Food and Chemical Toxicology 62 (2013) S51–S55

Contents lists available at ScienceDirect

Food and Chemical Toxicology

journal homepage: www.elsevier.com/locate/foodchemtox

Review

Fragrance material review on 2-cyclohexyl-1,6-heptadien-3-one

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ARTICLE INFO

Keywords:
Fragrance material
2-Cyclohexyl-1,6-heptadien-3-one
Review

ABSTRACT

A toxicologic and dermatologic review of 2-cyclohexyl-1,6-heptadien-3-one when used as a fragrance ingredient is presented. 2-Cyclohexyl-1,6-heptadien-3-one is a member of the fragrance structural group Alkyl Cyclic Ketones. These fragrances can be described as being composed of an alkyl, R_1, and various substituted and bicyclic saturated or unsaturated cyclic hydrocarbons, R_2, in which one of the rings may include up to 12 carbons. Alternatively, R_2 may be a carbon bridge of C2–C4 carbon chain length between the ketone and cyclic hydrocarbon. This review contains a detailed summary of all published and unpublished toxicology and dermatology papers that are related to this individual fragrance ingredient and is not intended as a stand-alone document. Available data for 2-cyclohexyl-1,6-heptadien-3-one were evaluated then summarized and includes physical properties, acute toxicity, skin irritation, mucous membrane (eye) irritation, skin sensitization, phototoxicity, photoallergy, repeated dose, and genotoxicity data. A safety assessment of the entire Alkyl Cyclic Ketones will be published simultaneously with this document; please refer to Belsito et al., 2013 for an overall assessment of the safe use of this material and all Alkyl Cyclic Ketones in fragrances.

Contents

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http://dx.doi.org/10.1016/j.fct.2013.08.069

1. Introduction

This document provides a comprehensive summary of the human health toxicological data currently available pertaining to the safety evaluation of 2-cyclohexyl-1,6-heptadien-3-one (See Fig. 1) when used as a fragrance ingredient. All safety data on 2-cyclohexyl-1,6-heptadien-3-one were compiled with due diligence including published and unpublished data. In 2013, a complete literature search was conducted on 2-cyclohexyl-1,6-heptadien-3-one. On-line toxicological 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.

Data from all relevant references are summarized in this FMR. Commonly used terms and their abbreviations are listed in Appendix A. 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. Papers in which the vehicles and/or the doses are not given were included and noted in this summary because either they demonstrated an adverse effect or there were limited to no data on this fragrance ingredient.

2. Identification

- 2.1. Synonyms: Cyclohexyl heptadienone; Pharaone
- 2.2. CAS registry number: 313973-37-4
- 2.3. EINECS number: N/A
- 2.4. Formula: $C_{13}H_{20}O$
- 2.5. Molecular weight: 192.3

3. Physical properties

- 3.1. Log K_{ow} (measured): 4.9[2]

4. Usage

2-Cyclohexyl-1,6-heptadien-3-one 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. The worldwide volume of use for 2-cyclohexyl-1,6-heptadien-3-one is in the region of 0.01–0.1 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 provide volume of use of fragrance ingredients for the majority of the fragrance industry.

[2] RIFM (Research Institute for Fragrance Materials, Inc.), 2001. Partition coefficient n-octanol/water of 1,6-heptadien-3-one, 2-cyclohexyl-(pharaone). Report number 59409 (RIFM, Woodcliff Lake, NJ, USA).

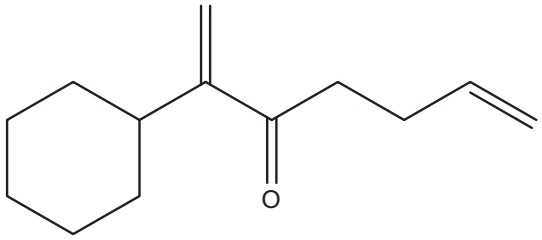

Fig. 1. 2-Cyclohexyl-1,6-heptadien-3-one.

4.1. Exposure assessment

The dermal systemic exposure to cosmetic products (see Table 1) is calculated based on the concentrations of the same fragrance ingredient in ten types of the most frequently used personal care and cosmetic products (anti-perspirant, bath products, body lotion, eau de toilette, face cream, fragrance cream, hair spray, shampoo, shower gel, and toilet soap). The concentration of the fragrance ingredient in fine fragrances is obtained from examination of several thousand commercial formulations and the upper 97.5th percentile concentration is calculated from the data obtained. This upper 97.5th percentile concentration is then used for all 10 consumer products. These concentrations are multiplied by the amount of product applied, the number of applications per day for each product type, and a "retention factor" (ranging from 0.001 to 1.0) to account for the length of time a product may remain on the skin and/or likelihood of the fragrance ingredient being removed by washing. The resultant calculation represents the total consumer exposure (mg/kg bw/day) (Cadby et al., 2002; Ford et al., 2000).

This is a conservative estimate of dermal systemic exposure because it makes the unlikely assumption that a consumer will use

Table 1
Calculation of the total human skin exposure from the use of multiple cosmetic products containing 2-cyclohexyl-1,6-heptadien-3-one.

Product type	Grams applied	Applications per day	Retention factor	Mixture /product (%)	Ingredient /mixture[a]	Ingredient mg/kg/day[b]
Antiperspirant	0.5	1	1	0.01	.02	0.0000
Bath products	17	0.29	0.001	0.02	.02	0.0000
Body lotion	8	0.71	1	0.004	.02	0.0001
Eau de toilette	0.75	1	1	0.08	.02	0.0002
Face cream	0.8	2	1	0.003	.02	0.0000
Fragrance cream	5	0.29	1	0.04	.02	0.0002
Hair spray	5	2	0.01	0.005	.02	0.0000
Shampoo	8	1	0.01	0.005	.02	0.0000
Shower gel	5	1.07	0.01	0.012	.02	0.0000
Toilet soap	0.8	6	0.01	0.015	.02	0.0000
Total						0.0005

[a] Upper 97.5th percentile levels of the fragrance ingredient in the fragrance mixture used in these products was not surveyed; a default value of 0.02% was used.
[b] Based on a 60 kg adult.