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The Effects of Propolis Consumption on Body Composition and Blood Pressure: A Systematic Review and Dose-Response Meta-Analysis ☆

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ABSTRACT

Introduction and Aim: Research on the effects of propolis consumption on body composition, and blood pressure (BP) has produced inconsistent results. This systematic review and dose-response meta-analysis was carried out to compile the data from the randomized controlled trials (RCTs) on how propolis supplementation affects body composition, and BP level in adults.

Materials and Methods: A systematic literature search was conducted using electronic databases, including PubMed, Embase, Scopus, Web of Science, and Cochrane library, up to January 2024. The RCTs, evaluating the effects of propolis consumption on weight, body mass index (BMI), waist circumference (WC), hip circumference (HC), waist-hip ratio (WHR), fat mass (FM), systolic BP (SBP), and diastolic BP (DBP), were included in the study. We used the random-effects model to establish the pooled effect size.

Results: A total of 22 RCTs involving 1082 participants were included in the study. Propolis supplementation demonstrated significant reductions in weight (weighted mean difference [WMD]: −0.37 kg; 95% confidence interval [CI]: −0.63 to −0.12), and BMI (WMD: −0.11 kg/m^2; 95% CI: −0.13 to −0.09). However, there were no significant effects on WC, WHR, FM, HC, SBP, and DBP levels. The dose-response analysis revealed a significant nonlinear relationship between propolis dosage and WC ($P = 0.020$). Moreover, the BMI ($P = 0.047$) and WC ($P = 0.004$) reduction trend continues until 8 weeks of intervention and then this impact plateaued.

Conclusions: Supplementation with propolis seems to be effective in reducing weight and BMI. However, it should be noted that the anti-obesity properties of propolis supplementation were small and may not reach clinical importance. Therefore, future well-designed studies with a large sample size are needed to investigate the effect of propolis on body composition and BP in adults.

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Introduction

Obesity is a significant public health concern that can be linked to an imbalance between energy intake and expenditure.[1] This condition is associated with a range of cardiometabolic diseases, including type 2 diabetes mellitus (T2DM), nonalcoholic fatty liver disease (NAFLD), hypertension (HTN), insulin resistance (IR), and cardiovascular disorders.[1] Despite being preventable, obesity has become a major public health issue, with the number of adults affected, increasing from 100 million in 1975 to 671 million in 2016.[2] Globally, it is estimated that approximately 30% of adults are affected by obesity, and this percentage is expected to reach to 33% by 2030.[3,4] Obesity can be attributed to several factors, such as genetic predisposition, consuming more energy than required, low physical activity, and sedentary behavior.[5] Moreover, not only general obesity but also central obesity and normal-weight obesity can have significant health risks, according to recent evidence.[6] Furthermore, clinical and animal studies have demonstrated a significant association between obesity and HTN.[7] Research has shown that obese subjects have a 3.5-fold increased risk of developing HTN, and 60% of HTN cases are attributed to an increase in adipose stores.[8]

Over a long period of time, calorie-restricted diets and exercise, which are commonly used to manage body weight (BW), have been shown to be relatively ineffective.[9,10] In addition, the long-term use of anti-obesity drugs is not recommended due to their side effects.[11] Complementary therapies, like anti-obesity supplements, can be a useful tool for promoting compliance and adherence to calorie-restricted diets and healthy dietary recommendations among obese subjects.[12] Propolis is a substance made by bees from plant material, bee's wax, and enzymes and saliva secreted by the bee's salivary glands.[13] Propolis' beneficial effects are mainly due to its phenolic components, including flavonoids (such as flavanones, flavones, flavonols, and dihydro flavanols), amino acids, steroids, aromatic aldehydes, and terpenoids.[14] Propolis is currently used a popular dietary supplement to promote the body's health. Compelling evidence indicates that propolis possesses anti-inflammatory, anti-diabetic, antimicrobial, antioxidant, cardioprotective immunomodulatory activities, anticancer agents.[15–18] Moreover, the use of both propolis and its constituents has been shown to be effective in treating and preventing cardiovascular risk factors, including obesity, HTN, atherosclerosis, dyslipidemia, and diabetes.[19] Animal and human studies have demonstrated that propolis is effective in enhancing immune system function, regulating glucose and lipid metabolisms, and improving blood pressure (BP).[20] The antihypertensive effects of propolis are thought to be achieved through mechanisms, such as the stimulation of endothelial-dependent vasodilation, vascular anti-inflammatory activity, and the suppression of catecholamine synthesis.[21]

Inconsistent results have been observed in various studies regarding the impact of propolis supplementation on obesity and BP. Despite this, the reasons or mechanisms behind improvements in these conditions have yet to be thoroughly explored. Clinical trials have shown that propolis supplementation has a positive effect on anthropometric indices, but other studies have not reported significant changes in anthropometric variables.[15,22–26] Prior meta-analyses evaluating the anti-obesity properties of propolis were limited to only four and five studies,[27,28] which revealed no significant effects on BW and body mass index (BMI). Additionally, critical anthropometric measures such as waist circumference (WC), hip circumference (HC), fat mass (FM), and waist-to-hip ratio (WHR) have yet to be thoroughly examined. Moreover, propolis supplementation was observed to have a beneficial effect on systolic BP (SBP) and diastolic BP (DBP) in some randomized controlled trials (RCTs),[20,29] while other RCTs did not report any significant changes in BP variables.[30–32] Furthermore, to the best of our knowledge, no meta-analysis has yet synthesized the findings from RCTs examining the effects of propolis supplementation on BP.

While previous systematic reviews and meta-analyses have examined the effects of propolis on anthropometric indices, several gaps remain in the current literature.[27,28] The meta-analyses mentioned earlier included a relatively small number of studies, which restricted their ability to assess effects across various population subgroups and dosing regimens. Furthermore, comprehensive dose-response analyses to explore potential nonlinear relationships between propolis supplementation and changes in body composition or BP outcomes have not been conducted. Given the inconsistent findings reported across individual trials, a more detailed investigation of potential sources of heterogeneity through subgroup and sensitivity analyses is warranted. To provide an inclusive conclusion, the current systematic review and meta-analysis aimed to investigate whether propolis consumption can favorably alter body composition (BW, BMI, WC, HC, FM, and WHR) and BP (SBP and DBP) in adults.

Materials and Methods

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) protocol was employed to report the systematic reviews and meta-analyses in this study (Supplementary Table 1).[33] The ethics committee of Isfahan University of Medical Sciences approved the study protocol (IR.MUI.PHANUT.REC.1403.030). In addition, the study protocol was documented in PROSPERO with the unique identifier: CRD42024507359.

Search strategy

The PICOS criteria, including the population (adult participants), intervention (supplementation of propolis), comparison (control or placebo), and outcomes (BW, BMI, WC, FM, HC, WHR, SBP, and DBP), were employed to design the study protocol. The literature search and study selection were independently conducted by two investigators (MV and NN). In the event of any inconsistencies, a third investigator (MAF) was consulted to finalize the study inclusion. The data search for all relevant published articles was performed by exploring PubMed, Embase, Scopus, Web of Science, and Cochrane library from their inception until January 2024. The following MESH and non-MESH terms were employed to conduct the search: propolis AND intervention study OR intervention* OR controlled trial OR random OR placebo OR clinical trial OR trial OR randomized controlled trial OR randomized clinical trial OR RCT OR clinical trials OR trials OR cross-over studies OR parallel. The search process was not restricted by publication date or the language in which the original text was printed. To ensure that no eligible publications were missed, reference lists of the selected articles were manually searched. If the manuscript did not contain the required data for meta-analysis, the corresponding author was contacted to obtain the data.

Eligibility criteria

Studies that met the following requirements were selected for further analysis: (1) parallel or crossover RCTs, (2) those with adult participants (≥18 years old), (3) RCTs investigating the impact of propolis supplementation on body composition indicators (BW, BMI, WC, HC, FM, and WHR) and BP (SBP and DBP) in both intervention and placebo groups, (4) RCTs that presented the means and standard deviations (SDs) for each variable or any other effect size that made it possible to calculate means and SDs. If a dataset was published in more than one article, the one with more comprehensive results or a larger number of participants was selected.

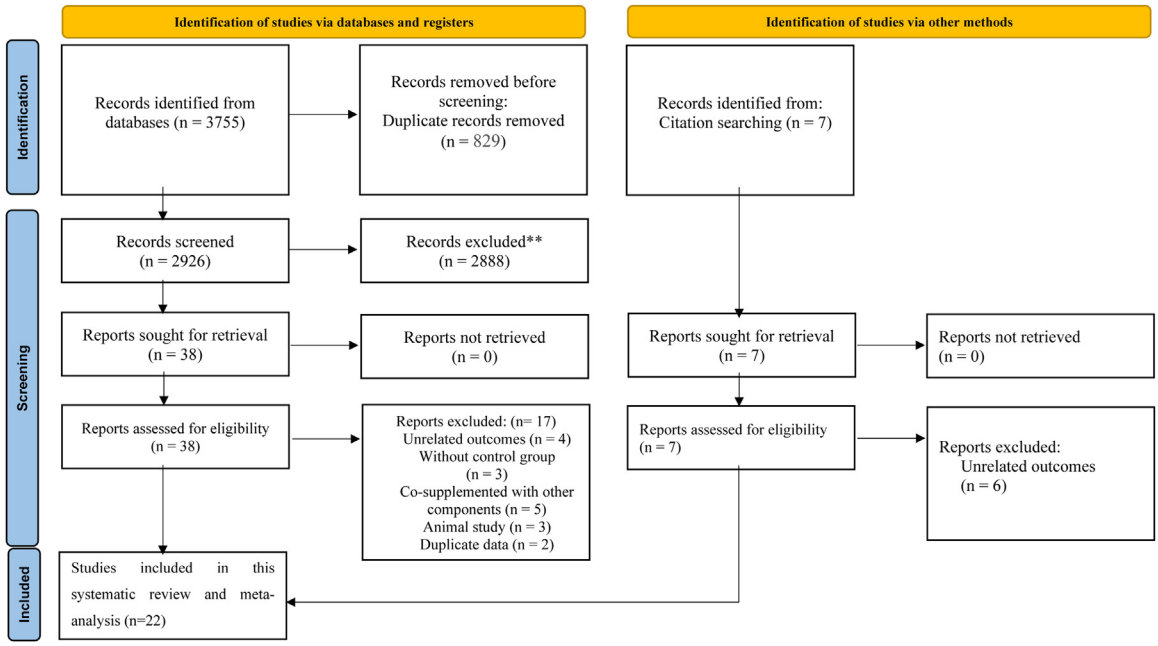


Figure 1. Flow diagram of study screening and selection process.

Exclusion criteria

Studies that had only one of the following criteria were removed: (1) animal studies, reviews, and in vitro studies, letters, conference abstracts, and observational studies, (2) RCTs without control or placebo, (3) trials conducted on pregnant women, children, or adolescents, (4) studies that prescribed propolis in combination with other ingredients, as it was impractical to assess the effect of propolis alone.

Data extraction

Data extraction was performed by two independent researchers, MV and NN. An additional reviewer (MAF) was consulted when there was a divergence of opinion regarding relevance. The following information was derived from the reports that were included: first author's name, publication year, location of trial, study design, sample size, mean age, gender, dose and duration of intervention, participants' health status, and mean changes and their SDs of values for the intervention and control groups.

Quality assessment

The Cochrane Collaboration's modified risk-of-bias tool was applied to appraise the quality of the trials included.[34] The quality of all eligible studies was assessed based on the following criteria: random sequence generation, blinding of outcome assessments, blinding of participants and personnel, allocation concealment, selective reporting, incomplete outcome data, and other sources of bias. Using the terms "low," "high," or "unclear," two independent investigators (MV and MAF) rated each of the seven domains. The investigators resolved any disagreement through discussion, and if any disagreement remained, a third assessor (GA) was consulted to make a final decision.

Statistical analysis

Statistical analyses were performed using STATA version 14.0 (STATA Corp, College Station, TX, USA). The statistical significance level was defined as $P < 0.05$. Using a random-effects model, the weighted mean difference (WMD) with the 95% confidence intervals (CIs) was determined.[35] The SD changes were calculated by using the following formula: SD change = square root ([SD baseline]^2 + [SD final]^2 − [2R × SD baseline × SD final]), where $R = (SD1^2 + SD2^2 - SDchange^2)/(2 \times SD1 \times SD2)$. Both Cochran's Q test and the inconsistency index (I^2) were employed to assess the heterogeneity between studies.[34] Heterogeneity was considered high when $I^2 \geq 50\%$ and the P value of the Q statistic was less than 0.1.[36] To determine potential sources of heterogeneity, a subgroup analysis was performed using preestablished variables. The analysis took into account various factors, including sample size (with groups of ≤50 compared to 51–94 participants), gender (male, female, and combined), age (20–40, 41–55, and 55–75 years), dosage (250–500, 600–900, and 1000–1500 mg/day), treatment duration (4–8, 10–12, and 24–48 weeks), and health status (diabetes, NAFLD, obesity, metabolic syndrome (Mets), and healthy subjects). We executed sensitivity analyses by excluding each study individually and recalculating the pooled estimates.[37] The nonlinear dose-response and linear meta-regression effects of propolis dosage and intervention duration on each outcome were evaluated using fractional polynomial modeling. The presence of publication bias was evaluated by visually examining funnel plots and statistically analyzing Egger's regression and Begg's tests.[38] The "trim and fill" method was used if publication bias was identified.

Results

Study selection

The process of selecting studies is shown in Figure 1. After searching the electronic datasets, 3762 studies were discovered, of which 829 were removed due to duplication and 2898 were excluded for irrelevancy based on the inclusion criteria. After applying the study inclusion criteria, 22 articles that satisfied the necessary data reporting requirements were included in the meta-analysis. The studies that were analyzed included 17 that investigated the impact of propolis consumption on BW,[13,15,20,22–26,29,32,39–45] 14 that provided data on BMI,[13,15,20,22,26,29,32,39,42–47] nine that focused on WC,[13,20,22,29,32,43–45,47] four that examined WHR,[22,23,29,44] three

Table 1
General characteristics of included studies.

First author	Year/country	Study design	Subject	Participants		Mean age		Baseline BMI		Duration (week)	Dose (mg/day)	Type of administration		**Outcome**
				Intervention	Control	Intervention	Control	Intervention	Control			Intervention	Placebo	
Mujica et al.	2017/Chile	Parallel, R, PC, DB	Individuals Healthy	35	32	48	44.5	27.9	28.2	12	30 drops	Propolis solution	Placebo (peppermint + fernet+ synthetic)	Weight, BMI, WC, SBP, DBP
Samadi et al.	2017/Iran	Parallel, R, PC, DB	T2DM	30	27	51.3	56.07	28.18	27.53	12	900	Propolis pill	Placebo	Weight, BMI, WC
Afsharpour et al.	2019/Iran	Parallel, R, PC, DB	T2DM	30	30	51.81	49.05	26.78	26.74	8	1500	Propolis capsule	Placebo (wheat flour capsule)	Weight, BMI
Silveira et al.	2019/Brazil	Parallel, R, PC, DB	Proteinuria + CKD	18	14	61.39	61.5	30.58	27.29	48	500	Brazilian green propolis tablet	Placebo	SBP, DBP
Zakerkish et al.	2019/Iran	Parallel, R, PC, DB	T2DM	50	44	55.4	54.86	30.04	29.02	12	1000	Propolis Iranian capsule	Placebo	Weight, BMI
Gholaminejad et al.	2019/Iran	Parallel, R, PC, DB	Asthenozoospermic men	29	28	31.61	30	27.02	26.52	10	1500	Propolis capsule	Placebo (wheat flour capsule)	Weight, BMI
Soleimani et al.	2021/Iran	Parallel, R, PC, DB	NAFLD	27	27	42.56	41.85	29.55	28.41	12	500	Propolis tablet+ microcrystalline cellulose	Placebo	Weight, FM
Soleimani et al.	2021/Iran	Parallel, R, PC, TB	Military cadets	24	25	24.21	24.2	23.82	23.22	4	900	Propolis tablet	Placebo (microcrystalline cellulose)	Weight, FM
Triyono et al.	2021/ Indonesia	Parallel, PC, DB	HIV+ ARV (anti-retroviral treatment)	19	24	36.8	37.1	NR	NR	24	600	Propolis capsule	Placebo	Weight
Nikbaf-Shandiz et al.	2022/Iran	Parallel, R, PC, DB	NAFLD	23	21	38.52	40.14	33.36	33	8	1500	Propolis capsule+ calorie restricted diet	Placebo (corn starch capsule) + calorie restricted diet	Weight, BMI, WC, WHR, HC
Miryan et al.	2022/Iran	Parallel, R, PC, DB	IBS	26	25	38.92	44.92	25.61	27.75	6	900	Propolis tablet	Placebo (microcrystalline cellulose)	Weight, BMI, WC
Davoodi et al.	2022/Iran	Parallel, R, PC, DB	Breast cancer + chemotherapy	26	24	49.3	44.36	27.9	27.63	12	500	Propolis capsule	Placebo (starch)	Weight, BMI
Rashvand et al.	2022/Iran	Parallel, R, PC	Endurance athletes	10	12	22	22	NR	NR	4	1000	Propolis capsule	Placebo (cellulose)	Weight
Abbasi et al.	2023/Iran	Parallel, R, PC, TB	PCOS	28	29	18–45	18–45	28.35	26.16	12	500	Propolis tablet	Placebo (microcrystalline cellulose)	Weight, BMI, WC, WHR, HC, SBP, DBP
Tutunchi et al.	2023/Iran	Parallel, R, PC, DB	Obesity+ NAFLD	24	24	37.5	36.33	34.1	33.75	8	1500	Propolis capsule+ maltodexterine+ dietary recommendation	Control (dietary recommendation)	Weight, BMI, WC, WHR, HC

(*continued on next page*)

Table 1 (*continued*)

First author	Year/country	Study design	Subject	Participants		Mean age		Baseline BMI		Duration (week)	Dose (mg/day)	Type of administration		**Outcome**
				Intervention	Control	Intervention	Control	Intervention	Control			Intervention	Placebo	
Moayedi et al. (a)	2023/Iran	Parallel, R, PC, SB	Dyslipidemia + T2DM	15	15	52.53	53.67	NR	NR	8	500	Propolis capsule	Placebo	Weight, WHR
Moayedi et al. (b)	2023/Iran	Parallel, R, PC, SB	Dyslipidemia + T2DM	15	15	54.07	51.67	NR	NR	8	500	capsule+ Propolis exercise	Exercise	Weight, WHR
Sani et al.	2023/France	Crossover, R, PC	Insulin resistant + obesity	9	9	49	49	31.5	31.7	12	6–9 capsules (250 mg) according to patient's weight	Propolis	Placebo	BMI, WC
Kanazashi et al.	2023/Japan	Parallel, R, PC, DB	Postmenopausal Healthy women	25	28	75	75	24	23	12	1362	Propolis capsule	Placebo (wheat germ oil capsule)	BMI, FM
Sajjadi et al.	2023/Iran	Parallel, R, PC, DB	Syndrome Metabolic	33	29	54.27	53.86	32.56	34.03	12	500	Propolis tablet+ microcrystalline cellulose	Placebo (microcrystalline cellulose)	Weight, BMI, WC, SBP, DBP
Maddahi et al.	2023/Iran	Parallel, R, PC, DB	Rheumatoid arthritis	23	22	46.56	47.90	27.89	26.84	12	1000	Propolis capsule	Placebo (corn starch capsules)	SBP, DBP
Anvarifard et al.	2023/Iran	Parallel, R, PC, DB	CKD	17	18	58.06	60.50	29.66	28.53	12	250	propolis capsule	Placebo (wheat starch)	SBP, DBP
Ochoa-Morales et al.	2022/Mexico	Parallel, R, PC, DB	T2DM	12	12	50	46	29	30.2	12	600	Propolis capsule	Placebo	Weight, BMI, WC

ARV = anti-retroviral; BMI = body mass index; CKD = chronic kidney disease; DB = double-blind; DBP = diastolic blood pressure; FM = fat mass; HIV = human immunodeficiency virus; IBS = irritable bowel syndrome; NAFLD = nonalcoholic fatty liver disease; NR = not reported; PC = placebo-controlled; R = randomized; SB = single-blind; SBP = systolic blood pressure; T2DM = type 2 diabetes mellitus; TB = triple-blind; WC = waist circumference.

Table 2
Quality assessment of clinical trials (according to the Cochrane guideline) investigating the associations between propolis consumption on body composition and blood pressure.

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias	Overall risk of bias
Mujica et al.	L	U	L	U	L	L	L	Fair
Samadi et al.	L	U	L	L	L	L	L	Good
Afsharpour et al.	L	U	L	L	L	L	L	Good
Silveira et al.	L	L	L	U	L	L	L	Good
Zakerkish et al.	L	L	U	L	L	L	L	Good
Gholaminejad et al.	L	L	L	U	L	L	L	Good
Soleimani et al.	L	L	L	L	L	L	L	Good
Soleimani et al.	L	L	L	L	L	L	L	Good
Triyono et al.	U	U	L	U	L	H	L	Poor
Nikbaf-Shandiz et al.	L	L	L	U	L	L	L	Good
Miryan et al.	L	L	L	U	L	H	L	Poor
Davoodi et al.	L	L	L	L	L	L	L	Poor
Rashvand et al.	U	U	U	U	L	L	L	Poor
Abbasi et al.	L	U	L	L	L	L	L	Good
Tutunchi et al.	L	L	L	L	U	U	L	Fair
Moayedi et al.	L	L	L	U	L	L	L	Good
Sani et al.	L	U	L	L	L	L	L	Good
Kanazashi et al.	L	L	L	L	L	U	L	Good
Sajjadi et al.	L	L	L	L	L	L	L	Good
Maddahi et al.	L	L	L	L	L	L	L	Good
Anvarifard et al.	L	L	L	L	L	L	L	Good
Ochoa-Morales et al.	L	L	L	U	L	L	L	Good

H = high risk of bias; L = low risk of bias; U = unclear risk of bias.

that investigated FM,[25,40,46] three reported data on HC,[22,29,44] six that analyzed SBP and DBP.[14,20,29–32]

Study characteristics

Table 1 provides a description of the characteristics of RCTs included in the current meta-analysis. Trials were carried out in Chile,[32] Iran,[13–15,20,22–26,29,30,39,40,42–44,48] Brazil,[31] Indonesia,[41] Japan,[46] France,[47] and Mexico[45] between 2017 and 2023. The sample size of the RCTs was 1082, with 548 participants in the intervention group and 534 in the control group, all of whom were aged between 22 and 61.39 years. Propolis was administered at dosages ranging from 250 to 1500 mg/day in different RCTs, with intervention durations varying between 4 and 48 weeks. All studies were conducted on both male and female participants, with three studies exclusively focusing on males[24,26,40] and four on females.[14,23,29,46] Selected studies enrolled participants with T2DM,[13,15,45,48] dyslipidemia,[23] rheumatoid arthritis,[14] metabolic syndrome,[20] polycystic ovary syndrome,[29] NAFLD,[25,44] obesity,[22] IR,[47] irritable bowel syndrome (IBS),[43] chronic kidney disease (CKD),[30,31] human immunodeficiency viruses,[41] breast cancer,[42] asthenozoospermia,[26] postmenopausal healthy women,[46] endurance athletes,[46] military cadets,[40] and healthy individuals.[32] Table 2 shows the details of the risk of bias assessment. Approximately 73% of studies had an overall low risk of bias, nearly 9% had an overall fair risk of bias, and almost 18% had an overall high risk of bias.

Effect of propolis supplementation on BW

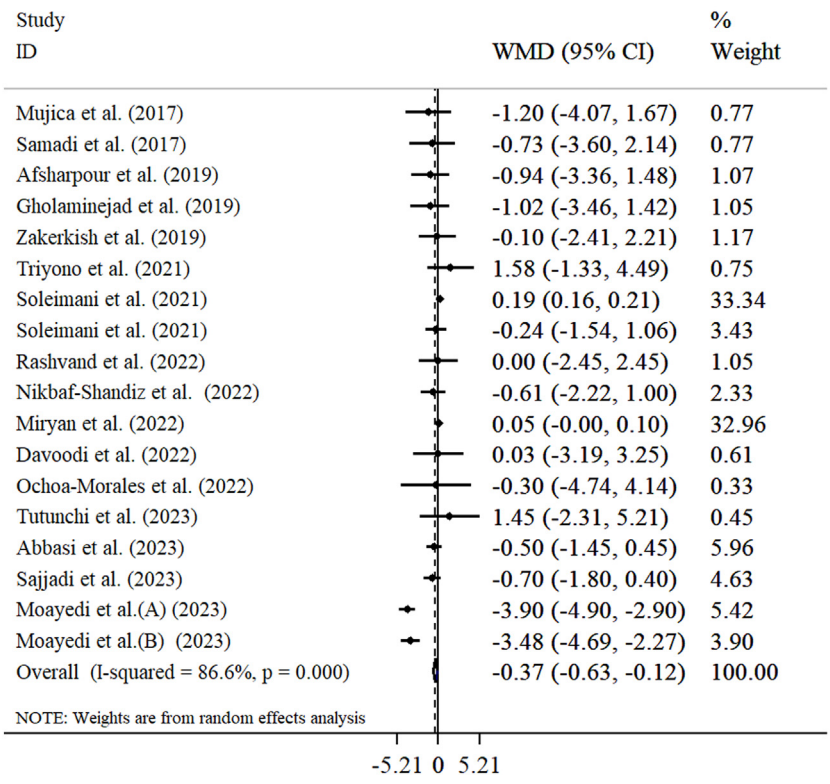
The effect of propolis supplementation on BW was investigated in 17 eligible articles (456 cases and 443 controls), which comprised 18 treatment arms.[13,15,20,22–26,29,32,39–45] According to the meta-analysis of the data, propolis consumption resulted in a significant reduction in BW (WMD: −0.37 kg; 95% CI: −0.63 to −0.12; $P = 0.004$; $I^2 = 86.6\%$; $P < 0.001$) (Figure 2A). Subgroup analysis revealed that the sources of between-study heterogeneity were sample size, gender, dose of propolis, health status, and duration of intervention. A subgroup analysis indicated that propolis consumption significantly reduced BW in participants aged 41–55 years, those diagnosed with diabetes, females, and individuals taking a propolis dosage of 250–500 mg/day. Conversely, an increase in BW was noted among subgroups of younger participants aged 20–40 years, those undergoing a 4–8 week intervention period, trials administering 600–900 mg/day of propolis, males, and healthy subjects after propolis consumption (Table 3 and Supplementary Table 2).

Effect of propolis supplementation on BMI

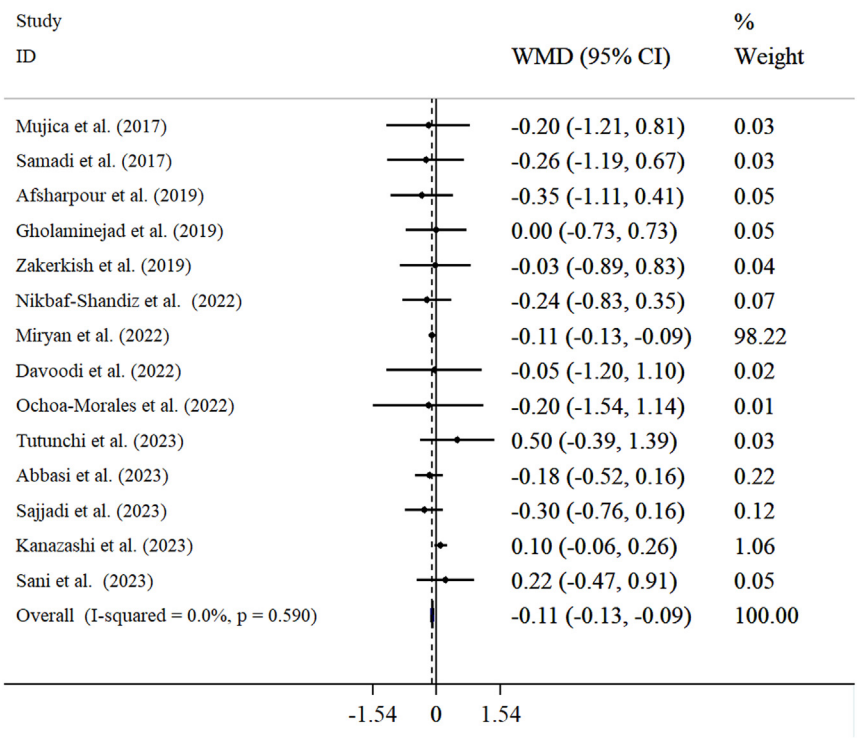
The effect of propolis supplementation on BMI was assessed by 14 trials (380 cases and 362 controls).[13,15,20,22,26,29,32,39,42–47] Pooled data showed that propolis intake had a significant effect on reducing BMI compared to the control group (WMD: −0.11 kg/m^2; 95% CI: −0.13 to −0.09; $P < 0.001$; $I^2 = 0.0\%$; $P = 0.590$) (Figure 2B). Subgroup analysis revealed that propolis consumption significantly impacted BMI in studies with intervention duration 4–8 weeks, both genders, trials with 51–94 individuals, studies with participants 20–40 years, and trials that administered 600–900 mg/day propolis (Table 3 and Supplementary Table 2).

Effect of propolis supplementation on WC

The effect of propolis supplementation on WC was studied in nine trials (220 cases and 208 controls).[13,20,22,29,32,43–45,47] According to a quantitative meta-analysis, propolis supplementation did not result in a significant change in WC when compared to the control group (WMD: −0.28 cm; 95% CI: −1.66 to 1.10; $P = 0.586$; $I^2 = 79.7\%$; $P < 0.001$) (Figure 2C). Subgroup analysis revealed that the sources of between-study heterogeneity were age of participants, sample size, dose of propolis, health status, and duration of

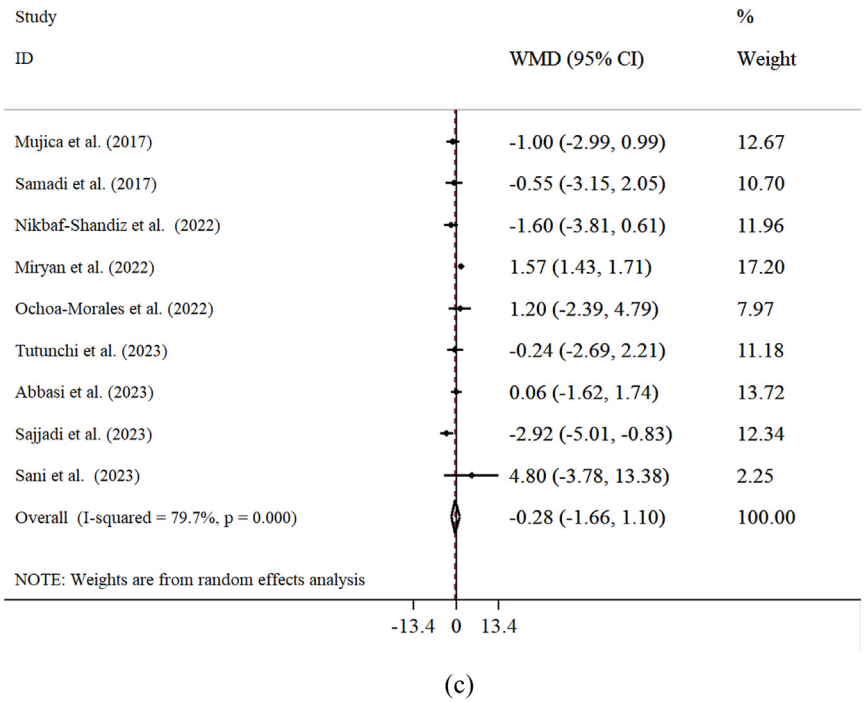


(a)



(b)

Figure 2. Forest plot illustrating weighted mean difference and 95% confidence intervals for the impact of propolis on BW (A), BMI (B), WC (C), WHR (D), FM (E), and HC (F).



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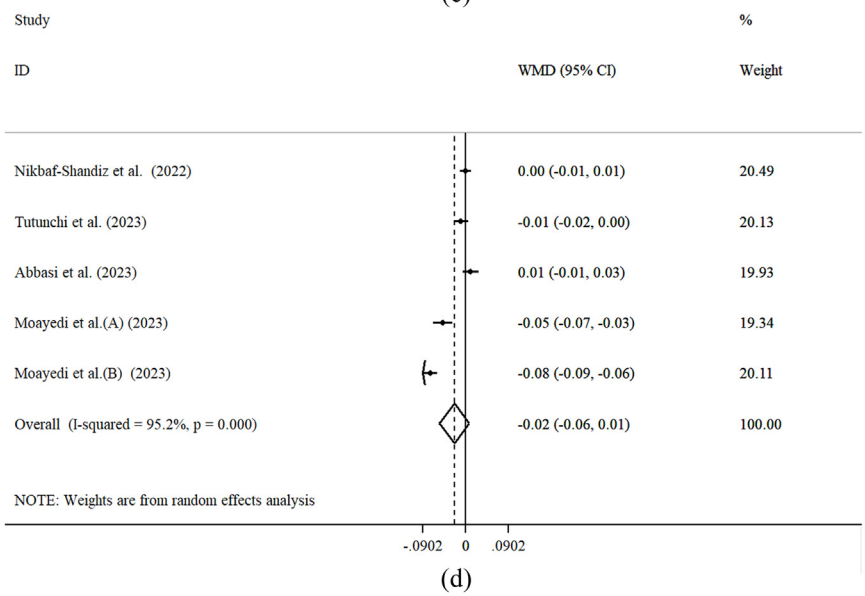
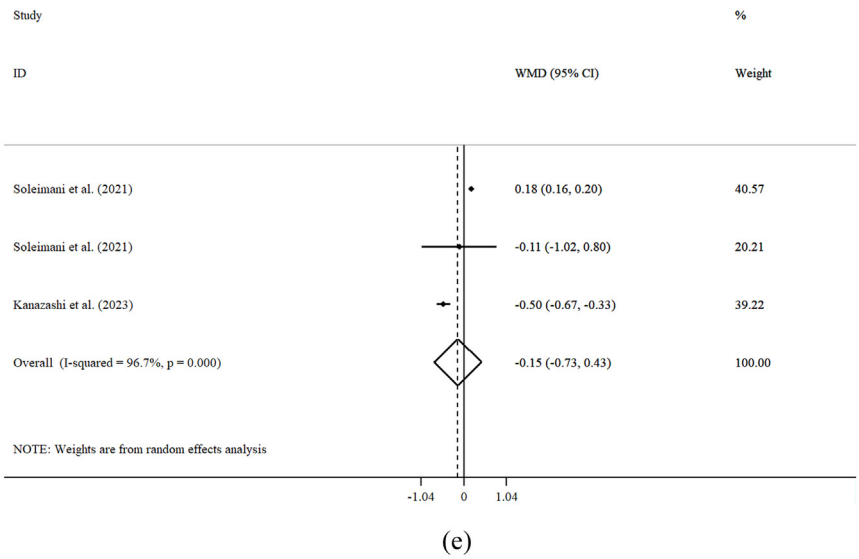
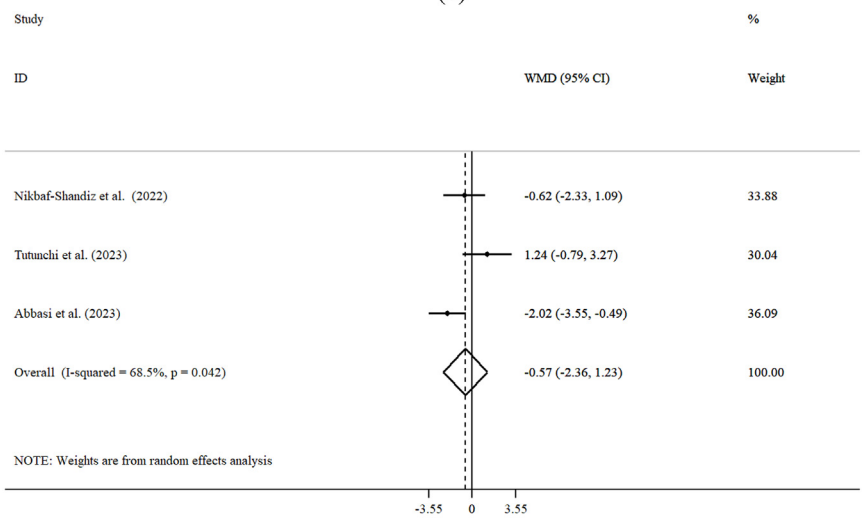


(d)

Figure 2. Continued



(e)



(f)

Figure 2. Continued

intervention. Propolis supplementation led to a significant decrease in WC in studies involving obese and Mets participants. Furthermore, Propolis intake led to a significant increase in WC in subgroups of patients aged 20–40 years, trials with 600–900 mg/day of propolis, both genders, trials with 51–94 participants, and studies with 6–8 weeks of intervention (Table 3 and Supplementary Table 2).

Effect of propolis supplementation on WHR

Four trials with five effect sizes (105 cases and 104 controls) investigated the impact of propolis consumption on WHR.[22,23,29,44] The random-effects model's combined results indicated that propolis consumption had no significant effect on WHR (WMD: −0.02; 95% CI: −0.06 to 0.01; $P = 0.126$; $I^2 = 95.2\%$; $P < 0.001$) (Figure 2D). Subgroup analysis revealed that the sources of between-study heterogeneity were age of participants, gender, dose of propolis, and health status. Propolis intake led to a significant reduction in WHR in subgroups of trials with sample size ≤50 participants, females, individuals with 41–55 years, studies that prescribed 500 mg/day propolis, diabetic patients, and trials with 8 weeks of intervention duration (Table 3 and Supplementary Table 2).

Effect of propolis supplementation on FM

The impact of propolis supplementation on FM was evaluated in three trials (76 cases and 80 controls).[25,40,46] The random-effects model's pooled estimate indicated that propolis had no significant impact on FM when compared to the control group (WMD: −0.15 kg; 95% CI: −0.73 to 0.43; $P = 0.619$; $I^2 = 96.7\%$; $P < 0.001$) (Figure 2E). The small number of studies available made it impractical to perform a subgroup analysis.

Effect of propolis supplementation on HC

Three studies (75 cases and 74 controls) were conducted to investigate the effect of propolis consumption on HC.[22,29,44] According to the pooled effect sizes from the random-effects model, propolis supplementation did not result in a significant change in HC compared to the control group (WMD: −0.57 cm; 95% CI: −2.36 to 1.23; $P = 0.537$; $I^2 = 68.5\%$; $P = 0.042$) (Figure 2F). It was not possible to carry out a subgroup analysis due to the limited number of studies available.

Table 3
Results of subgroup analyses for the effects of propolis supplementation on body composition and blood pressure according to dose and duration of intervention.

Study group	Effect size, *n*	WMD (95% CI)	*P*-effect	*P*-heterogeneity	I^2 (%)
Weight					
Dose (mg/day)					
250–500	6	−1.74 (−2.22, −1.26)	<0.001	<0.001	88.1
600–900	5	0.16 (0.13, 0.18)	<0.001	<0.001	80.8
1000–1500	6	−0.42 (−1.35, 0.51)	0.377	0.901	0
30 drops	1	−1.20 (−4.07, 1.67)	0.413	-	-
Duration (week)					
4–8	8	0.15 (0.13, 0.18)	<0.001	<0.001	94.1
10–12	9	−0.52 (−1.07, 0.02)	0.063	0.999	0
24–48	1	1.58 (−1.33, 4.49)	0.288	-	-
BMI					
Dose (mg/day)					
250–500	3	−0.21 (−0.48, 0.05)	0.117	0.882	0
600–900	3	−0.11 (−0.12, −0.09)	<0.001	0.944	0
1000–1500	6	0.06 (−0.07, 0.20)	0.349	0.644	0
30 drops	1	−0.20 (−1.21, 0.81)	0.698	-	-
6–9 capsules	1	0.22 (−0.47, 0.91)	0.535	-	-
Duration (week)					
4–8	4	−0.11 (−0.12, −0.09)	<0.001	0.498	0
10–12	9	0.01 (−0.11, 0.14)	0.823	0.821	0
WC					
Dose (mg/day)					
250–500	2	−1.11 (−2.42, 0.20)	0.097	0.030	78.8
600–900	3	1.56 (1.42, 1.70)	<0.001	0.274	22.8
1000–1500	2	−0.99 (−2.63, 0.65)	0.237	0.419	0
30 drops	1	−1.00 (−2.99, 0.99)	0.326	-	-
6–9 capsules	1	4.80 (−3.78, 13.38)	0.273	-	-
Duration (week)					
6–8	3	1.55 (1.41, 1.69)	<0.001	0.007	79.9
12	6	−0.76 (−1.73, 0.20)	0.121	0.165	36.2
WHR					
Dose (mg/day)					
500	3	−0.03 (−0.04, −0.02)	<0.001	<0.001	96.4
1500	2	−0.004 (−0.01, 0.005)	0.417	0.304	5.2
Duration (week)					
8	4	−0.02 (−0.03, −0.01)	<0.001	<0.001	95.5
12	1	0.01 (−0.007, 0.02)	0.235	-	-
SBP					
Dose (mg/day)					
250–500	4	−0.42 (−1.09, 0.25)	0.221	0.231	30.2
1000–1500	1	−0.53 (−11.55, 10.49)	0.925	-	-
30 drops	1	−3.60 (−5.84, −1.35)	0.002	-	-
Duration (week)					
12	5	−0.66 (−1.31, −0.02)	0.043	0.026	63.7
48	1	−2.84 (−10.10, 4.42)	0.443	-	-
DBP					
Dose (mg/day)					
250–500	4	0.03 (−0.59, 0.66)	0.915	0.097	52.5
1000–1500	1	−0.17 (−6.94, 6.60)	0.961	-	-
30 drops	1	−0.30 (−2.46, 1.86)	0.786	-	-
Duration (week)					
12	5	−0.05 (−0.65, 0.55)	0.864	0.902	0
48	1	8.50 (1.28, 15.72)	0.021	-	-

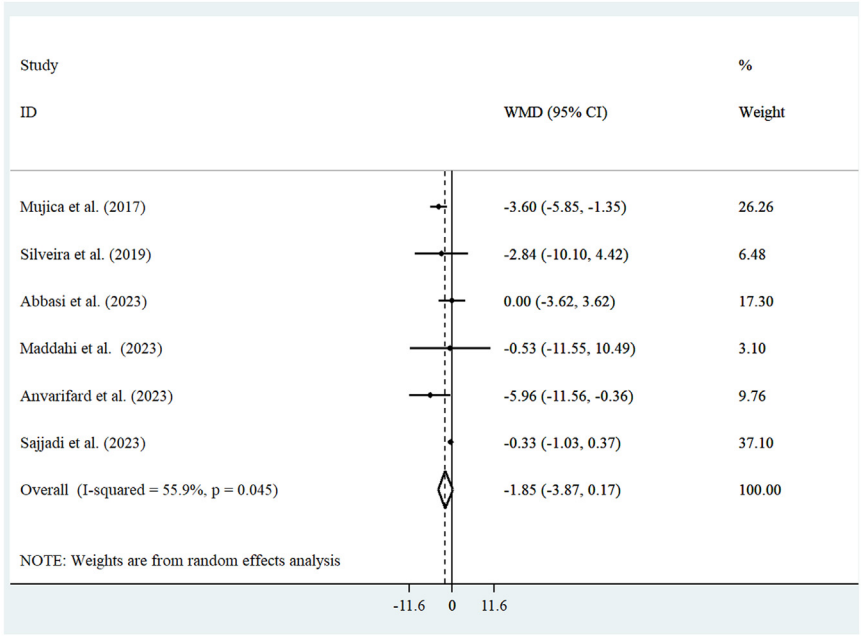
CI = confidence interval; WMD = weighted mean differences.

Effect of propolis supplementation on SBP

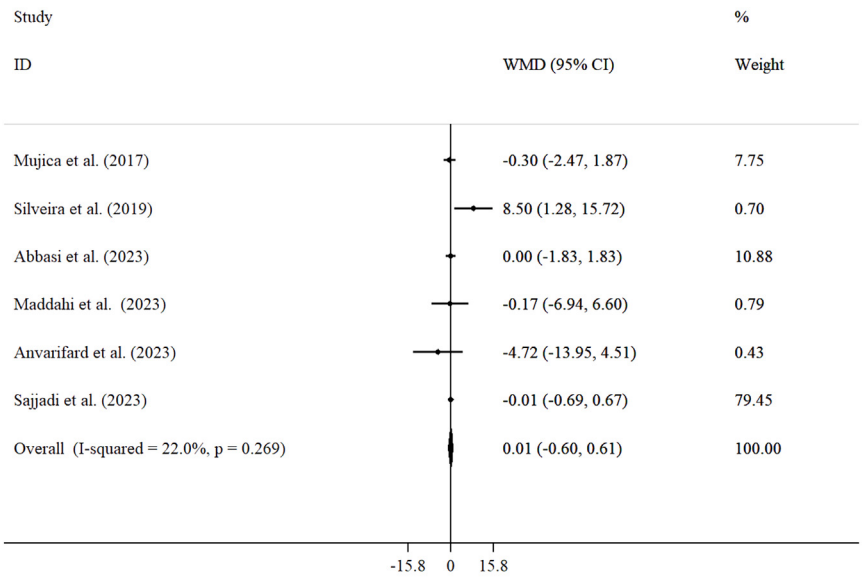
Six trials (154 cases and 144 controls) were conducted to investigate the effect of propolis supplementation on SBP.[14,20,29–32] The combined results from the random-effects model showed that propolis supplementation had no significant impact on SBP when compared to the control group (WMD: −1.85 mmHg; 95% CI: −3.87 to 0.17; $P = 0.073$; $I^2 = 55.9\%$; $P = 0.045$) (Figure 3A). Subgroup analysis revealed that the sources of between-study heterogeneity were age of participants, sample size, gender, dose of propolis, and health status. The results indicated that propolis supplementation could decrease SBP in trials involving 50 or fewer participants, inclusive of both genders and those aged 55–75 years. This effect was observed in studies that lasted for duration of 12 weeks, with a propolis dosage of 30 drops, and included patients with CKD as well as healthy individuals (Table 3 and Supplementary Table 3).

Effect of propolis supplementation on DBP

DBP was studied in six trials (154 cases and 144 controls) to determine the effect of propolis supplementation.[14,20,29–32] The results from the random-effects model indicate that propolis supplementation did not have a significant effect on reducing DBP (WMD: 0.01 mmHg; 95% CI: −0.60 to 0.61; $P = 0.121$; $I^2 = 22.0\%$; $P = 0.269$) (Figure 3B). The subgroup analysis revealed that propolis supplementation did not have a substantial change on DBP in any of the subgroups. However, in an RCT with a 48-week intervention period, propolis supplementation was observed to significantly affect DBP (Table 3 and Supplementary Table 3).



(a)



(b)

Figure 3. Forest plot illustrating weighted mean difference and 95% confidence intervals for the impact of propolis on SBP (A), and DBP (B).

Nonlinear dose-responses

A one-stage nonlinear dose-response analysis was performed to explore the relationship between propolis supplementation and BMI, BW, WC, SBP, and DBP. The intervention dose was found to have a significant nonlinear association with changes in WC ($P=0.020$), but no such relationship was observed for BMI ($P=0.344$), BW ($P=0.097$), SBP ($P=0.547$), and DBP ($P=0.347$). In addition, a significant association was detected between the duration of the intervention and alterations in BMI ($P=0.047$) and WC ($P=0.004$), whereas no significant relationship was identified for BW ($P=0.080$) (Supplementary Figure 1A–H).

Sensitivity analysis

To determine the impact of each individual trial on the pooled effect size, a sensitivity analysis was performed by eliminating each trial in turn. As a result, no individual trial had a significant impact on the overall effect size of WC, WHR, HC, FM, and DBP. The overall results of BW were significantly altered by omitting the studies by Miryan et al.[43] and Moayedi et al.[23] Furthermore, the overall effect of BMI was significantly changed by removing the study conducted by Miryan et al.[43] After removing the study performed by Sajjadi et al.,[20] the overall effect of SBP was also significantly changed (Supplementary Figure 2A–H).

Publication bias

Uponvisual inspection, the funnel plots were found to be asymmetrical. In addition, Begg's and Egger's tests did not indicate any publication bias for BMI (Begg's test; $P = 0.443$, Egger's test; $P = 0.499$), WHR (Begg's test; $P = 0.806$, Egger's test; $P = 0.530$), FM (Begg's test; $P = 1.000$, Egger's test; $P = 0.493$), SBP (Begg's test; $P = 0.707$, Egger's test; $P = 0.300$), and DBP (Begg's test; $P = 1.000$, Egger's test; $P = 0.731$). However, significant publication bias was identified for BW (Begg's test; $P = 0.015$, Egger's test; $P = 0.037$), WC (Begg's test; $P = 0.466$, Egger's test; $P = 0.019$), and HC (Begg's test; $P = 0.296$, Egger's test; $P = 0.042$). The trim and fill sensitivity method was employed, but the corrected effect size of publication bias did not change for BW and HC. However, the effect size of WC changed due to the presence of 10 imputed studies (WMD: −0.42 cm; 95% CI: −1.78 to 0.98) (Supplementary Figure 2A–H).

Discussion

This systematic review and meta-analysis of RCTs was conducted to examine propolis consumption's effects on body composition and BP in adults. Based on a pooled analysis, propolis consumption is associated with a reduction of BW and BMI. In contrast, propolis consumption did not significantly affect WHR, WC, FM, HC, SBP, and DBP compared to the control group. However, SBP, BW, and BMI levels were sensitive to the exclusion of some studies. After excluding the studies of Miryan et al.[43] and Moayedi et al.,[23] significant results in BW disappeared, and significant changes in BMI disappeared after removing Miryan et al.'s study.[43] There may be several reasons for the observed results, such as the different dosages of propolis, the different durations of interventions, and the different health status of the participants. In the Moayedi et al study, women with diabetes dyslipidemia were supplemented with 500 mg of propolis for 8 weeks, and in the Miryan et al study, IBS patients were given 900 mg of propolis per day for 6 weeks. Additionally, these individuals had an average BMI > 25 kg/m^2. Furthermore, the result of SBP was changed to be significant after omitting Sajjadi et al.'s study.[20] In the study, participants with metabolic syndrome received 500 mg of propolis, which was less than other studies' doses. Based on subgroup analysis, it was found that interventions lasting 8 weeks or less appeared to be more effective in reducing BMI and WHR and increasing BW and WC. These results should be interpreted with caution, and also longer-term studies are necessary. Subgroup analyses also took into account the age of participants. We found that BMI significantly reduced in participants younger than 40, while WC and BW significantly increased in this age group. However, it has been shown that propolis consumption could significantly lower BW, WHR in individuals between 41 and 55. The small number of studies in the subgroup of less than 40 years for BW and WC compared to BMI may be effective in the obtained results. However, the clinical significance of this finding remains unclear and more studies are needed to gain a better understanding. Additionally, the sample size of studies was considered in the subgroup analysis. In studies with fewer than 50 participants, WHR significantly improved. However, BMI decreased and WC increased in studies with more than 50 participants. As there have been only a few studies with large sample sizes, these results should be confirmed by larger studies. The health status of participants was also a crucial factor that was taken into account when analyzing subgroups. It was found that diabetics had a greater reduction in WHR and BW, and obese and Mets subjects had a greater decrease in WC. In clinical terms, these findings can be important, as improving anthropometric indicators in these patients may improve their condition. However, the BW significantly increased in healthy adults. Different propolis doses in studies and the consumption of propolis with other supplements may explain these contradictory results. A subgroup analysis based on dose propolis revealed that BW, WHR, and BMI significantly decreased in doses 500 mg and 600–900 mg, respectively, while WC and BW increased in dose of 600–900 mg.

To determine the appropriate dose of propolis consumption for improving body composition, a dose-response analysis was conducted in the present study. There was a nonlinear relationship between propolis consumption and WC. There was a greater decline in WC in doses over 1000 mg. The effects of propolis supplementation on other variables were not linearly related to dosage. A significant association was also found between alterations in BMI and WC and length of the intervention. A decline in WC and BMI levels was observed up to 8 weeks, followed by a reversal in this trend after 8 weeks. The findings of the present study were not consistent with the meta-analysis by Salehi-Sahlabadi et al.'s[49] study, suggesting that propolis did not show any significant effect on BW and BMI. The study differed from ours because the number of included studies was small. In agreement with our results, Tutunchi et al.'s[22] study detected significant effects on BW and BMI in obese patients with NAFLD after taking 1500 mg propolis for 8 weeks. Moreover, Samadi et al.[13] found that propolis consumption at 900 mg/day for 12 weeks reduced BW and BMI in T2DM patients. Propolis has also been shown to reduce obesity in several animal studies.[50–52]

In relation to BP, an improvement in SBP was observed in subgroups over 55 years of age, studies with fewer than 50 participants, studies lasting 12 weeks, and CKD patients. It is possible that the supplementation with propolis through tyrosine hydroxylase, which is the rate-limiting enzyme in the biosynthesis of catecholamine in nitric oxide inhibited hypertensive.[53] Moreover, propolis may increase the expression of endothelial nitric oxide synthase and decreased nicotinamide adenine dinucleotide phosphate oxidase (NOX) activity, also increase the endothelial NO bioavailability.[21] However, the number of studies included to investigate the effect of the propolis on BP was limited, which can cause the lack of beneficial effects of propolis in other subgroups, for this reason, it is necessary to conduct more studies in this field.

In addition, the possible mechanism that propolis may have beneficial effects on anthropometric indexes can attributed to having more than 300 compounds including flavonoids, caffeic acid phenethyl ester, polyphenols, amino acids, and vitamins, which have a variety of antibacterial, antioxidant, and anti-inflammatory properties.[54] Moreover, recent studies have indicated that propolis can boost thermogenesis by promoting lipid metabolism and brown adipose tissue growth.[55] As another mechanism, propolis may reduce fat absorption via increased excretion of fat in feces.[46] Another anti-obesity mechanism of propolis was its suppression of adipocyte differentiation.[56] Adipocyte differentiation refers to the proliferation and differentiation of adipocyte precursor cells, which determines the number and size of adipocytes within mature adipose tissue.[57] It is possible to reduce BW by inhibiting adipocyte differentiation. However, more research is needed to gain a better understanding of propolis' antiobesity effects.

Strengths and limitations

This meta-analysis has several strengths and some limitations. Firstly, to the best of our knowledge, this meta-analysis represents the first comprehensive evaluation of the overall effects of propolis on SBP, DBP, WC, HC, FM, and WHR. Secondly, the inclusion criteria for the studies were not restricted by publication date or language, aiming to create the most comprehensive review on propolis to date. Additionally, a standardized methodology and robust statistical methods were employed to evaluate the effects of propolis on body composition and BP. Thirdly, we took into account the dosage and duration of interventions in our dose-response analysis. Lastly,

we carried out subgroup analyses to investigate potential sources of heterogeneity and conducted sensitivity analyses to evaluate the robustness of our findings. However, there are a few limitations that should be taken into account. Firstly, the included studies used various dosages of propolis, durations, and health status of participants and some eligible trials had a small sample size which may affect the pooled effect size. Secondly, we observed heterogeneous results in the included studies, so subgroup analyses were performed to identify the underlying causes. Thirdly, most studies failed to take into account lifestyle factors (such as diet, physical activity, smoking, etc.) that may affect BP and body composition. Additionally, studies that reported body composition and BP changes as secondary outcomes were likely to produce biased estimates of intervention and control group differences.[58] Lastly, most of the studies were performed in Iran, and this issue reduces the generalizability of findings. Consequently, further RCTs are needed to investigate the effect of propolis on body composition and BP to confirm the result for BMI and BW.

Conclusion

Supplementation with propolis seems to be effective in reducing weight and BMI. However, based on our analysis, propolis failed to affect WC, WHR, FM, HC, SBP, and DBP levels. It should be noted that the anti-obesity properties of propolis supplementation were small and may not reach clinical importance. Therefore, future well-designed studies with a large sample size are necessary to derive definitive conclusions about the effects of propolis consumption on body composition and BP levels.

Ethical Approval

The study protocol was approved and registered by the Ethics Committee of Isfahan University of Medical Sciences (IR.MUI.PHANUT.REC.1403.030). The study protocol was registered in the PROSPERO system (registration number: CRD42024507359).

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Authors Contributions

All authors have reviewed and approved the final manuscript. **MV**, **MAF**, and **GA** were the primary researchers responsible for formulating the hypothesis and overseeing the project. **MV**, **NN**, and **FPFT** conducted the literature search and data screening. Data extraction and quality assessment were performed independently by **MV**, **NN**, **BA**, and **SGH**. **MV** and **MAF** analyzed and interpreted data and wrote the manuscript.

Declaration of competing interest

The authors declare that there are no conflicts of interest.

Data Availability

Data will be made available on request.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.curtheres.2024.100754.

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