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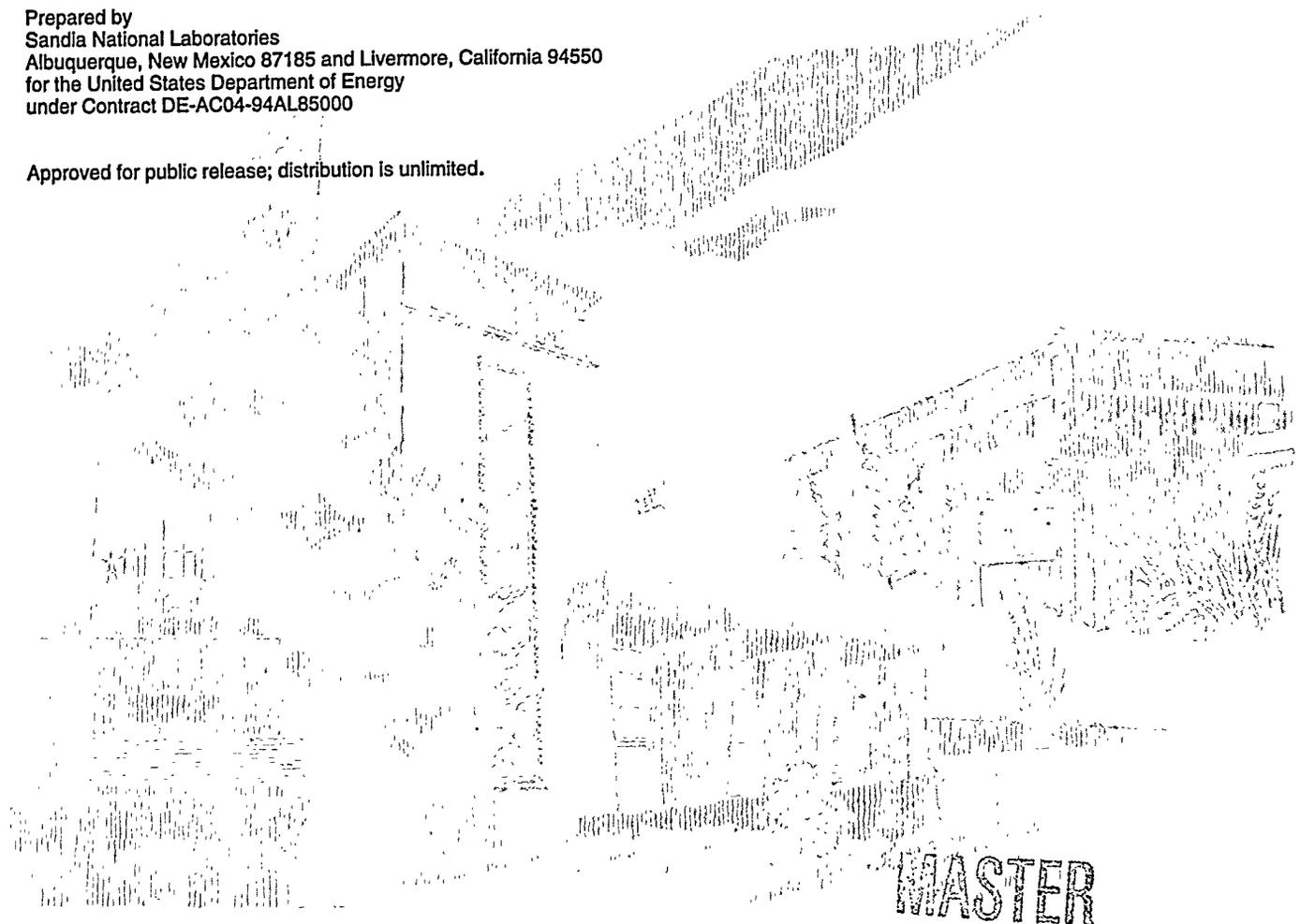
Printed October 1995

Oleoresin Capsicum Toxicology Evaluation and Hazard Review

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Prepared by
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for the United States Department of Energy
under Contract DE-AC04-94AL85000

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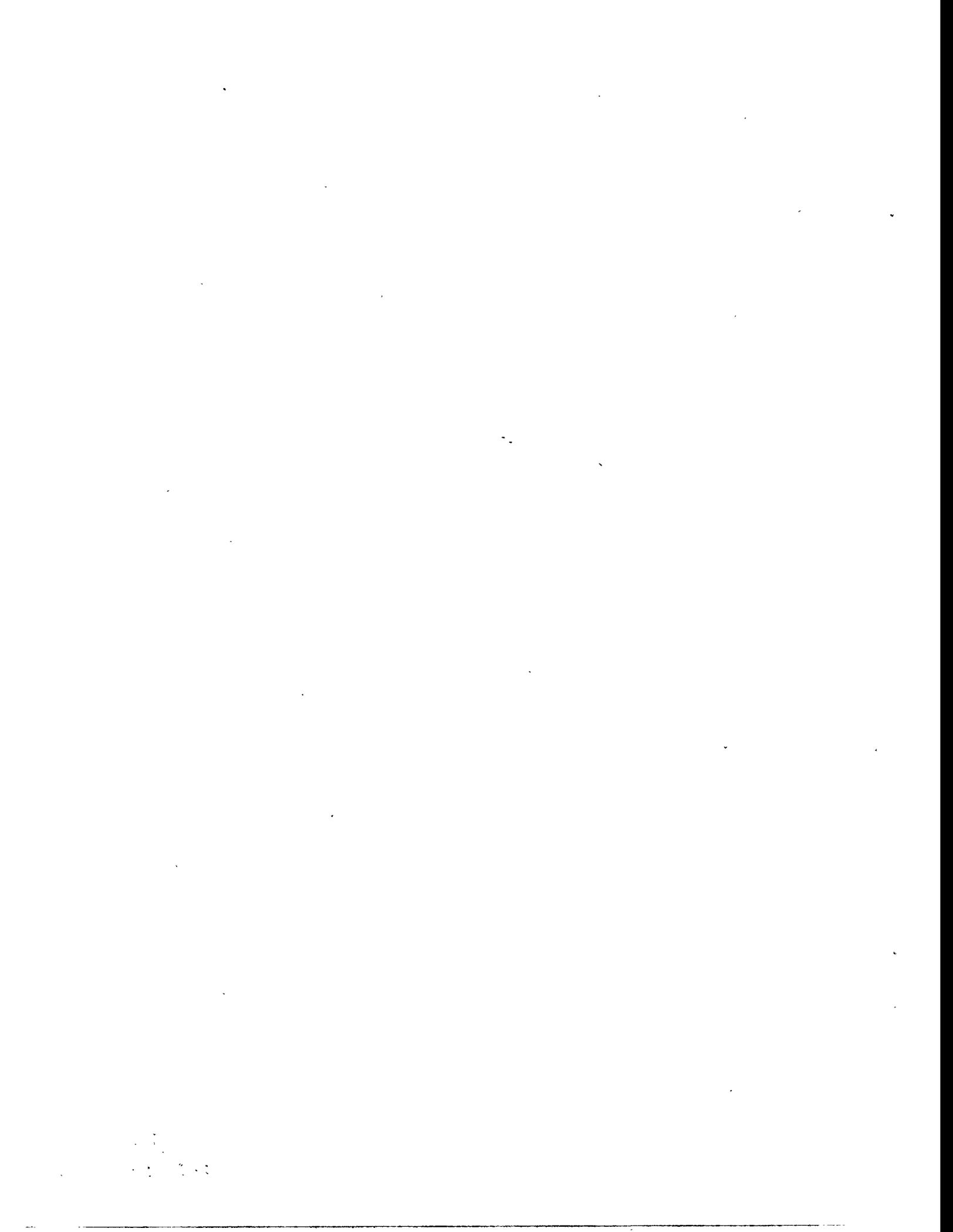
**OLEORESIN CAPSICUM
TOXICOLOGY EVALUATION AND HAZARD REVIEW**

**For the National Institute of Justice
Less-Than-Lethal Force Program**

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Abstract

Oleoresin Capsicum (OC) is an extract of the pepper plant used for centuries as a culinary spice (hot peppers). This material has been identified as a safe and effective Less-Than-Lethal weapon for use by Law enforcement and security professionals against assault. The National Institute of Justice (NIJ) is currently also evaluating its use in conjunction with other Less-Than-Lethal agents such as aqueous foam for use in corrections applications. Therefore, a comprehensive toxicological review of the literature was performed for the National Institute of Justice Less-Than-Lethal Force program to review and update the information available on the toxicity and adverse health effects associated with OC exposure. The results of this evaluation indicate that exposure to OC can result in dermatitis, as well as adverse nasal, pulmonary, and gastrointestinal effects in humans. The primary effects of OC exposure include pain and irritation of the mucous membranes of the eyes, nose, and lining of the mouth. Blistering and rash have been shown to occur after chronic or prolonged dermal exposure. Ingestion of capsicum may cause acute stinging of the lips, tongue, and oral mucosa and may lead to vomiting and diarrhea with large doses. OC vapors may also cause significant pulmonary irritation and prolonged cough. There is no evidence of long term effects associated with an acute exposure to OC, and extensive use as a culinary additive and medicinal ointment has further provided no evidence of long term adverse effects following repeated or prolonged exposure.



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Nomenclature

ACGIH	American Conference of Governmental Industrial Hygienists
ASTM	American Society for Testing and Materials
BEI	biological exposure indices
CEIL	ceiling, the concentration that should not be exceeded during any part of the working exposure.
COC	Cleveland Open Cup
CNS	central nervous system
HSDB	Hazardous Substances Data Bank
IARC	International Agency for the Research of Cancer
LC50	Lethal concentration - fifty = Concentration that leads to death in 50% of the population studied (used in inhalation studies).
LD50	Lethal dose fifty = Dose that leads to death in 50% of the population studied (generally oral or dermal studies).
NA	information not available
NCI	National Cancer Institute
NCITR	National Cancer Institute Toxicity Report
NIJ	National Institute of Justice
NIOSH	National Institute of Occupational Safety and Health
NTP	National Toxicology Program
OC	Oleoresin Capsicum
OSHA	Occupational Safety and Health Administration
PEL	permissible exposure limit
PM	Pensky-Martens Closed Cup
REL	recommended exposure limit
RTECS	Registry of Toxic Effects of Chemical Substances
S.H.U.	Scoville Heat Units
SNL	Sandia National Laboratories
STEL	short term exposure limit
TC	toxic concentration
TLV	threshold limit value
TWA	time weighted average (8 hour)
g	grams
hr	hours
kg	kilograms
l	liter
m ³	cubic meters
min.	minutes
mg	milligrams
ml	millimeters
ppm	parts per million

OLEORESIN CAPSICUM TOXICOLOGY EVALUATION AND HAZARD REVIEW

For the National Institute of Justice Less-Than-Lethal Force Program

Introduction

Oleoresin Capsicum (OC) is an organic oily resin derived from the pepper plant and is typically used for pharmacological (e.g. as a topical analgesic) and food seasoning purposes. The intensity of OC formulations and their toxicological effects are a direct function of the amount of capsiacinoids (capsaicin) present in the product.

OC "Pepper Spray" has generated interest and acceptance in law enforcement and police agencies as a safe and effective method of incapacitating violent or threatening subjects (1). It is naturally occurring, and its mechanism of action differs substantially from traditional chemical agents such as chloroacetophenone (CN) and *ortho*-chlorobenzylidene malononitrile (CS). Unlike these chemical irritants, which are primarily pain inducers and tearing agents, OC causes an incapacitating inflammatory response. When OC is inhaled, there is immediate inflammation in the respiratory tract and breathing is temporarily restricted to short, shallow breaths. Physical effects include involuntary closing of the eyes, coughing, choking, lack of upper body strength and coordination, and nausea. OC causes an almost immediate swelling of the eyes, with an intense burning sensation in the eyes, throat, and sprayed areas of the skin (2).

Current use of OC as a nonlethal spray weapon has been limited to police, security forces, and civilians for personal defense against assault. OC for defense formulas can vary in potency from 16,000 Scoville Heat Units (S.H.U.) to 1.5 million units, with a 5-10% solution generally recommended as an effective dose (13). However, because OC is inflammatory as well as irritating, increasing the strength also increases the safety risks.

OC has been proposed for use by the National Institute of Justice (NIJ) as a Less-Than-Lethal weapon to be used in conjunction with other such devices in corrections applications. The purpose of this study is to review the current literature and update the toxicity and adverse health effects data on oleoresin capsicum for the NIJ Less-Than-Lethal Program. This report summarizes the current chemical and toxicological literature on the adverse health effects associated with acute or chronic exposure to OC. Animal testing or human subjects testing with oleoresin capsicum was not performed by SNL for this study.

Toxicological Review of Oleoresin Capsicum

Chemical Name (3, 4):

Oleoresin capsicum (OC)
capsaicin (active ingredient in OC)
vanillyl amide
8-methyl-n-vanillyl-6-nonenamide

Molecular Formula (4):

$C_{18}H_{27}NO_3$

CAS Number (3):

404-86-4

Chemical and Physical Properties (4, 5):

Molecular Weight: 305.4 g/mol

Melting Point: <-60°C

Boiling Point: >187°C

Flash Point: 215°F (COC)

Appearance: Dark red viscous liquid

Odor: spicy odor with an odor threshold limit of approximately 10 PPM

Water solubility: Fully dispersible

Solvent solubility: Soluble in benzene, alcohol, ketone, ether, and paraffin oils.

pH: NA

Specific Gravity: 1.0073-1.1073 @ 25°C

Exposure Limits: No occupational exposure limits have been determined for this material by OSHA, NIOSH or ACGIH (6).

Toxicology: Oleoresin capsicum (OC) is a chemical inflammatory agent found in many plants. Contact with products containing capsaicin, the active ingredient in OC, produces local irritation, inflammation and lacrimation. Prolonged or repeated exposure to OC can result in dermatitis, as well as adverse nasal, pulmonary, and gastrointestinal effects in humans.

Inhalation Toxicity: Inhalation of capsaicin vapors may cause significant pulmonary irritation and prolonged cough. Exposure to concentrations of OC ranging from 0.6 to 19.8 g/m³ were examined for their effect on breathing in healthy individuals. OC at these concentrations induced a dose dependent cough response without serious pulmonary involvement even in subjects with mild asthma (7). Additional studies involving human exposure to aerosol solutions of 2 - 10% capsaicin have shown that upon exposure, coughing starts immediately but disappears promptly when the exposure is terminated (8).

Blanc et. al. measured three respiratory indices, prevalence of respiratory symptoms, alteration of lung function, and an increase in the cough threshold, to evaluate the effect of chronic exposure of workers to OC in the chili pepper industry. Inhalation exposure of these workers to capsaicin resulted in a lowered cough threshold with the induction of cough seen at concentrations of 3×10^{-7} to 3×10^{-6} M (i.e. 0.092 to 0.92 g/m³). Strong bronchial contractions were also measured *in vitro* in cultured bronchial tissue with 10^{-5} M (3.0 g/m³) capsaicin. However, no significant adverse effects on lung function or respiratory rates for these individuals were noted (9). In other human studies, nebulized capsaicin (10^{-7} M, 0.03 g/m³) was inhaled by 8 normal subjects to study its effects on the pattern of breathing. When compared to the diluent alone, capsaicin increased mean inspiratory flow through more rapid but not more shallow breathing (10).

The effect of inhaled capsaicin on airway conductance, or the ease in which air passes through the respiratory tract, in humans has also been studied. Inhaling 2.4×10^{-10} and 2.4×10^{-9} M (i.e. 0.73 and 7.3 g/m³) capsaicin resulted in a dose-dependent fall in specific airway conductance that was maximal within 20 seconds of exposure and lasted for less than 60 seconds. There was no difference in the magnitude or duration of bronchoconstriction between normal, smoking, or asthmatic subjects and there was no evidence for a reduced response on repeated exposure (11).

Philip et. al. examined a variety of acute secretory effects of capsaicin in the human nose. When sprayed into the nose, a concentration of 20 μ mol/L (6.1×10^{-3} mg/m³) capsaicin induced burning, runny nose, and tearing of the eyes. Capsaicin also induced a significant increase in total protein content of nasal lavage fluid after challenge. Unlike respiratory effects, repetitive capsaicin challenge every 10 minutes, led to a decrease in total protein secretion and lactoferrin secretion, indicators of sensory nerve inactivation in the nose (12).

Dermal Toxicity: Oleoresin capsicum is considered moderately toxic by the dermal route with a dermal LD₅₀ >512 mg/kg reported in the mouse. Dermal exposure to OC results in irritation, erythema or redness, and burning pain in humans. Blistering and rash has also occurred after chronic or prolonged exposure or in the presence of a preexisting dermatitis. The principal mechanism for the resulting pain following dermal exposure appears to be the release of "substance P" an undecapeptide which is the principal transmitter of pain impulses through specific peripheral sensory fibers to the central nervous system (CNS) (13).

In addition, a consistent finding throughout the scientific literature is that capsaicin or OC when applied to the skin or mouth, causes a local long lasting desensitization. Therefore, although the primary response is pain, also produced at the site of exposure is a long lasting desensitization to burning and pain by other agents (14). Therefore OC has been found effective when added to over-the-counter ointments as a topical analgesic (13). Furthermore, under experimental

conditions designed to obtain a controlled stimuli and to overcome the diffusion barrier of the skin, Simone et al. discovered that 0.1 µg was the lowest amount of capsaicin to evoke pain when delivered intradermally. Depending on the dose, the pain could endure from a couple of minutes to about 17 minutes (15).

Eye Toxicity: In studies examining the toxicity of OC to the eye, 0.1 ml of liquid from the test spray of a 5% solution of OC was introduced into the conjunctival sac of the left eye of 4 rabbits. The treated eyes were held closed for one second after instillation and were not washed. Untreated eyes served as controls. Gross signs of eye irritation and systemic toxicity were recorded at 24, 48, and 72 hours. The principle toxic effects of blinking, preening, and noisy discomfort were noted immediately after instillation. In three out of four rabbits, slight conjunctival erythema or redness was noted within the first 24 hours. This redness completely cleared by 48 hours in three of the eyes and cleared by 72 hours in the fourth eye (2). In other studies, 50 µg/ml capsaicin instilled in the eyes of rats caused obvious pain and spasmodic blinking. Furthermore, the blood vessels of the conjunctiva and lids of the rats became abnormally permeable (16).

The effects of OC on the eyes of rabbits have been studied by several manufacturers of OC defense products. Prolonged and repeated eye exposure to capsaicin was compared to the effects noted in the eyes of rabbits exposed to distilled water. Eye irritation was slightly greater in the OC exposed rabbits than in those exposed to distilled water. In addition, the irritation was confined to the conjunctiva and consisted of slight or moderate erythema of the lids and vascularization of the membranes. Maximum irritation was observed immediately following application and generally subsided by 96 hours. There was no significant increase in eye irritation with successive applications and no corneal or permanent eye damage was noted (17).

Oral Toxicity: Ingestion of OC in food has been documented in humans for many years. Ingestion may cause acute stinging of the lips, tongue, and oral mucosa, which may lead to vomiting and diarrhea. The guinea pig appears to be the species most susceptible to the toxicity of oral capsaicin exposure with an acute oral LD50 reported to be 1.10 mg/kg (18), while the acute oral LD50 in the mice was found to be >190 mg/kg. In male and female rats, the acute oral LD50 was determined to be 23.6 and 29.7 mg/kg, respectively (19). Gosselin et al. has determined OC to be moderately toxic and estimates the probable oral lethal dose in humans to be 0.5 - 5.0 g/kg or between 1 oz. and 16 oz. for a 70 kg person (20). The cause of death following toxic oral exposure is respiratory paralysis.

Subchronic (short term) and chronic (long term) oral exposure studies were conducted by administering 50 mg/kg crystalline capsaicinoids by stomach tube. The animals were allowed free access to normal feed and water. Comprehensive measurements and analyses were done for food and water intake, growth, rectal

temperature, blood and urine chemistry, and postmortem gross examination of different organs and their relative weights. There were no significant adverse effects associated with this exposure, which was 50-100 times the high, average daily intake of individuals in some Asian countries (21).

Reproductive Toxicity and Carcinogen Studies: This material is not listed as a carcinogen by IARC, NTP, or ACGIH. In addition, centuries of culinary use as a condiment and the absence of epidemiological evidence of any adverse effects due to eating chili peppers containing capsaicin, suggests that there are no cancer risks involved with capsaicin as a food ingredient (22). Similarly, the absence in the literature of case reports and results from studies showing no birth defects in the rat following oral gavage with capsaicinoid suggest an absence of teratogenesis as well (19, 22).

Human Exposure

According to a report from the U.S. Department of Justice Federal Bureau of Investigation, during the period from July 1987 to July 1989, >900 individuals were either sprayed directly in the face or placed in enclosed areas and exposed to solutions of OC ranging from 1% to 10% OC. The observed physiological effects on these individuals included eye irritancy that ranged from severe spasmodic blinking of the eyes to involuntary closing of the eyes; respiratory inflammation with symptoms that ranged from coughing and shortness of breath to gasping for breath with a gagging sensation in the throat; and dermal effects which ranged from a burning sensation to an acute burning sensation with redness of the skin. Respiratory functions and visual acuity returned to normal within 2 to 5 minutes after decontamination. In addition, depending on the breathing rates of the individuals and the amount of exposure time, various degrees of temporary paralysis of the larynx and the resulting inability to speak were observed but returned once OC exposure was discontinued. No permanent adverse effects were noted by any of the subjects studied following exposure to OC (2).

Midgren et.al. evaluated the cough response of capsaicin in healthy human subjects. Despite frequent coughing, the subjects could inhale repeated breaths of a 5% capsaicin aerosol for 60 seconds without difficulty. Coughing started immediately on inhalation and was most intense during the first 30 seconds. The cough response terminated quickly when the capsaicin exposure was stopped (8).

In studies of mild asthmatics, no evidence of hypersensitivity following exposure was noted (7), and there have been no reported cases of occupationally induced asthma due to OC (22). Furthermore, OC has been used in over the counter salves and ointments as a topical analgesic with no reported adverse effects.

Studies sponsored by the International Association of Chiefs of Police have reviewed data on in-custody death incidents where pepper spray had been used in the arrest procedure. These studies were undertaken to determine whether there is a possibility that OC could

be a factor in these in-custody deaths. In this study, a total of 30 incidents between August 1990 and December 1993 were evaluated. It was concluded from this study that in none of these cases was OC considered to be a cause of, or a contributor to, the deaths (23).

Environmental Concerns

Unlike *ortho*-chlorobenzylidene malononitrile (CS), or chloroacetophenone (CN), other chemical irritants, OC particles will dissipate from an individual's clothing in a relatively short period of time. Therefore, decontamination of individuals only involves removing them from the exposure to fresh air. Washing and rinsing of the eyes with water may also be required to eliminate the burning sensation. Area decontamination consists of ventilating the enclosed area by opening doors or windows. Cross ventilation is unnecessary since OC does not persist like CS or CN.

Conclusions

Analysis of the toxicological literature relating to OC and capsaicin leads to the conclusion that the hazard following acute exposure to OC appears to be limited to the characteristic burning sensation expected of the capsaicinoids and does not result in permanent adverse effects or tissue damage. OC is an inflammatory agent that causes swelling of the eyes and airways and makes vision and breathing difficult. Although few traditional toxicology studies exist on specific OC products, extensive experience with this product as a food ingredient or topical analgesic suggest limited systemic toxicity or long term target organ effects following exposure. Furthermore, the induction of allergies or asthma by capsaicinoids has not been reported in the literature and, although signs and symptoms may be descriptively similar to an allergic reaction, there is currently no known sensitization to capsaicin. Studies by Counterforce Technology have determined that a dose of 5-10% aerosol concentration of OC can be generated which is both safe and effective.

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