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Fragrance material review on *l*-borneol

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ABSTRACT

A toxicologic and dermatologic review of *l*-borneol when used as a fragrance ingredient is presented.

Introduction

In 2006, a complete literature search was conducted on *l*-borneol. 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. More details have been provided for unpublished data. 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 When Used as Fragrance Ingredients (Belsito et al., 2008) for an overall assessment of this material.

1. Identification (Fig. 1)

1.1 Synonyms: bicyclo[2.2.1]heptan-2-ol, 1,7,7-trimethyl-, (1S-endo)-; *l*-bornyl alcohol; *l*-2-camphanol.
1.2 CAS registry number: 464-45-9.
1.3 EINECS number: 207-353-1.
1.4 Formula: $C_{10}H_{18}O$.
1.5 Molecular weight: 154.25.

2. Physical properties

2.1 Boiling point: 212 °C at 5 mm Hg.
2.2 Flash point: >200 °F; CC.
2.3 Water solubility (calculated): 1186 mg/l at 25 °C.
2.4 Log K_{ow} (calculated): 2.85.
2.5 Melting point: 204.
2.6 Vapor pressure (calculated): 0.02 mm Hg 20 C.
2.7 Henry's law (calculated): 0.0000067 atm m^3/mol 25 °C.

3. Usage

l-Borneol 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 of 1–10 metric tonnes per annum.

The maximum skin level of *l*-borneol in formulae that go into fine fragrances has been reported to be 00.32% (IFRA, 2004), assuming use of the fragrance oil at levels up to 20% in the final product. The 97.5 percentile use level in formulae for use in cosmetics in general has been reported to be 0.18% (IFRA, 2004), which would result in a conservative calculated maximum daily exposure on the skin of 0.0046 mg/kg for high end users of these products (see Table 1).

4. Toxicology data

4.1. Acute toxicity (Table 2)

4.1.1. Oral studies

4.1.1.1. Ten male albino Wistar rats weighing 200–250 g were orally dosed with *l*-borneol at 5 g/kg. The animals were observed frequently on the test day and daily thereafter for 14 days. Death occurred in one animal during the study. Clinical signs observed were hyperactivity, 1/10 loss of righting reflex and death 6–8 h. No necropsies were performed (RIFM, 1972a).

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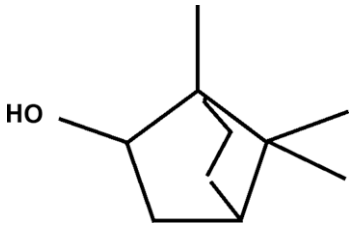

Fig. 1. *l*-Borneol.

4.1.1.2. The acute oral LD50 in 40 male albino rats (10/group) was determined to be 6.5 g/kg (95% C.I. 5.8 g/kg and 7.2 g/kg). *l*-Borneol was diluted in water and administered at doses: 4, 5, 6.25, and 7.8 g/kg. The animals were observed at 1 and 6 h after dosing and thereafter daily for 14 days. Death occurred in 1/10 animals at 5 g/kg, 4/10 at 6.25 g/kg and 10/10 in 7.8 g/kg. Gross necropsy revealed no abnormalities. Clinical signs included hyperactivity and loss of righting reflex (1/10) (RIFM, 1972b).

4.1.2. Dermal studies

4.1.2.1. Ten New Zealand white rabbits weighing 1.8–2.3 kg received a single 24-h dermal application of *l*-borneol at 2 g/kg to the clipped abraded abdominal skin. After 24 h of exposure the binders were removed and the animals were observed for 7 days. No deaths occurred. Gross necropsy performed on all animals revealed no abnormalities (RIFM, 1972c).

4.2. Skin irritation

4.2.1. Human studies (Table 3)

4.2.1.1. In two separate pre-tests for maximization tests, no irritation was observed to 20% *l*-borneol in petrolatum when applied for 48 h under occlusion on the backs of 23 and 5 male volunteers (RIFM, 1973; RIFM, 1972d).

4.2.1.2. In a pre-test for a maximization study, no irritation was observed to 8% *l*-borneol in petrolatum when applied for 48 h under occlusion on the backs of five healthy male volunteers (RIFM, 1972e).

4.2.2. Animal studies

4.2.2.1. Irritation was evaluated in New Zealand white rabbits, as part of the associated dermal toxicity study with neat *l*-borneol. Slight to moderate erythema and slight edema was observed. Irritation reactions persisted for 3 days (RIFM, 1972c).

Table 2
Summary of acute toxicity studies

Route	Species	No. animals/dose group	LD_{50} (g/kg)	References
Oral	Rats	10	>5.0	RIFM (1972a)
Oral	Rats	10	6.5	RIFM (1972b)
Dermal	Rabbits	10	>2.0	RIFM (1972c)

Table 3
Summary of irritation studies in humans

Method	Dose (%)	Results	Reference
Pre-test maximization	20% in petrolatum	0/23	RIFM (1973)
Pre-test maximization	20% in petrolatum	0/5	RIFM (1972d)
Pre-test maximization	8% in petrolatum	0/5	RIFM (1972e)

4.3. Mucous membrane (eye) irritation

No data available on this material.

4.4. Skin sensitization (Table 4)

4.4.1. Human studies

4.4.1.1. Induction studies. Series of maximization tests (Kligman, 1966; Kligman and Epstein, 1975) were conducted with *l*-borneol in petrolatum. *l*-Borneol was applied under occlusion to the same sites on volar aspects forearms or backs of all the subjects for five alternate-day 48-h period. Patch sites were pretreated with 5% aqueous SLS for 24-h under occlusion. Following a 10-day rest period challenge patches of the *l*-borneol was applied under occlusion for 48 h to fresh sites. The challenge applications were preceded by pretreatment with 10% SLS for 1 h. Reactions were read immediately after the removal of challenge patch and/or 48–72 h thereafter. The following results were obtained:

Table 4
Summary of sensitization studies in humans

Test method	Test concentration	Results	References
Maximization	20% in petrolatum	Mild sensitization 2/25	RIFM (1972d)
Maximization	8% in petrolatum	No sensitization was observed	RIFM (1972e)
Maximization	20% in petrolatum	No sensitization	RIFM (1973)

Table 1
Calculation of the total human skin exposure from the use of multiple cosmetic products containing *l*-borneol

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	0.18	0.0007
Face cream	0.80	2.00	1.000	0.003	0.18	0.0001
Eau de toilette	0.75	1.00	1.000	0.080	0.18	0.0018
Fragrance cream	5.00	0.29	1.000	0.040	0.18	0.0017
Antiperspirant	0.50	1.00	1.000	0.010	0.18	0.0002
Shampoo	8.00	1.00	0.010	0.005	0.18	0.0000
Bath products	17.00	0.29	0.001	0.020	0.18	0.0000
Shower gel	5.00	1.07	0.010	0.012	0.18	0.0000
Toilet soap	0.80	6.00	0.010	0.015	0.18	0.0000
Hair spray	5.00	2.00	0.010	0.005	0.18	0.0000
Total						0.0046

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