

**Evaluation of
Decanoic acid
for Use as a Cigarette Ingredient**

December 2005

INTRODUCTION

Decanoic acid (CAS # 334-48-5) is currently used worldwide at levels below **100 ppm** in selected cigarette brands manufactured and/or distributed by Philip Morris International. This document is a review of current published toxicology information on decanoic acid abstracted from online toxicity databases.

TOXICITY DATA ON UN-BURNED MATERIAL

The following information was generated from the MICROMEDEX database tool <http://csi.micromedex.com> on December 20th 2005, unless otherwise indicated.

Overview

The following information was generated from the HSDB – Hazardous Substances Data Bank, a database of MICROMEDEX Systems (<http://csi.micromedex.com>) on December 20th 2005.

Decanoic acid, also known as capric acid is a carboxylic acid that has been identified as a component of coffee aroma and bread flavour. It is commonly used as a flavouring agent in butter, coconut, fruit and also in perfumes.

As a food flavouring additive, the material has been assessed under the provisions of the *Federal Food, Drug and Cosmetic Act, section 201 (s)*, by the Expert Committee of the USA Flavour and Extract manufacturer's Association (FEMA), to be generally recognized as safe (GRAS) under current conditions of use.

The Joint FAO/WHO Expert Committee on Food Additives has assessed decanoic acid as presenting no safety concerns at current levels of intake when used as a flavouring agent. The daily per capita intake is estimated at 16 µg/kg bw/day in the USA and 24 µg/kg bw/day in Europe¹. It has also been defined as a flavouring substance which may be used as foodstuffs by the *Council of Europe Committee of Experts on Flavouring Substances* at an upper level of 10 mg/kg in foods.

Decanoic acid is a common cosmetic ingredient.

This material appears on the list of "Permitted Additives to Tobacco Products in the United Kingdom" (Department of Health, 2003) at a maximum level permitted for inclusion in cigarettes of 0.001 % w/w tobacco.

In a study of gastric lesions, 10% decanoic acid (about 5000 mg/kg bw per day) in the diet of rats for 150 days resulted in no observable changes in the forestomach or glandular stomach (Mori, 1953)¹.

An LD50 of 3301 mg/kg bodyweight was found for male rats after oral gavage with decanoic acid¹.

¹ Safety evaluations of certain food additives and contaminants, WHO Food Additive Series 40: Saturated aliphatic acyclic linear primary alcohols, aldehydes, and acids.
<http://www.inchem.org/documents/jecfa/jecmono/v040je10.htm>

A NOEL of >5000 mg/kg bw per day was found after oral administration of decanoic acid to the diets of rats for a period of 150 days¹.

The Rec assay, using *B. subtilis* strains H17 and M45 dosed with 18µg/disk of decanoic acid was negative¹.

The modified Ames test (preincubation method), using *S. typhimurium* strains TA98, TA100, TA1535, dose with up to 666 µg/plate of decanoic acid was also negative¹.

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Non-Human Toxicity Excerpts

1. Of the fatty acids tested, decanoic acid was most inhibitory to *L. citrovorum*. [**PEER REVIEWED**] [Kulshrestha DC, EH Marth; J Milk Food Technol 37(12) 600-5 (1974)]
2. Of 11 C6-22 even-numbered saturated & unsaturated fatty acids & their potassium salts tested for toxicity to balsam woolly aphid (*Adelges piceae*), the most effective fatty acids were capric acid (C10 saturated) & oleic acid (C18 unsaturated). [**PEER REVIEWED**] [Puritch GS; Can J for res 5(4) 515-22 (1975)]
3. Octanoic acid (100 millimoles) & decanoic acid (10 millimoles) induced contractures in isolated frog & rat muscles after 20-30 min exposure. [**PEER REVIEWED**] [Koessler F, Kuechler G; Acta boil med ger 36 (7-8) 1085-95 (1977)]
4. Among the saturated fatty acids tested, the C10, C12, & C14 acids inhibited prostaglandin synthetase to the greatest extent. [**PEER REVIEWED**] [Gryglewski RJ; Structure-activity relations of some prostaglandin synthetase inhibitors; prostaglandin synth inhibitors- Their eff physiol funct pathol states (Int symp) 33-52 (1974)]
5. The minimal growth-inhibitory amt of decanoate stopped growth, respiration, adenosine 5'-triphosphate synthesis, & amino acid transport of *Bacillus subtilis* in a culture containing amino acids & citrate as carbon sources. [**PEER REVIEWED**] [Levin BC, Freese E; Antimicrob agents chemother 12(3) 357-67 (1977)]
6. ...Rated 9 on rabbit eyes. ...Tested externally on eyes of rabbits &...rated numerically on scale of 1-10 according to degree of injury ..After 24 hr /observation/, paying particular attention to condition of cornea. Most severe injuries have been rated 10. [**PEER REVIEWED**] [Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986., p. 1008]
7. The compound was a moderate to severe irritant when applied undiluted for 24 hr to intact or abraded rabbit skin in an occluded patch test. Capric acid (mixed isomers) produces severe corneal burns when applied as a 5 percent solution (0.5 ml in water or propylene glycol) to rabbit eyes, and was moderately irritating to rabbit skin in an open patch test. No deaths occurred in rats exposed for 8 hr to concentrated capric acid vapor. [**PEER REVIEWED**] [Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene

- and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994., p. 3560]
8. No gastric lesions were evident in rats fed capric acid (10 percent in diet) for 150 days. Capric acid administered daily (37 mg/kg) to pregnant rabbits increased sensitivity to oxytocin-induced labor. **[**PEER REVIEWED**]** [Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994., p. 3560]
 9. The effects of sodium caprate and sodium caprylate on transcellular permeation routes were examined in rats. The release of membrane phospholipids was significantly increased only by caprate, while protein release did not change from the control in the presence of caprate or caprylate, indicating that the extent of membrane disruption was insufficient to account for the extent the enhanced permeation. Using brush border membrane vesicles prepared from colon, with their protein and lipid component labeled by fluorescent probes, the perturbing actions of caprate and caprylate toward the membrane were examined by fluorescence polarization. Caprate interacted with membrane protein and lipids, and caprylate mainly with protein, causing perturbation to the membrane. The release of 5(6)-carboxyfluorescein previously included in brush border membrane vesicles was increased by caprate but not by caprylate. These results suggest that caprate enhances permeability via the transcellular route through membrane perturbation. **[**PEER REVIEWED**]** [Tomita M et al; Pharm Res 5 (12): 786-9 (1988)]
 10. n-Decanoic acid was irritant ... to the skin and eyes of rabbits. ... Acute oral toxicity in rats and dermal toxicity in rabbits was generally low, with central nervous system effects being seen following oral administration. Limited studies in rats and dogs suggested a low toxicity upon repeated oral administration. When a mixture of decanoic acid and octanoic acid (as the triglycerides) was fed to rats through successive generations, an increased mortality rate (probably related to nutritional factors) was seen among the offspring comprising the third generation. Decanoic acid gave no evidence of carcinogenicity in very limited oral studies in rats, and no mutagenicity was noted in bacterial tests including Ames assays. **[**PEER REVIEWED**]** [Bibra Working Group; Bibra Toxicology International 6: (1996)]

The following information was generated from the RTECS – Registry of Toxic Effects of Chemical Substances, a database of MICROMEDEX Systems (<http://csi.micromedex.com>) on December 20th 2005.

Health hazard data

Acute toxicity

LD50/LC50 - LETHAL DOSE/CONC 50% KILL

Rat

LD50 - ROUTE: Oral; DOSE: >10 gm/kg [American Industrial Hygiene Association Journal. (AIHA, 475 Wolf Ledges Pkwy., Akron, OH 44311) V.19- 1958- (37,251,1976)]

Mouse

LD50 - ROUTE: Intravenous; DOSE: 129 mg/kg [Acta Pharmacologica et Toxicologica. (Copenhagen, Denmark) V.1-59, 1945-86. For publisher information, see PHTOEH (18,141,1961)]

TOXIC EFFECTS:

Behavioral - Convulsions or effect on seizure threshold

Mammal - Unspecified Species

LD50 - ROUTE: Oral; DOSE: >10 gm/kg [Federal Register. (U.S. Government Printing Office, Supt. of Documents, Washington, DC 20402) V.1- 1936- (68,7935,2003)]

LC50 - ROUTE: Skin; DOSE: >5 gm/kg [Federal Register. (U.S. Government Printing Office, Supt. of Documents, Washington, DC 20402) V.1- 1936- (68,7935,2003)]

Irritation

SKIN - STANDARD DRAIZE TEST

Rabbit

ROUTE: Skin; DOSE: 500 mg/24H; REACTION: Moderate [Food and Cosmetics Toxicology. (London, UK) V.1-19, 1963-81. For publisher information, see FCTOD7. (17,735,1979)]

SKIN - OPEN DRAIZE TEST

Rabbit

ROUTE: Skin; DOSE: 100%/24H ; REACTION: Severe [Federal Register. (U.S. Government Printing Office, Supt. of Documents, Washington, DC 20402) V.1- 1936- (68,7935,2003)]

Genetic effects

SEX CHROMOSOME LOSS/NONDISJUNCTION

Yeast - *S Cerevisiae*

DOSE: 14500 ppb [Annals of the New York Academy of Sciences. (New York Academy of Sciences, 2 E. 63rd St., New York, NY 10021) V.1- 1877- (407,186,1983)]

Other multiple dose toxicity data

Rat

TDLo - ROUTE: Oral; DOSE: 168 gm/kg/6W intermittent [Federal Register. (U.S. Government Printing Office, Supt. of Documents, Washington, DC 20402) V.1- 1936- (68,7935,2003)]

TOXIC EFFECTS:

Blood - Changes in serum composition (e.g., TP, bilirubin, cholesterol)

Nutritional and Gross Metabolic - Weight loss or decreased weight gain

Biochemical - Lipids including transport

TOXICITY DATA ON BURNT MATERIAL

Data on the toxicity of decanoic acid as a cigarette ingredient has been evaluated in a series of studies. The results of these studies may be found in the following references:

E.L. Carmines, 2002, "Evaluation of the Potential Effects of Ingredients Added to Cigarettes. Part I: Cigarette Design, Testing Approach and Review of Results," Food and Chemical Toxicology, 40:77-91. **PEER REVIEWED**

K. Rustemeier et al, 2002, "Evaluation of the Potential Effects of Ingredients Added to Cigarettes Part II. Chemical Smoke Composition," Food and Chemical Toxicology, 40:93 - 104. **PEER REVIEWED**

Roemer et al, 2002, "Evaluation of the Potential Effects of Flavor Ingredients Added to Cigarettes. Part 3. In Vitro Genotoxicity and Cytotoxicity," Food and Chemical Toxicology, 40:105-111. **PEER REVIEWED**

P.M. Vanscheeuwijck et al, 2002, "Toxicological Evaluation of Cigarettes without and with the Addition of Flavor Ingredients to the Tobacco. Part 4. Subchronic Inhalation Toxicity," Food and Chemical Toxicology, 40:113-131. **PEER REVIEWED**

Gaworski et al, 1998, "Toxicological evaluation of flavor ingredients added to cigarette tobacco: 13-week inhalation exposure in rats," Inhalation Toxicology, 10:357-381. **PEER REVIEWED**

Gaworski et al, 1999, "Toxicological evaluation of flavor ingredients added to cigarette tobacco: skin painting bioassay of cigarette smoke condensate in SENCAR mice," Toxicology, 139 1-17. **PEER REVIEWED**

These studies indicate that the ingredients used in the production of cigarettes do not increase the overall toxicity of cigarette smoke.

DATA ON THE EFFECTS ON HUMAN HEALTH

The following information was generated from the HSDB – Hazardous Substances Data Bank, a database of MICROMEDEX Systems (<http://csi.micromedex.com>) on December 20th 2005.

Human Toxicity Excerpts

Capric acid produced no irritation when applied to human skin as a 1% solution in petrolatum for 48 hr in a closed-patch test. At higher concentrations (up to 1.0 M in propanol), the compound produced signs of irritation within 8 days in occlusive patch tests in human volunteers. No sensitization reactions were seen. [Peer reviewed] [Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994., p. 3561]

Skin, Eye and Respiratory Irritations

n-Decanoic acid was irritant to the skin of humans ... No skin sensitization was induced in volunteers treated with a dilute solution. **[**PEER REVIEWED**]** [Bibra Working Group; Bibra Toxicology International 6: (1996)]

Probable Routes of Human Exposure:

NIOSH (NOES Survey 1981-1983) has statistically estimated that 2,939 workers (276 of these are female) are potentially exposed to capric acid in the US(1). Occupational exposure may be through dermal contact with this compound at workplaces where capric acid is produced or used(SRC). The general population will be exposed to capric acid via inhalation of ambient air, ingestion of food and drinking water, and dermal contact with vapors, food and other products containing capric acid(SRC). **[**PEER REVIEWED**]** [(1) NIOSH; National Occupational Exposure Survey (NOES) (1983)]

CONCLUSION

Cigarette smoking causes lung cancer, heart disease, emphysema and other serious diseases in smokers. Smokers are far more likely to develop serious diseases, like lung cancer, than non-smokers. There is no "safe" cigarette. Government health warnings about smoking apply to all cigarettes, regardless of the ingredients added, including those containing only tobacco and paper.

While Philip Morris International has not conducted human studies on the health effects of ingredients used in cigarette manufacture, studies have been conducted using scientifically accepted in vitro and in vivo toxicity assays with various ingredient mixtures (see Toxicity Data on Burnt Material above). These studies show there is no meaningful difference in the composition or toxicity of smoke when the smoke from cigarettes with added ingredients is compared to the smoke from cigarettes without added ingredients. These findings are supported by similar studies from the published literature. It is our scientific judgment, based on the best available data, that decanoic acid used in our cigarettes does not increase the overall toxicity of cigarette smoke.