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Effects of propolis consumption on blood pressure, lipid profile and glycemic parameters in adults: a GRADE-assessed systematic review and dose–response meta-analysis

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(Submitted 29 November 2023 – Final revision received 4 July 2024 – Accepted 17 July 2024)

Abstract

Propolis, as a by-product of honey production, has shown several beneficial effects on cardiovascular risks in past randomised controlled trials, although the findings are not conclusive. In this review, we intend to evaluate the effects of propolis consumption on cardiovascular risk factors by conducting a meta-analysis. The Web of Science, Medline and Scopus databases were comprehensively searched until September 2023. Eligible studies were identified by screening, and their data were extracted. Weighted mean differences with a 95 % CI for each outcome were estimated using the random-effects model. This meta-analysis revealed that propolis consumption led to a significant decrease in the levels of TAG (weighted mean differences (WMD): −10·44 mg/dl 95 % CI: −16·58, −4·31; $P = 0·001$), LDL-cholesterol (WMD: −9·31 mg/dl; 95 % CI: −13·50, −5·12 mg; $P < 0·001$), fasting blood glucose (WMD: −7·30 mg/dl; 95 % CI: −11·58, −3·02; $P = 0·001$), HbA1c (WMD: −0·32 %; 95 % CI: −0·60, −0·05; $P = 0·01$), insulin (WMD: −1·36 µU/ml; 95 % CI: −2·36, −0·36; $P = 0·007$), homeostatic model assessment for insulin resistance (WMD: −0·39; 95 % CI: −0·74, −0·03; $P = 0·020$) and systolic blood pressure (WMD: −2·24 mmHg 95 % CI: −4·08, −0·39; $P = 0·010$), compared with the control groups. Furthermore, propolis consumption had a significant increasing effect on HDL-cholesterol levels (WMD: 2·03 mg/dl; 95 % CI: 0·24, 3·83; $P = 0·020$). In contrast, the consumption of propolis had no significant effect on total cholesterol and diastolic blood pressure levels. This systematic review and dose–response meta-analysis suggested that propolis intake may be effective in cardiometabolic improvement in adults. Further, well-designed studies are required to confirm and elucidate all aspects of these findings.

Keywords: **Propolis: Blood pressure: Lipid profile: Glycemic control: Meta-analysis**

The maintenance of overall health and prevention of chronic diseases are closely linked to lifestyle and dietary factors. Indicators of cardiovascular health and metabolic function, such as blood pressure, lipid profile and glycaemic control, play a crucial role in this regard[1,2]. Unfortunately, these parameters are often compromised in conditions such as hypertension, dyslipidaemia and diabetes. Such conditions significantly increase the risk of severe complications, including kidney failure, stroke and heart attack. According to the American Heart Association, CVD accounted for 874 613 deaths in the USA in 2019 and was the leading global cause of death, accounting for approximately 19·05 million deaths in 2020. Stroke was the second leading cause of death worldwide, causing 6·2 million deaths in 2019[3]. Hypertension affects one in three adults worldwide and is a major risk factor for stroke, heart attack and kidney damage[4]. Approximately one in three adults with diabetes have chronic kidney disease, which can lead to kidney failure and require dialysis or transplantation[5]. It is therefore

Abbreviations: DBP, diastolic blood pressure; FBG, fasting blood glucose; HOMA-IR, homeostatic model assessment for insulin resistance; SBP, systolic blood pressure; TC, total cholesterol; WMD, weighted mean differences.

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essential to adopt healthy habits and consume foods that can modulate these parameters and protect against cardiovascular and metabolic disorders[1,6,7].

Propolis is a natural substance that bees collect from various trees and plants to protect their hives from external threats. For centuries, propolis has been used in traditional medicine to treat various ailments such as colds, flu, sore throat and skin infections[8]. This sticky substance consists of bioactive compounds such as flavonoids, phenolic acids and terpenes, which have been shown to possess potent medicinal properties such as antioxidant, anti-inflammatory, antimicrobial, anticancer and immunomodulatory effects[9]. Propolis has been shown to modulate carbohydrate and lipid metabolism by stimulating insulin synthesis and β-cell proliferation[10,11], inhibiting glucose production by the liver and glucose absorption by the gut[12], preventing lipid peroxidation and the rise of TAG and LDL-cholesterol[10,11], increasing HDL-cholesterol and enhancing cholesterol efflux from peripheral tissue[13,14]. Propolis may also influence blood pressure by inhibiting xanthine oxidase, chelating metal ions, regulating gene expression, suppressing cytokines, attenuating endothelial dysfunction and preventing platelet aggregation[15–17].

Recently, a systematic review and meta-analysis by Karimian *et al.*[18] evaluated the efficacy of propolis on markers of glycaemic control in adults with type 2 diabetes mellitus (T2DM). They found that propolis supplementation significantly reduced fasting blood glucose (FBG), and HbA1c, but had no effect on homeostatic model assessment for insulin resistance (HOMA-IR). However, this review did not include studies that assessed the effects of propolis on blood pressure and lipid profile, which are also important indicators of cardiovascular and metabolic health. Moreover, the quality of the included studies was low to moderate, and the heterogeneity among them was high. Additionally, the present review included more articles than the previous one and also considered more groups of participants rather than only diabetic patients. This may provide a more comprehensive and generalisable picture of the effects of propolis on cardiovascular and metabolic health in different populations and settings.

Several studies have investigated the effects of propolis consumption on blood pressure, lipid profile and glycaemic parameters in humans and animals. However, the results are inconsistent and conflicting. Some studies suggest that propolis can lower blood pressure[19], improve lipid profile[20] and reduce blood glucose levels[21], while others report no significant effects or even adverse effects[22–25]. These discrepancies may be due to differences in the type, dose, duration and quality of propolis used, as well as the characteristics of the study population, the methods of measurement and the confounding factors.

Therefore, there is a need for a systematic review and meta-analysis to address these inconsistencies and provide a comprehensive and reliable assessment of the effects of propolis consumption on blood pressure, lipid profile and glycaemic parameters. This study may contribute to the growing body of knowledge on propolis as a natural product with diverse health benefits.

Methods

In order to conduct this meta-analysis, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines was employed[26]. The protocol for conducting this systematic review has already been registered in the PROSPERO database with the registration ID: **CRD42023472448**.

Search strategy

A thorough search of the literature was conducted up until September 2023 in PubMed, Scopus and Web of Science to identify relevant articles without any restrictions on language or timeline. A search strategy using these specific search terms was designed: (propolis) AND (intervention OR intervention* OR 'controlled trial' OR 'randomized' OR 'randomised' OR 'randomly' OR placebo OR 'clinical trial' OR 'trial' OR 'randomized controlled trial' OR 'randomized clinical trial' OR 'RCT' OR 'blinded' OR 'double-blind' OR 'clinical trials' OR 'trials' OR 'Cross-Over' OR parallel) (online Supplementary Table 1).

Eligibility criteria

All the articles included in the analysis fulfilled the following criteria: (1) They were randomised controlled trials that investigated the impact of propolis consumption on blood pressure, lipid profile (TAG, total cholesterol, LDL-cholesterol, HDL-cholesterol) and glycaemic parameters (FBG, fasting insulin, HbA1c and HOMA) in adults outcome measures. (2) The research was conducted on adults aged 18 years or older who received propolis as an intervention; (3) the interventions lasted at least 4 weeks; (4) the studies had a parallel or crossover design and (5) the studies reported the outcome measures at both the beginning and end of the intervention.

Exclusion criteria

After conducting a thorough analysis of the full-text articles, the articles that met the following criteria were excluded: (1) Studies that focused on animals, reviews, ecological or observational studies. (2) Studies conducted on individuals below the age of 18. (3) Studies that lacked randomisation, placebo groups or control groups.

Data extraction

Information related to this review was extracted from studies entered by two authors (H.B. and K.G.) independently. The following information was extracted: the first author's name, publication year, study location and design, number of participants in each group, characteristics of the participants including gender, mean age and BMI, health status, the dosage of propolis used for intervention, intervention duration and the mean changes difference and standard deviation of outcomes for both intervention and control groups. Only the most recent data from each study at different time points were considered. Any disagreements were resolved through consultation.

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Quality assessment

The quality of the included studies was assessed independently by two separate researchers (M.Sh.J. and K.G.) using the Cochran scoring framework[27]. This framework included seven domains to evaluate the risk of bias: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other biases. Each domain was judged as 'Low', 'High' or 'Unclear' based on predefined criteria. Any discrepancies were resolved by the corresponding authors.

Data synthesis and statistical analysis

This meta-analysis utilised the random-effects model according to DerSimonian and Laird method to calculate the weighted mean differences (WMD) and SD of measures for both intervention and control groups[28]. The mean changes in cases of not reporting directly were calculated using the formula: mean change = final values – baseline values, and SD changes were calculated using the formula[29]:

$$\text{SD change} = \sqrt{[(\text{SD baseline})2 + (\text{SD final})2 - (2R \times \text{SD baseline} \times \text{SD final})}$$

Standard errors, 95 % CI and interquartile ranges were converted to SD using the method of Hozo *et al.*[30].

The included studies varied in terms of types, doses and duration of intervention, as well as the location and health status of participants. Due to this heterogeneity, the random-effects model was used. The heterogeneity among the included trials was evaluated by performing Cochran's Q test and measured using the I square (I^2)[31]. $P < 0{\cdot}05$ or $I^2 > 40$ % was considered as a significant heterogeneity between pooled studies[31]. Subgroup analyses were conducted in order to find the source of heterogeneity based on pre-planned criteria including country (Iran and non-Iran), gender (both sexes, only females), study duration (<12 weeks and 12 ≤), age (<50 years and 50<), baseline levels of BMI and propolis supplement dosage (<1000 and 1000 mg/d≤)[32]. To evaluate the impact of individual studies on the overall estimation, a sensitivity analysis was performed[33]. The publication bias among the studies investigating the effect of propolis intake on each outcome was assessed using Egger's regression test and the visually inspected funnel plot[34]. The linear and non-linear relationship between the changes in outcomes and the features of propolis supplementation (dose and duration) were assessed by performing meta-regression and fractional polynomial modelling, respectively[35,36]. Statistical analysis was conducted using STATA, version 11·2 (Stata Corp). In all the analyses performed, P values < 0·05 were considered statistically significant.

Results

Study selection

In Fig. 1, it can be seen that the search protocol initially yielded a total of 3686 studies. Out of these, 836 duplicates were identified and subsequently removed. Following this, an evaluation of the titles and abstracts based on inclusion criteria resulted in the exclusion of 2822 studies that were deemed irrelevant to the subject. A thorough assessment of the full text of twenty-eight studies led to the removal of six studies due to insufficient data reporting. Ultimately, a total of twenty-two studies met the criteria for inclusion in this meta-analysis.

Study characteristic

Table 1 provides information on the inclusion of twenty-two studies in this meta-analysis, which involved a total of 1164 participants (intervention groups: 596, control groups: 577). All qualified articles included in this analysis were published between 2015 and 2023. The qualified studies were conducted in several countries including Japan[37,38], China[24,39], Iran[40–51], Egypt[52], Chile[53], Mexico[54], Brazil[25], Greece[55] and France[56]. Three studies were executed on females[40,43,45], and the others were conducted on both sexes[24,25,37–39,41,42,44,46–56]. The sample sizes varied across the studies, ranging from nine[56] to ninety-four[51] participants. Out of the included studies, twenty-one had a parallel randomised controlled trial[24,25,37–55] design, while one had a crossover design[56]. The intervention periods in the included trials ranged from 4 weeks[55] to 48[25] weeks. The propolis type that was intervened was given as a solution in one study[53], as a drop in another[55] and as pills (tablets and capsules) in the other studies. The dosage of propolis supplement in the pill form in the included study ranged from 226·8[38] to 2000 mg/d[56]. The participants in these trials represented various populations, including healthy individuals[37,53,55], and patients with type 2 diabetes[38–40,46,47,50–52,54], type 2 diabetes and dyslipidaemia[40], insulin resistance[56], chronic kidney disease and proteinuria[25,42], metabolic syndrome[44], polycystic ovary syndrome[45], non-alcoholic fatty liver disease (NAFLD)[41,48,49] and rheumatoid arthritis[43].

Quality assessment

In terms of the general risk of bias in the qualified articles, it was found that twenty-one studies had a low risk of bias[24,25,37,38,40–56], and one article mentioned a high risk of bias[39]. Details of the risk of bias assessment are presented in Table 2.

Meta-Analysis

Effect of propolis consumption on lipid profile

Effect of propolis consumption on TAG. Assessing thirteen effect sizes indicated that propolis consumption led to a significant decrease in TAG levels compared with control groups (WMD: –10·44 mg/dl 95 % CI: –16·58, –4·31; $P = 0{\cdot}001$) (Fig. 2(a)). Additionally, a low degree of heterogeneity was detected between the included trials ($I^2 = 31{\cdot}4$ %, $P = 0{\cdot}13$). In subgroup analysis, it was found that short-term (<12 weeks) propolis consumption or intervention with propolis among obese (BMI > 30) or non-diabetic participants failed to significantly decrease TAG (Table 3).

Effect of propolis consumption on total cholesterol. Pooled data from seventeen effect sizes mentioned no significant impact

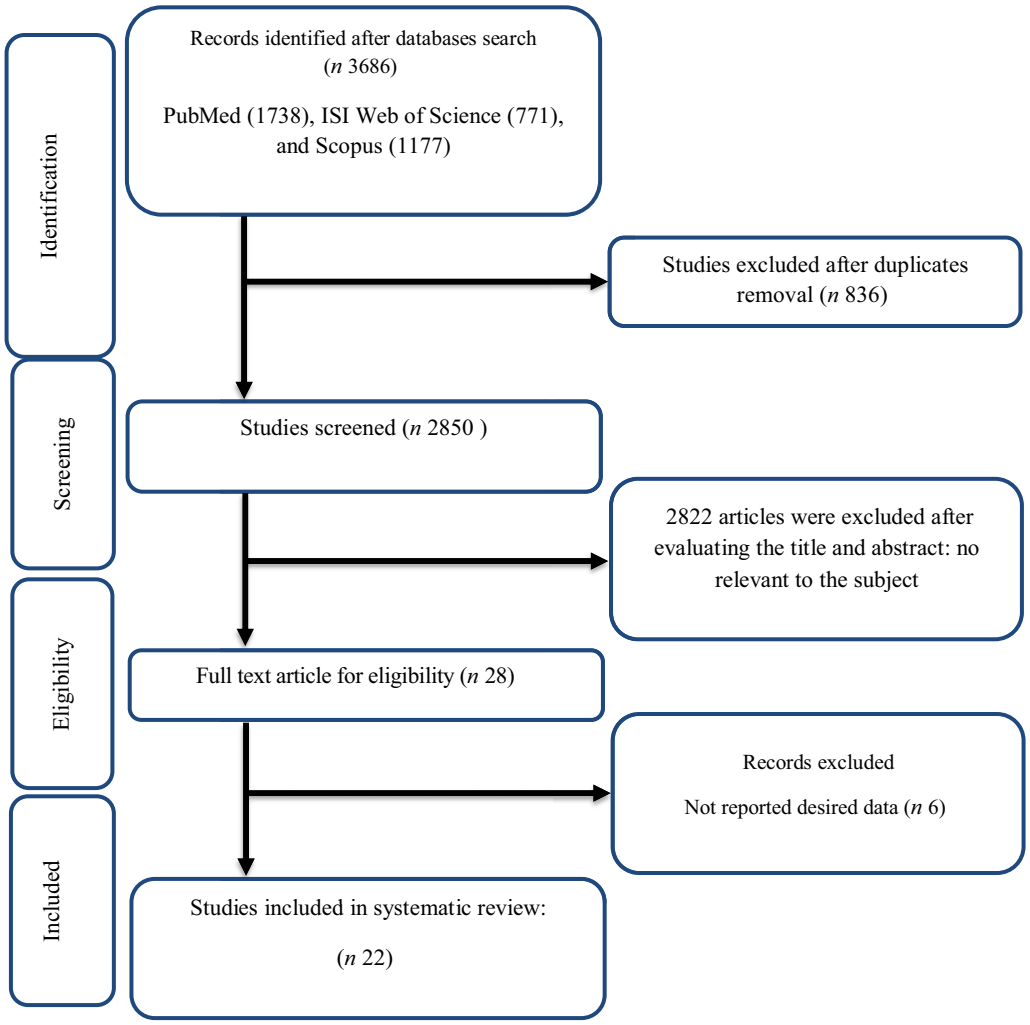

Fig. 1. Flow chart of study selection for inclusion trials in the systematic review.

of propolis intake on total cholesterol) (TC) levels compared with control groups (WMD: –2·53 mg/dl; 95 % CI: –7·00, 1·93; $P = 0·26$) (Fig. 2(b)). Moreover, a high degree of heterogeneity was observed among studies ($I^2 = 90·4$ %, $P < 0·001$). Subgroup analysis revealed that propolis consumption in the studies conducted in Iran had a significant reduction effect on TC levels (Table 3).

Effect of propolis consumption on LDL-cholesterol. The overall results from evaluating 16 effect sizes indicated a significant decrease in LDL-cholesterol levels following propolis consumption compared with control groups (WMD: –9·31 mg/dl; 95 % CI: –13·50, –5·12 mg; $P < 0·001$) (Fig. 2(c)). Moreover, a high degree of heterogeneity was observed among studies ($I^2 = 86·3$ %, $P < 0·001$). Subgroup analysis showed that propolis consumption with a high dosage (≥1000 mg/d) or propolis intake in the non-Iranian populations, people aged less than 50, individuals with NAFLD or healthy participants had no significant effect on LDL-cholesterol levels (Table 3).

Effect of propolis consumption on HDL-cholesterol. After evaluating seventeen effect sizes, it was found that propolis consumption showed a significant enhancing influence on HDL-cholesterol levels compared with control groups (WMD: 2·03 mg/dl; 95 % CI: 0·24, 3·83; $P = 0·02$) (Fig. 2(d)). In addition, a high between-studies heterogeneity was observed ($I^2 = 88·8$ %, $P < 0·001$). Moreover, the results of the subgroup analysis demonstrated that short-term propolis consumption or propolis intake in the Iranian population as well as in NAFLD patients significantly increased HDL-cholesterol levels (Table 3).

Effect of propolis consumption on blood pressure

Effect of propolis consumption on systolic blood pressure. Combining seven effect sizes revealed that propolis consumption significantly reduced systolic blood pressure (SBP) compared with control groups (WMD: –2·24 mmHg 95 % CI: –4·08, –0·39; $P = 0·01$) (Fig. 2(i)). Furthermore, there was no significant heterogeneity among the included studies ($I^2 = 0·6$ %, $P = 0·41$). Subgroup analysis demonstrated a significant reduction in SBP following propolis consumption in studies involving

Table 1. Characteristic of included studies in meta-analysis

Studies	Country	Study design	Participant	Sex	Sample size		Trial duration (week)	Means age		Means BMI		Intervention		
					IG	CG		IG	CG	IG	CG	Type	Dose (mg/day)	Control group
Fukuda *et al.* 2015	Japan	Parallel, R, PC, DB	T2DM	B	41	39	8	41	39	63·7	62·9	Brazilain green propolis	226·8	Safflower oil tablets
Zhao *et al.* 2016	China	Parallel, R, C	T2DM	B	33	32	18	33	32	59·5	60·8	Brazilain green propolis capsule	900	Without propolis consumption
El-Sharkawy *et al.* 2016	Egypt	Parallel, R, PC, DB	T2DM+periodontitis	B	24	26	24	24	26	48·9	51·2	Propolis capsule + scaling and root planing (SRP)	400	Placebo+SRP
Mujica *et al.* 2017	Chile	Parallel, R, PC, DB	Healthy individuals	B	35	32	12	35	32	48	44·5	Propolis solution	30 drops	Peppermint+ fernet+ synthetic
Samadi *et al.* 2017	Iran	Parallel, R, PC, DB	T2DM	B	30	27	12	30	27	51·3	56·07	Propolis pill	900	Placebo
Afsharpour *et al.* 2017	Iran	Parallel, R, PC, DB	T2DM	B	30	30	8	30	30	51·81	49·05	Propolis capsule	1500	Wheat flour capsule
Gao *et al.* 2018	China	Parallel, R, C	T2DM	B	25	30	18	25	30	57·7	60·6	Chinese propolis capsule	900	Without propolis consumption
Silveira *et al.* 2019	Brazil	Parallel, R, PC, DB	CKD+proteinuria	B	18	14	48	18	14	61·39	61·5	Brazilain green propolis tablet	500	Placebo
Zakerkish *et al.* 2019	Iran	Parallel, R, PC, DB	T2DM	B	50	44	12	50	44	55·4	54·86	Iranian propolis capsule	1000	Placebo
Soleimani *et al.* 2021	Iran	Parallel, R, PC, DB	NAFLD	B	27	27	12	27	27	42·56	41·85	Propolis tablet+ microcrystalline cellulose	500	Placebo
Asama *et al.* 2021	Japan	Parallel, R, PC, DB	Elderly	B	35	33	24	35	33	66·6	66·1	Propolis capsule	350	Starch
Ochoa-Morales *et al.* 2022	Mexico	Parallel, R, PC, DB	T2DM	B	11	11	12	11	11	50	46·7	Propolis capsule	600	Placebo
Nikbaf-Shandiz *et al.* 2022	Iran	Parallel, R, PC, DB	NAFLD	B	23	21	8	23	21	38·52	40·14	Propolis capsule+ calorie-restricted diet	1500	Corn starch capsule+ calorie-restricted diet
Tsamesidis *et al.* 2022	Greece	Parallel, PC	Blood donors	B	20	20	4	20	20	47	42	Propolis drop	1 drop	Without propolis consumption
Afsharpour *et al.* 2022	Iran	Parallel, R, PC, DB	T2DM	B	30	30	8	30	30	51·81	49·05	Propolis capsule	1500	Wheat flour capsule
Abbasi *et al.* 2023	Iran	Parallel, R, PC, TB	PCOS	F	28	29	12	28	29	18–45	18–45	Propolis tablet	500	Placebo
Sajjadi *et al.* 2023	Iran	Parallel, R, PC, DB	Metabolic Syndrome	B	33	29	12	33	29	54·27	53·86	Propolis tablet+ microcrystalline cellulose	500	Microcrystalline cellulose
Maddahi *et al.* 2023	Iran	Parallel, R, PC, DB	Rheumatoid arthritis	F	23	22	12	23	22	46·56	47·9	Propolis capsule	1000	Corn starch capsule
Anvarifard *et al.* 2023	Iran	Parallel, R, PC, DB	CKD	B	17	18	12	17	18	58·06	60·5	Propolis capsule+ bee pollen+ oat	250	Wheat starch+bee pollen+ oat
Tutunchi *et al.* 2023	Iran	Parallel, R, PC, DB	Obesity + NAFLD	B	24	24	8	24	24	37·5	36·33	Propolis capsule+ maltodexterine+ dietary recommendation	1500	Dietary recommendation
Sani *et al.* 2023	France	Crossover, R, PC	Insulin resistant + obesity	B	9	9	12	9	9	49	49	Propolis capsule	1500–2000	Placebo
Moayedi *et al.* 2023 (a)	Iran	Parallel, R, PC, SB	T2DM+ dyslipidemia	F	15	15	8	15	15	52·53	53·67	Propolis capsule	500	Without propolis consumption
Moayedi *et al.* 2023 (b)	Iran	Parallel, R, PC, SB	T2DM+ dyslipidemia	F	15	15	8	15	15	54·07	51·67	Propolis capsule+ exercise	500	Exercise

IG, intervention group; CG, control group; TB, triple blinded; DB, double blinded; SB, single blinded; PC, placebo controlled; CO, controlled; R, randomised; CKD, chronic kidney disease; NAFLD, non-alcoholic fatty liver disease; T2DM, type 2 diabetes mellitus; PCOS, polycystic ovary syndrome; NR, not reported.

Table 2. Risk of bias assessment

Study	Random sequence generation	Allocation concealment	Selective reporting	Other sources of bias	Blinding (participants and personnel)	Blinding (outcome assessment)	Incomplete outcome data	General risk of bias
Fukuda *et al.* 2015	L	U	L	U	L	L	L	Low
Zhao *et al.* 2016	L	U	L	U	U	U	L	Low
El-Sharkawy *et al.* 2016	L	L	L	U	L	L	L	Low
Mujica *et al.* 2017	L	U	L	L	L	U	L	Low
Samadi *et al.* 2017	L	U	L	L	L	L	L	Low
Afsharpour *et al.* 2017	L	U	L	L	L	L	L	Low
Gao *et al.* 2018	H	U	L	L	H	U	H	High
Silveira *et al.* 2019	L	L	L	U	L	U	L	Low
Zakerkish *et al.* 2019	L	L	L	L	U	L	L	Low
Soleimani *et al.* 2021	L	L	L	L	L	L	L	Low
Asama *et al.* 2021	L	U	U	L	L	U	L	Low
Ochoa-Morales *et al.* 2022	L	L	L	L	L	U	L	Low
Nikbaf-Shandiz *et al.* 2022	L	L	L	L	L	U	L	Low
Tsamesidis *et al.* 2022	U	U	L	L	U	U	L	Low
Afsharpour *et al.* 2022	L	U	L	L	L	L	L	Low
Abbasi *et al.* 2023	L	U	U	U	L	L	L	Low
Sajjadi *et al.* 2023	L	L	L	L	L	U	L	Low
Maddahi *et al.* 2023	L	U	U	L	L	U	L	Low
Anvarifard *et al.* 2023	L	L	U	U	L	U	L	Low
Tutunchi *et al.* 2023	L	L	L	L	U	U	L	Low
Sani *et al.* 2023	L	U	L	L	L	U	L	Low
Moayedi *et al.* 2023	L	L	L	U	L	U	L	Low

L, low risk of bias; H, high risk of bias; U, unclear risk of bias.
General low < 2 high risk.
General moderate = 2 high risk.
General high > 2 high risk.

both sexes, conducted on individuals aged less than 50 years, healthy participants or patients with chronic kidney disease (Table 3).

Effect of propolis consumption on diastolic blood pressure. Pooling seven effect sizes showed that propolis intake had no significant effect on diastolic blood pressure (DBP) compared with control groups (WMD: 0·02 mmHg 95 % CI: −1·36, 1·40; $P = 0·97$) (Fig. 2(j)). Furthermore, no significant heterogeneity between the included studies was detected ($I^2 = 0·0$ %, $P = 0·97$). Subgroup analysis demonstrated that propolis consumption failed to alter DBP in all pre-defined subgroups (Table 3).

Effect of propolis consumption on glycaemic control

Effect of propolis consumption on fasting blood glucose. According to the results from fifteen studies, propolis consumption had a significant diminishing impact on FBG levels compared with control groups (WMD: −7·30 mg/dl; 95 % CI: −11·58, −3·02; $P = 0·001$) (Fig. 2(e)). Also, high heterogeneity was observed among the included studies ($I^2 = 84·3$ %, $P < 0·001$). Following the results of subgroup analysis, short-term (<12 weeks) or high-dose (≥1000 mg/d) propolis intake or intervention among individuals who were under 50 years, in participants with obesity (BMI > 30), normal BMI (18·5–24·9 kg/m^2), NAFLD or chronic kidney disease, failed to diminish FBG significantly (Table 3).

Effect of propolis consumption on insulin. Pooling fifteen effect sizes demonstrated that propolis intake diminished fasting insulin levels significantly compared with control groups (WMD: −1·36 mU/ml; 95 % CI: −2·36, −0·36; $P = 0·007$) (Fig. 2(f)). Also, there was a high between-studies heterogeneity ($I^2 = 89·8$ %, $P < 0·001$). As a result, the outcomes of subgroup analysis revealed that propolis intake with a high dosage (≥1000 mg/d) or a long duration (≥12 weeks), as well as in the trials conducted on non-Iranian populations, both sexes, patients with NAFLD, chronic kidney disease or participants aged less than 50 years old, had no significant impact on fasting insulin levels.

Effect of propolis consumption on HbA1c. Analyzing fourteen overall effect sizes showed a significantly diminishing effect of propolis consumption on HbA1c compared with control groups (WMD: −0·32 %; 95 % CI: −0·60, −0·05; $P = 0·01$) (Fig. 2(g)). Also, there was a high between-studies heterogeneity ($I^2 = 86·2$ %, $P < 0·001$). Subgroup analysis demonstrated that propolis intake with a low dosage (<1000 mg/d) and in individuals aged less than 50, females, individuals with a BMI less than 30 kg/m^2 or non-diabetic patients did not significantly affect HbA1c levels (Table 3).

Effect of propolis consumption on homeostatic model assessment for insulin resistance. Pooled data from twelve studies mentioned a significant decrease in HOMA-IR by propolis consumption (WMD: −0·39; 95 % CI: −0·74, −0·03;

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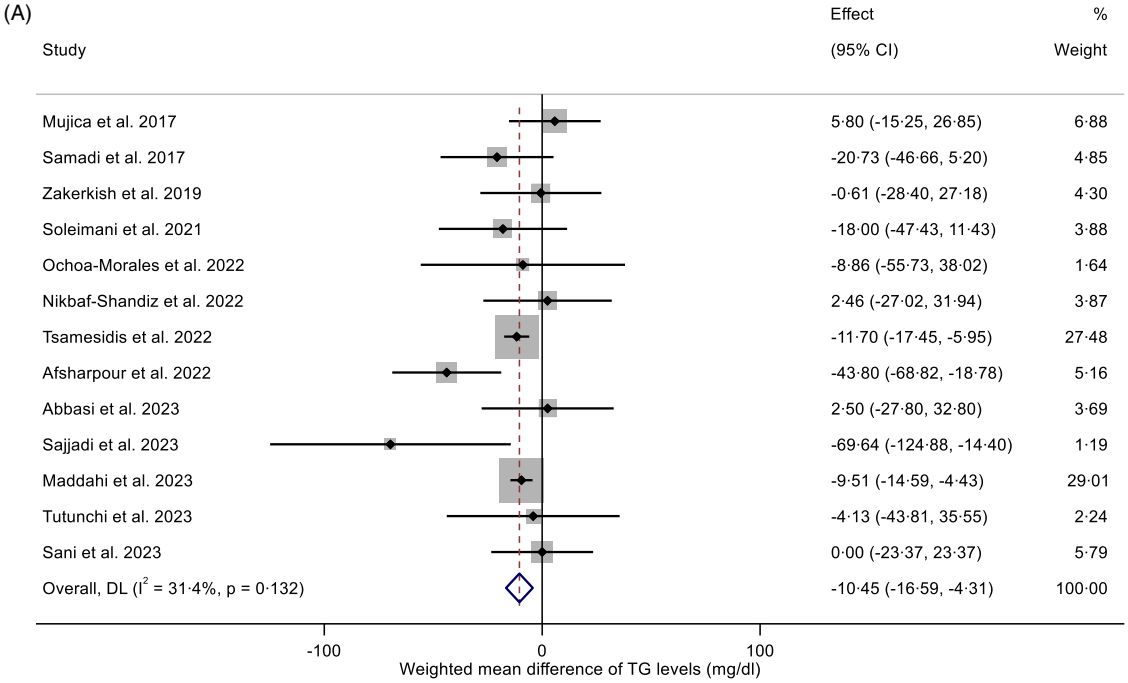
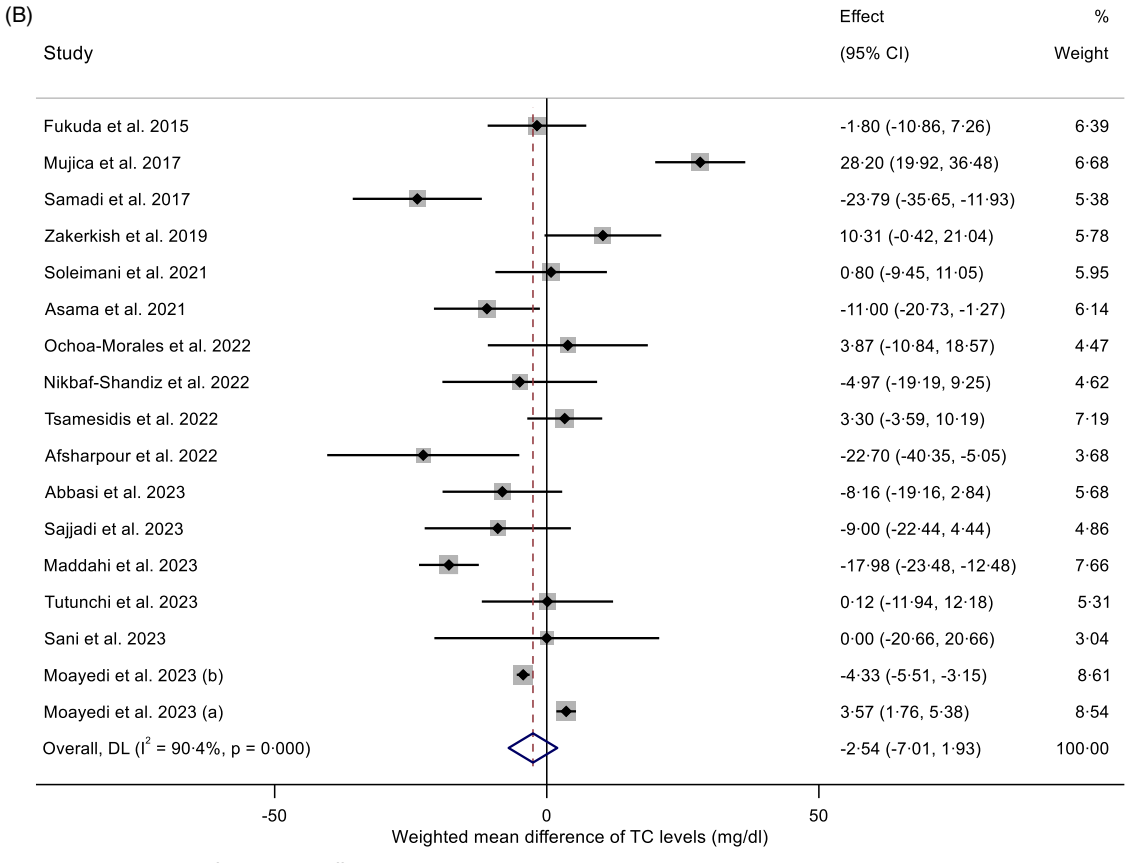


Note: Weights are from random-effects model



Note: Weigths are from random-effects model

Fig. 2. Forest plot detailing weighted mean difference and 95 % CI for the effect of propolis intake on A) TAG (mg/dl); B) TC (mg/dl); C) LDL-cholesterol (mg/dl); D) HDL-cholesterol (mg/dl); E) FBG (mg/dl); F) fasting insulin (uIU/ml); G) HbA1c (%); H) HOMA-IR; I) SBP (mmHg); and J) DBP (mmHg). FBG, fasting blood glucose; HOMA-IR, homeostatic model assessment for insulin resistance; SBP, systolic blood pressure.

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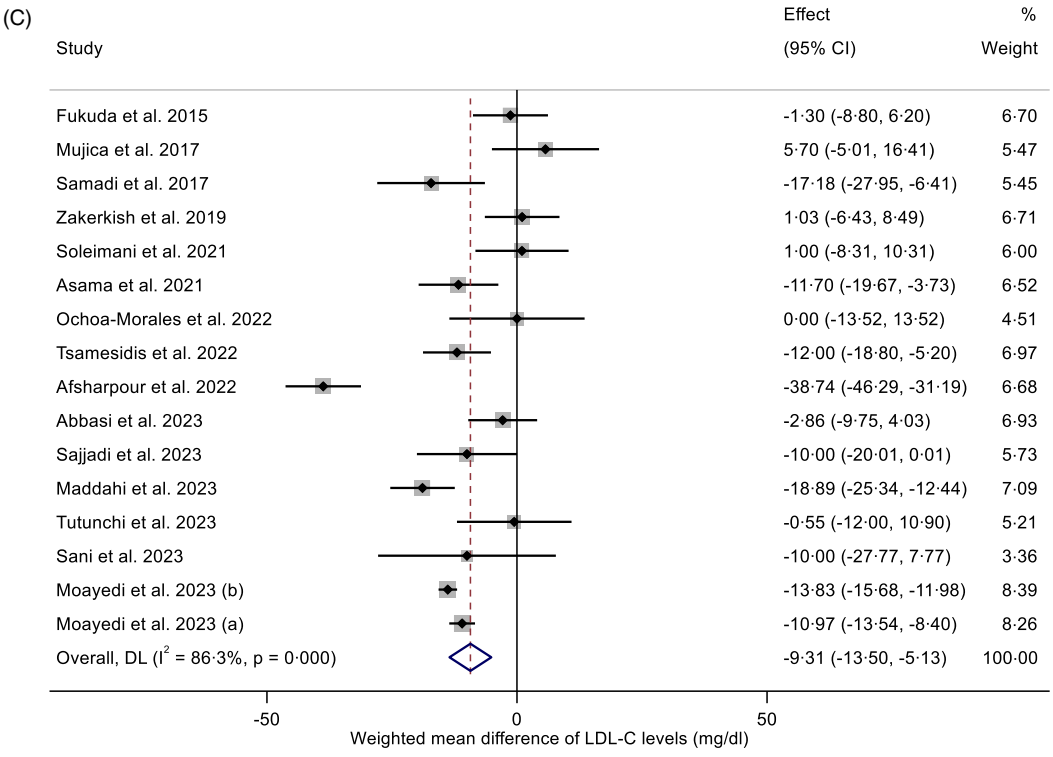

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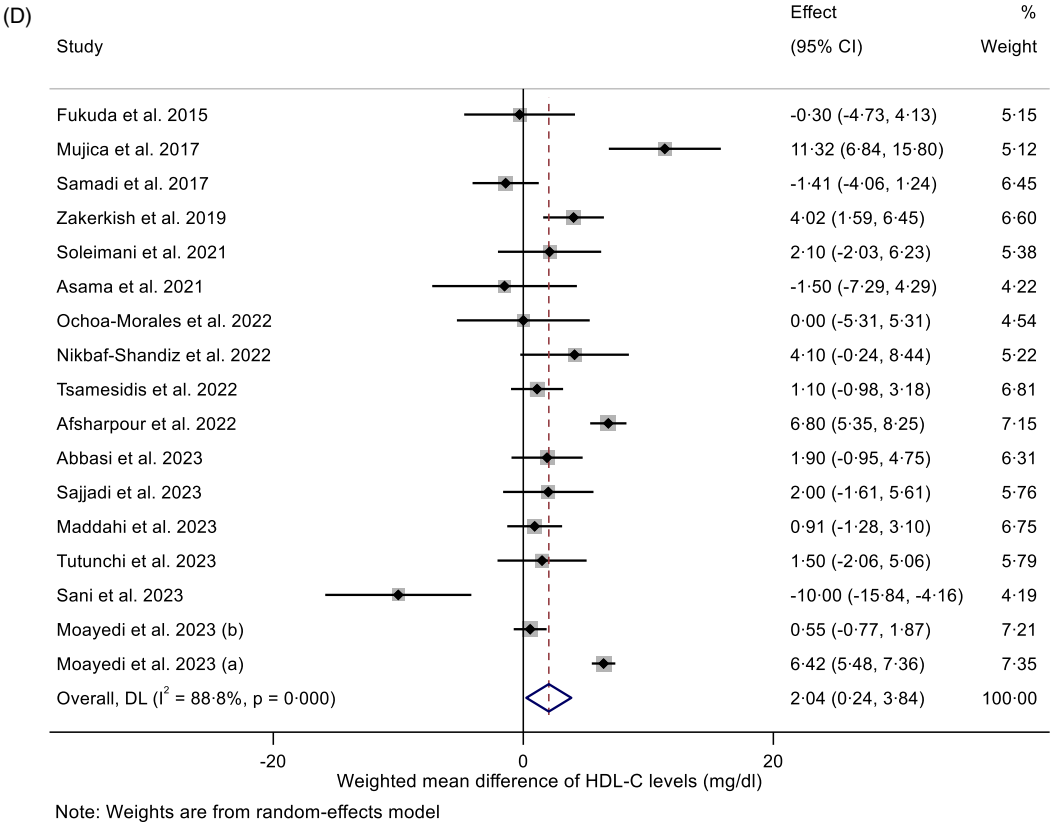
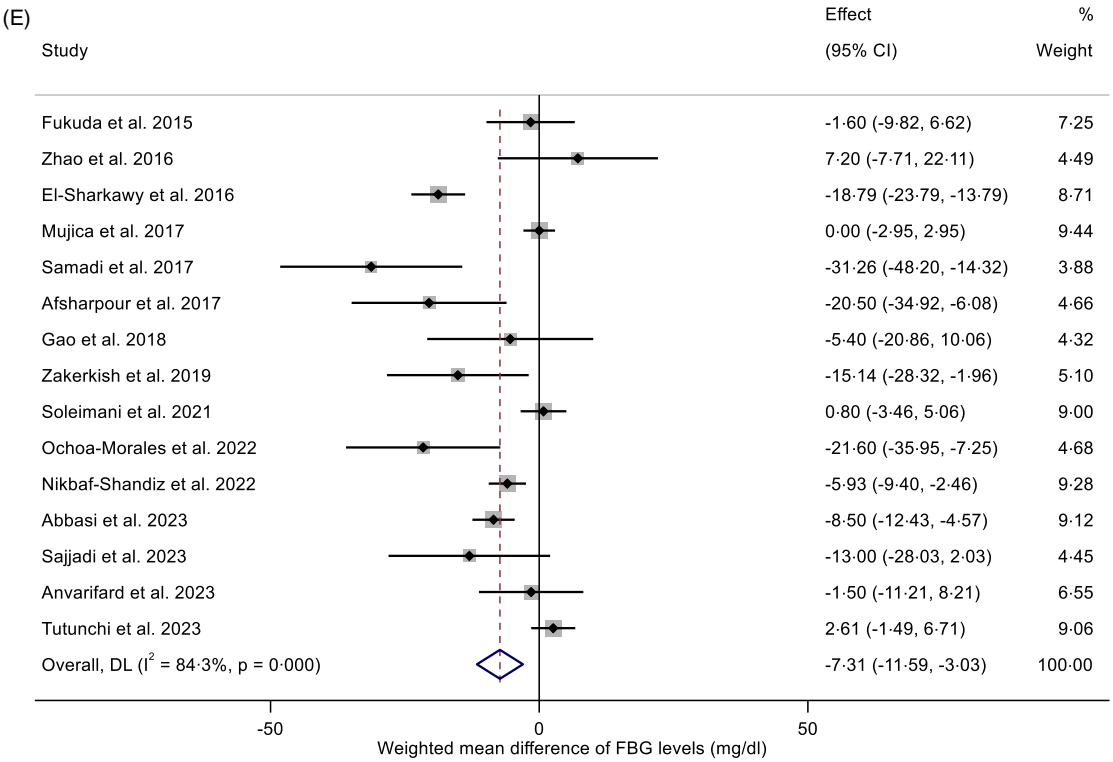


Note: Weights are from random-effects model

Fig. 2. (Continued)



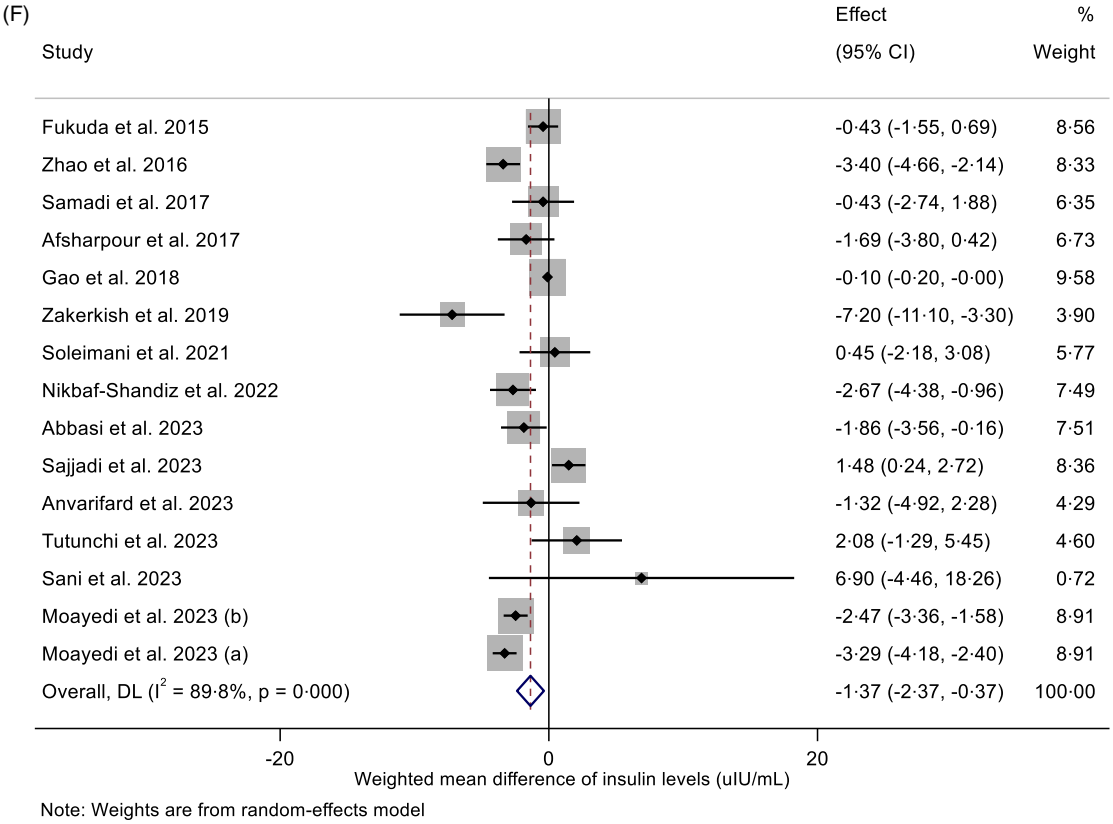


Fig. 2. (Continued)

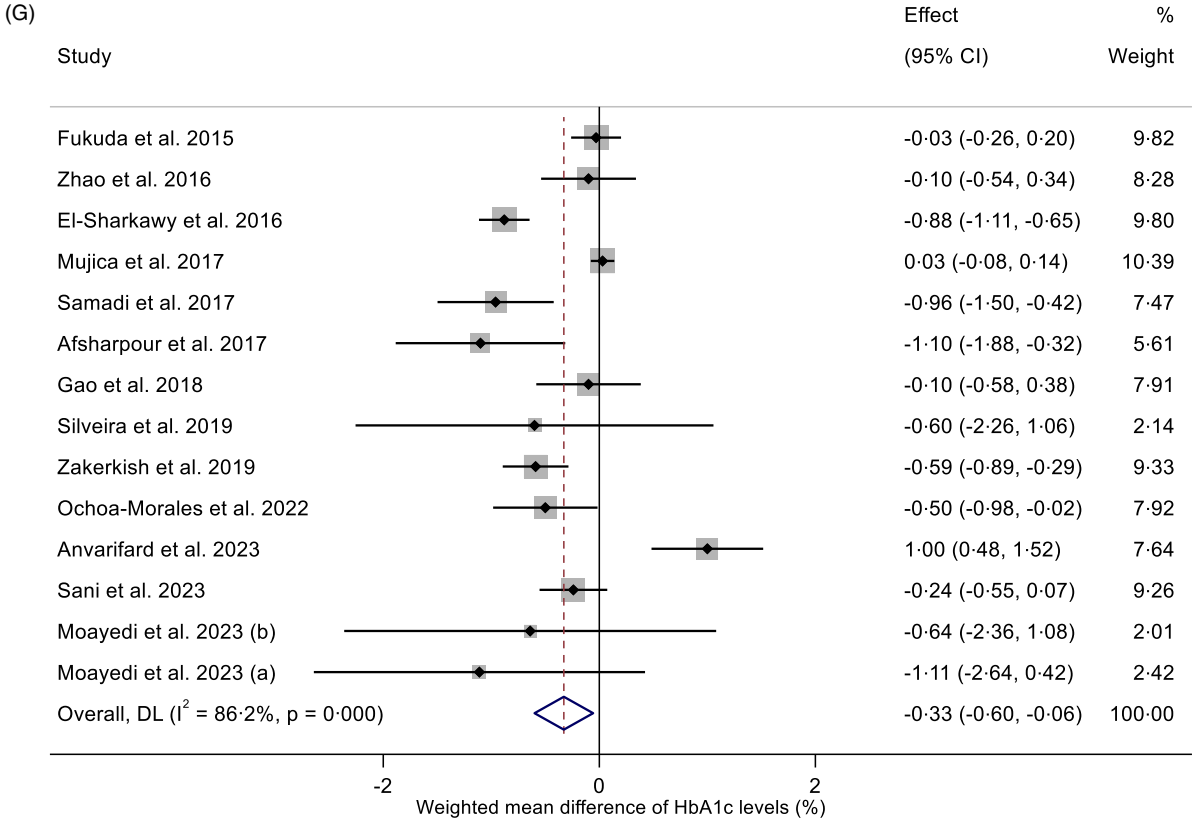


Fig. 2. (Continued)

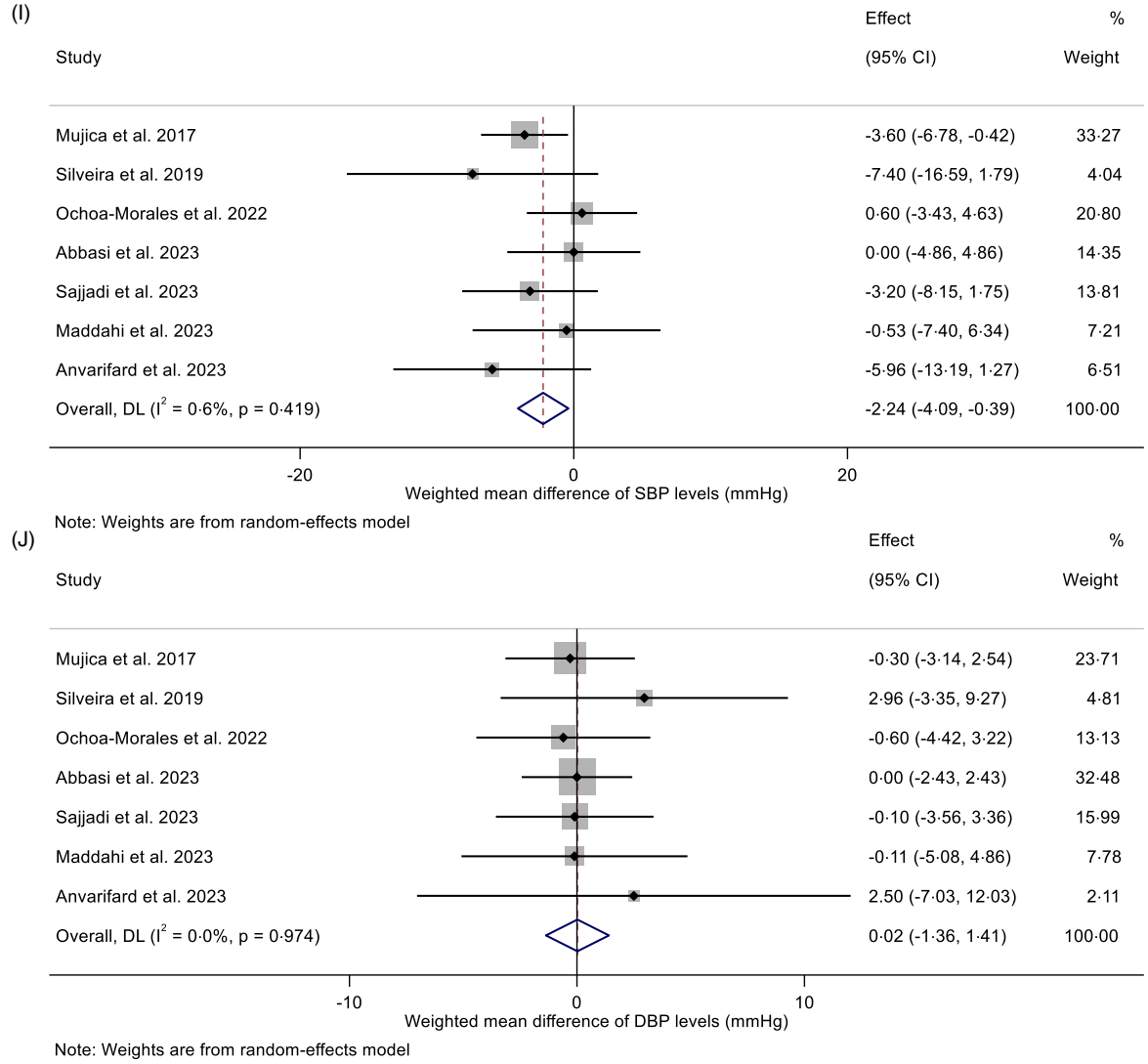


Fig. 2. (Continued)

$P = 0·02$) (Fig. 2(h)). Also, a high between-studies heterogeneity was found ($I^2 = 79·9$ %, $P < 0·001$). Moreover, the results of the subgroup analysis mentioned that high-dose (≥1000 mg/d) propolis consumption or intervention among female participants, or the Iranian population led to a significant reduction in HOMA-IR (Table 3).

Sensitivity analysis

To ascertain the impact of each study on the overall effect size, each included study was omitted from the analysis, respectively. By removing the studies Mujica *et al.* 2017 (WMD: 1·55 mg/dl, 95 % CI: –0·24, 3·35)[53], Zakerkish *et al.* 2019 (WMD: 1·88 mg/dl, 95 % CI: –0·03, 3·80)[51], Afsharpour *et al.* 2022 (WMD mg/dl: 1·67, 95 % CI: –0·20, 3·54)[47] and Moayedi *et al.* 2023 (a) (WMD: 1·71 mg/dl, 95 % CI: –0·06, 3·48)[40], the overall result of HDL-cholesterol was altered significantly. Moreover, by excluding Mujica *et al.* 2017 (WMD: –4·63 mg/dl, 95 % CI: –8·69, –0·58)[53], the pooled effect size for TC was significantly changed. Furthermore, by excluding Afsharpour *et al.* 2017 (WMD: –0·28, 95 % CI: –0·58, 0·02)[46], Zakerkish *et al.* 2019 (WMD: –0·31, 95 % CI: –0·64, 0·01)[51], Nikbaf-Shandiz *et al.* 2022 (WMD: –0·33, 95 % CI: –0·70, 0·04)[48] and Abbasi *et al.* 2023 (WMD: –0·36, 95 % CI: –0·75, 0·01)[45], the overall result for HOMA-IR was significantly changed. Finally, the overall result for SBP was significantly altered by omitting the trials Mujica *et al.* 2017 (WMD: –1·55 mmHg, 95 % CI: –3·81, 0·69)[53] and Sajjadi *et al.* 2023 (WMD: –2·07 mmHg, 95 % CI: –4·31, 0·16)[44]. However, other outcomes were not significantly influenced by the quality of one study.

Publication bias

Upon examination of the funnel plots and conducting Egger's test, it was observed that there is a notable publication bias in studies evaluating the effect of propolis consumption on HDL-cholesterol levels ($P = 0·04$). While among the studies examining other outcomes, no significant publication bias was detected (Fig. 3).

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Table 3. Subgroup analyses of propolis consumption and cardiometabolic risk factors in adults

	Number of effect sizes	WMD	95 % CI	*P* value	Heterogeneity		
					$P_{heterogeneity}$	I^2	$P_{between\ sub\text{-}groups}$
Propolis consumption on serum TC (mg/dl)							
Overall effect	17	−2·53	−7·00, 1·93	0·26	<0·001	90·4 %	
Gender							
Both	13	−1·51	−9·41, 6·38	0·70	<0·001	84·6 %	0·39
Females	4	−6·09	−13·06, 0·87	0·08	<0·001	96·4 %	
Age							
<50	7	1·41	−11·97, 14·81	0·83	<0·001	93·1 %	0·41
>50	9	−4·49	−9·60, 0·61	0·08	<0·001	89·9 %	
Trial duration (week)							
<12	7	−1·64	−6·64, 3·35	0·51	<0·001	89·9 %	0·86
≥12	10	−2·70	−13·87, 8·45	0·63	<0·001	91·5 %	
Intervention dose (mg/day)							
<1000	9	−4·63	−9·37, 0·10	0·05	<0·001	88·7 %	0·84
≥1000	6	−5·89	−17·36, 5·58	0·31	<0·001	82·1 %	
Baseline BMI (kg/m^2)							
Normal (18·5–24·9)	3	−2·61	−10·77, 5·54	0·53	0·06	63·8 %	0·77
Overweight (25–29·9)	7	−5·40	−20·83, 10·02	0·49	<0·001	94·0 %	
Obese (>30)	5	0·07	−7·16, 7·31	0·98	0·22	29·9 %	
Health status							
Healthy	2	15·64	−8·76, 40·04	0·20	<0·001	95·1 %	0·01
NAFLD	3	−0·75	−7·60, 6·08	0·82	0·80	0·0 %	
T2DM	7	−3·16	−8·88, 2·55	0·27	<0·001	92·0 %	
Others	5	−12·29	−17·82, −6·75	<0·001	0·21	30·5 %	
Origin of study							
Iran	11	−5·98	−10·96, −1·00	0·019	<0·001	90·8 %	0·134
Other countries	6	4·06	−8·10, 16·23	0·513	<0·001	88·4 %	
Propolis consumption on serum TG (mg/dl)							
Overall effect	13	−10·44	−16·58, −4·31	0·001	0·13	31·4 %	
Gender							
Both	11	−11·86	−21·29, −2·43	0·01	0·08	39·2 %	0·62
Females	2	−9·18	−14·19, −4·17	<0·001	0·44	0·0 %	
Age							
<50	7	−9·60	−13·22, −5·97	<0·001	0·64	0·0 %	0·14
>50	5	−25·58	−46·73, −4·42	0·01	0·08	51·2 %	
Trial duration (week)							
<12	4	−15·40	−32·87, 2·06	0·08	0·06	58·6 %	0·45
≥12	9	−8·24	−15·36, −1·11	0·02	0·32	12·9 %	
Intervention dose (mg/day)							
<1000	5	−17·46	−35·11, 0·18	0·05	0·26	24·2 %	0·49
≥1000	6	−10·07	−21·83, 1·67	0·09	0·11	44·1 %	
Baseline BMI (kg/m^2)							
Normal (18·5–24·9)	1	−11·70	−17·44, −5·95	<0·001	–	–	0·81
Overweight (25–29·9)	7	−12·50	−23·58, −1·42	0·02	0·09	44·4 %	
Obese (>30)	5	−6·12	−23·38, 11·13	0·48	0·21	30·7 %	
Health status							
Healthy	2	−6·00	−22·07, 10·07	0·46	0·11	59·5 %	0·70
NAFLD	3	−6·99	−25·44, 11·44	0·45	0·62	0·0 %	
T2DM	4	−20·56	−40·68, −0·43	0·04	0·13	45·5 %	
Others	4	−9·23	−24·85, 6·37	0·24	0·12	48·1 %	
Origin of study							
Iran	9	−14·25	−25·25, −3·25	0·011	0·076	43·8 %	0·423
Other countries	4	−8·96	−15·76, −2·16	0·010	0·361	6·4 %	
Propolis consumption on serum LDL-cholesterol (mg/dl)							
Overall effect	16	−9·31	−13·50, −5·12	<0·001	<0·001	86·3 %	
Gender							
Both	12	−7·98	−15·64, −0·33	0·04	<0·001	87·7 %	0·36
Females	4	−11·98	−15·93, −8·02	<0·001	0·002	79·4 %	
Age							
<50	6	−6·16	−14·51, 2·19	0·14	<0·001	78·8 %	0·26
>50	9	−11·78	−17·20, −6·36	<0·001	<0·001	89·4 %	
Trial duration (week)							
<12	6	−13·29	−19·58, −7·00	<0·001	<0·001	91·9 %	0·11
≥12	10	−6·40	−12·05, −0·75	0·02	<0·001	73·0 %	
Intervention dose (mg/day)							
<1000	9	−8·31	−11·99, −4·62	<0·001	<0·001	73·5 %	0·51
≥1000	5	−13·72	−29·50, 2·04	0·08	<0·001	93·7 %	

Table 3. (*Continued*)

	Number of effect sizes	WMD	95 % CI	*P* value	Heterogeneity		
					$P_{heterogeneity}$	I^2	$P_{between\ sub\text{-}groups}$
Baseline BMI (kg/m^2)							
Normal (18·5–24·9)	3	–8·37	–15·25, –1·48	0·01	0·07	61·4 %	0·42
Overweight (25–29·9)	7	–10·43	–22·52, 1·65	0·09	<0·001	92·6 %	
Obese (>30)	4	–3·40	–9·32, 2·50	0·25	0·28	20·4 %	
Health status							
Healthy	2	–3·65	–20·97, 13·66	0·67	0·006	86·6 %	0·05
NAFLD	2	0·38	–6·84, 7·60	0·91	0·83	0·0 %	
T2DM	7	–11·98	–18·41, –5·54	<0·001	<0·001	92·0 %	
Others	5	–10·87	–17·43, –4·31	0·001	0·02	64·2 %	
Origin of study							
Iran	10	–11·43	–16·64, –6·21	<0·001	<0·001	89·6 %	0·132
Other countries	6	–5·25	–11·38, 0·88	0·093	0·035	58·3 %	
Propolis consumption on serum HDL-cholesterol (mg/dl)							
Overall effect	17	2·03	0·24, 3·83	0·02	<0·001	88·8 %	
Gender							
Both	13	1·81	–0·51, 4·13	0·12	<0·001	85·0 %	0·75
Females	4	2·50	–1·09, 6·09	0·17	<0·001	95·1 %	
Age							
<50	7	1·79	–1·32, 4·90	0·26	<0·001	82·9 %	0·82
>50	9	2·22	–0·19, 4·64	0·07	<0·001	91·3 %	
Trial duration (week)							
<12	7	3·05	0·49, 5·61	0·01	<0·001	92·3 %	0·31
≥12	10	1·22	–1·21, 3·66	0·32	<0·001	79·5 %	
Intervention dose (mg/day)							
<1000	9	1·29	–1·30, 3·89	0·32	<0·001	89·9 %	0·81
≥1000	6	1·81	–1·57, 5·21	0·29	<0·001	89·1 %	
Baseline BMI (kg/m^2)							
Normal (18·5–24·9)	3	0·62	–1·17, 2·41	0·49	0·64	0·0 %	0·41
Overweight (25–29·9)	7	3·05	–0·10, 6·21	0·05	<0·001	88·7 %	
Obese (>30)	5	0·87	–2·83, 4·58	0·64	0·001	79·8 %	
Health status							
Healthy	2	6·01	–3·99, 16·01	0·23	<0·001	93·9 %	0·32
NAFLD	3	2·40	0·11, 4·70	0·03	0·65	0·0 %	
T2DM	7	2·59	–0·11, 5·31	0·06	<0·001	93·1 %	
Others	5	–0·55	–3·66, 2·55	0·72	0·006	72·6 %	
Origin of study							
Iran	11	2·70	0·74, 4·67	0·007	<0·001	89·6 %	0·355
Other countries	6	0·32	–4·31, 4·97	0·891	<0·001	85·8 %	
Propolis consumption on serum FBG (mg/dl)							
Overall effect	15	–7·30	–11·58, –3·02	0·001	<0·001	84·3 %	
Gender							
Both	14	–7·30	–12·00, –2·61	0·002	<0·001	84·6 %	0·70
Females	1	–8·50	–12·43, –4·56	0·000	–	–	
Age							
<50	5	–4·13	–10·52, 2·26	0·20	<0·001	92·8 %	0·19
>50	9	–10·58	–17·97, –3·18	0·005	0·003	65·6 %	
Trial duration (week)							
<12	4	–4·25	–11·04, 2·54	0·22	0·001	80·9 %	0·32
≥12	11	–8·71	–14·46, –2·96	0·003	<0·001	86·0 %	
Intervention dose (mg/day)							
<1000	10	–8·60	–14·84, –2·35	0·007	<0·001	83·2 %	0·79
≥1000	4	–7·27	–15·35, 0·81	0·07	<0·001	84·0 %	
Baseline BMI (kg/m^2)							
Normal (18·5–24·9)	1	–1·60	–9·81, 6·61	0·70	–	–	0·38
Overweight (25–29·9)	10	–8·81	–14·93, –2·69	0·005	<0·001	87·6 %	
Obese (>30)	4	–5·63	–12·93, 1·66	0·13	0·002	79·8 %	
Health status							
Healthy	1	0·00	–2·94, 2·94	1·000	–	–	0·001
CKD	1	–1·50	–11·21, 8·21	0·76	–	–	
NAFLD	3	–0·94	–6·32, 4·44	0·73	0·004	82·2 %	
T2DM	8	–13·10	–21·04, –5·15	0·001	<0·001	74·2 %	
Others	2	–8·78	–12·59, –4·98	<0·001	0·57	0·0 %	
Origin of study							
Iran	9	–7·16	–12·10, –2·22	0·004	<0·001	80·2 %	0·948
Other countries	6	–6·81	–16·32, 2·70	0·161	<0·001	89·7 %	
Propolis consumption on serum fasting insulin (μU/ml)							

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Table 3. (*Continued*)

	Number of effect sizes	WMD	95 % CI	*P* value	Heterogeneity		
					$P_{heterogeneity}$	I^2	$P_{between\ sub\text{-}groups}$
Overall effect	15	−1·36	−2·36, −0·36	0·007	<0·001	89·8 %	
Gender							
Both	12	−0·94	−1·98, 0·09	0·07	<0·001	81·7 %	0·006
Females	3	−2·71	−3·45, −1·98	<0·001	0·24	29·7 %	
Age							
<50	4	0·12	−2·81, 3·05	0·93	0·02	69·7 %	0·27
>50	10	−1·63	−2·83, −0·42	0·008	<0·001	92·6 %	
Trial duration (week)							
<12	6	−1·79	−2·98, −0·60	0·003	<0·001	77·7 %	0·44
≥12	9	−1·09	−2·44, 0·26	0·11	<0·001	84·5 %	
Intervention dose (mg/day)							
<1000	10	−1·20	−2·31, −0·08	0·03	<0·001	91·9 %	0·69
≥1000	5	−1·79	−4·53, 0·93	0·19	0·004	74·1 %	
Baseline BMI (kg/m^2)							
Normal (18·5–24·9)	1	−0·43	−1·55, 0·69	0·45	–	–	0·65
Overweight (25–29·9)	7	−1·24	−2·57, 0·08	0·06	<0·001	81·9 %	
Obese (>30)	5	−0·83	−4·13, 2·46	0·62	<0·001	86·9 %	
Health status							
CKD	1	−1·32	−4·91, 2·27	0·47	–	–	0·44
NAFLD	3	−0·31	−3·21, 2·59	0·83	0·01	75·0 %	
T2DM	8	−2·08	−3·46, −0·71	0·003	<0·001	93·9 %	
Others	3	0·33	−2·83, 3·50	0·83	0·004	81·7 %	
Origin of study							
Iran	11	−1·49	−2·74, −0·23	0·020	<0·001	82·6 %	0·690
Other countries	4	−1·05	−2·83, 0·73	0·249	<0·001	89·3 %	
Propolis consumption on HbA1c (%)							
Overall effect	14	−0·32	−0·60, −0·05	0·01	<0·001	86·2 %	
Gender							
Both	12	−0·30	−0·58, −0·02	0·03	<0·001	88·1 %	0·31
Females	2	−0·90	−2·04, 0·24	0·12	0·68	0·0 %	
Age							
<50	3	−0·35	−0·95, 0·23	0·23	<0·001	95·8 %	0·91
>50	11	−0·32	−0·66, 0·02	0·06	<0·001	77·9 %	
Trial duration (week)							
<12	4	−0·59	−1·33, 0·15	0·11	0·03	64·6 %	0·45
≥12	10	−0·27	−0·60, 0·04	0·09	<0·001	89·5 %	
Intervention dose (mg/day)							
<1000	10	−0·30	−0·71, 0·10	0·14	<0·001	85·5 %	0·43
≥1000	3	−0·53	−0·90, −0·15	0·006	0·07	61·1 %	
Baseline BMI (kg/m^2)							
Normal (18·5–24·9)	1	−0·03	−0·26, 0·20	0·79	–	–	0·08
Overweight (25–29·9)	8	−0·30	−0·72, 0·11	0·14	<0·001	91·6 %	
Obese (>30)	3	−0·42	−0·68, −0·16	0·002	0·28	20·4 %	
Health Status							
Healthy	1	0·03	−0·07, 0·13	0·58	–	–	0·003
CKD	2	0·40	−1·11, 1·91	0·60	0·07	69·4 %	
T2DM	10	−0·52	−0·81, −0·23	<0·001	<0·001	76·1 %	
Others	1	−0·24	−0·55, 0·07	0·13	–	–	
Origin of study							
Iran	6	−0·50	−1·23, 0·23	0·184	<0·001	86·8 %	0·565
Other countries	8	−0·26	−0·55, 0·02	0·071	<0·001	86·4 %	
Propolis consumption on HOMA-IR							
Overall effect	12	−0·39	−0·74, −0·03	0·02	<0·001	79·9 %	
Gender							
Both	11	−0·36	−0·75, 0·01	0·06	<0·001	81·6 %	0·44
Females	1	−0·63	−1·16, −0·09	0·02	–	–	
Age							
<50	5	−0·23	−0·77, 0·29	0·38	0·03	62·7 %	0·53
>50	6	−0·48	−1·04, 0·07	0·09	<0·001	88·4 %	
Trial duration (week)							
<12	4	−0·51	−1·13, 0·11	0·11	<0·001	86·5 %	0·50
≥12	8	−0·26	−0·61, 0·08	0·13	0·01	59·4 %	
Intervention dose (mg/day)							
<1000	6	−0·14	−0·34, 0·06	0·16	0·34	11·5 %	0·03
≥1000	5	−0·95	−1·65, −0·25	0·008	0·003	74·6 %	
Baseline BMI (kg/m^2)							
Normal (18·5–24·9)	1	−0·10	−0·51, 0·31	0·63	–	–	0·38

Table 3. (*Continued*)

	Number of effect sizes	WMD	95 % CI	*P* value	Heterogeneity		
					$P_{heterogeneity}$	I^2	$P_{between\ sub\text{-}groups}$
Overweight (25–29·9)	6	−0·30	−0·79, 0·18	0·22	<0·001	85·7 %	
Obese (>30)	5	−0·72	−1·52, 0·07	0·07	0·002	76·0 %	
Health status							
Healthy	1	−0·15	−0·61, 0·31	0·52	–	–	0·41
CKD	1	0·35	−0·63, 1·33	0·48	–	–	
NAFLD	3	−0·21	−1·05, 0·62	0·61	0·009	79·0 %	
T2DM	4	−0·74	−1·51, 0·02	0·05	<0·001	92·5 %	
Others	3	−0·44	−0·78, −0·09	0·01	0·58	0·0 %	
Origin of study							
Iran	9	−0·46	−0·90, −0·02	0·039	<0·001	83·9 %	0·219
Other countries	3	−0·12	−0·43, 0·18	0·420	0·836	0·0 %	
Propolis consumption on SBP (mmHg)							
Overall effect	7	−2·24	−4·08, −0·39	0·01	0·41	0·6 %	
Gender							
Both	5	−2·86	−5·20, −0·52	0·01	0·32	14·9 %	0·25
Females	2	−0·17	−4·14, 3·79	0·93	0·90	0·0 %	
Age							
<50	2	−3·05	−5·94, −0·17	0·03	0·42	0·0 %	0·88
>50	4	−2·72	−6·18, 0·74	0·12	0·23	29·9 %	
Intervention dose (mg/day)							
<1000	5	−1·89	−4·60, 0·81	0·17	0·29	18·1 %	0·71
≥1000	1	−0·53	−7·39, 6·33	0·88	–	–	
Baseline BMI (kg/m^2)							
Overweight (25–29·9)	5	−1·77	−3·98, 0·43	0·11	0·34	11·6 %	0·34
Obese (>30)	2	−4·14	−8·50, 0·21	0·06	0·43	0·0 %	
Health status							
Healthy	1	−3·60	−6·77, −0·42	0·02	–	–	0·16
CKD	2	−6·51	−12·19, −0·82	0·02	0·80	0·0 %	
T2DM	1	0·60	−3·43, 4·63	0·77	–	–	
Others	3	−1·35	−4·45, 1·73	0·39	0·64	0·0 %	
Origin of study							
Iran	4	−2·07	−4·91, 0·77	0·154	0·532	0·0 %	0·869
Other countries	3	−2·46	−6·21, 1·27	0·197	0·149	47·6 %	
Propolis consumption on DBP (mmHg)							
Overall effect	7	0·02	−1·36, 1·40	0·97	0·97	0·0 %	
Gender							
Both	5	0·04	−1·74, 1·84	0·95	0·87	0·0 %	0·96
Females	2	−0·02	−2·20, 2·16	0·98	0·96	0·0 %	
Age							
<50	2	−0·25	−2·72, 2·21	0·84	0·94	0·0 %	0·75
>50	4	0·27	−2·02, 2·58	0·81	0·76	0·0 %	
Intervention dose (mg/day)							
<1000	5	0·14	−1·52, 1·82	0·86	0·88	0·0 %	0·92
≥1000	1	−0·11	−5·07, 4·85	0·96	–	–	
Baseline BMI (kg/m^2)							
Overweight (25–29·9)	5	−0·13	−1·69, 1·42	0·86	0·98	0·0 %	0·67
Obese (>30)	2	0·60	−2·42, 3·64	0·69	0·40	0·0 %	
Health status							
Healthy	1	−0·30	−3·14, 2·54	0·83	–	–	0·74
CKD	2	2·82	−2·44, 8·08	0·29	0·93	0·0 %	
T2DM	1	−0·60	−4·42, 3·22	0·75	–	–	
Others	3	−0·04	−1·89, 1·80	0·96	0·99	0·0 %	
Origin of study							
Iran	4	0·05	−1·76, 1·86	0·958	0·966	0·0 %	0·963
Other countries	3	−0·02	−2·16, 2·12	0·987	0·612	0·0 %	

WMD, weighted mean differences; TC, total cholesterol; FBG, fasting blood glucose; HOMA-IR, homeostatic model assessment for insulin resistance; SBP, systolic blood pressure; DBP, diastolic blood pressure; CKD, chronic kidney disease; NAFLD, non-alcoholic fatty liver disease; T2DM, type 2 diabetes mellitus.

Non-linear dose–response analysis

A non-linear dose–response analysis was performed to investigate the non-linear relationship between changes in various outcomes and features of propolis supplementation (duration and dosage). The evaluation of the outcomes from the non-linear dose–response analysis revealed that there was no significant non-linear relationship between alterations in TC, TAG, LDL-cholesterol, HDL-cholesterol, FBG, insulin, HbA1c, HOMA-IR, SBP and DBP with the dosage and duration of propolis supplementation.

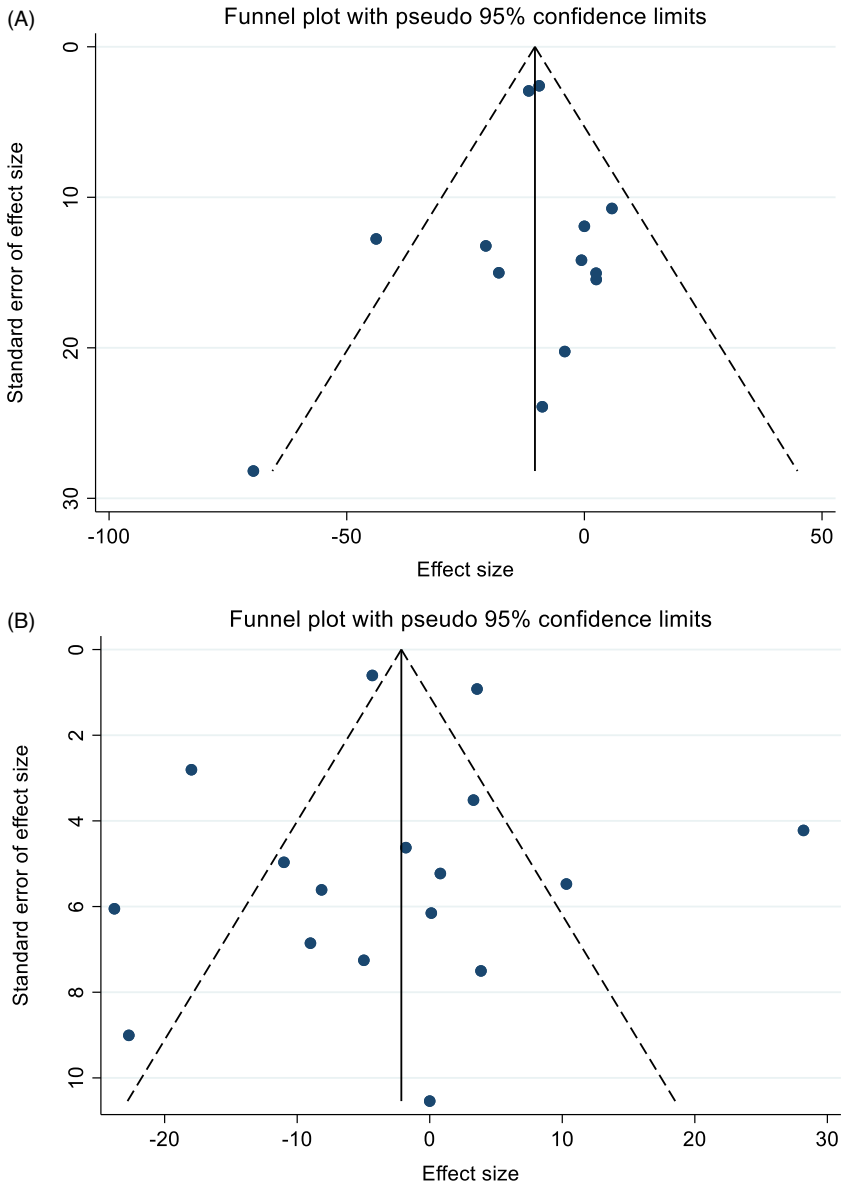

Fig. 3. Funnel plots for the effect of propolis intake on A) TAG (mg/dl); B) TC (mg/dl); C) LDL-cholesterol (mg/dl); D) HDL-cholesterol (mg/dl); E) FBG (mg/dl); F) fasting insulin (uIU/ml); G) HbA1c (%); H) HOMA-IR; I) SBP (mmHg); and J) DBP (mmHg). DBP, diastolic blood pressure; FBG, fasting blood glucose; HOMA-IR, homeostatic model assessment for insulin resistance; SBP, systolic blood pressure.

Meta-Regression analysis

Meta-regression analysis was performed to ascertain the linear relationship between changes in outcomes and propolis supplementation features (duration and dosage). The findings of the meta-regression test revealed that there was no significant linear relationship between the propolis supplementation features and changes in TC, TAG, LDL-cholesterol, HDL-cholesterol, FBG, insulin, HbA1c, HOMA-IR, SBP and DBP (online Supplementary Figs. 1–3).

GRADE analysis

This meta-analysis utilised the GRADE protocol to evaluate the quality of the evidence. The quality of evidence investigating the impact of propolis intake on LDL-cholesterol, HDL-cholesterol, FBG, insulin, HbA1c and HOMA was considered moderate. On the other hand, the quality of evidence for DBP was identified as high. Furthermore, trials assessing the effect of propolis on SBP and TAG had their evidence quality upgraded to very high levels (Table 4).

Discussion

In the present GRADE-assessed systematic review and dose–response meta-analysis, the results showed that propolis consumption resulted in a significant reduction in the TAG, LDL-cholesterol, FBG, HbA1c, insulin, HOMA-IR and SBP in comparison with control or placebo groups. Furthermore, propolis consumption had a significant increasing effect on

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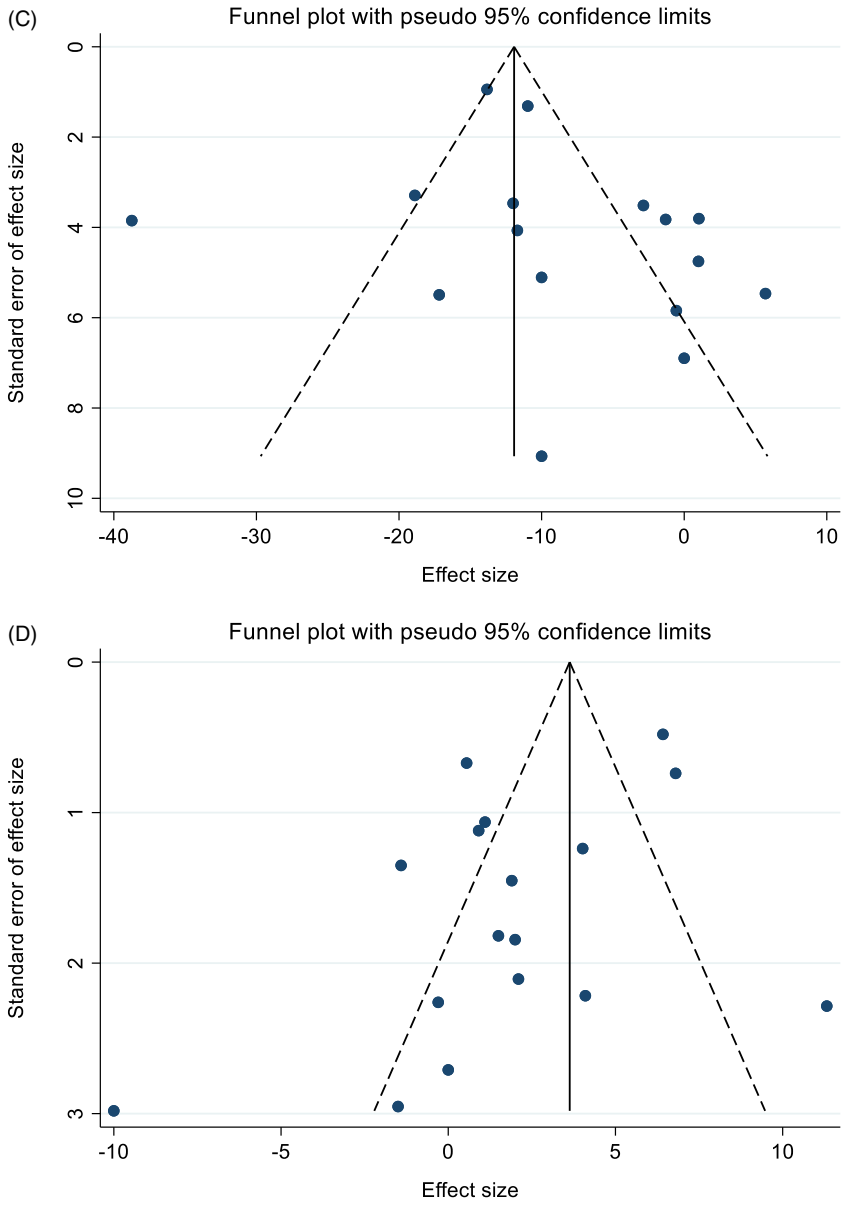

Fig. 3. (Continued)

HDL-cholesterol levels. While propolis intake had no significant effect on TC and DBP levels. Based on the non-linear dose–response analysis, a significant reducing effect of propolis intakes on TAG, LDL-cholesterol, FBG and insulin levels was found in less than 1000 mg/d, and it was not significant at higher dosages; however, for HOMA-IR and HbA1c, doses of 1000 mg/d and higher had significant effects, and these effects were not significant for doses lower than 1000 mg/d.

In Karimian *et al*. systematic review and meta-analysis, it was shown that propolis intake in T2DM patients caused a significant decrease in FBG and HbA1c levels; however, its effect on HOMA-IR and fasting insulin was not significant[18], the results of this study in terms of no effect on HOMA-IR and insulin are contrary to the results of present study, which is probably due to the low number of articles included in the study and the different doses of propolis used, as well as the fact that the patients are diabetic, also, the heterogeneity in their study was high and the source is unclear, as well as, in the sensitivity analysis, by removing some studies, our results changed, which shows that some studies can affect the overall results due to the low sample size, different study designs and the type of propolis used. In another study, Hallajzadeh *et al*. showed that glycaemic indices, including FBG, insulin, HbA1c and to some extent HOMA-IR, improved after consuming propolis, and the findings of this study confirmed the results of the present study[21]. Similar to the findings of the current study, in one interventional study, the consumption of propolis after 8 weeks (1500 mg/d) had significant effects on the improvement of FBG and HbA1c in T2DM patients[57]. A clinical trial study conducted by Samadi *et al*. showed that 12 weeks of propolis supplementation at a dose of 900 mg/d in T2DM patients significantly reduced FBG and HbA1c, while its effect on insulin and HOMA-IR was not

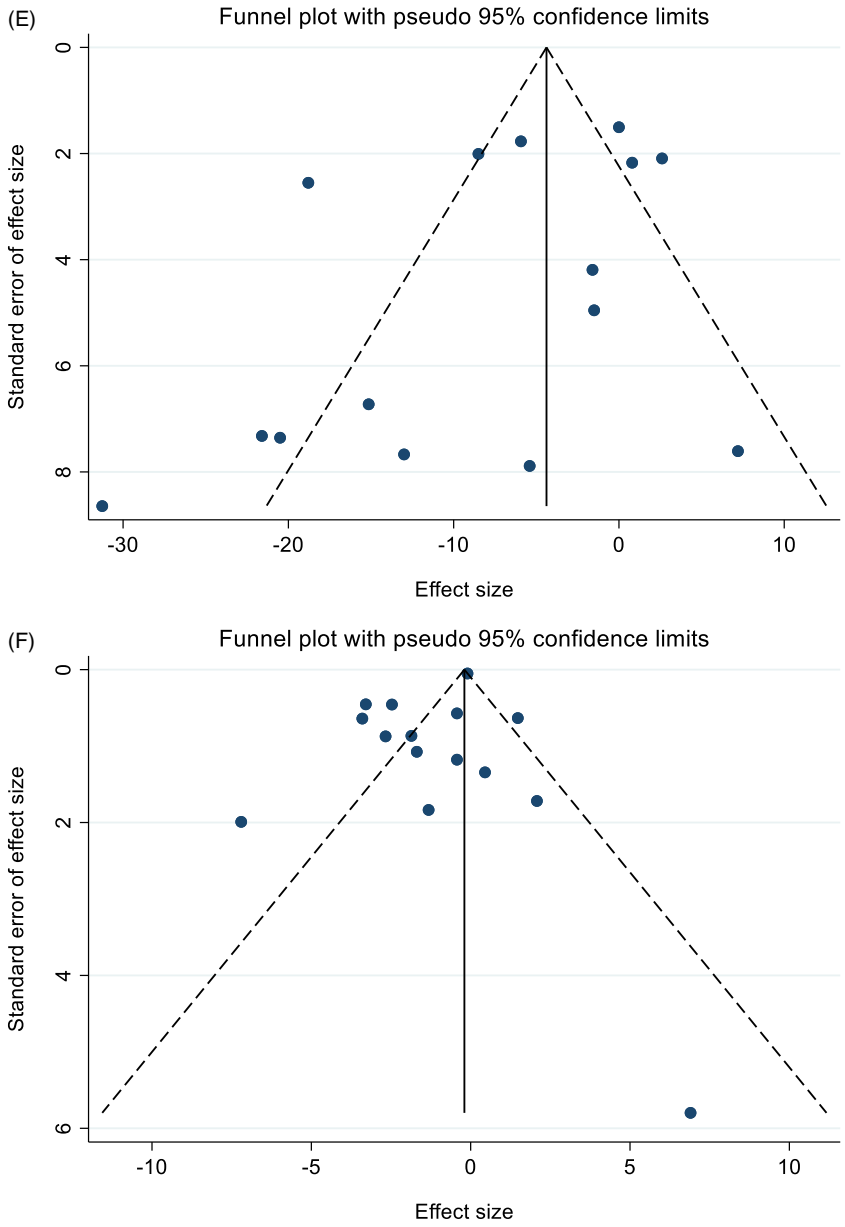

Fig. 3. (Continued)

significant[50], subgroup analysis in current study showed that propolis in doses less than 1000 mg/d and in less than 12 weeks duration causes significant effects on reducing insulin levels, that is not similar to the results of this study, which is probably due to the type of propolis and geographical region that propolis was gathered and it is also likely that confounders were not adjusted for in this study. The results of a clinical trial study showed that the Chinese propolis supplementation at a dose of 900 mg/d for 18 weeks in diabetic patients had no significant effect on serum glucose, HbA1c and insulin[39], which is contrary to the results of the present study, that is probably due to the propolis type and geographical region and also the health conditions of the participants. Also, in a similar study, receiving Brazilian green propolis at a dose of 226·8 mg/d for 8 weeks in diabetic patients did not have a significant effect on FBG, HbA1c and HOMA-IR[38], which does not confirm the results of the current study that the reason was due to the low dose of propolis and also kind and amount of propolis constituents in this study. It can be said that higher dosages of propolis supplementation, following long duration, might be necessary to observe definite effects of propolis on glycaemic indices in different conditions of health and illness of participants.

Although the mechanism of the effect of propolis on glycaemic indices has not been fully identified, it seems that one of the main probable mechanisms of propolis in improving glycaemic indices is increasing the activity of glucose transporter-4 in skeletal muscles, which increases glucose uptake, and on the other hand, propolis, by reducing the expression and activity of the glucose 6 phosphatase enzyme, causes decreasing effects on glycaemic indices[58,59]. Also, due to its antioxidant

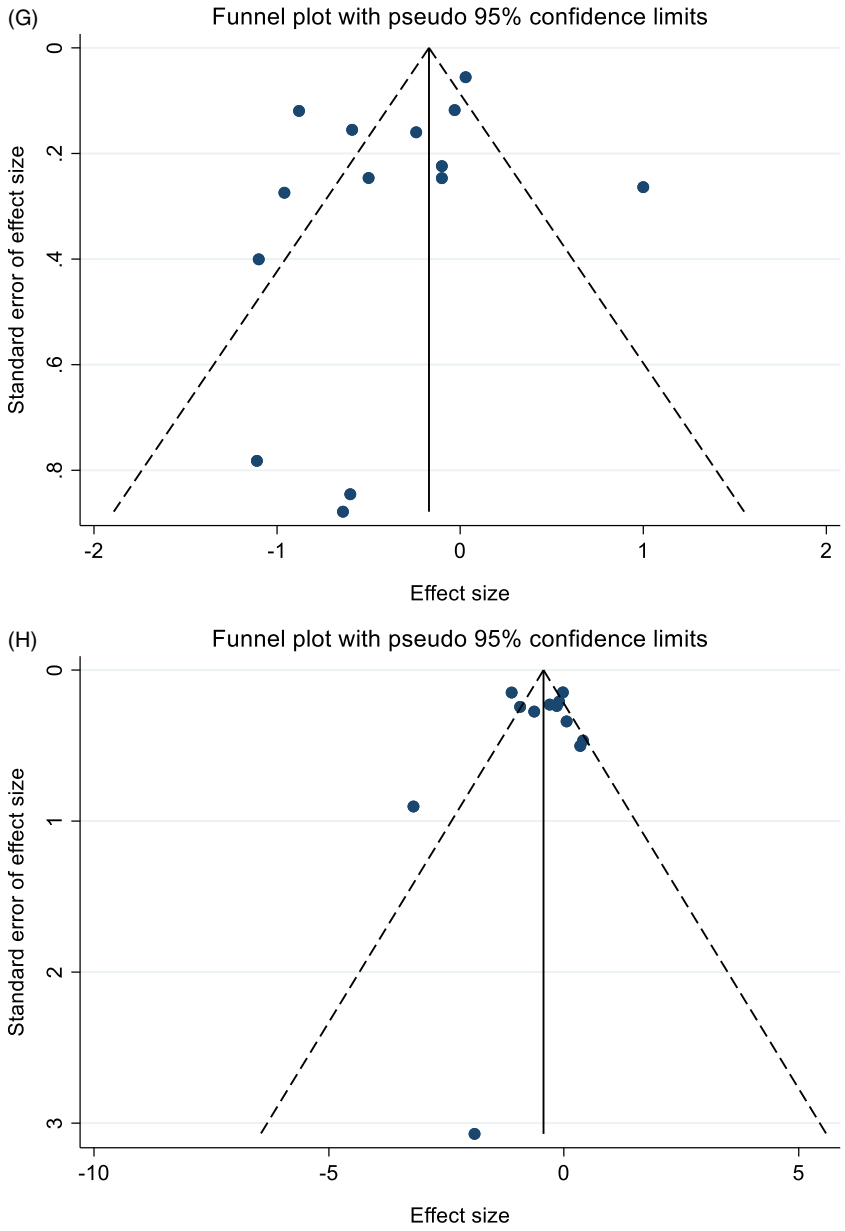

Fig. 3. (Continued)

properties, propolis can improve metabolic abnormalities and glycaemic indices and because of its bioactive compounds could elevate insulin production or/and increase cellular sensitivity response to insulin[53,60].

The findings of the present study revealed that propolis intakes resulted in a significant reduction in the TAG, and LDL-cholesterol and had a significant increasing effect on HDL-cholesterol levels. In contrast, propolis had no significant impact on TC levels. Consistent with the findings of the current study, a meta-analysis study conducted by Salehi-Sahlabadi *et al.* on five randomised controlled trials showed that propolis consumption significantly reduced TAG and increased HDL-cholesterol levels, but had no significant effect on cholesterol and LDL-cholesterol levels[23], and probably the reason that these effects on LDL-cholesterol were not significant (compared with current study) is the number of studies included in the analysis because in present study, between thirteen and seventeen effect sizes were evaluated for lipid profile. In another meta-analysis study, which included six studies, Gheflati *et al.* showed that propolis supplementation does not have a significant effect on TAG, TC, LDL-cholesterol, and HDL-cholesterol levels, and the findings of this study are somewhat contrary to the results of the current study[22], which is probably due to the small number of included studies, because in their study, despite decreasing (TAG, TC, LDL-cholesterol) and increasing (HDL-cholesterol) effects, these effects were not significant, also, due to the small number of included studies, another reason for this inconsistency of the results may be the study designs and the doses of propolis used. However, in the sensitivity analysis we performed, three of the studies included in the Gheflati *et al.* study had a significant effect

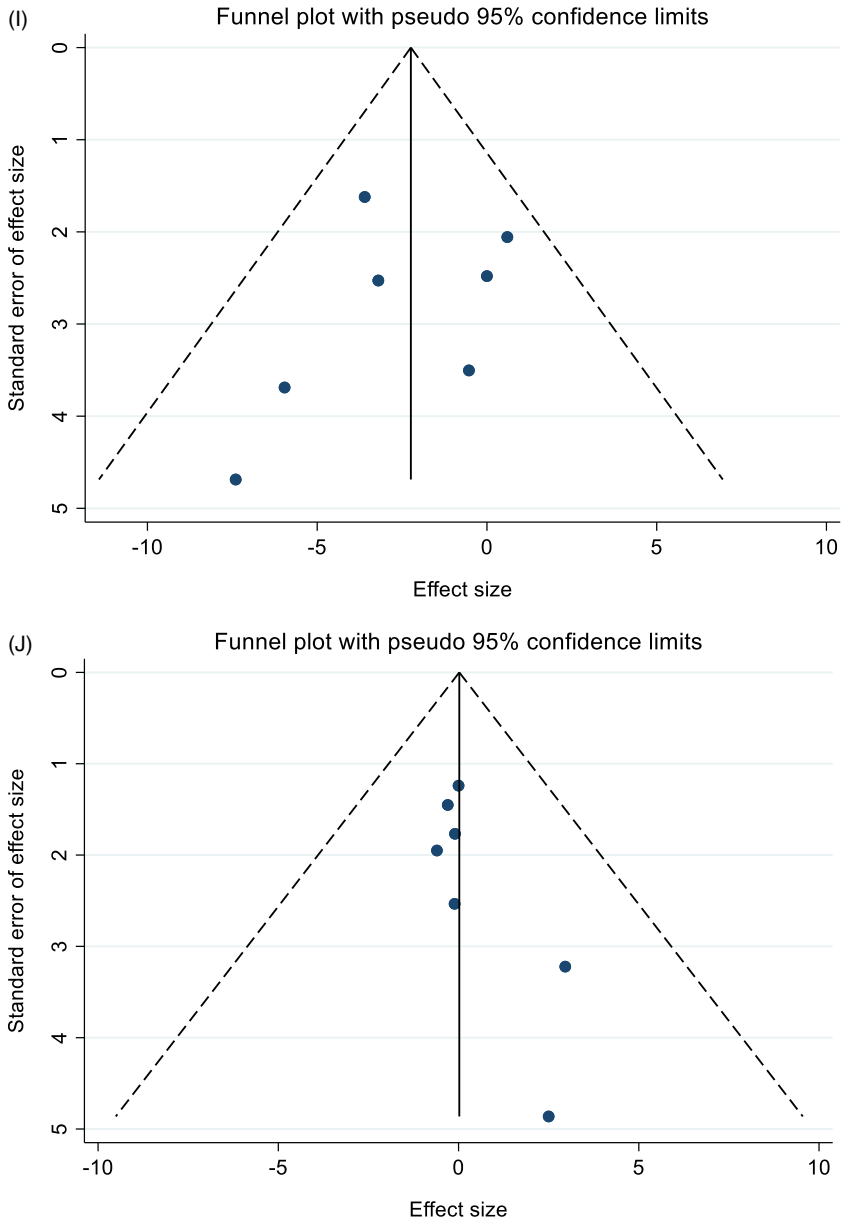

Fig. 3. (Continued)

on overall outcome when excluded from the analysis. In an intervention study, propolis with a dose of 900 mg/d for 12 weeks in patients with T2DM, although it did not have a significant effect on reducing TC and LDL-cholesterol levels before and after the intervention, compared with the placebo group, it caused significant effects and also did not have significant impacts on TAG and HDL-cholesterol levels[50]. In one study conducted on women with rheumatoid arthritis, propolis supplementation (1000 mg/d for 12 weeks) significantly reduced TC, TAG and LDL-cholesterol levels compared with placebo after adjusting for confounders, but its effects on HDL-cholesterol levels were not significant[43], unlike present study, in this study the effects of propolis on TC levels were significant and the reason for this can be seen in the subgroup analysis of current study, because in the subgroup analysis, the propolis effects in overweight participants and women on TC levels were reduced, which is similar to this study. A probable mechanism for the useful impact of propolis on lipid profile indices may be that ATP-binding cassette transporters, which are related to HDL-cholesterol arrangement and peripheral tissue efflux, are communicated to a more prominent degree within the liver proteins after propolis supplementation[50]. Another possible mechanism is that the propolis flavonoids can diminish the biosynthesis of cholesterol by inhibiting the hepatic 3-hydroxy-3-methylglutaryl-CoA reductase and acyl CoA: cholesterol o-acyltransferase, which decreases the acyl CoA: cholesterol o-acyltransferase activity leads to low availability of cholesterol ester for VLDL-cholesterol packing, that can reduce the secretion of VLDL-cholesterol from the liver[61–63]. Another probable mechanism of the beneficial impacts of propolis on the lipid profile modification is related to sterol regulatory element binding transcription factor 1 responsive

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Table 4. GRADE profile of propolis consumption for cardiometabolic risk factors in adults

Outcomes	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality of evidence
TC	No serious limitations	Very serious limitations*	No serious limitations	Serious limitations†	No serious limitations	⊕○○○ Low
TAG	No serious limitations	No serious limitations	No serious limitations	No serious limitations	No serious limitations	⊕⊕⊕⊕ Very high
LDL-cholesterol	No serious limitations	Very serious limitations*	No serious limitations	No serious limitations	No serious limitations	⊕⊕○○ Moderate
HDL-cholesterol	No serious limitations	Very serious limitations*	No serious limitations	No serious limitations	No serious limitations	⊕⊕○○ Moderate
FBG	No serious limitations	Very serious limitations*	No serious limitations	No serious limitations	No serious limitations	⊕⊕○○ Moderate
Insulin	No serious limitations	Very serious limitations*	No serious limitations	No serious limitations	No serious limitations	⊕⊕○○ Moderate
A1C	No serious limitations	Very serious limitations*	No serious limitations	No serious limitations	No serious limitations	⊕⊕○○ Moderate
HOMA-IR	No serious limitations	Very serious limitations*	No serious limitations	No serious limitations	No serious limitations	⊕⊕○○ Moderate
SBP	No serious limitations	No serious limitations	No serious limitations	No serious limitations	No serious limitations	⊕⊕⊕⊕ Very high
DBP	No serious limitations	No serious limitations	No serious limitations	Serious limitations†	No serious limitations	⊕⊕⊕○ High

TC, total cholesterol; FBG, fasting blood glucose; HOMA-IR, homeostatic model assessment for insulin resistance; SBP, systolic blood pressure; DBP, diastolic blood pressure.
* There is high heterogeneity ($I^2 > 75\%$).
† There is no significant effect of propolis consumption.

lipogenic genes, stearoyl-coenzyme A desaturase 1 and fatty acid-binding protein 5, which increases lipid oxidation and decrease its accumulation[64–66].

The results of the present study showed that propolis intakes lead to significant lowering effects on SBP, but its effects on DBP was not statistically significant. Two clinical trial studies showed that consumption of propolis (with a dose of 1000 mg/d in women with rheumatoid arthritis for 12 weeks and with a dose of 500 mg/d for 12 months in patients with chronic kidney disease) has not a significant effect on SBP and DBP[25,43], which are contrary to the results of current study in terms of no effect on SBP, which is probably due to the variable doses and health conditions of the participants. However, in confirmation of the findings of the present study, Mujica *et al.* showed that oral administration of propolis solution (30 drops of 3 % propolis extract after 3 months) caused a significant decrease in SBP and no effect on DBP[53]. In another study, it was shown that propolis (500 mg, twice daily) improved blood pressure in healthy individuals after 8 weeks of intervention[67]. It seems that the effects of propolis on blood pressure are probably due to its antioxidant and anti-inflammatory effects, which by reducing inflammation reduces vascular contraction, and by decreasing oxidative stress, improves the condition of atherosclerosis[67,68]. Also, another mechanism of propolis in improving blood pressure can be due to its effects in inhibiting nitric oxide synthase, which can reduce catecholamines associated with high blood pressure[69]; however, more studies with controlled doses and specific compositions of propolis are needed to evaluate its precise effects on blood pressure.

Generally in one comprehensive randomised controlled trial that was conducted on polycystic ovary syndrome women, 500 mg/d propolis supplement for 12 weeks was able to significantly reduce FBG, HOMA-IR and fasting insulin, but despite a significant reduction in the ratio of LDL-cholesterol/HDL-cholesterol had no significant effects on the levels of LDL-cholesterol, HDL-cholesterol, TC, TAG, SBP and DBP[45]. Considering the antioxidant, anti-inflammatory and antimicrobial effects of propolis with more than 300 effective compounds, its intake in safe doses seems to be effective in improving health and also in some chronic conditions[70,71].

From a clinical perspective, propolis consumption failed to have a clinically favourable effect on glycaemic parameters, lipid profile and blood pressure. Nevertheless, it is important to highlight that the statistically significant impact of propolis on glycaemic parameters, TAG, LDL-cholesterol, HDL-cholesterol and SBP was minor and may not have clinical significance. The minimal clinically important difference is defined as the minimum effect needed to generate clinically significant outcomes[72,73]. There is limited data on minimal clinically important difference for blood pressure and glycaemic and lipid profile, but multiple studies have indicated that minimal clinically important difference could be considered as 5 mmHg for SBP and DBP, >14 mg/dl for fasting blood glucose, >0·5 % for HbA1c, 10 % for LDL-cholesterol and HDL-cholesterol, and 30 % for TAG[74–76]. Given that the WMD of the impact of propolis on SBP, HbA1c, FBG, TAG, LDL-cholesterol and HDL-cholesterol is less than the minimal clinically important difference, we can contemplate that the favorable effects of propolis on blood pressure, glycaemic

parameters, and lipid profile are not clinically meaningful. Additional long-term and high-quality randomised controlled trials are necessary to further assess and validate the credibility of these findings.

To the best of our knowledge, the current GRADE-assessed systematic review and dose–response meta-analysis is one of the first comprehensive studies that evaluate the benefit of propolis effects on cardiometabolic markers in adults and also the general risk of bias was low in more than 95 % of the included studies, which indicates that the results can be more generalisable. Also, a subgroup analysis was performed to assess the effects of dose, gender, age, study durations and type of population on the changes in the cardiometabolic indices. However, the present study has some limitations, which should be considered when the data are interpreted. First, included articles have evaluated various types of propolis in different conditions, and it is unclear how much they differ in biological and bioactive components. Second, high heterogeneity because some studies were conducted on healthy participants and some on chronic conditions. Third, as most of the studies were done in Iran and Asia, possibly, the results could not be generalised to the general population of various areas, and these results should be interpreted with caution. Further studies in various populations or areas are recommended to achieve more definite results.

Conclusion

According to the findings of the present study, propolis intake can improve some cardiometabolic indices such as a significant reduction in the TAG, LDL-cholesterol, FBG, HbA1c, insulin, HOMA-IR and SBP. However, these effects were not clinically significant. Also due to the low significant side effects, it may be used as an auxiliary treatment in some chronic diseases and also as a health-promoting supplement in healthy participants in safe doses. Further, well-designed studies are required to confirm and elucidate all aspects of the findings of this study.

Acknowledgements

We would like to thank the Transplant Research Center, Mashhad University of Medical Sciences, for providing support in this manuscript.

The authors received no financial support for the research and/or publication of this article.

H. B. conceived and designed the research. S. T., K. G. and H. G. performed screening and data extraction. M. S. J. and H. B. analysed data. Z. N., N. P. and M. S. J. drafted the manuscript. N. P. and R. K. revised the manuscript. All authors have read and agreed to the published version of the manuscript.

Neither of the authors declared a conflict of interest.

All data generated or analysed during this study are included in this published article.

Supplementary material

For supplementary material/s referred to in this article, please visit https://doi.org/10.1017/S0007114524002010

References

1. Arnett DK, Blumenthal RS, Albert MA, *et al.* (2019) 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: executive summary: a report of the American college of cardiology/American heart association task force on clinical practice guidelines. *Circulation* **140**, e563–e595.
2. Yang Y, Jin H, Zhang P, *et al.* (2021) Influencing mechanisms of lifestyle and dietary factors on chronic diseases among community residents: updated evidence in Shanghai, China. *Public Health Nutr* **25**, 1–13.
3. Tsao CW, Aday AW, Almarzooq ZI, *et al.* (2022) Heart disease and stroke statistics—2022 update: a report from the American heart association. *Circulation* **145**, e153–e639.
4. Organization WH (2023) *First WHO Report Details Devastating Impact of Hypertension and Ways to Stop It*. Geneva: World Health Organization.
5. Koye DN, Magliano DJ, Nelson RG & Pavkov ME (2018) The global epidemiology of diabetes and kidney disease. *Adv Chronic Kidney Dis* **25**, 121–132.
6. Noce A, Romani A & Bernini R (2021) Dietary intake and chronic disease prevention. *Nutrients* **13**, 1358.
7. Locke A, Schneiderhan J & Zick SM (2018) Diets for health: goals and guidelines. *Am Fam Physician* **97**, 721–728.
8. Šuran J, Cepanec I, Mašek T, *et al.* (2021) Propolis extract and its bioactive compounds-from traditional to modern extraction technologies. *Mol* **26**, 2930.
9. Pasupuleti VR, Sammugam L, Ramesh N, *et al.* (2017) Honey, propolis, and royal jelly: a comprehensive review of their biological actions and health benefits. *Oxid Med Cell Longev* **2017**, 1259510.
10. Fuliang H, Hepburn H, Xuan H, *et al.* (2005) Effects of propolis on blood glucose, blood lipid and free radicals in rats with diabetes mellitus. *Pharmacol Res* **51**, 147–152.
11. Shinohara R, Ohta Y, Hayashi T, *et al.* (2002) Evaluation of antilipid peroxidative action of propolis ethanol extract. *Phytother Res* **16**, 340–347.
12. Matsui T, Ebuchi S, Fujise T, *et al.* (2004) Strong antihyperglycemic effects of water-soluble fraction of Brazilian propolis and its bioactive constituent, 3,4,5-tri-O-caffeoylquinic acid. *Biol Pharm Bull* **27**, 1797–1803.
13. Ichi I, Hori H, Takashima Y, *et al.* (2009) The beneficial effect of propolis on fat accumulation and lipid metabolism in rats fed a high-fat diet. *J Food Sci* **74**, H127–131.
14. Yu Y, Si Y, Song G, *et al.* (2011) Ethanolic extract of propolis promotes reverse cholesterol transport and the expression of ATP-binding cassette transporter A1 and G1 in mice. *Lipids* **46**, 805–811.
15. Braakhuis A (2019) Evidence on the health benefits of supplemental propolis. *Nutrients* **11**, 2705.
16. Zhu L, Zhang J, Yang H, *et al.* (2023) Propolis polyphenols: a review on the composition and anti-obesity mechanism of different types of propolis polyphenols. *Front Nutr* **10**, 1066789.
17. Gogebakan A, Talas ZS, Ozdemir I, *et al.* (2012) Role of propolis on tyrosine hydroxylase activity and blood pressure in nitric oxide synthase-inhibited hypertensive rats. *Clin Exp Hypertens* **34**, 424–428.
18. Karimian J, Hadi A, Pourmasoumi M, *et al.* (2019) The efficacy of propolis on markers of glycemic control in adults with type 2 diabetes mellitus: a systematic review and meta-analysis. *Phytother Res* **33**, 1616–1626.
19. Aoi W, Hosogi S, Niisato N, *et al.* (2013) Improvement of insulin resistance, blood pressure and interstitial pH in early developmental stage of insulin resistance in OLETF rats by intake of propolis extracts. *Biochem Biophys Res Commun* **432**, 650–653.

20. Maddahi M, Nattagh-Eshtivani E, Jokar M, *et al.* (2023) The effect of propolis supplementation on cardiovascular risk factors in women with rheumatoid arthritis: a double-blind, placebo, controlled randomized clinical trial. *Phytother Res* **37**, 5424–5434.
21. Hallajzadeh J, Milajerdi A, Amirani E, *et al.* (2021) Effects of propolis supplementation on glycemic status, lipid profiles, inflammation and oxidative stress, liver enzymes, and body weight: a systematic review and meta-analysis of randomized controlled clinical trials. *J Diabetes Metab Disorders* **20**, 831–843.
22. Gheflati A, Dehnavi Z, Yazdi AG, *et al.* (2021) The effects of propolis supplementation on metabolic parameters: a systematic review and meta-analysis of randomized controlled clinical trials. *Avicenna J Phytomed* **11**, 551.
23. Salehi-Sahlabadi A, Chhabra M, Rahmani J, *et al.* (2020) The effect of propolis on anthropometric indices and lipid profile: a systematic review and meta-analysis of randomized controlled trials. *J Diabetes Metab Disorders* **19**, 1835–1843.
24. Zhao L, Pu L, Wei J, *et al.* (2016) Brazilian green propolis improves antioxidant function in patients with type 2 diabetes mellitus. *Int J Environ Res Public Health* **13**, 498.
25. Silveira MAD, Teles F, Berretta AA, *et al.* (2019) Effects of Brazilian green propolis on proteinuria and renal function in patients with chronic kidney disease: a randomized, double-blind, placebo-controlled trial. *BMC Nephrol* **20**, 1–12.
26. Moher D, Liberati A, Tetzlaff J, *et al.* (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med* **151**, 264–269.
27. Higgins J & Green S (2010) *Cochrane Handbook for Systematic Reviews of Interventions*. Chichester (UK): John Wiley & Sons.
28. DerSimonian R & Laird N (1986) Meta-analysis in clinical trials. *Controlled Clin Trials* **7**, 177–188.
29. Borenstein M, Hedges LV, Higgins JP, *et al.* (2021) *Introduction to Meta-Analysis*. New York: John Wiley & Sons.
30. Hozo SP, Djulbegovic B & Hozo I (2005) Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med Res Method* **5**, 1–10.
31. Higgins JP, Thompson SG, Deeks JJ, *et al.* (2003) Measuring inconsistency in meta-analyses. *Bmj* **327**, 557–560.
32. Mitchell MN (2012) *Interpreting and Visualizing Regression Models Using Stata*, vol. 558. College Station, TX: Stata Press.
33. Tobias A (1999) Assessing the influence of a single study in the meta-analysis estimate. *Stata Tech Bull* **47**, 15–17.
34. Egger M, Smith GD, Schneider M, *et al.* (1997) Bias in meta-analysis detected by a simple, graphical test. *Bmj* **315**, 629–634.
35. Morton SC, Adams JL, Suttorp MJ, *et al.* (2010) *Meta-Regression Approaches: What, Why, When, and How?* Rockville, MD: Agency for Healthcare Research and Quality (US).
36. Xu C & Doi SA (2018) The robust error meta-regression method for dose–response meta-analysis. *JBI Evid Implementation* **16**, 138–144.
37. Asama T, Hiraoka T, Ohkuma A, *et al.* (2021) Cognitive improvement and safety assessment of a dietary supplement containing propolis extract in elderly Japanese: a placebo-controlled, randomized, parallel-group, double-blind human clinical study. *Evid-Based Complementary Altern Med* **2021**, 1–8.
38. Fukuda T, Fukui M, Tanaka M, *et al.* (2015) Effect of Brazilian green propolis in patients with type 2 diabetes: a double-blind randomized placebo-controlled study. *Biomed rep* **3**, 355–360.
39. Gao W, Pu L, Wei J, *et al.* (2018) Serum antioxidant parameters are significantly increased in patients with type 2 diabetes mellitus after consumption of Chinese propolis: a randomized controlled trial based on fasting serum glucose level. *Diabetes Ther* **9**, 101–111.
40. Moayedi F, Taghian F, Jalali Dehkordi K, *et al.* (2023) Cumulative effects of exercise training and consumption of propolis on managing diabetic dyslipidemia in adult women: a single-blind, randomized, controlled trial with pre–post-intervention assessments. *J Physiol Sci* **73**, 17.
41. Tutunchi H, Arefhosseini S & Ebrahimi-Mameghani M (2023) Clinical effectiveness of α-lipoic acid, myo-inositol and propolis supplementation on metabolic profiles and liver function in obese patients with NAFLD: a randomized controlled clinical trial. *Clin Nutr ESPEN* **54**, 412–420.
42. Anvarifard P, Anbari M, Ostadrahimi A, *et al.* (2023) Effects of Iranian propolis on renal function, prooxidant-antioxidant balance, metabolic status, and quality of life in patients with chronic kidney disease: a study protocol of an ongoing randomized, double-blind, placebo-controlled clinical trial. *Contemp Clin Trials Commun* **34**, 101159.
43. Maddahi M, Nattagh-Eshtivani E, Jokar M, *et al.* The effect of propolis supplementation on cardiovascular risk factors in women with rheumatoid arthritis: a double-blind, placebo, controlled randomized clinical trial. *Phytother Res* **37**, 5424–5434.
44. Sajjadi SS, Bagherniya M, Soleimani D, *et al.* (2023) Effect of propolis on mood, quality of life, and metabolic profiles in subjects with metabolic syndrome: a randomized clinical trial. *Sci Rep* **13**, 4452.
45. Abbasi E, Bagherniya M, Soleimani D, *et al.* (2023) The effects of propolis supplementation on high-sensitivity C-reactive protein, testosterone hormone, and metabolic profile in women with polycystic ovary syndrome: a randomized, triple-blinded, placebo-controlled clinical trial. *Phytother Res* **37**, 5366–5377.
46. Afsharpour F, Hashemipour S, Khadem-Haghighian H, *et al.* (2017) Effects of Iranian propolis on glycemic status, inflammatory factors, and liver enzyme levels in type 2 diabetic patients: a randomized, double-blind, placebo-controlled, clinical trial. *J Nutr Sci Diet* **9**, 7289.
47. Afsharpour F, Javadi M, Hashemipour S, *et al.* (2022) Changes in lipid profile, liver enzymes and inflammatory factors following oral supplementation with propolis in patients with type 2 diabetes. *Clin Diabetol* **11**, 224–231.
48. Nikbaf-Shandiz M, Tutunchi H, Khoshbaten M, *et al.* (2022) Propolis supplementation in obese patients with non-alcoholic fatty liver disease: effects on glucose homeostasis, lipid profile, liver function, anthropometric indices and meta-inflammation. *Food Funct* **13**, 11568–11578.
49. Soleimani D, Rezaie M, Rajabzadeh F, *et al.* (2021) Protective effects of propolis on hepatic steatosis and fibrosis among patients with nonalcoholic fatty liver disease (NAFLD) evaluated by real-time two-dimensional shear wave elastography: a randomized clinical trial. *Phytother Res* **35**, 1669–1679.
50. Samadi N, Mozaffari-Khosravi H, Rahmanian M, *et al.* (2017) Effects of bee propolis supplementation on glycemic control, lipid profile and insulin resistance indices in patients with type 2 diabetes: a randomized, double-blind clinical trial. *J Integr Med* **15**, 124–134.
51. Zakerkish M, Jenabi M, Zaeemzadeh N, *et al.* (2019) The effect of Iranian propolis on glucose metabolism, lipid profile, insulin resistance, renal function and inflammatory biomarkers in patients with type 2 diabetes mellitus: a randomized double-blind clinical trial. *Sci Rep* **9**, 7289.
52. El-Sharkawy HM, Anees MM & Van Dyke TE (2016) Propolis improves periodontal status and glycemic control in patients with type 2 diabetes mellitus and chronic periodontitis: a randomized clinical trial. *J Periodontol* **87**, 1418–1426.

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53. Mujica V, Orrego R, Pérez J, *et al.* (2017) The role of propolis in oxidative stress and lipid metabolism: a randomized controlled trial. *Evid Based Complement Altern Med* **2017**, 4272940.
54. Ochoa-Morales PD, González-Ortiz M, Martínez-Abundis E, *et al.* (2022) Anti-hyperglycemic effects of propolis or metformin in type 2 Diabetes Mellitus. *Int J Vitam Nutr Res* **93**, 498–506.
55. Tsamesidis I, Egwu CO, Samara D, *et al.* (2022) Effects of greek honey and propolis on oxidative stress and biochemical parameters in regular blood donors. *J Xenobiotics* **12**, 13–20.
56. Sani L, Cardinault N, Astier J, *et al.* (2023) Poplar propolis improves insulin homeostasis in non-diabetic insulin-resistant volunteers with obesity: a crossover randomized controlled trial. *Antioxidants* **12**, 1481.
57. Afsharpour F, Javadi M, Hashemipour S, *et al.* (2019) Propolis supplementation improves glycemic and antioxidant status in patients with type 2 diabetes: a randomized, double-blind, placebo-controlled study. *Complement Ther Med* **43**, 283–288.
58. Kang LJ, Lee HB, Bae HJ, *et al.* (2010) Antidiabetic effect of propolis: reduction of expression of glucose-6-phosphatase through inhibition of Y279 and Y216 autophosphorylation of GSK-3α/β in HepG2 cells. *Phytother Res* **24**, 1554–1561.
59. Ueda M, Hayashibara K & Ashida H (2013) Propolis extract promotes translocation of glucose transporter 4 and glucose uptake through both PI3K-and AMPK-dependent pathways in skeletal muscle. *Biofactors* **39**, 457–466.
60. Pahlavani N, Malekahmadi M, Firouzi S, *et al.* (2020) Molecular and cellular mechanisms of the effects of Propolis in inflammation, oxidative stress and glycemic control in chronic diseases. *Nutr Metab* **17**, 1–12.
61. Bok S-H, Lee S-H, Park Y-B, *et al.* (1999) Plasma and hepatic cholesterol and hepatic activities of 3-hydroxy-3-methyl-glutaryl-CoA reductase and acyl CoA: cholesterol transferase are lower in rats fed citrus peel extract or a mixture of citrus bioflavonoids. *J Nutr* **129**, 1182–1185.
62. Kurowska EM & Manthey JA (2004) Hypolipidemic effects and absorption of citrus polymethoxylated flavones in hamsters with diet-induced hypercholesterolemia. *J Agric Food Chem* **52**, 2879–2886.
63. Huang X, Wu X, Yan S, *et al.* (2018) Lipid-lowering effect of propolis in mice with Triton-WR1339-induced hyperlipidemia and its mechanism for regulating lipid metabolism. *J South Med Univ* **38**, 1020–1024.
64. Hulver MW, Berggren JR, Carper MJ, *et al.* (2005) Elevated stearoyl-CoA desaturase-1 expression in skeletal muscle contributes to abnormal fatty acid partitioning in obese humans. *Cell Metab* **2**, 251–261.
65. Ye M, Xu M, Ji C, *et al.* (2019) Alterations in the transcriptional profile of the liver tissue and the therapeutic effects of Propolis extracts in alcohol-induced steatosis in rats. *Anais da Academia Bras Ciências* **91**, e20180646.
66. Listenberger LL, Han X, Lewis SE, *et al.* (2003) Triglyceride accumulation protects against fatty acid-induced lipotoxicity. *Proceedings Natl Academy Sci* **100**, 3077–3082.
67. Khalaf DA & Thanoon IA (2018) Effects of bee propolis on blood pressure record and certain biochemical parameter in healthy volunteers. *Ann Coll Med Mosul* **40**, 20–26.
68. Fang Y, Sang H, Yuan N, *et al.* (2013) Ethanolic extract of propolis inhibits atherosclerosis in ApoE-knockout mice. *Lipids Health Dis* **12**, 1–6.
69. Gogebakan A, Talas ZS, Ozdemir I, *et al.* (2012) Role of propolis on tyrosine hydroxylase activity and blood pressure in nitric oxide synthase-inhibited hypertensive rats. *Clin Exp Hypertens* **34**, 424–428.
70. Nattagh-Eshtivani E, Pahlavani N, Ranjbar G, *et al.* (2022) Does propolis have any effect on rheumatoid arthritis? A review study. *Food Sci Nutr* **10**, 1003–1020.
71. Fokt H, Pereira A, Ferreira A, *et al.* (2010) How do bees prevent hive infections? The antimicrobial properties of propolis. *Curr Research, Technol Educ Top Appl Microbiol Microb Biotechnology* **1**, 481–493.
72. Cook CE (2008) Clinimetrics corner: the minimal clinically important change score (MCID): a necessary pretense. *J Man Manip Ther* **16**, E82–83.
73. Bahari H, Ashtary-Larky D, Goudarzi K, *et al.* (2024) The effects of pomegranate consumption on glycemic indices in adults: a systematic review and meta-analysis. *Diabetes Metab Syndr* **18**, 102940.
74. O'Brien MJ, Stephen JJ, Norton KL, *et al.* (2021) Integrating diabetes technologies with team-based primary care for type 2 diabetes: a pilot trial. *Prim Care Diabetes* **15**, 1104–1106.
75. Dankers M, Nelissen-Vrancken M, Hart BH, *et al.* (2021) Alignment between outcomes and minimal clinically important differences in the Dutch type 2 diabetes mellitus guideline and healthcare professionals' preferences. *Pharmacol Res Perspect* **9**, e00750.
76. Bradley R, Kozura E, Buckle H, *et al.* (2009) Description of clinical risk factor changes during naturopathic care for type 2 diabetes. *J Altern Complement Med* **15**, 633–638.

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