



SCIENTIFIC ADVISORY GROUP ON CHEMICAL SAFETY OF NON-FOOD AND NON-MEDICINAL CONSUMER PRODUCTS (SAG-CS)

Final Opinion on Daidzein in Cosmetic Products.

1. Introduction

1.1 Daidzein (7-hydroxy-3-(4-hydroxyphenyl)chromen-4-one; CAS No.486-66--8), Figure 1, has a maximum use concentration of 0.02% w/w in the EU as stipulated in Annex III of the EU Cosmetics Regulation (EC) No. 1233/2009¹. Daidzein is not currently regulated under the UK Cosmetics Products (Safety) Regulation No. 1223/2009².

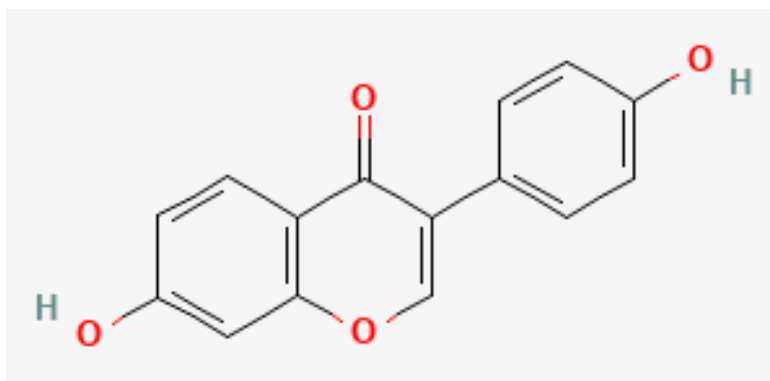


Figure 1: Structure of daidzein (Source: PubChem)

1.2 Daidzein has no classifications under the GB Classification, Labelling and Packaging regulation No 1272/2008 (as amended)³ and is

¹ [Regulation \(EC\) No. 1223/2009](#)

² Cosmetics product (safety) Regulations currently consists of the Regulation UK No 1223/2009 as amended by [SI 696/2019 Product Safety and Metrology \(EU Exit\) Regulations](#). The full consolidated UK text will be available in due course.

³ The GB CLP Regulation No 1272/2008 as amended by The Chemicals (Health and Safety) and Genetically Modified Organisms (Contained Use) (Amendment etc.) (EU Exit) Regulations 2019. The full consolidated UK text will be available soon.



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therefore not included in the GB Mandatory Classification and Labelling (MCL) list⁴.

1.3 In 2022, OPSS issued a call for data for cosmetic ingredients with suspected endocrine disrupting properties. Daidzein was included in this call, however no data was provided to OPSS by industry.

1.4 OPSS requested that the SAG-CS assess the safety of daidzein when intended to be used within cosmetic products based on available published data.

1.5 A summary of the key physicochemical and toxicological information as found in the literature was provided to the SAG-CS to assist with their review.

2. Background

Intended function and uses of daidzein.

2.1 Daidzein is a natural phytoestrogen (a plant-derived oestrogenic compound) belonging to the isoflavone class, which are predominantly found in soybeans and soy-based foods. To a lesser extent, daidzein can be found at low concentrations in other fruits and nuts ([Liggins et al., 2000](#)).

2.2 According to a submission to the [SCCS](#), daidzein (derived from soybean plants, also known as *Glycine max* L.) is used in the formulation of leave-on cosmetic products and has a variety of functions such as being an antioxidant, skin protectant, skin conditioning agent and a hair conditioning agent. Daidzein is predominantly found in products which claim to have anti-aging effects ([SCCS, 2022](#)).

3. Previous Scientific Opinions on Daidzein

3.1 The [SCCS](#) published a final opinion on daidzein in 2022. In summary, the SCCS concluded that “from the safety assessment based on the available relevant data on the aglycone form of daidzein⁵, and in consideration of the potential endocrine disrupting properties of phytoestrogens, the SCCS considers that the use of daidzein in cosmetic products up to a maximum concentration of 0.02% w/w is safe”.

⁴ Available at: <https://www.hse.gov.uk/chemical-classification/classification/harmonised-classification-self-classification.htm>

⁵ Aglycone daidzein (daidzein)



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When considering the oral route of exposure, the SCCS calculated a Margin of Safety (MoS) of 96, using a Lowest Observed Effect Level (LOEL) of 5 mg/kg bw/day, adjusted by an oral bioavailability factor of 25%, as the Point of Departure (POD). The LOEL was derived from an oral developmental study in Sprague-Dawley rats by Talsness et al., (2015) and considered to be a No Observed Adverse Effect Level (NOAEL) because the effects reported were not directly associated with reduced fertility performances in the female rats. For the subcutaneous route, the SCCS calculated a higher LOEL⁶ of 5 mg/kg bw/day as derived from a 90-day rat study by [Retana-Márquez et al., \(2016\)](#). Although the MoS calculated based on oral exposure to daidzein is less than 100, daidzein was deemed safe based on the MoS calculated from the subcutaneous exposure route. This is because the SCCS considered the subcutaneous route to be the more appropriate and reliable indicator of safety, given the uncertainties around the oral absorption of daidzein (reflected in the 25% bioavailability) in humans.

3.2 The European Food Safety Authority (EFSA) have published several opinions on soy isoflavones, which includes daidzein. Whilst the majority of these opinions look at the substantiation of health claims related to soy isoflavones (rather than their safety), one opinion by the EFSA Panel on Food Additives and Nutrient sources added to Food (ANS), carried out a risk assessment for peri- and post-menopausal women taking food supplements containing isolated isoflavones. The Panel were unable to derive a single health-based guidance value or a safe intake level for food supplements containing isoflavones, however, the recommended daily doses of the majority of marketed food supplements appeared to fall within the range for no observed effects in the three target organs (breast, uterus and thyroid). The conclusions of the opinion only applied to post-menopausal women due to insufficient data with respect to the uterus for peri-menopausal women ([EFSA, 2015](#)).

3.3 In 2020, a Cosmetic Ingredient Review (CIR) panel published a final report for a Safety Assessment of Soy-Derived ingredients as Used in Cosmetics. Overall, the Expert Panel for Cosmetic Ingredient Safety concluded that 24 soy-derived ingredients, which includes daidzein, are safe in cosmetics in the present practices of use and concentrations described in the safety assessment ([CIR, 2020](#)).

3.4 The Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) have published several statements on the dietary intake of phytoestrogens, which includes daidzein. The most recent statement, published in 2021, concerns the consumption of plant-based drinks (including soya) in children aged 6 months to 5 years of age ([COT,](#)

⁶ See 4.4. The SAG-CS did not deem this to be a 'true' LOEL since this was derived from a study using one dose concentration



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[2021](#)). This follows on from a 2013 statement which evaluated some of the potential risks of high levels of soya phytoestrogens in the infant diet. The main toxicological concern was the potential to disrupt the development and function of the reproductive system. Due to limitations in the available data and other uncertainties, it was not possible for the COT to set a health-based guidance value for soya isoflavones in infants ([COT, 2013](#)). Aside from a reduction in the estimated highest potential exposure of infants and children to phytoestrogens from consumption of soya drinks, the conclusions of the COT on the safety of soya phytoestrogens remained largely the same in their 2021 statement as in the 2013 statement ([COT, 2021](#)).

In 2015, the COT published a statement on the effects of soya phytoestrogen consumption on thyroid status. The COT concluded that “there are no indications that high intakes of soya impact materially on thyroid function in people in whom thyroid function is not already impaired”, however, there was inconsistent evidence that higher soya phytoestrogen intake could affect people with subclinical, compensated hypothyroidism, or have an effect on thyroxine used in the treatment of hypothyroidism ([COT, 2015](#)). In addition to the published statements, a COT report on phytoestrogens and health, published in 2003, offers a significant review of the health implications of dietary phytoestrogens ([COT, 2003](#)).

4. Discussion by the Scientific Advisory Group on Chemical Safety of Non-Food and Non-Medicinal Consumer Products (SAG-CS)

4.1 At their February 2024 meeting, the SAG-CS discussed a paper which focused on the risks posed to health by daidzein when used in cosmetic products. Since there was no industry response to the call for data issued by OPSS in 2022, members were presented with a literature review carried out by OPSS, as well as the [SCCS \(2022\)](#) opinion on daidzein.

4.2 A number of the papers reviewed in this assessment that considered daidzein also considered genistein. Genistein and daidzein are structural homologues. It should be noted that the SAG-CS has also reviewed genistein used in cosmetic products separately and their opinion will be published in due course.

4.3 Members discussed the analytical methods for daidzein. No specific analytical methods for cosmetics could be identified in the literature. There were, however, a significant number of papers which detailed the



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extraction of daidzein (or other isoflavones) from animal or human tissue/bodily fluids after dietary exposure, and from plants. Members noted that some of these methods, such as the QuEChERS⁷ method detailed in [Ding et al., 2016](#), along with methods detailed in the review by [Daems et al., 2016](#) could be adapted for use in cosmetics. Members were thus content that a reasonable analytical method could be available for daidzein in cosmetic products if fully developed and validated.

- 4.4 Members agreed with the Point of Departure (PoD) value of 5 mg/kg bw/day for both the subcutaneous route and the oral route as used by the SCCS in their safety assessment ([SCCS 2022](#)). For the subcutaneous route, the PoD was derived from a study by [Retana-Márquez et al., 2016](#) which evaluated the effects of genistein and daidzein, mesquite pod and *Leucaena* extracts on several aspects of behaviour and reproductive physiology of the male Wistar rat. The SCCS refer to this as a LOEL which the SAG-CS disagreed with given the study uses only one dose concentration. For the oral route, the PoD was derived from a modified (non-OECD guideline) one-generation reproductive toxicity study by [Talsness et al., 2015](#) in which the SCCS considered a NOAEL of 5 mg/kg bw/day based on changes in the ovaries of female Sprague Dawley rats. This was considered a NOAEL rather than a LOAEL because the reported effects were not directly associated with reduced fertility performance in female Sprague Dawley rats.
- 4.5 Members agreed with the SCCS that the PoD derived from the subcutaneous route is more appropriate and reliable to take forward for the safety assessment, acknowledging that this represents a worst exposure scenario. Using the oral route, a very conservative oral bioavailability factor of 25% has been applied by the SCCS. This is as a result of insufficient data on the oral absorption of daidzein and its extensive first-pass metabolism in the gut following systemic absorption, leading to low bioavailability of daidzein in humans ([SCCS, 2022](#)).
- 4.6 Members noted that daidzein, as a phytoestrogen, can bind to oestrogen receptors exhibiting both oestrogenic and anti-oestrogenic effects, ([Křížová et al., 2019](#); Intharuksa et al, 2025).

⁷ [QuEChERS](#) (Quick, Easy, Cheap, Effective, Rugged, and Safe) is a widely used, streamlined sample preparation technique for analysing chemical residues (mainly pesticides) in food and agricultural products. It uses solvent extraction followed by dispersive solid-phase extraction (dSPE) to clean up samples, removing fats, sugars and pigments before analysis ([Perestrelo et al., 2019](#))



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- 4.7 Members were content with the availability of endocrine activity and disruption data in the literature and concluded, based on the evidence available that daidzein likely has endocrine disruptive properties. Members noted that the two pivotal studies used to derive the PoD ([Retana-Márquez et al., 2016](#) and [Talsness et al., 2015](#)), along with other key supporting studies such as that by [Lamartiniere et al., \(2002\)](#), indicate that the PoD should be sufficiently protective of endocrine effects.
- 4.8 There was a lack of dermal absorption data available for daidzein. Of the few studies available, the most recent studies focus on the metabolism of daidzein. In the [SCCS \(2022\)](#) opinion, the default dermal absorption value of 50% was used in the safety assessment because none of the reported dermal absorption studies were carried out in accordance with the SCCS basic criteria for such studies.
- 4.9 Members concurred with the decision of the [SCCS \(2022\)](#) to use a dermal absorption of 50% but also considered two recently published papers by Génies et al., ([2024a](#) and [2024b](#)). The first paper is a comparative study of the absorption and metabolism of genistein and daidzein through four models, namely, human (fresh and frozen) skin, metabolically viable (fresh) pig skin and Phenion full-thickness (FT) models. The PhenionFT model is a 3D human skin equivalent that closely mimics the structure and physiological properties of native human skin. The fresh human skin data for daidzein is of particular relevance to the opinion and the study design is in general agreement with the SCCS criteria for dermal absorption studies ([SCCS, 2023](#)). 7 samples of human abdominal skin, 6 female and 1 male, were used in the study. 10 nmoles/cm² of both daidzein and genistein radiolabelled in ethanol was applied to skin mounted in an *in vitro* system and absorption followed for 24 hours. Dermal absorption was determined from radioactivity in receptor fluid and skin after removal of the stratum corneum. Mass spectrometry (MS) identification of metabolites showed glucuronides and sulphates which were measured by radiochromatography. Extensive metabolism was detected in receptor fluid and skin, accounting for 80% of radioactivity by 24 hours following daidzein and genistein application. Approximately 50% of the parent was present in the medium (receptor) by 24 hours but 20% when skin included. The dermal absorption of 10 nmoles/cm² genistein and daidzein and genistein in ethanol was comparable in all four models ([Génies et al., 2024a](#)). The dermal absorption results obtained for daidzein are therefore consistent with using a value of 50%.



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- 4.10 The second paper used the same approach described in paragraph 4.9 to compare the absorption of daidzein and genistein applied in ethanol and in a body lotion formulation. Dermal absorption was lower for both daidzein and genistein from the body lotion formulation compared to ethanol. The authors of the study concluded that “most of the dose applied in the formulation was retained on the skin surface, especially at 30 nmoles/cm² (60%–90%), resulting in much lower amounts in the medium and/or skin. In conclusion, all four skin models demonstrated first-pass metabolism of genistein and daidzein and a marked alteration in their disposition by applying them in a body lotion formulation” ([Géniès et al., 2024b](#)).
- 4.11 Members discussed the genotoxicity of daidzein. Since no original studies were submitted to OPSS, the SAG-CS members reviewed the studies summarised in the SCCS (2022) opinion in addition to any relevant studies found in the open literature. The SCCS examined all *in vitro* and *in vivo* studies identified in the published literature up to November 2021 which were relevant to the mutagenicity and genotoxicity of daidzein as well as an additional *in vitro* micronucleus assay on human lymphocytes (OECD TG 487) carried out in 2022 and submitted to the SCCS by the applicant. The SAG-CS recognised that the majority of studies identified in the literature were deemed by the SCCS to be of limited relevance and/or low priority, noting that several had not been conducted in accordance with current OECD Test Guidelines (TGs) or to Good Laboratory Practice (GLP). Mixed results were observed *in vitro*, with several positive Comet assays (Anderson et al., 1997a; Anderson et al., 1997b; Cemeli et al., 2004), along with a positive cell transformation assay and DNA adducts assay (Tsutsui et al., 2003) indicating that daidzein may cause DNA damage *in vitro*. However, an *in vitro* Comet assay of high reliability and relevance by Baechler et al., (2014) was negative. The *in vitro* micronucleus assay (2022) submitted by the applicant was also negative for mutagenicity. Of the limited number of *in vivo* studies identified, all three *in vivo* mammalian gene mutation studies were negative for genotoxicity (Aidoo et al., 2005; Manjanatha et al., 2006). A weakly positive result was observed in a sister chromatid exchange assay which is no longer recommended for regulatory purposes (Giri and Lu, 1995). Based on the weight of available evidence, members concurred with the SCCS that daidzein is unlikely to be genotoxic *in vivo*.
- 4.12 Overall, in the absence of any data submitted by industry, members concurred with the conclusions of the SCCS that daidzein is safe at a concentration of 0.02% in cosmetic products.



5. Conclusions

Members were content that a reasonable analytical method is available for daidzein, subject to matrix specific validation.

Members concluded that the available data in the literature suggest that daidzein has endocrine disruptive properties but noted that the Point of Departure used in the safety assessment should be protective of any adverse effects mediated by an endocrine mechanism.

Based on the evidence considered by members, daidzein was unlikely to have genotoxic potential in vivo.

Overall, the SAG-CS, consider daidzein to be safe for use in cosmetic products up to a maximum concentration of 0.02% w/w. This outcome is made in the absence of any additional data submitted by industry. It is based on the available published data and concurs with the SCCS conclusion that daidzein is safe for use in cosmetic products up to a maximum concentration of 0.02% w/w.

Scientific Advisory Group on Chemical Safety of Non-Food and Non-Medicinal Consumer Products

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Abbreviations

ANS	EFSA Panel on Food Additives and Nutrient Sources added to Food
CIR	Cosmetics Ingredient Review
CLP	Classification, Labelling and Packaging
COT	The Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
EFSA	European Food Safety Authority
GLP	Good Laboratory Practice
LOAEL	Low Observed Adverse Effect Level
LOEL	Low Observed Effect Level
MCL	Mandatory Classification and Labelling
MoS	Margin of Safety
NOAEL	No Observed Adverse Effect Level
PoD	Point of Departure
QuEChERS	Quick Easy Cheap Effective Rugged and Safe (analytical extraction method)
SCCS	Scientific Committee on Consumer Safety



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