Section 3: Appetite Suppression

Overview

A recent human trial of 30 obese subjects over eight weeks in India, showed that supplementation with 2800mg/day of HCA reduced food intake by 4% and body weight and BMI by 6.3%. This trial suggests that HCA may work better when administered with niacin bound chromium and extract of Gymnema sylvestre.

Previous tests to establish the appetite suppressing effects of HCA found that a single large oral dose or two divided oral doses totalling one-seventh the size of the single dose resulted in a 10% or greater reduction in food consumption in experimental animals fed a high sugar diet. This result continued over many weeks with the chronic ingestion of HCA.

The appetite control mechanism of HCA does not involve any conditioned aversion to food, i.e., HCA does not alter taste, cause gastric illness or distress, etc. Rather the primary control appears to stem from the increased production of glycogen and /or stimulation of glucoreceptors in the liver, either of which results in early satiety through signals sent to the brain via the vagus nerve. High fat diets and excess alcohol consumption may reduce the lipogenesis-inhibiting and appetite suppressing effects of HCA.

Further evidence is now emerging from *in vitro* studies to support the theory that HCA can inhibit [^{3}H]-5-HT uptake in rat brain cortex. [^{3}H]-5-HT is a neurotransmitter implicated in the regulation of eating behaviour and appetite control. The inhibition of [^{3}H]-5-HT uptake (and also increase 5-HT availability) in isolated rat cortical slices in a manner similar to that of SSRIs (Serotonin Receptor Reuptake Inhibitors) may prove beneficial in controlling appetite.

The Indian study also showed that HCA supplementation reduced serum leptin levels by 36.6%. Leptin is a protein hormone encoded by the obesity regulatory gene. It is synthesised by adipocytes (fat cells) and is present in the blood in amounts related to the amount of fat in the body. Leptin acts primarily on the brain where it binds to receptors and activates signals that inhibit food intake and increase energy expenditure. When plasma leptin levels increase, "leptin resistance" develops, i.e. leptin loses it's ability to inhibit food intake and increase energy expenditure. The authors hypothesise that the calcium-potassium salt of HCA may play a role in down regulating leptin, the obesity regulatory gene

HCA supplementation caused reduced appetite in a human study

***In vivo* human study:**

" ...our study was designed to better determine the effects of HCA on satiety.
A 2,000 kcal/day or 8372 kJ/day was administered, and all unconsumed food was weighed as an approximation of appetite reduction. Supplementation with HCA-SX (brand leading HCA product), ...significantly reduced appetite as determined by increased amounts of remaining food.

Harry G. Preuss, Debasis Bagchi, Manashi Bagchi, C.V. Sanyasi Rao, S. Satyanarayana, Dipak K. Dey 2003. **Efficacy of a novel, natural extract of (-)-hydroxycitric acid (HCA-SX) and a combination of HCA-SX, niacin bound chromium and *Gymnema sylvestre* extract in weight management in human volunteers: A pilot study.** Nutrition Research 24 (2004) 45-58

HCA reduces appetite without changes in water intake

***In vivo* study:**

Feed intake was significantly reduced in HCA-SX supplemented rats, demonstrating appetite suppression. None of the groups demonstrated any changes in water intake during the 90 days of treatment

Michael Shara, Sunny E. Ohia, Taharat Yasmin, Andrea Zardetto-Smith, Anthony Kincaid, Manashi Bagchi, Archana Chatterjee, Debasis Bagchi and Sidney J. Stohs: **Dose- and time- dependent effects of a novel (-)- hydroxycitric acid extract on body weight, hepatic and testicular lipid peroxidation, DNA fragmentation and histopathological data over a period of 90 days.** Molecular and Cellular Biochemistry 254: 339 –346, 2003

Effects of HCA are Dose Dependent
***In vivo* study:**

"...saline or various concentrations of (-)-hydroxycitrate [were give to 60 rats] either once a day (0.17, 0.66, 1.32, 2.63 mmoles/kg) or twice a day (0.33 mmoles/kg) for 30 days [to show the effects] on body weight gain in growing rats (160g). A dose related reduction in wt gain was observed with (-)-hydroxycitrate treatment. These decreases were significant at concentrations of 2.63 mmoles/kg once a day and 0.33mmoles/kg bid (twice a day). However, no significant reductions were observed with the single daily administration of 0.17, 0.66 and 1.32 mmoles/kg

Sullivan Ann C., Joseph Triscari, James G. Hamilton and O Neal Miller (1974b) **Effect of (-)-hydroxycitrate upon the accumulation of lipid in the rat: II.** Lipids 9,2 (1974) 129-134.

[redacted]

Tolerance Does Not Develop

In Vivo Study:

"In the studies reported here, (–)-hydroxycitrate was less effective in suppressing appetite only after 1 month or more of administration, depending on the model employed....Our previous investigations demonstrated a lack of tolerance to the inhibition of lipid synthesis produced by (–)-hydroxycitrate, because the acute or chronic dosing of (–)-hydroxycitrate produced an equivalent suppression of synthesis.

Sullivan, Ann C. and Joseph Triscari (1977a). Metabolic regulation as a control for lipid disorders. I. Influence of (–)-hydroxycitrate on experimentally induced obesity in the rodent. **The American Journal of Clinical Nutrition** 30, 5 (May 1977) 767-776.

Conditioned Aversion Is Not an Aspect of Anorexia with HCA

In Vivo Study:

"The present results indicate that (–)-hydroxycitrate at doses which have been found to be very effective in inhibiting lipid synthesis does not produce marked conditioned aversion in situations where the effects of lithium chloride are unmistakable and profound.

The present experiments also highlight the fact that the reduction in appetite seen after hydroxycitrate administration is modest—a 25% reduction in feeding under the most favorable testing conditions....

In summary, within the limits of conditions employed, (–)-hydroxycitrate sodium appears to be a safe and benign drug while certain other salts, specifically the ethylenediamine forms, can have undesirable behavioral effects."

Panksepp, Jaak, Alan Pollack, Rick B. Meeker, and Ann C. Sullivan (1977). (–)-Hydroxycitrate and conditioned aversions. **Pharmacology, Biochemistry & Behavior** 6, 6 (1977) 683-687.

Appetite Supression Is a Result of Metabolite Flux and Glycogen Production Without Effects upon Plasma Insulin Levels
***In vivo* study:**

"The (-)-hydroxycitrate mediated increase in apparent rate of glycogenesis was reflected in a significant elevation of liver glycogen. The treated animals demonstrated a significantly greater amount of glycogen (~20%) from 6 to 10 hours after feeding. At other intervals, glycogen levels in control and treated animals were similar.
These data suggest that the rates of absorption of carbohydrate from the gut and utilization by tissues were unaffected by (-)-hydroxycitrate.
No significant differences in circulating insulin levels were observed between control and treated rats, although mean plasma insulin values of control animals appeared to be greater than those in (-)-hydroxycitrate –treated rats in the 2-hr period."

Sullivan Ann C. and Joseph Triscari (1976). **Possible interrelationship between metabolite flux and appetite.** In D. Novin, W. Wyriwicka and G Bray, eds., Hunger: Basic Mechanisms and Clinical Implications (New York: Raven Press, 1976) 115-125

Human Trial Showed Effectiveness of HCA at Reducing Weight
Experimental Study:

"The results compare favourably with those achieved by my patients who are on appetite suppressants, diuretics, thyroid injections, and nutritional supplements."

Conte, Anthony A. (1993). **A non-prescription alternative in weight reduction therapy.** The Bariatrician (Summer 1993) 17 – 19

Articles

Michael Shara, Sunny E. Ohia, Taharat Yasmin, Andrea Zardetto-Smith, Anthony Kincaid, Manashi Bagchi, Archana Chatterjee, Debasis Bagchi and Sidney J. Stohs: **Dose- and time- dependent effects of a novel (-)- hydroxycitric acid extract on body weight, hepatic and testicular lipid peroxidation, DNA fragmentation and histopathological data over a period of 90 days.** Molecular and Cellular Biochemistry 254: 339 –346, 2003

Sullivan Ann C. and Joseph Triscari (1976). **Possible interrelationship between metabolite flux and appetite.** In D. Novin, W. Wyriwicka and G Bray, eds., Hunger: Basic Mechanisms and Clinical Implications (New York: Raven Press, 1976) 115-125.

Conte, Anthony A. (1993). **A non-prescription alternative in weight reduction therapy.** The Bariatrician (Summer 1993) 17 – 19.

Sullivan, Ann C., Joseph Triscari, and Karen Comai, **Pharmacological moderation of lipid metabolism for the treatment of obesity.** Department of Pharmacology, Hoffmann LaRoche, Inc , Nutley, NJ 07110, USA.

Ohia, Sunny E., Catherine A. Opere, Angela M. LeDay, Manashi Bagchi, Debasis Bagchi, and Sidney J. Stohs, **Safety and mechanism of appetite suppression by a novel hydroxycitric acid extract (HCA-SX).** Molecular and Cellular Biochemistry 238: 89-103, 2002.