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Review

# A comprehensive scientific overview of *Garcinia cambogia*

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ABSTRACT

The fruit rind of *Garcinia gummi-gutta*, commonly known as *Garcinia cambogia* (syn.), is extensively used traditionally as a flavourant in fish curries due to its sharp sour taste. Additional ethnobotanical uses include its use as a digestive and a traditional remedy to treat bowel complaints, intestinal parasites and rheumatism. This small fruit, reminiscent of a pumpkin in appearance, is currently most popularly used and widely advertised as a weight-loss supplement. Studies have shown that the extracts as well as (−)-hydroxycitric acid (HCA), a main organic acid component of the fruit rind, exhibited anti-obesity activity including reduced food intake and body fat gain by regulating the serotonin levels related to satiety, increased fat oxidation and decreased *de novo* lipogenesis. HCA is a potent inhibitor of adenosine triphosphate-citrate lyase, a catalyst for the conversion process of citrate to acetyl-coenzyme A, which plays a key role in fatty acid, cholesterol and triglycerides syntheses. The crude extract or constituents from the plant also exerted hypolipidaemic, antidiabetic, anti-inflammatory, anticancer, anthelmintic, anticholinesterase and hepatoprotective activities in *in vitro* and *in vivo* models. Phytochemical studies of various plant parts revealed the presence of mainly xanthones (e.g. carbogiol) and benzophenones (e.g. garcinol) together with organic acids (e.g. HCA) and amino acids (e.g. gamma aminobutyric acid). Currently, a large number of *G. cambogia*/HCA dietary supplements for weight management are being sold although the possible toxicity associated with the regular use of these supplements has raised concerns. In most cases, complaints have been related to multicomponent formulations and at this stage *G. cambogia* has not been confirmed as the potentially toxic culprit. This review presents a scientific overview of *G. cambogia* with reference to relevant botanical aspects, ethnobotanical uses, phytochemistry and biological activity as well as toxicity.



**Contents**



*Abbreviations:* Acetyl-CoA, acetyl coenzyme A; ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate aminotransferase; ATP, adenosine triphosphate; BW, body weight; cPLA2, cytosolic phospholipase A2; CRP, C-reactive protein; DPPH, 2,2-diphenyl-1-picrylhydrazyl; HCA, hydroxycitric acid; HCAL, hydroxycitric acid lactone; HIV, human immunodeficiency virus; $IC_{50}$, inhibitory concentration 50%; IFN, interferon; IL, interleukin; iNOS, inducible nitric oxide synthase; $LC_{50}$, lethal concentration 50%; LPS, lipopolysaccharide; MDI, 3-isobutyl-1-methylxanthine, dexamethasone and insulin; MPO, myeloperoxidase; PGE2, prostaglandin E2; p.o., per oral; mRNA, messenger RNA; miRNA, microRNA; NF-κB, nuclear factor kappa-light-chain-enhancer of activated B cells; NOAEL, no observed adverse effects level; ROS, reactive oxygen species; SSRI, selective serotonin reuptake inhibitor; TNBS, 2,4,6 trinitrobenzenesulfonic acid; TNF, tumour necrosis factor.

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## 1. Introduction

*Garcinia gummi-gutta* (L.) Roxb. or the Malabar tamarind, commonly known by its previous scientific name *Garcinia cambogia* (Gaertn.) Desr. (Clusiaceae), is native to Southeastern Asia. The fruit rind is commonly used as a food preservative, flavouring agent or food-bulking agent [1], and as a traditional remedy to treat constipation, piles, rheumatism, oedema, irregular menstruation and intestinal parasites in many Asian countries [2]. Earlier phytochemical reports on the plant led to the isolation of various organic acids [3], benzophenones [4] and xanthones [5] as major constituents and numerous scientific studies have indicated biological activity such as anti-obesity [6,7], hypolipidaemic [8] and anticancer activity [9] amongst numerous others.

Commercial products containing *G. cambogia* catapulted onto the market and have received considerable positive and negative media attention. It's popularity and notoriety is confirmed by the more than 11 million links displayed when entering the search term "*Garcinia cambogia*" on Google®. Perhaps its most positive (and negative) connotation was with the television personality Dr Mehmet Oz. Dr Oz has been quoted as saying that *G. cambogia* is the "Holy Grail of Weight-Loss" [10]. However, he has recently been reprimanded for his health claims in general by a senate subcomittee in the USA. *G. cambogia* is also mentioned fleetingly as one of "Dr Oz's three biggest weight-loss lies" [11]. It is evident that there is uncertainty about the use of this plant especially as more information becomes available. In an article in the popular media entitled "*Garcinia cambogia*: weight-loss supplement may be toxic to some", the author describes an incident of possible serotonin toxicity which may or may not be attributed to the concomitant consumption of *G. cambogia* and an antidepressant [12]. *Garcinia* supplements contain from 20 to 60% hydroxycitric acid (HCA), and many of these products are a combination of different active ingredients rather than *G. cambogia* alone [13]. This should also be considered when assessing the quality, efficacy and safety of these products. It has also been reported that in many products, the claimed concentration of HCA is lower than the value specified [14].

HCA, an α-, β-dihydroxy tricarboxylic acid [15], is the key component present in the fruit rind which may be responsible for its weight-loss property [16]. The fruit contains approximately 10% to 30% HCA which can be isolated in the free form, as a mineral salt or as a lactone [17]. HCA is available on the market in the form of its various salts such as calcium, magnesium and potassium as well as their mixtures [18]. HCA also occurs in various bacterial species, which could be an alternative source for natural HCA [19]. In addition, hydroxycitric acid can be synthesised using citric acid as starting material. Citric acid first undergoes dehydration to form aconitic acid, which forms hydroxycitric acid *via* oxidation [20]. It has been found that HCA reduced weight-gain by inhibiting adenosine triphosphate (ATP)-citrate lyase, the enzyme responsible for catalysing the extra mitochondrial cleavage of citrate to oxaloacetate and acetyl-coenzyme A (acetyl-CoA), a building block of fatty acid synthesis [21]. Various studies suggested that HCA promotes weight-loss in humans without stimulating the central nervous system [22]. It is evident that many conflicting views on the efficacy and safety of *G. cambogia* exists. This review presents a succint overview of the available scientific evidence of biological activity and toxicity of *G. cambogia* and HCA in addition to phytochemical, botanical and other important aspects.

## 2. Botanical description

*Garcinia* is the largest genus of the Clusiaceae family comprising of 390 species [23]. These polygamous trees or shrubs are mainly distributed in tropical Asia, Polynesia and Africa [24]. *Garcinia gummi-gutta* (L.) Roxb. is one of the most

medicinally important members of the Clusiaceae family. It is a small or medium size tree of up to 12 m tall with a rounded crown and drooping branches (Fig. 1A; B [25]). Young branchlets are subterete and glabrous and the trunk and bark is reddish-brown and lenticellate. The leaves are dark green, shiny, opposite and decussate with 5–16 cm long petioles and 5–13 × 2–6 cm laminae. The leaves are elliptic, oblanceolate to obovate in shape, and the apex is usually acute and rarely obtuse. The polygamous flowers are in axillary or terminal clusters and the sepals are cream while the petals are pink in colour (Fig. 1C; D [25]). Flowering occurs during the summer (March–May) while fruiting occurs during the rainy season (June–September). The ovoid fruits are about 5 cm in diameter with 6 to 8 grooves. The fruit can be yellow, orange or red when ripe and has 6 to 8 seeds surrounded by a succulent aril [26,27] (Fig. 1B; E [25]). Growth of the tree is slow and differentiation between male and female trees is known only at the flowering stage, at approximately 7–9 years [28].

## 3. Geographical distribution and habitat

*Garcinia cambogia* has a limited native global distribution, being restricted to India, Nepal and Sri Lanka, but it has been introduced elsewhere where it is distributed in the subtropical region of Asia including China, Malaysia and the Philipines. These trees are found mainly in the semi-evergreen to evergreen forests of Southwest India, predominantly in the Western Ghats (Maharashtra, Karnataka, Kerala and Tamil Nadu) (Fig. 2). This tree can grow on both hilltops and plain lands but grows best in dry or occasionally waterlogged or flooded soils in riverbanks and valleys. It is tolerant to fluctuating water tables and drought [29,30,31].

## 4. Ethnobotanical uses

*Garcinia cambogia* is an economically important spice tree valued for the sun-dried smoked rind which is widely used as a flavour condiment, especially in fish curries. The dried rind of the fruit acts as a bacteriostatic agent and in combination with salt it is used to cure fish in India and Sri Lanka [31–33]. It is also used as a substitute of Kokum butter (from *Garcinia indica* (Thouars) Choisy) and as a common additive to make meals more filling [31,34]. The fruit rind is used medicinally to treat rheumatism and bowel complaints and it is employed as a purgative, hydragogue, anthelmintic and emetic. It is also used in veterinary medicine where a rinse is used to treat mouth diseases in cattle [29]. The fruits are edible, but very acidic and are not generally eaten raw [31,33]. A tonic prepared from the fruit, which contains a high concentration of vitamin C, is used in India to treat various heart diseases [35]. *Garcinia cambogia* is not only used medicinally; the rind is used to polish gold and silver ornaments and as a substitute for acetic acid for the coagulation

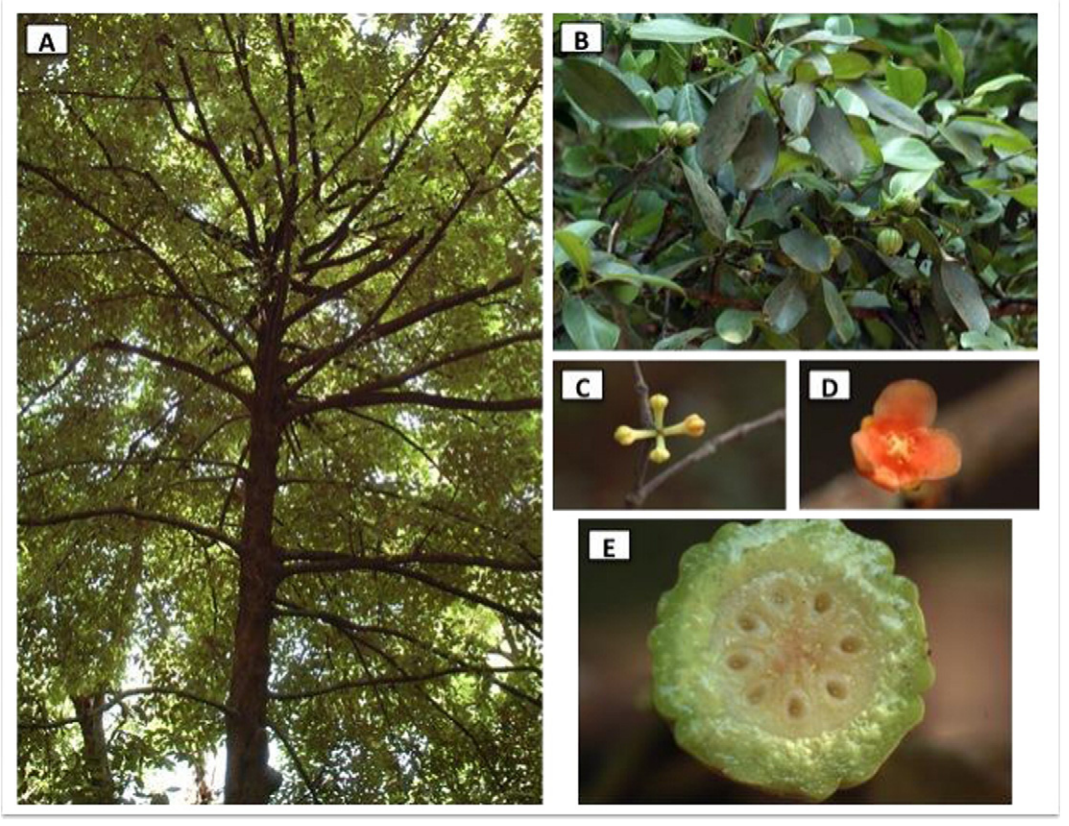



**Fig. 1.** Photographs of the *Garcinia cambogia* tree in habitat (A), a fruiting branch (B), inflorescence insertion (C), male flower (D) and a cross-section of the fruit (E). Photographs courtesy of Dr N Ayyappan, BIOTIK project (biotik.org) [25].


**Fig. 2.** Geographical distribution of *Garcinia cambogia* indicating the native and exotic ranges.

of rubber latex; the gum is used as a varnish and the resin is used as a pigment in miniature paintings and watercolours [29].

## 5. Phytochemistry

The phytochemistry of *G. cambogia* has not been studied and reported comprehensively. Preliminary phytochemical studies revealed the presence of alkaloids, flavanoids, phenolic compounds, saponins, tannins, carbohydrates and proteins [36]. Up to date, a few xanthones, benzophenones and organic and amino acids have been isolated from various parts of the plant.

### 5.1. Xanthones

Garbogiol (**1**) was isolated from the roots of the plant while rheediaxanthone A (**2**) was isolated from the bark [5]. The fruits yielded tetracyclic polyisoprenylated xanthones namely oxy-guttiferone I (**3**), oxy-guttiferone K (**4**), oxy-guttiferone K2 (**5**) and oxy-guttiferone M (**6**) [37]. The chemical structures of xanthones isolated from *G. cambogia* are provided in Fig. 3.

### 5.2. Benzophenones

Garcinol (camboginol or guttiferone E) (**7**) and isogarcinol (cambogin) (**8**) were reported from the bark [5] whereas guttiferone I (**9**), guttiferone N (**10**), guttiferone J (**11**), guttiferone K (**12**) and guttiferone M (**13**), the polyisoprenylated benzophenones, were isolated from the fruits [37,38]. The chemical structures of the benzophenones reported from *G. cambogia* are depicted in Fig. 4.

### 5.3. Organic acids

HCA (**14**) is the major organic acid occuring in the fruit [3] and also the major active ingredient. Other organic acids such as tartaric acid (**15**), citric acid (**16**) and malic acid (**17**) have been reported as minor constituents [39–42] but more recent reports state that the fruit contains only HCA and not citric acid or tartaric acid [33]. HCA lactone or *Garcinia* lactone (**18**) was also isolated from the fruit [43]. The chemical structures of organic acids reported from *G. cambogia* are given in Fig. 5.

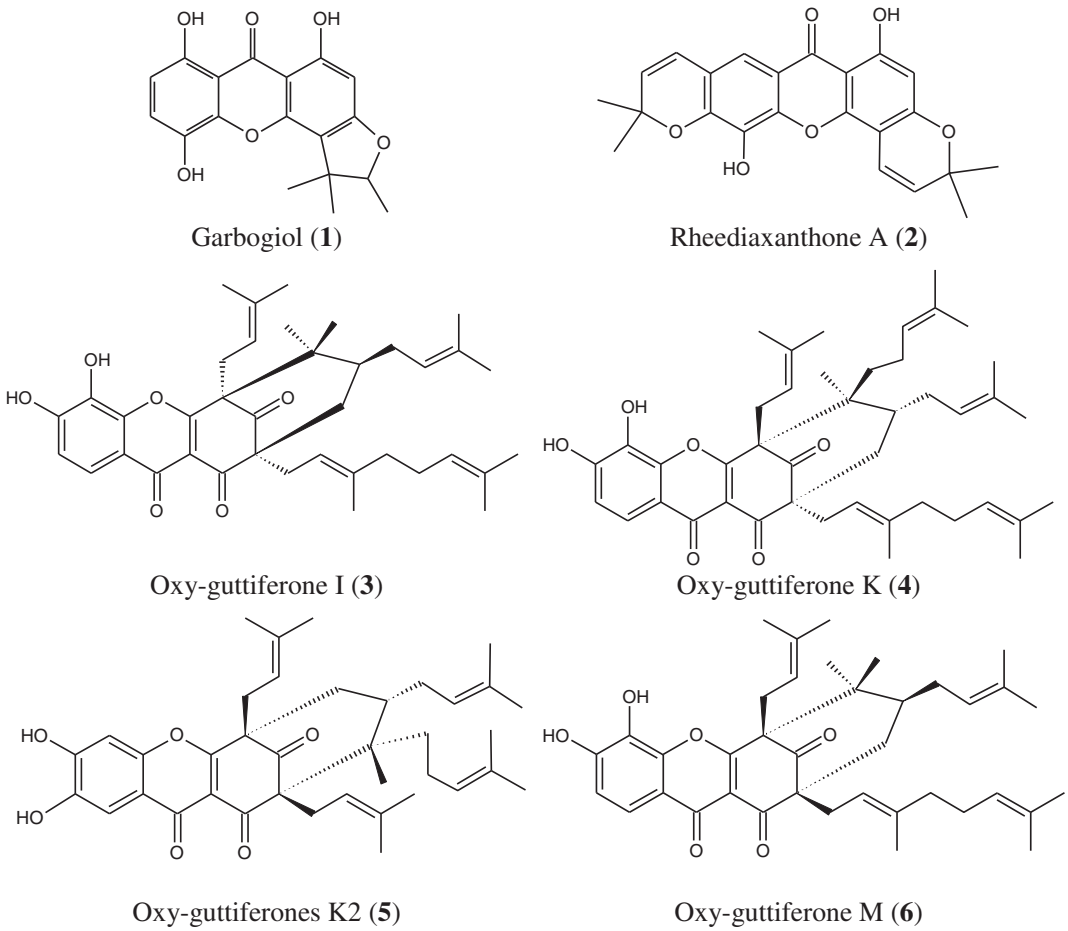



**Fig. 3.** Xanthones isolated from various parts of *Garcinia cambogia.*

*5.4. Amino acids*

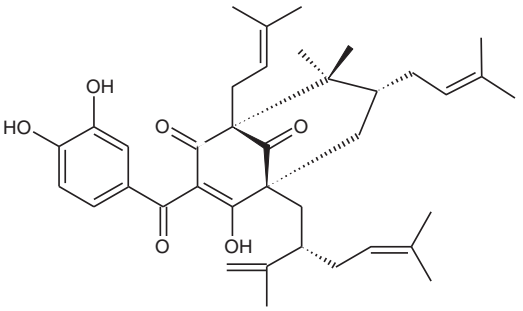
The amount of total free amino acids was determined to be less than 60 mg in 100 g of *G. cambogia* fruit. The amino acids detected include arginine, asparagine, glutamine, threonine, glycine, proline, γ-aminobutyric acid, leucine, isoleucine, ornithine and lysine [44].

## 6. Biological activity

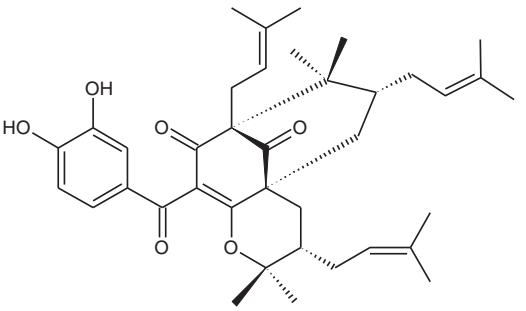
Various extracts, as well as pure compounds obtained mainly from *G. cambogia* fruit, have been shown to express biological activity in both *in vitro* and *in vivo* models. Clinical trial reports which are available, predominantly focus on the anti-obesity activity of *G. cambogia*/HCA supplements [45,46]. Although *G. cambogia* and *G. cambogia*-containing supplements are most popular for weight management, various other studies reported positive anti-inflammatory, antidiabetic, anti-oxidant, antimicrobial, anti-ulcer and hepatoprotective results.

*6.1. Appetite-suppressant activity*

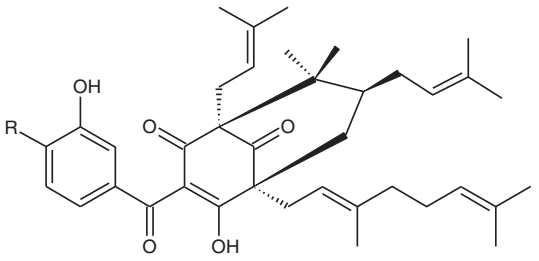
HCA as well as the lactone analogue (HCAL) was administered to Wistar albino rats at concentrations of 1.1, 3.7 and 5.5 mmol $kg^{-1}$ $day^{-1}$ over an 8-week period and the average feed intake and weight gain was measured. Feed intake was suppressed in both the HCA and HCAL groups with a lower intake reported for HCAL in all the dosage groups. The significant reduction in weight gain was dose-dependent. When compared to HCA, HCAL is more effective as these rats showed minimal weight gain initially and maximum weight loss at the end of the study period [47]. HCAL also showed anti-obesity activity in rats. Ohia et al. [48] found that HCA (10 μM to 1 mM) inhibited radiolabeled serotonin ([3H]-5-HT) uptake in isolated rat brain cortical slices *in vitro* similar to that of serotonin-specific reuptake inhibitors, fluoxetine (100 μM) plus clomipramine (10 μM). Hence, it could be useful in controlling appetite, and various serotonin-deficient conditions including depression and migraine. A formulation containing *G. cambogia* extract, *Ascophyllum nodosum* (L.) Le Jolis extract and L-carnitine was found to be an appetite modulator. The formulation was administered to 28 subjects using a random crossover design over a period of 1 week with no difference in energy intake between the groups. A reduction in subjective hunger sensations and an increase in satiety and fullness was reported acording to the Leeds Food Preferences Questionnaire and visual analogue scales [49]. However, Mattes and Bormann [50] reported that HCA did not have an effect on satiety or appetite variables.



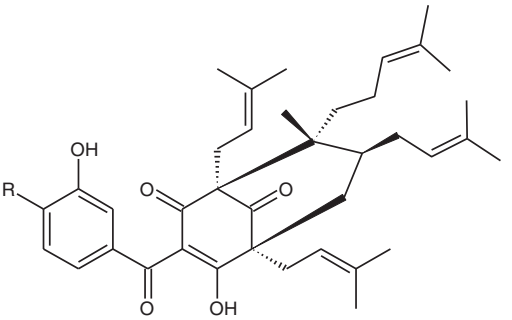
Garcinol (Camboginol or Guttiferone E) (**7**)



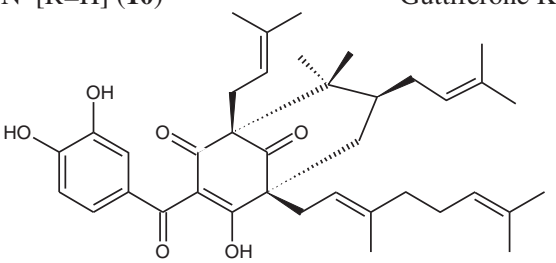
Isogarcinol (Cambogin) (**8**)



Guttiferone I [R=OH] (**9**)
Guttiferone N [R=H] (**10**)

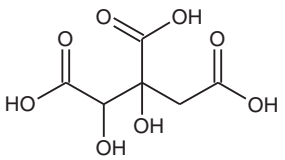


Guttiferone J [R=H] (**11**)
Guttiferone K [R=OH] (**12**)

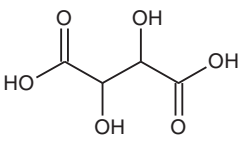


Guttiferone M (**13**)

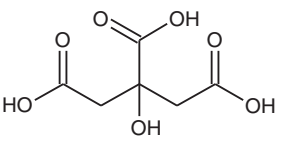
**Fig. 4.** Benzophenones isolated from various parts of *Garcinia cambogia.*



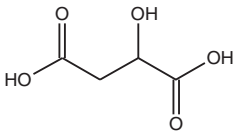
Hydroxycitric acid (**14**)



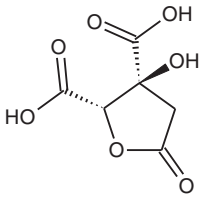
Tartaric acid (**15**)



Citric acid (**16**)



Malic acid (**17**)



Garcinia lactone (HCA lactone) (**18**)

**Fig. 5.** Organic acids reported from *Garcinia cambogia.*

### 6.2. Anti-obesity activity

Obesity is one of the chronic metabolic diseases commonly associated with various serious health disorders such as hyperglycaemia, myocardial infarction, hypertension and cancer [51]. Recently, the treatment of obesity with natural dietary supplements has gained popularity due to their high nutraceutical value and low rate of reported adverse effects [52]. A high number of *G. cambogia*/HCA products are widely marketed as dietary supplements. It has been found that HCA is effective in decreasing appetite, inhibiting fat synthesis and reducing body weight [53,54]. HCA inhibited ATP-citrate lyase, blocking the conversion of citrate to acetyl-CoA, the first step in fatty acid synthesis [55]. The enzyme ATP-citrate lyase (EC 4.1.3.8) also plays an important role in the lipogenic nutritional state produced by the consumption of a high-carbohydrate diet [56]. The daily administration of 300 mg HCA for 14 days was found to reduce body weight and 24-hour energy intake in humans. However, the appetite profile, dietary restraint, mood, taste perception and hedonics were found to be unchanged [57]. Ranjith et al. [58] found that HCA (300–1500 mg/kg, p.o.) and its lactone (212–1063 mg/kg, p.o.) potentially reduced food intake and body weight without showing any toxicity in rats. However, the effect of the lactone was found to be more pronounced than the effect of HCA. Short-term treatment using HCA (250 mg/day orally for 5 days) in women increased fat metabolism and enhanced exercise performance whereas a decrease in the respiratory exchange ratio and carbohydrate oxidation was noticed during exercise [59]. Anton et al. [60] investigated the effect of HCA on food intake, satiety, weight-loss and oxidative stress levels in humans. They used 2 doses, i.e. 2800 mg/day and 5600 mg/day, in obese individuals and found that both doses are safe for appetite suppression and weight management. HCA (500 mg/day for 3 days) reduced *de novo* lipogenesis in humans during overfeeding with carbohydrates and it was postulated that this may promote weight maintenance [61].

*Garcinia cambogia* extract (60% HCA) at a concentration of 1% suppressed the adipogenic differentiation of preadipocytes and intracellular lipid accumulation in differentiating adipocytes in the 3-isobutyl-1-methylxanthine, dexamethasone, and insulin (MDI)-induced mouse embryonic fibroblast-adipose-like cell line (3T3-L1). The expression of peroxisome proliferator-activated receptor γ2, CCAT/enhancer-binding protein a, and adipocyte protein aP2 were markedly inhibited after treatment [62]. An *in vitro* study by Blunden [63] suggested that *G. cambogia* fruit extract can inhibit lipid droplet accumulation in fat cells without affecting adipose conversion. The extract remarkably reduced body weight gain, visceral fat accumulation, blood and hepatic lipid concentrations, and plasma insulin and leptin levels in high-fat diet-induced obesity in mice. The extract also improved the high-fat diet-induced changes in the expression pattern of epididymal adipose tissue genes, adipocyte protein 2, sterol regulatory element-binding factor 1c, peroxisome proliferator-activated receptor γ2, and CCAT/enhancer-binding protein α [6,7]. An ethanolic extract administered orally at doses of 200 and 400 mg $kg^{-1}$ $day^{-1}$ for 5 weeks to rats, significantly reduced body weight and increased the red blood cell count [64]. A reduction in the plasma level of very-low-density lipoprotein and amplification in the level of chylomicrons were recorded after treatment. Ramos et al. [65] found that a lyophylised extract of *G. cambogia* at 500 mg 3 times per day for 8 weeks, potentially reduced the body weight, cholesterol and triglycerides in overweight humans, without showing any adverse effects [65]. Hayamizu et al. [66] found that *G. cambogia* extract reduced the accumulation of visceral fat in humans. In this study, a group of human subjects was treated with a *G. cambogia* extract (1000 mg HCA per day) for 12 weeks. A noticeable reduction was observed in visceral, subcutaneous and total fat areas and no severe adverse effecs were reported. An *in vivo* study by the same group [67] revealed that a *G. cambogia* extract-containing dip-sauce at doses of 5 g/kg BW/day orally for 3 months markedly reduced cumulative body weight gain together with serum levels of total cholesterol, total lipids and triglycerides in rats. *Garcinia cambogia* supplementation, at 1% (w/w) orally for 16 weeks, has been found to reduce visceral fat accumulation and adipocyte size in high-fat diet-fed obese mice. The supplement inhibited the activity of fatty acid synthase and its mRNA expression in visceral adipose tissue. In addition, it enhanced enzymatic activity and gene expression involved in adipose fatty acid β-oxidation. A reduction in glucose intolerance and blood plasma resistin was also noted after treatment. Hepatic collagen accumulation, lipid peroxidation and mRNA levels of genes related to oxidative stress and inflammatory responses were found to be increased in mice in the experimental group [68].

Bilal et al. [69] reported that *G. cambogia* (4.5% w/w), administered for 30 days, showed anti-obesity activity by increasing serum non-esterified fatty acid levels in atherogenic diet-fed rats. It was concluded that *G. cambogia* at higher doses can potentially increase serum non-esterified fatty acid concentrations perhaps due to increased fat degradation. A further study by the same group [8] reported that *Garcinia* extract (4.5% of diet, w/w) administered orally for 30 days increased the levels of serum apolipoprotein A1, a lipoprotein that offers protection from atherosclerosis, and total cholesterol in atherogenic-diet fed rats. However, the levels of serum lipoprotein (a) and apolipoprotein B in rats were found to be unchanged. In addition, the extract at similar doses exerted a suppressive effect against cardiac lipid and protein metabolism in high-lipid diet-fed rats [70]. The authors suggested that the extract could be useful against coronary heart disease through reducing cardiac triglyceride and cholesterol levels. A clinical trial revealed that Super CitriMax (*G. cambogia* extract) administered at an oral dose of 2800 mg/day for 8 weeks, resulted in weight management in all volunteers by maintaining their waist and hip circumferences and waist-hip ratios. A noteworthy decrease in aspartate aminotransferase and stabilisation of fasting blood glucose was recorded for all participants [71]. *G. cambogia*/HCA, at 50 mg/day orally for 12 weeks, was found to improve the damaging effects of a high-fat diet in rats through lowering food intake and brain oxidative stress as well as increasing brain nitric oxide [72,73]. The possible multiple mechanisms that contribute to the antiobesity effect of *G. cambogia*/HCA are summarised in Fig. 6 in which A and D contribute to the weight management effect while B and C contribute to antiobesity effect of *G. cambogia*/HCA.

Not all of the anti-obesity studies performed on *G. cambogia* reported positive results. Van Loon et al. [74] reported that *G. cambogia* extract even at higher doses (3.1 mL/kg BW) does not affect fat and carbohydrate oxidation rates in endurance-

trained humans. They suggested that HCA does not show a direct effect on fat oxidation, and, as a result, it could not be used as an anti-obesity or ergogenic agent. Another clinical trial on human volunteers suggested that *G. cambogia* extract, at 2000 mg/day for 10 weeks, does not promote weight-loss or any clinically significant change in body fat [75]. Moreover, the extract did not show any effect on triglycerides, non-high-density lipoprotein cholesterol, adipocytokines and anti-oxidants in plasma. A randomised trial on human subjects by Heymsfield et al. [45] also suggested that *G. cambogia* does not produce a significant effect on body weight. The study was conducted on a high number of subjects (treatment group; $n = 66$; control group; $n = 69$) treated with 1500 mg HCA per day for 12 weeks. After the treatment period was concluded, no significant weight or fat mass loss was observed. A further study by Kriketos et al. [76] found that (−)-HCA treatment at 3000 mg/day for 3 days did not affect energy expenditure and respiratory quotient in humans, and suggested that HCA does not alter the short-term rate of fat oxidation in the fasting state. Furthermore, Leray et al. [77] found that a *G. cambogia*-supplemented diet at a dose of 45 mg/kg BW per day for 6 months did not show any effect on the body weight of cats when compared to that of cats consuming a normal diet.

Several combination products have been tested to determine their effects on obesity. However, it must be noted that efficacy can then not be attributed to *G. cambogia* or HCA and therefore it has limited value in the assessment of *G. cambogia* as a useful anti-obesity agent. HCA-SX (4667 mg) alone or a combination of HCA-SX (4667 mg) with niacin-bound chromium (4 mg) and *Gymnema sylvestre* R.Br. (400 mg) administered for 8 weeks was found to reduce body mass index, food intake, total cholesterol, low-density lipoproteins, triglycerides and serum leptin levels in human volunteers. The treatment also increased high-density lipoprotein levels and the excretion of urinary fat metabolites [46,78,79]. A long-term study (90 days), suggested that HCA-SX at 2% and 5% of feed intake markedly decreased the body fat in rats without affecting haematology, clinical chemistry and histopathology [80]. An *in vivo* study in diabetic, obese and aged rats revealed that HCA-SX (200 mg/day for 6 weeks) reduced systolic blood pressure and body weight. The study suggested that similar supplementation could also be beneficial for elderly diabetic individuals [81].

A formulation of *G. cambogia*, soypeptide and L-carnitine (1.2:0.3:0.02; w/w/w) was found to reduce body weight gain and the accumulation of visceral fat mass in high-fat diet-induced obesity in rats. At a concentration of 0.38% of the total diet (w/w) for 9 weeks the formulation remarkably reduced blood and hepatic lipid concentrations and serum glucose, insulin, c-peptide, and leptin levels [82]. The oral administration of a combination of 2.4 g of *G. cambogia* (52.4% HCA) and 1.5 g of *Amorphophallus konjac* K.Koch (94.9% glucomannan)

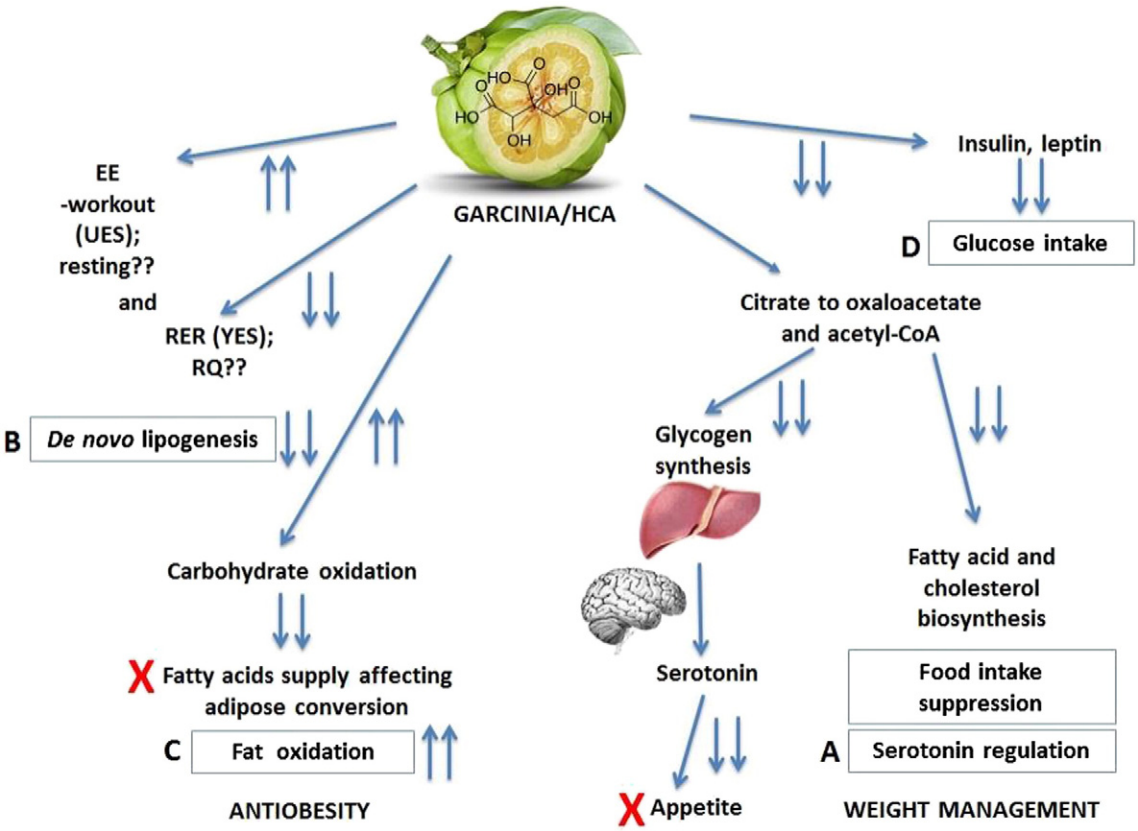



**Fig. 6.** Possible multiple mechanisms that contribute to the antiobesity effect of *Garcinia cambogia*/HCA. A: summary of serotonin regulation and food intake suppression; B: summary of reduction of *de novo* lipogenesis; C: summary of stimulation on fat oxidation; D: summary of reduce on glucose intake; ↑↑: increase or stimulation; ↓↓: reduce or inhibition;??: unknown effect (reproduced with permission from Chuah et al. [13]).

extracts 3 times a day for 12 weeks to obese humans was not found to be beneficial with regards to anthropometric parameters, resting energy expenditure, triglycerides or glucose levels. This combination did however, reduce total cholesterol and low-density lipoprotein cholesterol levels by 32 and 28.7 mg/dL, respectively [83]. The oral administration of Slim339 (560 mg, 3 times a day for 60 days), a supplement containing 132 mg of *G. cambogia* and 0.85 mg of a mixture of *Matricaria chamomilla* L., *Rosa damascena* Mill., *Lavandula officinalis* Chaix and *Cananga odorata* (Lam.) Hook.f. & Thomson (1:1:1:4) as well as 117 mg of calcium pantothenate, reduced the body weight of obese volunteers by up to 3 kg [84]. Supplementation with Hydroxycut, which contains HCA amongst many other ingredients, at various doses ranging from 43 to 129 mg $kg^{-1}$ $day^{-1}$ for 8 weeks, effectively reduced the fasting serum concentrations of cholesterol, triacylglycerol, low-density lipoprotein cholesterol, total apolipoprotein B, and low-density/high-density lipoprotein cholesterol ratio in rats without showing any adverse effects [85]. A mixture of Kidney bean pods, *G. cambogia* and chromium yeast in the form of tablets, administered orally twice a day for 12 weeks, enhanced the body composition improvement index and decreased body fat in humans [86]. OB-200G (500 mg/kg, p.o.), a polyherbal formulation consisting of aqeuous extracts of *G. cambogia, Gymnema sylvestre*, *Zingiber officinale* Roscoe, *Piper longum* Blume and *Commiphora mukul* Engl. resin, was investigated to determine possible serotonergic involvement in its biological effect. Results obtained using OB-200G in non-deprived female mice was compared with fluoxetine (10 mg/kg, i.p.), a serotonin reuptake inhibitor. Hyperphagic effects were significantly antagonised by OB-200G and it was suggested that serotonin may play a role in the mediation of satiety [87].

### 6.3. Hypolipidaemic activity

A strong lipid-lowering effect was recorded for a rich flavonoid extract prepared from the fruit rind after oral administration of 10 mg/kg BW/day for 45 days in rats. It was noted that the flavonoid extract, at higher doses, showed lesser activity in reducing lipid levels in serum and tissues. This indicated that the hypolipidaemic activity of the flavonoid-rich extract is perhaps due to lower lipogenesis and higher degradation rates [88,89]. *Garcinia cambogia* fruit extract, at an oral dose of 1000 mg/kg BW/day for 8 days, showed a notable hypolipidaemic effect on dexamethasone-treated rats. It normalised the increased levels of triglycerides and cholesterol, as well as free acids formed as a result of dexamethasone in the plasma and liver [90]. Weak preventive activity was recorded for the fruit extract (4.5% w/w with diet) against lipid metabolism and serum activity of alanine aminotransferase, aspartate aminotransferase and γ-glutamyl transferase in high-lipid diet-fed rats [91]. A clinical trial conducted on obese women receiving *G. cambogia* extract (50% HCA) at oral doses of 800 mg 3 times a day for 60 days revealed a reduction in triglycerides. However, other variables of the lipid profile, and leptin and insulin levels remained unchanged. The study concluded that *G. cambogia* has a hypotriglyceridaemic effect that is unrelated to changes in leptinaemia [92].

HCA (10 mg), in pure form, was found to promote lipid oxidation and spare carbohydrate utilisation in mice during exercise [93]. After 100 min of oral administration, the serum free fatty acid levels were notably higher, whereas after 16 h of treatment, the glycogen concentration in the gastrocnemius muscle was markedly higher than for the control group (water). Trisodium citrate (HCA salt) at 2% of the total diet administered for 15 days exerted a remarkable reduction in food intake, body weight, epididymal fat and serum triglyceride in lipogenic diet-fed rats. The treatment also exerted a reduction in the feed efficiency ratio in rats [94].

Antichol, a polyherbal formulation consisting of aqueous extracts of *Curcuma longa* L. (45% w/w), *Commiphora mukul* (10% w/w), *Emblica officinalis* Gaertn. (10% w/w), *Terminalia arjuna* (Roxb. Ex DC.) Wight & Arn. (10% w/w), *Terminalia bellirica* Roxb. (7% w/w), *Terminalia chebula* Retz. (5% w/w), *Garcinia cambogia* (8% w/w) and *Pterocarpus marsupium* Roxb. (5% w/w), at oral doses of 0.25 and 1.25 mg/kg, prevented cholesterol-cocktail-induced changes in serum glucose, lipid profile and alkaline phosphatase (ALP) levels in rats [95]. However, this effect can not be ascribed to *G. cambogia* alone.

### 6.4. Antidiabetic activity

Hayamizu et al. [96] found that 3.3% *Garcinia* extract with 10% sucrose administered daily to mice for 28 days did not show any effect on body weight, fat pad weight or serum glucose level of mice. However, it decreased the serum insulin level, leptin level and leptin/WAT ratio while improving glucose metabolism. Super CitriMax (HCA-SX) at a dosage of 500 mg/kg for the first 2 weeks followed by 1500 mg/kg BW per day up to 7 weeks, reduced the levels of malondialdehyde, protein carbonyl and protein tyrosine nitration in the liver and kidney of rats with type-2 diabetes-associated inflammation and oxidative stress. After supplementation, C-reactive protein and interleukin-6 levels in the plasma were found to decrease without the development of insulin resistance [97]. Oral administration of HCA at a dose of 310 mg/kg BW, delayed the intestinal absorption of enterally administered glucose at the level of the small intestinal mucosa in rats. It also attenuated postprandial plasma glucose levels after intragastric and intraduodenal glucose administration [98]. HCA supplementation, at 500 mg/day for 7 days, enhanced the glycogen synthesis rate and fatty acid translocase/CD36 mRNA expression in exercised human skeletal muscle and it also improved post-meal insulin sensitivity [99].

A polyherbal formulation consisting of *Gymnema sylvestre*, *Garcinia cambogia* and *Lagerstroemia speciosa* Pers. administered at doses of 412, 825 and 1625 mg/kg BW/day for 21 days, was found to be effective in obesity-associated diabetes in rats. The formulation reduced body weight, blood glucose, total cholesterol, triglycerides, low-density and very-low-density lipoproteins levels and increased the level of high-density lipoprotein. The formulation showed activity almost similar to that of the positive controls, glibenclamide (4 mg/kg, for diabetes) and sibutramine (5 mg/kg, for obesity) [100].

### 6.5. Anti-inflammatory activity

The oral administration of 500 and 1000 mg/kg BW of an extract obtained from the fruit rind, containing 51.2% (−)-HCA, showed anti-inflammatory activity in TNBS-induced colitis rats through improving macroscopic damage and causing substantial

reductions in increases in MPO activity, COX-2 and iNOS expression. The extract also reduced PGE 2 and IL-1β colonic levels in rats without producing any toxic effects [101]. The study suggested that the extract could be useful in the treatment of inflammatory bowel disease, caused by a dysregulated mucosal immune response.

Several compounds isolated from *G. cambogia* have shown anti-inflammatory activity. Garcinol (5 μM) inhibited NF-κB and/or JAK/STAT-1 activation in LPS-stimulated RAW264.7 murine macrophages [102]. It inhibited the expression of iNOS and COX-2 in LPS-activated macrophages and also lowered the LPS-induced increase of intracellular ROS. The release of arachidonic acid metabolites from human colon adenocarcinoma cell lines (HT-29 and HCT-116) and a rat normal immortalised intestinal cell line (IEC-6) was inhibited by 40–50% by garcinol at a concentration of 1 μM. The postulated mechanism of action was that garcinol modulates arachidonic acid metabolism by blocking the phosphorylation of cPLA2 and decreases iNOS protein levels by inhibiting STAT-1 activation [103].

Garcinol, guttiferone K and guttiferone M were found to modulate cytokine signaling in the cultured human breast cancer (MDA-MB-231) and rat insulinoma cell lines (INS-1E) by inhibiting STAT-1 nuclear transfer and DNA binding [104]. All the compounds inhibited cytokine IFNγ-induced STAT-1 activation in MDA-MB-231 cells. Garcinol (25 μM) was found to be the most effective followed by guttiferone M (50 μM) and guttiferone K (50 μM). Garcinol (25 μM) and guttiferone K (25 μM) also inhibited cytokine-induced STAT-1 activation in INS-1E cells whereas guttiferone M was only slightly inhibitory at a similar concentration. Moreover, garcinol also inhibited TNF-α-induced NF-κB activation in MDA-MB-231 cells at a concentration of 50 μM whereas at the same concentration, guttiferone K and guttiferone M showed only weak activity. Garcinol and guttiferone K at 25 μM noticeably reduced NF-κB activation in INS-1E cells, whereas guttiferone M was found to be inactive. Potassium-magnesium hydroxycitrate (KMgHCA) administered at doses of 28 and 84 mg/day p.o. improved systolic blood pressure and reduced carageenan-induced paw oedema in Sprague–Dawley rats by reducing CRP and TNF-α without any observed toxic effect. The activity was considered to be moderate when compared to that of the control group [105].

### 6.6. Anti-oxidant activity

An aqueous extract prepared from the fruit rind showed *in vitro* anti-oxidant activity in the DPPH, hydroxyl radical scavenging, ferric thiocyanate, total peroxy radical trapping and lipid peroxidation assays [36]. The extract showed activity against the DPPH radical, hydroxyl radical, peroxy radical and lipid peroxidation with $IC_{50}$ values of 36, 50, 44 and 62 μg/mL, respectively. Ascorbic acid ($IC_{50}$ of 10 and 24 μg/mL against DPPH radicals and lipid peroxidation, respectively), quercetin ($IC_{50}$ 36 μg/mL against hydroxyl radical) and TROLOX ($IC_{50}$ 18 μg/mL against peroxy radical) were used as positive controls. The study suggested that phenolic constituents present in the extract might be responsible for the activity. A subsequent study by Shivakumar et al. [106] revealed that hydro-alcoholic and ethanolic extracts from the fruit rind exerted *in vitro* anti-oxidant activity using the DPPH, hydroxyl radical scavenging and ferric thiocyanate assays. The extracts at a concentration of 300 μg/mL inhibited DPPH radicals by 79% (hydro-alcoholic) and 87% (ethanol), whereas ascorbic acid at the same concentration showed activity of 94%.

Hydro-alcoholic and ethanol extracts at a concentration of 1.4 mg/mL inhibited the hydroxyl radical by 82% and 62%, respectively when compared to ascorbic acid which inhibited the hydroxyl radical by 97% at 1.4 mg/mL. The ferric thiocyanate assay also revealed similar results for both extracts, which remarkably inhibited lipid peroxidation (positive control = α-tocopherol). Garcinol and guttiferone K isolated from the fruit showed *in vitro* protective effects against lipid and protein oxidation. They significantly reduced the formation of carbonyl groups in plasma and platelet proteins, and also the level of thiobarbituric acid reactive species induced by peroxynitrite at a concentration of 125 mg/mL in both cases. However, these compounds did not inhibit peroxynitrite-induced plasma and platelet protein nitration [107].

### 6.7. Hepatoprotective activity

The oral administration of a fruit extract at 1000 mg/kg BW per day for 45 days to rats reduced ethanol-induced peroxidative damage. The inhibitory effect of this extract on the lipid levels and peroxidative damage induced by ethanol is related to its anti-oxidant property. After treatment, the levels of serum aspartate aminotransferase (AST), alanine transaminase (ALT) and alkaline phosphatase (ALP) were found to be normal [108].

Although, *G. cambogia*/HCA has been suspected of causing hepatotoxicity in humans, an *in vitro* report showed that *G. cambogia* extract (60% HCA) at a 1% concentration attenuated palmitate-induced lipotoxicity in HepG2 cells by reducing cellular damage and reactive aldehydes induced by palmitate [62]. In addition, Antichol, which contains *G. cambogia* (8% w/w) as one of the active ingredients, prevented the cholesterol-induced fatty degeneration of the liver and changes in the liver anti-oxidant enzymes such as superoxide dismutases, glutathione and catalase in rats [95].

### 6.8. Anti-cancer activity

A preliminary *in vitro* screening study by Mazzio and Soliman [9] revealed that a fruit extract of *G. cambogia* expressed tumouricidal activity against the cell viability in the murine neuroblastoma cell line (Neuro-2A cells), derived from a spontaneous malignant tumour with an $LC_{50}$ value of 0.235 mg/mL [9]. Although *G. cambogia* has not been extensively investigated for its anti-cancer activity, garcinol, isolated from *G. indica* and also present in *G. cambogia* has received much scientific attention in this regard. A review by Saadat and Gupta [109] details the potential role of garcinol as an anticancer agent. Its effects appear to be as a result of its anti-oxidative, anti-inflammatory, antiproliferative, anti-angiogenic and proapoptotic activities in addition to the inhibition of histone acetyltransferases (HAT 300) and by possible posttranscriptional modulation by miRNA profiles involved in carcinogenesis. A host of *in vitro* studies have been performed to determine its effects in breast, colon, oesophageal, lung, kidney, pancreatic and prostate cancers as well as hepatocellular carcinoma, medulloblastoma, multiple myeloma, Burkitt's lymphoma and in HeLA cells [109].

### 6.9. Anti-ulcer activity

The oral administration of a fruit extract of *G. cambogia* at doses of 1000 mg/kg BW/day for 5, 10 or 15 days exerted protective effects against indomethacin-induced damage of the gastric mucosa in rats. The extract also reduced the acidity and increased the mucosal defence in the gastric areas [110]. A subsequent study by the same group [111] revealed that the extract at 1000 mg/kg BW/day at intervals of 7 and 15 days exhibited protective effects against HCl-ethanol-induced damage in gastric mucosa in rats by reducing the volume and acidity of gastric fluid. The extract also improved the increased lipid peroxidation, reduced anti-oxidant enzyme activity, and altered levels of protein and glycoproteins in the ulcerated mucosa. A polyherbal formulation consisting of *Glycyrrhiza glabra* L. (150 mg), *G. cambogia* (500 mg), deglycyrrhizinated licorice extract (200 mg) and *Azadirachta indica* A.Juss (150 mg) showed anti-ulcer activity against naproxen-, histamine-, cysteamine- and ethanol-induced ulcers in rats. The formulation administered at the doses of 300 and 600 mg/kg, p.o., exerted gastric healing activity, and remarkably reduced the ulcer index and ulcer area with a protection index of 80% [112].

### 6.10. Anticholinesterase activity

Acetylcholinesterase enzymes are present in neuro-muscular joints and cholinergic brain synapses, and plays a key role in the hydrolysis of acetylcholine, an important neurotransmitter. This enzyme is found to be responsible for the loss of cognitive ability, an initial stage of Alzheimer's disease, by terminating synaptic transmission [113]. The water extract of the fruit rind of *G. cambogia* produced significant anticholinesterase activity by inhibiting cholinesterase by 30% and 67% at a concentration of 500 and 1000 μg/mL, respectively. The activity was compared to the positive control neostigmine which inhibited cholinesterase by 78% and 92% at a concentration of 5 and 10 μg/mL, respectively [36].

### 6.11. Antimicrobial activity

Ethyl acetate, ethanol and hydro-alcoholic extracts from the fruit rind tested at a concentration of 25 mg/mL showed antimicrobial activity against *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Bacillus subtilis* and *Staphylococcus aureus* with inhibition zone diameters ranging from 15 to 34 mm. The ethyl acetate extract was found to be the most active followed by ethanol and hydro-alcoholic extracts whereas hexane extracts was found to be inactive against all the test pathogens [106]. Ethanolic and water extracts prepared from *G. cambogia* leaves exhibited inhibitory activity against the major HIV enzymes, HIV-1 protease and HIV-1 integrase. The $IC_{50}$ values for the water extract were determined to be 67 and 70 μg/mL against protease and integrase, respectively whereas the ethanolic extract showed comparatively weak activity with an $IC_{50}$ value of 100 μg/mL against both enzymes [114].

### 6.12. Anthelmintic activity

Various concentrations i.e. 20, 40 and 60 mg/mL of petroleum ether, choloroform and ethanolic extracts obtained from the leaves of *G. cambogia* were found to show activity against earthworms. The time taken for paralysis of earthworms was in the range of between 1.1 and 2.5 min whereas the time taken for death to occur was found to be between 3.1 and 7.4 min. Albendazole (positive control) produced paralysis within 1.2 min and caused death within 3.2 min at 60 mg/mL. The ethanol extract was found to be strongest anthelmintic followed by chloroform and petroleum ether extracts [115].

### 6.13. Effects on fertility

An ethanol extract prepared from the seeds of *G. cambogia* was administered for 6 days a week for 6 weeks to male rats to investigate its effects on the histology of the testis as well as sperm counts. The extract, at doses of 100 and 200 mg/kg BW/day, significantly increased the sperm count and interstitial spaces, and caused degeneration of the Leydig cells and distortion in the arrangement of the cells of spermatogenic series in all experimental rats [116]. Oral administration at a dosage of 102 mmol/kg BW to male rats lowered the level of testis meiosis-activating sterol, an intermediate in cholesterol biosynthesis from acetyl-CoA which might be responsible for transmitting a signal for spermatogenesis [117]. A subsequent study by same group revealed that (−)-HCA administered at a dosage of 154 mmol $kg^{-1}$ $day^{-1}$ for 4 weeks did not change the levels of the serum hormones i.e. follicle-stimulating hormone, luteinising hormone, oestradiol and progesterone in female rats. Follicle and corpus luteum, ovarian follicular fluid meiosis-activating sterol and testis meiosis-activating sterol concentrations were found to be unchanged during treatment. It was noted that the body weight and abdominal fat decreased after treatment [118].

### 6.14. Diuretic activity

Mathew et al. [119] investigated the diuretic activity of ethanolic and aqueous leaf extracts of *G. cambogia*. The oral administration of doses of 100 and 200 mg/kg BW/day to rats produced a diuretic effect (increased urine output) through the increased excretion of sodium, potassium and chloride (positive control = intraperitoneal furosemide 20 mg/kg) [119].

## 7. Toxicity studies

Recently, the safety of *G. cambogia* supplements for weight control has been called into question in various news reports. To add to the confusion, some researchers state that *G. cambogia* is safe while others disagree. A number of reports about the toxicity of *G. cambogia* itself or *G. cambogia*-containing supplements are available [120] and the majority of reports revealed that *G. cambogia* and/or HCA does not have significant toxic effects [51,121,122]. However, formulations containing *G. cambogia* as a key ingredient in addition to other ingredients have exibited various toxic effects such as toxicity towards spermatogenesis. The "no observed adverse effect level" (NOAEL) of up to 2800 mg/day suggests that it is safe for use [51].

Saito et al. [123] reported that a *G. cambogia* extract containing (−)-HCA administered at doses of 778 and 1244 mg/kg BW/day for 13 weeks showed strong testicular atrophy and toxicity in male Zucker rats. Diets containing 389 mg/kg BW/day did not cause these toxic effects and the authors determined this to be the NOAEL. In view of this

report, Hayamizu et al. [124] investigated the effect of *G. cambogia* extract (1667.3 mg/day = 1000 mg HCA/day) on serum sex hormones in humans ($n = 44$) when administered for a period of 12 weeks. They concluded that there were no significant changes in the serum testosterone, oestrone and oestradiol levels and that haematology, serum triacylglycerol and serum clinical pathology parameters did not indicate significant adverse effects. Ranjith et al. [58] also investigated pure HCAL to dispel negative health postulations by performing acute and chronic oral toxicity studies in Wistar rats. They reported no drug-related mortality and toxicity and determined the $LD_{50}$ of HCAL to be >5000 mg/kg BW. In addition, they showed that both HCA and HCAL are safe based on biochemical and histopathological analyses. Furthermore, Clouatre and Preuss [18] found that the administration of *G. cambogia* (1% w/w) for 16 weeks to obesity-prone C57BL/6 J mice did not promote inflammation or hepatotoxicity, but it in fact reduced markers of inflammation in the brain, intestines, kidney and serum. Ono et al. [125] determined that Ca-type *G. cambogia* extract (65% HCA) does not induce chromosome aberrations *in vitro* (Chinese hamster lung cells) or *in vivo* (bone marrow cells of Slc:DDY male mice) after a single oral administration of up to 2 mg/kg. Another study showed that *G. cambogia* extract (3.3%) does not show adverse effects on the skin properties of mice irrespective of excessive sucrose intake [126].

An *in vivo* study performed on Super Citrimax (HCA-SX), a calcium/potassium salt of (−)-HCA, showed non-toxicity in rats as the oral $LD_{50}$ dose was determined to be greater than 5000 mg/kg [16]. An *in vivo* study in a mouse model suggested that the intraperitoneal injection of HCA-SX, at doses of up to 12 500 μmol/kg, does not cause genotoxicity [127]. Deshmukh et al. [128,129] showed in a 10-week study that HCA-SX is non-teratogenic in rats and is safe at a dose of up to 1240 mg $kg^{-1}$ $day^{-1}$. An earlier study by Preuss et al. [130] also supported this fact. This study noted that the HCA-SX-supplement is not only safe but also effective in weight management in a study conducted for 8 weeks on 60 volunteers. In addition, a report by Stohs et al. [131] stated that the consumption of HCA-SX at the dose of up to 4667 mg/day is safe.

Perhaps the most relevant and recent example of suspected toxicity was a case study repoted by Lopez et al. [132]. A 35-year old woman taking a *G. cambogia*-containing supplement daily for 2–3 months presented with stuttering speech and profuse sweating. The supplement contained: 1000 mg *G. cambogia* fruit-rind extract (60% HCA), 200 μg chromium, 50 μg potassium and 50 μg calcium consumed at a dose of 2 capsules 3 times per day. She was previously stabilised on the antidepressant escitalopram 20 mg for more than 1 year, but about 1–2 months after starting to use the supplement she developed tremor, flushing and diaphoresis. Escitalopram was discontinued as she was diagnosed with serotonin toxicity. Sertraline 50 mg was initiated after a 2-week washout period and about one and a half weeks before this case study episode occurred. She was hypertensive (169/100 mmHg) and tachycardic (120 beats/min) and exhibited anxiety, diaphoresis, bilateral ocular clonus, ankle clonus in the lower extremities, rhythmic jaw motions and stuttering. According to the Hunter Serotonin Toxicity Criteria and the Sternbach Criteria, the patient's symptoms were consistent with serotonin toxicity. Neither the supplement, nor a selective serotonin reuptake inhibitor (SSRI) were re-introduced after this incident occurred and there is no definitive proof of a cause and effect relationship between *G. cambogia* and serotonin tocixity. However, it is important to note that the patient was stable on escitalopram without symptoms for an extended period of time and only developed serotonin toxicity when she started taking *G. cambogia* [132]. This possible interaction warrants further investigation.

Stohs et al. [122] reported in a 2009-review that a number of cases of toxicity and specifically hepatotoxicity have been attributed to the consumption of Hydroxycut and specifically to the HCA in these products. However, the large Hydroxycut product range includes some products which do not contain HCA and may contain up to 20 ingredients. Hydroxycut contained *Camellia sinensis* (L.) Kuntze, *Gymnema sylvestre, Amorphophallus konjac* and *Paullinia cupana* Kunth extracts together with *G. cambogia* at a stage, but prior to this formulation it also contained ephedra which was omitted after toxicity reports. It was premature to attribute the occurrence of liver toxicity to HCA specifically and each ingredient as well as the combination should be tested. The FDA (Food and Drug Administration) named Hydroxycut as a possible causative agent of hepatotoxicity and it was subsequently withdrawn by the manufacturer (and then reformulated) on 1 May 2009 [133]. The Hydroxycut products currently available on the market does not contain *G. cambogia*, however, the toxicity history will be briefly discussed. Narasimha et al. [134] published a case study which suggested that Hydroxycut may induce mania in humans. This report was based on a 23-year old male who was taking Hydroxycut supplements for 1 month, and presented with mania-related symptoms such as unprovoked anger outbursts and defiant behaviour. The study suggested that these symptoms were due to the regular use of Hydroxycut supplements. Hydroxycut was found to be a possible cause of rhabdomyolysis in an 18-year old Caucasian male who complained of bilateral leg pain and weakness [135]. Stevens et al. [136] reported a possible link between acute liver injury and Hydroxycut in 2 patients. Various other commercial weight-loss products such as Magri XS, Krea Slim, Chitosano 800 Complex Forte and Top Line Advantra Z, which contain *G. cambogia* as a key ingredient, together with many other herbs such as *Citrus aurantium* and *Gymnema sylvestre* have also been suspected as the causative agent of hypertension, palpitations and atrial tachycardia in women in Italy [137]. The Brazilian Pharmacovigilance System stated that the use of *G. cambogia* could cause serious adverse reactions including hepatotoxicity either during or after its use [138]. As discussed by Lobb [139], the case reports on the hepatotoxicity of Hydroxycut may not give a true reflection of the harm caused. This stresses the need for pre-marketing safety assessment as well as an effective post-marketing adverse effect surveillance system.

## 8. Conclusions and recommendations

*G. cambogia* fruit typically contains high concentrations of the organic acid, HCA (as indicated on most product labels), which is also the reported active ingredient. Several other compounds have been isolated from various plant parts, such as carbogiol from the roots, but it is the fruit which is chiefly used commercially. From the fruit, xanthones such as oxy-

guttiferones I, K, K2 and M, benzophenones such as guttiferones I, N, J, K and M and several organic and amino acids have been isolated. The phytochemistry of this popular commercial medicinal plant has not been comphrehensively studied. *G. cambogia* has been shown to possess numerous biological properties such as appetite-suppressant, anti-obesity and hyperlipidaemic activity. *In vivo* studies confirmed the role of *G. cambogia*/HCA in stimulating fat oxidation, increasing serotonin release in brain cortex and normalising lipid profiles in humans. Although *G. cambogia* extracts exerted *in vitro* anticancer and antimicrobial activities, its activity in *in vivo* models remains to be explored. According to clinical trial reports, *G. cambogia* extracts were beneficial to obese individuals in many cases. In addition, studies on the toxicity and observations during clinical trials indicate that *G. cambogia* is safe to use. Most of the negative reports have been related to cases where multi-ingredient formulations were consumed and the effect could not be attributed to a specific ingredient. However, as *G. cambogia* may increase the levels of serotonin, it is especially important to investigate a possible interaction between medicines that increase serotonin levels such as SSRIs and *G. cambogia*. Moreover, regulatory authorities should provide and enforce legislation requiring the compulsory basic safety demonstration of supplements pre-marketing and develop post-marketing surveillance systems.

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