors to the anti-obesity impact of quinoa, by a number of in vivo studies (Foucault et al., 2012). In these studies, quinoa supplementation has been associated with reduced adipose tissue development, due to reduced adipocyte size and lipid storage capacity, as well as downregulation of several genes involved in fat accumulation, such as lipoprotein lipase, and genes related to inflammatory adipokines, following a high-fat diet (Kizelsztein et al., 2009). Since same results were obtained for pure 20-hydroxyecdysone (Ecdysterone), it was suggested that phytoecdysteroids play the major role, regarding the anti-obesity effects of quinoa (Foucault et al., 2012). A few other mechanisms were proposed in this context. 20-hydroxyecdysone is structurally similar to vitamin D, and has the potential to bind the vitamin D receptors, thus has been proposed to affect the expression of genes responsible for lipid accumulation (Foucault et al., 2012). Quinoa consumption has been suggested to alter the level of hormones involved in appetite control, such as leptin, ghrelin, and cholecystokinin (Simnadis et al., 2015). Also, quinoa is a rich source of both soluble and insoluble dietary fibers, and dietary fiber intake has been associated with reduced energy intake, increased postmeal satiety, and modification of the gut dysbiosis, which is a major finding of gut bacterial composition in obese individuals (Cani, 2019; Howarth, Saltzman, & Roberts, 2001). Furthermore, saponins from quinoa have exhibited antiinflammatory properties in in vitro studies, mainly via inhibiting the release of inflammatory cytokines, including tumor necrosis factor-α and interleukin-6 (Yao, Yang, Shi, & Ren, 2014). Since low-grade systemic inflammation is considered a potential driver for obesity and obesity-related chronic diseases, the anti-obesity effects of quinoa can be explained partially by the presence of saponins (Heilbronn & Campbell, 2008).

Our finding on the beneficial effects of quinoa consumption on blood lipid levels, are in accordance with several previous preclinical animal studies (Anusha et al., 2018; Berger et al., 2003; Paśko, Zagrodzki, Bartoń, Chłopicka, & Gorinstein, 2010; Takao et al., 2005). However, such effects seems to be dose-dependent, and only appear when at least 2.5% of diet contains quinoa (Takao et al., 2005). The lipid-lowering properties of quinoa can be attributed to the presence of dietary fibers, phytosterols, 20-hydroxyecdysone, and quinoa protein. Owing to their gel formation ability, dietary fibers are able to promote satiety (Slavin & Green, 2007). Also, they interact with cholesterol absorption, as well as, enterohepatic cycle of bile acids, resulting in their increased disposal (Satija & Hu, 2012). Under fermentation in the gut, dietary fibers produce short-chain fatty acids, which decrease cholesterol synthesis in the liver (Surampudi, Enkhmaa, Anuurad, & Berglund, 2016). The protein isolated from quinoa has been shown to exert hypocholesterolemic impact through increasing bile acid excretion from the intestine, and reducing the expression of hepatic HMG-CoA reductase (Takao et al., 2005). Each 100 g of quinoa seeds contains up to 118 mg of various phytosterols, which among them b-sitosterol, campesterol, and stigmasterol are the most abundant (Filho et al., 2017). Their lipid-lowering impact has been well established, in several observational and intervention studies (Navruz-Varli & Sanlier, 2016). In the present study, we did not conclude a significant impact of quinoa on the HDL level. However, some preclinical evidence has reported the beneficial effects of quinoa on increasing serum HDL level, or inhibiting HDL reduction, following a high-fructose diet (Escudero et al., 2006; Paśko et al., 2010). Extending the intervention period or increasing the amount of administered quinoa may lead to a significant improvement in HDL concentration, in future clinical trials.

It is proposed that the mechanisms through which quinoa affects serum insulin level favorably, revolve around its ability to lower postprandial glucose, as well as to increase insulin sensitivity. 20-hydroxyecdysone treatment was associated with ameliorated insulin resistance and reduced hepatic gluconeogenesis, via affecting the upstream components of the PI3K-dependent insulin signaling pathway, in in vivo studies (Kizelsztein et al., 2009; Navruz-Varli & Sanlier, 2016). Also, polyphenols, especially flavonoids, may operate synergistically with 20-hydroxyecdysone, in these terms, or independently by affecting carbohydrate digestion and absorption (Graf et al., 2014). Quinoa, as a rich source of dietary fibers, and a low glycemic index food, has the potential to lower postprandial glucose response, through slowing gastric emptying and nutrient and energy absorption (De Carvalho et al., 2014). A possible explanation for the lack of any significant effect of quinoa on FBG, in the present meta-analysis, would be the major impact of quinoa on postprandial glucose response, rather than fasting glucose (Li et al., 2018).

To our knowledge, this is the first systematic review and meta-analysis conducted examining the effect of quinoa supplementation on cardiovascular risk factors in adults. Strengths of the study include a comprehensive coverage of the current literature via the utilization of a wide range of key words related to CVD, the searching through four scholarly databases (as recommended by the Cochrane Association guidelines and good practices for conducting systematic

reviews), the absence of language restriction, and a careful appraisal of study quality. However, it is important to consider some limitations of this meta-analysis when interpreting the results and producing conclusions. First, the results of most studies were not adjusted for confounding factors such as dietary intake and physical activity. Second, some cardio-metabolic risk factors such as inflammatory parameters and oxidative stress were not considered. Third, the evidence so far is limited, in this context. Since many of the included studies were of relatively short duration, and small number of participants, our results should be interpreted with caution. In addition, the present study was not registered in the International Prospective Register of Systematic Reviews (PROSPERO), which may be a limitation as well.

5 | CONCLUSION

Limited data propose that administration of quinoa may favorably affect body weight status, blood lipid profile, and serum insulin level. Further high-quality studies are warranted to confirm our findings. It should be considered that most of the studies discussed in the present review article have been not performed in accordance to a recent consensus document providing a perspective in best practice in pharmacological research on bioactive preparations from plants (Heinrich et al., 2020).

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Vihan Moodi and Jahangir Karimian contributed to the conception of research. Vihan Moodi and Sajjad Abedi searched databases, screened articles, and extracted data. Vihan Moodi performed statistical analysis; and all authors contributed to the writing and revision of the manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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