Original Article

Reduction of adipose tissue and body weight: effect of water soluble calcium hydroxycitrate in *Garcinia atroviridis* on the short term treatment of obese women in Thailand

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Fifty obese women with a body mass index (BMI) over 25 kg/m^2 were randomly allocated into two groups, 25 in each. Group 1, with a mean (±SEM) age of 40.0±2 years, received water soluble calcium hydroxycitrate (HCA) as *Garcinia atroviridis*. Group 2, with a mean age of 35.6±1.8 years, received placebo. All subjects were recommended a similar diet with 1000 Kcal/day. The trial lasted for 2 months. At baseline the means BMI of Group 1 and Group 2 were 27.5±0.2 kg.m^{-2} and 26.7±0.5 kg.m^{-2}, respectively. Group 1 lost significantly more weight (2.8 vs. 1.4 kg, $p<0.05$) and at a greater rate than Group 2 throughout the study. The decrease in their body weight was due to a loss of fat storage as evidenced by a significant decrease in the triceps skin fold thickness. On a short-term basis, HCA in *Garcinia atroviridis* was an effective for weight management.

Key Words: adipose tissue, obese women, *Garcinia atroviridis*

Introduction

Obesity is a global public health problem. About 315 million people worldwide are estimated to fall into the WHO-defined obesity categories.[1] Traditional herbal medicines may have some potential in managing obesity. Botanical dietary supplements often contain complex mixtures of phytochemicals that have additive or synergistic interactions. (-)-Hydroxy citric acid (HCA) is a principal constituent (10-30%) of the dried fruit rind of *Garcinia cambogia, Garcinia indica,* and *Garcinia atroviridis*, which are indigenous plants of Southeast Asia. The dried rind has been used for centuries throughout this part of the world as a food preservative, flavoring agent and carminative. Extensive experimental studies have shown that HCA inhibits fat synthesis and reduces food intake. However, a few clinical studies have shown contradictory findings.[2,3,4,5] The objective of this study was to evaluate the efficacy and safety of water soluble calcium hydroxycitrate from *Garcinia atroviridis* on the short term treatment of obese women.[6]

Subjects and Methods

A randomized double - blind, placebo - controlled trial study was conducted with 50 obese Thai women. The inclusion criteria were: female between 18 and 75 years old, obese with body mass index (BMI) between 25-30 kg/m^2. Exclusion criteria were diseases of endocrine origin, e.g., hypothyroidism, Cushing's syndrome, type I or type II diabetes, serious systemic or psychiatric illnesses, pregnancy or wishing to become pregnant or lactating women, or having taken drug treatment for obesity during the last 3 months.

The subjects were divided into 2 groups (Group I, n=25, Group II, n=25). Each subject in group I received one HCA sachet before meals, three times daily [HCA sachet contains 1.15 gram of *Garcinia atroviridis*] whereas group II received placebo sachet for 8 weeks. Each sachet was dissolved in water (200 ml) and taken before meals.

The diet was recommended to all patients throughout the study. The energy prescription was approximately 1,000 kcal /day which provided protein, fat, and carbohydrate as 50, 33 and 125 g, respectively.

To assess the efficacy of HCA, monthly body weight, body mass index, waist circumference, waist/hip ratio, handgrip strength, systolic and diastolic blood pressure were measured.

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Anthropometric parameters including Triceps, Biceps, Subscapular and Supra - iliac skinfold thicknesses by Harpenden caliper, body fat by BIA [Body stat 1500 ®] and by TBF-511 [TANITA®] were evaluated every 4 weeks. To assess safety of HCA, hematological, biochemical parameters and serum lipid profiles were measured before and after the program. Each subject was interviewed a questionnaire about compliance and adverse events at each visit.

All the subjects signed informed consent form. The study protocol was approved by the Institutional Review Board prior to the actual experimentation.

Statistical analysis

The statistical analysis was performed concerning efficacy and safety parameters. The results were expressed as rating scores in absolute values or percentage (%) with the mean and standard error of the mean (SEM). The comparisons were made by using Student's t- test operated on SPSS version 12.

Results

Table I shows the characteristics of the 2 groups, Group I (n=25) and Group II (n=25). Two subjects from Group I and six subjects from Group II were excluded because they did not return in the second week and refused the regular contact. There was no significant difference between the means of these 2 groups.The means of body weight and body mass index of Group I at week 4 and 8 decreased significantly from week 0 (p<0.05), whereas that of Group II at week 8 decreased significantly from week 0 (p<0.05). The waist circumference, waist hip ratio, handgrip strength and systolic blood pressure did not change in both groups, except that of the diastolic blood pressure of Group I at week 8 which decreased significantly from week 0 (Table 2). Mean ± SEM for cumulative weight loss after 1 month was 2.3±0.1 kg in Group I, and 0.5 ± 0.1 kg in Group II, respectively. The mean of the additional weight loss of 1.8 kg seen in Group I was highly significantly different (p<0.05) from that of Group II but in the second month there was no difference in the mean of the additional weight loss between the two groups. Significance of the difference between Group I and Group II of the difference from baseline at week 4 and 8 of body weight and body mass index was showed in Table 2. For the body composition measured by Harpenden caliper, Group I showed a gradual decrease in Triceps skinfold thickness at week 8. Significance of the difference between Group I and Group II of the difference from baseline at week 4 and 8 of the skinfold thicknesses of Biceps skinfold, Subscapular skinfold, Supra iliac creast skinfold, and upper arm circumference was showed in Table 3. The skinfold thicknesses of Biceps skinfold, Subscapular skinfold, Supra iliac creast skinfold, and upper arm circumference in Group I at week 4 and 8 decreased significantly from those at week 0. Subscapular and Supra iliac creast skinfold thicknesses at week 8 were significantly decreased from those at week 4. However, there was no significant change in the mid upper arm circumference of both groups (Table 3).

Table 1. Characteristics and anthropometry of obese women. (Mean ± SEM)

Parameters	Group I (HCA)	Group II (Placebo)
No of patients	23	19
Age (yr)	40 ± 2	36 ± 2
Height (cm)	158 ± 1	157 ± 1
Initial weight (kg)	69 ± 1	65 ± 1
Body mass index (kg/m^2)	27.5 ± 0.2	26.7 ± 0.5
Waist/hip ratio	0.8 ± 1.4	0.8 ± 1.5
Triceps skinfold thickness (cm)	38.6 ± 0.9	37.8 ± 0.8
Biceps skinfold thickness (mm)	28.2 ± 1.1	21.4 ± 0.9
Supscapular skinfold thickness (mm)	41.2 ± 1.3	35.1 ± 1.7
Suprailiac creast thickness (mm)	34.1 ± 1.3	29.7 ± 1.5
Upper arm circumference (cm)	30.6 ± 0.3	29.9 ± 0.4
Mid upper arm muscle circumference(cm)	18.7 ± 0.4	18.1 ± 0.3

Table 2. Mean ± SEM Actual change of body weight , body mass index and blood pressure.

Parameters	Group I	Group II
Body weight (kg)		
week 0-4	2.3 ± 0.1 [a]	0.5 ± 0.1*
week 4-8	0.5 ± 0.1	0.9 ± 0.1
week 0-8	2.8± 0.1[a]	1.4± 0.1*[a]
Body mass index (kg/m^2)		
week 0-4	0.8± 0.2[a]	0.3± 0.2*
week 4-8	0.1± 0.2	0.3± 0.2
week 0-8	0.9± 0.2 [ab]	0.6± 0.2* [a]
Diastolic BP (mmHg)		
week 0-4	3.0±0.8	2.0±0.8
week 4-8	1.0±0.8	-1.0±0.8
week 0-8	4.0±0.8[a]	1.0±0.8

* Significant difference from Group I, at p<0.05
[a] Significant difference from wk 0 at p<0.05

Table 3. The difference from baseline of triceps, biceps, subscapular and supra iliac crest skinfold thickness, upper arm circumference and midupper arm muscle circumference of both groups during the study

Parameters	Wk.	Group I	Group II
Triceps skinfold thickness (cm)	4	1.3 ± 0.1	0.4 ± 0.1
	8	1.7 ± 0.1	1.9 ± 0.1
Biceps skinfold thickness (mm)	4	4.7 ± 1.0[*a]	0.7 ± 0.1
	8	6.8 ± 1.0 [*a]	1.3 ± 0.1
Supscapular skinfold thickness (mm)	4	2.5 ± 0.3 [a]	0.9 ± 0.1
	8	4.6 ± 1.0 [*ab]	1.3 ± 1.7
Suprailiac creast thickness (mm)	4	3.4 ± 0.2[*a]	0.5 ± 0.4
	8	6.3 ± 0.3 [*ab]	0.7 ± 0.2
Upper arm circumference (cm)	4	0.4 ±0.1[*a]	-0.1 ± 0.1
	8	0.6 ± 0.1[*a]	0.2 ± 0.1
Mid upper arm muscle circumference(cm)	4	0.4 ± 0.1	0.1 ± 0.1
	8	0.3 ± 0.1	0.1 ± 0.1

[*] Significant difference from Group II at p <0.05
[a] Significant difference from wk 0 at p <0.05
[b] Significant difference from wk 4 at p <0.05

The body composition measured by BIA (Body stat 1500) showed a significant change only in Group I. The percentage of the body fat and the body fat in kilogram at week 8 decreased significantly from those at week 0 and week 4 (p<0.05). The percentage of the lean body mass and the body water at week 8 were significantly increased from week 0 (p<0.05) The percentage of the lean body mass in kilogram and the body water in litre at week 8 were significantly increased from week 4 (p<0.05). There was no significant change in the basal metabolic rate of both groups. The body fat measured by Tanita (TBF-511) showed a significant change only in Group I.The body fat at week 4 and 8 decreased significantly from week 0 (p<0.05) (Table 4).

Table 4. Mean ± SEM of body composition measured by BIA [Body stat 1500] and Tanita.

Parameters	wk	Group I	Group II
1. Body fat (%)	0	43.3 ± 1.7	36.1 ± 2.6
	4	43.1 ± 1.4	32.0 ± 1.5
	8	38.4±1.7[ab]	31.4 ± 1.6
Body fat (kg)	0	30.2 ± 1.3	23.6 ± 1.7
	4	28.6 ± 0.9	20.7 ± 0.9
	8	25.3 ± 1.1[ab]	22.1 ± 2.2
2. Lean body mass (%)	0	56.7 ± 1.7	63.9 + 2.6
	4	56.9 ± 1.4	68.1 ± 1.5
	8	61.7 ± 1.8 [ab]	68.7 ± 1.6
Lean body mass (kg)	0	39.2 ± 1.4	41.9 ± 2.0
	4	38.1 ± 1.3	41.3 ± 1.4
	8	40.5 ± 1.6[b]	41.4 ± 2.7
3. Body water (%)	0	40.8 ± 1.5	47.4 ± 2.2
	4	41.2 ± 1.3	51.2 ± 1.4
	8	45.6 ± 1.4 [a]	51.3 ± 1.1
Body water (liter)	0	28.6± 1.2	31.2 ± 1.4
	4	27.5 ± 0.9	34.0 ± 1.2
	8	30.3 ± 1.2[b]	33.3 ± 0.8
4. Basal metabolic rate (kcal/d)	0	1291 ± 62	1412 ± 43
	4	1319 ± 31	1442 ± 27
	8	1386 ± 38	1437 ± 32
5.Body fat (kg) by Tanita	0	40.9 ± 0.9	39.3 ± 1.1
	4	39.3 ± 1.0[a]	38.7 ± 1.2
	8	39.6 ± 1.1[a]	38.3 ± 1.3

[a] Significant difference from wk 0 at p<0.05
[b] Significant difference from wk 4 at p<0.05

The serum total cholesterol and HDL cholesterol did not change in each group except for the triglyceride level in Group I, at week 8, which was significantly decreased from the baseline (Table 5).

Biochemical parameters of fasting blood glucose, total protein, albumin, total bilirubin, direct bilirubin, serum AST, serum ALT, alkaline phosphatase, uric acid, urea nitrogen, creatinine, calcium, phosphorus, electrolytes and hematological parameters of each group before and after treatment were within normal limits (data not shown).

The 24-hour diet recall showed that the total energy intake of Group I at week 4 and 8 decreased significantly from week 0, and at week 8 increased significantly from week 4 (p<0.05), whereas in Group II at week 8 it decreased significantly from week 0 (p< 0.05). The total protein and the total fat intake of Group I at week 4 and 8 decreased significantly from week 0, whereas the total protein of Group II at week 8 decreased significantly from week 4 (p<0.05). There was no significant change of the total carbohydrate intake of Group I, whereas that of Group II at week 8 decreased significantly from week 0 (p<0.05)（Fig 1）.

Table 5. Mean ± SEM of total cholesterol, triglyceride and HDL during the study of both groups

Lipid profiles	Wk	Group I	Group II
1. Total cholesterol (mg/dL)	0	205.0± 9.0	207.9 ± 8.5
	4	198.4 ± 6.5	200.2 ± 13.6
	8	195.0 ± 8.3	199.2 ± 9.1
2. Serum triglycerides (mg/dL)	0	124.9 ± 11.4	86.5 ± 8.3
	4	101.5 ± 7.4	97.9 ± 7.5
	8	96.0 ± 7.8[a]	90.1 ± 7.2
3. Serum HDL (mg/dL)	0	48.6 ± 2.6	58.2 ± 3.2
	4	49.1 ± 2.6	51.3 ± 3.8
	8	50.1 ± 2.9	55.1 ± 2.8

Discussion

We have examined whether dietary supplementation of hydroxycitrate (HCA), a competitive inhibitor of the extramitochondrial enzyme ATP-citrate-lyase, where extensive animal studies[7] have indicated that (-)-HCA suppresses the fatty acid synthesis and lipogenesis, could suppress food intake and induce weight loss. In our study we found that cumulative weight loss of Group I decreased significantly from that of Group II (Table 3). The subcutaneous fat mass of trunkcal , Biceps skinfold and the body fat mass of Group I decreased significantly from those in Group II, as measured by the Harpenden caliper, BIA (Body stat 1500) or Tanita (TBF-511) (Tables 4, 5). These were correlated with the reduced dietary intake of the total calorie, protein and fat intake. The primary mechanism of action of HCA appears to be related to its ability to act as a competitive inhibitor of the enzyme ATP-citrate lyase, which catalyzes the extramitochondrial cleavage of citrate to oxaloacetate and acetyl-CoA: citrate + ATP + CoA → acetyl-CoA + ADP + P (i) + oxaloacetate. The inhibition of this reaction limits the availability of acetyl-CoA units required for fatty acid synthesis and lipogenesis. *Ohia et al* [8,9] have demonstrated a mechanism of appetite suppression of hydroxycitrate which can inhibit [3H]-5-HT uptake (and also increase 5-HT availability) in isolated rat brain cortical slices in a manner similar to that of SRRIs, and thus may prove beneficial in controlling appetite, as well as in treatment of depression, insomnia, migraine headaches and other serotonin-deficient conditions.

The body weight and body mass index of Group II decreased significantly from those of week 0 which were seen later at week 8 and could not be differentiated from which compartment of the body composition decreased. Dietary intake of total energy and carbohydrate of the placebo group showed a gradual decease and at week 8 they decreased significantly from week 0 (p<0.05) whereas protein intake at week 8 decreased significantly from week 4.

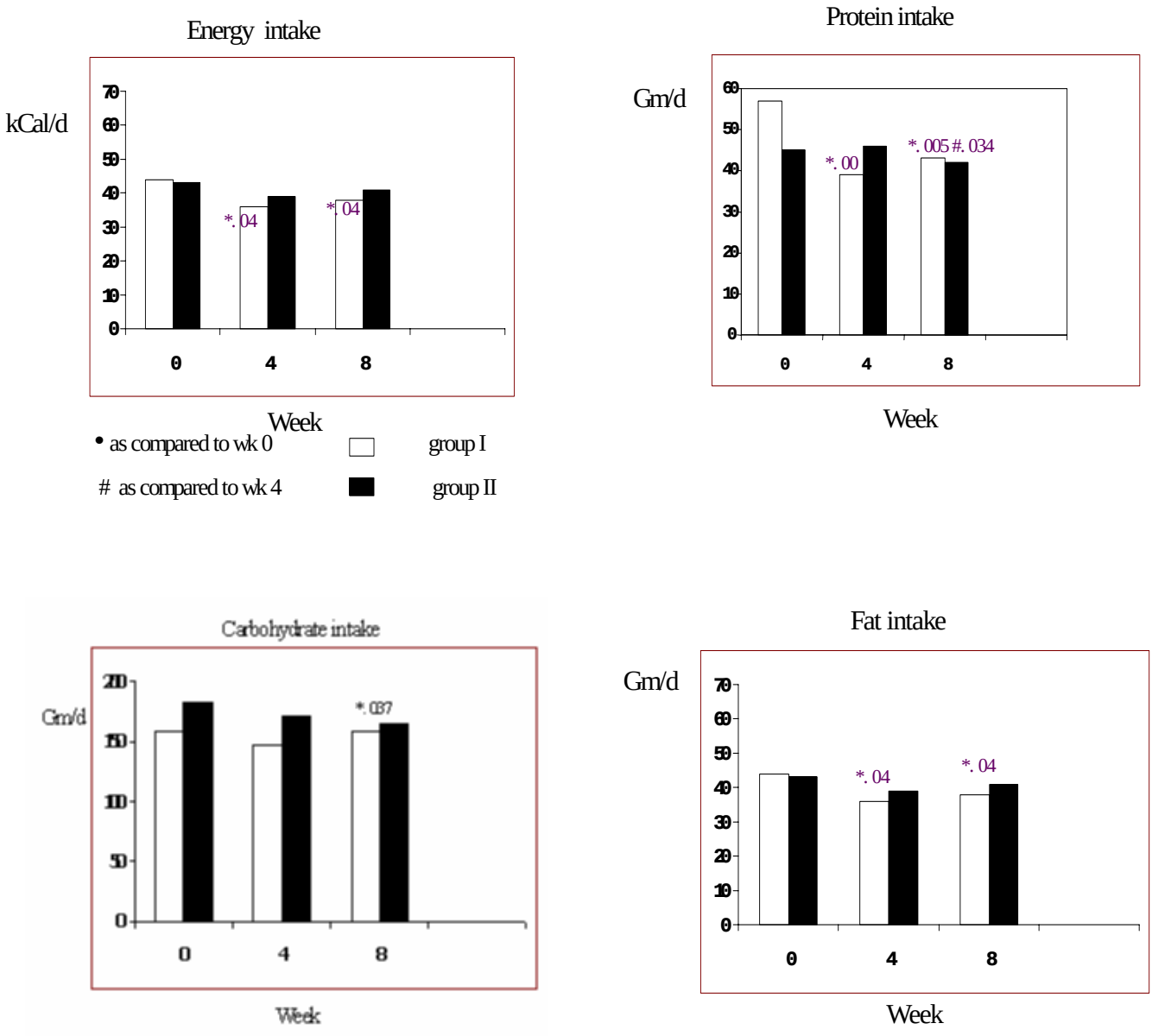

Figure 1. Mean ± SEM of energy, protein, carbohydrate and fat intake during the study of both groups.

The mid upper arm muscle circumference was maintained throughout the study in both groups. Only Group I demonstrated an increase in the lean body mass and the body water. Decreased diastolic blood pressure in Group I may be from lower body weight than that of group II.

Although the inhibition of reaction enzyme ATP-citrate-lyase limits the availability of acetyl-CoA units required for fatty acid synthesis and lipogenesis, primary building blocks of fatty acid and cholesterol synthesis, the lipid profiles of serum cholesterol level of Group I and Group II were not significantly changed from the beginning as well as those blood chemistry and hematological tests.

HCA is safe and effective in lowing the body weight [10] of an obese female but this was clearly seen only during the first 4 weeks (Table 3, Fig 1). In the second 4 weeks the mean ± SEM weight loss was not different between the HCA group and the placebo group. The dietary intake also showed a tendency to increase the total energy, protein, carbohydrate and fat intake in the HCA group.

Although HCA is a safe and effective agent, its application for the long-term treatment of obesity needs further investigations.

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Original Article

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藤黃果中水溶性烴化檸檬酸鈣對泰國肥胖女性的短期治療效果：脂肪組織與體重的降低

將 50 名身體質量指數(BMI)超過 25kg/m^2 的肥胖女性隨機分配成兩組，每組各 25 人。第一組，平均年齡(±SEM)為 40.0±2 歲，接受含有水溶性烴化檸檬酸鈣(HCA)的藤黃果。第二組，平均年齡為 35.6±1.8 歲，接受安慰劑。所有研究對象均建議攝取相同熱量的飲食，每日約 1000 大卡。這個試驗持續兩個月。在基線時第一組跟第二組平均 BMI 分別為 27.5±0.2 kg/m^2 及 26.7±0.5kg/m^2。整個研究期間，與第二組比較，第一組顯著降低較多體重(2.8 vs. 1.4 kg, p<0.05)，並且速度較快。由三頭肌皮層厚度顯著的減少可以證明他們體重的減輕是由於儲存脂肪的流失。藤黃果中的 HCA 對體重管理有短期的效果。

關鍵字：脂肪組織、肥胖女性、藤黃果。