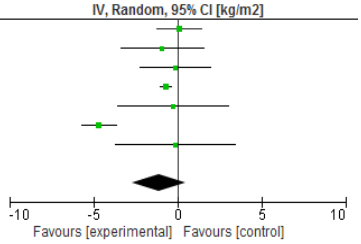
Supplementary file 1

(a) Outcomes: BMI

Study or Subgroup	Experimental Mean [kg/m2]	SD [kg/m2]	Total	Control Mean [kg/m2]	SD [kg/m2]	Total	Weight	Mean Difference IV, Random, 95% CI [kg/m2]
Ainehchi et al, 2019	-0.1	2.1	20	-0.2	2.2	20	16.6%	0.10 [-1.23, 1.43]
Arentz et al, 2017	-1.1	7.2	60	-0.2	6.8	62	12.9%	-0.90 [-3.39, 1.59]
Borzoei et al, 2018	-0.13	5.01	42	-0.01	4.85	42	14.2%	-0.12 [-2.23, 1.99]
Hajimonfarednejad et al, 2018	-0.19	0.7	29	0.52	0.64	30	18.7%	-0.71 [-1.05, -0.37]
Parseh et al, 2019	-0.13	4.24	10	0.14	3.2	10	10.5%	-0.27 [-3.56, 3.02]
Talaat.et al, 2018	-5.19	3.75	86	-0.52	3.21	89	17.4%	-4.67 [-5.71, -3.63]
Wiweko et al, 2017	-0.55	5.2	18	-0.42	6.1	20	9.6%	-0.13 [-3.72, 3.46]
Total (95% CI)			**265**			**273**	**100.0%**	**-1.10 [-2.70, 0.49]**

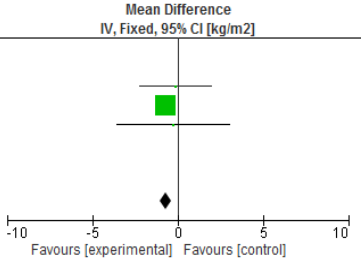
Heterogeneity: Tau² = 3.54; Chi² = 54.68, df = 6 (P < 0.00001); I² = 89%
Test for overall effect: Z = 1.35 (P = 0.18)



(b) Outcomes: BMI: Subgroup analysis of cinnamon alone (herbal mixture and metformin studies were excluded)

Study or Subgroup	Experimental Mean [kg/m2]	SD [kg/m2]	Total	Control Mean [kg/m2]	SD [kg/m2]	Total	Weight	Mean Difference IV, Fixed, 95% CI [kg/m2]
Ainehchi et al, 2019	-0.1	2.1	20	-0.2	2.2	20	0.0%	0.10 [-1.23, 1.43]
Arentz et al, 2017	-1.1	7.2	60	-0.2	6.8	62	0.0%	-0.90 [-3.39, 1.59]
Borzoei et al, 2018	-0.13	5.01	42	-0.01	4.85	42	2.5%	-0.12 [-2.23, 1.99]
Hajimonfarednejad et al, 2018	-0.19	0.7	29	0.52	0.64	30	96.4%	-0.71 [-1.05, -0.37]
Parseh et al, 2019	-0.13	4.24	10	0.14	3.2	10	1.0%	-0.27 [-3.56, 3.02]
Talaat.et al, 2018	-5.19	3.75	86	-0.52	3.21	89	0.0%	-4.67 [-5.71, -3.63]
Wiweko et al, 2017	-0.55	5.2	18	-0.42	6.1	20	0.0%	-0.13 [-3.72, 3.46]
Total (95% CI)			**81**			**82**	**100.0%**	**-0.69 [-1.03, -0.35]**

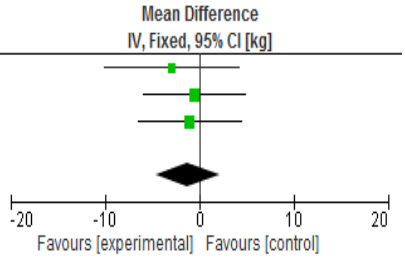
Heterogeneity: Chi² = 0.36, df = 2 (P = 0.84); I² = 0%
Test for overall effect: Z = 4.02 (P < 0.0001)



(c) Outcomes: Weight

Study or Subgroup	Experimental Mean [kg]	SD [kg]	Total	Control Mean [kg]	SD [kg]	Total	Weight	Mean Difference IV, Fixed, 95% CI [kg]
Arentz et al, 2017	-3	18.9	60	-0.1	21.3	62	22.5%	-2.90 [-10.04, 4.24]
Borzoei et al, 2018 (2)	-0.5	12.3	42	0	12.8	42	39.8%	-0.50 [-5.87, 4.87]
Hajimonfarednejad et al, 2018	-0.45	9.7	29	0.54	11.86	30	37.7%	-0.99 [-6.51, 4.53]
Total (95% CI)			**131**			**134**	**100.0%**	**-1.22 [-4.61, 2.16]**

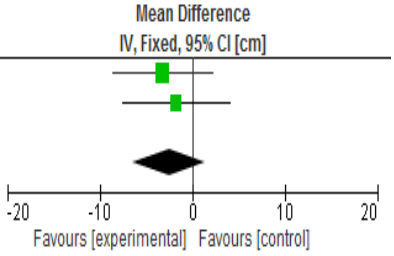
Heterogeneity: Chi² = 0.29, df = 2 (P = 0.87); I² = 0%
Test for overall effect: Z = 0.71 (P = 0.48)



(d) Outcomes: Waist circumference

Study or Subgroup	Experimental Mean [cm]	SD [cm]	Total	Control Mean [cm]	SD [cm]	Total	Weight	Mean Difference IV, Fixed, 95% CI [cm]
Arentz et al, 2017	-4.4	13	60	-1.2	17.1	62	53.7%	-3.20 [-8.58, 2.18]
Hajimonfarednejad et al, 2018	-0.72	10.9	29	1.03	11.8	30	46.3%	-1.75 [-7.54, 4.04]
Total (95% CI)			**89**			**92**	**100.0%**	**-2.53 [-6.47, 1.41]**

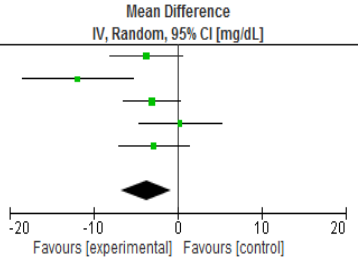
Heterogeneity: Chi² = 0.13, df = 1 (P = 0.72); I² = 0%
Test for overall effect: Z = 1.26 (P = 0.21)



(e) Outcomes: FBS

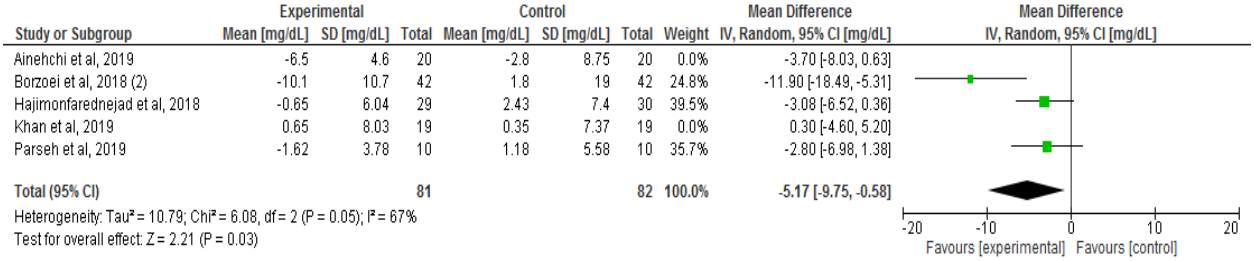
Study or Subgroup	Experimental Mean [mg/dL]	SD [mg/dL]	Total	Control Mean [mg/dL]	SD [mg/dL]	Total	Weight	Mean Difference IV, Random, 95% CI [mg/dL]
Ainehchi et al, 2019	-6.5	4.6	20	-2.8	8.75	20	21.1%	-3.70 [-8.03, 0.63]
Borzoei et al, 2018 (2)	-10.1	10.7	42	1.8	19	42	13.3%	-11.90 [-18.49, -5.31]
Hajimonfarednejad et al, 2018	-0.65	6.04	29	2.43	7.4	30	25.2%	-3.08 [-6.52, 0.36]
Khan et al, 2019	0.65	8.03	19	0.35	7.37	19	18.7%	0.30 [-4.60, 5.20]
Parseh et al, 2019	-1.62	3.78	10	1.18	5.58	10	21.7%	-2.80 [-6.98, 1.38]
Total (95% CI)			**120**			**121**	**100.0%**	**-3.69 [-6.67, -0.70]**

Heterogeneity: Tau² = 6.12; Chi² = 8.70, df = 4 (P = 0.07); I² = 54%
Test for overall effect: Z = 2.42 (P = 0.02)



Supplementary file 1

(f) Outcomes: FBS: Subgroup analysis (herbal mixture and metformin studies were excluded)

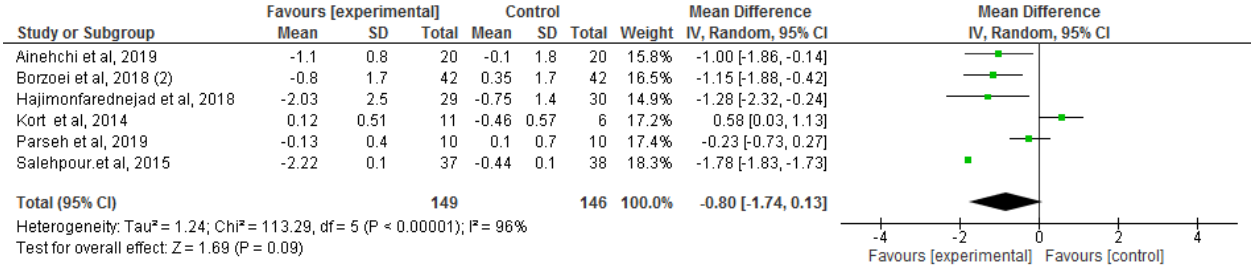


Study or Subgroup	Experimental Mean [mg/dL]	SD [mg/dL]	Total	Control Mean [mg/dL]	SD [mg/dL]	Total	Weight	Mean Difference IV, Random, 95% CI [mg/dL]
Ainehchi et al, 2019	-6.5	4.6	20	-2.8	8.75	20	0.0%	-3.70 [-8.03, 0.63]
Borzoei et al, 2018 (2)	-10.1	10.7	42	1.8	19	42	24.8%	-11.90 [-18.49, -5.31]
Hajimonfarednejad et al, 2018	-0.65	6.04	29	2.43	7.4	30	39.5%	-3.08 [-6.52, 0.36]
Khan et al, 2019	0.65	8.03	19	0.35	7.37	19	0.0%	0.30 [-4.60, 5.20]
Parseh et al, 2019	-1.62	3.78	10	1.18	5.58	10	35.7%	-2.80 [-6.98, 1.38]
Total (95% CI)			**81**			**82**	**100.0%**	**-5.17 [-9.75, -0.58]**

Heterogeneity: Tau² = 10.79; Chi² = 6.08, df = 2 (P = 0.05); I² = 67%
Test for overall effect: Z = 2.21 (P = 0.03)

Mean Difference IV, Random, 95% CI [mg/dL]
-20 -10 0 10 20
Favours [experimental] Favours [control]

(g) Outcomes: HOMA-IR

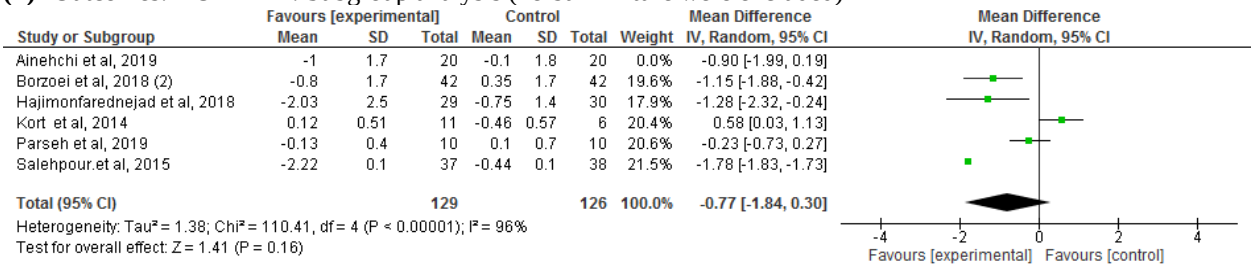


Study or Subgroup	Favours [experimental] Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Ainehchi et al, 2019	-1.1	0.8	20	-0.1	1.8	20	15.8%	-1.00 [-1.86, -0.14]
Borzoei et al, 2018 (2)	-0.8	1.7	42	0.35	1.7	42	16.5%	-1.15 [-1.88, -0.42]
Hajimonfarednejad et al, 2018	-2.03	2.5	29	-0.75	1.4	30	14.9%	-1.28 [-2.32, -0.24]
Kort et al, 2014	0.12	0.51	11	-0.46	0.57	6	17.2%	0.58 [0.03, 1.13]
Parseh et al, 2019	-0.13	0.4	10	0.1	0.7	10	17.4%	-0.23 [-0.73, 0.27]
Salehpour.et al, 2015	-2.22	0.1	37	-0.44	0.1	38	18.3%	-1.78 [-1.83, -1.73]
Total (95% CI)			**149**			**146**	**100.0%**	**-0.80 [-1.74, 0.13]**

Heterogeneity: Tau² = 1.24; Chi² = 113.29, df = 5 (P < 0.00001); I² = 96%
Test for overall effect: Z = 1.69 (P = 0.09)

Mean Difference IV, Random, 95% CI
-4 -2 0 2 4
Favours [experimental] Favours [control]

(h) Outcomes: HOMA-IR: Subgroup analysis (herbal mixture were excluded)

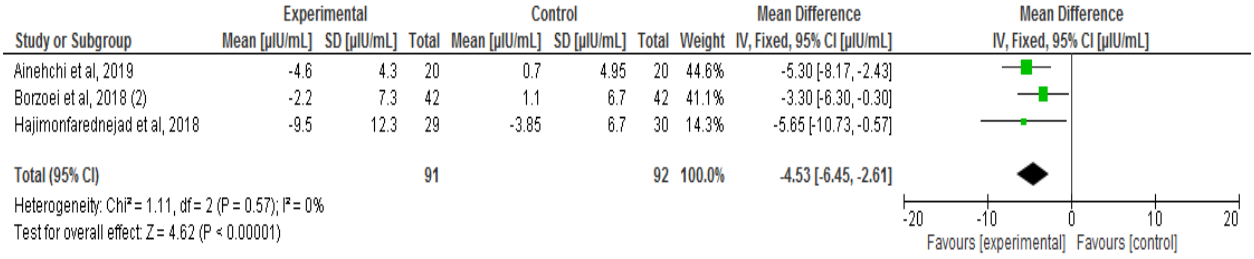


Study or Subgroup	Favours [experimental] Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Ainehchi et al, 2019	-1	1.7	20	-0.1	1.8	20	0.0%	-0.90 [-1.99, 0.19]
Borzoei et al, 2018 (2)	-0.8	1.7	42	0.35	1.7	42	19.6%	-1.15 [-1.88, -0.42]
Hajimonfarednejad et al, 2018	-2.03	2.5	29	-0.75	1.4	30	17.9%	-1.28 [-2.32, -0.24]
Kort et al, 2014	0.12	0.51	11	-0.46	0.57	6	20.4%	0.58 [0.03, 1.13]
Parseh et al, 2019	-0.13	0.4	10	0.1	0.7	10	20.6%	-0.23 [-0.73, 0.27]
Salehpour.et al, 2015	-2.22	0.1	37	-0.44	0.1	38	21.5%	-1.78 [-1.83, -1.73]
Total (95% CI)			**129**			**126**	**100.0%**	**-0.77 [-1.84, 0.30]**

Heterogeneity: Tau² = 1.38; Chi² = 110.41, df = 4 (P < 0.00001); I² = 96%
Test for overall effect: Z = 1.41 (P = 0.16)

Mean Difference IV, Random, 95% CI
-4 -2 0 2 4
Favours [experimental] Favours [control]

(i) Outcomes: Fasting Insulin

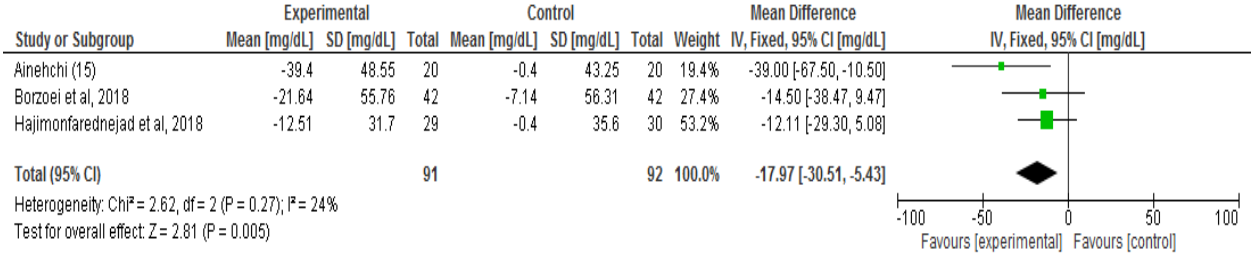


Study or Subgroup	Experimental Mean [µlU/mL]	SD [µlU/mL]	Total	Control Mean [µlU/mL]	SD [µlU/mL]	Total	Weight	Mean Difference IV, Fixed, 95% CI [µlU/mL]
Ainehchi et al, 2019	-4.6	4.3	20	0.7	4.95	20	44.6%	-5.30 [-8.17, -2.43]
Borzoei et al, 2018 (2)	-2.2	7.3	42	1.1	6.7	42	41.1%	-3.30 [-6.30, -0.30]
Hajimonfarednejad et al, 2018	-9.5	12.3	29	-3.85	6.7	30	14.3%	-5.65 [-10.73, -0.57]
Total (95% CI)			**91**			**92**	**100.0%**	**-4.53 [-6.45, -2.61]**

Heterogeneity: Chi² = 1.11, df = 2 (P = 0.57); I² = 0%
Test for overall effect: Z = 4.62 (P < 0.00001)

Mean Difference IV, Fixed, 95% CI [µlU/mL]
-20 -10 0 10 20
Favours [experimental] Favours [control]

(j) Outcomes: TG

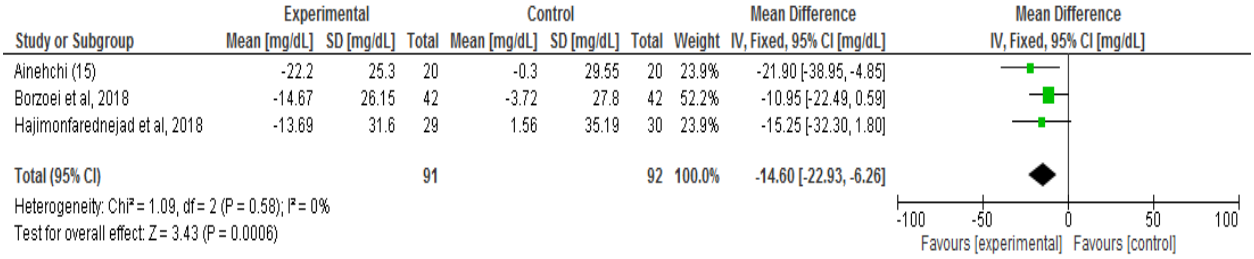


Study or Subgroup	Experimental Mean [mg/dL]	SD [mg/dL]	Total	Control Mean [mg/dL]	SD [mg/dL]	Total	Weight	Mean Difference IV, Fixed, 95% CI [mg/dL]
Ainehchi (15)	-39.4	48.55	20	-0.4	43.25	20	19.4%	-39.00 [-67.50, -10.50]
Borzoei et al, 2018	-21.64	55.76	42	-7.14	56.31	42	27.4%	-14.50 [-38.47, 9.47]
Hajimonfarednejad et al, 2018	-12.51	31.7	29	-0.4	35.6	30	53.2%	-12.11 [-29.30, 5.08]
Total (95% CI)			**91**			**92**	**100.0%**	**-17.97 [-30.51, -5.43]**

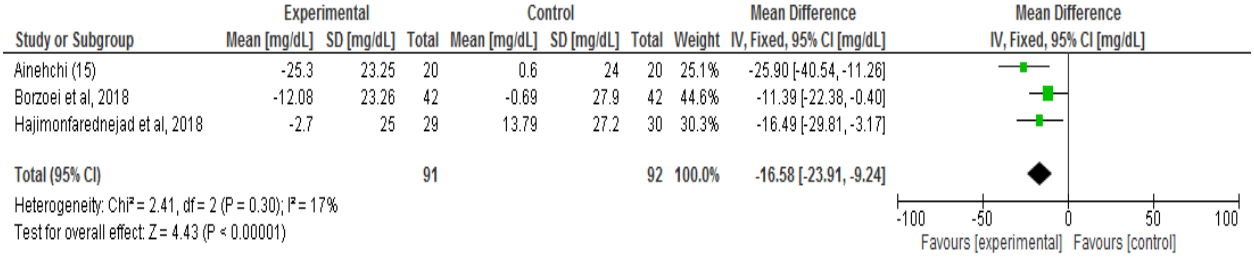
Heterogeneity: Chi² = 2.62, df = 2 (P = 0.27); I² = 24%
Test for overall effect: Z = 2.81 (P = 0.005)

Mean Difference IV, Fixed, 95% CI [mg/dL]
-100 -50 0 50 100
Favours [experimental] Favours [control]

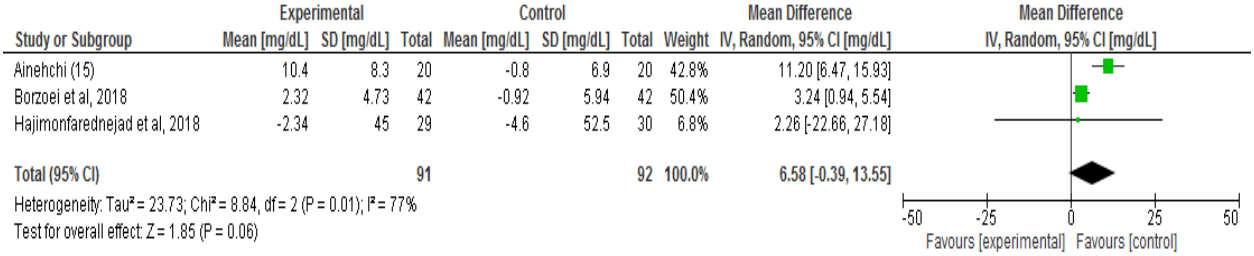
(k) Outcomes: TC



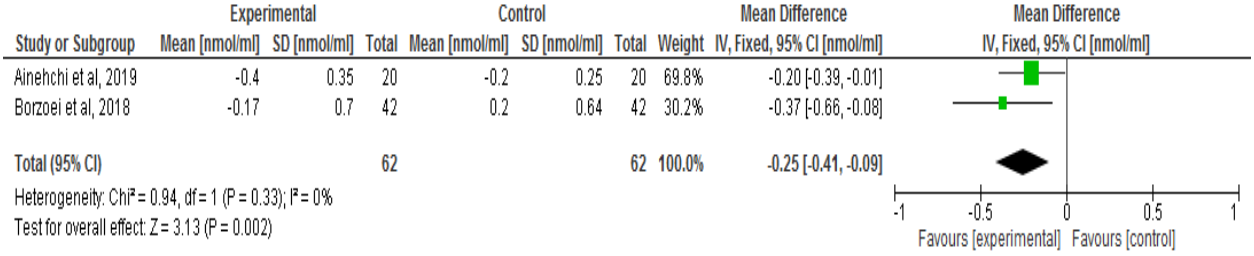
(l) Outcomes: LDL



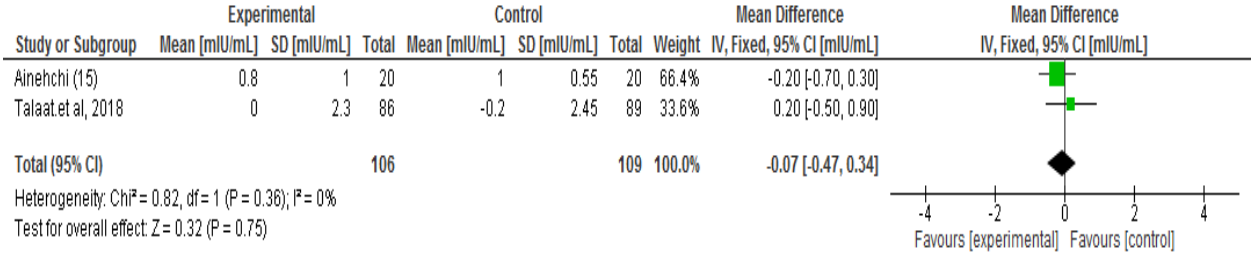
(m) Outcomes: HDL



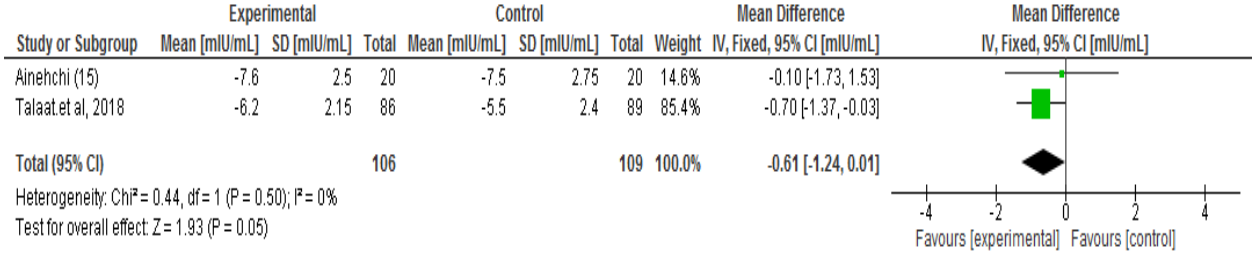
(n) Outcomes: MDA



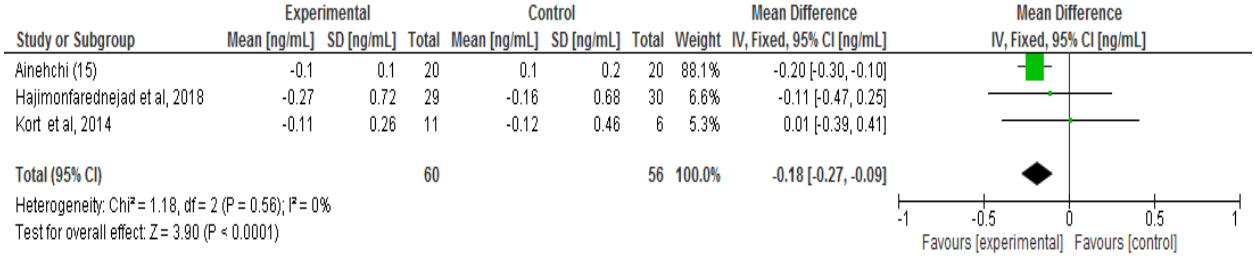
(o) Outcomes: FSH



(p) Outcomes: LH



(q) Outcomes: TT



(r) Outcomes: FT

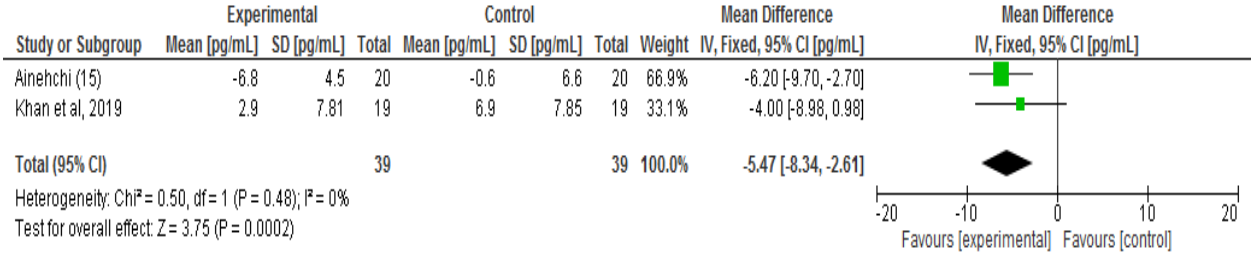


Figure S1. Meta-analysis of cinnamon and herbal mixture efficacy on PCOS patients' para clinical outcomes. (a) Effect of cinnamon alone and herbal mixture on BMI, (b) Subgroup analysis of BMI, (c) Effect of cinnamon alone and herbal mixture on weight, (d) Effect of cinnamon alone and herbal mixture on waist circumference, (e) Effect of cinnamon alone and herbal mixture on FBS, (f) Subgroup analysis of FBS, (g) Effect of cinnamon alone and herbal mixture on HOMA-IR, (h) Subgroup analysis of HOMA-IR, (i) Effect of cinnamon alone and herbal mixture on fasting insulin, (j) Effect of cinnamon alone and herbal mixture on TG, (k) Effect of cinnamon alone and herbal mixture on TC, (l) Effect of cinnamon alone and herbal mixture on LDL, (m) Effect of cinnamon alone and herbal mixture on HDL, (n) Effect of cinnamon alone and herbal mixture on MDA, (o) Effect of herbal mixture on FSH, (p) Effect of herbal mixture on LH, (q)Effect of cinnamon alone and herbal mixture on TT, (r) Effect of cinnamon alone and herbal mixture on FT.

Supplementary file 1

Table S1. Characteristics of studied articles about cinnamon alone included in the review

Authors (year)	*Type of study*	*Sample size*	*Sex*	*Drug*	*country*	*Participant age*	*Intervention (dosage and frequency)*	*Comparison (dosage and frequency)*	*Duration of follow-up*	*Outcomes (primary /secondary)*	*Method of measurements*	*Results*	*Side effects*
Borzoei, A., et al. (2018) (26)	RCT	Cinnamon group (n=42) Placebo group (n=42)	Female	Cinnamon capsules (cinnamon powder) Placebo capsules (wheat flour)	Iran	20-38	Cinnamon capsules (500 mg) for 3 times a day	Placebo capsules (500 mg) for 3 times a day	8 weeks	The effects of cinnamon on BMI, Energy, TAC, MDA, TC, LDL-C, HDL-C, and TG in women with PCOS	BMI: weight in kilogram divided by the height in meters squared Energy: 3-day average for energy and macronutrient intakes of all subjects was analysed by Nutritionist 4 software TAC: colorimetric method with commercial kits (TAC, RANDOX kits; UK) MDA: thiobarbituric acid test, TC, HDL-C, TG: enzymatic methods by Pars Azmun kit (Karaj, Iran) LDL-C (Friedewald formula: LDL-C=TC-(HDL-C+ TG/5	Cinnamon significantly increased TAC capacity (P=0.005). Cinnamon decreased MDA significantly compared to placebo (P=0.014). Cinnamon significantly improved TC, LDL-C, HDL-C (all $P < 0.05$). No significant effect was detected on BMI, Energy, and serum TG.	Patients did not report any side effects.

Supplementary file 1

Hajimonfarednejad, M., et al (2018) (27)	RCT	Cinnamon group (n=29) placebo group (n=30)	Female	Cinnamon capsules (cinnamon powder) + Medroxyprogesterone tablet Placebo capsules (450 mg starch + 50 mg cinnamon powder) + Medroxyprogesterone	Iran	18–45	Cinnamon capsule (500 mg) for 3 times a day + medroxyprogesterone tablet (10 mg) from the 15th day of menstruation cycle for 10 days	Placebo capsule (500 mg) for 3 times a day + medroxyprogesterone tablet (10 mg) from the 15th day of menstruation cycle for 10 days	12 weeks	Primary outcome: HOMA-IR Secondary outcomes: Weight, BMI, Waist circumference, FBS, insulin, 2hppG, HbA1c, TG, TC, LDL-C, HDL-C testosterone, DHEAS in women with PCOS.	HOMA-IR= Fasting blood glucose(mg/dl) ×Serum insulin level (mU=ml)/405 Method of other measurements were not explained	Cinnamon reduced level of fasting insulin (p=0.024), HOMA-IR (p=0.014) compared to placebo. Level of LDL (p=0.004) decreased compared to baseline There were not significant differences in Weight, BMI, Waist circumference, FBS, 2hppG, HbA1c, TG, TC, testosterone, DHEAS compared to placebo.	One patient after 5 days of using cinnamon capsule reported rash and itchiness.
Kort, D.H, et al. (2014)(28)	RCT	Cinnamon group (n=11) placebo group (n=6)	Female	Cinnamon capsules (cinnamon powder) Placebo capsules (ingredients were unknown)	New York	18-38	Cinnamon supplements (12 capsule 125 mg=1500 mg/day)	Placebo capsule (12 capsule 125 mg=1500 mg/day)	6 months	Primary outcome: Menstrual Cyclicity Secondary outcomes:, HOMA-IR, QUICK-I, AUC, SHBG, Total testosterone, DHEA-S, Weight, subcutaneous fat thickness, ovarian volume, glucose tolerance test	Total testosterone, DHEA-S, SHBG: chemiluminescence assays using Immulite. Menstrual Cyclicity: number menses/number months observed	Cinnamon improved menstrual cyclicity. There were not significant differences in Weight, subcutaneous fat thickness, ovarian volume, insulin resistance, glucose tolerance, DHEA-S, total Testosterone, SHBG.	Not reported in the article.
Wang, J.G., et al. (2007)(24)	Quasi-experimental	Cinnamon group (n=6) placebo group (n=7)	Female	Cinnamon capsules (cinnamon extract) Placebo capsules (ingredients	New York	31.1±2.0	cinnamon group (333 mg) for 3 times per day	placebo group (unknown mg) for 3 times per day	8 weeks	BMI, ovarian volumes, number of follicles, FBS, HOMA-IR, QUICKI, AUC,OGTT, insulin sensitivity	FSH, LH, TSH, total T, E2, insulin, and SHBG: chemiluminescence assays using Immulite HOMA-IR: fasting glucose (mmol/L) ×	Both cinnamon and placebo decreased FBS significantly (p<0.03) In placebo, level of BMI, Total T and E2, HOMA-IR, QUICKI, and insulin resistance	Patients did not report any side effects.

Supplementary file 1

				were unknown)						index, FSH, LH, TSH, total T, E2, insulin, SHBG	fasting insulin (μU/mL)/22.5, QUICKI: [log fasting glucose (mg/dL) + log fasting insulin (μU/mL)]$^{-1}$ AUC: trapezoidal method. Insulin sensitivity index (Matsuda method): 10,000× [fasting glucose (mg/dL) × fasting insulin (μU/mL) × mean glucose during OGTT (mg/dL) × mean insulin during OGTT (μU/mL)]-1/2	index remained unchanged. In cinnamon, BMI, total T, E2 remained the same. However, QUICKI increased (P<0.03) and HOMA-IR decreased (P<0.03), both consistent with improved insulin sensitivity. Also, level of OGTT reduce (P<0.03) and the insulin resistance index increased (P<0.05), consistent with improved insulin sensitivity.	
Khan, A.A.et al. (2019) (29)	RCT	Cinnamon (n=19) & (n=1; conceived) Metformin (n=19) & (n=1; conceived)	Female	Cinnamon capsules (cinnamon powder) Metformin capsules (metformin powder)	India	18–42	Cinnamon capsules (750 mg) 2x /day=3000 mg/day)	Metformin tablets (500 mg) 2x/day=1000 mg/day)	60 days	Duration of cycle (days), FBS, progesterone, free testosterone	Method of measurements were not explained	In both cinnamon and control group, menstrual cycle improved. Insulin resistance (p=0.899), post-ovulatory progesterone value (P=0.880) in both the cinnamon and the control group was similar at baseline and outcome. A remarkable change was observed in the ovarian size, and complete amelioration was reported in 6 patients in the control and 7 patients in the cinnamon group.	Adverse effect in 2 patients (one in the test group and the other in the control group) included gastric symptoms (epigastric burning & belching) happened. All adverse events resolved during the study period and no serious adverse events were reported.
Borzoei, A., M. et.al (2018) (30)	RCT	Cinnamon (n=42 Placebo (n=42)	Female	Cinnamon capsules (cinnamon powder) Placebo capsules	Iran	20-38	Cinnamon capsules (500 mg) for 3 times a day	Placebo capsules (500 mg) for 3 times a day	8 weeks	Weight, BMI, Energy, Carbohydrate, Protein, Total fat, FBS, Insulin, HOMA-IR,	Serum adiponectin level: ELISA method using Mediagnost kit (Germany). FBS: Enzymatic methods with commercially	Cinnamon significantly decreased FBS, insulin, HOMA-IR, TC and LDL and weight and increased HDL compared with placebo (all p<0.05).	Patients did not report any side effects.

Supplementary file 1

				(wheat flour)						Adiponectin, TC, TG, LDL, HDL	available Pars Azmun kit (Karaj, Iran). Insulin: ELISA method using Monobind kit (Monobind Inc, Lake Forest, CA, USA). HOMA-IR: fasting insulin (μU/mL) × fasting glucose (mg/dL) /405. TC, TG and HDL-C: enzymatic methods by Pars Azmun kit (Karaj, Iran). LDL-C : Friedewald formula = TC − (HDL-C + TG / 5)	TG and BMI significantly decreased in the cinnamon group, in comparison with baseline values (p=0.001 and p=0.002, respectively). No significant changes were seen in serum adiponectin in either group	
Parseh, S. et. Al. (2019) (31)	Quasi-experimental	Cinnamon (n=10) Control (n=10)	Female	Cinnamon capsules (cinnamon powder) Control (ingredients were unknown)	Iran	18-30	Cinnamon capsule (0.5 g) for 3 times a day	Control (unknown mg and serving times a day)	6 weeks	BMI, Fat percentage, Fat free mass, FBS, HOMA-IR	FBS: commercial kits (Pars Azemun, Isfahan, Iran) Insulin: ELISA (Monobind Inc.) BMI, fat percentage, and fat free mass: Body composition instrument (model Olympia 3.3 from South Korea) HOMA-IR= fasting insulin (microU/L) x fasting glucose (nmol/L)/22.5	Cinnamon significantly reduced BMI, FBS, and HOMA-IR	Not reported in the article.
Salehpour , S.et al (2015)(32)	RCT	Cinnamon extract (n=37) Placebo (n=38)	female	Cinnamon (cinnamon extract) Placebo (ingredients were unknown)	Ian	12.6-17	Cinnamon extract (500 mg) twice daily	Placebo (500 mg) twice daily	1 year	BMI, HOMA-IR, QUIKI, apoB/apoA1	Method of measurements were not explained	Cinnamon and metformin reduced HOMA-IR ($p<0.05$), QUICKI ($p<0.01$) and apoB/apoA1 significantly. Both of them decreased BMI compared to placebo ($P<0.05$) in obese adolescent girls with PCOS.	Not reported in the poster.

Supplementary file 1

Table S2. Characteristics of studied articles about herbal mixture containing cinnamon and other herbs included in the review

Authors Year	*Type of study*	*Sample size*	*Sex*	*Drug*	*country*	*Participant age*	*Intervention (dosage and frequency)*	*Comparison (dosage and frequency)*	*Duration of follow-up*	*Outcomes (primary/ secondary)*	*Method of measurements*	*Results*	*Side effects*
Wiweko, B. et al. (2017) (33)	RCT	DLBS3233 group (n=18) Metformin group (n=20)	female	DLBS3233 (Lagerstroemia spesiosa + Cinnamomum burmanii) Metformin	Indonesia	18 - 40	DLBS3233 group: 1 × 100 mg DLBS3233 and 2 placebos (unknown mg and ingredients) tablets daily	Metformin group: 2 × 750 mg metformin + 1 placebo (unknown mg and ingredients) tablet daily	6 months	AMH, urea, creatinine, alanine aminotransferase (ALT), and aspartate aminotransferase (AST), pregnancy	AMH: Beckman-Coulter gen II AMH assay (Beckman Coulter, Inc., Brea, CA, USA).	DLBS3233 reduced BMI significantly (P=0.017) 7 patients (18.42%) conceived naturally: 5 (13.16%) in the metformin group and 2 (5.26%) in the DLBS3233 group After 6 months, the decrease in AMH level was higher in the metformin group compared to the DLBS3233 group (P= 0.003)	In metformin group the most common side effect was nausea (P = 0.006) followed by diarrhea, vomiting, headache, and flu-like syndrome. In DLBS3233 group

Supplementary file 1

													induced minimal side effects (P = 0.01)
Arentz, S., et al. (2017)(34)	RCT	Herbal medicine + a lifestyle intervention (n=60) Lifestyle intervention alone (n=62)	female	Tablet 1 (Glycyrrhiza glabra + Paeonia lactiflora + Cinnamomum verum + Hypericum perforatum) Tablet 2 (Tribulus terrestris) Lifestyle: diet and a structured sequence of aerobic and progressive resistance exercises.	Australia	18-44	Tablet 1: 3 tablet (unknown mg) once a day. Tablet 2: 3 tablets (13.5 g) per day for ten consecutive days commenced on menstrual cycle day 5 for oligomenorrheawomen and within 1 week of trial commencement for women with amenorrhoea.	Lifestyle intervention	3 months	Primary outcomes: oligomenorrhoea/ amenorrhoea. Secondary outcomes: hormones, anthropometry, quality of life, depression, anxiety and stress, pregnancy, birth outcomes, and safety.	Menstrual cycle days: self-reported or websites E2, FSH, LH, testosterone, SHBG and free androgen index: by pathology companies Insulin and glucose serum: Quantitative Insulin Sensitivity Check Index HRQoL: PCO Questionnaire Depression, anxiety and stress: assessed by the short form (DASS 21) Pregnancy: β HCG	In the combination group recorded a reduction in oligomenorrhea ($p < 0.01$) compared to controls. BMI ($p < 0.01$); insulin ($p = 0.02$) and LH ($p = 0.04$); blood pressure ($p = 0.01$); quality of life ($p < 0.01$); depression, anxiety and stress ($p < 0.01$); and pregnancy rates ($p = 0.01$) were improved.	Two women were withdrawn from the trial with adverse events due to the herbal medicine.
Lai, L., et al., (2017) (25)	RCT	Standardised multiherb CHM (n=19) Individualised multiherb CHM (n=18)	female	Standardised multiherb (14 CHM) 16 g daily taken orally as a tea Individualised multiherb (20 CHM)	UK	Not reported in the article	Does not include a control group Standardised multiherb (8 g of granulated extracts) twice a day	Individualised multiherb (prescribing was provided by the study team)	6 months	primary outcome: oligomenorrhoea and amenorrhoea secondary outcomes: menstrual rate, BMI, weight and hirsutism.	Method of measurements were not explained	Improvements in menstrual rates were found within group for both standardised CHM ($p=0.0027$) and individualised CHM ($p<0.001$), though not between group ($p=0.26$). No improvements were observed for BMI nor for weight in either group. Improvements in hirsutism found within group for both groups were not statistically significant between group ($P=0.09$).	Minimal side effects were reported .

Supplementary file 1

Ushiroyama, T., et al. (2006) (23)	Quasi-experimental	Dang-gui-shao-yao-san (n=43) Gui-zhi-fu-ling-wan (n=21)	Female	Dang-Gui-Shao-Yao-San (Peony Root + Atractylodes Lancea Rhizome + Alisma Rhizome + Japanese Angelica Root + Hoelen + Cnidium Rhizome) Gui-zhi-fu-ling-wan (Cinnamon Bark + Peony Root + Peach Kernel + Hoelen + Moutan Bark))	Japan	18–33	Dang-gui-shao-yao-san: (2.5 g) in 100 ml of hot water before every meal: 3 times a day	Gui-zhi-fu-ling-wan: (2.5 g) in 100 ml of hot water before every meal: 3 times a day	8 weeks	Ovulation	Method of measurements were not explained	Ovulation of 10 women from 64 improved	Not reported in the article.
Talaat, B.et al. (2018) (35)	RCT	Cinnamon + metformin (n=86) Metformin (n=89)	Female	Cinnamon (cinnamon bark extract) + metformin Metformin	Egypt	18–35	Cinnamon (112 mg) three times a day + (500 mg) metformin three times a day with meals	Metformin tablet (500 mg) three times a day with meals	6 months	Resumption of menstrual regularity, BMI, waist/hip ratio, LH /FSH ratio, glycemic status (OGTT/A1C)	Method of measurements were not explained	Regular menstrua improved in both metformin group (P= 0.003) and in cinnamon + metformin group (P= 0.00). BMI reduced in cinnamon + metformin group (P= 0.00); however, there was no difference in metformin group (P= 0.36). Waist/Hip ratio decreased in cinnamon + metformin group (P = 0.00) in contrast	Not reported in the article.

Supplementary file 1

												with metformin (P = 0.74). Level of serum LH reduced in both group (P = 0.00). There was no difference in the FSH of the two groups. prediabetic patients: reduced in metformin (P= 0.038) and cinnamon + metformin group (P= 0.02)	
Ainehchi, N. et al (2019)(16)	RCT	Group 1 (Clomiphene citrate: CC) (n=20) Group 2 (cc+ herbal mixture) (n=20)	female	Clomiphene citrate Herbal mixture (250 mg spearmint + 200 mg ginger + 150 mg cinnamon + 100 mg C. sinensis)	Iran	18-35	Herbal mixture (750 mg) once a day + CC	CC (50–150 mg) for 3 menstrual cycles from the fifth day of menstruation for 5 days	3 months	Primary outcomes: MDA, SOD, GPx, CAT, Insulin, FBS, HOMA-IR Secondary outcome: total phenolic content (TPC), total flavonoid content (TFC), free radical scavenging activity, ferric reducing antioxidant potential (FRAP), and phytochemical analysis of herbal mixture as	MDA: thiobarbituric acid (TBA) test SOD: colorimetric method using an ELISA kit (RANDOX, Antrim, North Ireland UK) GPx: ELISA kit (RANDOX) CAT: ELISA kit (CUSABIO Kit, WUHAN HUAMEI BIOTECH Co., Ltd. Wuhan, China) Insulin: chemiluminescence assay (LIAISON C-Peptide, Byk-Sangtec) FBS: Commercial kits (Pars Azemun, Iran) and the auto-analyzer system (Selectra E, Vitalab, Netherland). HOMA-IR: (Glucose × Insulin)/405 Ultrasonography: ultrasound (5 MHz Ulramark 4 Plus; Advanced Technology	Levels of CAT, GPx and SOD in group 3 increased significantly (p<0.001). While FBS and MDA in group 3 significantly decreased compared to the group 1 (P<0.001). There were not significant difference in level of insulin and HOMA-IR	Patients did not report any side effects.

Supplementary file 1

											Laboratories, Bothell, WA, USA).		
Ainehchi (15)	RCT	Group 1 (Clomiphene citrate: CC) (n=20) Group 2 (cc+ herbal mixture) (n=20)	female	Clomiphene citrate Herbal mixture (250 mg spearmint + 200 mg ginger + 150 mg cinnamon + 100 mg C. sinensis)	Iran	18-35	Herbal mixture (750 mg) once a day + CC	CC (50–150 mg) for 3 menstrual cycles from the fifth day of menstruation for 5 days	3 months	Primary outcomes: HOMA-IR, FSH, LH, free-testosterone (T), total-testosterone (TT), E2, TC, TG, LDL-C, HDL-C, and VLDL-C Secondary outcomes: TSH, FT4, FT3, hirsutism, acne, oligomenorrhea, amenorrhea, menstrual regulation, and the rate of pregnancy	Level of FSH, LH, TT, and E2, as well as TSH, FT4, and FT3: Electrochemiluminescence (ECL) method using Cobas E 411 analyzer (Germany). Level of T: ELISA method using commercial kit (free testosterone: Monobind Inc., lake Forest, CA, USA). Insulin: Chemiluminescence assay (LIAISON C-Peptid, Byk-Sangtec). FBS: Commercial kits (Pars Azemun, Iran) and the auto-analyzer system (Selectra E, Vitalab, Netherland). HOMA-IR: (Glucose × Insulin)/405 TC, TG, LDL, HDL, and VLDL: Auto-analyzer system (Vita lab Selectra E, Netherland) Volume of ovary, numbers and the size of follicles: Vaginal ultrasound (5 MHz Ulramark 4 Plus; Advanced Technology Laboratories, Bothell, WA).	Level of LH, LH/FSH, decreased; however, level of FSH increased in all three groups (P<0.001). Level of TT just in group 2 and T in group 3 revealed a significant decrease compared to group 1. HOMA-IR in group 2 reduced significantly compared to group 1. TC, TG, LDL-C, and VLDL-C decreased significantly in group 2 and 3. However, high-density lipoproteins-cholesterol in group 2 and group 3 enhanced remarkably compared to group 1. Overall, clinical outcomes improved significantly in all groups (P<0.05).	Patients did not report any side effects.

Supplementary file 1

Table S3. Characteristics of studied article about spearmint included in the review

Authors year	*Type of study*	*Sample size*	*Sex*	*Drug*	*country*	*Participant age*	*Intervention (dosage and duration of treatment)*	*Comparison (dosage and duration of treatment)*	*Duration of follow-up*	*Outcomes (primary/secondary)*	*Method of measurements*	*Results*	*Side effects*
Grant, P.,et al (2010)(13)	RCT	Spearmint (n=21) Chamomile : placebo(n= 21)	female	Spearmint (dried leaves) Camomile (dried leaves)	UK	19–42	Spearmint (unknown mg) two cups of tea per day	Chamomile unknown mg) two cups of tea per day	1 months	FT(pg/mL) TT(ng/mL) DHEAS(mcg/mL) LH(mIU/mL) FSH(mIU/mL) DQLI (0–30) FG	Method of measurements were not explained	In the spearmint tea group levels of FT and TT were significantly reduced ($p < 0.05$). LH and FSH also increased ($p < 0.05$). Degree of hirsutism scored by the modifi ed DQLI were signify cantly reduced in the spearmint tea group ($p < 0.05$). There was, however, no significant reduction in the objective Ferriman-Galwey ratings of hirsutism between the two trial groups over the trial duration ($p = 0.12$).	Patients did not report any side effects. Just one patient who because of a dislike of the flavor of the chamomile tea discontinue d study.