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Fragrance material review on sclareol

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ABSTRACT

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

Introduction

In 2006, a complete literature search was conducted on sclareol. On-line 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 More details have been provided for unpublished data.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: Labd-14-ene-8,13-diol; 1-naphthalenepropanol, α-ethenyldecahydro-2-hydroxy-α,2,5,5,8a-pentamethyl-, [1*R*-[1.alph; sclareol.
1.2 CAS Registry number: 515-03-7.
1.3 EINECS number: 208-194-0.
1.4 Formula: $C_{20}H_{36}O_2$.
1.5 Molecular weight: 308.51.
1.6 Council of Europe (COE): Sclareol was included by the COE in the list of substances granted Waiting (COE No. 10311) (Council of Europe, 2000).
1.7 International Fragrance Association (IFRA): Sclareol used as fragrance ingredient should have a minimum purity of 98%.

2. Physical properties

2.1 Physical: A white crystalline powder.
2.2 Boiling point: >340 °C.
2.3 Melting point: 106 °C.
2.4 Melting point: 98–101 °C.
2.5 Water solubility (calculated): 0.082 mg/l at 25 °C.
2.6 Log K_{ow} (calculated): 6.
2.7 Vapor pressure (calculated): <0.001 mm Hg 20 °C.
2.8 Henry's law (calculated): 0.00000311 atm m^3/mol 25 °C.

3. Usage

Sclareol 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 less than 0.01 metric tonnes per annum.

The maximum skin level that results from the use of sclareol in formulae that go into fine fragrances has been reported to be 0.02% (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 0.03% (IFRA, 2004), which would result in a conservative calculated maximum daily exposure on the skin of 0.0008 mg/kg/day for high end users of these products (see Table 1).

4. Toxicology data

4.1. Acute toxicity

See Table 2.

4.1.1. Oral studies (gavage)

4.1.1.1. The LD_{50} in rats was determined to exceed 5.0 g/kg. Ten albino rats (5/sex) weighing 182–260 g were administered via gavage a single dose of sclareol at 5 g/kg body weight. Sclareol was administered as a 25% suspension in corn oil. The animals were observed at 1, 3, 6, and 24 h after treatment and daily thereafter for 14 days. No deaths occurred. Final weights increased, and ranged from 220–340 g. Gross necropsy revealed only a deposit of fibrous

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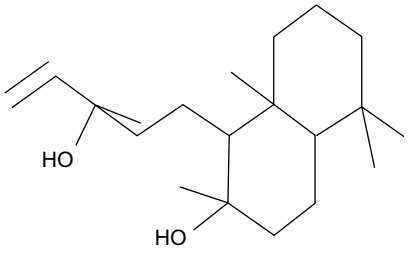

Fig. 1. Sclareol.

tissue in the thoracic cavity of one animal, which was not treatment related. This was a GLP study (RIFM, 1979a).

4.1.2. Dermal studies

4.1.2.1. Six New Zealand White rabbits (3/sex), weighing 1.72–2.09 kg received a single dermal application of sclareol at 5 g/kg body weight to the abraded skin of 3 animals and the intact skin of the remaining three animals. The test sites were occluded for 24 h. The animals were observed at 1, 3, 6, and 24 h after treatment and daily thereafter for a total of 14 days. No deaths occurred. Final weights increased, and ranged from 2.14–2.50 kg. Gross necropsy conducted on all animals revealed no abnormalities. The dermal LD_{50} in rabbits was determined to exceed 5 g/kg. This was a GLP study (RIFM, 1979a).

4.1.3. Intraperitoneal studies

4.1.3.1. Sclareol was evaluated for toxicity in 1–2 male Sprague Dawley rats using a Hippocratic screening open-field observational method. Sclareol at 0.100, 0.316, and 1 g/kg was suspended in sterile aqueous 0.25% agar and dosed via intraperitoneal route at 5 ml/kg/body weight (~5 g/kg). A decrease in the spontaneous motor activity and respiratory rate was observed at both the doses. Within 4 h recovery was essentially complete. One animal that received 0.316 g/kg dose was found dead on day 4 from peritonitis. Whereas, all the animals that received 0.100 and 1 g/kg doses survived the 7 day observation period. Necropsy revealed adhesions between the liver, spleen, stomach, and small intestine with white particles, apparent in the afflicted area (Malone et al., 1991).

4.2. Skin irritation

See Table 3.

4.2.1. Human studies

4.2.1.1. Irritation to sclareol was evaluated during the induction phase of two separate human repeated insult patch tests (HRIPTs) (see Section 4.4.1.1.1). Aliquots of 0.3 g or 0.2 ml sclareol at 3% concentration in alcohol SDA 39 °C (specially denatured alcohol 39 °C) or petrolatum were applied for 24 h under semi-occlusion using a 1 × 1 in. Webril patch affixed to 1 × 2 in. adhesive tape on each group of 35 and 39 male and female volunteers. Nine 24-hour applications were made over a 3-week period. No irritation was observed (RIFM, 1975a,b).

4.2.1.2. Three separate maximization pre-tests were conducted with 10% sclareol in petrolatum. The application was made on the backs of 23, 26, and 28 (male and female) volunteers for 48 h under occlusion. No irritation was observed (RIFM, 1979c, 1981, 1986).

4.2.1.3. Using the same method as above, maximization pre-test was conducted with 10% sclareol in petrolatum on 29 healthy male volunteers. No irritation was observed (RIFM, 1979b).

4.2.2. Animal studies

See Table 4.

4.2.2.1. Primary irritation to 3% sclareol in petrolatum was evaluated in 3 healthy albino rabbits (sex not specified). Prior to the experiment, 10% of the total body area of animals was clipped free of hair. Minor abrasions were made on the posterior of the clipped area, to penetrate the stratum corneum but not to disturb the derma. Sclareol at an aliquot of 0.5 ml each was patched over the scarified and the unscarified area. The 2 × 2 patch area was covered with Webril® patches and the entire experimental area was sealed with Blenderm Surgical Tape®. The animals were immobilized for a 24 h period. Reactions were assessed at 24 and 48 h using the Draize method. No irritation was observed (RIFM, 1975c).

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

Type of cosmetic product	Grams applied	Applications per day	Retention actor	Mixture/product	Ingredient/mixture[a]	Ingredient mg/kg/day[b]
Body lotion	8.00	0.71	1.000	0.004	0.03	0.0000
Face cream	0.80	2.00	1.000	0.003	0.03	0.0000
Eau de toilette	0.75	1.00	1.000	0.080	0.03	0.0001
Fragrance cream	5.00	0.29	1.000	0.040	0.03	0.0003
Antiperspirant	0.50	1.00	1.000	0.010	0.03	0.0000
Shampoo	8.00	1.00	0.010	0.005	0.03	0.0003
Bath products	17.00	0.29	0.001	0.020	0.03	0.0000
Shower gel	5.00	1.07	0.010	0.012	0.03	0.0000
Toilet soap	0.80	6.00	0.010	0.015	0.03	0.0000
Hair spray	5.00	2.00	0.010	0.005	0.03	0.0000
Total						0.0008

[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.

Table 2
Summary of acute toxicity studies

Route	Species	No. animals/dose group	LD_{50} (g/kg)	References
Oral	Rats	10 (5/sex)	>5	RIFM (1979a)
Dermal	Rabbits	6 (3/sex)	>5	RIFM (1979a)
Intraperitoneal	Rat	1–2	1	Malone et al. (1991)