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The effects of Garcinia cambogia on glycaemic control and liver enzymes in adults: a systematic review and meta-analysis of randomised controlled trials

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Review

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Abstract

Previous studies have assessed how supplementing with *Garcinia cambogia* affects glycaemic control and liver enzyme levels; nevertheless, the results were not consistent. The study aimed to evaluate the impact of *Garcinia cambogia* on glycaemic control and liver enzymes through a systematic review and meta-analysis. Searches were conducted from the beginning through February 2023, using online databases (Scopus, Web of Science, PubMed, and Cochrane Library). Trials examining the impact of *Garcinia cambogia* on serum levels of fasting blood sugar (FBS), serum level of insulin, alanine transaminase (ALT), and aspartate transaminase (AST) in adults were included. The overall estimates and their 95% confidence intervals (CIs) were calculated using a random-effects model. This meta-analysis includes nine publications with 444 participants. The results showed that *Garcinia cambogia* has no significant effect on FBS (weighted mean difference (WMD): 1.02 mg/dl, 95% CI: −1.29, 3.33), insulin (WMD: −0.12 mU/L, 95% CI: −1.50, 1.25), AST (Hedges' g: −0.08, 95% CI: −0.43, 0.26), and ALT (Hedges' g: 0.27, 95% CI: −0.20, 0.73). Subgroup analysis showed that *Garcinia cambogia* significantly increased insulin levels in females and also increased insulin and FBS levels in those with a BMI ≥30 kg/m^2. Nevertheless, the administration of *Garcinia cambogia* for more than 8 weeks significantly decreased insulin levels. This meta-analysis showed that supplementation with *Garcinia cambogia* has no significant effect on FBS, insulin, ALT, or AST levels compared with control groups; however, it seems that increasing the duration of the intervention may have a decreasing effect on insulin levels.

Introduction

In the current world population, some disorders like liver diseases, chronic obstructive pulmonary disease, cancer, diabetes, and CVDs are the leading causes of mortality. The prevalence of these disorders is closely correlated with lifestyle choices like physical activity, diet, smoking, and alcohol use[1–4]. Alanine transaminase (ALT) and aspartate transaminase (AST) are two important enzymes in diagnosing liver diseases. An increase in the level of these enzymes indicates liver damage. It has been demonstrated that variations in the amounts of these two enzymes have negative effects on one's health[5,6]. On the other hand, the importance of glycaemic management for human health has been demonstrated in earlier research[7,8]. *Garcinia cambogia* (native to Southeast Asia) is one of the plants that has been shown to play an important role in human health. This plant has anti-inflammatory and antioxidant characteristics and is effective in the management of liver abnormalities and glycaemic control. A bioactive compound called hydroxycitric acid (HCA) is mainly responsible for these therapeutic effects[9].

Previous studies on the use of *Garcinia cambogia* in the adult population have yielded conflicting results when examining metabolic indicators such as insulin, blood glucose, ALT, and AST. It seems that age, sex, BMI, and intervention duration were the main potential sources of heterogeneity. In one study, it was found that orlistat in combination with *Garcinia cambogia*

or each alone did not have a significant effect on postprandial glucose and fasting blood glucose in obese men[10]. Other studies have also shown that *Garcinia cambogia* extract supplementation does not have a considerable effect on glycaemic control and liver transaminases in healthy individuals[11–16]. A study conducted on obese adults in Taiwan showed that the serum AST level in the group receiving only *Garcinia cambogia* significantly decreased, but insulin and glucose levels and serum ALT did not change significantly[17]. On the contrary, *Garcinia cambogia* extract along with a calorie-restricted diet has led to increased liver enzymes and failure to control glycaemic parameters[18].

Therefore, considering the conflicting and heterogeneous results of previous studies, the objective of this study is to systematically review and meta-analyse the existing research on the impact of *Garcinia cambogia* supplementation on glycaemic control and liver enzymes in the adult population.

Methods

Search strategy

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed when conducting the current systematic review and meta-analysis[19] and were registered at PROSPERO (CRD42023428039). The systematic literature search of Scopus, Web of Science, PubMed/Medline, Google Scholar, and Cochrane Library databases was conducted up to 9 February 2023. In order to conduct our search technique, the following MeSH and non-MeSH phrases were combined: ('Garcinia cambogia' OR 'Hydroxycitric Acid' OR Hydroxycitrate OR brindleberry OR 'Malabar tamarind' OR kudampuli) AND (intervention OR RCT OR Randomly OR randomised OR random OR Placebo OR trials OR trial OR randomised). There was no time limit, and we included only English-language articles. Two independent authors (MRA, ST) reviewed the titles and abstracts to find related publications. Additionally, to guarantee that all potentially relevant papers were found, the reference lists of the included research and pertinent reviews were carefully searched.

Selection criteria

To determine eligibility, the population, intervention, comparison, outcome, and study design (PICOS) criteria[20] were used.

Studies were selected based on the following inclusion criteria: (1) designed as randomised controlled trials (RCT) (either parallel or crossover); (2) examined the effects of *Garcinia cambogia* in humans (either healthy or unhealthy subjects); (3) investigated fasting blood sugar (FBS), insulin, ALT, and AST levels for both treatment and control groups at baseline and at the end of the study; (4) involved adult individuals (aged ≥ 18 years); and (5) provided means and SDs of desired outcomes or any other effect sizes being convertible to means and SDs. We excluded articles with non-randomised study designs, animal studies, observational studies, *in vitro* research, papers without a placebo group, studies conducted on children or adolescents, conference abstracts, and reviews.

Data extraction

Two different researchers (MRA and ST) independently extracted the pertinent information from each included article using common data extraction forms, such as the name of the first author, the year that the work was published, the nation, the study's design, the participant's health status, their gender, the sample size, their average age and BMI, the duration of the intervention, the dosage of *Garcinia cambogia* supplementation (and its equivalent in HCA), the comparison group, and the averages and standard deviations of their FBS, insulin, ALT, and AST levels both before and after the intervention for the treatment and control groups. Our primary outcome was FBS levels. The secondary outcomes were insulin, ALT, and AST levels. In studies where relevant information was not provided, the respective authors were emailed to ask for more details.

Quality assessment

Two reviewers (MRA and ST) independently assessed the methodological quality of the chosen papers using the Cochrane risk-of-bias tool for randomised trials (RoB 1),[21] which rate the quality of studies based on random sequence generation, allocation concealment, selective reporting, blinding of participants, and staff, blinding of outcome assessment, incomplete outcome data, and other likely sources of bias. Any disagreements were handled through conversation. Methodological defects affecting the findings of the study gave rise to a 'high risk' score for each domain, while a 'low risk' score was given to each defect-free domain. When the information was not sufficient to evaluate the impact, the domain was scored 'unclear risk'. According to the Cochrane Handbook's guideline, the studies were finally classified as having a low risk of bias, a high risk of bias, or an uncertain bias[21] (Table 1).

Statistical analysis

Using the random-effects method (DerSimonian and Laird)[22], standardised mean differences, estimated by Hedges' g, with the 95% confidence intervals (CIs) of ALT and AST were used as opposed to weighted mean differences (WMDs) with 95% CIs for glucose and insulin. Also, in studies that only provided SEM (standard error of the mean), SDs were derived using the following formula: $SD = SEM \times \sqrt{n}$, where n is the number of participants in each group. When medians and interquartile ranges were presented instead of mean and SD values, SDs were obtained using SD = interquartile range/1.35 (symmetrical data distribution)[23]. If RCTs did not report the SDs of the change, we calculated them using the following formula in which the correlation coefficient (R) was considered 0.8: $SD_{difference}$ = Square Root $[(SD_{pre\text{-}treatment})^2 + (SD_{post\text{-}treatment})^2 - (2 \times R \times SD_{pre\text{-}treatment} \times SD_{post\text{-}treatment})]$[24]. Using the Cochrane's Q-test and the *I*-squared (I^2) values, the heterogeneity among studies was evaluated. If I^2 values >50% or P<0.05, between-study heterogeneity was regarded as significant[25,26]. We conducted a stratified analysis to determine the cause of the heterogeneity among the examined studies. Sensitivity analyses were carried out by excluding each study individually and rerunning the pooled analysis in order to examine the impact of each study on the overall effect size. To identify the likely publication bias, Egger's regression test was used[27]. All statistical tests were performed using STATA, version 14 (StataCorp, College Station, Texas, USA). Statistics were considered significant for P-values under 0.05.

Results

Search results

A primary systematic search of databases turned up 569 papers in all, and manual searching turned up one study. After excluding duplicates, 464 articles were reviewed based on the title and

Table 1. Risk of bias for randomised controlled trials, assessed according to the revised Cochrane risk-of-bias tool for randomised trials (RoB 1)

Publications	Random sequence generation	Allocation concealment	Selective reporting	Blinding (participants and personnel)	Blinding (outcome assessment)	Incomplete outcome data	Other source of bias
1. Hayamizu (2001)	L	L	L	L	H	L	L
2. Kovacs (2006)	L	U	L	L	H	L	H
3. Hayamizu (2008)	L	L	L	L	H	L	L
4. Kim (2011)	L	L	L	L	H	L	L
5. Lu (2012)	L	U	L	L	H	L	L
6. Vasques (2014)	L	U	L	L	H	H	L
7. Chong (2014)	L	L	L	L	H	L	L
8. Al-kuraishy (2016)	L	U	L	H	H	L	L
9. Arefhosseini (2022)	L	L	L	H	H	L	L

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

abstract screening approach, which resulted in the exclusion of 440 articles due to no relevant or original data (n = 196), animal studies (n = 160), and reviews (n = 84). From twenty-four studies that entered the full-text examination, fifteen studies were excluded because of the following reasons: irrelevant research (n = 9), no control group (n = 2), inadequate data of interest (n = 1), the same participants (n = 2), and combined intervention (n = 1). Nine RCTs[10–18] were finally included in the qualitative and quantitative synthesis (Fig. 1).

Study characteristics

The detailed characteristics of selected studies are summarised in Table 2. These trials have involved 444 participants. The range of publication years of selected articles was between 2001 and 2022. Two studies were carried out in Japan[14,15], one in the Netherlands[12], one in Korea[13], one in Taiwan[17], one in Brazil[11], one in Germany[16], one in Iraq[10], and one in Iran[18]. All studies were RCTs that were conducted on adult subjects aged ≥ 18 years. Two studies included only women[11,18], two included only men[10,12], and the rest of the RCTs were conducted on both genders[13–17]. The mean BMI varied from 21.8 to 38.1 kg/m^2 among eligible articles. Except for two studies conducted on obese[10] and non-alcoholic fatty liver disease[18] patients, other studies involved healthy individuals[11–17]. The sample size of the eligible studies ranged between ten and eighty-four subjects in both treatment and control groups. The dose of *Garcinia cambogia* extract supplementation ranged between 166 and 2800 mg/d. The control group received a placebo except for two studies in which the control group received orlistat[10] and a calorie-restricted diet[18]. The range of intervention length was from 11 d to 16 weeks among RCTs.

Risk of bias assessment

As shown in Table 1, in terms of random sequence generation, all studies[10–18] were scored with low risk since they mentioned random sequence generation methods. Additionally, five studies were evaluated as low risk for allocation concealment[13–16,18]; however, four were rated with unclear risk[10–12,17]. Researchers blinding was performed in no studies and was, thus, identified as high risk. Except for two studies that were considered as having a high risk of bias in the participants blinding[10,18], others reported that the participants were blinded and were given a low risk score. All studies were considered as having a low risk of bias in selective reporting. Eight RCTs explicitly mentioned incomplete outcome data receiving a low risk of bias[10–13,15–18]. Since all studies were rated as having a high risk of bias in one domain (blinding of outcome assessment), they were considered as low quality.

Primary outcomes

Effect of Garcinia cambogia on FBS

As an end measure, the effects of *Garcinia cambogia* administration on FBS levels were investigated in seven trials[10,12,14–18]. The random-effects model's overall findings showed that taking *Garcinia cambogia* supplements did not significantly alter FBS levels (WMD: 1.02 mg/dl, 95% CI: −1.29, 3.33, P = 0.378) (I^2 = 52.4%, P = 0.050) (Fig. 2). According to Egger's regression test, we did not find any evidence of publication bias for FBS concentrations (P = 0.335). To determine the impact of a single study on the total effect size, the sensitivity analysis was conducted by excluding each trial one at a time. Sensitivity analysis indicated that the overall effect of *Garcinia cambogia* supplementation on FBS was not dependent on any single study.

Due to significant heterogeneity among studies, subgroup analysis was also performed in which we stratified RCTs based on the intervention duration (≤ 8 or > 8 weeks), age (< 40 or ≥ 40 years), BMI (< 25, 25–29.9, or ≥ 30 kg/m^2), and sex (both, male, or female). The heterogeneity was reduced when subgroup analysis was performed based on intervention duration (I^2 = 0%, P = 0.779), age (I^2 = 0%, P = 0.779), and sex (I^2 = 0%, P = 0.948). When individuals were < 40 years and the duration of intervention was less than 8 weeks, *Garcinia cambogia* supplementation reduced FBS levels; however, it was not statistically significant (WMD: −0.38 mg/dl, 95% CI: −2.3, 1.54, P = 0.134), and (WMD: −0.38 mg/dl, 95% CI: −2.3, 1.54, P = 0.134), respectively. In studies that mean BMI of participants was ≥ 30 kg/m^2, FBS increased following *Garcinia cambogia* consumption (WMD: 3.57 mg/dl, 95% CI: 0.34, 6.80, P = 0.030). Similarly, female participants experienced increased levels of FBS following *Garcinia cambogia* supplementation (WMD: 5.41 mg/dl, 95% CI: 1.21, 9.61, P = 0.012) (Table 3).

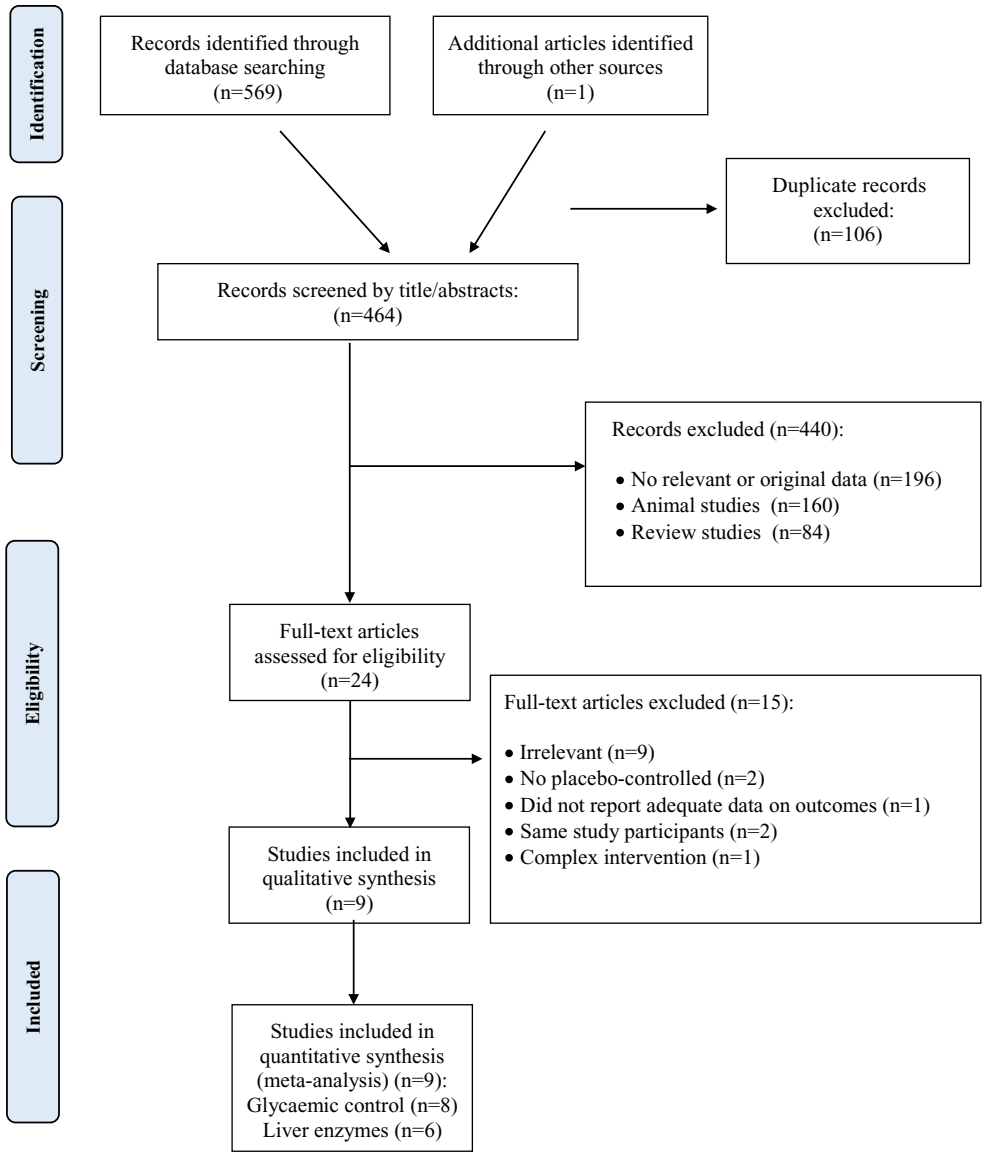

Figure 1. Flow chart of the number of studies identified and selected into the meta-analysis.

Secondary outcomes

Effect of Garcinia cambogia on insulin

The effect of *Garcinia cambogia* supplementation on insulin concentrations was considered in six RCTs[11,12,14,15,17,18]. Combined results using the random-effects model (Fig. 3) showed that there was no significant effect of *Garcinia cambogia* consumption on insulin levels (WMD: −0.12 mU/L, 95% CI: −1.50, 1.25, P = 0.861) with significant between-study heterogeneity (I^2 = 64.2%, P = 0.016). There was no evidence of publication bias (P = 0.719). The results of the sensitivity analysis showed that none of the individual studies had a significant effect on the overall effect size of findings.

When the BMI (I^2 = 47.3%, P = 0.150) and sex (I^2 = 47.3%, P = 0.150) subgroups were analysed, the heterogeneity vanished. Most reduction in insulin was found among participants of normal range (BMI = 18.5-24.9) when compared to participants with overweight (BMI = 25–29.9) following intervention (WMD: −1.05 mU/L, 95% CI: −2.68, 0.58, P = 0.207 vs. WMD: −0.64 mU/L, 95% CI: −1.78, 0.51, P = 0.276). Likewise, the reducing effect of *Garcinia cambogia* on insulin was greater in males (WMD: −1.05 mU/L, 95% CI: −2.68, 0.58, P = 0.207 compared by both genders (WMD: −0.64 mU/L, 95% CI: −1.78, 0.51, P = 0.276). These results also demonstrated that insulin levels significantly increased in trials conducted on females (WMD: 1.81 mU/L, 95% CI: 0.28, 3.34, P = 0.021) and participants with mean BMI ≥ 30 kg/m^2 (WMD: 1.81 mU/L, 95% CI: 0.28, 3.34, P = 0.021) (Table 3).

Effect of Garcinia cambogia on ALT

A total of six studies[13–18] provided changes in ALT levels as an outcome measure. The results of the pooled analysis (Fig. 4) revealed that *Garcinia cambogia* supplementation did not alter ALT concentrations significantly (Hedges' g: 0.27, 95% CI: −0.20, 0.73, P = 0.264) (I^2 = 76.9%, P = 0.001). Egger's regression test found no significant publication bias among selected trials (P = 0.330). The findings were unchanged when any RCT was eliminated and no significant changes to our results occurred.

Table 2. Demographic characteristics of the included studies

First author (year)	Location	Study design	Health status	Sex	Sample size	Duration (week)	Mean age (year)	Baseline BMI (kg/m^2)	Intervention group	Comparator group	Outcome
1. Hayamizu (2001)	Japan	RCT	Healthy	Both	40	8	36.8	27.8	1667.3 mg/d *Garcinia cambogia* extract (equivalent to 1000 mg HCA/d)	Placebo	FBS/insulin/ALT/AST
2. Kovacs (2006)	Netherlands	RCT	Healthy (sedentary lean male)	Male	10	11 d	24	21.8	1447.5 mg/d HCA	Placebo	FBS/insulin
3. Hayamizu (2008)	Japan	RCT	Healthy	Both	39	16	42.5	28.7	1667.3 mg/d *Garcinia cambogia* extract (equivalent to 1000 mg HCA/d)	Placebo	FBS/insulin/ALT/AST
4. Kim (2011)	Korea	RCT	Healthy	Both	58	10	33.9	25.4	2000 mg/d *Garcinia cambogia* extract (60% HCA)	Placebo	ALT/AST
5. Lu (2012)	Taiwan	RCT	Healthy	Both	71	8	27	28.8	2800 mg/d *Garcinia cambogia* extract (1380.4 mg/d HCA)	Placebo	FBS/insulin/ALT/AST
6. Vasques (2014)	Brasil	RCT	Healthy	Female	43	60 d	40	32.24	2400 mg/d *Garcinia cambogia* extract (50% HCA)	Placebo	Insulin
7. Chong (2014)	Germany	RCT	Healthy	Both	84	12	42.8	28.8	1950 mg/d *Garcinia cambogia* extract (60% HCA)	Placebo	FBS/ALT/AST
8. Al-kuraishy (2016)	Iraq	RCT	Obese male patients	Male	59	12	41.5	38.1	166 mg/d *Garcinia cambogia* extract plus 120 mg/d orlistat	120 mg/d orlistat	FBS
9. Arefhosseini (2022)	Iran	RCT	NAFLD	Female	40	8	36.15	33.9	1875 mg/d *Garcinia cambogia* bark leaf extract (1122 mg/d HCA) accompanied by receiving a calorie-restricted diet (−700 kcal/d)	control group (receiving only a calorie-restricted diet)	FBS/insulin/ALT/AST

RCT, randomised controlled trial; HCA, hydroxycitric acid; ALT, alanine aminotransferase; AST, aspartate aminotransferase; FBS, fasting blood sugar; NAFLD, non-alcoholic fatty liver disease.

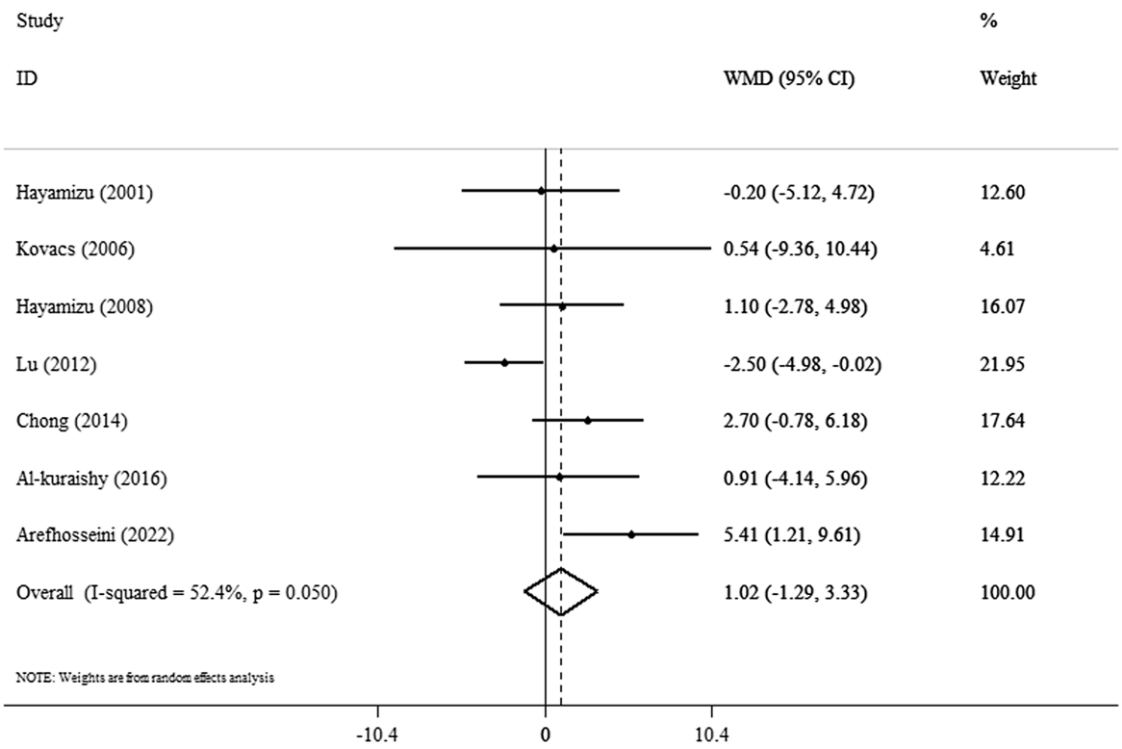

Figure 2. Forest plot detailing weighted mean difference and 95% confidence intervals (CIs) for the effect of *Garcinia cambogia* on glucose.

Due to the significant heterogeneity among RCTs, stratified analysis was also carried out by trial duration ($I^2 = 26.1\%$, P = 0.258) and age ($I^2 = 0\%$, P = 0.492), which decreased heterogeneity (Table 3). Non-significant changes in ALT levels were observed when studies were classified based on trial duration and age.

Effect of Garcinia cambogia on AST

The pooled mean differences of six trials[13–18] illustrated a non-significant effect on AST levels compared to the control group following *Garcinia cambogia* intervention (Hedges' g: −0.08, 95% CI: −0.43, 0.26, P = 0.632) (Fig. 5). We found no evidence of publication bias for AST levels (P = 0.638). According to the results of the sensitivity analysis, none of the studies exerted significant effects on the combined effect size.

Although there was a lot of heterogeneities among the articles, it was reduced when trials were grouped by age ($I^2 = 5.7\%$, P = 0.303) and the duration ($I^2 = 34.5\%$, P = 0.217) of the intervention (Table 3). The non-significant effect of *Garcinia cambogia* on AST levels remained after classifying articles by aforementioned variables with a higher reducing effect among subjects aged > 40 years (Hedges' g: −1.01, 95% CI: −0.37, 0.34, P = 0.951).

Discussion

The primary outcome of the current systematic review and meta-analysis was that there was no significant effect on FBS. The secondary outcomes indicated consumption of *Garcinia cambogia* has no significant influence on insulin, AST, or ALT. Although subgroup analysis showed *Garcinia cambogia* significantly increased FBS and insulin levels in women with a BMI ≥30, it significantly reduced insulin levels when it was used for more than 8 weeks of administration.

Primary outcomes

Effect of Garcinia cambogia on FBS

Our results are in agreement with previous studies. In animal studies, Hayamizue et al. demonstrated that the administration of garcinia daily to mice for a duration of 28 d had no effect on the serum glucose level of the mice[28]. Moreover, Shetty et al found no hypoglycaemic effect on diabetic rat models treated with *Garcinia cambogia* for 21 d[29]. Another study in healthy obese men has indicated that treatment with 166 mg/d *Garcinia cambogia* for 3 months did not affect glucose levels[10]. According to Chonge et al.'s study, administering *Garcinia cambogia* extract with 50% HCA (1950 mg) twice daily for a duration of 12 weeks did not result in any significant alteration in glucose levels in healthy overweight adults[16]. In an animal study, oral administration of HCA at a dose of 310 mg/kg/bw reduced glucose levels in rats[30]. In another animal study, Kirana et al. showed the aqueous extract of *Garcinia cambogia* rind at 100 and 200 mg/kg/bw decreased glucose in diabetic rat models[31]. Differences in studies may be attributed to differences in population, intervention duration, doses, and formulation of *Garcinia cambogia*, which influence the bioavailability of *Garcinia cambogia*. The phytochemical makeup of a plant extract also influences its biological capabilities. The phytochemical composition can vary depending on geographical location, climate, and soil type[32,33]. Moreover, the common significant effect of *Garcinia cambogia* on the reduction of glucose levels was seen in subjects with a high baseline range of glucose levels[34].

Secondary outcomes

Effect of Garcinia cambogia on insulin

Furthermore, according to the results of our study, Vasque et al. reported that insulin levels did not change after receiving 2.4 g of

Table 3. Subgroup analysis of included randomised controlled trials in meta-analysis of the effect of *Garcinia cambogia* on glycaemic control and liver enzymes

Group	No. of trials	WMD (95% CI)	P value	I^2 (%)	P-heterogeneity	P for between subgroup heterogeneity
FBS						
Pooled effect size	7	1.02 (−1.29, 3.33)	0.378	52.4	0.050	–
Duration (week)						0.161
≤ 8	4	−0.38 (−2.30, 1.54)	0.134	70.4	0.017	
> 8	3	1.76 (−0.54, 4.07)	0.341	0.0	0.779	
Mean age						0.161
< 40	4	−0.38 (−2.30, 1.54)	0.134	70.4	0.017	
≥ 40	3	1.76 (−0.54, 4.07)	0.341	0.0	0.779	
Mean BMI						0.110
< 25	1	0.54 (−9.336, 10.44)	0.915	—	—	
25-29.9	4	−0.34 (−2.02, 1.35)	0.694	53.0	0.094	
≥ 30	2	3.57 (0.34, 6.80)	0.030	44.5	0.180	
Sex						0.045
Both	4	−0.34 (−2.02, 1.35)	0.694	53.0	0.094	
Female	1	5.41 (1.21, 9.61)	0.012	—	—	
Male	2	0.83 (−3.67, 5.33)	0.694	0.0	0.948	
Insulin						
Pooled effect size	6	−0.12 (−1.50, −1.25)	0.861	64.2	0.016	–
Duration (week)						0.026
≤ 8	5	0.19 (−0.64, 1.02)	0.659	55.5	0.061	
> 8	1	−3.30 (−6.25, −0.35)	0.028	—	—	
Mean age						0.283
< 40	4	0.14 (−0.75, 1.03)	0.753	66.4	0.030	
≥ 40	2	−0.97 (−2.81, 0.86)	0.298	74.4	0.048	
Mean BMI						0.017
< 25	1	−1.05 (−2.68, 0.58)	0.207	—	—	
25-29.9	3	−0.64 (−1.78, 0.51)	0.276	47.3	0.150	
≥ 30	2	1.81 (0.28, 3.34)	0.021	52.0	0.149	
Sex						0.017
Both	3	−0.64 (−1.78, 0.51)	0.276	47.3	0.150	
Female	2	1.81 (0.28, 3.34)	0.021	52.0	0.149	
Male	1	−1.05 (−2.68, 0.58)	0.207	—	—	
ALT						
Pooled effect size	6	0.27 (−0.20, 0.73)	0.264	76.9	0.001	–
Duration (week)						0.414
≤ 8	3	0.30 (−0.03, 0.63)	0.078	89.1	<0.001	
> 8	3	0.11 (−0.18, 0.41)	0.446	26.1	0.258	
Mean age						0.608
< 40	4	0.15 (−0.13, 0.43)	0.294	85.7	<0.001	
≥ 40	2	0.27 (−0.09, 0.62)	0.140	0.0	0.492	

(*Continued*)

Table 3. (*Continued*)

Group	No. of trials	WMD (95% CI)	P value	I^2 (%)	P-heterogeneity	P for between subgroup heterogeneity
AST						
Pooled effect size	6	−0.08 (−0.43, 0.26)	0.632	59.2	0.031	–
Duration (week)						0.597
≤ 8	3	−0.04 (−0.36, 0.29)	0.825	77.6	0.011	
> 8	3	−0.15 (−0.45, 0.14)	0.301	34.5	0.217	
Mean age						0.526
< 40	4	−0.16 (−0.43, 0.12)	0.266	72.2	0.013	
≥ 40	2	−1.01 (−0.37, 0.34)	0.951	5.70	0.303	

FBS, fasting blood sugar; ALT, alanine aminotransferase; AST, aspartate aminotransferase; WMD, weight mean difference.

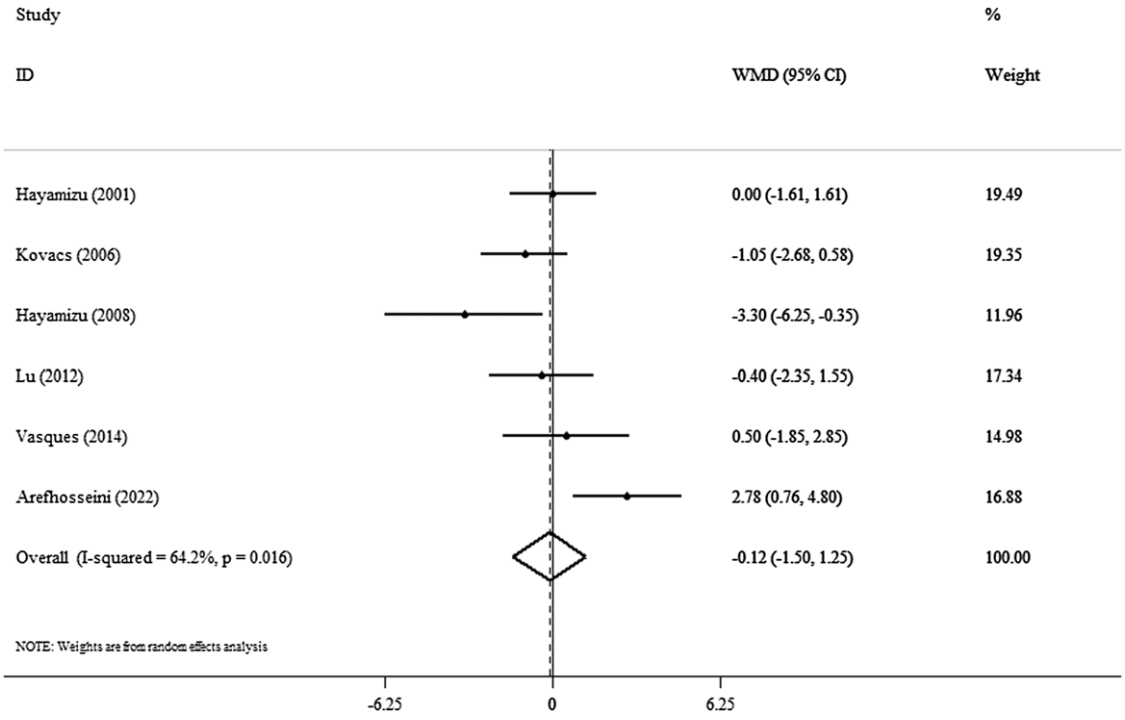

Figure 3. Forest plot detailing weighted mean difference and 95% confidence intervals (CIs) for the effect of *Garcinia cambogia* on insulin.

Garcinia cambogia extract with 50% HCA for 60 d[11]. In patients with type 2 diabetes, small intestinal infusions of 2800 mg HCA did not affect blood glucose or plasma insulin[35]. In contrast, HCA supplementation in exercised individuals at 500 mg/d for 7 d enhanced post-meal insulin sensitivity[36]. Differences among studies may be for various populations, intervention duration, *Garcinia cambogia* doses, and formulation of *Garcinia cambogia*, which may influence the bioavailability of *Garcinia cambogia*.

One possible mechanism that explains the link between *Garcinia cambogia* and glycaemic factors is a competition of HCA with citric acid for citrate lyase, which leads to reduced decomposition of citric acid and increased cellular citric acid that cause inhabitation of glycolysis and facilitated glycogenesis and resulted in reduction of glucose concentrations[37,38]. As a result, the amount of insulin that should be secreted to regulate blood glucose is reduced[38]. The HCA isomer (2s,3r) also inhibited intestinal and pancreatic glucosidase, which reduced glucose absorption and carbohydrate metabolism and ultimately lowered blood sugar levels[34]. Moreover, *Garcinia cambogia* may decrease intestinal uptake of glucose by releasing serotonin[39].

Effect of Garcinia cambogia on ALT and AST

In this study, we systematically reviewed the effect of *Garcinia cambogia* on AST and ALT levels. Consistent with our findings, an animal study by Clouatre and his colleagues indicated no change in AST and ALT in rats who received HCA for 16 weeks[40]. Besides, a clinical study showed AST and ALT levels did not change in overweight adults who received *Garcinia cambogia* (containing

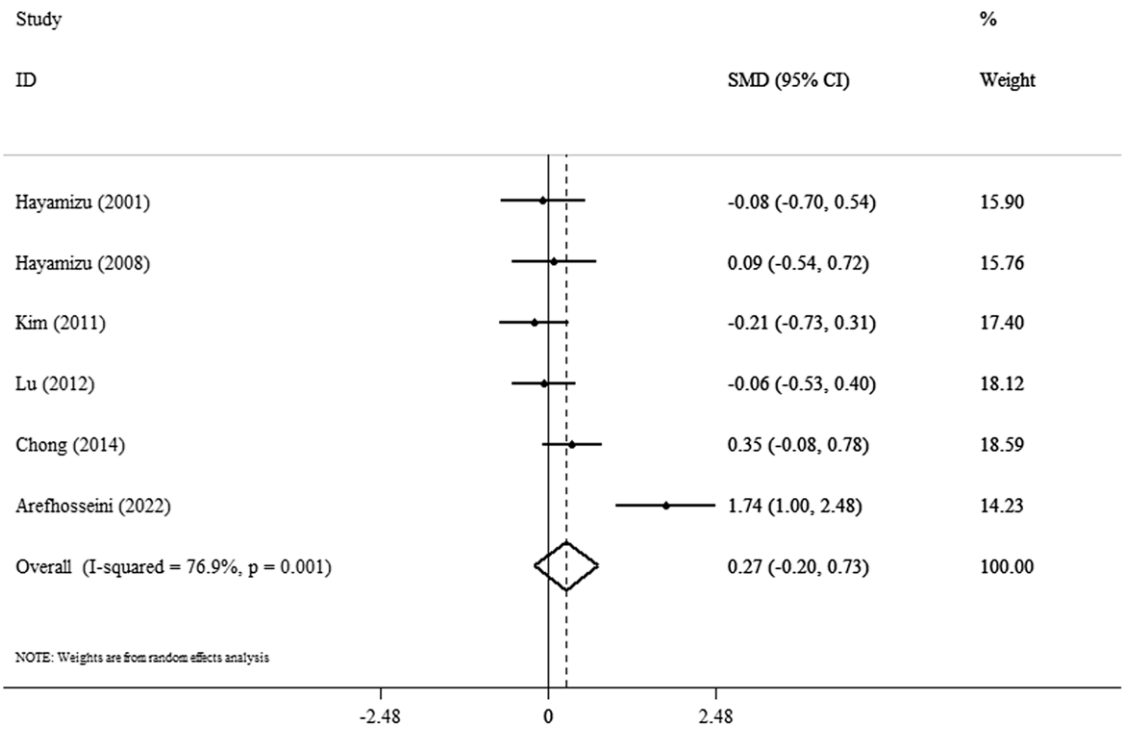

Figure 4. Forest plot detailing weighted mean difference and 95% confidence intervals (CIs) for the effect of *Garcinia cambogia* on alanine transaminase.

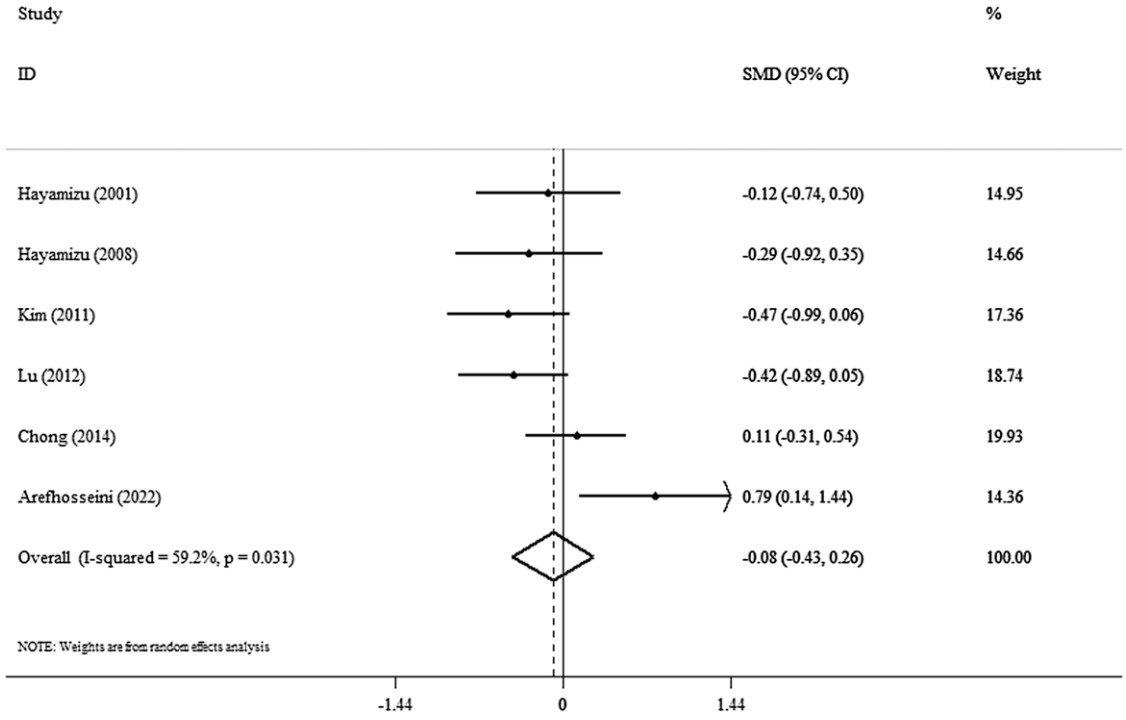

Figure 5. Forest plot detailing weighted mean difference and 95% confidence intervals (CIs) for the effect of *Garcinia cambogia* on aspartate transaminase.

1000 mg of HCA per day) for 12 weeks[14]. However, Stohs et al. found that in participants who received 4600 mg of HCA for 8 weeks, the AST and ALT levels decreased significantly[41]. A recent study has reported six cases that had a rise in AST and ALT levels associated with weight loss with HCA[42]. In an animal study, Sanchez et al. reported that mice supplemented with *Garcinia cambogia* showed increased plasma AST and ALT levels[43]. Discrepancies among studies may partly be due to differences in age, gender, health conditions, sample size, dose, and duration of interventions.

Consistent with our results, evidence has shown that Antichol, which contains *Garcinia cambogia* (8% w/w), inhibits cholesterol-induced fatty degeneration of the liver and changes in the liver enzymes[44]. Another study revealed the antioxidant property of *Garcinia cambogia* could keep the AST and ALT at normal levels[45].

In the sub-group analysis, *Garcinia cambogia* increased glucose and insulin levels in the females with BMI $\geq$ 30; however, it was still in the standard range of healthy humans. In fact, the level of increasing glucose and insulin was statistically significant, but this was not clinically significant. Furthermore, the sub-group analysis based on the duration of the study showed that the administration of *Garcinia cambogia* for more than 8 weeks decreased insulin levels.

Strengths and limitations

Our understanding allows us to say that the current meta-analysis is the first meta-analysis of the effects of *Garcinia cambogia* on glycaemic control and liver enzymes. Moreover, we assessed publication bias by the results of Egger's test, and no evidence of publication bias was indicated which caused more reliability of our results. However, our results should be explained cautiously considering some of the limitations in the present meta-analysis. Most importantly, few studies were eligible, and the majority of them had small sample sizes. In addition, the significant differences in methodology, sample sizes, ages of patients, health conditions, and countries of participants indicated significant heterogeneity among the studies.

Conclusion

The findings of this meta-analysis demonstrated that *Garcinia cambogia* could be effective in reducing insulin levels when administered for more than 2 months. However, further well-designed clinical trials with long-term intervention and different doses of *Garcinia cambogia*, especially in pre-diabetic and diabetic subjects and patients with liver diseases, are advised to confirm our results.

Authorship. MRA created the research. Data screening and literature searches were carried out by ST and MS. MRA independently extracted data and evaluated its quality. The text was written by ST, MS, RR, MAS, and MA after data interpretation. The study was headed by AH. The final manuscript was read and approved by all writers.

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Competing interests. The authors declared no conflicts of interest.

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