

NATURAL HEALTH PRODUCT

CAYENNE – *CAPSICUM ANNUUM* L.

This monograph is intended to serve as a guide to industry for the preparation of Product Licence Applications (PLAs) and labels for natural health product market authorization. It is not intended to be a comprehensive review of the medicinal ingredient.

Notes

- ▶ Text in parentheses is additional optional information which can be included on the PLA and product label at the applicant's discretion.
- ▶ The solidus (/) indicates that the terms and/or the statements are synonymous. Either term or statement may be selected by the applicant.

Date September 27, 2013

Proper name(s)

Capsicum annuum L. (Solanaceae) (USDA 2010)

Common name(s)

- ▶ Cayenne (McGuffin et al. 2000)
- ▶ Chili pepper (Blumenthal et al. 2000)
- ▶ Paprika (Blumenthal et al. 2000)
- ▶ Red pepper (Blumenthal et al. 2000)

Source material(s)

Fruit (Bradley 2006; Felter and Lloyd 1983 [1898])

Route(s) of administration

- ▶ Oral
- ▶ Topical

Dosage form(s)

- ▶ The acceptable pharmaceutical dosage forms include, but are not limited to capsules, chewables (e.g. gummies, tablets), liquids, powders, strips or tablets.

- ▶ Those pharmaceutical dosage forms suited to topical administration.
- ▶ This monograph is not intended to include foods or food-like dosage forms such as bars, chewing gums or beverages.

Use(s) or Purpose(s) Statement(s) to the effect of

ORAL

- ▶ Traditionally used in Herbal Medicine to aid digestion (Bradley 2006; Ellingwood 1983 [1919]; Felter and Lloyd 1983 [1898]).
- ▶ Traditionally used in Herbal Medicine to help support peripheral circulation (Bradley 2006; Ellingwood 1983 [1919]; Wren 1907).

TOPICAL

- ▶ Traditionally used in Herbal Medicine (as a rubefacient/counterirritant) (Blumenthal et al. 2000; BHP 1983; Ellingwood 1983 [1919]; Felter 1983 [1922]) to help relieve the symptoms of rheumatism (Lust 1987; BPC 1934) and/or muscle and joint pain (BHP 1983; Felter and Lloyd 1983 [1898]).
- ▶ Used for the temporary relief of muscle and joint pain associated with rheumatoid arthritis or osteoarthritis, and pain of tendons and ligaments (McCarthy et al. 1992; Deal et al. 1991).
- ▶ Used to relieve cutaneous pain (Hautkappe et al. 1998) associated with conditions such as post-herpetic neuralgia (Watson et al. 1993; Bernstein et al. 1989) and diabetic neuropathy (Tandan et al. 1992; Scheffler et al. 1991; The Capsaicin Study Group 1991).

Table 1: Recommended Conditions of Use	Oral	Topical	
		Traditional	Non-Traditional
Dose (Adults ≥ 18 years)	Preparations equivalent to 15-650 mg dried fruit, per day (Bradley 2006; Blumenthal 2003; Hoffmann 2003; Lust 1987; Felter and Lloyd 1983 [1898]; Grieve 1971 [1931])	Preparations equivalent to 20-70 mg dried fruit, per day (BHP 1983)	<p><i>Relief muscle, joint, tendons and ligaments pain</i> Preparations equivalent to 0.025-0.075% capsaicin (McCarthy et al. 1992; Deal et al. 1991)</p> <p><i>Relief of cutaneous pain</i> Preparations equivalent to 0.075% capsaicin (Watson 1993; Tandan et al. 1992; Scheffler et al. 1991; The Capsaicin Study Group 1991; Bernstein et al. 1989)</p>
Directions of Use	No statement required.	Apply as needed.	Apply thinly and evenly to affected area up to 3-4 times



			per day. Rub and/or massage into skin until solution vanishes (US FDA 1979).
Duration of Use	No statement required.	No statement required.	Use for a minimum of 1-4 weeks to see beneficial effects (Berardi 2002; McCarthy et al. 1992; Deal et al. 1991).
Caution(s) and warning(s)	Keep out of the reach of children.		
	If overdose or accidental ingestion occurs, call a Poison Control Center immediately (CPS 2008).		
	If symptoms persist or worsen, consult a health care practitioner. If you are pregnant or breastfeeding, consult a health care practitioner prior to use (Bradley 2006; Boon and Smith 2004). If you have stomach ulcers or inflammation, consult a health care practitioner prior to use (Brinker 2001).	For external use only. Avoid contact with the eyes and mucous membranes (US FDA 1983). Do not apply to wounds or damaged skin (US FDA 1983). Do not tightly bandage (US FDA 1983). Do not apply with external heat, such as an electric heating pad, as this may result in excessive skin irritation or skin burn (Pray 2006; APhA 2002).	
Contraindication(s)	No statement required.		
Known adverse reaction(s)	No statement required.	Headache (McCleane 2000), erythema, redness, rashes and/or burning discomfort, and hypersensitivity have been known to occur (Martindale 2010; Zhang et al. 2008; APhA 2002; McCleane 2000, Hoffman 2003).	

Note

- ▶ A claim for traditional use must include the term “Herbal Medicine”.
- ▶ Refer to Appendix 1 for examples of dosage preparations and directions for use, according to the cited references. The purpose of Appendix 1 is to provide guidance to industry.

Non-medicinal ingredients

Must be chosen from the current NHPD *Natural Health Products Ingredients Database* (NHPID) and must meet the limitations outlined in the database.



Storage conditions

Statement(s) to the effect of

No statement required.

Specifications

- ▶ The finished product specifications must be established in accordance with the requirements described in the NHPD *Quality of Natural Health Products Guide*.
- ▶ The medicinal ingredient must comply with the requirements outlined in the *Natural Health Products Ingredients Database* (NHPID).

References cited

APhA 2002: Berardi RR, DeSimone EM, Newton GGD, Oszko MA, Popovich NG, Rollins CJ, Shimp LA, Tietze KJ, editors. Handbook of Nonprescription Drugs: An interactive approach to self-care. 13th edition. Washington (DC): American Pharmaceutical Association; 2002.

Bernstein JE, Korman NJ, Bickers DR, Dahl MV, Millikan LE. Topical capsaicin treatment of chronic postherpetic neuralgia. *Journal of the American Academy of Dermatology* 1989;21(2):265-270.

BHP 1983: British Herbal Pharmacopoeia. Cowling (GB): British Herbal Medical Association; 1983.

Blumenthal M. ABC Clinical Guide to Herbs. New York (NY): Theime; 2003.

Blumenthal M, Goldberg A, Brinkmann J, editors. Herbal Medicine: Expanded Commission E Monographs. Boston (MA): Integrative Medicine Communications; 2000.

Boon H, Smith MJ. The Complete Natural Medicine Guide to the 50 Most Common Medicinal Herbs, 2nd edition. Toronto (ON): Robert Rose Inc; 2004.

BPC 1934: The British Pharmaceutical Codex, 1934: An imperial dispensatory for the use of medical practitioners and pharmacists. London (GB): The Pharmaceutical Press; 1934.

Bradley PR, editor. British Herbal Compendium: A Handbook of Scientific Information on Widely Used Plant Drugs, Volume 2. Bournemouth (GB): British Herbal Medicine Association; 2006.

Brinker F. Herb Contraindications and Drug Interactions, 3rd edition. Sandy (OR): Eclectic Medical Publications; 2001.



CPhA 1996: Carruthers-Czyzewski P, editor. Non-Prescription Drug Reference for Health Professionals. First Edition. Ottawa (ON): Canadian Pharmaceutical Association; 1996.

CPS 2008: Repchinsky C, Welbanks L, Bhalla A, Fortin K, Jarvis B, Jovaisas B, Acharya S. Compendium of Pharmaceutical Specialties. Ottawa (ON): Canadian Pharmacists Association; 2008.

Deal CL, Schnitzer TJ, Lipstein E, Seibold JR, Stevens RM, Levy MD, Albert D, Renold F. Treatment of arthritis with topical capsaicin: a double-blind trial. *Clinical Therapeutics* 1991;13(3):383-395.

Ellingwood F. *American Materia Medica, Therapeutics and Pharmacognosy*. Sandy (OR): Eclectic Medical Publications; 1983 [Reprint of 1919 original].

Felter HW. *The Eclectic Materia Medica, Pharmacology and Therapeutics*. Sandy (OR): Eclectic Medical Publications; 1983 [Reprint of 1922 original].

Felter HW, Lloyd JU. *King's American Dispensatory, Volume 1*, 18th edition. Sandy (OR): Eclectic Medical Publications; 1983 [Reprint of 1898 original].

Grieve M. *A Modern Herbal, Volume 1*. New York (NY): Dover Publications; 1971 [Reprint of 1931 Harcourt, Brace & Company publication].

Hautkappe M, Roizen MF, Toledano A, Roth S, Jeffries JA, Ostermeier AM. Review of the effectiveness of capsaicin for painful cutaneous disorders and neural dysfunction. *The Clinical Journal of Pain* 1998;14(2):97-106.

Hoffman D. *Medical Herbalism: The Science and Practice of Herbal Medicine*. Rochester (VT): Healing Arts Press; 2003.

Lust J. *The Herb Book*. New York (NY): Bantam Books Incorporated, published by arrangement with Benedict Lust Publications; 1987.

Martindale 2010: Sweetman SC, editor. *Martindale: The Complete Drug Reference*. London (GB): Pharmaceutical Press; Copyright 1933-2010. [*Capsicum*: Last modified: 2010 Mai 21; Accessed 2013 May 5].

McCarthy GM, McCarty DJ. Effect of topical capsaicin in the therapy of painful osteoarthritis of the hands. *Journal of Rheumatology* 1992;19(4):604-607.

McGuffin M, Kartesz JT, Leung AY, Tucker AO, editors. *Herbs of Commerce*, 2nd edition. Silver Spring (MD): American Herbal Products Association; 2000.

McCleane G. Topical application of doxepin hydrochloride, capsaicin and a combination of both produces analgesia in chronic human neuropathic pain: a randomized, double-blind, placebo-controlled study. *British Journal of Clinical Pharmacology* 2000; 49:574-579.



Pray WS. Non-Prescription Product Therapeutics. 2nd edition. New York (NY): Lippincott Williams & Wilkins; 2006.

Scheffler NM, Sheitel PL, Lipton MN. Treatment of painful diabetic neuropathy with capsaicin 0.075%. *Journal of the American Podiatric Medical Association* 1991;81(6):288-293.

Tandan R, Lewis GA, Krusinski PB, Badger GB, Fries TJ. Topical capsaicin in painful diabetic neuropathy. Controlled study with long-term follow-up. *Diabetes Care* 1992;15(1):8-14.

The Capsaicin Study Group. Treatment of painful diabetic neuropathy with topical capsaicin. A multicenter, double-blind, vehicle-controlled study. *Archives of Internal Medicine* 1991;151(11):2225-2229.

USDA 2008: United States Department of Agriculture, Agricultural Research Service, National Genetic Resources Program. Germplasm Resources Information Network (GRIN). *Capsicum Annuum*. National Germplasm Resources Laboratory, Beltsville (MD). [Accessed 2008-01-07]. Available at: http://www.ars-grin.gov/cgi-bin/npgs/html/tax_search.pl

US FDA 1983: United States Food and Drug Administration. External Analgesics Drug Products for Over-the-Counter Human Use; Tentative Final Monograph [online]. Federal Register, Volume 48, Number 27, February 8, 1983, Proposed Rules. Rockville (MD): United States Department of Health and Human Services, U.S. Food and Drug Administration. [Accessed 2013 May 8]. Available from: http://www.fda.gov/ohrms/DOCKETS/ac/05/briefing/2005-4099B1_03_FDA-Tab3.pdf

US FDA 1979: The USA Department of Health and Human Services: Food and Drug Administration. 21 CHR Part 348. External analgesics drug products for over-the-counter human use: establishment of a monograph and notice of proposed rulemaking, 1979. [Accessed 2013 May 8]. Available from: <http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Over-the-CounterOTCDrugs/StatusofOTCRulemakings/UCM077916.pdf>

Watson CP, Tyler KL, Bickers DR, Millikan LE, Smith S, Coleman E. A randomized vehicle-controlled study of topical capsaicin in the treatment of post-herpetic neuralgia. *Clinical Therapeutics* 1993;15(3):510-526.

Wren RC. *Potter's Cyclopedia of Botanical Drugs and Preparations*. London (GB): Potter and Clark; 1907.

Zhang W, Moskowitz, RW, Nuki G, Abramson S, Altman RD, Arden N, Bierma-Zeinstra S, Brandt KD, Croft P, Doherty M, Dougados M, Hochberg M, Hunter DJ, Kwoh K, Lohmander LS, Tugwell P. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence--based, expert consensus guidelines. *Osteoarthritis and Cartilage* 2008;16:137-162.



References reviewed

Ahuja KDK, Robertson IK, Geraghty DP, Ball MJ. The effect of 4-week chilli supplementation on metabolic and arterial function in humans. *European Journal of Clinical Nutrition* 2007;61(3):326–333.

Barnes J, Anderson LA, Philipson JD. *Herbal Medicines*, 3rd edition. London (GB): The Pharmaceutical Press; 2007.

Bernstein JE, Bickers DR, Dahl MY, Roshal JY. Treatment of chronic post-herpetic neuralgia with topical capsaicin. A preliminary study. *Journal of the American Academy of Dermatology* 1987;17(1):93-96.

Bortolotti M, Coccia G, Grossi G, Miglioli M. Treatment of functional dyspepsia with red pepper. *Alimentary Pharmacology and Therapeutics* 2002;16(6):1075-1082.

Charkoudian N, Fromy B, Saumet JL. Reflex control of the cutaneous circulation after acute and chronic local capsaicin. *Journal of applied physiology* 2001;90(5):1860-1864.

Deng PY, Li YJ. Calcitonin gene-related peptide and hypertension. *Peptides* 2005;26(9):1676-1685.

Desai HG, Venugopalan K, Anita FP. Effect of red chilli powder on the DNA content of gastric aspirates. *Gut* 1973;14:974-976.

Ferrell WR, Wong BB, Lockhart JC, Ramsay JE. Gender differences in regional cutaneous microcirculatory responses to capsaicin. *Fundamentals of Clinical Pharmacology* 2004;18(2):195-200.

Gupta S, Lozano-Cuenca J, Villalón CM, de Vries R, Garrelds IM, Avezaat CJ, van Kats JP, Saxena PR, MaassenVanDenBrink A. Pharmacological characterisation of capsaicin induced relaxations in human and porcine isolated arteries. *Naunyn-Schmiedeberg's archives of pharmacology* 2007;375(1):29–38.

Heck AM, DeWitt BA, Lukes AL. Potential interactions between alternative therapies and warfarin. *American Journal of Health-System Pharmacy* 2000;57(13):1221-1227.

Helme RD, McKernan S. Neurogenic flare responses following topical application of capsaicin in humans. *Annals of Neurology* 1985;18(4):505-509.

Hogaboam CM, Wallace JL. Inhibition of platelet aggregation by capsaicin. An effect unrelated to actions in sensory afferent neurons. *European Journal of Pharmacology* 1991;202(1):129-131.

Johnson W. Final report on the safety assessment of *Capsicum Annuum* extract, *Capsicum Annuum* fruit extract, *Capsicum Annuum* Resin, *Capsicum Annuum* fruit powder, *Capsicum*



Frutescens resin, and Capsaicin. *International Journal of Toxicology* 2007;26(Supplement 1):3-106.

Joliffe VA, Anand P, Kidd BL. Assessment of cutaneous sensory and autonomic axon reflexes in rheumatoid arthritis. *Annals of the Rheumatic Diseases* 1995;54(4):251-255.

Kumar N, Vij JC, Sarin SK, Anand BS. Do chillies influence healing of duodenal ulcer? *British Medical Journal* 1984;288(6433):1803-1804.

Lee YS, Kho HS, Kim YK, Chung SC. Influence of topical capsaicin on facial sensitivity in response to experimental pain. *Journal of Oral Rehabilitation* 2007;34(1):9-14.

Matucci-Cerinic M, Marabini S, Jantsch S, Cagnoni M, Partsch G. Effects of capsaicin on the metabolism of rheumatoid arthritis synoviocytes in vitro. *Annals of the Rheumatic Diseases* 1990;49(8):598-602.

Morris VH, Cruwys SC, Kidd BL. Characterization of capsaicin induced mechanical hyperalgesia as a marker for altered nociceptive processing in patients with rheumatoid arthritis. *Pain* 1997;71(2):179-186.

Rodriguez-Stanley S, Collings KL, Robinson M, Owen W, Miner PB. The effects of capsaicin on reflux, gastric emptying and dyspepsia. *Alimentary Pharmacology and Therapeutics* 2000;14(1):129-134.

Satyanarayana MN. Capsaicin and gastric ulcers. *Critical Reviews of Food Science and Nutrition* 2006;46(4):275-328.

Schnitzer TJ, Morton C, Coker S, Flynn P. Effectiveness of reduced applications of topical capsaicin (0.025%) cream in osteoarthritis. *Arthritis and Rheumatism* 1992;35:S132.

Shalansky S, Lynd L, Richardson K, Ingaszewski A, Kerr C. Risk of warfarin-related bleeding events and supratherapeutic international normalized ratios associated with complementary and alternative medicine: a longitudinal analysis. *Pharmacotherapy* 2007;27(9):1237-1247.

Simone DA, Ochoa J. Early and late effects of prolonged topical capsaicin on cutaneous sensibility and neurogenic vasodilation in humans. *Pain* 1991;47(3):285-294.

Tsuchiya H. Biphasic membrane effects of capsaicin, an active component in capsicum species. *Journal of Ethnopharmacology* 2001;75(2-3):295-299.

Van der Schueren BJ, de Hoon JN, Vanmolkot FH, Van Hecken A, Depre M, Kane SA, De Lepeleire I, Sinclair SR. Reproducibility of the capsaicin-induced dermal blood flow response as assessed by laser Doppler perfusion imaging. *British Journal of Clinical Pharmacology* 2007;64(5):580-590.



Visudhiphan S, Poolsuppasit S, Piboonnukarintr O, Tumliang S. The relationship between high fibrinolytic activity and daily capsicum ingestion in Thais. *American Journal of Clinical Nutrition* 1982;35(6):1452-1458.

Wang DH. The vanilloid receptor and hypertension. *Acta Pharmacologica Sinica* 2005;26(3):286–294.

Westerterp-Plantenga MS, Smeets A, Lejeune MPG. Sensory and gastrointestinal satiety effects of capsaicin on food intake. *International Journal of Obesity* 2005;29(6):682–688.

Willams SR, Clark RF, Dunford JV. Contact dermatitis associated with capsaicin: Human hand syndrome. *Annals of Emergency Medicine* 1995;25(5):713-715.

Yoshioka M, St-Pierre S, Drapeau V, Dionne I, Doucer E, Suzuki M, Tremblay A. Effects of red pepper on appetite and energy intake. *British Journal of Nutrition* 1999;82(2):115–123.



Appendix 1 Examples of dosage preparations and directions for use

ORAL

Dried fruit

- ▶ 30-120 mg, 3 times per day (Bradley 2006)
- ▶ 120-145 mg, 2-3 times per day (Blumenthal 2003)
- ▶ 65-200 mg, per day (Lust 1987)
- ▶ 65-400 mg, per day (Felter and Lloyd 1983 [1898])
- ▶ 65-650 mg, per day (Grieve 1971 [1931])

Direction for use: Take with meals (Blumenthal 2003).

Infusion

- ▶ 140-280 mg dried fruit, per day (Blumenthal 2003; Hoffmann 2003; Lust 1987)
- ▶ 400 mg dried fruit, per day (Grieve 1971 [1931])

Tincture

15-50 mg dried equivalent, 3 times per day (1:20, 60% alcohol, 0.3-1 ml) (Bradley 2006)

TOPICAL

Tincture

20-70 mg dried equivalent, per day (1:3, 60% alcohol, 0.06-0.2 ml) (BHP 1983)

Directions for use: Apply as needed.

Other preparations

- ▶ 0.025% capsaicin cream (Deal et al. 1991)
- ▶ 0.075% capsaicin cream (Watson 1993; McCarthy et al. 1992; Tandan et al. 1992; Scheffler et al. 1991; The Capsaicin Study Group 1991; Bernstein et al. 1989)

Directions for use: Apply 4 times per day (Watson 1993; McCarthy et al. 1992; Tandan et al. 1992; Deal et al. 1991; Scheffler et al. 1991; The Capsaicin Study Group 1991; Bernstein et al. 1989).