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Safety and efficacy of a feed additive consisting of a dried extract from the roots of *Arctium lappa* L. (*A. lappa* dry extract) for use in cats and dogs (C.I.A.M.)

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Abstract

Following a request from the European Commission, the EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) was asked to deliver a scientific opinion on the safety and efficacy of a dried extract prepared from the roots of *Arctium lappa* L. (*A. lappa* dry extract) when used as a sensory additive (flavouring compound) in feed for cats and dogs. *A. lappa* dry extract is specified to contain at least 2% inulin. Since uncertainty remains concerning the nature of up to 77% of the additive, the FEEDAP Panel was unable to conclude on the safety of the extract at the proposed use levels of up to 40 mg/kg complete feed for cats and dogs. In the absence of data, no conclusions can be drawn on the safety for the user. In the absence of convincing evidence that the extract acts as a flavour in animal feed or has an effect on palatability, the FEEDAP Panel was unable to conclude on the efficacy of the additive.

Keywords: sensory additives, *Arctium lappa* L., *Arctium lappa* dry extract, Great Burdock extract, inulin, safety, efficacy

Requestor: European Commission

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1. Introduction

1.1. Background and Terms of Reference

Regulation (EC) No 1831/2003[1] establishes the rules governing the Community authorisation of additives for use in animal nutrition. In particular, Article 10(2) of that Regulation specifies that for existing products within the meaning of Article 10(1), an application shall be submitted in accordance with Article 7, within a maximum of seven years after the entry into force of this Regulation.

The European Commission received a request from C.I.A.M. S.r.l.[2] for re-evaluation of the product *Arctium lappa* L. extract (Great Burdock extract CoE 57), when used as a feed additive for cats and dogs (category: sensory additives; functional group: flavouring compounds).

According to Article 7(1) of Regulation (EC) No 1831/2003, the Commission forwarded the application to the European Food Safety Authority (EFSA) as an application under Article 10(2) (re-evaluation of an authorised feed additive). EFSA received directly from the applicant the technical dossier in support of this application. The particulars and documents in support of the application were considered valid by EFSA as of 4 June 2018.

According to Article 8 of Regulation (EC) No 1831/2003, EFSA, after verifying the particulars and documents submitted by the applicant, shall undertake an assessment in order to determine whether the feed additive complies with the conditions laid down in Article 5. EFSA shall deliver an opinion on the safety for the target animals and the user, and on the efficacy of the product *A. lappa* L. dry extract, when used under the proposed conditions of use (see Section 3.2.3).

1.2. Additional information

A. lappa L. (Great Burdock extract CoE 57, synonym *Arctium majus* Bernh) is currently listed in the European Union Register of Feed Additives pursuant to Regulation (EC) No 1831/2003 (2b natural products – botanically defined). It has not been previously assessed by EFSA as feed additive.

Great Burdock extract is listed by the Council of Europe as a natural source of food flavouring (CoE 57).

A. lappa extract from the roots of the Burdock is listed in the European list of Cosmetics and Ingredients and Substances as soothing, antiseborrhoeic, skin conditioning, astringent and tonic agent.[3]

For human traditional medicinal uses, the European Medicines Agency (EMA) issued a herbal monograph and an assessment report on *A. lappa* L., radix (EMA, 2011a,b). In 2020, EMA published an addendum to the assessment report (EMA, 2020).

2. Data and methodologies

2.1. Data

The present assessment is based on data submitted by the applicant in the form of a technical dossier[4] in support of the re-evaluation of *A. lappa* dry extract as a feed additive.

The FEEDAP Panel used the data provided by the applicant together with data from other sources, such as previous risk assessments by EFSA or other expert bodies, peer-reviewed scientific papers, other scientific reports and experts' knowledge, to deliver the present output.

EFSA has verified the European Union Reference Laboratory (EURL) report as it relates to the methods used for the control of the additive's phytochemical markers in animal feed. The Executive Summary of the EURL report can be found in Annex A.[5]

[1] Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.
[2] C.I.A.M. S.r.l., via Piemonte 4, 63100 Ascoli Piceno (AP), Italy.
[3] Commission Decision 2006/257/EC of 9 February 2006 amending Decision 96/335/EC establishing an inventory and a common nomenclature of ingredients employed in cosmetic products, OJ L 97, 5.4.2006, p. 1–528.
[4] FEED dossier reference: FAD-2010-0301.
[5] The full report is available on the EURL website: https://ec.europa.eu/jrc/sites/jrcsh/files/finrep_fad-2010-0301_greatb_arctiumlappa.pdf

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of *A. lappa* dry extract, is in line with the principles laid down in Regulation (EC) No 429/2008[6] and the relevant guidance documents: Guidance for the preparation of dossiers for sensory additives (EFSA FEEDAP Panel, 2012a), Guidance on studies concerning the safety of use of the additive for users/workers (EFSA FEEDAP Panel, 2012b), Guidance on the assessment of additives intended to be used in pets and other non food-producing animals (EFSA FEEDAP Panel, 2011).

3. Assessment

The additive under assessment, *A. lappa* dry extract, is prepared from the roots of *A. lappa* L. and is intended for use as a sensory additive (functional group: flavouring compounds) in feed for cats and dogs.

3.1. Origin and extraction

A. lappa L. (Great Burdock) is a biennial plant, belongs to the *Asteraceae* family and is native to the temperate regions of Europe, Russia and northern Asia. In Asia, it is generally cultivated as a food, while in Europe, although there are records of food use, it is more commonly found as a garden plant. In Asia, the plant is grown primarily for its roots but the stem also finds culinary use. Both roots and the aerial parts of the plant are used in traditional medicine.

The *A. lappa* dry extract is prepared from crushed and chopped roots by extraction with water. After a period of extraction, the liquor is separated from the insoluble biomass. The extract is then concentrated to an ~ 50% dry matter, maltodextrin is added and the concentrated extract is spray-dried. Finally, the spray-dried extract is ground, sieved and packed for distribution.

3.2. Characterisation

3.2.1. Characterisation of the extract

A. lappa dry extract is identified by the Council of Europe (CoE) number 57, the Chemical Abstract Service (CAS) number 84012-13-5 and the European Inventory of Existing Commercial chemical Substances (EINECS) number 281-658-8. The additive is described as a brown fine powder, with a characteristic odour. It has a density of 450–700 kg/m^3. The additive is partially soluble in water and organic solvents.

According to the specification proposed by the applicant, *A. lappa* dry extract contains at least 2% inulin (selected as the marker compound). Loss on drying is specified to be ≤ 5%, and ash ≤ 15%. Data were provided for four batches of the *A. lappa* dry extract, which showed an average content of inulin of 33.2% (range 22.9–39.9%).[7] However, certificates of analysis were not provided.

The applicant did not provide the full characterisation of the additive, despite being requested. Although the additive contains maltodextrin, the amount added is unknown and, as a result, uncertainty remains concerning the nature of up to 77% of the extract.

The applicant provided a commercial information sheet for the *A. lappa* dry extract,[8] which includes the limits applied for chemical impurities and microbiological contamination. Specifications for chemical impurities include heavy metals (lead ≤ 3.0 mg/kg, cadmium ≤ 1.0 mg/kg and mercury ≤ 0.1 mg/kg), mycotoxins (aflatoxin B1 ≤ 5.0 μg/kg, aflatoxins B1, B2, G1 and G2 ≤ 10.0 μg/kg) and pesticide residues (which are declared to comply with the maximum limits of Regulation (EU) No 396/2005[9]). Specifications for microbial contamination include aerobic bacteria ≤ 50,000 colony forming unit (CFU)/g, fungi (yeast/moulds) ≤ 500 CFU/g, Bile-tolerant Gram-negative bacteria ≤ 100 CFU/g, *Salmonella* spp. absent in 25 g,

[6] Commission Regulation (EC) No 429/2008 of 25 April 2008 on detailed rules for the implementation of Regulation (EC) No 1831/2003 of the European Parliament and of the Council as regards the preparation and the presentation of applications and the assessment and the authorisation of feed additives. OJ L 133, 22.5.2008, p. 1.

[7] Technical dossier/Section II/Annex II_1_03_ Analysis batches.

[8] Technical dossier/Section II/Annex II_1_01_Data_sheet_Arctium_lappa.

[9] Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC Text with EEA relevance. OJ L 70, 16.3.2005, p. 1–16.

E. coli absent in 1 g. However, analytical data supported by certificates of analysis were not provided. The FEEDAP Panel notes that the specification for aerobic bacteria is very high.

Particle size analysis (by sieving) of the additive showed that 90% of particles passed a 300 μm sieve, and 39–53% of three batches of *A. lappa* dry extract passed a 50 μm sieve. No data were provided on the dusting potential of the additive.

3.2.2. Stability

The applicant stated that the typical shelf-life of *A. lappa* dry extract is at least three years when stored in closed containers protected from heat, light and humidity.[10] Stability studies provided showed that the content of inulin (the marker compound) was on average 90% of the initial content in one batch of *A. lappa* dry extract after 3-year storage (storage conditions not reported).[11]

3.2.3. Conditions of use

A. lappa dry extract is intended for use in feedingstuffs, premixtures and complementary feed for cats and dogs, up to the maximum use level of 40 mg/kg complete feed.

3.3. Safety for the target species and the user

No specific studies were provided on absorption, distribution, metabolism and excretion with the extract under assessment or with the individual constituents.

Tolerance studies and/or toxicological studies made with the additive under application were not submitted. In addition, the additive was insufficiently characterised to allow an assessment based on the individual components.

The applicant made reference to a draft EMA herbal monograph on *A. lappa* L., radix (EMA, 2011a) and to carcinogenicity data in rat, also mentioned in an EMA assessment report on *A. lappa* L., radix (EMA, 2011b). The carcinogenicity data on the roots of *A. lappa* L. comes from a very limited study by Hirono (1977). The test item is not specified in any detail and the study is inadequate to conclude on carcinogenicity. No tests on preparations from *A. lappa* root have been performed.

Considering that there is uncertainty about the composition up to 77% of the additive and in the absence of adequate toxicological data, the FEEDAP Panel cannot conclude on the safety of the additive for cats and dogs.

No specific data were provided by the applicant regarding the safety of the additive for the user and, consequently, no conclusions can be drawn on the additive's potential to be dermal/eye irritant or skin sensitiser. The additive contains about 50% of particles of thoracic size (< 50 μm). In the absence of data on their dusting potential, it is not possible to estimate exposure of users to dust.

In the absence of adequate data, the FEEDAP Panel cannot conclude on the safety of the additive under assessment for the target animals or the users.

3.4. Efficacy

A. lappa L. is listed in Fenaroli's Handbook of Flavour Ingredients (Burdock, 2010) under the heading 'Burdock' without any indication of its particular use. It is, however, not recognised by the Flavour and Extract Manufactures Association (FEMA) and is without an FEMA number. The European Inventory of Existing Commercial chemical Substances (EINECS) references its use only as a cosmetic ingredient for skin conditioning, and not for fragrance or flavour use.

In the absence of convincing evidence that the extract acts as a flavour in animal feed or has an effect on palatability, the FEEDAP Panel is unable to conclude on the efficacy of the additive.

4. Conclusions

Since up to 77% of the additive remains uncharacterised, the FEEDAP Panel cannot conclude on the safety of the extract derived from the roots of *A. lappa* L. at the proposed use levels of up to 40 mg/kg complete feed for cats and dogs.

In the absence of data, no conclusions can be drawn on the safety of the additive for the user.

[10] Technical dossier/Section II/Annex II_4_01_Stability statement of supplier.
[11] Technical dossier/Section II/Annex II_4_02_Stability shelf life.

In the absence of convincing evidence that the extract acts as a flavour in animal feed or has an effect on palatability, the FEEDAP Panel is unable to conclude on the efficacy of the additives.

5. Documentation as provided to EFSA/Chronology

Date	Event
05/11/2010	Dossier received by EFSA. *Arctium lappa* L. (Great Burdock extract CoE 57) for cats and dogs. Submitted by C.I.A.M. S.r.l.
24/04/2018	Reception mandate from the European Commission
04/06/2018	Application validated by EFSA – Start of the scientific assessment
22/06/2018	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. *Issues: characterisation, safety for the target species, safety for the user, efficacy*
05/09/2018	Comments received from Member States
04/10/2018	Reception of the Evaluation report of the European Union Reference Laboratory for Feed Additives
11/10/2019	The applicant informed the European Commission on the impossibility to provide the information requested in line with Article 8(1)(2) of Regulation (EC) No 1831/2003
17/03/2021	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

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Abbreviations

CAS	Chemical Abstracts Service
CFU	colony forming unit
DM	dry matter
EINECS	European Inventory of Existing Commercial chemical Substances
EMA	European Medicines Agency
EURL	European Union Reference Laboratory
WHO	World Health Organization

Annex A – Executive Summary of the Evaluation Report of the European Union Reference Laboratory for Feed Additives on the Method(s) of Analysis for *Arctium lappa* extract (Great Burdock extract CoE 57)

In the current application, authorisation is sought under Article 10(2) for the botanically defined *Arctium lappa* extract (Great Burdock extract CoE 57) under the category/functional group (2 b) 'sensory additives'/'flavouring compounds', according to the classification system of Annex I of Regulation (EC) No 1831/2003. Specifically, the *feed additive* is sought to be used for cats and dogs.

According to the Applicant, the phytochemical marker of the *feed additive* is *inulin*; at least 2% of *inulin* is included in the product.

The *feed additive* is intended to be incorporated directly into *feedingstuffs* or through *premixtures*. The Applicant did not propose a minimum or maximum level of the *feed additive*; however, a maximum content of 40 mg *feed additive*/kg *feedingstuffs* was suggested.

For the determination of the phytochemical marker *inulin* in the *feed additive,* the Applicant submitted the ring trial validated AOAC Official Method 997.08 which has the scope to determine added fructans (*inulin* and fructo-oligosaccharides – FOS) in processed foods. The analytical method is based on Ion Exchange Chromatography (IEC) coupled with Pulsed Amperometric Detection (PAD). The Applicant, in the frame of the dossier, presented tests in which the AOAC method for the determination of *inulin* was applied directly to the *feed additive*. Based on the results presented for three different lots of the same product, the EURL calculated a relative standard deviation for repeatability (RSDr) of 7.5%.

Based on the available performance profile, the EURL recommends for official control the ring trial validated AOAC method based on IEC-PAD for the determination of the selected phytochemical marker in the *feed additive*.

The Applicant did not provide experimental data or analytical method for the determination of *Arctium lappa* extract in *premixtures* and *feedingstuffs* as the unambiguous determination of the *feed additive* added to the matrices is not achievable experimentally. Therefore, the EURL cannot evaluate nor recommend any method for official control for the determination of *Arctium lappa* extract in *premixtures* and *feedingstuffs*.

Further testing or validation of the methods to be performed through the consortium of National Reference Laboratories as specified by Article 10 (Commission Regulation (EC) No 378/2005, as last amended by Regulation (EU) 2015/1761) is not considered necessary.