Hydroxycitric Acid

https://pubmed.ncbi.nlm.nih.gov/32666259/
In S. cerevisiae hydroxycitric acid antagonizes chronological aging and apoptosis regardless of citrate lyase 2020
Caloric restriction mimetics (CRMs) are promising molecules to prevent age-related diseases as they activate pathways driven by a true caloric restriction. Hydroxycitric acid (HCA) is considered a bona fide CRM since it depletes acetyl-CoA pools by acting as a competitive inhibitor of ATP citrate lyase (ACLY), ultimately repressing protein acetylation and promoting autophagy. Importantly, it can reduce inflammation and tumour development.

https://bmcmedicine.biomedcentral.com/articles/10.1186/s12916-017-0873-x
When less may be more: calorie restriction and response to cancer therapy 2017
Given the nutritional concerns of CR(Calorie Restriction) and fasting in some cancer patients, CR mimetics, namely pharmacological agents that target pathways affected by CR, such as rapamycin, metformin, resveratrol, and hydroxycitrate, are attractive strategies to mimic the protective effects of CR both for cancer prevention and as adjuvant therapies without dietary restriction. These CR mimetics affect systemic and tumor-specific inflammation and metabolism, and targeting these pathways may sensitize cancers to traditional and emerging anti-cancer therapies by reducing tumor-associated inflammation or causing metabolic stress in the cancer cell.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5715805/
Caloric Restriction Mimetics Enhance Anticancer Immunosurveillance 2017
Caloric restriction mimetics (CRMs) mimic the biochemical effects of nutrient deprivation by reducing lysine acetylation of cellular proteins, thus triggering autophagy. Treatment with the CRM hydroxycitrate, an inhibitor of ATP citrate lyase, induced the depletion of regulatory T cells (which dampen anticancer immunity) from autophagy-competent, but not autophagy-deficient, mutant KRAS-induced lung cancers in mice, thereby improving anticancer immunosurveillance and reducing tumor mass. Short-term fasting or treatment with several chemically unrelated autophagy-inducing CRMs, including hydroxycitrate and spermidine, improved the inhibition of tumor growth by chemotherapy in vivo. This effect was only observed for autophagy-competent tumors, depended on the presence of T lymphocytes, and was accompanied by the depletion of regulatory T cells from the tumor bed.

https://www.nature.com/articles/s41598-019-39109-1
Metabolic therapies inhibit tumor growth in vivo and in silico 2019
In the early 20th century, Otto Warburg revealed that cancer cells rely on the cytoplasmic fermentation of glucose to lactic acid for energy synthesis (called "Warburg effect"). Our investigations aim to reverse this effect in reprogramming cancer cells' metabolism. In this work, we present a metabolic therapy specifically targeting the activity of specific enzymes of central carbon metabolism, combining the METABLOC bi-therapeutic drugs combination (Alpha Lipoic Acid and Hydroxycitrate) to Metformin and Diclofenac, for treating tumors implanted in mice. Furthermore, a dynamic metabolic model describing central carbon metabolism as well as fluxes targeted by the drugs allowed to simulate tumors progression in both treated and non-treated mice, in addition to draw hypotheses on the effects of the drugs on tumor cells metabolism. Our model predicts metabolic therapies-induced reversed Warburg effect on tumor cells.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9268148/
Hydroxycitric Acid Inhibits Chronic Myelogenous Leukemia Growth through Activation of AMPK and mTOR Pathway 2022
We found that hydroxycitric acid (HCA), a natural, safe bioactive from the plant *Garcinia gummi-gutta* (*cambogia*), has potent AMPK activity in chronic myelogenous leukemia (CML) cell line K562. HCA is a known competitive inhibitor of ATP citrate lyase (ACLY) and is widely used as a weight loss inducer. We found that HCA was able to inhibit the growth of K562 cells in in vitro and in vivo xenograft models.

https://pubmed.ncbi.nlm.nih.gov/32439410/
Hydroxycitric acid potentiates the cytotoxic effect of tamoxifen in MCF-7 breast cancer cells through inhibition of ATP citrate lyase 2020
Hydroxycitric acid (HCA), a dietary-derived weight loss supplement, competitively inhibits ATP citrate lyase (ACLY). Tamoxifen (TAM) is the most frequently used therapy for estrogen receptor (ER)-positive breast cancer patients, but its application was restricted due to efficacy related issues. Lipid metabolic reprogramming plays a key role in cancer progression and response to treatment. This study will test the hypothesis that targeting lipid metabolic enzymes could enhance TAM effect against breast cancer cells. MCF-7 ER-positive breast cancer cell line was used, and the cytotoxic effect of TAM treatment, alone and in combination with HCA was evaluated.
Treatment with TAM or HCA significantly reduced cell viability in a concentration-dependent manner whereas co-treatment synergistically reduced cell viability, promoted apoptosis, and decreased the expression of ACLY, ACC-α, and FAS. Intracellular triglyceride and cholesterol were accumulated in response to treatment with TAM and/or HCA. Moreover, either solitary TAM or TAM/ HCA co-treatment increased ER-α protein levels non significantly. Our results revealed that TAM effects on breast cancer are mediated, in part, through the regulation of key genes involved in lipid metabolism. Accordingly, inhibition of ACLY by HCA might be beneficial to enhance the therapeutic index of TAM against breast cancer.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3424601/
In Vitro and In Vivo Toxicity of Garcinia or Hydroxycitric Acid: A Review 2012
Obesity is one of the pandemic chronic diseases commonly associated with health disorders such as heart attack, high blood pressure, diabetes or even cancer. Among the current natural products for obesity and weight control, *Garcinia* or more specifically hydroxycitric acid (HCA) extracted from *Garcinia* has been widely used. The evaluation of the potential toxicity of weight control supplement is of the utmost importance as it requires long term continuous consumption in order to maintain its effects. Majority of reports demonstrated the efficacy of *Garcinia*/HCA without any toxicity found. However, a few clinical toxicity reports on weight-loss diet supplements of which some were combinations that included *Garcinia*/HCA as an active ingredient showed potential toxicity towards spermatogenesis. Nonetheless, it cannot be concluded that *Garcinia*/HCA is unsafe. Those products which have been reported to possess adverse effects are either polyherbal or multi-component in nature. To date, there is no case study or report showing the direct adverse effect of HCA. The structure, mechanism of action, long history of the use of *Garcinia*/HCA and comprehensive scientific evidence had shown "no observed adverse effect level (NOAEL)" at levels up to 2800 mg/day, suggesting its safety for use.

https://pubmed.ncbi.nlm.nih.gov/22797854/
Tumor regression with a combination of drugs interfering with the tumor metabolism: efficacy of hydroxycitrate, lipoic acid and capsaicin 2013
Cellular metabolic alterations are now well described as implicated in cancer and some strategies are currently developed to target these different pathways. In previous papers, we demonstrated that a combination of molecules (namely alpha-lipoic acid and hydroxycitrate, i.e. Metabloc™) targeting the cancer metabolism markedly decreased tumor cell growth in mice. In this work, we demonstrate that the addition of capsaicin further delays tumor growth in mice in a dose

dependant manner. This is true for the three animal model tested: lung (LLC) cancer, bladder cancer (MBT-2) and melanoma B16F10. There was no apparent side effect of this ternary combination. The addition of a fourth drug (octreotide) is even more effective resulting in tumor regression in mice bearing LLC cancer. These four compounds are all known to target the cellular metabolism not its DNA. The efficacy, the apparent lack of toxicity, the long clinical track records of these medications in human medicine, all points toward the need for a clinical trial. The dramatic efficacy of treatment suggests that cancer may simply be a disease of dysregulated cellular metabolism.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9960359/

Cancer Metabolism: Fasting Reset, the Keto-Paradox and Drugs for Undoing 2023

In previous works, we tested lipoic acid and hydroxycitrate in pursuit of this goal; more information can be found in Refs. [11,12]. We found that, respectively, these substances inhibit the citrate formation and ACL, beginning the cytosolic synthesis of fatty acids. However, tumor cells are still able to incorporate exogenous acetate, converting it into acetyl-CoA in the cytosol; "via" acetyl-CoA synthetase, we can inhibit this entry with allicine [13] or orotic acid [14].
In earlier works we showed that Lipoic acid and Hydroxycitrate from Garcinia were able to limit the citrate efflux from mitochondria and inhibit ATP citrate lyase (ACL) in the cytosol, which cuts the lipogenic supply. These effects are strengthened if one uses allicine or orotic acid to block the direct incorporation of external acetate via acetyl-CoA synthetase. Moreover, one can impair the synthesis of lipid membranes with DHA through the inhibition of AMP deaminase, which leaves more AMP to stimulate AMP kinase.

https://pubmed.ncbi.nlm.nih.gov/20372858/

A combination of alpha lipoic acid and calcium hydroxycitrate is efficient against mouse cancer models: preliminary results 2010

The impact of metabolic dysregulation on tumor development has long been established. We have targeted two enzymes that are altered during carcinogenesis: pyruvate dehydrogenase (PDH), which is down-regulated, and ATP citrate lyase, which is overexpressed in cancer cells. Alpha lipoic acid is a cofactor of PDH, while hydroxycitrate is a known inhibitor of ATP citrate lyase. Our hypothesis is that a combination of these drugs may have antitumoral potential.
When hydroxycitrate and lipoic acid were used together, there was a major cytotoxic effect: complete cell death was seen following 8 microM lipoic acid and 300 microM hydroxycitrate treatment for 72 h. The combination of alpha lipoic acid and hydroxycitrate was administered to healthy mice, at doses currently utilized for other indications than cancer; no demonstrable toxicity was observed. The combination was used to treat mouse syngenic cancer models: MBT-2 bladder transitional cell carcinoma, B16-F10 melanoma and LL/2 Lewis lung carcinoma. The efficacy of this combination appears similar to conventional chemotherapy (cisplatin or 5-fluorouracil) as it resulted in significant tumor growth retardation and enhanced survival.

https://jeffreydachmd.com/2016/05/alpha-lipoic-acid-anticancer-agent-burt-berkson-md/

Addition of Hydroxy Citrate improves effect of ALA
In a series of studies authored by Laurent Schwartz, the addition of hydroxycitrate increases the effect of ALA. Hydroxycitrate is a known inhibitor of ATP citrate lyase (also called ATP-citric synthase), an enzyme frequently upregulated in cancer cells, a useful anti-cancer target, and the subject of a patent.

https://aacrjournals.org/cancerres/article/72/8_Supplement/3832/580877/Abstract-3832-Tolerance-of-oral-lipoid-acid-and

Abstract 3832: Tolerance of oral lipoid acid and hydroxycitrate combination in cancer patients: first approach of the cancer metabolism research group 2012

Introduction: our previous publications demonstrate that lipoïc acid (ALA) and hydroxycitrate (HCA) combination decreases the tumor growth in mice with either lung cancer, bladder cancer or melanoma. ALA is a well known treatment of the diabetic neuropathy but its interest in cancer is growing. In fact, ALA is a cofactor in mitochondrial energy metabolism and a potent regulator of the cell's redox status with effects on P13K and AMPK signaling and related transcriptional pathways. These mechanisms increase its interest in cancer and aging relative diseases.
French experience: Jan 08 to Nov 11, 13 p. with local relapse and/or metastatic cancer with a combination of ALA -HCA, 7 M, 6 F, median age 45 y (28 –74) 2 colon, 1 lung, 1 hepatocarcinoma, 5 sarcomas, 1 neuro-endocrine. HCA was administered orally, 3 g / d (1 g x3/d). ALA 1,8 g /D (600 m g x3/d) and from Oct 11 increased to 6 g /d for 3 last 6 p. Median duration: 3 months (15 d - 5 m, 1 pt 20m). Results: This association was well tolerated with few clinical disturbances: vomiting, nausea, 5 patients had a gastric protective treatment and 2 because of corticotherapy. The increased dose of ALA was well tolerated. No hepatic toxicity found, no weight loss, no hypoglycemia. A problem was the bad and discontinued observance for patients in relation with the cost of these medicines, the difficulty to buy them (only by online pharmacy for ALA in France).The tolerance of HCA was mild because of gastric pain but patients continue the treatment. Conclusion: ALA - HCA a combination well tolerated is a promising treatment in cancer patients. The switch to IV ALA will permit to obtain higher blood peaks and better observance.

https://pubmed.ncbi.nlm.nih.gov/20931262/

Adding a combination of hydroxycitrate and lipoic acid (METABLOC™) to chemotherapy improves effectiveness against tumor development: experimental results and case report 2012

We recently published results obtained with a combination of two drugs, lipoic acid and hydroxycitrate, targeting metabolic enzymes particularly affected in cancer: ATP citrate lyase and pyruvate dehydrogenase kinase. This treatment was as efficient as chemotherapy in the three mouse cancer models that were tested. In this work, we asked if our drug combination could be used in conjunction with standard cytotoxic chemotherapy, in particular cisplatin, to improve basic protocol efficacy.
We demonstrate that the triple combination lipoic acid + hydroxycitrate + cisplatin or methotrexate is more efficient than cisplatin or methotrexate used individually or the combination of lipoic acid and hydroxycitrate administered alone. Of particular note are the results obtained in the treatment of an 80 year-old female who presented with ductal adenocarcinoma of the pancreas accompanied by liver metastases. A treatment course using gemcitabine plus α-lipoic acid and hydroxycitrate gave highly promising results.

https://pubmed.ncbi.nlm.nih.gov/24511042/

Metabolic treatment of cancer: intermediate results of a prospective case series 2014

Background: The combination of hydroxycitrate and lipoic acid has been demonstrated by several laboratories to be effective in reducing murine cancer growth.
Patients and methods: All patients had failed standard chemotherapy and were offered only palliative care by their referring oncologist. Karnofsky status was between 50 and 80. Life expectancy was estimated to be between 2 and 6 months. Ten consecutive patients with chemoresistant advanced metastatic cancer were offered compassionate metabolic treatment. They were treated with a combination of lipoic acid at 600 mg i.v. (Thioctacid), hydroxycitrate at 500 mg t.i.d. (Solgar) and low-dose naltrexone at 5 mg (Revia) at bedtime.
Results: One patient was unable to receive i.v. lipoic acid and was switched to oral lipoic acid (Tiobec). Toxicity was limited to transient nausea and vomiting. Two patients died of progressive disease within two months. Two other patients had to be switched to conventional chemotherapy combined with metabolic treatment, one of when had a subsequent dramatic tumor response. Disease in the other patients was either stable or very slowly progressive. The patient with hormone-resistant prostate cancer had a dramatic fall in Prostate-Specific Antigen (90%), which is still decreasing.

Conclusion: These very primary results suggest the lack of toxicity and the probable efficacy of metabolic treatment in chemoresistant advanced carcinoma. It is also probable that metabolic treatment enhances the efficacy of cytotoxic chemotherapy. These results are in line with published animal data. A randomized clinical trial is warranted.

https://pubmed.ncbi.nlm.nih.gov/36401980/

Hydroxycitric acid reverses tamoxifen resistance through inhibition of ATP citrate lyase 2022

Lipid metabolic reprogramming is involved in mediating tamoxifen (TAM) response in breast cancer cells. Published microarray data indicated that ATP citrate lyase (ACLY) is overexpressed in TAM-resistant BC cells. Hydroxycitric acid (HCA) is a powerful competitive inhibitor of the enzyme ACLY, which links carbohydrates and lipids metabolism. However, whether inhibition of ACLY could modulate TAM response in TAM-resistant BC cells remained unexplored. Thus the current study aimed to explore the effect of ACLY inhibition on TAM-resistant BC cells. The cytotoxicity of TAM and/or HCA on LCC2 and its TAM-sensitive counterpart MCF7 cells was evaluated. Also, the effect of TAM and/or HCA treatments on ACLY protein levels were investigated by western blotting. In addition, the effects of TAM and/or HCA on caspase-3, Bax, and Bcl2 levels were evaluated by ELISA.; besides, and flow cytometric analysis was performed for the detection of apoptosis. Moreover, cholesterol and triglyceride contents of LCC2 and MCF7 were quantified colorimetrically. Our results demonstrated that TAM/HCA co-treatment synergistically diminished LCC2 and MCF7 cell viability, with the effect being more significant on LCC2. Mechanistically, TAM/HCA co-treatment decreases the expression level of ACLY in LCC2 by 74 %, while in MCF7 by only 59 %. Moreover, apoptosis marker caspase-3 and Bax were increased, while the anti-apoptotic Bcl2 was decreased. Furthermore, the cholesterol and TG contents were increased in LCC2 than in MCF7. Our data revealed that ACLY plays a key role in TAM resistance and ACLY inhibition by HCA-mediated sensitization of BC-resistant cells to TAM.

https://pubmed.ncbi.nlm.nih.gov/30195238/

ATP citrate lyase (ACLY) inhibitors: An anti-cancer strategy at the crossroads of glucose and lipid metabolism 2018

ATP citrate lyase (ACLY) is a cytosolic homotetrameric enzyme that catalyzes the conversion of citrate and coenzyme A (CoA) to acetyl-CoA and oxaloacetate, with the simultaneous hydrolysis of ATP to ADP and phosphate. Interestingly, ACLY is a strategic enzyme linking both the glycolytic and lipidic metabolism. In tumour cells characterized by an altered energetic metabolism, an increased glucose uptake and an accelerated glycolytic flux lead to an intensified production of mitochondrial citrate. Once transported to the cytosol, citrate is here converted by ACLY to acetyl-CoA, an essential biosynthetic precursor for fatty acid synthesis and mevalonate pathway. ACLY expression and activity proved to be aberrantly expressed in many types of tumours, and its pharmacological or genetic inhibition significantly inhibited cancer cell proliferation and induced apoptosis. Increasing evidences highlight the central role of ACLY, conferring a great therapeutic potential to this enzyme as a key target for the treatment of cancer. ACLY inhibitors, previously developed for metabolic disorders, have recently attracted interest as promising anti-cancer agents. After a brief introduction to the structure and the pathophysiological role of ACLY, this review article provides an overview of the main ACLY inhibitors reported in the literature.

https://pubmed.ncbi.nlm.nih.gov/11754536/

Chemistry and biochemistry of (-)-hydroxycitric acid from Garcinia 2002

(-)-Hydroxycitric acid [(-)-HCA] is the principal acid of fruit rinds of Garcinia cambogia, Garcinia indica, and Garcinia atroviridis. (-)-HCA was shown to be a potent inhibitor of ATP citrate lyase (EC 4.1.3.8), which catalyzes the extramitochondrial cleavage of citrate to oxaloacetate and acetyl-CoA: citrate + ATP + CoA --> acetyl-CoA + ADP + P(i) + oxaloacetate. The inhibition of this reaction limits the availability of acetyl-CoA units required for fatty acid synthesis and lipogenesis during a lipogenic diet, that is, a diet high in carbohydrates. Extensive animal studies indicated that (-)-HCA suppresses the fatty acid synthesis, lipogenesis, food intake, and induced weight loss.

https://pubmed.ncbi.nlm.nih.gov/18084863/

An overview of the safety and efficacy of a novel, natural(-)-hydroxycitric acid extract (HCA-SX) for weight management 2004

Garcinia cambogia-derived (-)-hydroxycitric acid (HCA) is a safe, natural supplement for weight management. HCA is a competitive inhibitor of ATP citrate lyase, a key enzyme which facilitates the synthesis of fatty acids, cholesterol and triglycerides.

Furthermore, clinical studies to evaluate the safety and efficacy of HCA-SX over a period of eight weeks were conducted in 60 human volunteers. Subjects were given a 2,000 kcal diet/day, participated in a 30 min walking exercise program 5 days/week and given an oral dose of placebo or 4666.7 mg HCA-SX (providing 2,800 mg HCA) in three equally divided doses 30-60 min 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 excretion of urinary fat metabolites (a biomarker of fat oxidation) significantly increased. No significant adverse effects were reported. These results demonstrate the safety, bioavailability and efficacy of HCA-SX in weight management.

https://pubmed.ncbi.nlm.nih.gov/34400337/

Garcinia cambogia, Either Alone or in Combination With Green Tea, Causes Moderate to Severe Liver Injury 2022

Background & aims: Garcinia cambogia, either alone or with green tea, is commonly promoted for weight loss. Sporadic cases of liver failure from G cambogia have been reported, but its role in liver injury is controversial.

Methods: Among 1418 patients enrolled in the Drug-Induced Liver Injury Network (DILIN) from 2004 to 2018, we identified 22 cases (adjudicated with high confidence) of liver injury from G cambogia either alone (n = 5) or in combination with green tea (n = 16) or Ashwagandha (n = 1). Control groups consisted of 57 patients with liver injury from herbal and dietary supplements (HDS) containing green tea without G cambogia and 103 patients from other HDS.

Results: Patients who took G cambogia were between 17 and 54 years, with liver injury arising 13-223 days (median = 51) after the start. One patient died, one required liver transplantation, and 91% were hospitalized. The liver injury was hepatocellular with jaundice. Although the peak values of aminotransferases were significantly higher (2001 ± 1386 U/L) in G cambogia group ($P < .018$), the median time for improvement in total bilirubin was significantly lower compared with the control groups (10 vs 17 and 13 days; $P = .03$). The presence of HLA-B∗35:01 allele was significantly higher in the G cambogia containing HDS (55%) compared with patients because of other HDS (19%) ($P = .002$) and those with acute liver injury from conventional drugs (12%) ($P = 2.55 \times 10\text{-}6$).

Conclusions: The liver injury caused by G cambogia and green tea is clinically indistinguishable. The possible association with HLA-B∗35:01 allele suggests an immune-mediated mechanism of injury.

https://pubmed.ncbi.nlm.nih.gov/38132462/

Hydroxycitric Acid Alleviated Lung Ischemia-Reperfusion Injury by Inhibiting Oxidative Stress and Ferroptosis through the Hif-1α Pathway 2023

Lung ischemia-reperfusion injury (LIRI) is a prevalent occurrence in various pulmonary diseases and surgical procedures, including lung resections and transplantation. LIRI can result in systemic hypoxemia and multi-organ failure. Hydroxycitric acid (HCA), the primary acid present in the peel of Garcinia cambogia, exhibits anti-inflammatory, antioxidant, and anticancer properties. However, the effects of HCA on LIRI remain unknown. To investigate the impact of HCA on LIRI in mice, the mice were randomly divided into four groups: the control group, the I/R model group, and the I/R + low- or high-dose HCA groups.

We found that HCA could also alleviate endothelial barrier damage in H/R-induced HUVECs in a concentration-dependent manner. In addition, overexpression of Hif-1α counteracted HCA-mediated inhibition of H/R-induced endothelial cell ferroptosis. In summary, these results indicate that HCA alleviated LIRI by inhibiting oxidative stress and ferroptosis through the Hif-1α pathway.

https://pubmed.ncbi.nlm.nih.gov/30915494/

Hydroxycitrate: a potential new therapy for calcium urolithiasis 2019

Alkali supplements are used to treat calcium kidney stones owing to their ability to increase urine citrate excretion which lowers stone risk by inhibiting crystallization and complexing calcium. However, alkali increases urine pH, which may reduce effectiveness for patients with calcium phosphate stones and alkaline urine. Hydroxycitrate is a structural analog of citrate, widely available as an over-the-counter supplement for weight reduction. In vitro studies show hydroxycitrate has the capacity to complex calcium equivalent to that of citrate and that it is an effective inhibitor of calcium oxalate monohydrate crystallization. In fact, hydroxycitrate was shown to dissolve calcium oxalate crystals in supersaturated solution in vitro. Hydroxycitrate is not known to be metabolized by humans, so it would not be expected to alter urine pH, as opposed to citrate therapy. Preliminary studies have shown orally ingested hydroxycitrate is excreted in urine, making it an excellent candidate as a stone therapeutic. In this article, we detail the crystal inhibition activity of hydroxycitrate, review the current knowledge of hydroxycitrate use in humans, and identify gaps in knowledge that require appropriate research studies before hydroxycitrate can be recommended as a therapy for kidney stones.

https://pubmed.ncbi.nlm.nih.gov/37592762/

Hydroxycitric acid prevents hyperoxaluric-induced nephrolithiasis and oxidative stress via activation of the Nrf2/Keap1 signaling pathway 2023

Our results showed that HCA administration significantly reduced crystal deposition and kidney injury induced by glyoxylate. HCA also alleviated oxidative stress via upregulating the antioxidant enzyme activities of superoxide dismutase (SOD) and catalase (CAT) and reducing the malondialdehyde (MDA) content. Moreover, HCA treatment promoted cell proliferation and inhibited apoptosis of renal tubular epithelial cells exposed to hyperoxaluria. Of note, Nrf2 activator dimethyl fumarate (DMF) exerted the same beneficial effects as HCA in nephrolithiasis. Mechanistically, HCA prevented crystal deposition and oxidative stress induced by hyperoxaluria through targeting the Nrf2/Keap1 antioxidant defense pathway, while knockdown of Nrf2 significantly abrogated these effects. Taken together, HCA exhibited antioxidation and anti-apoptosis activities in nephrolithiasis induced by hyperoxaluria via activating Nrf2/Keap1 pathway, suggesting that it may be an effective therapeutic agent for the prevention and treatment of nephrolithiasis.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5143754/

Dangerous dietary supplements: Garcinia cambogia-associated hepatic failure requiring transplantation 2016

He imbibed two 80 mg capsules of “Garcinia Cambogia 5:1 Extract” three times daily before meals for five months preceding initial presentation.
This is one of the first reported cases of acute liver failure specifically associated with a “purified” supplement of G. cambogia. The patient had histologic evidence of drug-induced liver injury in the absence of other medication or alcohol use. Viral, autoimmune, and genetic (i.e., hemochromatosis and Wilson’s disease) causes of acute liver failure were definitively ruled-out, and G. cambogia intake was the only apparent risk factor.

https://pubs.sciepub.com/jfnr/10/1/6/index.html

Orlistat and Hydroxycitrate Ameliorate Colon Cancer in Rats: The Impact of Inflammatory Mediators 2022

This study aimed to investigate the possible protective effects of orlistat and hydroxycitrate (HCA) against dimethylhydrazine (DMH) and high-fat diet (HFD)-induced CC in adult male rats.
Administration of orlistat and HCA improved the measured markers of a colon tumor, inflammatory mediators, oxidative stress, as well as caspase-3 (an apoptotic marker) in the colon tissue compared with the CC group. Furthermore, orlistat and HCA corrected the histopathological lesions in the colon lining. These findings revealed that orlistat and HCA had a positive chemopreventive efficacy and could be viewed as a possible clinical solution for colon cancer.