Substance Information Document

Cascarilla bark oil

1. Substance identity

Name	Cascarilla bark oil
Synonyms	Cascarille Cascarilla oil Cascara bitterless extract Croton eluteria bark oil
IUPAC Name	N/A*
CAS	8007-06-5

*Non answered, IUPAC Name was not found.

2. Toxicological information

Cascarilla bark oil is obtained from the bark of the Croton trees. Traditionally, it is used as a therapeutic aromatic bitter tonic for the treatment of various stomach ailments. Today, the oil is used for commercial perfume and flavor marketplace.

Not much toxicological data can be found for Cascarilla bark oil. The CAS no. 8007-06-5 has three entries in FEMA, i.e., FEMA 2253, 2254, and 2255. And all three numbers are included in GRAS report.

The CAS no. 8007-06-5 is not registered under REACH in EU. But Classification & Labelling (C&L) notification indicates that cascarilla bark oil might be sensitizing to skin.

Major constituents of cascarilla bark oil include cymene, diterpene, limonene, caryophyllene, terpineol, and eugenol, among others. Monocyclic and monoaromatic terpene hydrocarbons like cymene and limonene have been assessed by FEMA for their use as flavors (Adams et al., 2011). Both cymene and limonene are not acutely toxic when being administered orally to rodents. The oral LD50s were > 4000 mg/kg bw. Limonene has been evaluated in several short- and long-term toxicity studies via oral gavage. Depends on the testing species and exposure duration, the NOAEL was between 5 to 1650 mg/kg bw/day, mainly based on decrease in body weight gain. It has been observed that limonene induced renal tubular tumors in male rats, however, the underlying mechanism has been demonstrated as not relevant for humans and confirmed by IARC. Neither cymene nor limonene is mutagenic in Ames assays, and limonene was negative in mouse lymphoma assay (MLA) as well. Limonene has been evaluated in various reproductive toxicity studies with rodents. Some developmental effects were observed in the offspring, however, all of them occurred at the doses that induced maternal toxicity as well. Based on those results, FEMA concluded that the group of aliphatic and aromatic monoterpene hydrocarbons is generally recognized as safe (GRAS) under conditions of intended use as flavor ingredients. Caryophyllene is another constituent that is often present in essential oils. It is registered under EU REACH. Based on the studies included in the dossier, it is not acutely toxic when administered to mice orally. The resulting LD50 was > 5000 mg/kg bw. Caryophyllene has been demonstrated as not being irritating to either skin or eye. Two skin sensitization studies are available on caryophyllene, being OECD TG 406 (FCAT) and 429 (LLNA). Both

studies indicated that caryophyllene is a skin sensitizer with low to moderate potency. No evidence of genotoxicity was identified in Ames tests (OECD TG 471) and MLA (OECD TG 476). Terpineol, belonging to the aliphatic acyclic and alicyclic terpenoid tertiary alcohol group, has been assessed by FEMA for use as flavoring agents (Marnett, et al., 2014). Based on data from other members in the group, the oral acute toxicity of tertiary alcohols and related esters is considered as extremely low (LD50 range from 1300 to > 36300 mg/kg bw). In short- and mid/long- term oral toxicity studies (10- 196 days), no major adverse outcome was observed for the group members tested. The NOEAL was between 3 to < 1860 mg/kg bw/day, depends on the testing species, exposure route, and study duration. Various group members were being evaluated in either in vitro assays like Ames or MLA, and in vivo models for their genotoxic potential. All results are negative. Reproductive toxicity data are available for two members of the group. Only one chemical induced reduced numbers of live fetuses and reduced fetal weights at high dose (2794 mg/kg bw/day) in rats and rabbits. Based on those results, FEMA concluded that the group of aliphatic acyclic and alicyclic terpenoid tertiary alcohol is generally recognized as safe (GRAS) under conditions of intended use as flavor ingredients. Eugenol has been registered under EU REACH. Based on the studies included in the dossier, it is not acutely toxic either via oral or inhalation exposure. Skin irritation potential is low, but it has been demonstrated to be moderately irritating to eyes in rabbits. Based on the results from LLNA (OECD TG 429) and GPMT (OECD TG 406) assays, eugenol is a skin sensitizer with low to moderate potency. Several repeated dose toxicity studies are available for eugenol. The NOAEL varies between 300 to 1250 mg/kg bw/day, depends on the testing species and study duration. No specific organ toxicity, reproductive toxicity, or carcinogenicity was observed in those studies.

Based on the results of major constituents in cascarilla bark oil, it is likely that its skin sensitizing property is due to the presence of caryophyllene and eugenol.

JECFA	-
FEMA	3. GRAS Substances(2001-3124)_0.pdf (femaflavor.org)
EFSA	-
ECHA – REACH dossier	-
PUBCHEM	SID 135307965 - PubChem (nih.gov)
CIR	-
OSHA	-

3. Addictiveness and attractiveness

No substance specific data were identified.

SCENIHR	-
EMA	-
PUBMED	-

Reference

Adams et al., 2011. The FEMA GRAS assessment of aliphatic and aromatic terpene hydrocarbons used as flavor ingredients (femaflavor.org)
Marnett et al., 2014. GRASr2 Evaluation of Aliphatic Acyclic and Alicyclic Terpenoid Tertiary Alcohols and Structurally Related Substances Used as Flavoring Ingredients (wiley.com)