



Review

Fragrance material review on 3-phenylpropyl isobutyrate

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ABSTRACT

A toxicologic and dermatologic review of 3-phenylpropyl isobutyrate when used as a fragrance ingredient is presented. 3-Phenylpropyl isobutyrate is a member of the fragrance structural group cinnamyl phenylpropyl compounds. The common characteristic structural element of cinnamyl phenylpropyl materials is an aryl substituted primary alcohol/aldehyde/ester. They are simple aromatic compounds with saturated propyl or unsaturated propenyl side chains containing a primary oxygenated functional group which has little toxic potential. 3-Phenyl-1-propyl derivatives participate in the same beta oxidation pathways as do their parent cinnamic acid derivatives. This review contains a detailed summary of all available toxicology and dermatology papers that are related to this individual fragrance ingredient and is not intended as a stand-alone document. Available data for 3-phenylpropyl isobutyrate was evaluated then summarized and includes physical properties, acute toxicity, skin irritation and skin sensitization. A safety assessment of all cinnamyl phenyl propyl compounds will be published simultaneously with this document. Please refer to Belsito et al. (2011) for an overall assessment of the safe use of this material and all cinnamyl phenylpropyl materials in fragrances.

Belsito, D., Bickers, D., Bruze, M., Dagli, M.L., Fryer, A., Greim, H., Miyachi, Y., Saurat, J.H., Sipes, I.G., 2011. A toxicologic and dermatologic assessment of cinnamyl phenylpropyl compounds when used as fragrance ingredients.

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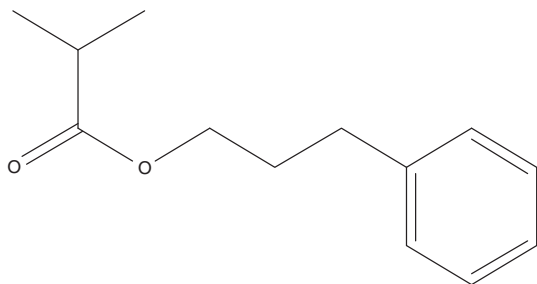


Fig. 1. 3-Phenylpropyl isobutyrate.

1. Introduction

This document provides a summary of the human health toxicological data currently available pertaining to the safety evaluation of 3-phenylpropyl isobutyrate when used as a fragrance ingredient. All safety data on 3-phenylpropyl isobutyrate was compiled with due diligence including published and unpublished data.

In 2006, a complete literature search was conducted on 3-phenylpropyl isobutyrate, followed by an update in 2009. On-line databases were searched including those from the Chemical Abstract Services, [e.g., ToxCenter (which in itself contains 18 databases including Chemical Abstracts)], and the National Library of Medicine [e.g., Medline, Toxnet (which contains 14 databases)] as well as 26 additional sources (e.g., BIOSIS, Embase, RTECS, OSHA, ESIS). In addition, all RIFM sponsored studies and studies from fragrance companies are included in this summary.

This document provides a summary of the available toxicological data of 3-phenylpropyl isobutyrate when used as a fragrance ingredient. The safety data on this material has been reviewed by Opdyke, 1978. Data from all relevant references are summarized in this document. More details have been provided for unpublished data. The number of animals, sex and strain are always provided unless they are not given in the original report or paper.

2. Identification (Fig. 1)

- 2.1 Synonyms: Hydrocinnamyl isobutyrate; hydrocinnamyl 2-methylpropanoate; β -phenylpropyl 2-methylpropanoate; 3-phenylpropyl 2-methylpropanoate; propanoic acid, 2-methyl-3-phenylpropyl ester.
- 2.2 CAS Registry number: 103-58-2.
- 2.3 EINECS number: 203-125-0.
- 2.4 Formula: $C_{13}H_{18}O_2$.
- 2.5 Molecular weight: 206.29.

- 2.6 Council of Europe: 3-Phenylpropyl isobutyrate was included by the Council of Europe in the list of substances granted B – information required – hydrolysis study (COE No. 303) (COE, 2000).
- 2.7 FDA: 3-Phenylpropyl isobutyrate was approved by the FDA as a flavor (21 CFR 172.515).
- 2.8 FEMA: Flavor and Extract Manufacturers' Association states: Generally Recognized as Safe as a flavor ingredient – GRAS 3. (2893) (FEMA, 1965).
- 2.9 Joint Expert Committee on Food Additives: The Joint FAO/WHO Expert Committee on Food Additives concluded that the substance (JECFA No. 640) does not present a safety concern at current levels of intake when used as a flavoring agent (JECFA, 2000).

3. Physical properties

- 3.1 Physical form: Colorless liquid with a fruity-balsamic, sweet odor.
- 3.2 Flash point: $>200^\circ\text{F}$; CC.
- 3.3 Henry's Law (calculated): 0.000044 atm m³/mol 25 °C.
- 3.4 Log Kow (calculated): 3.97.
- 3.5 Specific gravity: 0.977.
- 3.6 Vapor pressure (calculated): 0.02 mm Hg at 20 °C.
- 3.7 Water solubility (calculated): 16.47 mg/l @ 25 °C.
- 3.8 UV spectra available at RIFM; peaks at 210 nm and returns to base line at: 230 nm.

4. Usage

3-Phenylpropyl isobutyrate is a fragrance ingredient used in many compounds. It may be found in fragrances 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. It is a colorless liquid, possessing a fruity-balsamic but refreshingly sweet odor of considerable tenacity (Arctander, 1969). The worldwide volume of use for 3-phenylpropyl isobutyrate is in the region of <0.1 metric tons per year (IFRA, 2008). This reported volume is for its use as a fragrance ingredient in fragrance compounds (mixtures) found in all finished consumer product categories. The volume of use is surveyed by IFRA approximately every four years through a comprehensive survey of IFRA and RIFM member companies. As such the volume of use data from this survey provides volume of use of fragrance ingredients for the majority of the fragrance industry.

4.1. Exposure assessment

The dermal systemic exposure from cosmetic products is calculated based on the concentrations of the same fragrance

Table 1

Calculation of the total human skin exposure from the use of multiple cosmetic products containing 3-Phenylpropyl isobutyrate.

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	0.006	0.0000
Face cream	0.80	2.00	1.000	0.003	0.006	0.0000
Eau de toilette	0.75	1.00	1.000	0.080	0.006	0.0001
Fragrance cream	5.00	0.29	1.000	0.040	0.006	0.0001
Antiperspirant	0.50	1.00	1.000	0.010	0.006	0.0000
Shampoo	8.00	1.00	0.010	0.005	0.006	0.0000
Bath products	17.00	0.29	0.001	0.020	0.006	0.0000
Shower gel	5.00	1.07	0.010	0.012	0.006	0.0000
Toilet soap	0.80	6.00	0.010	0.015	0.006	0.0000
Hair spray	5.00	2.00	0.010	0.005	0.006	0.0000
Total						0.0002

^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.

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