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## Garcinia Cambogia, Diabetic Ketoacidosis, and Pancreatitis

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### **Key Words**

garcinia cambogia, hydroxycitric acid, pancreatitis, diabetic ketoacidosis

### **Introduction**

Obesity affects 36.5% of all American adults,<sup>1</sup> and many people struggle to achieve sustained weight-loss. Lifestyle modifications like dieting and exercising are effective, but difficult, so patients often try dietary supplements to more quickly and easily lose weight. However, supplement intake is not without its risks. Dietary supplement products are portrayed as treatment of a disease, despite insufficient evidence to support their use. Furthermore, a recent report analyzing emergency room visits due to supplement intake showed that 25.5% of cases implicated a weight-loss product.<sup>2</sup>

Garcinia cambogia (GC) is a dietary supplement marketed primarily for weight loss, as well as for appetite suppression, cholesterol reduction, and blood sugar control. Hydroxycitric acid (HCA) is the active ingredient in GC products. The primary mechanism of action of HCA for weight loss is via inhibition of adenosine triphosphatase (ATP) citrate-lyase, preventing the conversion of citrate to oxaloacetate and acetyl coenzyme A (ACA). Inhibiting the formation of oxaloacetate and ACA reduces fatty acid synthesis in the cell cytosol.<sup>3</sup> There have been several

reports of adverse effects associated with consumption of GC including hepatotoxicity,<sup>4</sup> rhabdomyolysis,<sup>5</sup> nephropathy,<sup>6</sup> serotonin toxicity<sup>7</sup> and cardiovascular toxicity.<sup>8</sup> We report the case of a 56-year-old woman who presented with diabetic ketoacidosis (DKA), pancreatitis, and stress cardiomyopathy after several weeks of GC consumption.

### **Case Report**

A 56-year-old woman with a history significant for insulin-dependent diabetes mellitus, hypertension, hepatitis C infection, and opioid abuse, abstinent for more than 18 years, presented to the emergency room with altered mental status. On the day of admission, she had been found by her son in the bathroom, lethargic and confused. Earlier that day, she had reported mild abdominal pain and vomiting. Her outpatient medications had not been significantly adjusted in the last three years (**Table 1**). On admission, her pulse was 103 beats/min and regular, respiratory rate 24 breaths/ min, blood pressure 115/70 mmHg, and temperature 95.8 degrees Fahrenheit. Her Glasgow Coma Scale was 13. There were no focal neurological deficits, and her mucous membranes were dry. Initial laboratory data was significant for a plasma glucose of 1,150 mg/dL, arterial pH of 7.33, serum bicarbonate of 7 mmol/L, serum beta hydroxybutyrate of 5.4 mmol/L, serum anion gap of 35, troponin I of 5.12 ng/mL, and serum lipase of 861 U/L. A computed tomography of the abdomen without contrast showed peripancreatic stranding, as well as possible pancreatic atrophy. Initial electrocardiogram revealed normal sinus tachycardia without acute ST-segment changes.

The patient was admitted to the intensive care unit for management of DKA, pancreatitis and elevated troponin. She was treated with aggressive hydration, insulin drip, and electrolyte repletion. Her DKA and pancreatitis resolved within three days. Her mental status improved in

three days and she reported excellent adherence to all of her medications and no dietary transgressions. In fact, she had been trying and had successfully lost approximately 40 pounds in the last month. When the medical team inquired further, the patient admitted to taking GC for the last month. She had been taking two tablets of GC by mouth three times a day with meals (1,400–1,440mg HCA per day depending on the brand) in addition to taking an unknown quantity of another dietary supplement, *Irvingia gabonensis* or African Mango. Her hospital course was complicated by atrial fibrillation with rapid ventricular response, which was treated with amiodarone. A transthoracic echocardiogram revealed significantly depressed left ventricular function. The mid to distal anterolateral, anteroseptal, inferior, and entire apical wall appeared severely hypokinetic, consistent with stress cardiomyopathy. The patient was discharged after seven days, fully recovered.

## **Discussion**

Pancreatitis is caused by inflammation, leading to inappropriate activation of amylase and lipase and autodigestion of the gland. Pancreatitis can be idiopathic or caused by gallstones, alcohol, illicit drugs, infections, diabetic ketoacidosis, or medications. Typical cases of medication-induced pancreatitis involve antimicrobials, valproic acid, furosemide, thiazide diuretics, immunosuppressants, NSAIDs, tamoxifen, L-asparaginase, and estrogen.<sup>9</sup> Of these agents, the patient had only reported taking her prescription aspirin and hydrochlorothiazide. Case reports have suggested that a few other medications on her list may rarely cause pancreatitis: statins, angiotensin converting enzyme (ACE) inhibitors, and metformin.<sup>10</sup>

Diabetic ketoacidosis is a physiological adaptation to starvation. Common causes of DKA are insulin non-adherence, starvation, infection, acute stress, pancreatitis, or medications including

antipsychotics, cocaine, alcohol, corticosteroids, glucagon, interferon, sympathomimetics, and thiazide diuretics. DKA is more common in Type I diabetes than Type II diabetes. When cells lack sufficient intracellular glucose to function, the body begins breaking down fat. ACA is then metabolized to acetone, acetoacetate, and beta hydroxybutyrate (ketone bodies) rather than entering the citric acid cycle. The accumulation of ketone bodies lowers pH and patients often experience nausea, vomiting, abdominal pain, confusion, hyperglycemia, and ketonuria. By losing 40 pounds in one month, the patient was essentially in starvation mode.<sup>11,12</sup>

Based on the mechanism of action, it is possible that GC caused her weight loss, in addition to the unwanted side effects of DKA and pancreatitis. GC works to reduce weight by altering the availability of oxaloacetate and ACA, but this may also alter glucose and fatty acid metabolism. Low levels of oxaloacetate shunt ACA from the citric acid cycle to the ketogenic pathway.<sup>13</sup> This patient was already at risk for ketosis due to her sudden weight loss. Therefore, GC could have caused ketosis both indirectly through weight loss, and directly by inhibiting the production of oxaloacetate and shunting ACA into the ketogenic pathway.

Since being featured on television and endorsed by celebrities, GC has been widely used by women for weight loss, despite lack of evidence to support efficacy or safety. Various products recommend different daily doses of GC and contain different percentages of HCA. There is no standardized dosing for GC, and clinical trial doses vary from 1g to 2.8g of HCA daily. A meta-analysis of twelve small, randomized, double-blinded placebo controlled trials demonstrated a statistically significant difference in weight loss versus placebo, with an average of -1% body weight loss in the HCA group versus placebo. Of note, all twelve studies had at least one methodological weakness and provided little or no information regarding blinding procedure,

allocation, or randomization. A sub-analysis of the two highest quality GC trials from the meta-analysis showed no statistical difference between groups.<sup>14</sup>

Since the passage of the Dietary Supplement Health and Education Act (DSHEA) in 1994, dietary supplements have been recognized as a distinct class of products that contain a vitamin, mineral, herb/botanical, or amino acid, intended for ingestion for the purpose of supplementing the diet. While medications in the US must be approved by the FDA before marketing, dietary supplements are not held to these standards of safety and efficacy. The FDA only regulates dietary supplements to ensure that good manufacturing practices and minimum labeling requirements are met. Therefore, the primary method of identifying potential dietary supplement toxicity is through post-market patient reports. Manufacturers are required to report serious adverse events to the FDA. Health care professionals, public health officials, researchers, and citizens are also encouraged to report dietary supplement adverse events to the FDA.<sup>15</sup>

Hepatic toxicity associated with the use of GC has been reported for over a decade,<sup>4</sup> but pancreatitis may be an under-recognized adverse effect. There is only one other published case of pancreatitis associated with GC. In 2016, a middle-aged woman with a history of type 2 diabetes mellitus, hypertension, and chronic hepatitis C developed acute pancreatitis after using GC for weight loss.<sup>16</sup> While a home medication list was not included in this case report, it seems reasonable to assume that the patient case from 2016 and our patient would be taking similar drugs due to overlapping comorbidities of diabetes, hypertension, and opioid use disorder. As previously stated, thiazide diuretics, ACE inhibitors, statins, aspirin, and metformin have all been associated with acute pancreatitis.<sup>10</sup> However, our patient had been receiving these medications chronically, with no recent dose changes and no previous episodes of pancreatitis. The supplements may have had an additive effect in these two patients with high baseline risk.

While no definitive cause was determined, the use of GC may have contributed to her DKA and pancreatitis based on the Naranjo algorithm for estimating adverse drug reaction causality.<sup>17</sup>

Each of the ten questions in the algorithm is scored, and the total is summed. The likelihood of an adverse drug-event is categorized as definite, probable, possible, or doubtful based on high to low total score. The patient's total score was five, which coincides with a probable adverse drug reaction.

## **Conclusion**

Garcinia cambogia supplements may have serious adverse effects, especially in patients with pre-existing metabolic disorders. Patients may not always mention their dietary supplement use during medication reconciliation and may be surprised to learn that dietary supplements can potentially be deleterious to their health. Our patient assumed that GC must be safe because it was endorsed by a trusted TV figure.

Providers must be sure to identify patients that use dietary supplements, counsel these patients on their risks, and report any possible adverse effects to the FDA.

(FDA Safety Reporting Portal at US Department of Health and Human Services:

<https://www.safetyreporting.hhs.gov>)

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**Image 1: *Garcinia cambogia*, a topical fruit found in the forests of Southeast Asia, India, and Africa.**

Attribution: [Vssun](#) at [ml.wikipedia](#)



**Table 1. Outpatient Medications on Admission.**

<b>Drug, Dose, Route, Frequency</b>	<b>Indication</b>
Diazepam, 10 mg, PO, daily	Anxiety
Methadone, 125 mg, PO, daily	Opioid abuse
Aspirin, 81mg, PO, daily	Primary prevention
Metoprolol tartrate, 25 mg, PO, twice daily	Hypertension
Metformin, 1,000 mg, PO, twice daily	Diabetes mellitus
Hydrochlorothiazide, 12.5 mg, PO, daily	Hypertension
Lisinopril, 5 mg, PO, daily	Hypertension
Atorvastatin, 20 mg, PO, daily	Hyperlipidemia
Insulin glargine, 75 U, SubQ, daily	Diabetes mellitus

**NOTE: PO - by mouth; SubQ - subcutaneous.**