

# Carbohydrate Metabolism

Slowing Lipid Synthesis



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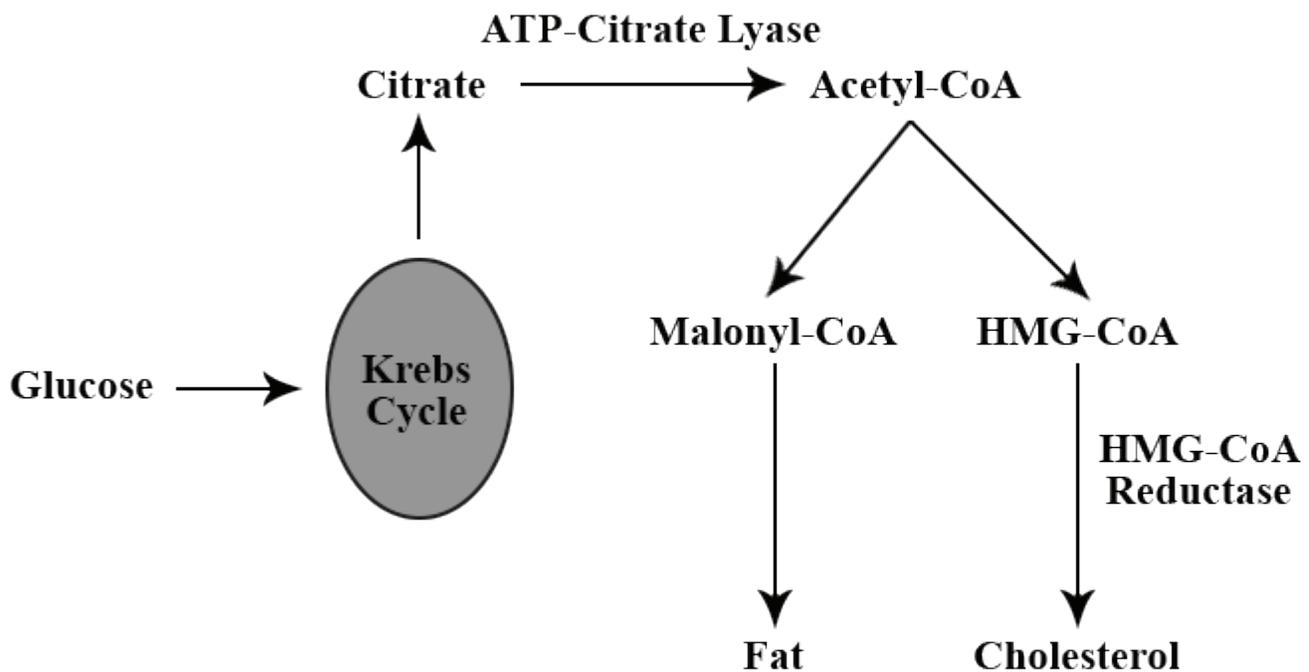
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## Carbohydrate Metabolism

When carbohydrates enter the body they are converted to glucose or stored as glycogen. The body has a limited capacity for storing glycogen and once this is attained, the excess glucose is converted to fat and stored in the adipose tissue.

To accomplish this, the glucose is converted first to pyruvate and transported into the mitochondria where it is converted to acetyl-CoA. Acetyl-CoA enters the Krebs cycle where the enzyme citrate synthase combines acetyl-CoA with oxaloacetate to form citrate. While some of this citrate continues along the Krebs cycle creating ATP, the presence of excess carbohydrates and increased insulin causes citrate derived from glucose to be transported out of the mitochondria and split into cytosolic acetyl-CoA by the enzyme ATP-citrate lyase, the first step in lipogenesis and cholesterologenesis.

Lipogenesis converts cytosolic acetyl-CoA to malonyl-CoA to form fat; Cholesterologenesis converts cytosolic acetyl-CoA to HMG-CoA to form cholesterol.



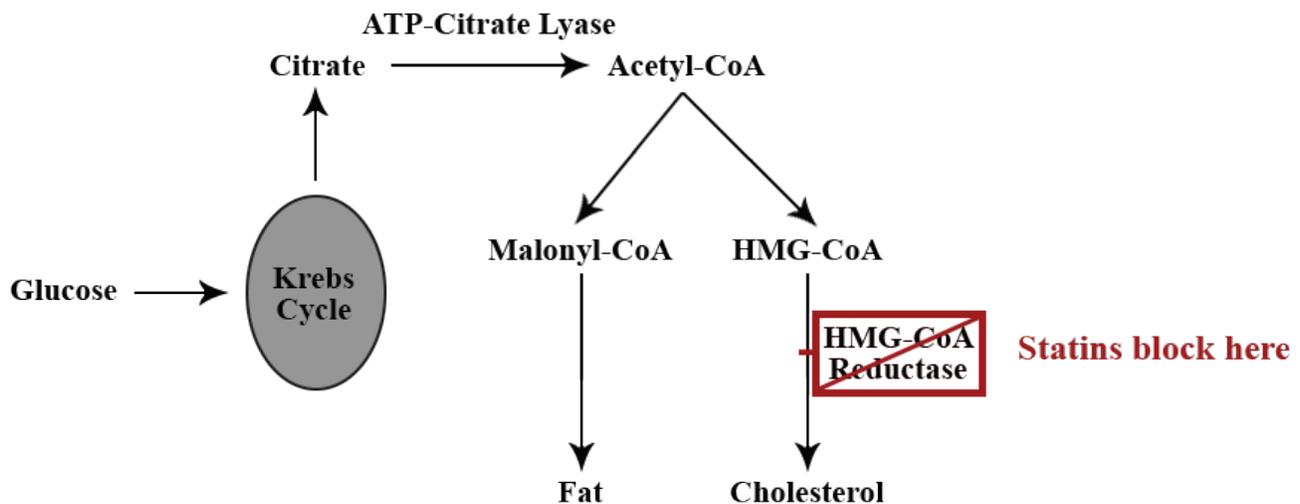
## Statin Drugs

Statins, a class of drugs used for lowering cholesterol, work by blocking the enzyme HMG-CoA reductase. This enzyme catalyses the conversion of HMG-CoA to mevalonic acid, a necessary step in the biosynthesis of cholesterol.

Statins also come with side effects. Studies<sup>1</sup> have shown an association of statin use with decreased myocardial function. Researchers noted "[t]here was significantly better function noted with SI [Strain Imaging] in the control group vs the statin group."

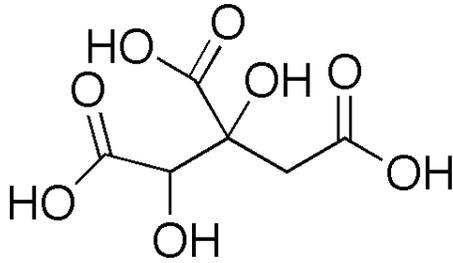
Although side effects can vary between different statins, common side effects include:

- nose bleeds
- sore throat
- a runny or blocked nose
- headache
- problems with the digestive system
- muscle and joint pain
- increased blood sugar level (hyperglycemia)
- an increased risk of diabetes



## Garcinia Cambogia

Garcinia Cambogia is a small or medium-sized tree with horizontal or drooping branches and dark, green leaves approximately 2-5 inches long. The tree is native to Asia, Polynesia, and parts of Africa. The fruit of the garcinia cambogia tree are almost pumpkin-shaped, green in color, or yellow/red when ripe.



Hydroxycitric Acid

The fruit of the Garcinia Cambogia tree has been used in cooking in the coastal cities of India and Sri Lanka for centuries. The biological properties of Hydroxycitric Acid, found within the fruit, has attracted the interest of Biochemists and health practitioners alike.



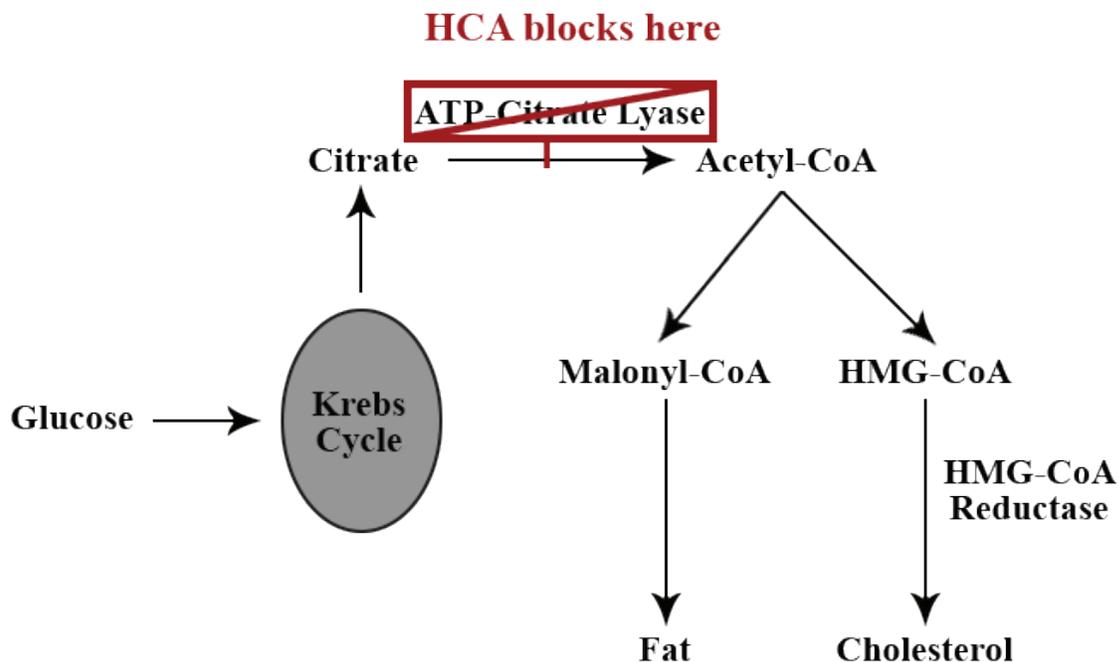
## Hydroxycitric Acid - Primary Mechanism of Action

Increased insulin levels, such as after a meal, results in increased ATP-Citrate lyase activity. A study<sup>2</sup> published in 2007 found that this relationship can also move in the opposite direction. The study showed that selective inhibition of ATP-Citrate lyase was accompanied by a reduction in glucose induced insulin secretion and an increase in fatty acid oxidation.

**Hydroxycitric Acid (HCA)** inhibits the enzyme ATP-Citrate lyase, effectively slowing the creation of fat. The inhibition of this reaction limits the availability of acetyl-CoA units required for fatty acid synthesis. As stated above, this also leads to an increase in fatty acid oxidation and a decrease in glucose induced insulin secretion.

The action of HCA has been shown in multiple studies:

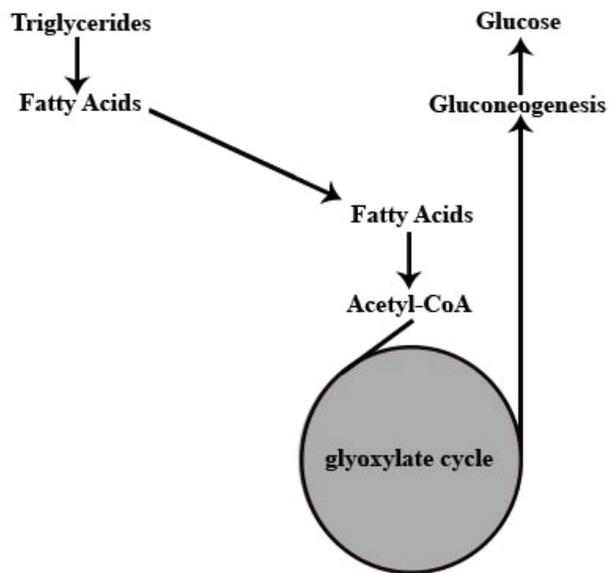
- HCA profoundly inhibited the glucose-stimulated insulin secretion (GSIS).<sup>3</sup>
- HCA was associated with a remarkable rate of body-fat loss and thermogenesis, strongly suggestive of uncoupled fatty acid oxidation.<sup>3</sup>
- HCA led to an increase in the intensity and duration of satiety, possibly due to fatty acid oxidation.<sup>4</sup>
- Inhibition of ATP-citrate lyase by HCA significantly reduced the level of malonyl-CoA, indicating that citrate was the major substrate for the formation of cytosolic acetyl-CoA.<sup>3</sup> "There is sufficient evidence that HCA inhibits ATP-citrate lyase, limiting the pool of cytosolic acetyl-CoA, the precursor of malonyl-CoA."



## Hydroxycitric Acid - Effects on Satiety

Inhibition of ATP-Citrate lyase results in an increase of cytosolic citrate. It seems levels of cytosolic citrate play some role in the effect of satiety. Thus, HCA appears to affect satiety at the metabolic level and not directly at the central nervous system as typical appetite suppressants do.

High levels of cytosolic citrate has an inhibitory effect of glycolysis and promotes gluconeogenesis. During gluconeogenesis, fatty acids are oxidized to generate glucose.<sup>5</sup> The resulting intestinal glucose release activates hypothalamic nuclei involved in the regulation of food intake, resulting in a decrease in hunger.<sup>6</sup>



The glucose generated by oxidation of fatty acids is converted to Acetyl-CoA inside the mitochondria whereas fatty acids are synthesized from cytosolic Acetyl-CoA generated by ATP-Citrate lyase. These pathways are mutually inhibitory, preventing the acetyl-CoA produced by fatty acid oxidation from entering the synthetic pathway.<sup>7</sup>

## HCA Produces Results

In two experiments<sup>8</sup> designed as a double-blind crossover test, six subjects ingested 250 mg of HCA or placebo for 5 days and then participated in cycle ergometer exercise. HCA tended to decrease the respiratory exchange ratio (RER) and carbohydrate oxidation during 1 hour of exercise. In addition, exercise time to exhaustion was significantly enhanced. These results suggest that HCA increases fat metabolism, which may be associated with enhanced exercise performance.

Another limited study reported that an extract of *Garcinia cambogia* with 60% hydroxycitric acid increased serum serotonin levels and HDL cholesterol and lowered serum leptin levels, LDL cholesterol, and triglycerides in human subjects in an 8-week clinical trial.<sup>9</sup>

When 42 subjects<sup>10</sup> were randomly assigned to take HCA or placebo for 16 weeks, the HCA group had significantly reduced visceral, subcutaneous, and total fat areas compared to placebo. No side effects were observed at any time during the treatment period.

A 1993 study using 50 obese volunteers over 8 weeks saw an average weight loss of 11.14 lbs, compared to 4.2 lbs in the placebo group.<sup>11</sup> Those taking HCA also reported appetite suppression and increased energy levels.

A randomized, placebo-controlled, double-blind study of 60 overweight men and women for a period of 8 weeks saw equally impressive results.<sup>12</sup> The HCA group had an average weight loss of 14.11 lbs, compared to 8.37 lbs in the placebo group. In addition to weight loss, appetite scores were significantly reduced for the HCA group, but not in the placebo group.

Another 8 week trial, consisting of patients aged 20 to 64, also saw significant weight loss.<sup>13</sup> Physicians who conducted the study also observed a significant decrease in LDL and an increase in HDL.

A separate study observing long-term use of HCA saw a significant weight reduction, with an average of over 10 lbs, as well as an improvement in lipid profiles, as shown below.<sup>13</sup>

<b>Long-term Trial</b>		
	<b><u>Before Treatment</u></b>	<b><u>After Treatment</u></b>
Body mass index	27.2	24.1
Triglyceride levels	178 mg/dL	141.2 mg/dL
Cholesterol	210.5 mg/dL	191.9 mg/dL

## Bio-Citrin™



Garcinia Cambogia is a chemically unique compound that has been studied extensively for its effects on metabolizing carbohydrates and total body lipids, as well as appetite regulation.

### Each capsule contains:

Garcinia Cambogia	500 mg
(60% Hydroxycitric Acid stabilized 300 mg)	
Chromium Polynicotinate	100 mcg
Bioperine®	2.5 mg

Legere Pharmaceuticals was the first to market, over 25 years ago, with a standardized extract of Garcinia Cambogia. **Bio-Citrin™** contains 500mg of Garcinia Cambogia extract with 60% HCA combined with chromium polynicotinate and bioperine for increased effectiveness.

Chromium polynicotinate is a superior form of chromium which has been shown to be 18-times more bioactive than other chromium complexes tested.<sup>14</sup> Clinical research shows that chromium polynicotinate helps support healthy blood sugar levels, cholesterol levels, and weight management.

Bioperine is derived from black pepper and increases the absorption of other ingredients. Studies have shown that Bioperine can increase bioavailability by over 200%, leading to enhanced blood levels.<sup>15</sup>

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\*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, mitigate or prevent any disease.