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TOX/2025/41

Committee on the Toxicity of Chemicals in Food, Consumer Products and the Environment

Scoping paper on the potential risk(s) of *Garcinia cambogia* oral consumption

Background

1. In March 2025, the French Agency for Food, Environmental and Occupational Health and Safety (ANSES) published an opinion on their assessment of adverse reactions to the consumption of food supplements containing *Garcinia cambogia* (*G. cambogia*) (document in French). Their official webpage provided an overview and advised consumers to not consume food supplements containing *G. cambogia*.
2. Currently in the United Kingdom (UK), there are no safe levels or set limits established for the use of *G. cambogia* in food and drinks, including food supplements. In response to the ANSES review, the Food Standards Agency (FSA) and Food Standards Scotland (FSS) requests the Committee on Toxicity of Chemicals found in Food, Consumer Products and the Environment (COT) to perform a review of the opinion published by ANSES and assess the risk(s) associated with consumption of *Garcinia cambogia* in food supplements. In addition, the Committee is also requested to consider whether a safe level or maximum limit of *G. cambogia* for use in food and drink, including food supplements can be derived based on the current available data.
3. Points of consideration include:
 - i. What is the maximum dietary level of *G. cambogia* that can be added to/used in food and drink, including food supplements, to be consumed daily without appreciable health risk?
 - ii. Is there a link between consumption of food, drinks and food supplements, containing *G. cambogia* and adverse effects on health?

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- iii. What are possible subgroups of the general population that are more vulnerable or more sensitive to the adverse effects caused by *G. cambogia*?

4. The Secretariat has summarised the information presented in the ANSES Opinion from paragraph 17-92, as well as collated information from other regulatory authorities. The translation of the ANSES Opinion is attached as Annex A and B of this paper. It should be noted that the translation is not an official ANSES translation and was commissioned by the FSA for FSA use.

5. A literature search was carried out using the search string "Garcinia cambogia" AND "toxicity" in PubMed, Science Direct and Google Scholar. No filters or restrictions were used.

Introduction

6. The genus *Garcinia*, native to Asia and Africa, belongs to the *Clusiaceae* family and includes more than 300 species, such as *G. cambogia*. Various therapeutic effects have been attributed to this genus including anti-obesity, anti-ulcerogenic, antioxidant, anti-diabetes, anti-fungal, anti-inflammatory and anti-neoplastic (Chuah *et al.*, 2013). The fruit has been consumed as a tea in Ayurvedic medicine for inflammation and stomach complaints, while the fruit rind has a history of traditional use as a food ingredient and preservative.

7. The European Novel Food List does not consider *G. cambogia* as a novel food; however, advises that other legislation may restrict the placing on the market as a food in the EU or in some Member States (EC, 2023).

8. The UK Medicines and Healthcare products Regulatory Agency (MHRA) deems that products containing *G. cambogia* are not classed as medicinal provided that they contain the whole herb and not the extract; hydroxycitric acid (HCA). While the whole herb is not regarded as medicinal and is known to have common food uses, when HCA is extracted from the herb its concentration will greatly exceed that

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found in the natural fruit and it is regarded as a medicinal substance with a known ability to modify physiological functions.

9. This only applies to ingested products. Neither whole *G. cambogia* nor its HCA extract is known to be capable of exerting a pharmacological effect when used topically, for example in cosmetics.

10. It is important to note that not all *G. cambogia* extracts are created using the same manufacturing process or have the same HCA inclusion rate in the final product. The anti-obesity properties of *G. cambogia* have been attributed to HCA, which is present in the rind or epicarp of the fruit at 10-30% by weight. Extracts can contain between 20–60% HCA (Semwal *et al.*, 2015; Jakopin, 2019). HCA is susceptible to lactonization during manufacturing (evaporation and concentration), as such in commercially available samples of *G. cambogia*, HCA is present as its calcium salt for stability (Jena *et al.*, 2002).

Chemical composition

11. The bioactive compounds which are extracted and isolated from *G. cambogia* are shown in Table 1 and Figure 1.

Table 1 - list of bioactive compounds from plant parts of *G. cambogia* and their related bioactivities (reproduced from Espirito Santo *et al.*, 2020).

Xanthones	Plant part	Activity
Garbogirol	Roots	Inhibition of α -glucosid
Rheedia xanthone A	Peel	Not applicable*
Oxy-guttiferone i	Fruits	Not applicable*
Oxy-guttiferone k	Fruits	Not applicable*
Oxy-guttiferone k2	Fruits	Not applicable*
Oxy-guttiferone m	Fruits	Not applicable*
Benzophenones	Not applicable*	Not applicable*
Garcinol	Peel	Anticancer, anti-inflammatory, antiparasitic, action on nervous system

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Isogarcinol	Peel	Anticancer, anti-inflammatory, antiparasitic, action on nervous system
Guttiferone i	Fruits	Not applicable*
Guttiferone n	Fruits	Not applicable*
Guttiferone j	Fruits	Not applicable*
Guttiferone k	Fruits	Topoisomerase II inhibitor
Guttiferone m	Fruits	Topoisomerase II inhibitor
Organic acids	Not applicable*	Not applicable*
Heterocyclic amines	Fruits	Antiobesity
Tartaric acid	Fruits	Not applicable*
Citric acid	Fruits	Not applicable*
Malic acid	Fruits	Antimicrobial
Garcinialactone	Fruits	Not applicable*

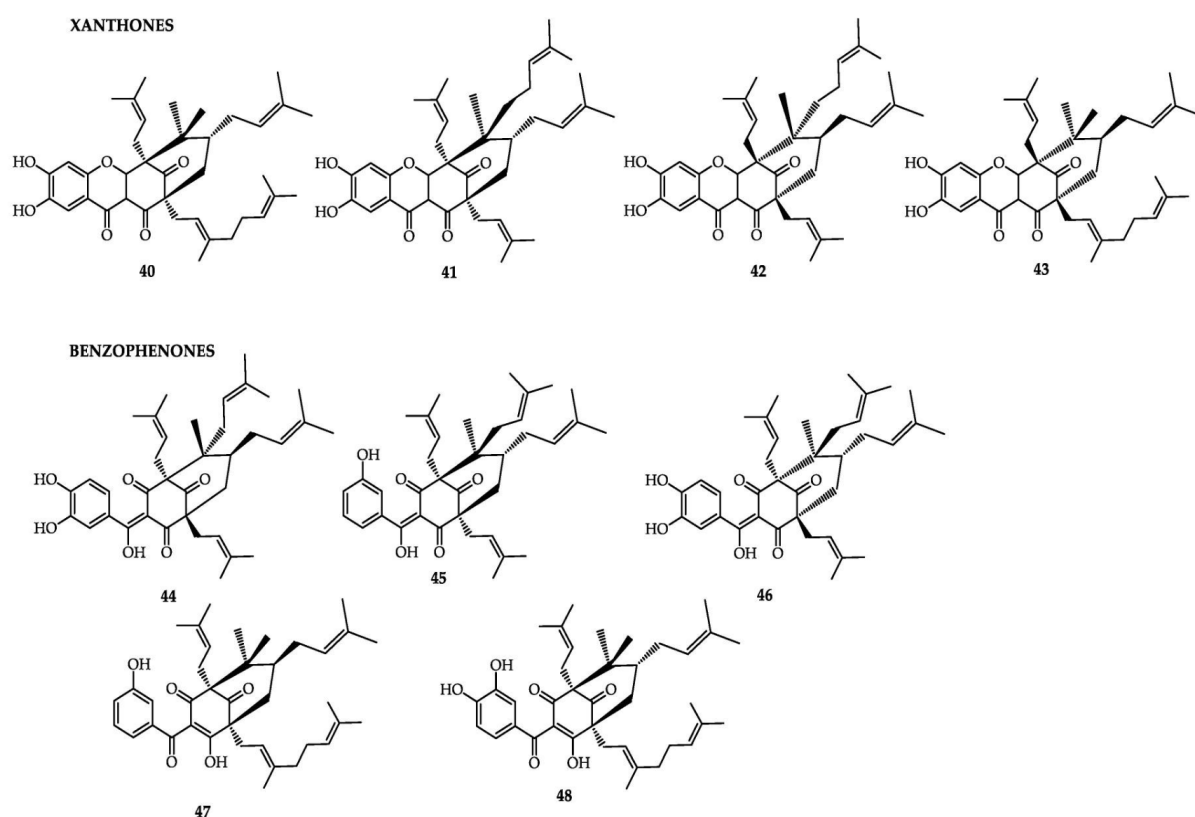


Figure 1 - chemical structures of the xanthone and benzophenone classes of bioactive compounds from *G. cambogia*. Xanthones: 40) oxy-guttiferone-i; 41) Oxy-guttiferone k; 42) Oxy-guttiferone k2 and 43) Oxy-guttiferone k. Benzophenones: 44)

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guttiferone-l; 45) guttiferone-j; 46) guttiferone-k; 47) guttiferone-n and 48) guttiferone-m (reproduced from Espirito Santo *et al.*, 2020).

12. The HCA present in *G. cambogia* is a “potent” and “competent” inhibitor of adenosinetriphosphate (ATP) citrate lyase, which is a key enzyme in the synthesis of fatty acids, cholesterol, and triglycerides. It also regulates the level of serotonin, which has been associated with satiety, increased oxidation of fat, and decreased gluconeogenesis (Semwal *et al.*, 2015; Preuss *et al.*, 2004). HCA compromises a citric acid with a hydroxyl group at the second carbon. HCA has two diastereomers as there are two chiral centres, as such there are four stereoisomers of HCA, compromising two pairs of enantiomers (see Figure 2). Each of the stereoisomers can form a γ -lactone ring and in general solution, HCA is a mixture of non-lactone and lactone forms (Yamada *et al.*, 2007).

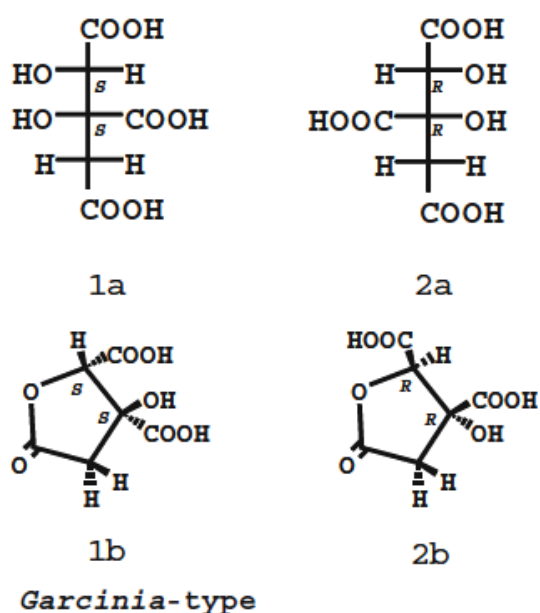


Figure 2 - Structures of HCA derived from *Garcinia* ssp. Upper and bottom structures show the non-lactone and lactone forms, respectively. (2S,3S)-HCA (a mixture of 1a and 1b) is found in *G. cambogia*. The other isomers (2R,3R)-HCA (a mixture of 2a and 2b) and (2R,3S)-HCA have not been isolated from natural sources (reproduced from Yamada *et al.*, 2007).

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Data from authoritative bodies

13. Multiple authoritative bodies have reviewed the data on *G. cambogia*. For example, in European and international vigilance systems several reports of hepatic, digestive (pancreatitis), cardiac and muscular (rhabdomyolysis) damage as a result of consumption of supplements containing *G. cambogia* have been identified.

ANSES

14. It should be noted that paragraphs 16 and 17 were summarised from the relevant webpage of ANSES (ANSES, 2025) rather than information from their opinion which is published in French.

15. The ANSES assessment highlighted 38 cases of adverse effects reported between 2009 and March 2024 (as identified in the French nutravigilance scheme). They further “identified several drug interactions that can lead to an increase in adverse effects or cause medicines to lose their efficiency.”, from their analysis of other vigilance systems and literature review.

16. From their review of the literature, adverse effects were observed in people with various health issues like psychiatric disorders, pancreatitis or hepatitis, diabetes, obesity or hypertension. Those on certain medications that affect liver function, antiretroviral treatments or antidepressants were also seen to be negatively affected by consumption of *G. cambogia*. Those without any previous medical problems were also reported to have severe health effects following consumption of *G. cambogia*.

17. The FSA have commissioned a translation of the ANSES opinion, it is not an official ANSES translation. The following paragraphs provide a summary of the approach used by ANSES and their conclusions. The full ANSES opinion is attached in Annexes A and B of this paper.

18. ANSES’ goal was to review the existing data on the physicochemical [and toxicological] properties of *G. cambogia* Desr., and analyse clinical cases from literature and vigilance reports to draw conclusions.

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Classification and Taxonomy

19. *G. gummi-gutta* (L.) N. Robson is commonly known as the Malabar tamarind tree. In the scientific literature or on the labelling of marketed products it is referred to as *G. cambogia* Desr., It belongs to the *Clusiaceae* family and has 18 genera. The genus *Garcinia* was found to include nearly 404 species.

20. The French regulations allow the use of the fruit, fruit peel, and gum resin from *G. gummi-gutta*, as well as the fruit, fruit pulp, and pericarp (rind) of *G. mangostana* in food supplements.

21. ANSES observed that researchers and regulatory bodies utilise the name *G. cambogia* for *G. gummi-gutta*, which creates confusion. As such in their assessment, *G. cambogia* Desr., denotes *G. gummi-gutta*.

Botanical data and geographical distribution

22. ANSES described that the species of the genus *Garcinia* is widespread in tropical regions. *G. cambogia* Desr., is native to India, Sri Lanka and Nepal but has been introduced to other subtropical areas in Asia including China, Malaysia, Indonesia and the Philippines, as well as to West Africa and Polynesia.

Traditional uses of the plant and associated economic activities

23. ANSES found that the Indian populations had historic use of *G. cambogia* Desr., in several applications: medicinal, culinary, crafts and construction.

24. The fruits are edible; however, they are too acidic to eat raw and are processed into marmalade, vinegar or dried to use in condiments. The pericarp [rind] is sun-dried and are sold as is or ground into powder. It is traditionally used as a spice to act as a flavour enhancer and/or a preservative. Other food uses for the rind

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include non-alcoholic drinks and syrup. The bark has been used to produce fermented alcoholic drinks, whilst the seeds can be extracted for vegetable oil.

25. In Indian folk medicine, *G. cambogia* Desr., has been used to treat oedema, delayed menstruation, digestive disorders (in particular, chronic diarrhoea). The emetic properties of *G. cambogia* Desr., have been described as treatment for intestinal parasites. Various decoctions have been described to treat rheumatism and management of cardiovascular conditions.

26. It was found that the literature attributed these food and medicinal uses to other species of *Garcinia*, thus it is difficult to definitively associate them with *G. cambogia* Desr.

27. In 2014-2015, the Indian industry was reported to have an annual use of ~300 tonnes (dry weight) of *G. cambogia* Desr., fruit. Exported quantities ranged from 100 to 5,000 tonnes per year between 2005-2015, where more than half was destined for the United States of America, and the remainder exported to South Korea, Japan, Germany and Australia.

Chemical composition of the plant

28. The pericarp of *G. cambogia* Desr., contains 10 to 30% organic acids, calculated as citric acid equivalents, including less than 1% citric, oxalic, tartaric, and acetic acids; more than 4% malic acid; and up to over 15% HCA. It was identified that other *Garcinia* ssp., also contained HCA though typically at lower levels.

29. HCA (C₆H₈O₈) is a derivative of citric acid that has an additional hydroxyl group on the second carbon, creating two chiral centres at positions C-2 and C-3. HCA exists as four stereoisomers: (-)-HCA (2S,3S), (+)-HCA (2R,3R), (+)-*allo*-HCA (2S,3R) et (-)-*allo*-HCA (2R,3S).

30. In *G. cambogia* Desr., this compound [HCA] appears in the (2S,3S) or (-)-HCA configuration and serves as a competitive inhibitor of ATP-citrate lyase, an enzyme that drives fatty acid synthesis. Each stereoisomer can cyclise to a γ -lactone. In *G. cambogia* Desr., HCA occurs in both its non-lactonic form and its

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lactonic form, known as garcinia lactone or (2S,3S)-3-hydroxy-5-oxo-2,3,4,5-tetrahydrofuran-2,3-dicarboxylic acid. From the literature, it was described that the lactonic form of (2S,3S)-HCA inhibits ATP citrate lyase less effectively than the non-lactonic form. It is also less bioavailable.

31. Industrial processes generally stabilise HCA as a single, double, or triple salt to prevent its cyclisation into the lactone form. The most common are calcium, magnesium, or potassium salts because they offer greater stability, higher solubility, and lower hygroscopicity compared to sodium salts.

32. The fruit of *G. cambogia* Desr., contains 6.25% carbohydrates, 3.25% protein, less than 0.0060% amino acids, and 0.34% lipids. The dried pericarp of *G. cambogia* Desr., contains 14.4 mg vitamin C. The bark has also been reported to contain certain B-group vitamins: 48 µg vitamin B1, 275 µg vitamin B2, 45 µg vitamin B3 and 8.8 µg vitamin B12 per 100 g. The dried fruit bark also contains minerals: 2.8 mg sodium, 26.6 mg potassium, 12.7 mg calcium, 14.4 mg magnesium, 9 mg iron and 5.3 mg phosphorus per 100g.

33. *G. cambogia* Desr., has been described to contain polyisoprenylated benzophenones (precursors of xanthenes). Studies have isolated garcinol, isogarcinol from the plant's bark and fruit. Both compounds have been shown to have antitumour, antimicrobial, antioxidant, anti-inflammatory, and central nervous system effects, especially *in vitro* and in animal models. Other isolated polyisoprenylated benzophenones are presented in Appendix 2a and 2b of the ANSES Opinion (see Annex A).

34. The xanthone content of the fruit was estimated to be 1.96%. The total phenol content is estimated to be 3.26%. Flavone heterosides (apigenin, luteolin) and flavanols (kaempferol, quercetin) have been detected in *G. cambogia* Desr., fruits.

35. Glycosylated derivatives of caffeic acid (caffeoyl glucose), esterified with quinic acid (dicaffeoyl-quinic acid) as well as *p*-coumaroyl-quinic acid have also been detected in fruits.

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Regulatory status in different fields of use and geographic regions

United States

36. Several clinical trials had not revealed any health risks, and *G. cambogia* Desr., was used as an ingredient in food supplements, most notably in the Hydroxycut® range sold in the U.S. in the early 2000s. However, shortly after they were marketed, reports of hepatic, muscular, cardiac and neurological damage, sometimes serious, were reported in the United States and Canada. In 2009, the United States Food and Drug Administration (US FDA) requested the withdrawal of *G. cambogia* Desr., from Hydroxycut® preparations. It should be noted that consumers continued to use these products for several years following withdrawal from the market, due to remaining stock or illegal sales.

Europe

37. Several European Union member states, including Belgium, Italy, and Hungary, have authorised the use of *Garcinia cambogia* Desr., in food supplements. Between 2008 and 2010, applicants submitted requests to the European Food Safety Authority (EFSA) for the evaluation of health claims related to the species *G. cambogia* Desr., including in extract form. These health claims relate to weight control, reducing fat storage and hunger, controlling blood sugar and cholesterol levels. These are said to still be awaiting assessments. In addition, HCA is also the subject of a health risk assessment by EFSA, which is yet to be published.

France

38. The French National Agency for the Safety of Medicines and Health Products (ANSM), classifies *G. cambogia* Desr., as a medical product due to its hypoglycaemic and lipid-lowering effects associated with HCA. However, given the lack of proven therapeutic benefit and an unfavourable benefit/risk ratio due to adverse effects reported in the U.S. and Canada, the ANSM Director General issued a ban on 12

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April 2012. The decision prohibits the import, preparation, prescription, and dispensing of preparations containing *G. cambogia*, as well as its use in humans.

39. The French “plants” decree which establishes the list of plants authorised for use in food supplements and their conditions of use, does not include *G. cambogia* Desr.; however, the General Directorate for Competition, Consumer Affairs and Fraud Control (DGCCRF) registered it by mutual recognition under the incorrect name *G. gummi-gutta* (L.) Roxb. The latter appears on the list of plants permitted in food supplements.

40. Data from the Télécare database show that the DGCCRF registered 340 food supplements containing *G. cambogia* Desr., between April 2016 and January 2023. Based on the information gathered from these products, the average HCA intake was 752 mg/day for products that contained only *G. cambogia* Desr. The range was 1.25 – 2,850 mg/day, with 747 mg/day as the median. For multi-ingredient dietary supplements (MIDS) containing HCA, the average HCA intake was 255 mg/day. The range was 0 – 2,070 mg/day, with 150 mg/day as the median.

41. HCA analyses were conducted separately by Service commun des laboratoires and shared between the DGCCRF and customs. The HCA intake was calculated to consider the manufacturer’s advice for use. The average daily intake was 412 mg/day. The range was 21 – 2,000 mg/day, with a median of 203 mg/day.

42. Seventy-four percent [of the registered 340 food supplement products] combined *G. cambogia* with other ingredients that are known to cause liver toxicity in experimental models and clinical studies. These included: green tea containing epigallocatechin gallate; curcuma containing curcumin; red yeast rice containing monacolin K and coumarin. The Plants Working Group (WG) identified other substances that were suspected to be hepatotoxic (as suggested by the literature). These included: conjugated linoleic acid (unspecified isomers), hydroxyanthracene derivatives, forskolin, salicin, methyl salicylate and salicylated derivatives, *Equisetum arvense* [horsetail], gingerol, ginsenosides, gymnemic acid, and parsley. The Plants WG and Human Nutrition Expert Committee further noted that 89% [of the registered

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340 food supplement products] contained at least one other ingredient that is known to be hepatotoxic: chromium, caffeine or piperine.

Adverse effects linked to the consumption of *G. cambogia* Desr

Data from French vigilance systems

43. Since launching in 2009 and up to March 2024, ANSES has received 38 reports of adverse reactions likely linked to food supplements containing *G. cambogia* (or *G. gummi-gutta*), the products labels did not display the full scientific names. All admissible cases (n=35/38) were hepatic, cardiovascular and digestive. Of the 35 reported cases, 18 had sufficient information to assess the product's causal relationship with the observed adverse effects. The number of reports where the causal relationship of the product was very likely was (n = 1/18), likely (n = 7/18), possible (n = 8/18), doubtful (n = 1/18) or excluded (n = 1/18). The reader is referred to Table 2 of Annex A of TOX/2025/41 for additional information. It should be noted that the majority of the products are MIDS (n=16/18), with the remaining 2 stated to contain *G. cambogia* only.

44. The reported cases with a possible causal relationship associated with hepatic effects were further analysed by ANSES. Five of the six reported liver damage cases involved cytolytic hepatitis. In each case, the person either took *G. cambogia* alongside another potentially hepatotoxic ingredients in the supplement or used a hepatotoxic drug at the same time. In addition, all consumers have co-morbidities, or even risk factors for liver damage (obesity, significant and rapid weight loss).

45. Six additional case reports from the pharmacovigilance system were provided by the French ANSM. Three of which had enough information for the Nutrivigilance WG to assess the causal relationship of *G. cambogia* consumption with the observed adverse effects. The Nutrivigilance WG determined that 2 of the 6 cases had a possible or a very likely causal relationship.

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46. Twenty out of 30 additional case reports from the toxicovigilance system were reviewed by the Nutrivigilance WG, they identified that the adverse effects were mostly cardiovascular (n=8/20; tachycardia) and digestive effects (n=6/20; abdominal pain, vomiting). Other effects included general symptoms (n=5/20; dizziness, malaise, fatigue, excessive sweating, dilated pupils) and skin reactions (itchy erythema).

Data from other vigilance system

Europe

47. In October 2020, ANSES contacted its European counterparts to gather more data on adverse effects potentially linked to the consumption of food supplements containing *G. cambogia* or *G. gummi-gutta* (under their truncated names). Of the 37 countries contacted, 21 responded. Table 6 of Annex A of TOX/2025/41 provides additional information. In brief, most of the 21 respondents (Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Estonia, Hungary, Iceland, Ireland, Latvia, Lithuania, Malta, Slovakia, Spain, Switzerland) were not aware of any cases of adverse reactions related to *G. cambogia* (truncated names).

48. In Belgium, the Federal Public Service for Public Health, Food Chain Safety and the Environment authorises the use of "gum-resin (from the whole fruit or the pericarp)" of *Garcinia* in food supplements. Companies have currently notified and obtained authorisation for over 300 such products on the Belgian market. In Hungary, manufacturers have used this plant in food supplements on the market for over 20 years, and in 2020, they notified 152 products containing it. Some of these contain HCA at a dose higher than the 1,000 mg considered acceptable in Hungary. In these two countries, despite the notification of several hundred dietary supplements containing *G. cambogia*, authorities have not received any reports of adverse reactions.

49. In contrast, Germany (which recorded at least 167 notified products containing *G. cambogia* in 2020), along with Italy, Norway, Slovenia, and the

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Netherlands, have reported cases. The effects were primarily hepatic (n=13), followed by cardiovascular (n=8), psychiatric (n=6), and neurological issues (n=6).

50. In 2018, the Slovenian National Institute of Public Health published information relating to dietary supplements for weight control, specifying the risks and benefits of the ingredients frequently used in their composition. Regarding *G. cambogia*, liver damage is mentioned.

51. In 2019, the Spanish Scientific Committee of the Spanish Agency for Food Safety and Nutrition (AESAN) published a report on the risks linked to consuming dietary supplements containing *G. gummi-gutta* (AESAN, 2019). The report emphasised the existence of sufficient clinical evidence connecting the consumption of *G. gummi-gutta* to the occurrence of hepatic events. This agency also stressed the need to monitor psychiatric disorders (manic attacks, psychoses) reported in the literature in connection with the consumption of this plant.

Canada

52. From the 1st of January 1965 to 31st of August 2023, 93 reports involving at least one product containing one of the following ingredients: '*garcinia*', '*garcinia gummi-guta*', '*garcinia gummigutta*', '*garcinia gummi- guta extract*', '*garcinia gummi-guta fruit*', '*garcinia gummi-gutta gum resin*' (names registered in the database), were recorded. The average age was 42 [note that 12% of the data did not have information on age], and over 80% were women. The mean BMI where available (62% missing data) was 29.9 ($\pm$ 5.2) kg/m². The commonly reported adverse reactions included general symptoms (headache, dizziness), digestive issues (abdominal pain, nausea, vomiting), cardiovascular problems (palpitations, high blood pressure), and psychiatric or neurological effects. Of these 93 reports, 4 were reports of liver damage.

United States

53. According to the US FDA-Medwatch database, authorities had received 40 adverse reaction reports up until the 14th of December 2023 [the start date was not

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provided]. Of these 40 adverse reaction reports, 35 involved women. The average age (with 17% of data missing) was 43 years ($\pm$ 12.9). The adverse effects reported were mainly of a hepatic, digestive and cardiovascular nature. The Plants WG and the Human Nutrition Expert Committee reviewed the cases submitted by all foreign vigilance systems but could not establish a causal relationship due to a lack of information.

Data published in the literature

54. The clinical cases reported in the literature up to October 2024 were mainly hepatic effects (n = 35). Psychiatric (n = 8), cardiovascular (n = 3), digestive (n = 3), muscular (n = 2) and metabolic (n = 2) disorders were the subject of several publications. Authors of these publications utilised *G. cambogia* and did not further allow for accurate scientific identification.

Hepatotoxicity

55. Thirty-six cases of liver damage have been published, observations by ANSES are detailed in Appendix 3 of Annex B of TOX/2025/41. Readers are also referred to Table 9 of Annex A of TOX/2025/41 for further information.

56. In brief, hepatitis of the cytolytic type were observed (86%), followed by cholestatic hepatitis (8%) and mixed hepatitis (6%). Grade 2 hepatitis was observed with elevation of transaminases (greater than 3 times the normal range) in the majority of cases; however, some were life-threatening (n=6), or even fatal (n=1). 60% of the reported cases involved women aged 37 years on average (35 years as the median; 19 – 64 years age range).

57. In 20 of the 36 publications, co-morbidities were reported, including hypertension, heart or kidney failure, diabetes, haemochromatosis, allergy, hypothyroidism, adenoma, chronic pain, dyslipidaemia, or hepatic steatosis. Authors of the publications identified risk factors for certain pathologies, including high BMI, hypocaloric diets, intense physical activity, a history of hepatitis, rapid and significant weight loss, alcohol use, and smoking.

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58. In 29 of the 36 publications, the composition of the food supplements was of sufficient detail to identify other ingredients. Within these 29, 24 involved dietary supplements containing *G. cambogia* in combination with other hepatotoxic ingredients: caffeine, piperine or chromium. Most cases involving multi-ingredient products have been reported in the United States in people who have consumed products from the Hydroxycut® range. The composition of Hydroxycut® products in reported cases is often vague or entirely unknown.

59. Besides these occasional published cases, research teams have also analysed database records of liver damage linked to toxic drugs or plant-based products.

60. As part of the US Drug Induced Liver Injury Network (DILIN), Vuppalanchi *et al.*, (2022) published their analysis of the 22 cases related to *G. cambogia* hepatotoxicity. Five of the twenty-two cases could be attributed to *G. cambogia* alone, in combination with green tea (n=16/22) or *Withania somnifera* [ashwagandha] (n=1/22). Statistical tests comparing control groups—patients with liver injury linked to green tea supplements without *G. cambogia* (n=57) or to other herbal supplements (n=103) showed that liver damage caused by *G. cambogia* and green tea was clinically indistinguishable. Patients who developed liver damage from dietary supplements containing *G. cambogia* showed a significantly higher frequency of the HLA-B*35:01 allele compared to those whose liver injuries were linked to other herbal supplements or conventional medications. The authors concluded that this association suggested a mode of action that is mediated by the immune system.

61. Bessone *et al.*, (2022) analysed the Latin America-Drug Induced Liver Injury (LATINDILI) database, they found that out of 367 cases, 8% were attributed to herbal food supplements. *Camellia sinensis* [green tea], Herbalife® products, and *G. cambogia*—mostly used for weight loss—were the most frequently identified as causes.

Psychiatric disorders

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62. Four of the eight cases involved people with a history of psychiatric disorders. This was identified to be a potential risk factor, although adverse reactions have also occurred in individuals without any known psychiatric history. The studies reviewed as part of the ANSES opinion are summarised in Table 2.

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Table 2 - Summary of data on psychiatric disorders linked to the consumption of *G. cambogia* Desr., reported in the literature (reproduced from the ANSES Opinion, 2025).

Author, date	Sex, age	Psychiatric history	Treatments	Consumption and context of use	Effects	Score assigned by the authors
Narasimha, 2013	Man, 23 years old.	None.	No information.	Hydroxycut® containing caffeine, guarana, <i>G. cambogia</i> , <i>Gymnema sylvestre</i> , glucomannan, green tea and willow bark.	Mania.	Linked to Hydroxycut® but authors suspect caffeine and guarana.
Beecheno, 2016	Woman, 33 years old.	None.	None.	Graviola® + spray containing levocarnitine, chromium, lipoic acid and dried fruit extracts from <i>G. cambogia</i> , leaves of <i>Gymnema sylvestre</i> , tea leaves and seeds of <i>Avena sativa</i> .	Psychosis	Naranjo 5, "probable" level according to WHO (positive reintroduction).
Hendrickson, 2016	Man, 50 years old.	Type I bipolar disorder.	None.	Food supplement based on <i>G. cambogia</i> . Diet or even exercise context.	Severe manic bipolar disorder (DSM-5)*.	None.
Hendrickson, 2016	Man, 25 years old.	None.	No information.	Food supplement based on <i>G. cambogia</i> . Diet or even exercise context.	Severe manic bipolar	None.

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					disorder (DSM-5)*.	
Hendrickson, 2016	Woman, 34 years old.	Type II bipolar disorder, hypomania induced by selective serotonin reuptake inhibitors.	Aripiprazole, bupropion and topiramate.	Food supplement based on G. cambogia. Diet or even exercise context.	Severe manic bipolar disorder (DSM-5)*.	None
Cotovio, 2017	Woman, 51 years old.	Stabilised type I bipolar disorder and occasional episodes of hypomania or moderate depression.	Valproic acid and paroxetine.	Product contains G. cambogia calcium, chromium and potassium.	Hypomanic episode.	Probable according to the authors (suggestive development).
Nguyen, 2019	Woman, 22 years old.	Traumatic episode in adolescence.	Subdermal etonogestrel implant.	Garcinia cambogia Plus®, containing G. cambogia extract with 60% HCA, and Cleanse and Detox®, containing raspberry ketone, liquorice root, pumpkin seeds, buckthorn root, cascara (Rhamnus purshiana), mango,	Mania with psychosis.	Naranjo 3, level "Possible" according to WHO.

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				rhubarb, citrus pectin, L. acidophilus, and Cape aloe.		
Guu, 2020	Woman, 20 years old.	History of overweight (BMI=25.6) and early-onset type 2 diabetes.	Metformin.	G. cambogia extract.	Autoimmune psychosi.	None.

*Fifth Edition of the Diagnostic and Statistical Manual of Mental Disorders.

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Cardiovascular disorders

63. Two cases of cardiomyopathy and one case of giant cell myocarditis have been reported in the literature. They are detailed in Appendix 3 of Annex B of TOX/2025/41.

64. The Plants WG and the Human Nutrition Expert Committee noted that both cases of cardiomyopathy involved women with no prior medical history. The clinical observations were deemed to be severe; one led to cardiac arrest, and the other caused high blood pressure with cardiac dysfunction, requiring ongoing cardiology follow-up.

Digestive disorders

65. The Plants WG and Human Nutrition Expert Committee noted that acute lithiasis pancreatitis often occurs in cases of obesity and diabetes. These three cases of pancreatitis occurred in people with diabetes and hypertension. Two of the three cases involved a history of obesity and chronic hepatitis C. They are detailed in Appendix 3 of Annex B of TOX/2025/41.

Muscle disorders

66. Two cases of rhabdomyolysis following consumption of Hydroxycut® have been reported in the literature. During periods of consumption (prior to 2009 [when the US FDA requested the withdrawal of *G. cambogia* from the product – see paragraph 36]), ephedra, caffeine, chromium, *G. cambogia* and *Gymnema sylvestre* [gymnema] were part of the composition of Hydroxycut®. These cases involved women who were either overweight or had recently increased their physical activity.

Metabolic disorders

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67. Roche *et al.*, (2014) reported a case of hypoglycaemia (blood glucose at 33 mg/dl) leading to syncope in a 67-year-old woman. The woman had been taking the following medications: venlafaxine, lisinopril-hydrochlorothiazide and alprazolam. She had started taking a dietary supplement containing *G. cambogia* two days before the onset of hypoglycaemia. The symptoms disappeared after administration of glucose. The author suspected *G. cambogia* because of the temporality of the events and the nonrecurrence of similar events following discontinuation of the product.

68. Bystrak *et al.*, (2017) reported a case involving digestive complications in a 56-year-old consumer with diabetes, the patient developed diabetic ketoacidosis. The authors suggested *G. cambogia* may have triggered ketosis by increasing ketone body production.

69. These studies detailed in Appendix 3 of Annex B of TOX/2025/41.

Other types of disorders

70. A 35-year-old woman with no known medical history or medication use reported an ocular disorder unilateral vision loss and eye pain after taking over 1,500 mg of HCA daily from *G. cambogia* extract for one week (Cho *et al.*, 2019). These ocular complications resolved after the extract was discontinued and treatment with topical and oral steroids was initiated.

71. Other publications of adverse reactions suspected to be related to consumption of *G. cambogia* provided little descriptive information on the product label and in general e.g. dose, exposure duration, presence of other hepatotoxic ingredients. Two studies (Sikka *et al.*, 2016; Graf *et al.*, 2020) reported cases of thrombocytopenia in connection with taking dietary supplements containing *G. cambogia*. Li and Bordelon (2011) reported a case of nephropathy occurring in a 51-year-old woman with no previous medical history in association with one month's consumption of a dietary supplement containing *G. cambogia*.

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Clinical trials

72. Several clinical trials have investigated the pharmacological effects of *G. cambogia* (Girola *et al.*, 1996; Hayamizu *et al.*, 2008; Heymsfield *et al.*, 1998). Most patients either reported no adverse events or showed no significant difference from the control group.

73. Cheng *et al.*, (2012) assessed the effects of a single oral HCA supplementation on postprandial glycogen synthesis in skeletal muscle in physically active men. Eight men aged on average 22 years (mean BMI 25.2 kg/m²) and in apparent good health were dosed with 500 mg of HCA, immediately after exercise. They noted an increase in fat oxidation after HCA supplementation and suggested this may present a risk of increased ketosis in patients with severe diabetes.

74. In another study (phase I observational study), 10 healthy men aged 26-56 years with no digestive disorders received 3,000 mg/day of HCA for 30 days. Although the measured parameters: anthropometric indices, clinical examinations, and serum testosterone levels remained unchanged, two subjects experienced anorexia and a third reported a headache (Hayamizu *et al.*, 2003).

Drug interactions

75. 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)

76. 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 (see case no. 2021-129 in Table 4 of Appendix 3 in Annex B of TOX/2025/41). A few days to weeks after starting the product, a 31-year-old woman

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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)

77. 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 (see case no. 2021 in Table 4 of Appendix 3 in Annex B of TOX/2025/41). 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.

78. In the study by Bolla *et al.*, (2021) garcinol exhibited strong inhibitory effects on CYP2D6 ($IC_{50} = 9,5 \mu M$) and CYP1A2 ($IC_{50}=7.6 \mu M$). Significant inhibitions were also reported for CYP2C9 ($IC_{50} = 8.0 \mu M$), 2B6 ($IC_{50} = 2.1 \mu M$) and 3A4 ($IC_{50}=5.1 \mu M$).

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79. 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.

80. 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

81. 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*.

82. 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

83. 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

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involved in a drug-drug interaction context without providing formal evidence (Lopez *et al.*, 2014).

84. 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.

85. 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).

86. 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.

87. 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

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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.

Conclusions of the Plants WG and the Human Nutrition Expert Committee

88. The Plants WG and the Human Nutrition Expert Committee:

- Noted that the EU has not harmonised the lists of authorised plants and plant parts for *G. cambogia* Desr., nor their uses and doses in food supplements, or the related restrictions and warnings. Therefore, they recommended proper characterisation of the raw material, including measuring HCA and conducting a botanical identification utilising appropriate analytical techniques to discriminate between the different species.
- Highlighted that many of the reported studies in the literature and vigilance reports poorly characterise *G. cambogia* Desr., extracts and thus urge operators to clearly define their extracts by detailing the composition and specifying the exact production conditions, including the extraction and purification methods and the solvents used.
- Noted that only HCA has been investigated in clinical studies, other components may contribute to adverse reactions. They recommended conducting studies on constituents found in fruit extracts—particularly benzophenones and polyisoprenylated xanthenes to investigate and clarify their potential role in adverse reactions.
- Noted that there is ambiguity in the plant parts present in *G. cambogia* Desr., food supplements.
- Advise individuals with psychiatric disorders, certain cardiometabolic diseases (diabetes, obesity, hypertension), and those with a history of pancreatitis or hepatitis to not consume food products (including

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supplements) containing *G. cambogia* Desr., based on the information from the literature and various vigilance systems.

- Further advise against the use of food supplements containing *G. cambogia* Desr., in children and pregnant or breastfeeding women [due to the lack of information].
- Recommend not combining the intake of *G. cambogia* Desr., with other hepatotoxic ingredients or foods (such as green tea extract, red yeast rice, turmeric or sources of coumarin).
- Recommended to avoid the use of this plant in combination with drugs known to affect liver function, anti-depressants, and antiretrovirals. More broadly, those taking drugs that are substrates of CYP3A4, CYP2B6, and Pg-P—to avoid consuming food supplements containing *G. cambogia* Desr. They also warn that *G. cambogia* may interact with substrates of CYP1A2, CYP2C9, and CYP2D6, and emphasise that these interactions remain a credible risk.

89. The Plants WG and the Human Nutrition Expert Committee reiterate the opinion of ANSES on slimming diets. Any weight-loss programme requires specialist medical support.

Conclusions of ANSES

90. In brief, ANSES highlighted the inconsistency of the regulatory status of the plant *G. cambogia* Desr., (also known as *G. gummi-gutta* (L.) N. Robson) in France. ANSES further noted that since 2012, the import, preparation, prescription and dispensing of medicines or preparations containing *G. cambogia* Desr., have been prohibited in France, as these preparations have not proven their efficacy and may expose the patient to health risks.

91. Based on the conclusions of the Human Nutrition Expert Committee and the Plants WG, ANSES advises against using *G. cambogia* Desr., products in individuals

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with psychiatric disorders, cardiometabolic conditions (diabetes, obesity, hypertension), or a history of pancreatitis or hepatitis. Use is also discouraged for those on liver-affecting drugs, antiretrovirals, or antidepressants. Given reports of severe adverse reactions in consumers without prior medical history. ANSES extends its recommendation to the entire population. It advises against consuming food supplements made from this plant or preparations containing it.

92. In general, ANSES highlights the need for European harmonisation regarding authorised plants, plant parts, uses and doses in food supplements, along with related restrictions and warnings.

AESAN

93. In 2019, the Scientific Committee of the Spanish Agency for Food Safety and Nutrition (AESAN) reviewed the risk associated with the consumption of food supplements that contain *G. gummi-gutta*.

94. They state that it is recommended to not exceed a daily dose of 3,000 mg of standardised extract at 50-60% HCA (dose equivalent to 1,500 – 1,800 mg of HCA), administered orally in three “shots”, 30-60 minutes before three main meals.

95. It was found that different supplements marked in Spain containing *Garcinia* and/or HCA were in the form of tablets, capsules, sachets or vials with differing compositions of *G. cambogia* and/or HCA content. The range of recommended daily allowances in these products was 30 – 2,070 mg of HCA.

96. AESAN noted that consumption of supplements containing *Garcinia* and/or HCA has been linked to toxic effects including hepatotoxicity, rhabdomyolysis, nephropathy, cardiovascular toxicity, hypomania and serotonin toxicity and psychosis; however, it has not been confirmed if *Garcinia* is the main toxicant, as it is often found in products with other ingredients.

97. AESAN concluded that there was “sufficient clinical evidence to establish a causal association between the consumption of garcinia and the duration of treatment, and the development of acute liver injury, with an obvious improvement in liver function

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after the withdrawal from the garcinia food supplement.” This conclusion was based on the literature reviewed by AESAN including Lunsford *et al.*, (2016) (see paragraphs 153-155), Crescioli *et al.*, (2018) (see paragraphs 143-149, 181), and Sharma *et al.*, (2018) (see paragraphs 150-152), among others.

98. Further to this, AESAN highlighted the importance of regulatory authorities to develop systems for post-market surveillance and for healthcare professionals, researchers and citizens to report adverse effects.

Australian TGA

99. The Australian Department of Health, Disability and Ageing Therapeutic Goods Administration (TGA) have also been aware of an increasing number of cases in scientific literature, by consumers who had taken products containing *G. gummi-gutta* or HCA. One of the five cases which reported liver transplantation was an Australian case. In response, the TGA completed an investigation into the risk of liver injury for the ingredient *G. gummi-gutta* (*G. cambogia*) and its naturally occurring component HCA. They concluded that “available evidence shows that there may be a rare risk of liver injury from taking *Garcinia gummi-gutta* (*Garcinia cambogia*).” (TGA, 2024a).

100. The TGA states that they will continue to monitor the issue and considering further regulatory action following a consultation on proposed requirements for a label warning. The consultation has ended, and final changes commenced 1st of March 2025, and a 12-month transition period was given to ensure product compliance. These changes are: 1) replacing “rare” with “very rare”; 2) provisions relating to liver-related warnings, and 3) references to the plant part for *G. gummi-gutta* will be changed from “rind of the fruit” to “fruit peel” to align with the plant parts in the TGA Code Tables (TGA, 2024b).

BfR (German Federal Institute for Risk Assessment)

101. Although not an official published risk assessment, a slide deck on “Risk Assessment Approaches and Methodology – an Overview” presented HCA from *G.*

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cambogia extracts as a case study - is publicly available (Hirsch-Ernst, 2022). In this, it was noted that doses via supplements was up to 3,000 mg HCA/day.

102. Three animal studies (oral administration, rats) were summarised (see Figure 3). It was observed that at high doses male rats showed signs of testicular toxicity and/or impaired spermatogenesis (i.e. sperm quality and sperm count).

Figure 3 – Animal studies as summarised in Hirsch-Ernst, (2022) (reproduced from Hirsch-Ernst, 2022).

Animal studies: Oral administration, rats		
Study	preparation tested	Results
90-day	Garcinia c. extract (41,2% HCA)	Testicular atrophies, germ cell degeneration, impaired spermatogenesis LOAEL: 778 mg HCA/kg bw; NOAEL: 389 mg HCA/kg bw
90-day	Ca ²⁺ /K ⁺ -HCA (60% HCA)	No testicular toxicity reported; hematology, clinical chemistry, histopathology without changes NOAEL: 1500 mg HCA/kg bw
Reprod. toxicity	Ca ²⁺ /K ⁺ -HCA (60% HCA)	No effects on the reproductive system of ♂/♀ animals observed; sperm quality & reproductive parameters of ♂ animals not affected NOAEL(♂): 611 mg HCA/kg bw (= highest tested dose)

103. In human intervention studies that assessed the safety of HCA intake, the observed adverse effects were mostly non-specific and were in similar occurrence as in control groups. The parameters of potential effects on spermatogenesis were not investigated.

104. The risk assessment was as follows. It was unclear whether the reproductive toxicological effects observed in male rats were due to the possible impurities in the extracts or were compound-specific to high doses of HCA intake. The lowest no-observed adverse effect level (NOAEL) was determined to be 389 mg HCA/kg bw per day (*G. cambogia* extract, 41.2% HCA). The human data were found to be inadequate with regards to considerations for the male reproductive system. The lack of specifications for HCA preparations/*G. cambogia* extracts added to food supplements was noted, and as such “transferability” of the above NOAEL to other preparations of food supplements may not be appropriate. Lastly, uncertainties regarding the health assessment of prolonged HCA intakes, especially at high doses (3,000 mg HCA/day) were noted.

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EFSA

105. The EFSA are currently in the process of writing a scientific opinion on the evaluation of the safety in use of hydroxycitric acid and plant preparations containing hydroxycitric acid (under EFSA query: EFSA-Q-2022-00805). The protocol of which has been published in 2023 (EFSA, 2023a). In brief, the protocol is based on a narrative review of the evidence and on expert knowledge. The overarching risk assessment questions are:

- a) Is there a link between dietary exposure to HCA and adverse effects on health?
- b) Is there a link between consumption of HCA in the plant preparations listed in Table 1 (covers *G. gummigutta* (L.) N.Robson, *G. indica* (Thouars) Choisy, *G. mangostana* L., *Hibiscus sabdariffa* L. with their respective plant parts e.g. fruit, resin, peel, flower, leaf, seed, bloom, twig) and adverse effects on health?
- c) What is the maximum level of total chronic dietary exposure (i.e. over a substantial part of the lifespan) to HCA and HCA in plant preparations and foods containing HCA, which is unlikely to pose a risk of adverse effects to humans?

106. In 2023, EFSA issued a call for data specifically for: occurrence data (analytical data on the content of HCA in plant preparations and food, including food supplements); use of levels of supplements (use levels recommended by manufacturers for food supplements containing HCA) and biological and toxicological data (to support the assessment of a causal relationship between dietary exposure to HCA as single substance and/or in plant preparations and the a priori identified adverse effects, including data on absorption, digestion, absorption and metabolism for HCA and within the food matrix). The call for evidence ended on the 12th of January 2024 (EFSA, 2023b).

107. Publicly available minutes for the EFSA Scientific Panel on Nutrition, Novel

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Foods and Allergens show that the Working Group on substances other than vitamins and minerals last discussed the draft opinion on the 4th of June 2025 (EFSA, 2025).

Health Canada

108. An entry was found in Health Canada's Licensed Natural Health Products Database for brand name *G. Cambogia* produced by New Roots Herbal Inc (Applicant) (Health Canada, 2024a). The accompanying monograph to which the Applicant attested to provides details on the dosage form and quantities. The route of administration is oral and can be taken by adults 18 years and older. The recommended dose is 2-3 grams of extract standardized to 50-60% hydroxycitric acid, per day; 1.5-2 grams of extract per single dose and is to be taken before meals.

109. These dose range were based on the studies by (Kim *et al.*, 2011; Gatta *et al.*, 2009; Ishii *et al.*, 2003; Heymsfield *et al.*, 1998).

110. Health Canada states that the monograph "is intended to serve as a guide to industry for the preparation of Product Licence Applications (PLAs) and labels for natural health product market authorisation. It is not intended to be a comprehensive review of the medicinal ingredient." (Health Canada, 2018, 2024b).

NCCIH

111. The United States National Centre for Complementary and Integrative Health (US NCCIH) states that "it may be unsafe to consume garcinia cambogia products, including multi-ingredient products containing garcinia cambogia extract. Several cases of liver damage have been reported. Some of these cases were severe, but this appears to be uncommon."

112. Other reported side effects include headache, nausea, diarrhoea, and other gastrointestinal symptoms. Interactions between *G. cambogia* and some drugs affecting the liver and serotonin have been reported. Limited information is available on the safe use of *G. cambogia* during pregnancy or while breastfeeding (US NCCIH, 2025).

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Data from literature search

113. As mentioned in paragraph 5, a literature search was carried out using the search string "Garcinia cambogia" AND "toxicity" in PubMed, Science Direct and Google Scholar. No filters or restrictions were used. These were in addition to the data reviewed by ANSES.

Toxicokinetics

114. van Loon *et al.*, (2000) investigated the acute effects of ingestion of HCA ("6-30 times the reported dosage applied in human weight-loss studies) on plasma HCA availability. They further investigated whether systemic HCA availability altered fat oxidation rates and plasma metabolite concentrations at rest and during moderate-intensity exercise in "endurance-trained" humans by assessing total fat and oxidation rate calculations. Ten cyclists presumed to be male (sex based on information from a pilot study (n=3 males; these males were not included in the main study); aged 25 ± 2 years; BMI 22.1 ± 0.5 kg/m²) received a total of 0.5 g/kg bw of a liquid *G. cambogia* extract - Citrimax HCA-450-LS (48% HCA), which was divided over 4 boluses. This resulted in 18 ± 0.4 g HCA being ingested by every subject in the HCA trial. The placebo was water; the number of subjects in the control group were not detailed. It should be noted that beverages (HCA drink or water) were provided in a randomised order. A blood sample was taken at rest, and subjects were provided with either HCA or water to drink 45 mins before exercise. Blood samples were taken at 15 minutes intervals until t=0. Subjects received their second dose 15 minutes before exercise. Following a warm-up period (5 minutes), subjects started cycling at a moderate intensity of 50% Wmax for 2 h (t = 0–120). During exercise, subjects received another bolus of test drink at t = 30 and at t = 60. During exercise, blood samples were taken at 30-min intervals (t = 30 and 60).

115. In the pilot study, it was determined that plasma HCA concentrations increased over time after ingestion of a single dose of HCA solution 4.4g over a 3.5-hour period. Maximal values were attained after 60-90 minutes at 0.12 ± 0.03

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mmol/L, after which the concentration decreased. No HCA was detected in the samples collected in the placebo trial.

116. In the main study, plasma HCA concentrations increased up to 0.08 ± 0.01 mmol/L (16.6 mg/L) after the ingestion of 4.4 ± 0.1 g HCA at $t = -45$ and $t = -15$ during resting conditions. Plasma HCA concentrations increased further up to 0.39 ± 0.02 mmol/L (82.0 ± 4.8 mg/L) after the ingestion of 4.4 ± 0.1 g HCA after 30 and 60 min of exercise. It was concluded by the authors that plasma HCA availability does not increase energy expenditure or stimulate skeletal fat muscle fat oxidation at rest or during exercise.

117. Loe *et al.*, (2001) dosed fasting humans ($n=4$; 3 males and one female, subjects were anonymised; age range 21-42; weight range 52.3-86.2 kg) with 2 g of HCA (in the form of CitriMax HCA-600-SXP capsules, ~500 mg) to assess the [bio]availability in humans using a novel gas chromatography/mass spectrometry (GC/MS) method. The subjects were all “healthy, non-smokers that had no history of cardiovascular disease or diabetes”. Blood samples were collected 30 minutes after ingestion of the supplement and every 30 minutes thereafter over a period of 3.5 to 4 hours. A 50 mL blood sample from a control subject (who did not take the supplement) was also collected to construct a standard curve. The peak plasma HCA concentration was observed 2 hours after administration, measuring 8.4 µg/mL, which demonstrated that HCA absorption is relatively fast.

118. Cruz *et al.*, (2021) aimed to determine the main pharmacokinetic parameters of *G. cambogia* extract/HCA in “healthy” women ($n=16$ fasted period and $n=13/16$ for fed period; ages 21-41 years with BMI 20.29–25.82 kg/m²), and to evaluate the food effects on HCA absorption. Subjects received 1,500 *G. cambogia*, of which 750 mg is HCA extract under 8 hours of fasting. In the fed period, a high-calorie breakfast (~600 calories) was given after dosing. Plasma HCA concentrations were significantly higher in the fasted state (1.21 µg/mL) compared to the fed state (0.40 µg/mL). Overall, plasma concentrations ranged from 0.05 – 2.74 µg/mL. Peak plasma concentration (C_{max}) and area under the curve time concentration ($AUC_{0-10hrs}$) were 3-fold and 2-fold lower ($p<0.001$, 0.01), in the fed-condition, respectively. The maximum concentration for both groups were similar with 2 hours as the

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median. In the presence of food, it was observed that, HCA elimination was reduced (5 hours vs 3 hours under fasted conditions). The authors further noted substantial inter-individual variation for the different pharmacokinetic parameters in both periods. The authors suggested that “HCA might suffer an active absorption uptake and intense adsorption on food.”

119. Heymsfield *et al.*, (1998) evaluated the efficacy of *G. cambogia* for body weight and fat mass loss in “overweight but otherwise healthy adults” (aged 18-65 years; BMI range 27 - 38 kg/m²). The total daily dose of *G. cambogia* extract was 3,000 mg, of which 1,500 mg was HCA or a placebo was received. Both groups were prescribed a high-fibre, low energy diet. A total of 135 subjects were randomised to either active HCA (n=66) or placebo (n=69) groups; 42 (64%) in the active HCA group and 42 (61%) in the placebo group completed 12 weeks of treatment ($P=.74$). It was found that the co-administration of HCA with a high-fibre diet and low-energy may have inhibited the gastrointestinal absorption of HCA. There was no significant difference in group weight loss (mean [SD], 3.2 [3.3] kg vs 4.1 [3.9] kg; $P=.14$) between the exposed and placebo groups.

120. In the literature, (2S,3S)-HCA has been described to inhibit the ATP-citrate lyase enzyme (Jakopin, 2019). This is the primary enzyme responsible for the synthesis of cytosolic acetyl-CoA in many tissues. The product, acetyl-CoA, serves several important biosynthetic pathways, including lipogenesis and cholesterologenesis. In nervous tissue, ATP citrate-lyase may be involved in the biosynthesis of acetylcholine (NCBI, 2025). Thus, it is believed that HCA is widely distributed.

121. No other data were available for distribution, metabolism and excretion. It is also unclear if different *Garcinia* species influences the bioavailability of HCA.

Review articles

122. Andueza *et al.*, (2021) performed a review to investigate the effectiveness and side-effects of nutritional supplements based on *G. cambogia* to promote weight loss. The efficacy of other *Garcinia* species was also provided. They utilised the

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Cochrane and PubMed databases; 13/51 and 29/53 articles were selected for detailed review, respectively. They concluded that toxicity cannot be reliably attributed to *Garcinia*, as it is typically present in MIDS. The authors were of the opinion that case reports describing adverse effects usually reflect the associations between the observed toxicity and the intake of the dietary supplement, rather than causality. Furthermore, the authors note that the use of these supplements should be discouraged for pregnant and lactating women, since HCA can affect the production of fatty acids and cholesterol, which can directly influence the production of sterols and steroid hormones.

123. Data from the LiverTox database noted that studies in rats and other animal models have suggested that *G. cambogia* and HCA do not have significant toxicities, although testicular toxicity was found with high doses (Saito *et al.*, 2005). In humans, *Garcinia* has been linked to rare reports of serotonin syndrome, rhabdomyolysis and hepatic toxicity; however, the role of *Garcinia* as opposed to other components of MIDS typically used in humans is yet to be fully elucidated. The frequency of hepatic adverse reactions was estimated to be 1:10,000 and it was concluded that consumption of *G. cambogia* is likely a rare cause of clinically apparent liver injury (NCBI, 2019).

124. Márquez *et al.*, (2012) noted that caution should be exercised when interpreting the results from human studies as other randomized, placebo-controlled clinical trials have not reported the same outcomes. Furthermore, most studies in humans have been conducted on small samples and mainly in the short term. None of them have shown whether these effects persist beyond 12 weeks of intervention. Therefore, there is still little evidence to support the potential effectiveness and long-term benefits of *G. cambogia* extracts. Regarding toxicity and safety, it is important to note that except in rare cases, studies conducted in experimental animals have not reported increased mortality or significant toxicity. Furthermore, at the doses usually administered, no differences have been reported in terms of side effects or adverse events (those studied) in humans between individuals exposed to *G. cambogia* and controls.

125. Chuah *et al.*, (2013) “critically assessed” the evidence from the *in vitro*, *in*

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vivo, and clinical trials on the safety of *Garcinia*/HCA as a dietary supplement for treating obesity. The methodology in which the authors collected and reviewed studies in the literature was not described. The following endpoints were considered: cytotoxicity, genotoxicity, acute toxicity (oral, dermal, dermal irritation and eye irritation), sub-chronic (90 days) toxicity and reproductive and teratogenic toxicity. The authors summarised that *G. cambogia*/HCA is generally safe and a NOAEL up to 1, 240 mg/kg per day based on a developmental toxicity study in rats by Deshmukh et al., (2008a) (see Subchronic section).

Genotoxicity

126. Lee & Lee (2007) evaluated the genotoxicity of HCA isolated from *G. cambogia* using three tests: the Ames test, the *in vitro* chromosomal aberration test, and an *in vivo* micronucleus test. The test item was described as “a natural, highly water-soluble, calcium-potassium salt of 60% HCA extract”; commercially known as Super CitriMax HCA-600-SXS (HCA-SX).

127. The Ames *Salmonella* mutation test was used according to the plate incorporation procedure described by Maron and Ames (1983). The five strains of *Salmonella typhimurium* (TA98, TA100, TA102, TA1535, and TA1537) were provided by Prof. B. N. Ames (University of California Berkeley). The assay was performed with and without metabolic activation using an S9 mixture. Negative and positive controls were used for each strain. The positive controls performed without metabolic activation were: 2-nitrofluorene (1 µg per plate) for TA98, sodium azide (1.5 µg per plate) for TA100 and TA1535, mitomycin (1 µg per plate) for TA102, and acridine mutagen (1 µg per plate) for TA1537. The positive controls performed with metabolic activation was 2-aminoanthracene (1 µg per plate) for all strains. Six concentrations of HCA-SX were examined with triplicate plates per dose: 0, 20, 200, 500, 2,500, and 12,500 µM/plate. HCA-SX did not induce mutagenic activity in any of the five bacterial strains tested, under any of the activation conditions examined.

128. For the chromosomal aberration test, the Chinese hamster ovary (CHO) cell line was provided by the Cancer Research Institute, Seoul National University,

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Korea. CHO cells were maintained under monolayer conditions in Eagle's minimum essential medium supplemented with 10% foetal bovine serum, with L-glutamine and ampicillin at 37°C in a 5% CO₂ atmosphere. For each treatment, 3×10^5 cells were cultured in duplicate in 5 mL of culture medium in a 2.5-L flask. After the cells were incubated for 24 h, they were treated with an HCA-SX 10 µL reaction volume. A 5-hr pulse treatment was then carried out with and without the S9 mixture (used at a final concentration of 10% in the treatment medium). Benzo[a]pyrene (BaP) was used as a positive control in the presence of S9. Mitomycin C (MMC) was used as a positive control in the absence of S9 mixture. Chromosomal aberration percentages included by HCA-SC in the treated groups were >3% and 4%, respectively. In the positive control groups, the percentage of structural chromosome aberrations in the BaP and MMC-treated groups were >21% with S9 and >25% without S9, respectively. HCA-SX was not observed to induce any cytotoxic effect.

129. For the micronucleus test, 7- to 8-week-old ICR male mice (n=5/group) were acclimatised for at least 7 days prior to the start of the test. HCA-SX were dissolved in dimethyl sulfoxide (DMSO). The groups were as follows: DMSO (negative control), 20, 100, 500, 2,500 or 12,500 HCA-SX µmol/kg dissolved/suspended in DMSO, mitomycin C at 2 mg/kg (positive control). Animals were administered the treatments by intraperitoneal injection and were sacrificed by cervical dislocation 24 hours after the test substance administration. Numbers of micronucleated cells were determined by counting the number of polychromatic erythrocytes (PCEs) from at least 1,000 PCEs per animal. The micronucleated polychromatic erythrocytes (MNPCEs) that contained micronuclei were counted from at least 1,000 PCEs. No mortality was observed. MNPCE/1,000 PCEs were induced at the highest HCA-SX dose (12,500 µmol/kg) and PCE/(PCE + NCE) ratios decreased with increasing dose.

130. The authors concluded that HCA-SX was not found to be genotoxic by bacterial or by chromosome aberration testing. It demonstrated "a weak mutagenic effect by micronucleus testing but did not induce structural chromosomal aberrations or significantly induce MNPCEs at the doses used.

131. The article by Lee & Lee (2007) (as summarised in paragraphs 126-130) was refuted by Lau *et al.*, (2008), stating that for the *in vivo* micronucleus test, the

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authors: i) selected an inappropriate route of administration intraperitoneal rather than the oral route; ii) the use of vehicle for the test item (DMSO) was not justified and varied to that of the positive control (water), as DMSO may react with the test compound to induce an adverse effect; iii) a dose-range finding test was not performed and the range of selected doses (separated by a factor of 5) differed from conventional dose levels used in toxicological studies; iv) discrepancy with reporting of results; v) “very weak” statistical analysis, where a *t*-test was utilised without performing a one-way analysis of variance previously; a regression or correlation analyses was also not performed.

132. Ghosh & Mukherjee (2017) evaluated the *in vitro* genotoxicity of HCA (50.9% HCA in calcium salt of HCA) in human lymphocytes. The following methods were used: trypan blue dye exclusion test, MTT assay, Comet assay and a DNA diffusion assay. The trypan blue and MTT assay were performed according to the test methods of Tennant (1964) and Mosmann (1983), respectively, with modifications by Sinha *et al.*, (2014). The Comet assay was performed following the method of Tice *et al.*, (2000), with modifications based on Sinha *et al.*, (2014). Cells were exposed to HCA (0, 10, 20, 40 or 100 µg/mL) for 3 hours or 24 hours and processed for cytotoxicity and genotoxicity analyses. The effects of HCA on erythrocytes were determined by a haemolysis test using the same doses and exposure duration. Results from the trypan blue and MTT assay in human lymphocytes demonstrated the absence of significant induction of cytotoxicity when compared to the positive control groups. However, as observed in the Comet assay, HCA induced DNA damage that was statistically significant at concentrations of 40 and 100 µg/mL. The authors noted that these concentrations were “almost identical to and approximately double the maximum permitted dose [author does not detail if this the human equivalent dose] (i.e. 900 – 2,800 mg/day or 15 – 47 mg/kg/day, respectively).” Oxidative stress, as a potential mechanism of DNA damage was evaluated using DCFH-DA dye. A significant increase in reactive oxygen species (ROS) production was found at concentrations of 40 and 100 µg/mL at both time points compared to the respective controls. As for the effects on the erythrocytes, no haemolytic potential was observed. The authors concluded that HCA-induced genotoxicity may not lead to apoptotic/necrotic cell death. The observed DNA damage can be

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attributed to oxidative stress, which was independent of mitochondrial ROS generation.

Human data

Clinical data

133. Onakpoya *et al.*, (2010) performed a systematic review and meta-analysis of RCTs on the use of *Garcinia* extract (HCA) as a weight loss supplement. Twenty-three eligible trials were identified of which twelve were further analysed. Nine of the twelve trials provided data for statistical pooling (see Figure 4). The dosage of HCA and the duration of the study were varied, ranging from 1-2.8 grams daily and from 2 to 12 weeks, respectively. The adverse effects reported in the RCTs included headache, skin rash, common cold, and gastrointestinal symptoms. In most of the studies there were no “major” differences in adverse events between the HCA treatment and placebo groups. Except for one trial where gastrointestinal symptoms were twice as frequent in the HCA group compared to the placebo group (Heymsfield *et al.*, 1998).

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Figure 4 - Results table for studies with adequate data for meta-analysis (reproduced from Onakpoya *et al.*, 2011).

Author Year Country	HCA formulation	Randomised/ Analysed	Age in yrs	HCA Dosage	Treatment Duration	Baseline weight indices for HCA/placebo groups	Mean change in weight indices for HCA/placebo groups	Adverse events (AE)	Control for lifestyle factors
Hayamizu et al. 2001 Japan [24]	Tablets	40/40	37.1 ± 12.5 (HCA) 36.5 ± 10.7 (PLA)	1 g daily	8 weeks	BW: 75.6 ± 10.3/73.3 ± 10.7 BMI: 27.9 ± 1.8/27.8 ± 1.8	BW: 0 ± 11.5/0.5 ± 11.7 BMI: 0 ± 1.97/0.3 ± 2.3	No serious AE reported	Dietary control
Heymsfield et al. 1998 U.S.A. [25]	Capsules	135/135	38.6 ± 7.7 (HCA) 39.4 ± 7.2 (PLA)	1.5 g daily	12 weeks	BW: 83.8 ± 10.7/88.2 ± 13.0 BMI: 31.2 ± 2.8/31.9 ± 3.1	BW: -3.2 ± 3.3/ -4.1 ± 3.9	Headache, URTI & GI symptoms	High fibre diet, stable physical activity levels
Kovacs et al. 2001 Netherlands [26]	Unspecified	21/21	43 ± 10 for both HCA&placebo groups	1.5 g daily	2 weeks	Mean BW: 79.3 ± 9.0 Mean BMI: 27.6 ± 2	BW: -0.4 ± 0.9/-0.5 ± 1.4	Not reported	No restriction on food intake; 1 glass of alcohol maximum daily
* § Kovacs et al. 2001 Netherlands [27]	Unspecified	11/11	47 ± 16 for both HCA&placebo groups	1.5 g daily	2 weeks	Mean BW: 85.4 ± 25.8 Mean BMI: 27.4 ± 8.2	BW: -1.5 ± 1.66/ -1.0 ± 1.34	Not reported	No restriction on food intake; 1 glass of alcohol maximum daily
Mattes and Bormann 2000 U.S.A. [5]	Caplets	167/89	40.97 ± 10 (HCA) 44.0 ± 9.5 (PLA)	1.2 g daily	12 weeks	BW: 75.5 ± 10.2/75.8 ± 12.6 BMI: 28.3 ± 0.6/28.8 ± 0.7	BW: -3.7 ± 3.1/-2.4 ± 2.9	Not reported	Dietary control, exercise encouraged, but no formal regimen prescribed
§ Preuss et al. 2004 India [29]	Unspecified	60/53	Range: 21–50	2.8 g daily	8 weeks	BW: 91.7 ± 15.7/80.4 ± 36.9 BMI: 34.7 ± 5.5/32.5 ± 2.6	BW: -4.5 ± 16.6/ -1.6 ± 34.1 BMI: -1.7 ± 5.8/-0.7 ± 2.74	Gas, stomach burn, headache, skin rash	Dietary control, walking exercise programme
§ Preuss et al. 2004 India [6]	Unspecified	30/29	Range: 21–50	2.8 g daily	8 weeks	BW: 88.5 ± 21.8/87.4 ± 15.9 BMI: 33.6 ± 6.2/34.0 ± 4.5	BW: -5.5 ± 23.7/ -1.4 ± 17.3 BMI: -2.1 ± 6.85/-0.5 ± 4.8	No serious AE reported	Dietary control, walking exercise programme
Ramos et al. 1995 Mexico [30]	Capsules	40/ 35	35.3 ± 11.8 (HCA) 38.7 ± 12.3 (PLA)	1.5 g daily	8 weeks	BMI: 32.6 ± 4.3/33.2 ± 4.4	BW: -4.1 ± 1.8/-1.3 ± 0.9	Nausea, headache	Dietary control
Roongpisu- thipong et al. 2007 Thailand [2]	Sachets	50/42	40.0 ± 10.0 (HCA) 36.0 ± 10.0 (PLA)	Unclear	8 weeks	BW: 69.0 ± 5.0/65.0 ± 5.0 BMI: 27.5 ± 1.0/26.7 ± 2.5	BW: -2.8 ± 0.5/-1.4 ± 0.5 BMI: -0.9 ± 1.0/-0.6 ± 1.0	Not reported	Dietary control

Abbreviations: HCA: Hydroxycitric acid; PLA: Placebo; BW: Body Weight; BMI: Body Mass Index.

^bUnless otherwise specified, values for age, baseline weight and mean change in weight indices have been reported as means with standard deviations.

*Studies included as crossover design, otherwise all included trials had parallel-study design.

§Studies with 3 intervention groups.

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134. Amini *et al.*, (2024) performed a systematic review and meta-analysis of RCTs on the use of *G. cambogia* (HCA) on serum leptin concentrations. Eight studies were included in the meta-analysis (see Figure 5). Leptin is a peptide hormone that is produced and secreted by adipose tissue. It plays a role in appetite control, immune system modulation, insulin sensitivity, blood pressure regulation and energy homeostasis. The authors observed that several of the included studies found no adverse effects of supplementation. In one study, 38.4% of participants reported the following side effects during treatment: gastrointestinal symptoms, thirst, dizziness and diuresis with gastric discomfort being the commonly reported (Vasques *et al.*, 2014). It was noted by the authors that the treatment period in the selected trials ranged from 11 days to 10 weeks and the long-term side effects of supplementation requires further evaluation as several case reports observed liver injury following *G. cambogia* supplementation.

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Figure 5 - Demographic characteristics of the included studies (reproduced from Amini *et al.*, 2024).

First Author (year)	Location	Study Design	Health status	Sex	Sample size	Duration (week)	Mean age (year)	Baseline BMI (kg/ m ²)	Intervention group	Comparator group	Outcome	Assess potency of the Garcinia cambogia product used)	Assess purity of the Garcinia cambogia product used)
1. Preuss (a) (2004)	India	RCT	Healthy	Both	20	8	35.5	40.4	4667 mg/day hydroxycitric acid (HCA-SX) (60 % HCA providing 2800 mg HCA/day)	Placebo	Leptin	Yes	Yes
2. Preuss (b) (2004)	India	RCT	Healthy	Both	35	8	35.5	42.7	4667 mg/day hydroxycitric acid (HCA-SX) (60 % HCA providing 2800 mg HCA/day)	Placebo	Leptin	Yes	Yes
3. Preuss (2005)	India	RCT	Healthy	Both	54	8	35.5	33.6	4667 mg/day hydroxycitric acid (HCA-SX) (60 % HCA providing 2800 mg HCA/day)	Placebo	Leptin	Yes	Yes
4. Kovacs (2006)	Netherlands	RCT	Healthy (sedentary lean male)	Male	10	11 day	24	21.8	1447.5 mg/day HCA	Placebo	Leptin	Yes	No
5. Kim (2011)	Korea	RCT	Healthy	Both	58	10	33.9	25.4	2000 mg/day Garcinia cambogia extract (60 % HCA)	Placebo	Leptin	Yes	No
6. Lu (2012)	Taiwan	RCT	Healthy	Both	71	8	27	28.8	2800 mg/day Garcinia cambogia extract (1380.4 mg/day HCA)	Placebo	Leptin	Yes	No
7. Vasques (2014)	Brasil	RCT	Healthy	Female	43	60 day	40	32.24	2400 mg/day Garcinia cambogia extract (50 % HCA)	Placebo	Leptin	Yes	Yes
8. Tutunchi (2023)	Iran	RCT	NAFLD	Female	39	8	34	33.7	3000 mg/day HCA + Received low-calorie diet	Received low-calorie diet	Leptin	Yes	No

Abbreviations: RCT, Randomized controlled trial; BMI, Body mass index; NAFLD, Nonalcoholic fatty liver disease; HCA, Hydroxycitric acid;

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Hepatotoxic case reports

DILIN network

135. The United States Drug-Induced Liver Injury Network (DILIN) have published several articles concerning herb related drug injury. Articles that referred to *G. cambogia* are summarised in chronological order.

136. In 2015, Navarro *et al.*, noted that *G. cambogia* was implicated with herbal products in the DILIN database; however, the role of this herb in causing liver injury was difficult to assign since there was a lack of documentation of their chemical presence and purity, the possibility of contamination with other herbal products or mislabelling of the ingredients.

137. In 2022, Vuppalanchi *et al.*, described the hepatotoxic effects of *G. cambogia*, either alone or in combination with green tea extract (catechins) consumption. Among the 1,418 patients enrolled in the DILIN from 2004-2018, it was identified that 22 cases of liver injury could be attributed to *G. cambogia* alone (n=5/22), in combination with green tea (n=16/22) or in combination with ashwagandha (n=1/22). 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.

138. Patients who took *G. cambogia* (see Figure 6) were aged 17 and 54 years (n=22; 12 females and 10 males) with liver injury arising 13-223 days (median = 51 days) following the first dose. The doses for each product type were not made readily available, and it should be noted that although one of the products claimed the presence of *Garcinia*/HCA, it was not detected.

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Figure 6 - Names and products linked to *G. cambogia* and green tea extract (catechins) induced liver injury (reproduced from Vuppalanchi *et al.*, 2022).

Patient		<i>Garcinia cambogia</i> /HCA		GT extract/EGCG	Total catechins	EGCG
		Label claim	Chemical profiling	Label claim	Chemical profiling	
1.	Mega-T Green Tea Extract	No	Not detected	Yes	Detected	Detected
2.	Hydroxycut	Yes	Detected	Yes	Detected	Detected
3.	Quick Loss Diet Spray with Hoodia	Yes	Detected	Yes	Not detected	Not detected
4.	Visalus Sciences Vi-Slim Metab-Awake	No	Not detected	Yes	Detected	Detected
	OmegaKrill Pure Concentrated Krill Oil	No	Not detected	No	Not detected	Not detected
	Visalus Sciences Neuro	No	Not detected	Yes	Detected	Detected
	Visalus Sciences Vi-Trim	Yes	Detected	No	Not detected	Not detected
5.	Hydroxycut	No	Not detected	Yes	Detected	Detected
6.	Fat Burner	Yes	Detected	Yes	Detected	Detected
	Great Start-Energy Formula	No	Not detected	Yes	Detected	Detected
7.	Garcinia Cambogia X Treme	Yes	Detected	No	Not detected	Not detected
8.	Super Plus Weight Loss Enhancer	Yes	Not detected	Yes	Detected	Detected

EGCG, epigallocatechin gallate; GC, *Garcinia cambogia*; GT, green tea; HCA, hydroxycitric acid.

139. Of these patients, one died, one required liver transplantation and 20 were hospitalised. The liver injury was hepatocellular with jaundice. Peak values of aminotransferases were significantly higher ($2,001 \pm 1,386$ U/L) in the *G. cambogia* group ($P < .018$), the median time for improvement in total bilirubin (TB) was significantly lower compared with the control groups (10 vs 17 and 13 days; $P = .03$).

140. 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%) ($P = 2.55 \times 10^{-6}$). The authors concluded that liver injury caused by *G. cambogia* and green tea was clinically indistinguishable and hypothesised that there is possible association immune-mediated mechanism of injury via HLA-B*35:01 allele.

LATINDILI

141. Bessone *et al.*, (2025) published a “comprehensive analysis” of patients enrolled into the Latin American DILI Network over a decade. Chemicals suspected of causing DILI were classified according to the Anatomical Therapeutic Chemical classification. Causality was assessed using the Roussel Uclaf Assessment method. Overall, 468 idiosyncratic DILI cases were analysed, it was observed that 62% were women (mean age 49 years). Of the cases, 4.1% had a fatal outcome, and 24

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patients (12%) developed chronic DILI. The most common drug classes were systemic anti-infectives (31%), musculoskeletal agents (12%), antineoplastic and immunomodulating agents (11%), and herbal and dietary supplements (9%). A total of 6 cases were attributed to *G. cambogia*.

Other literature

142. Al-Khazraji *et al.*, (2020) [abstract only – poster for symposium] claimed to report the first human case report of *G. cambogia* induced autoimmune hepatitis. A 39-year-old female with no past medical history presented with fatigue and dark coloured urine. Clinical exam demonstrated a palpable liver and scleral icterus. The patient reported using a “slimming herbal tea supplement” containing pure GC for weight loss 5 weeks prior to presentation [no further information on dose or HCA content]. Elevated transaminase levels were observed and were considered significant: alanine transaminase (ALT) 1803 IU/L; aspartate aminotransferase (AST) 1026 IU/L; alkaline phosphatase (ALP) 139 mg/dL and TB 5.2 mg/dL. Further liver work up revealed an elevated anti-nuclear antibody (ANA) 1:160 titer; anti-smooth muscle antibodies (ASMA) 1:320; and immunoglobulin G 1,814. The normal range for these parameters were not detailed in the paper. A liver biopsy was performed, which demonstrated moderate mixed inflammatory cells including lymphocytes, plasma cells, neutrophils and “rare” eosinophils in the portal tracts. Interface hepatitis and cholestasis was also noted. The authors stated that findings were consistent with DILI with a background of autoimmune hepatitis. The patient was treated with steroids (Prednisone 40 mg orally, daily), upon tapering of her steroids; her liver function began to rise, and she was started on immunosuppressive therapy for long term maintenance with “good response”. The authors further stated that *G. cambogia* liver injury can last for 2–3 months with normalizing of liver function tests by 5 months.

143. Crescioli *et al.*, (2018) presented four cases of acute liver failure in women taking *G. cambogia* extract for weight loss, and a literature review of clinical evidence about hepatic toxicity in patients taking dietary supplements containing *G. cambogia* extract.

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144. For Case 1, a 61-year-old woman presented to the emergency department with symptoms of abdominal pain, nausea, progressive weakness, jaundice, dark urine, and acholic stools. The patient's anamnesis denoted cholecystectomy, mixed dyslipidemia, and hypothyroidism in treatment with levothyroxine. There was no history of alcoholism or exposure to hepatotoxins; she also denied paracetamol abuse. She reported taking one envelope/daily of SUPER ANANAS SLIM®, for a period of 2 months to lose weight. This contained extracts of *G. cambogia* (HCA 60%), *Ananas comosus* (bromelain 334 GDU; gelatine dissolving units), and *Ilex paraguariensis* [Yerba mate] (caffeine 2%). Laboratory tests revealed that ALT, AST, TB, ALP, gamma-glutamyl transferase (GGT), direct bilirubin and albumin were higher than the normal total range at 1,629 U/L, 1,121 U/L, 22.5 mg/dL, 16.7 mg/dL and 2.2 g/dL, respectively. The normal range for each parameter is 0-35 U/L, 0-40 U/L, 0.2-1 mg/dL, 0-0.25 mg/dL and 3.5-5 g/dL, respectively. Serology was negative for hepatitis viruses or autoantibodies. A check-up 3-months prior had found these parameters to be normal. The abdominal computed tomography scan revealed a small peritoneal effusion, perihepatic lymphadenopathy, and a hepatic biopsy which was consistent with cholestatic hepatitis. Four weeks after the cessation of the supplement intake, patient symptoms and liver function tests gradually improved, and the patient was discharged with no need for liver transplant. Four months later, the levels of the previously tested markers reverted to normal values.

145. For Case 2, a 39-year-old woman presented to the emergency department with symptoms of jaundice, asthenia, loss of appetite, and right hypochondrial pain. Her anamnesis denoted arterial hypertension, obesity (BM 44.9 kg/m²), and hiatal hernia. Her medication at the time of admission were methyldopa 500 mg/day, domperidone 20 mg 3 times/day and omeprazole two 20 mg capsules/day. She also reported taking two dietary supplements for weight loss recommended by her dietician. The first, OBLESS®, contained in each capsule: *C. aurantium* [bitter orange] 140 mg of extract 10% (14 mg of synephrine), *G. cambogia* (72 mg of HCA), *Orthosiphon stamineus* [cat's whiskers or Java tea] (0.2 mg of sinensetin), and *Griffonia simplicifolia* [African black bean] (75 mg of 5-hydroxy-L-tryptophan). The second dietary supplement was a magistral preparation containing in each capsule: *C. aurantium* [bitter orange] 350 mg of extract 6% (21 mg of synephrine), *Rhodiola rosea* [Roseroor or Goldenroot] 150 mg extract, and *O. stamineus* [cat's whiskers or

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Java tea] 200 mg extract. The patient declared that she had been taking the first dietary supplement for the previous month (1 capsule/day) and the magistral preparation for 15 days (1 capsule/day), simultaneously. Laboratory tests performed revealed that ALT, AST and TB were higher than the normal ranges at 1,554 U/L, 1,071 U/L and 15.2 mg/dL, respectively. The normal range for each parameter is 0-35 U/L, 0-40 U/L, 0.2-1 mg/dL, respectively. Serology was negative for hepatitis viruses, cytomegalovirus, and varicella-zoster virus. Non-specific antinuclear antibodies and biliary antibodies were positive. Abdominal ultrasound was normal and did not reveal steatosis. Liver biopsy was not performed. Supplement intake was ceased. After 12 days of hospitalisation, the patient was discharged with no need of supplementary therapies, and a diagnosis of acute cholestatic hepatitis related to consumption of OBLESS® was made.

146. For Case 3, a 47-year-old woman was admitted to the emergency department with symptoms of severe abdominal pain (right hypochondrial). Her anamnesis denoted hyperthyroidism (treated with levothyroxine 100 µg/day), arterial hypertension (treated with enalapril 20 mg/day), and mild obesity. She also reported taking of THERMO GIALLO®, as self-medication for weight control. Each capsule contains 50 µg chromium and 400 mg *G. cambogia* of which 50% was HCA (200 mg), the patient reported that she had been consuming 2 capsules/day for a month. Laboratory tests revealed elevation of ALT, AST and TB at 299 U/L, 67 U/L and 0.7 mg/dL, respectively. The normal range for each parameter is 0-35 U/L, 0-40 U/L, 0.2-1 mg/dL, respectively. Serology was negative for hepatitis or autoantibodies. No clinical evidence of steatosis was observed, and a liver biopsy was not performed. During the patient's hospital stay, after cessation of weight-loss supplement, the levels of TB spontaneously declined, and her symptoms and liver function tests "rapidly improved", without the need of therapies. The patient was discharged with a diagnosis of acute hepatitis.

147. For Case 4, a 52-year-old woman was admitted to the emergency department and was diagnosed with acute hepatitis. No "significant" diseases and medication therapies were reported in anamnesis. However, she was taking two JILL COOPER BE SLIM® products (1 capsule/day for each product) for weight control, containing 400 mg *G. cambogia* of which 60% was HCA (240 mg), and 400 mg green coffee of

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which 50% was chlorogenic acid (200 mg), respectively. These products were purchased via T-commerce and were used for a month prior to the emergency department visit. Laboratory tests revealed elevation of ALT, AST, and TB at 1,819 U/L, 1,442 U/L and 14.7 mg/dL, respectively. The normal range for each parameter is 0-35 U/L, 0-40 U/L, 0.2-1 mg/dL. Serologies for hepatitis viruses and autoantibodies were also negative. No clinical evidence of steatosis was observed, and a liver biopsy was not performed. During the following days [number of days not specified] and cessation of the supplement products, liver parameters “spontaneously declined” and acute hepatitis “completely resolved” with no need of supplementary therapies.

148. As previously mentioned, Crescioli *et al.*, (2018) also performed a literature review related of four areas: i) general information for *G. cambogia*; ii) its use in humans for weight control; iii) the safety of *G. cambogia*, iv) *G. cambogia* dietary supplements. The criteria were filtered for human case reports and series only, published between January 2000 and October 2017. The final selection were 24 case reports and 8 case series reporting adverse effects in a total of 66 patients who consumed *G. cambogia* extract. Five studies reported single cases of myocarditis (Allen *et al.*, 2014), cardiomyopathy (Joseph *et al.*, 2014), serotonin toxicity (Lopez *et al.*, 2014), hypoglycaemia (Roche *et al.*, 2014), and thrombocytopenic purpura (Sikka *et al.*, 2016). Two patients presented acute pancreatitis (Sidhu & Khehra, 2016) and diabetic ketoacidosis (Bystrak *et al.*, 2017), three patients experienced rhabdomyolysis (Dehoney & Wellein, (2009); Hines *et al.*, (2015); Mansi & Huang, (2004)), and in five studies the authors described adverse events of mania (Cotovio & Oliveira-Maia, (2017); Narasimha *et al.*, (2013); Hendrickson *et al.*, (2016)) and multiple psychotic symptoms (Nguyen *et al.*, (2017); Wong *et al.*, (2016)). The patients were mostly women (62%) with no relevant medical history. Seventeen out of the 32 studies described cases of acute liver injury, liver failure, and hepatotoxicity, observed in 50 patients who consumed *G. cambogia* dietary supplements or *G. cambogia* “pure extract” (Actis *et al.*, (2007), Chen *et al.*, (2010), Corey *et al.*, (2016), Dara *et al.*, (2008), Elinav *et al.*, (2007), Fong *et al.*, (2010), Jones & Andrew (2007), Kothadia & Olivera-Martinez, (2016), Lunsford *et al.*, (2016), McDonnell *et al.*, (2009), Melendez-Rosado *et al.*, (2015), Schoepfer *et al.*, (2007),

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Shim & Saab, (2008), Smith *et al.*, (2016), Stevens *et al.*, (2005), Stickel *et al.*, (2009), Vitalone *et al.*, (2011).

149. According to Crescioli *et al.*, (2018), all patients with hepatic adverse effects consumed their food supplements according to the manufacturer's recommendations and yet developed similar symptoms, including jaundice, weakness, abdominal pain, dark urine, nausea, and vomiting, which were the most reported. The duration of exposure varied with some patients taking supplements for a few days or weeks to more than one year. Of the 50 patients, the symptoms of 38 improved, while 8 required liver transplantation, 1 was diagnosed with liver cirrhosis and 2 died.

150. Sharma *et al.*, (2018) presented a case report with "severe" liver toxicity following exposure to Hydroxycut®.

151. A 19-year-old man with no "significant" past medical history presented to a community medical centre with 2-day history of fever (103°F/39.4°C on presentation), severe fatigue, myalgia, arthralgias and an erythematous rash over his lower extremities. He started using Hydroxycut® [product formulation or HCA content not specified] approximately one week prior to presentation for fat burning and muscle building. He denied any smoking or alcohol use and was taking no other prescription or over the counter medication apart from Hydroxycut® and Myoflex® cream. His blood test revealed an AST level of 23 U/L, ALT of 81 U/L, alkaline phosphatase of 298 U/L white blood cell count of $31 \times 10^9/L$, haemoglobin level of 12.7 g/dL and a normal platelet count. TB was 7.3 mg/dL and he had a prothrombin time of 16.7 seconds. The paper did not provide details of the normal range for these parameters. Blood cultures, urine analysis, chest X-ray, abdominal ultrasound, computed tomography scan and magnetic resonance cholangiopancreatography results were normal. His liver appeared normal in size and texture and there was no evidence of mass, vascular compromise, stone disease, ascites or biliary ductal dilatation. The patient continued to have rising bilirubin levels over the next 3 days and despite antibiotics (Piperacillin and Tazobactam) had a persistent fever. On day 4, the patient was transferred to a hospital for possible urgent liver transplant evaluation due to rising TB of 12.7 mg/dL and a prothrombin time of 21.7 seconds. His hepatic profile showed AST at 27 U/L, ALT at 24 U/L, alkaline phosphatase at

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152 U/L, bilirubin at 12.4 mg/dL, a prothrombin time of 15.4 seconds, ammonia at 38 µg/dL, a white blood cell count of $34.8 \times 10^9/L$ (71 neutrophils and 24 bands), haemoglobin level at 11.2 g/dL, and a platelet count of 237,000/µL. Repeat blood cultures and sputum cultures, as well as urine analysis showed no evidence of infection. Serologies for hepatitis A, B, and C, anti-mitochondrial antibody, anti-nuclear antibody, anti-smooth muscle antibody, F actin IgG, liver kidney Microsomal antibody-1, cytomegalovirus, Epstein Barr virus, *Herpes Simplex* virus, Group A streptococcal antigen, Coxsackie virus, Monospot virus and leptospirosis were all negative. Ceruloplasmin and Alpha-1 anti-trypsin levels were normal. Human immunodeficiency virus and Rapid plasma reagin tests were negative. Alpha-fetoprotein level was normal at 1 ng/mL. Iron studies were notable for mild iron deficiency and a ferritin level of 463 ng/mL. A comprehensive urine toxicity screen was negative for any drugs except for opiates which he was administered at the hospital for pain management. A liver biopsy done on the 7th day of hospitalization showed acute cholangitis with scant micro vascular fatty changes (<5%) and no evidence of lobulitis, hepatocytes necrosis, cholestasis, fibrosis, parasite, ova, vasculitis, thrombosis, viral inclusions or neoplasm. Infectious disease consultation was obtained, and Vancomycin was added to his antibiotic regimen. No infectious aetiology could be determined and the patient continued to have hyperbilirubinemia. He was started on Ursodiol 600 mg orally twice a day. His bilirubin level peaked at 18.6 milligram/dL, (direct at 10.2) and started to decrease after day 6 of hospitalization. Peak alkaline phosphatase was on day 3 of admission at 298 units/L and peak AST/ALT levels were 110/142 units/L respectively on days 11 and 13. All abnormal levels gradually started to decrease. Antibiotics were discontinued after a total of 14 days of therapy. The patient was discharged from hospital on day 17 with a bilirubin level of 6.8 mg/dL (direct at 3.2), AST level of 68 U/L, ALT level of 108 U/L, alkaline phosphatase level of 160 U/L. The patient had gradual recovery of liver functions and at 14 weeks after initial onset of symptoms his liver function tests had returned to normal.

152. The authors acknowledged that “whilst causation is difficult to prove in any drug induced injury, the temporal relationship after Hydroxycut® exposure and gradual improvement after withdrawing the involved medication plus the absence of any other aetiologies despite comprehensive testing would point to Hydroxycut®

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being the most likely possible cause for hepatotoxicity.”

153. Lunsford *et al.*, (2016) reported “the first known case” of fulminant hepatic failure associated with dietary intake of a “pure” *G. cambogia* supplement.

154. A 34-year-old Hispanic male presented with nausea, vomiting, abdominal pain, and dark urine. Testing revealed elevated transaminases and TB; however, imaging failed to demonstrate cirrhosis or anatomic abnormality. Hepatitis work-up, including testing for viral hepatitis, hemochromatosis, Wilson’s disease, and autoimmune hepatitis, was unremarkable with the exception of an elevated Ferritin level of 7,089 mg/dL. Genetic testing for hemochromatosis was negative. His medical history was only positive for occasional social alcohol use, and the drug toxicology testing was negative. He denied use of energy drinks, herbs, Chinese teas, or muscle milk. He was advised to discontinue alcohol use, which he did, and his symptoms initially seemed to abate. Six weeks later, the patient developed asterixis, jaundice, and confusion. Follow-up imaging was concerning for rapid onset of cirrhosis or infiltrative hepatocellular carcinoma. On admission, transaminases were elevated with AST 624 U/L, alanine ALT 520 U/L and TB of 34.7 mg/dL. Autoantibody titers demonstrated a positive antinuclear antibody, but no other positive autoantibodies. Evaluation of Wilson’s disease demonstrated normal ceruloplasmin and copper levels; however, 24-h urine copper was elevated. Serum ferritin but not transferrin was elevated. A liver biopsy was performed and demonstrated sub-massive necrosis with collapse of the hepatic architecture involving about 70% of the liver parenchyma. Mild lymphocytic inflammatory infiltration and minimal canalicular cholestasis were seen. No viral inclusions or other infectious agents were identified by histology or immunohistochemistry. No evidence of granuloma, tumour, or features of cirrhosis were demonstrated. Periodic acid-Schiff stain with diastase was negative for alpha-1 antitrypsin globules. Iron stain showed only mild iron deposition in Kupffer cells and hepatocytes. Quantitative tissue copper was within normal limits. Findings were suspected to be potentially related to drug-induced liver injury. After questioning, the patient confirmed intake of *G. cambogia*, purchased on the Internet. He was taking two 80 mg capsules of “Garcinia Cambogia 5:1 Extract” three times daily before meals for five months preceding initial presentation. Since not advised against intake, he continued the

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supplement after initial presentation. He denied any other medications or supplements and reported no alcohol intake for two months. An 80 mg tablet of a 5:1 concentrate of *G. cambogia* was determined to be equivalent to 400mg of standard preparation. Other listed ingredients include rice flour, gelatine, magnesium stearate, and silica. However, it was confirmed that the manufacturer does not perform assays to determine HCA concentration. The patient's status declined and his mental status deteriorated; he was listed for liver transplantation and received an orthotopic liver transplant. Histopathologic examination of the explanted liver demonstrated near total hepatic necrosis with massive hepatocellular dropout and mixed inflammatory cell infiltrates, consistent with severe drug-induced liver injury.

155. The authors concluded that “while evidence from a case report rarely offers proof of causality, this case, in conjunction with known cases of hepatotoxicity and liver failure associated with other *G. cambogia*-containing supplements warrants a high index of suspicion.”

156. García-Cortés *et al.*, (2016) reviewed the reported cases of hepatotoxicity by dietary supplements. Two case-studies were summarised relating to *G. cambogia* induced hepatotoxicity. Corey *et al.*, (2015) reported a 52-year-old female requiring liver transplant after taking *G. cambogia* extract 936 mg (2 capsules per day) with 60% HCA (USA Nutra Labs) for 15 days. To note that the supplement also contained calcium (50 mg), chromium (200 µg), and potassium (50 mg) at the ingested amount.

157. Melendez-Rosado *et al.*, (2015) reported a 42-year-old female with elevated transaminase levels (ALT at 1,277 U/L and AST at 2,792 U/L, which are 70 and 45 times the upper limit of normal, respectively) and coagulopathy. It should be noted that the woman had a medical history of hypertension, chronic kidney disease (stage V), diabetes mellitus type 2, chronic back pain, haemochromatosis, and obesity. Abdominal ultrasound showed mildly coarse hepatic echotexture with no intrahepatic or extrahepatic dilatation, and abdominal computed tomographic scan showed a surgically absent gallbladder and no hepatic parenchymal abnormalities. A week before presentation, the patient started taking “pure *G. cambogia*” for weight loss. The supplement was discontinued, and the patient was empirically treated with N-acetylcysteine due to concerns of acetaminophen toxicity. After several days of

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supportive care, the patient's abdominal pain resolved, and liver enzymes recovered to baseline. The patient was discharged after 4 days. Four months later, the patient's symptoms had not recurred, and normalisation of her liver function studies was noted. The authors were of the opinion that the development of acute abdominal pain with elevated liver enzymes in the setting of a baseline liver inflammation in combination with the use of acetaminophen and the introduction of a hepatotoxic herbal supplement makes the diagnosis of acute hepatitis secondary to *G. cambogia* "very likely". No other information on the supplement, dose or exposure time could be obtained.

Animal studies

Subchronic effects

158. Shara *et al.*, (2003) evaluated the dose- and time-dependent effects of HCA-SX in male and female Sprague-Dawley rats on body weight, hepatic and testicular lipid peroxidation, DNA fragmentation, liver and testis weight, expressed as such and as a percentage of body weight and brain weight, and histological changes over a period of 90 days. An animal research protocol (ARC# 0598) was obtained from Creighton University Medical Center. HCA-SX "a natural, highly water-soluble", calcium-potassium salt of 60% HCA extract from *G. cambogia* – commercially known as SuperCitriMax HCA-600 SXS was dissolved in water and administered by gavage at 0, 0.2, 2.0 and 5% of feed intake. Control animals received the vehicle (water). Food and water consumption were measured 2-3 times weekly. Mortality/morbidity was assessed once daily throughout the study period. Clinical signs were evaluated once to twice daily. Body weights were recorded on day 1, twice weekly thereafter and before necropsy. Animals were sacrificed on days 30, 60 and 90 of treatment and the target organs were either processed immediately, preserved in 10% buffered formalin for histopathology, or stored at -80°C. The number of animals per dose group was not explicitly stated by the authors; however, it was detailed that all result values were reported as a mean $\pm$ standard deviation from 5-7 samples.

159. By day 90, feed intake was reduced by 13.7, 26.7 and 25.6% in male rats following supplementation of HCA-SX at the aforementioned doses (0 (water), 0.2, 2.0 and 5% of feed intake), respectively, when compared to their corresponding

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controls. In females, the values were 16.3, 19.6 and 22.8%, respectively. Regarding changes in body weight, ~11.2, 12.4 and 15.8% reduction in body weight in male rats following supplementation at the tested dose levels, respectively. For females these values were ~11.1, 18.1 and 13.0%, respectively. These were considered as significant by the authors. Regarding changes in testicular weight (expressed as a percentage of body weight and brain weight), a small but not statistically significant increase in testis weight with increasing age was observed in control animals. The testis weights in the exposed groups were similar to the control animals. Regarding the effects of HCA-SX on hepatic and testicular lipid peroxidation, a time-dependent increase in hepatic lipid peroxidation was generally observed in all samples; however, these were not significant in the HCA-SX exposed groups. A small but non-significant increase in testicular lipid peroxidation was observed in the control group as well as the HCA-SX exposed group. Regarding the effects of HCA-SX on hepatic and testicular DNA fragmentation, the results showed that there were no significant HCA-SX treatment related effects on these parameters (in male rats for the latter) when compared with their respective controls. Histopathological analyses on the liver, brain and testis, revealed that HCA-SX exposure did not cause any morphological alterations in these tissues.

160. The authors were of the opinion that these results indicated that HCA-SX was “safe and efficacious in weight management” under the test conditions.

Reproductive toxicity

161. Deshmukh *et al.*, (2008a) evaluated the effects of a novel calcium/potassium salt of HCA on the reproductive systems of male and female rats, the postnatal maturation and reproductive capacity of their offspring, and possible cumulative effects through multiple generations. The study was performed in compliance with a standard study protocol based on the US FDA Redbook Guidelines for Reproductive Studies IV.C.9.a, and Guidelines for Developmental Toxicity Studies IV.C.9.B., Feed Additive Safety (US FDA, 1993), and the OECD principles of Good Laboratory Practice.

162. The test article, HCA-SX, commercially known as Super CitriMax was mixed

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with powdered rodent diet to obtain three concentration levels. A small volume of diet premix was prepared, which was then mixed with the remaining portion of the diet in a mechanised ribbon blender for about 20 minutes to obtain the desired homogeneity of the test article concentration in diet. The experimental diets were prepared once a week based upon the results of the stability tests on HCA-SX. The diet preparation procedure was subsequently validated by conducting stability studies and homogeneity on exposed diets.

163. Sprague-Dawley rats (n=30/sex per dose group) were administered feed containing HCA at dose levels of 0, 1,000, 3,000, or 10,000 ppm for 10 weeks prior to mating, during mating, and, for females, through gestation and lactation, across two generations. The control group of animals were fed normal diet. The male and female rats of the F₀ generation from each dose group were mated and allowed to deliver normally. At weaning, one male and one female pup from each litter from the control and treatment dose groups were selected for the F₁ generation. The selected F₁ animals were exposed to HCA-SX for 10 weeks before mating and then they were mated to produce a second generation F_{2a}. During the period of study, animals were examined daily for signs of clinical toxicity and their body weight and feed consumption (g/rat/day) were recorded twice a week. N.B. A discrepancy was noted where the abstract states the latter was performed twice a week recording, whilst the methods section describes one weekly recording. For the parents (F₀ and F₁) and the offspring (F₁ and F_{2a}), reproductive parameters such as fertility and mating, gestation, parturition, litters, lactation, sexual maturity, and development of offspring were assessed. At termination, necropsy and histopathological examinations were performed on all animals.

164. Data on feed consumption by the parental male and female rats of both (F₀ and F₁) generations during the premating and mating periods, for both sexes, and during gestation and lactation in the case of female rats, did not reveal any “remarkable” treatment-related changes in the average daily feed intake by the male and female rats compared to the respective control groups, across the different dose levels for each of the F₀ and F₁ generations and also when compared across these two generations. Based on feed intake, the resulting dose of HCA-SX for the highest-dose groups of male and female was calculated as 813 and 1,205

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mg/kg/day, respectively, for the F₀ generation, while the same was respectively 1,018 and 1,524 mg/kg/day in the case of the F₁ generation. The total daily dose of HCA-SX for all groups are provided in Table 3.

Table 3 – Daily dose of HCA-SX (mg/kg bw per day) during the premating period (reproduced from Deshmukh *et al.*, (2008a).

HCA-SX level in diet (ppm)	F₀ Males (mg/kg bw per day)	F₀ Females (mg/kg bw per day)	F₁ Males (mg/kg bw per day)	F₁ Females (mg/kg bw per day)
Control (0)	0	0	0	0
Low (1,000)	80	109	89	135
Mid (3,000)	246	354	268	447
High (10,000)	813	1,205	1,018	1,524

165. Dietary exposure to all animals and offspring at the F₀ and F₁ generations, did not reveal significant incidence of mortality or abnormal clinical signs. Compared to the respective controls, the HCA treatment groups at all dose levels, did not have different feed consumption or body weight. All deaths and abnormal clinical signs observed in the rats during F₀ and F₁ generations, such as transient/reversible spells of emaciation, abdominal breathing, respiratory rates, hypoactivity, circling disorder, and lacrimation, were considered to be incidental and not test substance related.

166. The average bodyweight and body weight gains on the parental F₀ and F₁ generations up to all stages including lactation of female rats of the exposed groups at all doses, did not reveal any significant differences when compared to the respective control groups. Although, a mild but significant lowering of body weight gain in F₁ male offspring was noted in the highest dose level after they were weaned, between 3 to 7 weeks of their life. For the duration of the study, the difference in body weights persisted; however, it was not significant, and the percentage gain in body weights between control and exposed groups of male rats was found to be comparable on week 31 (it was slightly higher in the high dose group than the control group). The authors did not count this as an adverse effect while deciding the NOAEL, as it was considered to be a likely effect of the pharmacological activity of

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HCA-SX. There were other “occasional” instances of group mean values of exposed animals differing from those of the respective control; however, these were not considered of no toxicological significance due to the “small magnitude of variation”.

167. During the gestation period in all females exposed to HCA-SX, no treatment-related adverse effects on reproductive performance in terms of fertility and mating, gestation, parturition, and the litters born were observed. The values of male fertility indices for the exposed groups in the F_0 and F_1 generations did not differ significantly from those of the controls and also compared well with the historical control data at the test facility. The sperm motility of the F_1 parents was lower than the F_0 parents (in exposed groups). The authors did not consider this to be related to HCA-SX exposure, as the lowering was also observed in the concurrent control group of rats.

168. All the gross and microscopic findings of the parental organ weights, necropsy and histopathology were considered to be incidental as the incidence was found to be comparable among the control group and the treatment groups, without any dose-dependent trend.

169. Offspring observations are hereby summarised. The body weights of some of the pups selected as parents for the next generation were recorded at ~4 weeks after they were weaned at the end of their lactation; in male offsprings exposed at the highest dose (10,000 ppm), the group mean body weights were significantly lower than those of the control group; however, this effect was not considered as an adverse effect [was considered as a pharmacological effect]. When compared with their respective controls, data on survival and clinical observations recorded for the offspring of both generations F_1 and F_{2a} during the lactation period of 21 days did not reveal any remarkable differences. Nor were there any adverse effects on their litter sizes, sex ratio of litters, live birth indices and the viability of litters, which were calculated on days 4, 7, 14 and 21 of lactation from parental females exposed to HCA-SX at all dose levels. The sexual maturation [age at which there is balanopreputial separation in males and vaginal opening in females] was only measured for the F_{2a} groups. It was observed that exposure to HCA-SX at any of the dose levels did not affect the age of sexual maturity of the offspring belonging to the F_{2a} generation. Exposure of the parental animals of both the F_0 and F_1 generation to

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HCA-SX at the tested dose levels had no adverse effect on the physical development of their litters, compared to the respective control groups. The group mean values of absolute and relative weights of the brain, spleen, and thymus of the pups of the F₁ and F_{2a} generation did not significantly alter between the control and treatment groups. The study authors considered that all the gross and microscopic pathology findings in this study were accidental as the incidence was found to be comparable among the control group and the treatment groups, without any dose-dependent trend. HCA-SX treatment did not cause any significant histopathological changes in any organ.

170. The authors noted that exposure to HCA-SX did not affect reproductive performance as evaluated by sexual maturity fertility and mating, gestation, parturition, litter properties, lactation, and development of the offspring. Nor did it induce any systemic toxicity in the parental rats and their offspring at the tested concentration levels. Based on the results of this study, the authors determined a NOAEL to be greater than 10,000 HCA ppm in the diet or equivalent to 1,018 and 1,524 HCA mg/kg bw per day in male and female rats, respectively.

171. Saito *et al.*, (2005) investigated the ability of *G. cambogia* extract to suppress body fat accumulation in developing male Zucker obese (fa/fa) rats. 6-week-old rats (n=6 per dose group) were fed diets containing HCA powder (41.2 wt%: ratio of free to lactone form was 36.6 to 63.4) at 0, 2, 10.1, 20.1 and 30.2 g HCA/kg diet for 92 or 93 days. All groups had free access to water. Each diet group was pair-fed to the 30.2 g HCA/kg diet group. On the last experimental day, the rats were allowed to consume three-quarters of the food intake of the previous day and were then killed by cardiac puncture. Liver, kidney, spleen, spleen, testis, and epididymal fat pads were excised, washed with isotonic saline and weighed. The liver, spleen and testis were fixed with 10% formalin neutral buffer solution, pH 7.4 and histopathological examinations were performed after haematoxylin-eosin staining. At the highest dose, there was significant suppression of epididymal fat accumulation in developing male Zucker obese rats, compared with the other groups. The higher dose groups (20.1 and 30.2 g HCA/kg diet) caused “potent” testicular atrophy and toxicity, whereas diets containing 10.1 g HCA/kg diet or less did not. The authors derived a NOAEL of 10.1 g HCA/kg diet equivalent to 389 mg HCA/kg BW per day.

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172. Burdock *et al.*, (2005) performed a “critical review” of the article by Saito *et al.*, (2005) (as summarised in paragraph 171) and raised the following comments: (1) the form of HCA and toxicity; (2) experimental study design and results; (3) Zucker rat model and testicular toxicity; and (4) dietary ingredients and testicular toxicity. The form of HCA can vary its toxic profile, dietary supplements containing HCA consist of various salts, including HCA–sodium, –calcium, –potassium, –magnesium, or combinations thereof. Depending on the salt(s) used and the extraction process, the solubility, bioavailability, bioefficacy and lactone content can vary considerably.

173. Limitations on the experimental design were noted: the amount of food received by pair-fed animals was approximately 10% less (compared to ad libitum fed control, which was not included). Burdock *et al.*, further state that HCA is known to affect satiety, effectively preventing consumption of food at high levels. Secondly, the investigators reported severe diarrhoea at the highest use levels (1,244 mg HCA/kg/day), which may have further affected the feed intake in this group and other groups (as a result of pair feeding). Thirdly, Saito *et al.*, (2005) stated that Zucker obese rats (or models with higher lipogenic properties) may be insensitive to HCA at usual dietary levels; however, a biphasic effect of HCA on fat accumulation in the liver was noted. The selection of Zucker rat model was thought to be inappropriate since serum concentrations of testosterone in obese male Zucker rat at the age of 2-, 3- and 4-months were lower when compared to lean male Zucker rats. Testes morphology of Zucker rats was also found to be different from lean rats.

174. It was not made clear by Saito *et al.*, (2005), whether dietary imbalance or nutritional imbalance (use of high levels of the extract, pair feeding) may have contributed to the observed testicular toxicity at two highest doses of *G. cambogia* extract.

Developmental toxicity

175. Deshmukh *et al.*, (2008b) conducted a follow-up study (summarised in paragraphs 161-170) to evaluate maternal toxicity and effects on the developing embryo in Sprague-Dawley rats (effects included death, structural abnormalities, and altered or retarded growth) when exposed to HCA-SX. The study was performed as

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per the previous protocol in Deshmukh et al., (2008a). A total of 30 males and 30 female pups per dose group (except the 3,000 ppm (mid) dose group where 25 of each sex were available), including the concurrent control group. The animals in this study were selected randomly after weaning from each F_{2b} litter of the F₁ generation from the two-generation reproductive toxicity study (as summarised in paragraphs 161-170). Therefore, the rats in the treatment group were exposed directly to HCA-SX via feed, prior to which they had indirect exposure to HCA during lactation. The dietary exposure levels were the same as those employed for the two-generation reproductive toxicity study: 0, 1,000, 3000, or 10,000 ppm. Following mating at maturity, the pregnant rats were observed twice daily for clinical signs of adverse effects, and body weight and feed consumption were recorded. On day 20 of gestation, animals were subjected to a necropsy and caesarean section to examine the uterus, ovaries, and foetuses for assessment of different parameters of pregnancy and embryo-foetal defects.

176. The daily amount of HCA-SX consumed at dietary feed levels of 1,000, 3,000 or 10,000 (ppm) (equivalent to 0.1%, 0.3% and 1.1%) were calculated as 103, 352, or 1,240 mg/kg bw per day, respectively.

177. Comparison indices of sperm-positive females (mating behaviour), maternal deaths during pregnancy, number of pregnant/non-pregnant females, pregnancy rate (%), and females with resorptions (%) were evaluated between the control group and the HCA-SX exposed groups. At the dose levels administered, no adverse effects were observed. Maternal body weight changes during gestation were recorded for the following periods: days 0, 7, 14 and 20. The group mean values of body weight gain for each period did not show any significant differences between the exposed and control groups. On the 20th day of gestation, a significant decrease (by 13%) in mean body weight of the rats maintained on the highest dose (10,000 ppm) was noted. During the study, no treatment-related clinical effects were observed in any of the groups. However, the following incidences were reported: i) wryneck and a transient period of emaciation were observed in females during the course of the study [was deemed to be not dose related by the authors]; ii) on day 17 of gestation, one pregnant female from the highest dose group died – profuse haemorrhage [by vaginal bleeding] was identified as the probable cause of death. No other mortalities

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were noted in any of the groups during the course of the study. Observations made on the gravid uteri of females euthanised on day 20 of gestation did not reveal any “remarkable” alterations indicative of adverse effects of HCA-SX on absolute uterus weight, number of: corpora lutea, implantations, live and dead implants, early and late resorptions, and post-implantation losses (%). Observations made on the litters of females euthanised on day 20 of gestation did not reveal any remarkable treatment-related alterations in litter size, number of foetuses, sex ratios and foetal weights. The group mean litter size from the highest-dose group of HCA-SX was significantly lower than the control group ($p < 0.05$). However, these observations deemed to be not of biological significance by the authors as the changes were smaller in magnitude compared to the variation observed in the historical control data.

178. Observations in the foetal groups are summarised. The number of foetuses examined in the control, 1,000, 3,000 and 10,000 ppm dose groups were 226, 227, 158 and 160, respectively. The only “major malformation” was an omphalocele [birth defect, where the intestine or other abdominal organs stick out of the belly button], which was found in two foetuses: one in the control and high-dose groups. This was considered incidental by the authors. Two other “minor malformations” were observed. An incidence of a small haematoma at the tip of the tail in three foetuses: one in the control, low-dose and mid-dose groups. One foetus in the high-dose group was small (runt). No treatment-related significant incidence of soft tissue alterations in foetuses of dams exposed to HCA-SX at the tested doses were noted ($n=108$, 106, 74, 76 for the control and each HCA-SX dose groups, respectively). Small incidences of “minor anomalies” were observed including, globular heart and unilateral enlargement of the ventricle of the heart, mottled lungs, unilateral displacement of adrenal, and unilateral hypoplasia of kidney in foetal soft tissues. These were considered as incidental and of no toxicological significance by the authors. The only abnormal finding classified under “major anomalies” was unilateral cerebral hypoplasia observed in one of the foetuses in the low-dose group; this was considered to be incidental by the authors, in light of its isolated incidence (0.94%). There was no incidence of any significant and treatment related skeletal abnormalities in foetuses of dams exposed to HCA-SX. Any abnormalities were considered incidental or of no toxicological significance due to either being a normal

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variant, minor in nature or the incidence was in isolation and/or comparable to the control dose group.

179. The authors concluded that HCA-SX was not found to be teratogenic in Sprague-Dawley rats at dietary exposure levels of 1,000, 3000, and 10,000 ppm, equivalent to the dose levels of 103, 352, or 1,240 mg/kg/day, respectively. Based on the results of the study, the NOAEL of HCA-SX was determined by the authors at 1,240 mg/kg per day.

Mode of action

180. The cause of hepatotoxicity from *G. cambogia* is unclear. *In vitro* studies suggest that HCA may be toxic to the liver in high doses, but the rare instances of acute liver injury that occur with *G. cambogia* suggest an idiosyncratic form of injury. The possibility of mislabelling or adulteration with hepatotoxic herbal products has been identified as an issue in herbal related injury.

181. In the literature review by Crescioli *et al.*, (2018), it was noted that HCA mechanism of toxicity is not clearly defined; however, HCA increases hepatic collagen accumulation, lipid peroxidation, mRNA levels of genes related to oxidative stress (superoxide dismutase and glutathione peroxidase), and inflammatory responses (tumour necrosis factor- α and monocyte chemoattractant protein-1). It was suggested that certain patients could have genetic predisposition leading to hepatotoxicity, such as cytochrome P450 polymorphisms promoting toxic accumulation of metabolites. The information suggested that there is a potential causal relationship between *G. cambogia* product exposure and development of herb induced liver injury (HILI); however, these were limited by the lack of data on factors influencing the severity of HILI, especially for cases derived from the literature.

Exposure

Brief market analysis

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182. A brief market analysis was carried out using the search term on Google: “*Garcinia cambogia* buy UK”. This information was collated into tables 4 and 5. The FSA’s Exposure Assessment Team (EAT) have quality assured this data by reviewing the transcription of the information in the table is correct according to the weblinks.

183. The Holland & Barret website states that “Most studies have been based on 900 mg to 3,000mg of HCA of *garcinia cambogia* daily. Dosage recommendations on commercially available pills are generally lower, around 300mg – 1,600mg daily.” (Holland & Barrett, 2019). At the time of writing, two products (each available in different pack sizes) were available that contained *G. cambogia* in MIDS: *G. cambogia* and green coffee bean capsules (600 mg *G. Cambogia* (fruit) per day (2 capsules)) in 60 or 100 capsule bottles; protein shakes (150 mg *G. cambogia* extract/55g per scoop; instructions state to add 2 scoops per serving and recommends 1-3 servings daily – total of up to 900 mg *G. cambogia* extract/day) in 1 or 2 kg tubs (Holland & Barrett, 2025).

184. Other online retailers such as Amazon, Superdrug, Grape Tree, Natur House and various body building supplement & nutrition websites offer *G. cambogia* capsule products with daily doses of HCA ranging from 80 – 10,000 mg. However, the product description and labelling are inconsistent with some listings simply stating *G. cambogia* extract without describing whether it is HCA nor the standardised HCA content. A powdered product of *G. Cambogia* extract was also available, where half a teaspoon serving gave a dose of 500 mg HCA (60% standardised (Oils and Herbs, 2025). It may be possible that other (non-)UK retailers offer products with higher concentrations of HCA than identified in this discussion paper.

Estimated exposure

185. A comprehensive exposure assessment using consumption data from years 1-11 of the National Diet and Nutrition Survey (NDNS) (Bates *et al.*, 2014; Bates *et al.*, 2016; Roberts *et al.*, 2018; Bates *et al.*, 2020) was not possible, for the following

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reasons:

- Specific food supplements containing *G. cambogia* are not in the NDNS.
- Specific food/drink products containing *G. cambogia* are not in the NDNS. Whilst consumption estimates for food/drink products containing *G. cambogia* could be based on consumption of “normal” versions of the food in NDNS, it was noted these products are uncommon; this approach may have resulted in a significant overestimation of exposure.
- The use of the rind for culinary purposes was not in scope for the exposure assessment. In this instance, using the identified dose for use as a supplement was considered the most appropriate approach.

186. Therefore, the exposure estimates provided for the identified products of the market analysis are based on the recommended dose/serving size and the average body weights of adults (aged 19-64 years) and toddlers (aged 1.5-3 years) from the NDNS (78.6 and 14.6 kg, respectively).

187. Most products in the market analysis included warning information that recommended the product was suitable for adults only. However, consumption by other age groups could not be ruled out completely. Therefore, toddlers have been chosen as the age group for worst case exposure estimates.

188. Table 4 provides dosage information for *G. cambogia* only supplements, whilst Table 5 provides dosage information for multi-ingredient *G. cambogia* dietary supplements, as sold in UK online retailers at the time of the assessment.

189. Table 6 and Table 7 provide the exposure estimates for adults (*G. cambogia* only and MIDS products respectively), while Table 8 and Table 9 provide the exposure estimates for toddlers (*G. cambogia* only and MIDS products respectively). There are exposure estimates for both *G. cambogia* and HCA, where possible. In some cases, insufficient information was provided to perform an exposure assessment for one or the other.

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Table 4 - Dosage information for *G. cambogia* only supplements, as sold in UK online retailers at the time of the assessment.

Supplement name	Supplement type	Recommended daily serving	<i>G. cambogia</i> concentration per unit (capsule/ tablet/ scoop etc) (mg)	<i>G. cambogia</i> concentration in a daily serving (maximum serving size*) (mg)	HCA content % (mg in maximum daily serving*)
BodyBuilding Warehouse Pure <i>Garcinia cambogia</i>	Capsules	1-2 capsules	500	1000	60% (600)
UK Health House <i>Garcinia Cambogia</i> - High Strength - 1000mg Tablets 60% HCA Max	Tablets	1-2 tablets	1000	2000	60% (1200)
HERBASENSE GARCINIA CAMBOGIA EXTRACT – 60% HCA by HPLC	Powder	3 spoons (1.5g)	1500	4500	60% (2700)
NOW Foods, Garcinia, 120 Tablets	Tablets	1-3 tablets	1000	3000	50% (1500)
Fitimins <i>Garcinia Cambogia</i> Extract 1000mg Capsule	Capsules	2 capsules	1000	2000	60% (1200)
BioTechUSA HCA - 100 caps	Capsules	3 capsules	1000	3000	60% (1800)
Woods Supplements <i>Garcinia</i>	Capsules	1 capsule	1000	1000	Not provided

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Supplement name	Supplement type	Recommended daily serving	<i>G. cambogia</i> concentration per unit (capsule/ tablet/ scoop etc) (mg)	<i>G. cambogia</i> concentration in a daily serving (maximum serving size*) (mg)	HCA content % (mg in maximum daily serving*)
<i>Cambogia</i> 1000mg					
Paradise Herbs, Garcinia Extract, 500 mg, 60 Vegetarian Capsules	Capsules	1-3 capsules	500	1500	50% (750)
Inlife Garcinia 1600 MG Capsules - 120 Capsules	Capsules	2-3 capsules	1600	4800	>60% (>2880)
Himalaya, Organic Garcinia, 60 Caplets	Caplets	2 caplets	600	1200	66% (792)
Swanson <i>Garcinia Cambogia</i> 5:1 Extract, 80mg - 60 caps	Capsules	1 capsule	80	80	Not provided
Sotya Garcinia	Capsules	3 capsules	250	750	60% (450)
DR WAKDE'S Garcinia Fruit Powder - 100g (3.5oz) Pure, Raw & Dried Powder Ayurvedic Herb Vegan Nothing Added, Nothing Removed Same Day	Powder	1-2 teaspoons (5-10g)	5,000 (5g teaspoon)**	10,000**	Not provided

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Supplement name	Supplement type	Recommended daily serving	<i>G. cambogia</i> concentration per unit (capsule/ tablet/ scoop etc) (mg)	<i>G. cambogia</i> concentration in a daily serving (maximum serving size*) (mg)	HCA content % (mg in maximum daily serving*)
Dispatch					
<i>Garcinia Cambogia</i> 1500mg 120 Vegan Capsules High Strength 20:1 Whole Fruit Powder Premium Quality Supplement by Horbaach	Capsules	1 capsule	1500	1500	Not provided
Black Swan Hydroxycitric Acid Capsules - 500mg HCA Garcinia Cambogia Enhanced Mood Weight Management Metabolic Support Natural Food Supplement - 30 Capsules 1 Month Supply	Capsules	1-2 capsules	Not provided**	Not provided**	Percentage content not provided** (1000)

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* Maximum serving assumes the maximum amount recommended on the packaging or website of the supplement. E.g. if recommended to take 1-2 capsules per day, this table assumes 2 capsules would be taken. Another example is if the website suggests a serving of 2 capsules a day, but the packaging suggests 3, then the highest suggestion has been used.

**An assumption has been made regarding the value, see Table 1 (Appendix A of TOX/2025/41) for more details.

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Table 5 Dosage information for multi-ingredient *G. cambogia* dietary supplements, as sold in UK online retailers at the time of the assessment.

Supplement name	Supplement type	Recommended daily serving	<i>G. cambogia</i> concentration per unit (capsule/ tablet/ scoop etc) (mg)	<i>G. cambogia</i> concentration in a daily serving (maximum serving size*) (mg)	HCA content % (mg in maximum daily serving*)
Swiss Bioenergetics <i>Garcinia cambogia</i>	Capsules	3-6 capsules	500	3000	Not provided
Nutralie <i>Garcinia cambogia</i> complex fat burner	Capsules	3 capsules	667	2000	60% (1200)
Holland & Barrett <i>Garcinia Cambogia</i> & Green Coffee Bean 100 Capsules	Capsules	2 capsules	300	600	Not provided
HERBASENSE <i>Garcinia Cambogia</i> Plus Jar – 60% HCA by HPLC + Green Coffee Bean + Green Tea Extracts	Powder	3 spoons (1.5g)	1500	4500	60% (2700)
Sensilab Essentials <i>Garcinia Cambogia</i> 1,800mg High	Capsules	3 capsules	600	1800	60% (1080)

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Dose - Vegan, 90 Capsules					
Sensilab Garcinia Slim	Capsules	2 capsules	209	417	60% (250)
GARCINIA ULTRA BLEND (with Acai & Green Tea) 60 Vegetarian Capsules	Capsules	1-2 capsules	100	200	55% (110)
<i>Garcinia Cambogia</i> - 90 Capsules - 1500mg Daily Dosage - Premium Quality Supplement - UK formulated - Vegetarian & Vegan Suitable - Optimum Strength For Maximum Results - Garcinia Clean For Men & Women	Capsules	3 capsules	500	1500	No provided
Apple Cider Vinegar with Cayenne Pepper, Turmeric & Ginger Root + <i>Garcinia Cambogia</i> with Calcium, Potassium, Chromium, etc. - UK Formulated Food Supplements Capsules –	Capsules	3 capsules	1500**	4500**	15% (675)**

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Both Vegan & Vegetarian Suitable					
Prowise Healthcare Essentials <i>Garcinia Cambogia</i> High Dose - Vegan, 180 Capsules	Capsules	2 capsules	1000	2000	Not provided
Troo Health Care <i>Garcinia Cambogia</i> Complex Supplement - 90 Capsules UK Manufactured	Capsules	3 capsules	500	1500	Not provided
<i>Garcinia Cambogia</i> 1500mg Daily Dosage –with Added Chromium Picolinate for Rapid Absorption – 30 Day Supply of The Super Strength Whole Fruit – Manufactured in The UK	Capsules	3 capsules	500	1500	Not provided

*Maximum serving assumes the maximum amount recommended on the packaging or website of the supplement. E.g. if recommended to take 1-2 capsules per day, this table assumes 2 capsules would be taken. Another example is if the website suggests a serving of 2 capsules a day, but the packaging suggests 3, then the highest suggestion has been used.

**An assumption has been made regarding the value, see Table 1 (Appendix A of TOX/2025/41) for more details.

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Table 6 - Exposure estimates for adults from *G. cambogia* only supplements, as sold in UK online retailers at the time of the assessment.

Supplement name	<i>G. cambogia</i> concentration in a daily serving (maximum serving size*) (mg)	HCA content % (mg in maximum daily serving*)	Exposure to <i>G. cambogia</i> (maximum daily serving*) (mg/ kg bw/day)	Exposure to HCA (maximum daily serving*) (mg/ kg bw/day)
BodyBuilding Warehouse Pure <i>Garcinia cambogia</i>	1000	60% (600)	13	7.6
UK Health House <i>Garcinia Cambogia</i> - High Strength - 1000mg Tablets 60% HCA Max	2000	60% (1200)	25	15
HERBASENSE GARCINIA CAMBOGIA EXTRACT – 60% HCA by HPLC	4500	60% (2700)	57	34
NOW Foods, <i>Garcinia</i> , 120 Tablets	3000	50% (1500)	38	19
Fitimins <i>Garcinia Cambogia</i> Extract 1000mg Capsule	2000	60% (1200)	25	15
BioTechUSA HCA - 100 caps	3000	60% (1800)	38	23
Woods Supplements <i>Garcinia Cambogia</i> 1000mg	1000	Not provided	13	Not provided
Paradise Herbs, <i>Garcinia</i> Extract, 500 mg, 60 Vegetarian Capsules	1500	50% (750)	19	9.5
Inlife <i>Garcinia</i> 1600 MG Capsules - 120 Capsules	4800	>60% (>2880)	61	37
Himalaya, Organic <i>Garcinia</i> , 60 Caplets	1200	66% (326)	15	10
Swanson <i>Garcinia Cambogia</i> 5:1 Extract, 80mg - 60 caps	80	Not provided	1.0	Not provided
Sotya <i>Garcinia</i>	750	60% (450)	9.5	5.7

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DR WAKDE'S Garcinia Fruit Powder - 100g (3.5oz) Pure, Raw & Dried Powder Ayurvedic Herb Vegan Nothing Added, Nothing Removed Same Day Dispatch	10,000**	Not provided	130	Not provided
<i>Garcinia Cambogia</i> 1500mg 120 Vegan Capsules High Strength 20:1 Whole Fruit Powder Premium Quality Supplement by Horbaach	1500	Not provided	19	Not provided
Black Swan Hydroxycitric Acid Capsules - 500mg HCA Garcinia Cambogia Enhanced Mood Weight Management Metabolic Support Natural Food Supplement - 30 Capsules 1 Month Supply	Not provided**	Percentage content not provided** (1000)	Not provided	13

* Maximum serving assumes the maximum amount recommended on the packaging or website of the supplement. E.g. if recommended to take 1-2 capsules per day, this table assumes 2 capsules would be taken. Another example is if the website suggests a serving of 2 capsules a day, but the packaging suggests 3, then the highest suggestion has been used.

**An assumption has been made regarding the value, see Table 1 (Appendix A of TOX/2025/41) for more details.

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Table 7 - Exposure estimates for adults from multi-ingredient *G. cambogia* dietary supplements, as sold in UK online retailers at the time of the assessment.

Supplement name	<i>G. cambogia</i> concentration in a daily serving (maximum serving size*) (mg)	HCA content % (mg in maximum daily serving*)	Exposure to <i>G. cambogia</i> (maximum daily serving*) (mg/ kg bw/day)	Exposure to HCA (maximum daily serving*) (mg/ kg bw/day)
Swiss Bioenergetics <i>Garcinia cambogia</i>	3000	Not provided	38	Not provided
Nutralie <i>Garcinia cambogia</i> complex fat burner	2000	60% (1200)	25	15
Holland & Barrett <i>Garcinia Cambogia</i> & Green Coffee Bean 100 Capsules	600	Not provided	7.6	NA
HERBASENSE <i>Garcinia Cambogia</i> Plus Jar – 60% HCA by HPLC + Green Coffee Bean + Green Tea Extracts	4500	60% (2700)	57	34
Sensilab Essentials <i>Garcinia Cambogia</i> 1,800mg High Dose - Vegan, 90 Capsules	1800	60% (1080)	23	14
Sensilab <i>Garcinia Slim</i>	417	60% (250)	5.3	3.2
GARCINIA ULTRA BLEND (with Acai & Green Tea) 60 Vegetarian Capsules	200	55% (110)	2.5	1.4
<i>Garcinia Cambogia</i> - 90 Capsules - 1500mg Daily Dosage - Premium Quality Supplement - UK formulated - Vegetarian & Vegan Suitable - Optimum Strength For Maximum Results - <i>Garcinia Clean</i> For Men & Women	1500	No provided	19	Not provided

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Apple Cider Vinegar with Cayenne Pepper, Turmeric & Ginger Root + <i>Garcinia Cambogia</i> with Calcium, Potassium, Chromium, etc. - UK Formulated Food Supplements Capsules – Both Vegan & Vegetarian Suitable	4500**	15% (675)**	25	8.6
Prowise Healthcare Essentials <i>Garcinia Cambogia</i> High Dose - Vegan, 180 Capsules	2000	Not provided	25	Not provided
Troo Health Care <i>Garcinia Cambogia</i> Complex Supplement - 90 Capsules UK Manufactured	1500	Not provided	19	Not provided
<i>Garcinia Cambogia</i> 1500mg Daily Dosage – with Added Chromium Picolinate for Rapid Absorption – 30 Day Supply of The Super Strength Whole Fruit – Manufactured in The UK	1500	Not provided	19	Not provided

* Maximum serving assumes the maximum amount recommended on the packaging or website of the supplement. E.g. if recommended to take 1-2 capsules per day, this table assumes 2 capsules would be taken. Another example is if the website suggests a serving of 2 capsules a day, but the packaging suggests 3, then the highest suggestion has been used.

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Table 8 - Exposure estimates for toddlers from *G. cambogia* only supplements, as sold in UK online retailers at the time of the assessment.

Supplement name	<i>G. cambogia</i> concentration in a daily serving (maximum serving size*) (mg)	HCA content % (mg in maximum daily serving*)	Exposure to <i>G. cambogia</i> (maximum daily serving*) (mg/ kg bw/day)	Exposure to HCA (maximum daily serving*) (mg/ kg bw/day)
BodyBuilding Warehouse Pure <i>Garcinia cambogia</i>	1000	60% (600)	68	41
UK Health House <i>Garcinia Cambogia</i> - High Strength - 1000mg Tablets 60% HCA Max	2000	60% (1200)	140	82
HERBASENSE GARCINIA CAMBOGIA EXTRACT – 60% HCA by HPLC	4500	60% (2700)	310	180
NOW Foods, <i>Garcinia</i> , 120 Tablets	3000	50% (1500)	210	100
Fitimins <i>Garcinia Cambogia</i> Extract 1000mg Capsule	2000	60% (1200)	140	82
BioTechUSA HCA - 100 caps	3000	60% (1800)	210	120
Woods Supplements <i>Garcinia Cambogia</i> 1000mg	1000	Not provided	68	Not provided
Paradise Herbs, <i>Garcinia</i> Extract, 500 mg, 60 Vegetarian Capsules	1500	50% (750)	100	51
Inlife <i>Garcinia</i> 1600 MG Capsules - 120 Capsules	4800	>60% (>2880)	330	200
Himalaya, Organic <i>Garcinia</i> , 60 Caplets	1200	66% (326)	82	54
Swanson <i>Garcinia Cambogia</i> 5:1 Extract, 80mg - 60 caps	80	Not provided	5.5	Not provided

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Sotya Garcinia	750	60% (450)	51	31
DR WAKDE'S Garcinia Fruit Powder - 100g (3.5oz) Pure, Raw & Dried Powder Ayurvedic Herb Vegan Nothing Added, Nothing Removed Same Day Dispatch	10,000**	Not provided	680	Not provided
<i>Garcinia Cambogia</i> 1500mg 120 Vegan Capsules High Strength 20:1 Whole Fruit Powder Premium Quality Supplement by Horbaach	1500	Not provided	100	Not provided
Black Swan Hydroxycitric Acid Capsules - 500mg HCA Garcinia Cambogia Enhanced Mood Weight Management Metabolic Support Natural Food Supplement - 30 Capsules 1 Month Supply	Not provided**	Percentage content not provided** (1000)	Not provided	68

* Maximum serving assumes the maximum amount recommended on the packaging or website of the supplement. E.g. if recommended to take 1-2 capsules per day, this table assumes 2 capsules would be taken. Another example is if the website suggests a serving of 2 capsules a day, but the packaging suggests 3, then the highest suggestion has been used.

**An assumption has been made regarding the value, see Table 1 (Appendix A of TOX/2025/41) for more details.

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Table 9 - Exposure estimates for toddlers from multi-ingredient *G. cambogia* dietary supplements, as sold in UK online retailers at the time of the assessment.

Supplement name	<i>G. cambogia</i> concentration in a daily serving (maximum serving size*) (mg)	HCA content % (mg in maximum daily serving*)	Exposure to <i>G. cambogia</i> (maximum daily serving*) (mg/ kg bw/day)	Exposure to HCA (maximum daily serving*) (mg/ kg bw/day)
Swiss Bioenergetics <i>Garcinia cambogia</i>	3000	Not provided	210	Not provided
Nutralie <i>Garcinia cambogia</i> complex fat burner	2000	60% (1200)	140	82
Holland & Barrett <i>Garcinia Cambogia</i> & Green Coffee Bean 100 Capsules	600	Not provided	41	Not provided
HERBASENSE <i>Garcinia Cambogia</i> Plus Jar – 60% HCA by HPLC + Green Coffee Bean + Green Tea Extracts	4500	60% (2700)	310	180
Sensilab Essentials <i>Garcinia Cambogia</i> 1,800mg High Dose - Vegan, 90 Capsules	1800	60% (1080)	120	74
Sensilab <i>Garcinia Slim</i>	417	60% (250)	29	17
GARCINIA ULTRA BLEND (with Acai & Green Tea) 60 Vegetarian Capsules	200	55% (110)	14	7.5
<i>Garcinia Cambogia</i> - 90 Capsules - 1500mg Daily Dosage - Premium Quality Supplement - UK formulated - Vegetarian & Vegan Suitable - Optimum Strength For Maximum Results - <i>Garcinia Clean</i> For Men & Women	1500	No provided	100	Not provided

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Apple Cider Vinegar with Cayenne Pepper, Turmeric & Ginger Root + <i>Garcinia Cambogia</i> with Calcium, Potassium, Chromium, etc. - UK Formulated Food Supplements Capsules – Both Vegan & Vegetarian Suitable	4500**	15% (675)**	310	46
Prowse Healthcare Essentials <i>Garcinia Cambogia</i> High Dose - Vegan, 180 Capsules	2000	Not provided	140	Not provided
Troo Health Care <i>Garcinia Cambogia</i> Complex Supplement - 90 Capsules UK Manufactured	1500	Not provided	100	Not provided
<i>Garcinia Cambogia</i> 1500mg Daily Dosage – with Added Chromium Picolinate for Rapid Absorption – 30 Day Supply of The Super Strength Whole Fruit – Manufactured in The UK	1500	Not provided	100	Not provided

* Maximum serving assumes the maximum amount recommended on the packaging or website of the supplement. E.g. if recommended to take 1-2 capsules per day, this table assumes 2 capsules would be taken. Another example is if the website suggests a serving of 2 capsules a day, but the packaging suggests 3, then the highest suggestion has been used.

**An assumption has been made regarding the value, see Table 1 (Appendix A of TOX/2025/41) for more details.

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Uncertainties in the exposure assessment

190. It should be highlighted that the UK market analysis of *G. cambogia* dietary supplements was performed in brief and as such, may not include all products that are available online. Thus, products with higher dosage recommendations and resulting in higher estimated exposures may exist on the UK market.

191. Some assumptions have been made where dosage recommendations are varied. In cases where the dosage is given as a range (e.g. 1-3 capsules per day), the highest possible amount has been assumed to be consumed (e.g. 3 capsules per day). Also, where there is a discrepancy between the packaging image and website instructions, the highest dosage has been assumed e.g. if the website suggests a serving of 2 capsules a day, but the packaging suggests 3, then the value of 3 has been used.

192. Some assumptions have been made where *G. cambogia* or HCA content has not been explicitly stated. E.g. for pure *G. cambogia* it is assumed that 5g-10g of the powder is equal to 5000-10,000 mg of *G. cambogia* (1g = 1000mg). I.e. it is assumed that no other ingredient(s) are present.

193. As stated in paragraph 187, most supplements in the market analysis, provided warnings on the website/ packaging recommending that that the product is only suitable for adults. However, exposures for other age groups could not be completely excluded. Toddlers have been selected as the age group for worst case exposure estimates, which are expressed on a per kg bodyweight basis. This is expected to be a conservative assessment and likely to be protective of other age groups under the age of 18 due to the average bodyweight of toddlers being lower than older children.

194. Infants have not been included in the assessment as it is assumed that supplements intended for weight loss and provided as small capsules or powders that could cause a choking hazard would not be used for infants.

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Uncertainties

195. The following uncertainties have been noted:

- Dietary supplement labels often do not list the full scientific name/specie of *G. cambogia* nor the part of the plant that the extract(s) is/are derived from. This represents an uncertainty as it does not allow accurate determination of the components of the food product (including food supplements).
- *G. cambogia* products have inconsistent labelling. Some are simply marketed as *G. cambogia* or *G. cambogia* extract without describing whether it is HCA nor the standardised HCA content. This poses an issue for both exposure and risk assessment as the HCA content is unknown.
- The percentage of standardised HCA in *G. cambogia* extract or the salt form of HCA in food supplement products is not always disclosed and there is inconsistency in labelling of said products. Depending on the amount of concentrate and the form of HCA salt, the toxicological profile could potentially be different.
- *G. cambogia* (and/or its extract; HCA) is more commonly present in MIDS that have other active compounds that may or may not be fully disclosed, which does not allow for a comprehensive risk assessment.
- If *G. cambogia* (and/or its extract) is present in MIDS there is a potential synergistic effect of the mixture, the potential risk(s) of which is unknown.
- Consumers may use more than one HIDS and/or in combination with prescription drugs. Incorrect dosing is also possible should the consumer not follow the manufacturers' instructions.
- Considerations for the presence of contaminants such as heavy metals, extraction solvents (from the manufacturing process), pesticides or any other chemicals that could pose a risk to health have not been considered in this assessment.

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- Case reports in the literature are limited to certain brands and formulations of *G. cambogia* and may not always provide the holistic state of the consumer: granularity on duration of exposure and dose, health status of the consumer (e.g., do they have suspected liver injury or immunocompromised or any other, fasting or non-fasting, physically active or not active), concomitant with other drugs or MIDS. Thus, identification of sensitive population and establishment of a mode of action for the toxicity observed in these cases is always not possible.
- Possible drug-drug interactions have been reported in some case-studies (e.g., anti-depression (serotonergic drugs), drugs affecting the liver). However, there is little scientific information to be able to fully assess this potential risk. Furthermore, it is unknown if other types of medication can cause adverse drug interaction.
- The long-term safety of *G. cambogia* (and/or its extract; HCA) has not been established.

Risk Characterisation

196. The presence of HCA in food supplements is considered medicinal according to the UK MHRA (see paragraph 8). From the Brief market analysis described in the Exposure section it is clear that some products are medicinal.

197. Data from nutrивigilance programs/schemes of authoritative bodies and literature have reported the following adverse effects following consumption of supplements containing *G. cambogia*: hepatic, digestive (pancreatitis), cardiac and muscular (rhabdomyolysis) damage, psychiatric, metabolic disorders, as well as drug-drug interactions. However, the mode of action of *G. cambogia* and its extracts have yet to be fully elucidated.

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Questions to the Committee

198. The Committee are asked to consider the following questions:

- a) Does the Committee agree with the conclusions reached by ANSES?
- b) Based on the current data, is the Committee able to identify a no-observed effect level or any other options, to derive a health-based guidance value?
 - i) If no, what additional information would the Committee require to provide a risk assessment?
- c) Does the Committee have any other comments?

October 2025

Secretariat

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Abbreviations

AESAN	Spanish Scientific Committee of the Spanish Agency for Food Safety and Nutrition
AhR	Aryl hydrocarbon receptor
AIDS	Acquired immune deficiency syndrome
ALP	alkaline phosphatase
ALT	Alanine transaminase
ANA	Anti-nuclear antibody
ANSES	French Agency for Food, Environmental and Occupational Health and Safety
ANSM	French National Agency for the Safety of Medicines and Health Products
ASMA	Anti-smooth muscle antibodies
ASP	Aspartate aminotransferase
ATP	Adenosinetriphosphate
BaP	Benzo[a]pyrene
BMI	Body mass index
CHO	Chinese hamster ovary cell line
COT	Committee on the Toxicity of Chemicals in Food, Consumer Products and the Environment
CYP	Cytochrome P450
DCFH-DA	2'- 7'- dichlorodihydrofluorescein diacetate
DGCCRF	General Directorate for Competition, Consumer Affairs and Fraud Control
DILIN	US Drug Induced Liver Injury Network
DMSO	Dimethyl sulfoxide
EAT	Exposure assessment team
FSA	Food Standards Agency
FSS	Food Standards Scotland
GGT	Gamma-glutamyl transferase
HCA	Hydroxycitric acid
HDS	Herbal and dietary supplements
HepG2	Hepatocellular carcinoma cell line
HIV	Human immunodeficiency virus

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IC50	Half maximal inhibitory concentration
IPS	Italian Phytovigilance System
LATINDILI	Latin America-Drug Induced Liver Injury database
MDCK-MDR1	Madin-Darby Canine Kidney-Human Multidrug Resistance gene-1 cell line
MHRA	Medicines and Healthcare products Regulatory Agency
MIDS	Multi-ingredient dietary supplements
MMC	Mitomycin C
MNPCE	Micronucleated polychromatic erythrocytes
MTT	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
NCE	Normochromatic erythrocytes
NDNS	National Diet and Nutrition Survey
NOAEL	No observed adverse effect level
PXR	Pregnane X receptor
RCT	Randomised clinical trial
ROS	Reactive oxygen species
TB	Total bilirubin
TGA	Australian Department of Health, Disability and Ageing Therapeutic Goods Administration
UK	United Kingdom
US FDA	United States Food and Drug Administration
US NCCIH	United States National Centre for Complementary and Integrative Health
WG	Working Group
WHO	World Health Organisation

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