1-OCTANOL

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I. IDENTIFICATION

Chemical Name: 1-Octanol

Synonyms: Alcohol C-8; capryl alcohol; caprylic alcohol; n-caprylic alcohol; heptyl carbinol; 1-hydroxyoctane; n-octanol; n-octyl alcohol; octanol; octilin; octyl alcohol; primary octyl alcohol; Alfol 8; Dytol M-83; FEMA No. 2800; Lorol 20; n-octan-1-ol; octyl alcohol, normal-primary; Sipol L8.[1,2]

In industrial practice, the term octyl alcohol has been used for both 1-octanol (CAS 111–87–5) and 2-ethylhexanol (CAS 104–76–7).[3]

Apparently, the term octyl alcohol is also applied to methyl heptanol (mixed primary isomers), 2-ethyl-4-methyl-1-pentanol (CAS 106–67–2) and 2,2,4 trimethy-1-pentanol (CAS 123–44–4).[4]

The term octanol also refers to a mixture of primary isomers containing 75% 2-ethylyhexanol and 25% 2-ethyl-4methyl pentanol.[5]

CAS Number: 111–87–5.

Molecular Formula: $C_8H_{18}O$

Structural Formula: $CH_3(CH_2)_6CH_2OH$

II. CHEMICAL AND PHYSICAL PROPERTIES

Physical State: Colorless Liquid[6]

Molecular Weight: 130.23[7]

Conversion: 1 ppm (v/v) = 5.35 mg/m^3

Boiling Point: 194.4°C (382°F) at 760 mmHg[7]

Melting Point: -16.7°C (2°F)[7]

Vapor Pressure: 0.08 mmHg at 25°C (77°F)[8]
1 mmHg at 54°C (129°F)[9]
5 mmHg at 76.5°C (170°F)[9]
10 mmHg at 88.3°C (191°F)[9]

Saturated Vapor Concentration: 105 ppm at 25°C (calculated from vapor pressure)[8]

Odor Description and Threshold: Fresh orange rose odor[1,10]; penetrating aromatic odor[1,10]; lemon-like solvent cleaner odor[11]; Threshold: 1 ppm[10]; average 0.13 ppm; range 0.0087–0.56 ppm concentration in water for 10 panelists and 10 observations.[10]

Flash Point: 81°C (178°F)[3]

Autoignition Temperature: No data found.

Specific Gravity: 0.827 at 20°C (68°F)[7]

Solubility in Water: Insoluble[6]

Stability: Stable[10]

III. USES

1-Octanol is used in the manufacture of perfumes and esters,[6] as a synthetic flavoring ingredient,[12] a solvent, and an antifoaming agent.[3] 1-Octanol has been in commercial use since 1900.

The concentration of 1-octanol in various fragrance products varies from 0.03% (300 ppm) to 0.2% (2000 ppm). 1-Octanol was reported as being used as a flavor ingredient in various beverages and foods at levels from 0.9 to 57 ppm.[12]

1-Octanol is also a metabolic by-product of certain plants and fungi.[13,14]

IV. TOXICITY DATA

A. Acute Toxicity

1. Oral

Rat: LD_{50} >5.0 g/kg[15]

Rat LD_{50} >25 g/kg.[16] In this acute oral LD_{50} study, 1 of 10 young adult male ChR-CD rats that were administered 25,000 mg/kg (25 g/kg) by intragastric intubation died 2 days after treatment, and demonstrated acute chemical gastroenteritis upon gross pathological examination. 3 of 4 rats that were examined 14 days after exposure demonstrated gastritis with epithelial

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hyperplasia and hyperkeratosis in the cardiac portion of the stomach.[16]

Mouse: LD_{50} = 1.79 g/kg[17,18]

2. *Eye Toxicity*

Von Oettingen[19] reported that the vapors of octyl alcohol caused irritation of the mucous membrane of the eyes and upper respiratory tract. However, Weiss[20] reported that the vapors were not irritating to the eyes and throat. Exposure levels and durations are not reported in either study.

3. *Skin Toxicity*

a. Absorption

Rabbit: LD_{50} > 5 g/kg[5,15]

b. Irritation

Weiss[20] reported that 1-octanol is practically harmless to human skin.

c. Sensitization

No information found.

4. *Inhalation*

In a 4-hour exposure study, 3 of 10 rats exposed to 5600 mg/m^3 (1052 ppm) died within 2 days of exposure.[18,21] "Lung lesions were noted and consisted of necrosis of the bronchial epithelium with alveolar edema and an accumulation of alveolar macrophages."[21]

A sensory irritation study using mice reported an RD_{50} value of 50 ppm for n-octanol.[22] It should be noted that the Mueller (1984) study references a manuscript that is "non encore publiés, 1983" (not yet published, 1983). The Mueller (1984) manuscript does not provide the methodology, mouse strain, or data analysis techniques used to derive the reported RD_{50} values. A literature search failed to find any published study that has the RD_{50} results of the Mueller study at any previous or future date. It is believed that the OF strain of mouse was used for the Mueller (1984) study; however, this is impossible to corroborate. Since the OF strain of mouse has previously demonstrated a highly variable response when compared to the Swiss Webster mouse (the standard for RD_{50} determination) and there is no conformation of methodology, the practice of multiplying the RD_{50} by 0.03 was not employed in the determination of the exposure limit.

5. *Other*

Aspiration of 0.2 mL of 1-octanol (~165 mg 1-octanol) killed 10 of 10 male albino rats (Sprague-Dawley). Death came after only a few breaths.[23]

Mouse: LD_{50}, intravenous: 69 mg/kg[24,25]

Cultured rat hepatocytes exposed to 0.1 mmol (13.0 mg/l) did not demonstrate any evidence of peroxisome proliferation.[26]

B. Genotoxicity

1-octanol was not active in a sister chromatid exchange assay (SCE) at 10^{-3} M (0.13 mg/ mL) with V79 Chinese hamster lung fibroblasts.[27] However, it should be noted that this is regarded with caution since only one concentration of 1-octanol was tested in the Stahl et al. (1981) study.[28]

An *in vitro* cytogenetic *S. cerevisiae* yeast test showed positive reaction at 2 millimole/tube.[29]

C. Metabolism and Pharmacokinetics

In a general discussion of the metabolism and pharmacokinetics of alcohols, Williams[30] indicates that:

> "Primary aliphatic alcohols undergo two general reactions *in vivo*, namely oxidation to carboxylic acids and direct conjugation with glucuronic acid. The first reaction proceeds with the intermediate formation of an aldehyde and the carboxylic acid. This form may be either oxidized completely to carbon dioxide or excreted as such or combined with glucuronic acid as an ester glucuronide. The extent to which an alcohol undergoes the second reaction, *i.e.*, direct conjugation to an ether glucuronide, appears to depend upon the speed of the first reaction..."

D. Developmental and Reproductive Toxicity

To examine the potential developmental toxicity of 1-octanol, Nelson et al. (1990) exposed pregnant Sprague-Dawley rats to 65 ppm vapor (350 mg/m^3) for 7 hours/day on Gestational Days 1 through 19.[31] No external, skeletal, or visceral fetal malformations, fetal resorptions, or fetal weight changes were observed. Also, no maternal signs of toxicity were reported, as exposed dams demonstrated normal food consumption and weight gain, with no signs of CNS depression.

E. Subacute Toxicity

No Information found.

F. Subchronic Toxicity

A Soviet study[17] indicated that no cumulative effects were found in mice after intragastric administration of 179 mg/kg octyl alcohol for 1 month.

G. Chronic Toxicity and Carcinogenicity

1. Dermal Carcinogenicity

1-Octanol was studied in an initiation-promotion dermal skin-painting study wherein a group of 40 female Swiss mice were treated 3 times a week, for 60 weeks, with one drop (approximately 20 microliters) of 1-octanol dissolved in cyclohexane (20 g/100 mL). This treatment began 1 week after an initiation treatment with a noncarcinogenic dose of 7,12-dimethylbenz(a)anthracene. One skin papilloma appeared after 25 weeks, and developed into a squamous cell carcinoma. The authors concluded that octanol probably has a weak tumor-promoting effect.[32]

H. Other

1. Intraperitoneal (IP) Carcinogenicity

Groups of 30 A/He mice (15 male, 15 female) were given intraperitoneal injections of 1-octanol (89% to 99% pure) dissolved in 0.1 mL of tricaprylin 3 times/week for 8 weeks.[33] The doses used were 100 and 500 mg/kg per injection for a total of 2.40 and 12.00 g/kg; 500 mg/kg was determined to be the maximum tolerable dose (MTD) in mice. After 24 weeks, the animals were sacrificed. The incidence of tumors was similar in test and control groups.

In a study conducted to evaluate the effects of alcohols on the liver, Bleyman[34] reported that unlike *t*-butanol and *n*-butanol, 1-octanol did not affect the elimination rate of ethanol in Sprague Dawley rats. 1-Octanol did induce a decrease in body temperature after an i.p. injection. This effect was also seen with the other alcohols.[34]

V. HUMAN USE AND EXPERIENCE

An *in vitro* study using human epidermis demonstrated a dermal flux of 0.008 mg/cm^2/h.[35] This rate of dermal flux suggests a low rate of penetration through the epidermis (skin),[35,36] consistent with the dermal LD_{50}. Human patch tests performed in two separate laboratories indicate that 1-octanol is not a significant irritant.[37]

Soviet experiments using electroretinography, determination of the retinocortical period, and a study of the conditioned reflexes indicate that 10 mg/m^3 (1.88 ppm) is the maximum acceptable concentration (MAC) for alcohols from hexyl to decyl.[38]

Octyl alcohol caused transient injury to the corneal epithelium in two patients, with recovery 48 hours after denuding the eye.[39,40] One anecdotal report regarding 99+% 1-octanol listed eye irritation and headache as effects, after inhaling an estimated 166 ppm saturated concentration for only a few minutes in a laboratory setting.[11]

VI. RATIONALE

1-Octanol has a low order of acute toxicity following oral ingestion, dermal contact, and inhalation in laboratory rodents. The primary toxic observation following high acute doses/exposures to 1-octanol in animals is edema and irritation to the epithelial layers of the mucous membranes. Pregnant rats that inhaled 65 ppm 1-octanol, 7 hours/day for 19 days, demonstrated no clinical signs of toxicity, and genotoxicity studies with 1-octanol have been equivocal.

There is limited human experience with exposure to 1-octanol. While acute animal studies demonstrate low toxicity, 1-octanol appears to have an irritating property. There are no known reports of adverse heath effects since 1986 when the occupational exposure level (OEL) of 50 ppm was originally published. Therefore, it is believed that the current OEL of 50 ppm is adequate to prevent irritation.

VII. RECOMMENDED OEL

8-hr time-weighted average (TWA): 50 ppm (265 mg/m^3)

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