

## SHORT COMMUNICATION

# The effect of (–)-hydroxycitrate on energy intake and satiety in overweight humans

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**OBJECTIVE:** Assessment of the effects of 2 weeks of daily administration of HCA on energy intake and satiety in overweight men and women.

**DESIGN:** A 6-week randomized placebo-controlled single-blinded cross-over trial. Subjects consumed three times daily for 2 weeks 100 ml tomato juice (placebo) and, separated by a 2 week wash-out period, 100 ml tomato juice with 300 mg HCA.

**SUBJECTS:** Twelve males and 12 females (body mass index  $27.5 \pm 2.0$  kg/m<sup>2</sup>; age  $37 \pm 10$  y).

**MEASUREMENTS:** After 2 weeks, 24 h energy intake (EI), appetite profile, hedonics, mood and possible change in dietary restraint were assessed in the laboratory restaurant. Prevention of degradation and bio-availability was documented.

**RESULTS:** Twenty-four-hour EI was decreased by 15–30% ( $P < 0.05$ ) with HCA treatment compared to placebo, without changes in the appetite profile, dietary restraint, mood, taste perception and hedonics, while body weight tended to decrease ( $P = 0.1$ ).

**CONCLUSION:** HCA treatment reduced 24 h EI in humans while satiety was sustained.

*International Journal of Obesity* (2002) **26**, 870–872. doi:10.1038/sj.ijo.0801979

**Keywords:** obesity; *Garcinia cambogia* (–)-hydroxycitrate; satiety; energy intake regulation; humans

Obesity is a medical condition associated with a relatively high rate of morbidity, if it remains untreated.<sup>1</sup> Weight control methods often produce short-term success, but sustained weight maintenance is difficult to attain.<sup>2–4</sup> Moreover, the increasing prevalence of obesity<sup>5</sup> requires preventive treatments of obesity. Substances that reduce energy intake without a major reduction in satiety would prove to be useful. We therefore investigated the potential of (–)-hydroxycitrate (HCA) in overweight men and women. HCA is an ingredient extracted from the rind of the fruit *Garcinia cambogia*, a native species from India, and is promoted as a weight loss agent. HCA is an inhibitor of ATP-citrate lyase, a cytosolic (extramitochondrial) enzyme that catalyses the cleavage of citrate to oxaloacetate and acetyl-CoA.<sup>6–8</sup> Limitation of acetyl-CoA for lipid synthesis during carbohydrate feeding results in increased hepatic glycogen synthesis, which might result in reduction of energy intake.<sup>9,10</sup> Results on the effects of HCA on appetite and

body weight regulation in humans showed positive<sup>11</sup> and negative<sup>12,13</sup> outcomes. In this study we assessed the efficacy of HCA with respect to energy intake and satiety, hypothesizing that, when HCA is effective in reducing energy intake, satiety is sustained.

Twenty-four healthy, overweight, dietary unrestrained<sup>14,15</sup> subjects: 12 males and 12 females (body mass index (BMI)  $27.5 \pm 2.0$  kg/m<sup>2</sup>; age  $37 \pm 10$  y) were enrolled for the trial. The Medical Ethics Committee approved of the protocol, and all subjects signed informed consent forms. During the single-blinded, randomized and placebo-controlled study, subjects consumed HCA or placebo during 2 weeks as drinks, three times per day. Before and after 2 weeks they came for 24 h energy intake, satiety and body weight assessment to the laboratory.

The drinks consisted of either 100 ml tomato juice alone or 100 ml tomato juice with HCA—500 mg SuperCitri-max/100 ml tomato juice (ie 300 mg (–)-hydroxycitrate HCA from 500 mg SuperCitrimax HCA 600 SGX dissolved). The composition of Citrimax HCA 600 SGX is 58.7% HCA, 11% calcium, 16% potassium, 1% moisture; the rest is carbohydrate and fat (EuroChem Feinchemie GmbH, München, Germany). Thus the dosage was 900 mg HCA/day. Prevention of degradation was confirmed by an efficacy

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Received 13 August 2001; accepted 17 October 2001

study in rodents, using HCA from the same batch, showing consistent positive results twice, also 3 months after our study was finished.<sup>16</sup> Water solubility and pH level mainly determine the bio-availability. A compound complexed with calcium and potassium is nearly 100% soluble and creates a pH level favourable for gastrointestinal absorption. Bio-availability of HCA in humans was checked by analysing the concentration of HCA in plasma.<sup>17</sup> HCA was analysed with a concentration gradient of NaOH, starting with 0.5 mM NaOH during 2.5 min, followed by subsequent linear concentration gradients of 0.5–5 mM NaOH during 3.5 min, and 5–38.25 mM NaOH during 12 min (Dionex DX 500 chromatography system; IonPac AS 11 column 4.6×250 mm, Dionex, Sunnyvale, California, USA; flow rate 2 ml/min). Ingestion of a single dose of HCA resulted in maximal plasma HCA concentration of 1.4%,<sup>17</sup> 60–90 min after ingestion, thereafter decreasing linearly to zero over at least 3 h.<sup>17</sup> Thus we instructed the subjects to take the drinks 1 h before lunch and dinner, and a drink 2 h after dinner, to prevent snacking in the evening.

After the 2 weeks, food intake was assessed in the laboratory restaurant, and analysed using the Dutch food composition table (Stichting Nederlands Voedingsstoffenbestand<sup>18</sup>) and the accessory computer program (Becel Nutrition Program<sup>18</sup>). Twenty-four-hour energy intake, body weight, scores on appetite profile, mood, taste perception, hedonics, and dietary restraint (mean ± s.d.) were tested for significant differences between the HCA and placebo treatments, using two-factor ANOVA repeated measures (STATVIEW + GRAPHICS; Abacus Concepts Inc., Berkeley, CA, USA); statistical significance was set at  $P < 0.05$ .

Twenty-four-hour energy intake on the test-day after 2 weeks of treatment with HCA was significantly reduced compared to placebo, mainly due to a significant decrease in snack intake (Table 1), with a tendency to a decrease in body weight of 0.5 kg ( $P = 0.1$ ; Table 2). On the test-day, the appetite profile, changes in dietary restraint, taste perception, hedonics or mood did not differ with the HCA treatment compared to placebo. Reported compliance to the drinks was 90% on average, without complaints or negative effects.

In this randomized placebo-controlled crossover design, (-)-hydroxycitrate, consumed three times daily (300 mg

**Table 2** Subject characteristics before and after 2 weeks of treatment with 300 mg (-)-hydroxycitrate/100 ml tomato juice, three times daily, or 2 weeks with placebo (100 ml tomato juice, three times daily)<sup>a</sup>

	Before treatment	After treatment
Age (y)	37 ± 11	
Placebo (n = 24)		
Body weight (kg)	85.2 ± 12	85.2 ± 11
Body mass index (kg/m <sup>2</sup> )	27.2 ± 2.8	27.2 ± 2.8
Hydroxycitrate (n = 24)		
Body weight (kg)	84.2 ± 12	83.7 ± 11
Body mass index (kg/m <sup>2</sup> )	26.9 ± 2.8	26.7 ± 2.7

<sup>a</sup>(Mean ± s.d.); n = 24 (12 men and 12 women).

dissolved in tomato juice) for 2 weeks by overweight males and females, showed a significant reduction in 24 h energy intake, while satiety was sustained. The fact that the main energy intake reduction took place between meals might indicate that HCA works by increasing fat oxidation (inhibiting malonyl-CoA synthesis, thus stimulating carnitine palmitoyl transferase activity) since fat is oxidized after protein and carbohydrate, thus later during the intermeal interval.<sup>15</sup> During this interval satiety might be sustained by increased fat oxidation and ketone body formation. We also observed a tendency toward reduction in body weight with HCA compared to placebo, but the treatment period may have been too short to result in a significant body weight loss. Our results are in line with results from a recent study by Mattes and Bormann,<sup>11</sup> reporting a larger body weight loss in subjects using HCA for 12 weeks, compared to placebo. Reasons for the controversial results reported on HCA, may be possible degradation and bio-availability of the HCA used, which we controlled for, and timing of HCA administration according to the peak level of HCA in plasma. Also the number of obese subjects, as in the study by Heymsfield *et al*<sup>12</sup> who report a negative result, may be a reason, since resistance to HCA in obese rats was shown.<sup>19</sup>

Summarizing, we showed that daily administration of a relatively low dosage of HCA (900 mg/day), during 2 weeks, reduced energy intake in overweight subjects, while satiety was sustained. HCA might not primarily be a weight loss agent, as indicated by the minor changes observed in body weight, but might be effective in preventing weight (re)gain in humans.<sup>20</sup>

## Acknowledgements

This study was financially supported by Novartis Consumer Health Ltd (Nyon, Switzerland) and by Novartis Pharma (Basel, Switzerland, and Summit, NJ, USA).

## References

- 1 National Institutes of Health Consensus Developments Panel on the Health Implications of Obesity. Health Implications of obesity. *Ann Intern Med* 1985; 103: 1073–1077.

**Table 1** Twenty-four-hour energy intake (EI) in MJ on the test-day at the end of 2 weeks with 300 mg (-)-hydroxycitrate/100 ml tomato juice, three times daily; or 2 weeks with placebo (100 ml tomato juice, three times daily)<sup>a</sup>

	Placebo (n = 24)	HCA (n = 24)
24 h EI	9.4 ± 2.2	7.0 ± 2.1*
EI at breakfast	1.0 ± 0.6	0.8 ± 0.8
EI at lunch	3.1 ± 2.5	2.0 ± 1.9
EI at dinner	2.7 ± 1.2	2.5 ± 0.5
EI between meals	2.7 ± 1.9	1.6 ± 1.5*

<sup>a</sup>(Mean ± s.d.); n = 24 (12 men and 12 women).

\* Significantly different from placebo;  $P < 0.05$ .

- 2 Pasma WJ, Rössner S, Westerterp-Plantenga MS, Saris WHM. Body weight changes after treatment of obesity or pregnancy. In: Westerterp-Plantenga MS, Steffens A, Tremblay A (eds). *Regulation of food intake and energy expenditure*. EDRA, Medical Publishing and New Media: Milan; 1999. pp 269–284.
- 3 Westerterp-Plantenga MS, Kempen KP, Saris WHM. Determinants of weight maintenance in women after diet-induced weight reduction. *Int J Obes Relat Metab Disord* 1998; 22: 1–6.
- 4 Pasma WJ, Saris WHM, Westerterp-Plantenga MS. Predictors of weight maintenance. *Obes Res* 1999; 7: 43–50.
- 5 Kuczmarski RJ, Flegal M, Campbell SM, Johnson CL. Increased prevalence of overweight among US adults. The National Health and Nutrition examination surveys, 1960–1991. *JAMA* 1994; 272: 205–211.
- 6 Watson JA, Fang M, Lowenstein JM. Tricarballylate and hydroxycitrate: substrate and inhibitor of ATP: citrate oxaloacetate lyase. *Arch Biochem Biophys* 1969; 135: 209–217.
- 7 Sullivan AC, Hamilton JG, Miller ON, Wheatley VR. Inhibition of lipogenesis in rat liver by (-)-hydroxycitrate. *Arch Biochem Biophys* 1972; 150: 183–190.
- 8 Szutowicz A, Stepień M, Lysiak W, Angielski S. Effect of (-)-hydroxycitrate on the activities of ATP citrate lyase and the enzymes of acetyl-CoA metabolism in rat brain. *Acta Biochim Pol* 1976; 23: 227–234.
- 9 Hellerstein MK, Xie Y. The indirect pathway of hepatic glycogen synthesis and reduction of food intake by metabolic inhibitors. *Life Sci* 1993; 53: 1833–1845.
- 10 Melanson KJ, Westerterp-Plantenga MS, Campfield LA, Saris WHM. Appetite and blood glucose profiles in humans after glycogen-depleting exercise. *J Appl Physiol* 1999; 87: 947–954.
- 11 Mattes RD, Bormann L. Effects of (-)-hydroxycitric acid on appetitive variables. *Physiol Behav* 2000; 71: 87–94.
- 12 Heymsfield SB, Allison DB, Vasselli JR, Pirotbelli A, Greenfield D, Nunez C. *Garcinia cambogia* (hydroxycitric acid) as a potent antiobesity agent. *JAMA* 1998; 280: 1596–1600.
- 13 Kovacs EMR, Westerterp-Plantenga MS, Saris WHM. The effect of ingestion of (-)-hydroxycitrate and (-)-hydroxycitrate combined with medium-chain triglycerides on appetite, energy expenditure and body weight. *Int J Obes Relat Metab Disord* 2001; 25: 1087–1094.
- 14 Stunkard AJ, Messick S. The three-factor eating questionnaire to measure dietary restraint, disinhibition, and hunger. *J Psychosom Res* 1985; 29: 71–83.
- 15 Westerterp-Plantenga MS, Rolland V, Wilson SAJ, Westerterp KR. Satiety related to 24 h diet-induced thermogenesis during high protein/carbohydrate vs high fat diets measured in a respiration chamber. *Eur J Clin Nutr* 1999; 53: 495–502.
- 16 Leonhardt M, Hrupka B, Langhans W. Effect of hydroxycitrate on food intake and body weight regain after food restriction in male rats. *Physiol Behav* 2001; 74: 191–196.
- 17 Loon L van, Rooijen JJM van, Niesen B, Verhagen H, Saris WHM, Wagenmakers AJM. Effects of (-)-hydroxycitrate supplementation on substrate metabolism at rest and during exercise in humans. *Am J Clin Nutr* 2000; 72: 1445–1450.
- 18 Stichting Nederlands Voedingsstoffenbestand. *Nevo Tabel Voorlichtingsbureau voor de voeding*: Den Haag, 1996.
- 19 Greenwood MRC, Cleary MP, Gruen R, Blasé D, Stern JS, Triscari J, Sullivan AC. Effect of (-)-hydroxycitrate on development of obesity in the Zucker obese rat. *Am J Physiol* 1981; 240: E72–78.
- 20 Kovacs EMR, Westerterp-Plantenga MS. Does (-)-hydroxycitrate reduce *de novo* lipogenesis? *Int J Obes Relat Metab Disord* 2001; 25: S127.



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