

## Review Article

# The Use of *Garcinia* Extract (Hydroxycitric Acid) as a Weight loss Supplement: A Systematic Review and Meta-Analysis of Randomised Clinical Trials

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The aim of this systematic review is to examine the efficacy of *Garcinia* extract, hydroxycitric acid (HCA) as a weight reduction agent, using data from randomised clinical trials (RCTs). Electronic and nonelectronic searches were conducted to identify relevant articles, with no restrictions in language or time. Two independent reviewers extracted the data and assessed the methodological quality of included studies. Twenty-three eligible trials were identified and twelve were included. Nine trials provided data suitable for statistical pooling. The meta-analysis revealed a small, statistically significant difference in weight loss favouring HCA over placebo (MD:  $-0.88$  kg; 95% CI:  $-1.75$ ,  $-0.00$ ). Gastrointestinal adverse events were twice as common in the HCA group compared with placebo in one included study. It is concluded that the RCTs suggest that *Garcinia* extracts/HCA can cause short-term weight loss. The magnitude of the effect is small, and the clinical relevance is uncertain. Future trials should be more rigorous and better reported.

## 1. Introduction

The prevalence of overweight and obesity has increased over the last decade [1], and current measures have not been able to stem the tide. A wide variety of weight management strategies are presently available, and some involve the use of dietary supplements marketed as slimming aids. One such slimming aid is *Garcinia* extract, (-)-hydroxycitric acid (HCA).

HCA is a derivative of citric acid and can be found in plant species native to South Asia such as *Garcinia cambogia*, *Garcinia indica*, and *Garcinia atroviridis* [2]. HCA is usually marketed as a weight loss supplement either alone or in combination with other supplements [2, 3]. Some authors have suggested that HCA causes weight loss by competitively inhibiting the enzyme adenosine triphosphatase-citrate-lyase [3–6]. HCA has also been reported to increase the release or availability of serotonin in the brain, thereby leading to appetite suppression [7]. Other postulated weight loss mechanisms include inhibition of pancreatic alpha amylase and

intestinal alpha glucosidase, thereby leading to a reduction in carbohydrate metabolism [8].

Animal studies have suggested that HCA causes weight loss [3, 9], and human trials involving the use of HCA as a weight loss supplement have been carried out [3].

The primary objective of this systematic review was to examine the efficacy of HCA in reducing body weight in humans, using data from randomised clinical trials.

## 2. Methods

Electronic searches of the literature were conducted in the following databases: Medline, Embase, *The Cochrane Library*, Amed, and Cinahl. The search terms used included dietary supplements, antiobesity agents, body weight, hydroxycitrate, *garcinia*, and derivatives of these. Each database was searched from inception until March, 2010. We also searched the Internet for relevant conference proceedings and hand searched relevant medical journals, and our own files. The bibliographies of all located articles were also searched.

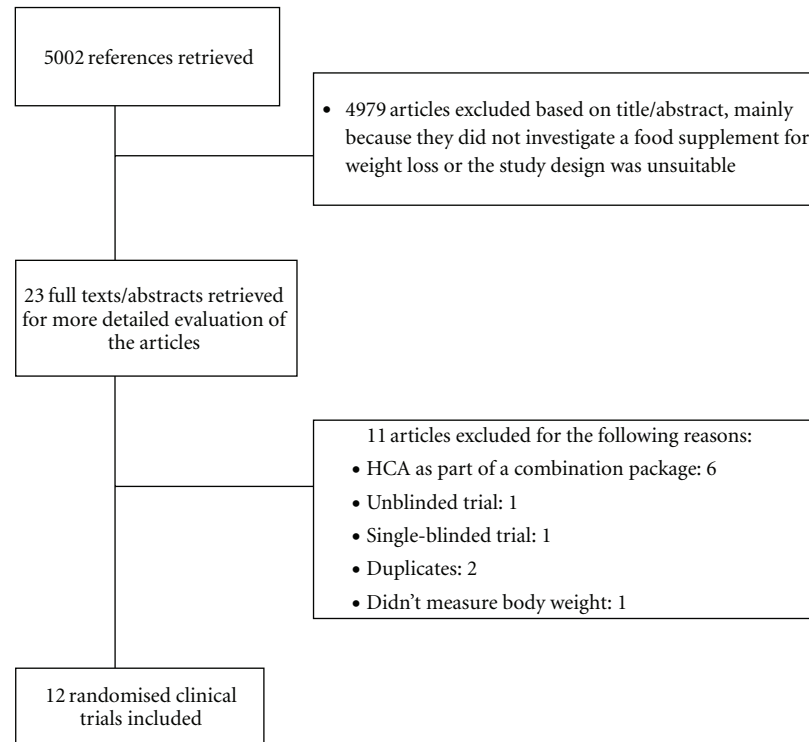


FIGURE 1: Flow chart showing the process for the inclusion of randomised controlled trials.

Only randomised, double-blind, placebo-controlled studies were included in this paper. To be considered for inclusion, studies had to test the efficacy of oral HCA or any of its salts for weight reduction in obese or overweight humans. Included studies also had to report body weight as an outcome. No age, time, or language restrictions were imposed for inclusion of studies. Studies which involved the use of HCA as part of a combination treatment (dietary interventions containing other supplements in addition to HCA), or not involving obese or overweight subjects based on body mass index (BMI) values, were excluded from this paper.

Two independent reviewers assessed the eligibility of studies to be included in the paper. Data were extracted systematically by two independent reviewers according to the patient characteristics, interventions, and results. The methodological quality of all included studies was assessed by the use of a quality assessment checklist adapted from the Consolidated Standard of Reporting Trials (CONSORT) guidelines [10, 11]. In addition, the Jadad score [12] was also used to assess the quality of included studies. Disagreements were resolved through discussion with the other authors.

Data are presented as means with standard deviations. Mean changes in body weight were used as common endpoints to assess the differences between HCA and placebo groups. Using the standard meta-analysis software [13], we calculated mean differences (MDs) and 95% confidence intervals (CIs). Studies included in the meta-analysis were weighted by SD (a proxy for study size). If a trial had 3 arms, only the HCA and placebo arms were included in the

meta-analysis. The  $I^2$  statistic was used to assess for statistical heterogeneity amongst studies. A funnel plot was used to test for publication bias.

### 3. Results

Our searches produced 5002 “hits” of which 23 potentially relevant articles were identified (Figure 1). Six trials were excluded because they involved the use of HCA in combination with other therapies [7, 14–18]. One trial was excluded because it was not blinded [19], and another because it was single blinded [20]. Two articles were excluded because they were duplicates. One of these articles [21] was the same trial published in another journal which had been earlier excluded, while the other article [22] was a report of two individual trials which were included in this systematic review. One trial was excluded because the investigators did not measure weight as an outcome [23]. Thus 12 randomised clinical trials (RCTs) including a total of 706 participants met our inclusion criteria, and were included in this systematic review [2, 4–6, 24–31]. Their key details are summarized in Tables 1, 2, and 3.

All of the studies had one or more methodological weaknesses (Table 1). None of the included studies reported on how double blinding was carried out, and all studies were also unclear about how the allocation was concealed. The randomization procedure was clear in only a third of included studies [4, 6, 25, 29].

Three RCTs [4, 28, 31] did not provide actual values to enable statistical pooling (Table 3). One of these RCTs

TABLE 1: Characteristics of included studies.<sup>a</sup>

Authors Year	Main outcome (s)	Main diagnoses of participants	Randomisation appropriate?	Allocation concealed?	Groups similar at baseline?	Similar follow-up of groups?	Outcome assessor blinded?	Care provider blinded?	Patients blinded?	Attrition bias?	ITT analysis?	Jadad Score
Hayamizu et al. 2001 [24]	Visceral fat, BW indices	Overweight subjects	?	?	+	+	?	?	?	—	—	2
Hayamizu et al. 2003 [4]	Visceral fat, BW indices	Overweight subjects	+	?	+	+	?	?	?	?	—	3
Heymsfield et al. 1998 [25]	BW, fat mass	Overweight subjects	+	?	+	+	?	?	?	?	+	5
Kovacs et al. 2001 [26]	Satiety, food intake, BW	Normal to moderately obese subjects	?	?	?	+	?	?	?	—	—	3
Kovacs et al. 2001 [27]	Satiety, food intake, BW	Normal to moderately obese subjects	?	?	?	+	?	?	?	—	—	3
Mattes and Bormann 2000 [5]	Satiety, body composition	Overweight subjects	?	?	+	+	?	?	?	?	—	2
*Preuss et al. 2002 [28]	BW, BMI, appetite	Moderately obese subjects	?	?	?	?	?	?	?	?	?	2
Preuss et al. 2004 [29]	BW, BMI, lipid profile, appetite	Healthy, obese volunteers	+	?	+	+	?	?	?	?	—	3
Preuss et al. 2004 [6]	BW, BMI, lipid profile, appetite	Healthy, obese volunteers	+	?	?	+	?	?	?	?	—	4
Ramos et al. 1995 [30]	BW, BMI, lipids	Obese subjects	?	?	?	?	?	?	?	?	?	2
Roongpisu- thipong et al. 2007 [2]	BW, BMI, BP, waist-hip ratio	Healthy, overweight volunteers	?	?	+	+	?	?	?	?	—	2
Thom 1996 [31]	BW, BP, total cho-sterol, appetite	Obese subjects	?	?	?	?	?	?	?	?	?	2

<sup>a</sup> Quality assessment checklist adapted from The CONSORT Statement and Jadad criteria [10–12].

TABLE 2: Results table for studies with adequate data for meta-analysis.<sup>b</sup>

Author Year Country	HCA formulation	Randomised/ Analysed	Age in yrs	HCA Dosage	Treatment Duration	Baseline weight indices for HCA/placebo groups	Mean change in weight indices for HCA/placebo groups	Adverse events (AE)	Control for lifestyle factors
Hayamizu et al. 2001 Japan [24]	Tablets	40/40	37.1 ± 12.5 (HCA) 36.5 ± 10.7 (PLA)	1 g daily	8 weeks	BW: 75.6 ± 10.3/73.3 ± 10.7 BMI: 27.9 ± 1.8/27.8 ± 1.8	BW: 0 ± 11.5/0.5 ± 11.7 BMI: 0 ± 1.97/0.3 ± 2.3	No serious AE reported	Dietary control
Heymsfield et al. 1998 U.S.A. [25]	Capsules	135/135	38.6 ± 7.7 (HCA) 39.4 ± 7.2 (PLA)	1.5 g daily	12 weeks	BW: 83.8 ± 10.7/88.2 ± 13.0 BMI: 31.2 ± 2.8/31.9 ± 3.1	BW: -3.2 ± 3.3/-4.1 ± 3.9 BMI: -1.0 ± 1.34	Headache, URTI & GI symptoms	High fibre diet, stable physical activity levels
Kovacs et al. 2001 Netherlands [26]	Unspecified	21/21	43 ± 10 for both HCA&placebo groups	1.5 g daily	2 weeks	Mean BW: 79.3 ± 9.0 Mean BMI: 27.6 ± 2	BW: -0.4 ± 0.9/-0.5 ± 1.4	Not reported	No restriction on food intake; 1 glass of alcohol maximum daily
*§Kovacs et al. 2001 Netherlands [27]	Unspecified	11/11	47 ± 16 for both HCA&placebo groups	1.5 g daily	2 weeks	Mean BW: 85.4 ± 25.8 Mean BMI: 27.4 ± 8.2	BW: -1.5 ± 1.66/ -1.0 ± 1.34	Not reported	No restriction on food intake; 1 glass of alcohol maximum daily
Mattes and Bormann 2000 U.S.A. [5]	Caplets	167/89	40.97 ± 10 (HCA) 44.0 ± 9.5 (PLA)	1.2 g daily	12 weeks	BW: 75.5 ± 10.2/75.8 ± 12.6 BMI: 28.3 ± 0.6/28.8 ± 0.7	BW: -3.7 ± 3.1/-2.4 ± 2.9	Not reported	Dietary control, exercise encouraged, but no formal regimen prescribed
SPreuss et al. 2004 India [29]	Unspecified	60/53	Range: 21–50	2.8 g daily	8 weeks	BW: 91.7 ± 15.7/80.4 ± 36.9 BMI: 34.7 ± 5.5/32.5 ± 2.6	BW: -4.5 ± 16.6/ -1.6 ± 34.1 BMI: -1.7 ± 5.8/-0.7 ± 2.74	Gas, stomach burn, headache, skin rash	Dietary control, walking exercise programme
SPreuss et al. 2004 India [6]	Unspecified	30/29	Range: 21–50	2.8 g daily	8 weeks	BW: 88.5 ± 21.8/87.4 ± 15.9 BMI: 33.6 ± 6.2/34.0 ± 4.5	BW: -5.5 ± 23.7/ -1.4 ± 17.3 BMI: -2.1 ± 6.85/-0.5 ± 4.8	No serious AE reported	Dietary control, walking exercise programme
Ramos et al. 1995 Mexico [30]	Capsules	40/35	35.3 ± 11.8 (HCA) 38.7 ± 12.3 (PLA)	1.5 g daily	8 weeks	BW: 32.6 ± 4.3/33.2 ± 4.4	BW: -4.1 ± 1.8/-1.3 ± 0.9	Nausea, headache	Dietary control
Roongpisu- thipong et al. 2007 Thailand [2]	Sachets	50/42	40.0 ± 10.0 (HCA) 36.0 ± 10.0 (PLA)	Unclear	8 weeks	BW: 69.0 ± 5.0/65.0 ± 5.0 BMI: 27.5 ± 1.0/26.7 ± 2.5	BW: -2.8 ± 0.5/-1.4 ± 0.5 BMI: -0.9 ± 1.0/-0.6 ± 1.0	Not reported	Dietary control

Abbreviations: HCA: Hydroxycitric acid; PLA: Placebo; BW: Body Weight; BMI: Body Mass Index.

<sup>b</sup>Unless otherwise specified, values for age, baseline weight and mean change in weight indices have been reported as means with standard deviations.

\* Studies included as crossover design, otherwise all included trials had parallel-study design.

§ Studies with 3 intervention groups.

TABLE 3: Results of included studies without suitable data for meta-analysis.<sup>P</sup>

Author Year Country	HCA formulation	Randomised/ Analysed	Age in yrs	HCA Dosage	Treatment Duration	Baseline weight indices for HCA/placebo groups	Main Results	Adverse events (AE)	Control for lifestyle factors
Hayamizu et al. 2003 Japan [4]	Tablets	44/39	43.7 ± 11.9 (HCA) 45.2 ± 13.0 (PLA)	1 g daily	12 weeks	BW: 75.1 ± 12.3/ 75.9 ± 11.5 BMI: 28.9 ± 4.7/ 28.5 ± 4.6	No significant differences in BMI or body weight at week 12	Common cold, toothache, diarrhea	Dietary control
Preuss et al. 2002 (abstract) India [28]	Unspecified	48/unclear	Not reported	2.8 g daily	8 weeks	Not reported	4.8% loss in body weight, and 6.8% decrease in BMI for HCA group	Not reported	Diet control, exercise
Thom 1996 (abstract) Norway [31]	Capsule	60/unclear	Not reported	1.32 g daily	8 weeks	Not reported	Significant decrease in body weight in HCA group compared with placebo ( <i>P</i> < .001)	Stomach ache	Low fat diet, exercise

Abbreviations: HCA: Hydroxycitric acid; PLA: Placebo; BW: Body Weight; BMI: Body Mass Index.

<sup>P</sup>Unless otherwise stated, all trials are parallel-study designs.

reported a nonsignificant difference in BMI or body weight between groups [4], another reported a significant difference (*P* < .001) in the HCA group compared with placebo [31]. The third RCT [28] reported a decrease in body weight and (BMI) from baseline for the HCA group, without providing results of intergroup differences.

A forest plot (random effect model) for studies with data suitable for statistical pooling is shown in Figure 2. The meta-analysis reveals a statistically significant difference in body weight between the HCA and placebo groups. The average effect size was, however, small (MD: −0.88 kg; 95% CI: −1.75, −0.00), with a *P* value of .05. This translates to about 1% in body weight loss in HCA group compared with placebo. The *I*<sup>2</sup> statistic suggests that there was considerable heterogeneity amongst the trials, the duration of treatment, and the dosages of HCA used in the different trials varied widely. A funnel plot of mean difference plotted against trial sample size (Figure 3) indicated that most of the studies (which had small sample sizes) were distributed around the mean difference of all the trials.

Sensitivity analyses were performed to test the robustness of the overall analysis. The first included 7 trials [2, 5, 6, 24, 25, 29, 30] with parallel-group design, excluding two studies which were crossover [26, 27]. Meta-analysis of these trials revealed MD of −1.22 kg (95% CI: −2.29, −0.14). Heterogeneity was substantial. A second meta-analysis for studies with parallel group designs and dosage ranges of HCA between 1 and 1.5 g per day [5, 24, 25, 30] did not reveal a significant difference between HCA and placebo; heterogeneity was also substantial in this analysis. A third meta-analysis excluding three studies with outlying data for MD [6, 29, 30] did not reveal a significant difference in weight loss between HCA and placebo, but heterogeneity was considerable. A further meta-analysis of the two trials

with good methodological quality [6, 25] revealed a non-significant difference in weight loss (MD: 0.88 kg; 95% CI: −0.33, 2.10) between HCA and placebo, with *I*<sup>2</sup> value of 0, suggesting that heterogeneity might not be important. Finally, a meta-analysis of the change in BMI for four studies [6, 24, 29, 31] did not reveal any significant difference between HCA and placebo (MD: −0.34 kg; 95% CI: −0.88, 0.20), with *I*<sup>2</sup> value of 0.

One study [2] reported a significant decrease in fat mass in the HCA group compared with placebo (*P* < .05), while two studies [4, 24] reported a significant decrease in visceral, subcutaneous, and total fat areas in the HCA group compared with placebo (*P* < .001). In contrast two other studies [5, 25] found no significant difference in body fat loss between HCA and placebo.

Adverse events reported in the RCTs included headache, skin rash, common cold, and gastrointestinal (GI) symptoms. In most of the studies, there were no major differences in adverse events between the HCA and placebo groups. However, in one trial, GI adverse events were twice as frequent in the HCA group compared with the placebo group [25]. In total, there were 88 drop outs. A further 45 participants were reported to have been excluded from the analysis in one trial [5] because they either took a mixture of HCA and placebo (28), or were males (17).

#### 4. Discussion

The objective of this systematic review was to assess the efficacy and effectiveness of HCA as a weight reduction agent. The overall meta-analysis revealed a small difference in change in body weight between the HCA and placebo groups. The effect is of borderline statistical significance and is no longer significant on the basis of a sensitivity analysis

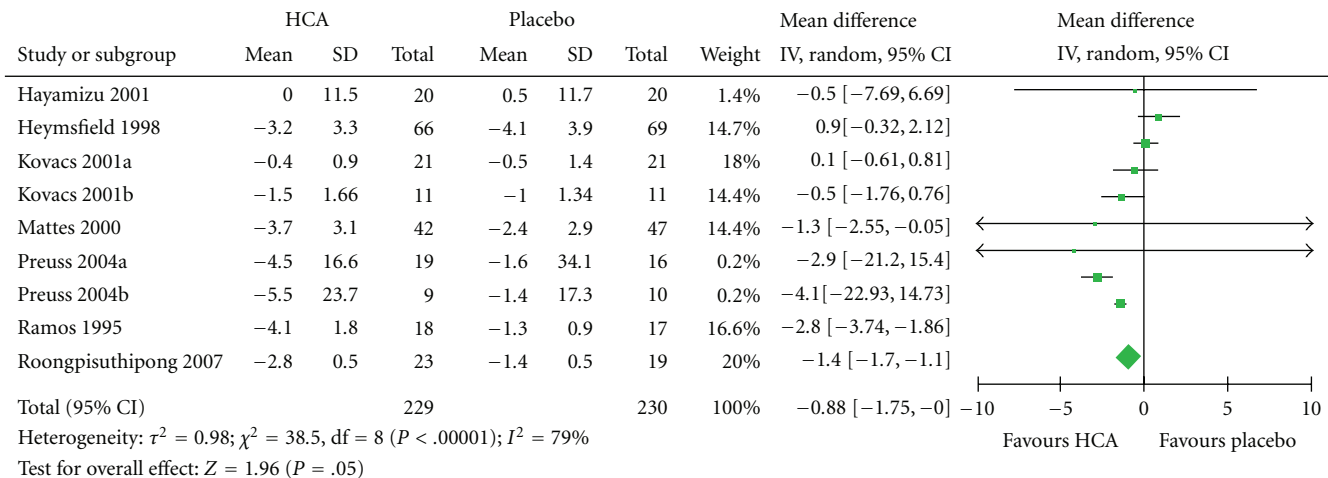


FIGURE 2: Forest plot of comparison showing the effect of hydroxycitrate on body weight. The vertical line represents no difference in weight loss between HCA and placebo.

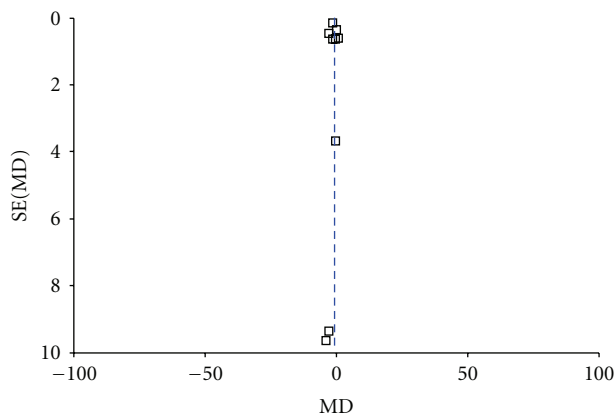


FIGURE 3: Funnel plot of the mean difference in body weight reduction trials of HCA, plotted against sample size. The vertical line depicts the weighted mean difference of all trials.

of rigorous RCTs. Arguably the overall effect size is also too small to be of clinical relevance. The overall meta-analytic result corroborates the findings from one of the studies without suitable data for statistical pooling [31], but is at variance with another study [4].

The overall result should be interpreted with caution. The pooled data from some of the studies were adjusted values. Three studies with small sample sizes [6, 29, 30] seemed to have influenced the overall meta-analytic result in favour of HCA over placebo. If these three trials are excluded, the meta-analysis result is no longer significant. The largest and most rigorous RCT [25] found no significant difference in weight loss between HCA and placebo.

The result of our systematic review corroborates the findings from a previous systematic review of weight loss supplements, which reported that the weight reducing effects of most dietary supplements is not convincing [32]. HCA is a commonly marketed as a complementary weight loss

supplement. The meta-analysis from this systematic review suggests that HCA is not as effective as conventional weight loss pills, for example, orlistat. In a meta-analysis report of 16 studies including over 10 000 participants [33], overweight and obese patients taking orlistat had a clinically significant reduction in body weight compared to placebo (MD: 2.9 kg; 95% CI: 2.5, 3.2). Participants taking orlistat achieved a 5% and 10% weight loss compared to placebo in the results from pooled data. This contrasts quite sharply with the results from the meta-analysis of HCA clinical trials.

All of the studies included in this review had methodological issues, which are likely to have affected the outcomes in these trials. This is supported by the  $I^2$  values from the overall meta-analysis result which suggested substantial heterogeneity. Most of the studies included in this systematic review had small sample sizes. Only one included study [25] reported that they performed a power calculation. Larger study sizes with *a priori* sample size calculation will help eliminate a type II error (i.e., failure to reject the null hypothesis when it should have been rejected). Only one study [25] performed an intention to treat (ITT) analysis, while all the participants in three other studies [24, 26, 27] were reported to have completed the trial. The failure of about 66% of the included studies to report ITT analyses casts a doubt as to the validity of their results. In several of the RCTs, drop-outs/attrition was unclear. In one study [5], participants were excluded due to mixed-pill ingestion (an error in coding of pill bottles resulted in some participants receiving a mixture of HCA and placebo). Male participants were also excluded from the analysis of this RCT because they were too few in number compared with females in the trial. It was also unclear to which intervention group the excluded participants belonged to in this study.

The dosage of HCA, and the duration of study also varied amongst the RCTs. The dosage of HCA used ranged from 1 g to 2.8 g daily. The optimal dose of HCA is currently unknown. Two included studies which differed widely in results [25, 29] also differed widely in dosage of HCA.



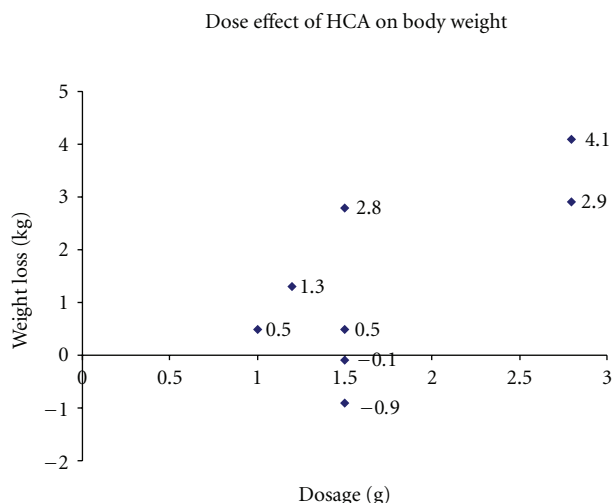


FIGURE 4: Effect of dosage of HCA on body weight. The dosages from included RCTs did not produce a linear effect on body weight.

Though one of these studies claimed the bioavailability of the HCA used in their trial was high [25], the dosage of HCA used was almost twice that used in the other trial [29]. It is not clear if the higher HCA dosage ensures a higher bioavailability of HCA. A nonlinear, significant ( $P < .05$ ) correlation between the dosage of HCA and body weight loss seems to exist (Figure 4). *Garcinia cambogia* was the main source of HCA in most studies, with *Garcinia atroviridis* being the source of HCA in one included study [2]. None of the trials used *Garcinia indica* as an intervention. It is unclear if the strain of *Garcinia* species influences the bioavailability of HCA. Furthermore HCA is also reported to be found in *Hibiscus subdariffa* [8], and none of the studies included in this review used HCA extracted from this plant species. The duration of the studies included in the review also differed, with a range of 2 to 12 weeks, and mode of 8 weeks. This is probably too short a time to assess the effects of HCA on body weight.

There was some variation in the design of the RCTs included in the review. All of the studies included had parallel-study designs except two which were crossover trials [26, 27]. Four included RCTs comprised three intervention groups [6, 26, 27, 29]. None of the included studies indicated whether or not outcome assessors were blinded, and seven studies did not specify the source of funding [2, 4, 6, 24, 28, 29, 31]. The failure of study investigators to adhere strictly to the CONSORT guidelines [10, 11] may have contributed to the variation in methodology (and heterogeneity) of the trials included in the review.

Most (7/12) RCTs reported adverse events, with headache, nausea, upper respiratory, and gastrointestinal tract symptoms being the most frequent ones. In most of the trials, there were no significant differences in adverse events between HCA and placebo. This seems to corroborate the report in another article [34] which suggested that HCA is safe for human consumption. A few of the studies reported a

positive effect of HCA on the blood lipid profile [6, 24, 29–31], while one did not find any significant difference between HCA and placebo on this blood parameter [2]. However, given the short duration of the studies involving the use of HCA, it is unclear how safe this dietary supplement is on the intermediate and long term. In 2009, the Food and Drug Administration (FDA) warned consumers about the potential for serious adverse effects associated with the consumption of hydroxycut, a popular HCA-containing slimming pill. This resulted in the withdrawal of this supplement from the market [35].

All of the studies included in this review except two [26, 27] incorporated some form of dietary control into their trials, with participants in one study receiving high fibre diets [25]. The daily caloric intake for participants in the trials included in this review ranged from as low as 1,000 kcal [2, 30], to as high as 3,009 kcal [27]. Half the number of studies in this review did not institute any form of exercise. The extent to which the variation in these lifestyle adjustment factors could have influenced study results is uncertain. Two studies [28, 31] reported a significant reduction in appetite in the HCA group ( $P < .001$ ), but not with placebo. Three other studies did not find any significant difference between HCA and placebo groups in terms of satiety effect [5, 26, 27].

All of the studies described their participants as overweight, obese, or both. However, in one RCT [2], the definition of the participants as obese individuals is questionable, because they had a BMI between 25–30 kg/m<sup>2</sup>. Based on the World Health Organisation definition [36], a BMI between 25–29 kg/m<sup>2</sup> is considered overweight, while a BMI  $\geq 30$  kg/m<sup>2</sup> is termed obese.

This systematic review has several limitations. Though our search strategy involved both electronic and non-electronic studies, we may not have identified all the available trials involving the use of HCA as a weight loss supplement. Furthermore, the methodological quality of most of the studies identified from our searches is poor, and most studies are of short duration. These factors prevent us from drawing firm conclusions about the effects of HCA on body weight.

## 5. Conclusion

The evidence from RCTs suggests that *Garcinia* extracts/HCA generate weight loss on the short term. However, the magnitude of this effect is small, is no longer statistically significant when only rigorous RCTs are considered, and its clinical relevance seems questionable. Future trials should be more rigorous, longer in duration, and better reported.

## Conflict of Interests

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