

# CAPSAICIN

## TECHNICAL FACT SHEET

NPIC Technical Fact Sheets provide information that is complex and intended for individuals with a scientific background and/or familiarity with toxicology and risk assessment. This document is intended to promote informed decision-making. Please refer to the General Fact Sheet for less technical information.

### Chemical Class and Type:

- Capsaicin is an animal repellent that has also been registered for use as an insecticide, miticide, rodenticide, and feeding depressant.<sup>1</sup> The International Union of Pure and Applied Chemistry (IUPAC) chemical name is 8-methyl-n-vanillyl-6-nonenamide and the Chemical Abstracts Service (CAS) registry number is 404-86-4.<sup>2</sup> Capsaicin is a phenylpropanoid compound.<sup>3</sup>
- Capsaicin is obtained from peppers which are the fruit from plants in the genus *Capsicum*. The peppers are ground into a fine powder. This may be further refined to the oleoresin, which is a reddish-brown liquid with little odor.<sup>2</sup> When extracted from plants, the capsicum oleoresin may contain many volatile compounds in addition to capsaicin.<sup>4</sup> *Capsicum annum* fruits contained 1.27% capsaicinoids, and 0.03% capsaicin.<sup>5</sup>
- Capsaicin was first registered for use in the United States in 1962.<sup>2</sup> It is classified as a biochemical pesticide due to its mode of action and the fact that it is a naturally occurring substance.<sup>2</sup> See the text box on **Laboratory Testing**.

**Laboratory Testing:** Before pesticides are registered by the U.S. EPA, they must undergo laboratory testing for short-term (acute) and long-term (chronic) health effects. Laboratory animals are purposely given high enough doses to cause toxic effects. These tests help scientists judge how these chemicals might affect humans, domestic animals, and wildlife in cases of overexposure.

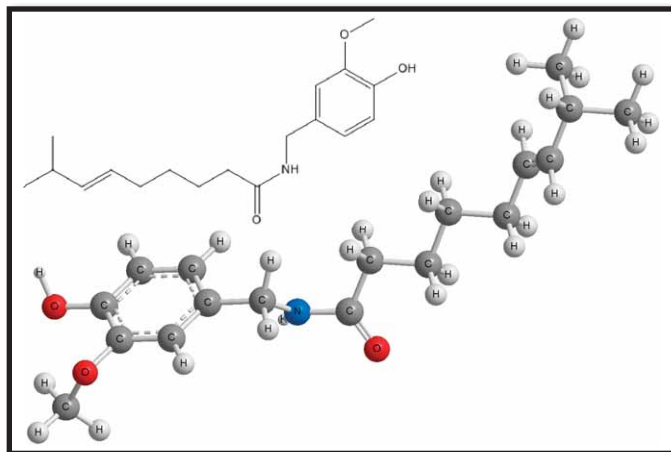
### Physical / Chemical Properties:

- Vapor pressure<sup>6</sup>: Very low
- Octanol-Water Partition Coefficient ( $\log K_{ow}$ )<sup>7</sup>: 3.04
- Henry's constant<sup>7</sup>:  $1 \times 10^{-13}$  atm·m<sup>3</sup>/mol at 25 °C
- Molecular weight<sup>7</sup>: 305.462 g/mol
- Solubility (water)<sup>7</sup>: 10.3 mg/L at 25 °C
- Soil Sorption Coefficient ( $K_{oc}$ )<sup>7</sup>:  $1.10 \times 10^3$

### Uses:

- Capsaicin is used on vegetation such as crops and trees, buildings, and garbage containers. It is registered to repel vertebrate pests such as rabbits, squirrels, deer, voles, raccoons, cats, dogs, and skunks. It is also used as an attack deterrent for dogs and bears.<sup>1</sup> Uses for individual products containing capsaicin vary widely. Always read and follow the label when applying pesticide products.
- It is applied to foliage of plants to deter feeding by insects such as spider mites, lace bugs, and other invertebrates.<sup>1</sup> Capsaicin is used as an insecticide in addition to its use as a repellent.<sup>8</sup>
- Capsaicin is toxic to some bacteria and has been evaluated for use as a marine antifoulant.<sup>9</sup>
- Signal words for products containing capsaicin may range from Caution to Danger. The signal word reflects the combined toxicity of the active ingredient and other ingredients in the product. See the pesticide label on the product and refer to the NPIC fact sheets on [Signal Words](#) and [Inert or "Other" Ingredients](#).

### Molecular Structure - Capsaicin



# CAPSAICIN

## TECHNICAL FACT SHEET

- To find a list of products containing capsaicin which are registered in your state, visit the website <http://npic.orst.edu/state1.htm> and search by "active ingredient."
- In addition to its use as a pesticide, capsaicin is used in law enforcement and as an ingredient in cosmetics.<sup>10</sup> Medical researchers have studied capsaicin and its interaction with the TRVP1 receptor for use in pain management.<sup>11,12</sup> Capsaicin also has been evaluated for treatment of some cancers.<sup>14</sup>

### Mode of Action:

#### Target Organisms

- Inhalation results in inflammation of pulmonary tissue and damage to respiratory cells.<sup>15</sup> Capsaicin also irritates skin, sometimes severely.<sup>16,17</sup>
- In insects, capsaicin's toxicity appears to be through metabolic disruption, membrane damage, and nervous system dysfunction.<sup>8</sup> Capsaicin has also been shown to repel insects as well as kill them.<sup>18</sup>
- Capsaicin triggers the release of the neuropeptide P from the sensory nerve fibers of the C type.<sup>3</sup> In mammals, capsaicin binds to the TRPV1 vanilloid receptor.<sup>15</sup> The TRPV1 receptor then releases sensory neuropeptides that trigger a neurogenic inflammatory response.<sup>13,19</sup>

#### Non-Target Organisms

- Modes of toxicity for non-target organisms are expected to be similar to those of targeted insects and mammals. Capsaicin is considered toxic to honeybees and other beneficial insects.<sup>8</sup> Although birds have the TRPV1 receptor, it is not activated by capsaicin.<sup>20,21</sup> No information was available regarding toxicity of capsaicin to fish or other aquatic life.<sup>2</sup>

### Acute Toxicity:

#### Oral

- Acute oral LD<sub>50</sub> values were determined to be 97.4 mg/kg and 118.8 mg/kg in female and male mice, respectively, and 148.1 mg/kg and 161.2 mg/kg in female and male rats, respectively.<sup>22</sup> See the text boxes on **Toxicity Category** and **LD<sub>50</sub>/LC<sub>50</sub>**.

TOXICITY CATEGORY - CAPSAICIN				
	High Toxicity Category I	Moderate Toxicity Category II	Low Toxicity Category III	Very Low Toxicity Category IV
Acute Oral LD <sub>50</sub>	Up to and including 50 mg/kg (≤ 50 mg/kg)	Greater than 50 through 500 mg/kg (> 50 – 500 mg/kg)	Greater than 500 through 5000 mg/kg (> 500 – 5000 mg/kg)	Greater than 5000 mg/kg (> 5000 mg/kg)
Inhalation LC <sub>50</sub>	Up to and including 0.05 mg/L (≤ 0.05 mg/L)	Greater than 0.05 through 0.5 mg/L (>0.05 – 0.5 mg/L)	Greater than 0.5 through 2.0 mg/L (> 0.05 – 2.0 mg/L)	Greater than 2.0 mg/L (> 2.0 mg/L)
Dermal LD <sub>50</sub>	Up to and including 200 mg/kg (≤ 200 mg/kg)	Greater than 200 through 2000 mg/kg (> 200 – 2000 mg/kg)	Greater than 2000 through 5000 mg/kg (>2000 – 5000 mg/kg)	Greater than 5000 mg/kg (> 5000 mg/kg)
Primary Eye Irritation	Corrosive (irreversible destruction of ocular tissue) or corneal involvement or irritation persisting for more than 21 days	Corneal involvement or other eye irritation clearing in 8 – 21 days	Corneal involvement or other eye irritation clearing in 7 days or less	Minimal effects clearing in less than 24 hours
Primary Skin Irritation	Corrosive (tissue destruction into the dermis and/or scarring)	Severe irritation at 72 hours (severe erythema or edema)	Moderate irritation at 72 hours (moderate erythema)	Mild or slight irritation at 72 hours (no irritation or erythema)

Modeled after the U.S. Environmental Protection Agency, Office of Pesticide Programs, Label Review Manual, Chapter 7: Precautionary Labeling.  
<http://www.epa.gov/oppfead1/labeling/lrm/chap-07.htm>

# CAPSAICIN

## TECHNICAL FACT SHEET

- Additional LD<sub>50</sub> values for male mice were 60-75 and 190 mg/kg depending on the carrier solution when the capsaicin was administered within the stomach.<sup>23</sup>
- Studies using mice have reported LD<sub>50</sub> values ranging from 47.2 mg/kg<sup>25</sup> to 2500.0 mg/kg.<sup>24</sup>
- The LD<sub>50</sub> in humans has been estimated at 0.5-5.0 g/kg.<sup>25</sup>

### Dermal

- Capsaicin can cause skin irritation.<sup>10,16</sup> Little absorption occurs across the skin.<sup>12</sup> Edema following dermal exposure in mouse ears in several studies peaked within 1 hour of application, although subsequent applications produced less of a response.<sup>10</sup>
- Capsaicin can severely irritate the eyes, and was found to cause corneal lesions in rats and mice.<sup>8,10</sup>
- The dermal LD<sub>50</sub> was determined to be >512 mg/kg in mice, however no signs of toxicity were noted at the doses tested.<sup>23</sup>

**LD<sub>50</sub>/LC<sub>50</sub>:** A common measure of acute toxicity is the lethal dose (LD<sub>50</sub>) or lethal concentration (LC<sub>50</sub>) that causes death (resulting from a single or limited exposure) in 50 percent of the treated animals. LD<sub>50</sub> is generally expressed as the dose in milligrams (mg) of chemical per kilogram (kg) of body weight. LC<sub>50</sub> is often expressed as mg of chemical per volume (e.g., liter (L)) of medium (i.e., air or water) the organism is exposed to. Chemicals are considered highly toxic when the LD<sub>50</sub>/LC<sub>50</sub> is small and practically non-toxic when the value is large. However, the LD<sub>50</sub>/LC<sub>50</sub> does not reflect any effects from long-term exposure (i.e., cancer, birth defects or reproductive toxicity) that may occur at levels below those that cause death.

### Inhalation

- No inhalation LC<sub>50</sub> was found.
- Capsaicin temporarily causes bronchoconstriction, coughing, nausea, and incoordination in the upper body in humans following inhalation.<sup>26</sup>
- Airway resistance increased following inhalation of capsaicin in both mild asthmatics and non-asthmatic people at doses that are below those eliciting the cough response.<sup>27</sup>
- People suffering from asthma and other respiratory diseases may be more sensitive to capsaicin than other individuals.<sup>26</sup>
- A more recent study suggested that people with sensory hyperreactivity have enhanced sensitivity to capsaicin. This was associated with increased levels of serum nerve growth factors in nasal lavage fluid.<sup>28</sup>

### Signs of Toxicity - Animals

- Capsaicin produces its repellent effect when it contacts either eye or respiratory tract mucus membranes. Signs of acute exposure include coughing, inability to vocalize, and temporary blindness.<sup>29</sup>
- Mice and rats dosed orally with 96 to 200 mg/kg capsaicin demonstrated immediate salivation, convulsions, reddening of the skin, and dyspnea, or labored breathing. Animals either died within 26 minutes of dosing, or showed no further symptoms 24 hours after dosing.<sup>22</sup>
- Inhalation exposure to capsaicinoids in pepper sprays damaged rat bronchial, tracheal, nasal, and alveolar cells, causing acute inflammation.<sup>15</sup>

### Signs of Toxicity - Humans

- Exposure to capsaicin pepper spray results in temporary blindness, lacrimation (tear production), burning sensation, pain and redness on the skin, nasal irritation, coughing, bronchoconstriction, and dyspnea.<sup>26</sup>
- Capsaicin administered in a nasal spray resulted in human volunteers experiencing greatly increased nasal discharge and lacrimation, and burning sensation.<sup>30</sup>

- Mucous membranes throughout the gastrointestinal tract from mouth to anus may be temporarily irritated by ingestion of capsaicin. In addition to irritation, diarrhea and vomiting may occur.<sup>31</sup>
- Always follow label instructions and take steps to avoid exposure. If any exposures occur, be sure to follow the First Aid instructions on the product label carefully. For additional treatment advice, contact the Poison Control Center at 1-800-222-1222. If you wish to report an incident, please call 1-800-858-7378.

## Chronic Toxicity:

### Animals

- Chronic feeding studies in rodents consistently demonstrated weight loss when animals were either dosed via gavage or when the capsaicin was mixed with the food.<sup>10</sup> However, another feeding study showed no such effects using ground red pepper *Capsicum annuum* at up to 10% of the total diet in mice.<sup>36</sup>
- Different diets affected the toxic effects of capsaicin on the liver and spleen in rabbits, such that effects were greatest in animals fed the high-fat diets. In contrast, animals fed high protein, high carbohydrate diets showed no effects relative to controls. Test animals were given 5 g/kg of “red pepper” daily for one year.<sup>32</sup>
- Researchers applied pure capsaicin topically to the backs of mice once weekly for 26 weeks. Doses of 0.64, 1.28, and 2.56 mg/mouse/week resulted in skin abnormalities including inflammation, epidermal crusts, epidermis thickening, and ulcerations.<sup>33</sup> Other signs included gross lesions in the stomach, salivary glands, and oral cavity.<sup>33</sup>
- Capsaicin applied to the hind paws of rats twice daily for 10 weeks led to increased pain sensitivity in the animals exposed to the highest dose (0.75% capsaicin) although this sensitivity decreased with time.<sup>34</sup> Rats treated with a lower dose (0.075% capsaicin) demonstrated reduced function in certain cells known as C fibers following prolonged dosing, but this impairment disappeared after treatment stopped.<sup>34</sup>

### Humans

- No information was found regarding NOEL, LOEL, PAD, or RfD values for capsaicin. See the text box on **Exposure**.

**Exposure: Effects of capsaicin on human health and the environment depend on how much capsaicin is present and the length and frequency of exposure. Effects also depend on the health of a person and/or certain environmental factors.**

- Chronic exposure to capsaicin in a factory setting resulted in cough thresholds that were related to the extent of exposure on the job.<sup>35</sup> Workers exposed to capsaicin demonstrated a bimodal cough threshold response that was not observed in unexposed workers, who showed a unimodal response. Some exposed workers were much more sensitive to capsaicin than other exposed workers.<sup>35</sup>
- A condition known as “Hunan hand”, which is a form of contact dermatitis, has been noted in workers handling peppers.<sup>16,17</sup>

## Endocrine Disruption:

- No data were found regarding possible effects of capsaicin on endocrine systems.

## Carcinogenicity:

### Animals

- Several researchers reviewed evidence that capsaicin is carcinogenic in animals and found that the evidence was inconclusive.<sup>10,28,38</sup>

# CAPSAICIN

## TECHNICAL FACT SHEET

- Researchers have demonstrated that capsaicin is mutagenic and genotoxic in some studies using bacterial and rodent models<sup>36</sup> but not in others.<sup>37,38</sup>
- Researchers applied pure *trans*-capsaicin to the dorsal skin of mice weekly for 26 weeks at rates of 0.64, 1.28, or 2.56 mg/mouse/week.<sup>33</sup> No increase of neoplastic skin lesions or other abnormal skin growth was noted over control mice.<sup>33</sup>
- A lifetime diet containing 0.03% capsaicin fed to mice led to slight increases in benign tumors of the cecum.<sup>39</sup>
- Capsaicinoids fed to male mice at 1% of the diet for 79 weeks resulted in kidney lesions in male mice.<sup>40</sup> However, female mice fed a diet of 0.25% capsaicinoids for 83 weeks developed fewer tumors compared with controls. Hepatocellular neoplasms, or abnormal growths in the liver, also occurred less often in male and female mice fed greater concentrations of capsaicinoids in their diet.<sup>40</sup>

### Humans

- Neither the U.S. EPA nor the International Agency for Research on Cancer (IARC) has published a cancer rating for capsaicin. See the text box on **Cancer**.

**Cancer: Government agencies in the United States and abroad have developed programs to evaluate the potential for a chemical to cause cancer. Testing guidelines and classification systems vary. To learn more about the meaning of various cancer classification descriptors listed in this fact sheet, please visit the appropriate reference, or call NPIC.**

- Capsaicin has demonstrated mutagenic effects in some research<sup>46</sup> but not in other studies.<sup>26</sup> Impurities in the extract may be responsible for mutagenic effects because the studies that failed to demonstrate mutagenic effects used pure capsaicin.<sup>26,43</sup>
- People consuming 90-250 mg of capsaicin per day (in the form of jalapeno peppers) had a greater risk of gastric cancer compared with people who consumed less capsaicin (0-29.9 mg capsaicin per day).<sup>41</sup>
- Capsaicin exerted an anti-proliferative effect on human prostate cancer cells *in vitro* in a dose-dependent manner, completely halting proliferation at  $5 \times 10^{-4}$  mol/L.<sup>14</sup>

### Reproductive or Teratogenic Effects:

#### Animals

- Offspring of pregnant rats treated with 8% wet weight capsaicin via a 50 cm<sup>2</sup> dermal patch had delayed ossification in their metatarsal bones. This dose was above the NOEL for the mothers.<sup>42</sup> See the text box on **NOAEL, NOEL, LOAEL, and LOEL**.
- Rabbit fetuses were unaffected at all maternal doses tested although the dams showed signs of toxicity at the higher doses.<sup>42</sup> The authors concluded that *trans*-capsaicin should not be considered a developmental toxicant.<sup>42</sup>
- A review of studies that involved injecting capsaicin into subject animals documented developmental and reproductive effects such as reduced growth and contraception rates in some studies, but no effects in others.<sup>10</sup>

**NOAEL: No Observable Adverse Effect Level**  
**NOEL: No Observed Effect Level**  
**LOAEL: Lowest Observable Adverse Effect Level**  
**LOEL: Lowest Observed Effect Level**

#### Humans

- No human data were found on the teratogenic or reproductive effects of capsaicin.

### Fate in the Body:

#### Absorption

- Little absorption occurs across the skin.<sup>12</sup>
- Researchers applied 0.8 g of gel containing 0.075% of capsaicin to the skin of six human volunteers for 8 hours of exposure. They then calculated the average absorbed dose as 22.65  $\mu\text{g}/\text{cm}^2$  with a standard deviation of 3.73  $\mu\text{g}/\text{cm}^2$ .<sup>49</sup>
- Topical application of pure capsaicin to the skin of mice resulted in peak plasma concentrations occurring 4 to 12 hours later, and capsaicin was detectable in the blood 24 hours after dosing. Doses of 5.12 mg/mouse/week led to maximum plasma concentrations of 51.50 ng/mL in male and 84.80 ng/mL in female mice.<sup>33</sup>
- Capsaicin fed to rats was rapidly absorbed from the stomach, with 85% of a 3 mg dose absorbed within 3 hours.<sup>43</sup>

#### Distribution

- Rats injected intravenously accumulated capsaicin primarily in the brain and spinal cord 3 minutes after dosing, with lower levels found in the liver and blood. Ten minutes after dosing, the greatest concentrations remained in the spinal cord.<sup>44</sup>
- When the capsaicin was injected subcutaneously, rat blood concentrations peaked 5 hours following dosing, and brain and spinal cord tissue concentrations were somewhat lower. Kidneys contained the greatest concentrations and liver concentrations were low. Researchers detected capsaicin in all tissues 10 minutes following dosing but residues were undetectable in any tissues 17 hours later.<sup>44</sup> The researchers concluded that the low concentrations in the liver were due to metabolic breakdown of the capsaicin.
- Distribution data for capsaicin in humans were not found.

#### Metabolism

- Metabolism occurs primarily by the liver in the rat.<sup>45</sup>
- Metabolism of capsaicin by P450 enzymes may follow a number of pathways and produce a variety of metabolites, some of which may be associated with increased toxicity.<sup>46</sup>
- Research using human, rat, mouse, goat, and rabbit liver and lung microsomes demonstrated that metabolism rates were much greater in liver microsomes compared with lung microsomes for each species. Although the same metabolites were produced, the relative amounts of each metabolite were species-dependent.<sup>47</sup>
- No metabolism data were found for humans.

#### Excretion

- Less than 10% of an oral dose of capsaicin given to rats was excreted unchanged 48 hours after dosing.<sup>43</sup>
- No information on urinary/fecal metabolites and biomarkers was available.
- No data for human excretion were found.

### Medical Tests and Monitoring:

- Medical tests are not generally available to detect or quantify capsaicin in the human body.

### Environmental Fate:

#### Soil

- Capsaicin should not be very mobile in soil based on its chemical properties.<sup>7</sup> See the text box on **Half-life**.

The "half-life" is the time required for half of the compound to break down in the environment.

1 half-life = 50% remaining

2 half-lives = 25% remaining

3 half-lives = 12% remaining

4 half-lives = 6% remaining

5 half-lives = 3% remaining

Half-lives can vary widely based on environmental factors. The amount of chemical remaining after a half-life will always depend on the amount of the chemical originally applied. It should be noted that some chemicals may degrade into compounds of toxicological significance.

- Volatilization from either wet or dry soil is not expected based on the Henry's Law Constant and the vapor pressure, respectively.<sup>7</sup>
- Soil bacteria break capsaicin down into vanillylamine, which is further broken down into vanillin, vanillyl alcohol and vanillic acid.<sup>48</sup>
- Capsaicin applied to a compacted sandy loam with 2.5% organic matter and a pH of 7.9 did not move from the point of application over a 9-day period, with unspecified irrigation or rainfall.<sup>49</sup> Researchers concluded that soil compaction may have prevented movement.<sup>49</sup>
- Researchers studying persistence of capsicum oleoresin in a sandy loam soil estimated half-lives of 2 to 8 days.<sup>50</sup> Researchers suspected that the capsicum oleoresin leached from the test soil based on the color of the water collected at the base of the test bins.<sup>50</sup>

### Water

- Breakdown by photolysis or hydrolysis is not expected due to capsaicin's molecular structure and solubility.<sup>7</sup>
- Based on its  $K_{ow}$  and  $K_{oc}$  values, capsaicin is predicted to bind to the surface of sediments and suspended solids.<sup>7</sup> Therefore, the potential for groundwater contamination by capsaicin is low.
- Capsaicin has a low potential for volatilization based on its vapor pressure.<sup>7</sup>
- Laboratory and field data related to capsaicin's fate in water were not available.

### Air

- Due to its low vapor pressure, capsaicin will exist only in particulate form in the atmosphere, and be subject to wet and dry deposition processes.<sup>7</sup>
- Capsaicin's chemical structure suggests that photolysis will not be a major degradation pathway.<sup>7</sup>

### Plants

- Capsaicin is an extract of the fruits of the plants in the genus *Capsicum*.<sup>2</sup>
- No information was found regarding the transport, distribution, or metabolism of capsaicin in plants, nor were data available for the foliar half-life of capsaicin.

### Indoor

- No data were found on capsaicin's indoor persistence.

### Food Residue

- Capsaicin has been used in human cuisine as an ingredient and as a condiment for many years.<sup>16,17,41</sup>
- Capsaicin is exempted from the requirement of a residue tolerance.<sup>51</sup>

## Ecotoxicity Studies:

### Birds

- No toxicity information or field studies involving birds were found for capsaicin.
- Birds do not detect capsaicin. Although birds possess the TRVP1 receptor in their nerve cells, it is not activated by capsaicin as it is in mammals.<sup>20,21</sup>
- Ecologically, capsaicinoids may function to protect the seeds within the fruit.<sup>52</sup> They may also influence seed dispersal patterns by influencing gut retention times of the seeds, resulting in more successful plant reproduction.<sup>53</sup>

### Fish and Aquatic Life

- No studies were found evaluating the toxicity of capsaicin to aquatic life.
- In its Reregistration Eligibility Decision, the U.S. EPA waived the ecological effects studies that are typically required because it was determined that restrictive labeling would adequately protect aquatic species.<sup>2</sup>
- Based on its chemical characteristics, a moderate potential for bioconcentration is expected for capsaicin.<sup>7</sup>

### Terrestrial Invertebrates

- Capsaicin is toxic to bees and other beneficial insects.<sup>8</sup>
- No other information for terrestrial invertebrates was found.

### Regulatory Guidelines:

- No RfD exists for capsaicin. See the text box on **Reference Dose (RfD)** text box.
- No cancer classification has been made for capsaicin.

**Reference Dose (RfD):** The RfD is an estimate of the quantity of chemical that a person could be exposed to every day for the rest of their life with no appreciable risk of adverse health effects. The reference dose is typically measured in milligrams (mg) of chemical per kilogram (kg) of body weight per day.

U.S. Environmental Protection Agency. Office of Water. 2002 Edition of the Drinking Water Standards and Health Advisories. EPA 822-R-02-038.  
<http://www.epa.gov/ost/drinking/standards/dwstandards.pdf>

**Date Reviewed: October 2008**

### References

1. Pesticide Products. *Pest-Bank* [CD-ROM] 2007.
2. *Reregistration Eligibility Decision (RED) Capsaicin, Case 4018*; U.S. Environmental Protection Agency, Office of Prevention, Pesticides, and Toxic Substances, Office of Pesticide Programs, U.S. Government Printing Office: Washington, DC, 1992.
3. Flomenbaum, N. E.; Goldfrank, L. R.; Hoffman, R. S.; Howland, M. A.; Lewin, N. A.; Nelson, L. S. *Goldfrank's Toxicologic Emergencies*, 8th ed.; McGraw Hill: New York, 2006.
4. Lee, R. J.; Yolton, R. L.; Janin, M. L. *Personal Defense Sprays: Effects and Management of Ocular and Systemic Exposure*. <http://www.opt.pacificu.edu/ce/catalog/13541-SD/pepper.html> (accessed Dec 2003), updated 2006.
5. Azizan, A.; Blevins, R. D. Mutagenicity and antimutagenicity testing of six chemicals associated with the pungent properties of specific spices as revealed by the Ames *salmonella*/microsomal assay. *Arch. Environ. Contam. Toxicol.* 1995, 28, 248-258.
6. Tucker, S. P. Capsaicin and Dihydrocapsaicin: Method 5041. *NIOSH Manual of Analytical Methods*, 4th ed.; Schlecht, P. C.; O'Connor, P. F., Eds.; U.S. Department of Health and Human Services, Centers for Disease Control, National Institute for Occupational Safety and Health: Atlanta, 1996.
7. *Hazardous Substances Data Bank (HSDB), Capsaicin*; U.S. Department of Health and Human Services, National Institutes of Health, National Library of Medicine: Bethesda, MD, 2006.
8. Copping, L. G. *The BioPesticide Manual*, 2nd ed.; British Crop Protection Council: Farnham, UK, 2001; pp 171-172.
9. Xu, Q.; Barrios, C. A.; Cutright, T.; Newby, B. Z. Evaluation of toxicity of capsaicin and zosteric acid and their potential application as antifoulants. *Environ. Toxicol.* 2005, 20 (5), 467-474.
10. Johnson Jr., W. Final report on the safety assessment of *Capsicum annum* extract, *Capsicum annum* fruit extract, *Capsicum annum* resin, *Capsicum annum* fruit powder, *Capsicum frutescens* fruit, *Capsicum frutescens* fruit extract, *Capsicum frutescens* resin, and capsaicin. *Int. J. Toxicol.* 2007, 26 (Suppl. 1), 3-106.
11. Mason, L.; Moore, R. A.; Derry, S.; Edwards, J. E.; McQuay, H. J. Systematic review of topical capsaicin for the treatment of chronic pain. *Br. Med. J.* 2004, 328 (7446), 991-994.

# CAPSAICIN

## TECHNICAL FACT SHEET

12. Knotkova, H.; Pappagallo, M.; Szallasi, A. Capsaicin (TRPV1 agonist) therapy for pain relief: farewell or revival? *Clin. J. Pain* 2008, 24 (2), 143-154.
13. Pall, M. L.; Anderson, J. H. The vanilloid receptor as a putative target of diverse chemicals in multiple chemical sensitivity. *Arch. Environ. Health* 2004, 59 (7), 363-375.
14. Mori, A.; Lehmann, S.; O'Kelly, J.; Kumagai, T.; Desmond, J. C.; Pervan, M.; McBride, W. H.; Kizaki, M.; Koeffler, H. P. Capsaicin, a component of red peppers, inhibits the growth of androgen-independent, p53 mutant prostate cancer cells. *Cancer Res.* 2006, 66 (6), 3222-3229.
15. Reilly, C. A.; Taylor, J. L.; Lanza, D. L.; Carr, B. A.; Crouch, D. J.; Yost, G. S. Capsaicinoids Cause Inflammation and Epithelial Cell Death through Activation of Vanilloid Receptors. *Toxicol. Sci.* 2003, 73, 170-181.
16. Burnett, J. W. Capsicum Pepper Dermatitis. *Cutis* 1989, 43, 534.
17. Williams, S. R.; Clark, R. F.; Dunford, J. V. Contact Dermatitis Associated with Capsaicin: Hunan Hand Syndrome. *Ann. Emerg. Med.* 1995, 25, 713-715.
18. Antonious, G. F.; Meyer, J.; Snyder, J. C. Toxicity and repellency of hot pepper extracts to spider mite, *Tetranychus urticae* Koch. *J. Environ. Sci. Health B* 2006, 41, 1383-1391.
19. Gharat, L.; Szallasi, A. Medicinal chemistry of the vanilloid (Capsaicin) TRPV1 receptor: current knowledge and future perspectives. *Drug Develop. Res.* 2007, 68, 477-497.
20. Geisthövel, E.; Ludwig, O.; Simon, E. Capsaicin fails to produce disturbances of autonomic heat and cold defence in an avian species (*Anas platyrhynchos*). *Pflügers Arch.* 1986, 406, 343-350.
21. Jordt, S.-E.; Julius, D. Molecular basis for species-specific sensitivity to "hot" chili peppers. *Cell* 2002, 108, 421-430.
22. Saito, A.; Yamamoto, M. Acute Oral Toxicity of Capsaicin in Mice and Rats. *J. Toxicol. Sci.* 1996, 21, 195-200.
23. Glinsukon, T.; Stitmunnaithum, V.; Toskulkaeo, C.; Buranawuti, T.; Tangkrisanavinot, V. Acute toxicity of capsaicin in several animal species. *Toxicon* 1980, 18, 215-220.
24. Meister, R. T.; Sine, C., *Capsaicin*. Meister Media Worldwide: Willoughby, OH, 2007; Vol. 93.
25. Lewis Sr., R. J. *Sax's Dangerous Properties of Industrial Materials*, 10th ed.; John Wiley & Sons, Inc.: New York, 2000; p 702.
26. Chanda, S.; Erexon, G.; Raich, C.; Innes, D.; Stevenson, F.; Murli, H.; Bley, K. Genotoxicity studies with pure *trans*-capsaicin. *Mutat. Res.* 2004, 557, 85-97.
27. Gosselin, R. E.; Hodge, H. C.; Smith, R. P.; Gleason, M. N. *Clinical Toxicology of Commercial Products*, 4th ed.; The Williams and Wilkins Company: Baltimore, 1976; p 145.
28. Busker, R. W.; van Helden, H. P. M. Toxicologic Evaluation of Pepper Spray as a Possible Weapon for the Dutch Police Force. *Am. J. Forensic Med. Pathol.* 1998, 19 (4), 309-316.
29. Fuller, R. W. Pharmacology of inhaled capsaicin in humans. *Respir. Med.* 1991, 85 (Suppl. A), 31-34.
30. Collier, J. G.; Fuller, R. W. Capsaicin inhalation in man and the effects of sodium cromoglycate. *Br. J. Pharmac.* 1984, 81, 113-117.
31. Millqvist, E.; Ternesten-Hasseus, E.; Stahl, A.; Bende, M. Changes in levels of nerve growth factor in nasal secretions after capsaicin inhalation in patients with airway symptoms from scents and chemicals. *Environ. Health Perspect.* 2005, 13 (7), 849-852.
32. Miller, D. S. Review of oleoresin capsicum (pepper) sprays for self-defense against captive wildlife. *Zoo Biol.* 2001, 20, 389-398.
33. Philip, G.; Baroody, F. M.; Proud, D.; Naclerio, R. M.; Togias, A. G. The human nasal response to capsaicin. *J. Allergy Clin. Immunol.* 1994, 94, 1035-1045.
34. Tominack, R. L.; Spyker, D. A. Capsicum and Capsaicin - A Review: Case Report of the Use of Hot Peppers in Child Abuse. *Clin. Toxicol.* 1987, 25 (7), 591-601.

# CAPSAICIN

## TECHNICAL FACT SHEET

35. Jang, J. J.; Devor, D. E.; Logsdon, D. L.; Ward, J. M. A 4-Week Feeding Study of Ground Red Chilli (*Capsicum Annuum*) in Male B6C3F<sub>1</sub> Mice. *Food Chem. Toxicol.* 1992, 30 (9), 783-787.
36. Lee, S. O. Studies on the influence of diets and lipotropic substances upon the various organs and metabolic changes in rabbits on long term feeding with red pepper. *Korean J. Intern. Med.* 1963, 6 (7), 383-395.
37. Chanda, S.; Erexon, G.; Frost, D.; Babbar, S.; Burlew, J.-A.; Bley, K. 26-week dermal oncogenicity study evaluating pure trans-capsaicin in Tg.AC hemizygous mice (FBV/N). *Intern. J. Toxicol.* 2007, 26, 123-133.
38. McMahon, S. B.; Lewin, G.; Bloom, S. R. The consequences of long-term topical capsaicin application in the rat. *Pain* 1991, 44, 301-310.
39. *R.E.D. Facts Capsaicin*; U.S. Environmental Protection Agency, Office of Prevention, Pesticides, and Toxic Substances, Office of Pesticide Programs, U.S. Government Printing Office: Washington, DC, 1992.
40. Blanc, P.; Liu, D.; Juarez, C.; Boushey, H. A. Cough in Hot Pepper Workers. *Chest* 1991, 99, 27-32.
41. Marques, S.; Oliveira, N. G.; Chaveca, T.; Rueff, J. Micronuclei and sister chromatid exchanges induced by capsaicin in human lymphocytes. *Mutat. Res.* 2002, 517, 39-46.
42. Proudlock, R.; Thompson, C.; Longstaff, E. Examination of the potential genotoxicity of pure capsaicin in bacterial mutation, chromosome aberration, and rodent micronucleus tests. *Environ. Mol. Mutagen.* 2004, 44, 441-447.
43. Toth, B.; Gannett, P. Carcinogenicity of lifelong administration of capsaicin of hot pepper in mice. *In Vivo* 1992, 6, 59-63.
44. Akagi, A.; Sano, N.; Uehara, H.; Minami, T.; Otsuka, H.; Izumi, K. Non-carcinogenicity of capsaicinoids in B6C3F<sub>1</sub> mice. *Food Chem. Toxicol.* 1998, 36, 1065-1071.
45. Richeux, R.; Cascante, M.; Ennamany, R.; Sabureau, D.; Creppy, E. E. Cytotoxicity and genotoxicity of capsaicin in human neuroblastoma cells SHSY-5Y. *Arch. Toxicol.* 1999, 73, 403-409.
46. Lopez-Carrillo, L.; Lopez-Cervantes, M.; Robles-Diaz, G.; Ramirez-Espitia, A.; Mohar-Betancourt, A.; Meneses-Garcia, A.; Lopez-Vidal, Y.; Blair, A. Capsaicin consumption, *Helicobacter pylori* positivity and gastric cancer in Mexico. *Intern. J. Cancer* 2003, 106, 277-282.
47. Chanda, S.; Sharper, V. A.; Hoberman, A. M.; Bley, K. Developmental toxicity study of pure trans-capsaicin in rats and rabbits. *Intern. J. Toxicol.* 2006, 25, 205-217.

# CAPSAICIN

## TECHNICAL FACT SHEET

48. Fang, J.; Tsai, M.; Huang, Y.; Wu, P.; Tsai, Y. Percutaneous absorption and skin erythema: quantification of capsaicin and its synthetic derivatives from gels incorporated with benzalkonium chloride by using non-invasive bioengineering methods. *Drug Develop. Res.* 1997, 40, 56-67.
49. Kawada, T.; Suzuki, T.; Takahashi, M.; Iwai, K. Gastrointestinal Absorption and metabolism of Capsaicin and Dihydrocapsaicin in Rats. *Toxicol. Appl. Pharmacol.* 1984, 72, 449-456.
50. Saria, A.; Skofitsch, G.; Lembeck, F. Distribution of capsaicin in rat tissues after systemic administration. *J. Pharm. Pharmacol.* 1982, 34, 273-275.
51. Donnerer, J.; Amann, R.; Schuligoi, R.; Lembeck, F. Absorption and metabolism of capsaicinoids following intragastric administration in rats. *Naunyn Schmiedeberg's Arch. Pharmacol.* 1990, 342, 357-361.
52. Reilly, C. A.; Yost, G. S. Metabolism of capsaicinoids by P450 enzymes: a review of recent findings on reaction mechanisms, bio-activation, and detoxification processes. *Drug Metab. Rev.* 2006, 38, 685-706.
53. Reilly, C. A.; Ehlhardt, W. J.; Jackson, D. A.; Kulanthaivel, P.; Mutlib, A. E.; Espina, R. J.; Moody, D. E.; Crouch, D. J.; Yost, G. S. Metabolism of capsaicin by cytochrome P450 produces novel dehydrogenated metabolites and decreases cytotoxicity to lung and liver cells. *Chem. Res. Toxicol.* 2003, 16, 336-349.
54. Onozaki, H.; Asai, H.; Isshiki, S.; Esaki, H. Bacterial metabolism of vanillylamine and vanilline. *Hakkokagu Kaishi* 1986, 64, 425-430.
55. Sterner, R. T.; Kimball, B. A. Slow migration of capsicum oleoresin in a sandy loam soil. *Int. Biodeterior. Biodegradation* 2005, 56, 188-191.
56. Sterner, R. T.; Ames, A. D.; Kimball, B. A. Persistence of capsicum oleoresin in soil. *Int. Biodeterior. Biodegradation* 2002, 49, 145-149.
57. Meat Meal and Red Pepper; Exemption from the Requirement of a Tolerance. *Fed. Regist.* March 27, 1996, 61 (60), 13424-13426.
58. Tewksbury, J. J.; Reagan, K. M.; Machnicki, N. J.; Carlo, T. A.; Haak, D. C.; Calderon Penaloza, A. L.; Levey, D. J. Evolutionary ecology of pungency in wild chilies. *Proc. Natl. Acad. Sci. U.S.A.* 2008, 105 (33), 11808-11811.
59. Tewksbury, J. J.; Levey, D. J.; Huizinga, M.; Haak, D. C.; Traveset, A. Costs and benefits of capsaicin-mediated control of gut retention in dispersers of wild chilies. *Ecology* 2008, 89 (1), 107-117.