Substance Information Document

D,L-Citronellol

1. Substance identity

Name	D,L-Citronellol
Synonyms	(+-)-Citronellol; (+-)-beta-Citronellol; 3,7-Dimethyl-6-octen-1-ol; 3,7-Dimethyloct-6-en-1-ol; 2,3-Dihydrogeraniol
IUPAC Name	3,7-dimethyloct-6-en-1-ol
CAS	106-22-9

2. Toxicological information

In its review of aliphatic, branched-chain saturated and unsaturated alcohols, aldehydes, acids, and related esters, including D,L-citronellol, the EFSA CEF Panel concluded that "genotoxicity is not of concern for all the 23 substances in FGE.72Rev1". Also, according to the EFSA CEF Panel available citronellol data gave no rise to safety concern with respect to carcinogenicity.

32% D,L-citronellol was moderately irritating to the skin of men topically exposed for 48 hours; 20% D,L-citronellol applied to the skin for 48 hours was not irritating, and no irritation occurred when undiluted D,L-citronellol was applied to human skin for 4 hours under occlusion. Although skin irritation is reported from animal experiments, no skin irritation was seen when Pitman-Moore miniature swine were exposed to neat D,L-citronellol for 48 hours under occlusion. Moderate conjunctival irritation was detected 24 hours after undiluted D,L- citronellol was instilled into the eyes of rabbits. Citronellol is included in a table of established contact allergens in humans (indicating that there is "sufficient human evidence present"), being placed in category ++ (indicating that 11-100 positive test reactions have been reported in >1000 patients tested). Citronellol is restricted for use in fragrances due to its sensitisation potential (maximum concentration limits of 0.67-87% in the final product). Human Repeat Insult Patch and Human maximisation test revealed NOEL for sensitization of 29.5 mg/cm^2 and 4.1 mg/cm^2, respectively.

An ED_{25} value of 999 mg/m3 was reported in female CF-1 mice exposed for one minute to an atmosphere containing D,L-citronellol using a nebuliser. No reduction in respiratory rate was seen when mice were exposed by tracheal cannula, indicating a lack of (significant) respiratory tract irritation. The oral LD_{50} value for D,L-citronellol was determined to be 3450 mg/kg bw in rats, indicating a low order of acute oral toxicity. The dermal LD_{50} value for rabbits was determined as 2650 mg/kg bw, and clinical signs included ataxia and papillary dilation. The LD_{50} value in mice after intramuscular injections of neat D,L-citronellol was given as 4000 mg/kg bw, while subcutaneous injections of D,L-citronellol in olive oil in the back, lead to a LD_{50} value of 880 mg/kg bw, and the principal sign of toxicity was leg paralysis. A 100- day rat inhalation study reported a NOAEC of 0.3 mg/m^3 based on unspecified central nervous system effects and olfactory function effects occurring at 1 month as well as on changes in the liver and immunological reactivity included alkaline phosphatase, alanine aminotransferase, lysozyme in the serum and SH group content in the blood.

EFSA concluded that the use of citronellol as a food flavouring is of "no safety concern" at then-current estimated intakes of 320 and 0.5 µg/person/day in Europe and the US, respectively. JECFA has set a group ADI of 0-0.5mg/kg bw, expressed as citral, for citral, geranyl acetate, citronellol, linalool, and linalyl acetate.

JECFA	WHO_TRS_922 ALIPHATIC BRANCHED-CHAIN SATURATED AND UNSATURATED ALCOHOLS, ALDEHYDES, ACIDS, AND RELATED ESTERS (JECFA 52, 2004) (inchem.org)
FEMA	0320 FEMA GRAS 29 (femaflavor.org)
EFSA	https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2013.3392 https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2013.3091 https://efsa.onlinelibrary.wiley.com/doi/full/10.2903/j.efsa.2016.4559 https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2020.6029
ECHA – REACH dossier	Registration Dossier - ECHA (europa.eu)
PUBCHEM	Citronellol | C10H20O - PubChem (nih.gov)
CIR	-
OSHA	-

3. Addictiveness and attractiveness

Male C57BL/6 mice that inhaled beta-citronellol (either CAS 106-22-9 or 7540-51-4 26) for 30 minutes showed an increase in anxiety-like behaviour in the elevated plus maze and open field tests. There were also no treatment-related effects in other behavioural tests assessing nociception (hot plate test), motor function (grip strength test) or depressive behaviour (tail suspension test and forced swim test). Intraperitoneal doses of 25-100 mg/kg bw were antinociceptive in formalin, capsaicin and glutamate tests on mice, in the acetic acid-induced writhing and thermal pain tests, and when the hind paw was injected with carrageenan. After one month exposure to 2.8 mg/m3 unspecified CNS effects occurred in rats.

SCENIHR	-
EMA	Information for the package leaflet for fragrances containing allergens used as excipients in medicinal products for human use (europa.eu)
PUBMED	https://pubmed.ncbi.nlm.nih.gov/32475228/ https://pubmed.ncbi.nlm.nih.gov/22350215/ https://pubmed.ncbi.nlm.nih.gov/23035741/ https://pubmed.ncbi.nlm.nih.gov/26141506/ Kostrodymov NN (1981). Experimental features of biological activity of synthetic fragrant substances. Gigiena i Sanitariya 9, 20-22