

NATURAL HEALTH PRODUCT

CAYENNE – *CAPSICUM ANNUUM*/CAPSAICIN Topical

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 statements are synonymous. Either term or statement may be selected by the applicant.

Date March 19, 2021

Proper name(s), Common name(s), Source information

Table 1. Proper name(s), Common name(s), Source information

Proper name(s)	Common name(s)	Source information			
		Source ingredient(s)	Source material(s)	Part(s)	Preparation(s)
<i>Capsicum annuum</i>	<ul style="list-style-type: none"> • Cayenne • Cayenne pepper • Chili pepper • Paprika • Red pepper 	N/A	<i>Capsicum annuum</i>	Fruit	Dried
<ul style="list-style-type: none"> • (6E)-N-[(4-Hydroxy-3-methoxyphenyl)methyl]-8-methyl-6-nonenamide • (E)-8-Methyl-N-vanillyl-6-nonenamide 	Capsaicin	Capsaicin ¹	<i>Capsicum annuum</i>	Fruit	N/A
		Capsaicin ²	N/A	N/A	N/A

References: Proper names: USDA 2018; USP 36 2013, NLM 2012; Common names: Blumenthal et al. 2000, McGuffin et al. 2000, NLM 2012; Source information: USP 36 2013, Bradley 2006, Felter and Lloyd 1983.

¹ Isolate

² Synthetic



Route of administration

Topical

Dosage form(s)

The following dosage forms are acceptable when used according to the requirements indicated in this monograph: Cream; Fluid extract; Gel; Liniment; Liquid; Lotion; Oil; Ointment; Salve; Solution; Tincture; Topical liquid.

Use(s) or Purpose(s)

Cayenne powder or extracts

Used in Herbal Medicine (as a rubefacient/counterirritant) to help (temporarily) relieve the symptoms of rheumatism and/or muscle and joint pain (Blumenthal et al. 2000; Lust 1987; BHP 1983; Ellingwood 1983; Felter 1983; Felter and Lloyd 1983; BPC 1934).

Cayenne extracts or Capsaicin (isolate; synthetic)

- ▶ 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 skin (cutaneous) pain associated with conditions such as post-herpetic neuralgia and/or diabetic neuropathy (Hautkappe et al. 1998; Watson et al. 1993; Tandan et al. 1992; Scheffler et al. 1991; The Capsaicin Study Group 1991; Bernstein et al. 1989).

Dose(s)

Subpopulation(s)

Adults 18 years and older

Quantity(ies)

Cayenne powder or extracts

Herbal Medicine use

Methods of preparation: Powdered standardized, Standardised Extracts (Dry extract, Tincture, Fluid extract, Decoction, Infusion)

The percentage of the medicinal ingredient in the product formulation and the percentage of the potency constituent, capsaicin, in the medicinal ingredient are not restricted as long as the concentration of capsaicin in the finished product is equivalent to:



0.01-0.05% capsaicin (BHP 1983)¹

Cayenne extracts

Relief of muscle, joint, tendons and ligaments pain

Methods of preparation: Standardised Extracts (Dry extract, Tincture, Fluid extract, Decoction, Infusion)

The percentage of the medicinal ingredient in the product formulation and the percentage of the potency constituent, capsaicin, in the medicinal ingredient are not restricted as long as the concentration of capsaicin in the finished product is equivalent to:

0.025-0.075% capsaicin (McCarthy et al. 1992; Deal et al. 1991)¹

Relief of skin (cutaneous) pain

Methods of preparation: Standardised Extracts (Dry extract, Tincture, Fluid extract, Decoction, Infusion)

The percentage of the medicinal ingredient in the product formulation and the percentage of the potency constituent, capsaicin, in the medicinal ingredient are not restricted as long as the concentration of capsaicin in the finished product is equivalent to:

0.075% capsaicin (Watson1993; Tandan et al. 1992; Scheffler et al. 1991; The Capsaicin Study Group 1991; Bernstein et al. 1989)¹

Capsaicin (isolate; synthetic)

Relief of muscle, joint, tendons and ligaments pain

Methods of preparation: Isolate, Synthetic

0.025-0.075% capsaicin (McCarthy et al. 1992; Deal et al. 1991)

Relief of skin (cutaneous) pain

Methods of preparation: Isolate, Synthetic

0.075% capsaicin (Watson1993; Tandan et al. 1992; Scheffler et al. 1991; The Capsaicin Study Group 1991; Bernstein et al. 1989)

Note:

¹ For standardized Cayenne fruit powder or extract, the percentage of capsaicin in the finished product should also be included on the product label.

e.g.

Cayenne extract (*Capsicum annuum* - fruit) 30%, standardized to 0.1% capsaicin is equivalent to

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0.03 % capsaicin in the finished product

Direction(s) for use

Herbal Medicine use

Apply as needed.

Other uses

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).

Combination rule

No permitted combinations. This monograph only supports single ingredient products.

Duration(s) of use

Herbal Medicine use

No statement required.

Other uses

Use for at least 1-4 weeks to see beneficial effects (Berardi 2002; McCarthy et al. 1992; Deal et al.1991).

Risk information

Caution(s) and warning(s)

All products

- ▶ Keep out of the reach of children.
- ▶ Call a Poison Control Center immediately if overdose or accidental ingestion occurs (CPS 2008).
- ▶ 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; Berardi 2002).

Contraindication(s)

No statement required.

Known adverse reaction(s)

All products

Stop use if headache, erythema, redness, rashes, burning discomfort or hypersensitivity occurs (Martindale 2010; Zhang et al. 2008; Hoffman 2003; Berardi 2002; McCleane 2000).

Non-medicinal ingredients

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

Storage conditions

No statement required.

Specifications

- ▶ The finished product specifications must be established in accordance with the requirements described in the Natural and Non-prescription Health Products Directorate (NNHPD) Quality of Natural Health Products Guide.
- ▶ The medicinal ingredient must comply with the requirements outlined in the NHPID.

References cited

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



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.

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 Dispensary, Volume 1, 18th edition. Sandy (OR): Eclectic Medical Publications; 1983 [Reprint of 1898 original].

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.

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.

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



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

NLM 2012: National Institute of Medicine. ChemIDplus advanced [Internet]. Search term: "Capsaicin"; Bethesda (MD): Specialized Information Services, United States National Library of Medicine, National Institutes of Health, United States Department of Health & Human Services. [Accessed 2017 January 30]. Available from: <http://chem.sis.nlm.nih.gov/chemidplus/>

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 2018: 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 2018 August 15]. 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 2018 August 15]. Available from: <http://cdn.loc.gov/service/ll/fedreg/fr048/fr048027/fr048027.pdf#page=138>

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 2018 August 15]. Available from: <http://cdn.loc.gov/service/ll/fedreg/fr044/fr044234/fr044234.pdf#page=168>

USP 36: United States Pharmacopeia and the National Formulary (USP 36 - NF 31). Rockville (MD): The United States Pharmacopeial Convention; 2013.

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

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.