Drug interactions

In this guide

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74. Some reported cases in the literature and in vigilance systems raise suspicions of drug interactions involving *G. cambogia* and other medications.

Effects on P-glycoprotein (P-gp)

75. The Nutrivigilance WG suspects a drug interaction between antiretroviral treatments and the ingredients of the herbal tea blend Thé Catherine®, which includes *G. cambogia*, senna leaves and pods, and *Chrysanthemum morifolium* Ramat. A few days to weeks after starting the product, a 31-year-old woman with stage B3 HIV showed an increase in viral load. Ritonavir and darunavir (medication for HIV/AIDS) act as both substrates and inhibitors of P-glycoprotein (P-gp or MDR1; membrane efflux transporters). Bolla *et al.,* (2021) investigated the effect of garcinol (a polyisoprenyl benzophenone present in *G. cambogia* Desr.,). on the P-gp transporter in rats. Concomitant administration of garcinol to digoxin, a P-gp substrate, decreased the area under the curve of digoxin measured in rat plasma. The authors suggested that this was due to increased expression of the gene encoding P-gp in the brain and digestive tract. Thus, co-administration of Thé Catherine® with ritonavir and darunavir may reduce exposure to these antiviral treatments and therefore contribute to an increase in viral load. An in vitro study on a 95% ethanolic extract of *Garcinia cambogia* in MDR1-MDCK epithelial cells showed an inhibitory effect at the highest dose tested (50 µg/mL) (Husain *et al*., 2023). Boonyong *et al*., (2024) investigated the effects of guttiferone K (a polyisoprenylated benzophenone found in *G. cambogia* Desr.) in Caco-2 cells and its P-gp function. Results showed that guttiferone K could inhibit P-gp.

Effects on cytochrome P450 monooxygenases (CYP)

76. A drug interaction was suspected in a case where a 38-year-old woman developed hypokalaemia and cardiorespiratory arrest with no relevant medical or family history. The cardiorespiratory arrest due to hypokalaemia occurred two to three days after taking the food supplement Eafit Ultra Slim Burner® (with *G. cambogia*), combined with Maté®, Spasfon®, and Primpéran®. The Nutrivigilance WG highlighted the large number of cofactors potentially responsible for adverse reactions, including Primpéran® (metoclopramide), known to lengthen the QT interval, and Maté®, which is rich in caffeine, known for its arrhythmogenic effects.

77. In the study by Bolla *et al*., (2021) garcinol exhibited strong inhibitory effects on CYP2D6 (IC50 = 9,5 µM) and CYP1A2 (IC50=7.6 µM). Significant inhibitions were also reported for CYP2C9 (IC50 = 8.0 µM), 2B6 (IC50 = 2.1 µM) and 3A4 (IC50=5.1 µM).

78. Yu *et al*., (2017) examined the inhibitory effects of a *G. cambogia* extract on CYP enzymes. The results showed significant dose-dependent inhibitory effects of *G. cambogia* extract on CYP2B6 activity, effects that did not appear with HCA, which was also tested.

79. An *in vitro* study using recombinant cytochromes found that a hydro-alcoholic extract (95% ethanol) of *G. cambogia* weakly inhibited CYP3A4, with an IC50 around 25 µg/mL (Husain *et al*., 2023). Another in vitro study on human hepatocytes showed that the same type of extract induced over 50% activity of CYP3A4 and CYP1A2 at concentrations below 10 µg/mL (Haron *et al*., 2023).

Effects on nuclear receptors PXR and AhR

80. In an *in vitro* study conducted by (Haron *et al.,* 2023), an activating effect of the nuclear receptors PXR and AhR humans transfected into HepG2 cells (human hepatocytes) were also observed when exposed to a hydro-alcoholic extract (95% ethanol) of *G. cambogia*.

81. Another study describes the agonist effect of the same type of extract on PXR and AhR receptors in HepG2 liver cells and AhR-reporter cells respectively. The authors showed that *G. cambogia* was an activator of PXR and AhR (Husain *et al*., 2023).

Pharmacodynamic reactions

82. A 35-year-old woman developed serotonin syndrome marked by tremors, hot flushes, and diaphoresis after one month of taking a supplement containing *G. cambogia*, chromium, calcium, and potassium. She was also on escitalopram, baclofen, gabapentin, omeprazole, oxycodone, cannabinoids, silodosin, solifenacin, and diphenhydramine. Treatment was changed from escitalopram to sertraline, and the patient kept taking the dietary supplement. One week following change of medication, she was admitted to accident and emergency with a stammer and excessive sweating. On admission, she had tachycardia, hypertension, clonus, leucocytosis and hypokalaemia. The authors concluded that *G. cambogia* could be involved in a drug-drug interaction context

without providing formal evidence (Lopez *et al*., 2014).

83. Roy *et al*., (2004) exposed Sprague-Dawley rats with a calcium-potassium salt of 60% HCA extract from *G. cambogia* (commercially known as Super Citrimax HCA-600-SXS) orally for 8 weeks (5 days a week) at a dose of 10 mg/kg and then performed transcriptomic analysis. A significant increase in the expression of genes encoding the serotonin receptors 5HT2A, 5HT3A, 5HT2B, 5HT4, and 5HT7, with expression levels in abdominal adipose tissue rising by a factor of 1.3.

84. Ohia *et al.,* (2001) utilised the same extract (Super Citrimax HCA-600-SXS) in an *ex vivo* rat model (cortex sections) and it was shown to induce serotonin release at the highest concentration (300 µM) and an inhibition of the reuptake of this neurotransmitter (at 300 and 1 mM; following an 1 h exposure) (Ohia *et al*., 2002).

85. A review was carried out by Leite *et al.,* (2021) on the concomitant use of plants with treatment with warfarin. Between 2016 and 2021, 114 medicinal plants were noted to interact with warfarin. *G. cambogia* (Gaertn.) Desr., (Incorrect designation) was identified as one of the plants that affected platelet activation by lowering adhesion, aggregation, and secretion, which raises the risk of bleeding.

86. Other authors have studied the toxicity of *G. cambogia* (Gaertn.) based products. Desr., (misnomer) and the mechanisms involved (Di Giacomo *et al*., 2023). Researchers examined several suspected hepatotoxic reactions linked to products containing *G. cambogia* (Gaertn.) Desr., based on reports collected through the Italian Phytovigilance System (IPS). Eight cases of hepatic adverse reactions associated with *G. cambogia* (Gaertn.) Desr., were reported to the IPS over a period of 20 years. One of these cases involves a fatal acute hepatitis in a 45-year-old woman who had taken a dietary supplement containing *G. cambogia* (Gaertn.) Desr., She was also taking montelukast to manage her asthma—a drug known to cause liver toxicity, frequently raising serum transaminase levels and, in rare cases, triggering hepatitis. An *in vitro* study was performed to assess the mechanisms possibly responsible for liver toxicity, focusing on modulation of oxidative stress and Nrf2 expression. Low cytotoxicity was observed. However, its combination with montelukast significantly reduced cell viability, increased intracellular levels of reactive oxygen species, and affected cytoplasmic expression of Nrf2, suggesting an impairment of antioxidant and cytoprotective defences.