Meeting

Draft Scientific Opinion on the safety of hydroxycitric acid and plant preparations containing hydroxycitric acid for public consultation

This is a paper for discussion. This does not represent the views of the Committee and should not be cited.

Introduction

1. Following a risk assessment by the Spanish Agency for Food Safety and Nutrition (AESAN) which raised concerns regarding a potential risk to consumers linked with the consumption of foods containing the pericarp of the fruit of Garcinia gummi-gutta (L.) Roxb. (syn. Garcinia cambogia (Gaertn.) Desr.), the European Commission requested EFSA to deliver a scientific opinion on opinion on the safety for human consumption of hydroxycitric acid (HCA) and HCA-containing plant preparations. The Panel on Nutrition, Novel Foods and Food Allergens (NDA) assessed the safety of plant preparations containing (–)-HCA, i.e. Garcinia gummi-gutta (L.) Roxb. pericarp or aril and Garcinia indica (Thouars) Choisy pericarp or aril preparations as well as the safety of plant preparations containing (+)-allo-HCA, i.e. Hibiscus sabdariffa L. calyx or petals. Preparations produced with non-polar solvents as well as medicinal products and novel foods were excluded from the assessment. Moreover, the Panel noted that a risk-benefit analysis was outside the scope of the assessment.

2. The Opinion considered previous evaluations from EFSA, other EU bodies and other regulatory bodies. They noted that EFSA's Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) was unable to conclude on the safety and the efficacy of a dried extract from the fruit rind of G. gummi-gutta (L.) N. Robson, as sensory additive in feed for cats and dogs, due to lack of

characterisation of the extract and the absence of complete toxicological data. The French National Agency for the Safety of Medicines and Health Products prohibited the importation, preparation, prescription and dispensing of magistral, officinal and hospital preparations, as well as the prescription, dispensing or administration to humans of G. gummi-gutta (plant part not specified). The decision was based on an unfavourable risk-benefit assessment, taking into account reports of serious adverse effects, including hepatotoxicity, cardiac injury, neurotoxicity, and muscle toxicity, documented in case reports from the United States and Canada. The Opinion also references the 2025 ANSES report on G. gummi-gutta preparations which the COT has previously reviewed (in February 2026) and which concluded that these preparations were poorly characterised in terms of HCA dosage, composition and extraction conditions. ANSES recommended to discourage the use of G. gummi-gutta supplements in individuals with psychiatric disorders, cardiometabolic diseases (diabetes, obesity, hypertension), history of pancreatitis or hepatitis, children and pregnant or breastfeeding women. Finally, They note that in 2009 the FDA had warned consumers a warning to consumers to stop using 'Hydroxycut®' products, which are food supplements containing HCA and other ingredients following reports of serious health problems ranging from jaundice and elevated liver enzyme concentrations, an indicator of potential liver injury, to liver damage requiring a liver transplant and a death due to liver failure.

3. With regards to their approach, the Panel outlined the protocol for the evaluation of the safety in use of hydroxycitric acid and plant preparations containing hydroxycitric acid (EFSA, 2023). EFSA collected data via systematic searches and considered available studies in animals and humans as well as in silico data on genotoxicity. Human randomised controlled studies (RCTs) investigating supplementation with HCA and HCA containing plant preparations were also included in the assessment. Further to the above, a call for data was launched aiming to collect:

- Analytical data on the content of (–)-HCA or (+)-allo-HCA in plant preparations and food, including food supplements.
- Use levels recommended by manufacturers for food supplements containing (–)-HCA or (+)-allo-HCA.
- Data (published and unpublished) on the ADME of (–)-HCA or (+)-allo-HCA (i.e. when consumed in a food matrix) and biological and toxicological data on the relationship between dietary exposure to (–)-HCA or (+)-allo-HCA as pure substance and/or in plant preparations and the identified potential adverse effect.

4. With regards to exposure, the EFSA Comprehensive European Food Consumption Database was used to provide estimates of exposure to (+)-allo-HCA from the habitual diet in EU populations. Data on the concentration of HCA in foods, including food supplements, on the European market were retrieved from the Mintel Global New Products Database (GNPD) .

5. Chronic dietary exposures to (–)-HCA or (+)-allo-HCA were calculated by combining content values of (+)-allo-HCA in hibiscus infusions with its average daily consumption at individual level in each dietary survey and age class, whilst it was not possible to determine exposure to (–)-HCA through the habitual diet, i.e. from the use of G. gummi-gutta or G. indica preparations as condiments due to the lack of content and consumption data.

6. The exposure to (–)-HCA from food supplements containing G. gummi-gutta preparations was estimated as mean dose/day based on the proposed uses from manufacturers extracted from the Mintel GNPD. No data were retrieved which would have allowed to estimate the exposure to (–)-HCA from food supplements containing G. indica preparations or (+)-allo-HCA from food supplements containing H. sabdariffa preparations.

7. An expert-guided approach was used to weigh the evidence and draw conclusions regarding the relationship between the exposure to (–)-HCA or (+)-allo-HCA, and to preparations of the plant species and parts included in the assessment and the endpoints considered. For genotoxicity, the reliability of the studies was scored using numerical values based on the scoring system by Klimisch et al. (1997). The relevance of the test system and studies were also considered, and they were scored as ‘high’, ‘limited’ or ‘low’ relevance. Additionally, a QSAR analysis on the similarity between guttiferone A (not present in the Garcinia species under assessment, however, has known genotoxicity concerns) and polyisoprenylated benzophenones occurring in G. gummi-gutta and G. indica was performed by EFSA to quantify the structural similarity. This was done using two approaches: unsupervised using VEGA similarity and supervised using expert evaluation of the structure.

8. With regards to the other endpoints, adverse effects on body weight were defined as a ≥10% difference between the dosed and the control group when the dosed group showed a lower body weight. Weight loss in growing animals was always considered to be adverse. For organ weights, adverse effects were considered to be present when differences were ≥10%. The internal validity (risk of bias, RoB) of all eligible animal studies identified through the literature search was critically appraised using the Office of Health Assessment and Translation

(OHAT) RoB tool developed by the US National Toxicology Program (NTP) (OHAT-NTP, 2019).

9. Section 3 of the Opinion addresses the Assessment of (–)-hydroxycitric acid and of (–)-hydroxycitric acid-containing plant preparations for which the following data have been considered: characterisation of 3.1. Characterisation of (–)-hydroxycitric acid containing plant preparations in 3.1.1. Garcinia gummi-gutta (aril and pericarp and 3.1.2. Garcinia indica (aril and pericarp), absorption, distribution, metabolism and excretion (ADME), genotoxicity, acute toxicity, general toxicity, reproductive and developmental toxicity, neurotoxicity in animals. Mechanistic studies were also considered in each section. For human data, case reports as well as other data from RCTs which reported side effects of the intervention were considered. Overall, the Panel reached the following conclusions on the safety of (–)-hydroxycitric acid and of (–)-hydroxycitric acid-containing plant preparations:

- The available data are insufficient to confirm or exclude genotoxicity off (–)-HCA, G. gummi-gutta or G. indica aril or pericarp preparations.
- (–)-HCA induced testicular toxicity in experimental rodent studies, primarily affecting Sertoli cells; a potential contribution of genotoxic damage in germ cells, particularly at meiotic stages, cannot be excluded.
- In humans, consumption of products labelled as containing G. gummi-gutta has been linked to idiosyncratic herb-induced liver injury; individuals in the general population who may be susceptible cannot currently be identified, and uncertainty remains as to whether (–)-HCA and G. indica preparations may also cause idiosyncratic liver injury.
- A safe dose for (–)-HCA, both in isolated form and in aqueous G. gummi-gutta pericarp preparations, could be established on the basis of data on testicular toxicity for the general, population, provided that concerns regarding genotoxicity are resolved; this dose may not protect susceptible individuals against idiosyncratic liver injury, for whom no safe level can be defined.
- No toxicological studies are available for non-aqueous preparations of G. gummi-gutta, for preparations of G. gummi-gutta aril and of G. indica aril or pericarp; therefore, no safe dose can be derived.
- The currently available data are insufficient to establish safe intake level for (–)-HCA, G. gummi-gutta or G. indica aril or pericarp preparations during human pregnancy or lactation.

10. Section 4 addresses the assessment of (+)-allo-hydroxycitric acid and (+)-allo-hydroxycitric acid-containing plant preparations. This section considered data

on: characterisation of Hibiscus sabdariffa (calyx and petals), ADME, genotoxicity, acute and general toxicity, chronic toxicity, reproductive and developmental toxicity and immunotoxicity in animals. Mechanistic studies were also considered where available. For humans, no reports were retrieved from the systematic literature search which reported adverse effects following the consumption of H. sabdariffa preparations, whilst data was retrieved from 5RCTs that reported adverse events or on markers of liver and kidney function after consumption of H. sabdariffa calyx preparations.

11. Overall, the following conclusions were reached:

- The available data are insufficient to confirm or exclude genotoxicity of (+)-allo-HCA or H. sabdariffa calyx/petal preparations; H. sabdariffa preparations may exert transplacental genotoxicity but this needs to be confirmed in an additional study.
- H. sabdariffa calyx/petal preparations induced testicular, kidney and liver toxicity in experimental rodent studies; concerns for a delayed onset in puberty of female rats following transplacental exposure also exist.
- Testicular toxicity has been observed with an infusion at a dose of 200 mg/kg bw per day of calyx equivalents in mice; however, the evidence is insufficient to identify a NOAEL; a dose which is associated with kidney and liver toxicity can also not be identified.
- The currently available data are insufficient to establish a safe intake for humans for (+)-allo-HCA or H. sabdariffa calyx/petal preparations.

12. In the abstract, the Panel notes that due to identified safety concerns and insufficient data, safe intake levels for humans for (–)-HCA, G. gummi-gutta, G. indica aril or pericarp or H. sabdariffa calyx or petal preparations cannot be set.

13. This item is presented for discussion of the COT as a whole. The consultation period closes on 04/05/2026 and therefore the Secretariat welcomes comments until COP 17th of April, after which the Committee comments will be compiled and submitted on behalf of the COT. A summary document will be placed in the collaboration folder for comments, or these can be sent to the Secretariat directly. Please provide page and line numbers in your comment submissions.

Questions to the Committee:

i) Based solely on the information that has been evaluated by EFSA within this Opinion, does the COT agree with the overall conclusions reached for each of the components under assessment?
ii) Does the COT have any comments with regards to the overall scientific methodology, scoring of the studies and weighing of evidence?
iii) Does the COT have any comments on the structure and clarity of the EFSA Opinion?
iv) Does the COT have any other comments?

Secretariat
March 2026

Annex A to TOX/2026/15

Link to consultation:

Public Consultation: Draft scientific opinion on the safety of hydroxycitric acid and plant preparations containing hydroxycitric acid

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