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Fragrance material review on geraniol

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ABSTRACT

A toxicologic and dermatologic review of geraniol when used as a fragrance ingredient is presented.

Introduction

In 2006, a complete literature search was conducted on geraniol. Online databases that were surveyed included Chemical Abstract Services and the National Library of Medicine. In addition, fragrance companies were asked to submit pertinent test data. All relevant references are included in this document. Any papers in which the vehicles and/or the doses are not given have not been included in this review. The number of animals, sex and strain are always provided unless they are not given in the original report or paper.

This individual Fragrance Material Review is not intended as a stand alone document. Please refer to the Toxicologic and Dermatologic Assessment of Cyclic and Non-Cyclic Terpene Alcohols (Belsito et al., 2008) for an overall assessment of this material.

1. Identification (Fig. 1)

1.1 Synonyms: 2,6-Dimethyl-2,6-octadien-8-ol; *trans*-3,7-Dimethyl-2,6-octadien-1-ol; *trans*-3,7-Dimethyl-2,7-octadien-1-ol; Geraniol Coeur; Meranol; 2,6-Octadien-1-ol, 3,7-dimethyl-, (e)-.
1.2 CAS Registry Number: 106-24-1.
1.3 EINECS Number: 203-377-1.
1.4 Formula: $C_{10}H_{18}O$.
1.5 Molecular weight: 154.25.
1.6 COE: Geraniol was included by the Council of Europe in the list of substances granted A – may be used in foodstuffs (COE No. 60).
1.7 FEMA: Flavor and Extract Manufacturers' Association: Generally Recognized as Safe as a flavor ingredient – GRAS 3 (FEMA, 1965).
1.8 FDA: Geraniol was approved by the FDA as GRAS (21 CFR 182.60).
1.9 JECFA: The Joint FAO/WHO Expert Committee on Food Additives (JECFA No. 1223) concluded that the substance does not present a safety concern at current levels of intake when used as a flavoring agent (JECFA, 2004).
1.10 IFRA: Geraniol has an International Fragrance Association standard – see Section 4.4.1 for details (IFRA, 2007).

2. Physical properties

2.1 Water solubility (measured): Practically insoluble.
2.2 Log K_{ow} (calculated): 3.47.
2.3 Vapor pressure (calculated): 0.02 mmHg at 20 °C.
2.4 Flash point: >100 F; CC.
2.5 Boiling point: 230 °C.

3. Usage (Table 1)

Geraniol is a fragrance ingredient used in decorative cosmetics, fine fragrances, shampoos, toilet soaps and other toiletries as well as in non-cosmetic products such as household cleaners and detergents. Its use worldwide is in the region greater than 1000 metric tonnes per annum.

The maximum skin level that results from the use of geraniol in formulae that go into fine fragrances is defined by the IFRA Standard (IFRA, 2007) for this material. The recently revised standard is based on the dermal sensitization quantitative risk assessment (QRA) approach for fragrance ingredient (QRA Expert Group,

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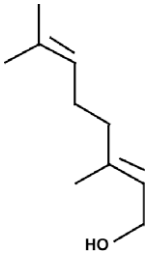

Fig. 1. Geraniol.

2006). The details of the standard can be found in Section 4.4.1 of this Fragrance Material Review.

4. Toxicology data

4.1. Acute toxicity (Table 2)

4.1.1. Oral studies

4.1.1.1. The acute oral (gavage) LD_{50} was reported to be 3.6 g/kg in 10 Osborne-Mendel rats (5/sex). Clinical signs in treated rats included depression, wet fur and coma (Jenner et al., 1964; Bar and Griepentrog, 1967).

4.1.1.2. The acute oral LD_{50} was calculated as 4.8 g/kg in mixed bred rats that received 0.001, 0.005, 0.01, 0.1, 1.0, 2.0 or 5.0 g/kg geraniol in propylene glycol. Three (3/5) animals died at 5.0 g/kg. All animals had mucous stools within 24–48 h. Necropsy revealed geraniol odor in the lung, and accumulation of bloody serum in respiratory tract and bronchi, with sporadic blood spots in alveolar tissue (Yamawaki, 1962).

4.1.2. Dermal studies

4.1.2.1. The acute dermal LD_{50} was greater than 5 g/kg based on no deaths at that dose. Three rabbis received a single dermal application of neat geraniol at 5 g/kg. No clinical signs were observed (RIFM, 1972).

4.1.3. Intramuscular studies

4.1.3.1. The intramuscular LD_{50} in mice was reported to be 4 g/kg. Groups of 10 mice per dose received intramuscular injections of test material at dose levels of 4, 6, 8, 10 or 12 g/kg (Northover and Verghese, 1962).

4.1.4. Subcutaneous studies

4.1.4.1. Groups of 5 mice per dose received subcutaneous injections of geraniol into the back at various dose levels. Test material was diluted with olive oil to obtain injection consistency of 0.3 cm^3. Paralysis in four legs was the principal toxic effect observed. The calculated LD_{50} was reported to be 1.1 g/kg (Nozawa, 1952).

4.1.5. Inhalation studies

4.1.5.1. The respiratory irritation potential of geraniol was assessed in CF-1 female mice by recording respiratory rate using a whole body plethysmograph. Mice were exposed to test materials for 1 minute using a nebulizer for aerosolization in a 2600 ml chamber. Materials shown to be sensory irritants were further tested in mice cannulated via the trachea and compared to an intact mouse breathing through its nose. Comparisons made were between the preexposure and exposure rate values for each material at each dose level. Mild to moderate respiration depression was observed via nose. No effects when inhaled through tracheal cannula. The ED_{25} was reported to be 570 μg/l (Troy, 1977).

4.1.5.2. The effect of inhaled geraniol on the output and the composition of respiratory tract fluid was measured in rabbits. No effects were observed at 1.0 and 1.5 mg/ml geraniol in ethyl alcohol. Increase in volume output and total solids and significant decrease in specific gravity was observed at 3.0, 9.0 and 27 mg/ml. Marked odor and no augmentation of volume output was observed at 81 mg/ml (Boyd and Sheppard, 1970).

4.2. Skin irritation

4.2.1. Human studies (Table 3)

Irritation was evaluated as a part of four Human Repeated Insult Patch tests (HRIPT). Aliquots of 0.3 ml geraniol in specific vehicle

Table 1
Calculation of the total human skin exposure from the use of multiple cosmetic products containing geraniol

Type of cosmetic product	Grams applied	Applications per day	Retention factor	Mixture/product	Ingredient/mixture[a]	Ingredient (mg/kg/day)[b]
Body lotion	8.00	0.71	1.000	0.004	5.3	0.0201
Face cream	0.80	2.00	1.000	0.003	2.8	0.0022
Eau de toilette	0.75	1.00	1.000	0.080	5.3	0.0530
Fragrance cream	5.00	0.29	1.000	0.040	5.3	0.0512
Antiperspirant	0.50	1.00	1.000	0.010	0.4	0.0003
Shampoo	8.00	1.00	0.010	0.005	5.0	0.0003
Bath products	17.00	0.29	0.001	0.020	5.0	0.0001
Shower gel	5.00	1.07	0.010	0.012	5.0	0.0005
Toilet soap	0.80	6.00	0.010	0.015	5.0	0.0006
Hair spray	5.00	2.00	0.010	0.005	5.3	0.0004
Total						0.1289

[a] Upper 97.5 percentile levels of the fragrance ingredient in the fragrance mixture used in these products (IFRA, 2003).
[b] Based on a 60-kg adult.

Table 2
Summary of acute toxicity studies

Route	Species	Number of animals/dose group	LD50	Reference
Oral	Rat	10 (5/sex)	3.6 g/kg	Jenner et al. (1964) and Bar and Griepentrog (1967)
Oral	Rat	5	4.8 g/kg	Yamawaki (1962)
Dermal	Rabbit	3	>5 g/kg	RIFM (1972)
Intramuscular	Mouse	10	4 g/kg	Northover and Verghese (1962)
Subcutaneous	Mouse	5	1.1 g/kg	Nozawa (1952)