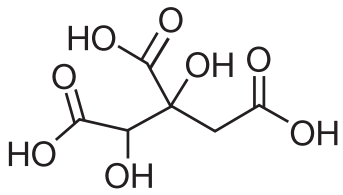
Structure/Function Substantiation

# (-)(-) Hydroxycitric Acid (HCA)

## BRIEF BACKGROUND




HCA is widely used as a popular dietary supplement ingredient for weight loss. **(-)(-) Hydroxycitric Acid** (HCA) extracted from the rind of ***Garcinia Cambogia*** has been extensively researched and is believed to have beneficial effects related to weight loss by **reducing appetite**, **increasing fat metabolism**, **decreasing glycogen utilization**, and **lowering LDL cholesterol levels**. [1]

Several publications have reported the efficacy of HCA in weight management [2-6]. HCA has been reported to reduce appetite, contribute to weight loss in humans by inhibiting fat synthesis without stimulating the central nervous system [7] and has been reported to reduce food intake in experimental animals, suggesting its role in weight reduction [8-12]. Additionally, HCA is believed to **enhance exercise performance** by increasing fat oxidation [8] and **improve mood** (related to overeating) by increasing bioavailability of serotonin [13].

## MECHANISM OF ACTION

HCA is a competitive inhibitor of the enzyme ATP citrate-lyase, an extra-mitochondrial enzyme which is involved in the initial steps of *de novo* lipogenesis in the body. [8-12]. Consequently, HCA reduces the transformation of citrate into acetyl coenzyme A, a step necessary for the formation of fatty acids in the liver. In addition, there is an increased production of hepatic glycogen in the presence of HCA, which may activate glucoreceptors leading to a sensation of fullness and reduced appetite. [10,12] The increased bioavailability of serotonin is thought to be related to appetite suppressing effects of supplemental HCA [13]. Another possible mechanism of action may be HCA's ability to down-regulate Leptin, an amino acid hormone that influences obesity and body weight. [14-16].

## CLINICAL RESEARCH

Clinical studies to evaluate the safety and efficacy of HCA over a perior of eight weeks were conducted in 60 human volunteers. Subjects were given a 2,000 kCal daily diet, participated in a 30 minute walking exercise programs 5 days per week, and given an oral dose of placebo or 4,666.7mg 60% HCA (providing 2,800 mg HCA) in three equally divided doses 30 to 60 minutes before meals. Body weight, BMI, lipid profiles, serum leptin, serotonin and excretion of urinary fat metabolites were determined at 0, 4 and 8 weeks of treatment. At the end of 8 weeks, body weight and BMI decreased by 5.4% and 5.2% respectively. Food intake, total cholesterol, LDL, triglycerides and serum leptin levels were significantly reduced, while HDL and serotonin levels, and the excretion of urinary fat metabolites (a biomarker of fat oxidation) significantly increased. Improvement of BMI indicates sparing of lean muscle and burning fat, as demonstrated by enhanced excretion of urinary fat metabolites. No significant adverse effects were reported. These results demonstrate the safety, bioavailability and efficacy of HCA in weight management. [1]

In contrast, a twelve week, double-blind, placebo-controlled trial of 135 overweight individuals, who were given either a placebo or 500mg of 50% HCA three times daily, found no effect on body weight or fat mass [17]. However, this study has been criticized for using a high-fiber diet, which is thought to impair HCA absorption. Additionally, the concentration of HCA and the daily dose was significantly less than the aforementioned study. At this time, there is a lack of high-quality human trials supporting the efficacy of HCA for any indication other than weight loss and exercise performance.

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## SAFETY CONCERNS

***Garcinia Cambogia***, from which HCA is extracted, is a traditional food and flavoring in Southeast Asia. No serious side effects have been reported from animal or human studies involving either fruit extracts or the concentrated (-)(-) Hydroxycitric acid extracted from the rind of the fruit. HCA has undergone considerable formal safety study, without the evidence of toxicity appearing [1, 8, 10-13]. HCA does not cause nervousness, rapid heart rate, high blood pressure, or insomina symptoms that are often associated with dietary supplements such as ephedra, caffeine or phenylpropanolamine [18] . HCA has been well tolerated for up to 12 weeks in available human trials, and is regarded as safe in recommended doses. Maximum safe doses have not been established, especially for pregnant or nursing women, young children, or individuals with severe liver or kidney disease. HCA may lower blood sugar levels [7]. Caution is advised in patients with diabetes or hypoglycemia, or those taking medications or supplements that affect blood sugar.

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