Cayenne

***Capsicum* spp.**

Capsicum annuum L. var. *annuum*; C. *annuum* L. var. *glabriusculum* (Dunal) Heiser & Pickersgill [syn. C. *frutescens* L.]; C. *baccatum* L.; C. *chinense* Jacq.

[Fam. *Solanaceae*]

Overview

Cayenne is marketed in the U.S. as a food, spice, and dietary supplement in tablets, capsules, and occasionally as a tincture. Common names for cayenne include cayenne pepper, chili pepper, paprika, red pepper, tabasco pepper, bird pepper, African bird pepper, piquin, aji pepper, Brown's pepper, Peruvian pepper, piris, habañero pepper, and bonnet pepper. Cayenne is one of the fastest growing botanical imports, accounting for approximately 12% of the total annual value of U.S. spice imports. New Mexico alone produces approximately 100 million pounds of dried peppers annually. Twenty-three percent of natural food store consumers purchased cayenne at least once during the first half of 1999. Preparations made from the oleoresin in cayenne, and the oleoresin's isolated constituent capsaicin, are used in topical, over-the-counter (OTC) drug products. Capsicum oleoresin topical analgesic lotions and creams, containing the pure compound capsaicin, are available OTC in three strengths (0.025%, 0.075%, and 0.25%) for the following uses: inflammation and pain due to shingles, pain associated with postherpetic neuralgia, rheumatoid arthritis, osteoarthritis, diabetic neuropathy, and post-surgical pain. Other off-label uses for these lotions and creams are to relieve pain associated with psoriasis, chronic neuralgia unresponsive to other forms of therapy, and intractable pruritus.

Primary Uses

External

Capsaicin preparations

- Neuralgia, postherpetic (acute and chronic pain)
- Neuropathy, diabetic
- Psoriasis
- Osteoarthritis

Other Potential Uses

Internal

Cayenne preparations

- Peptic ulcer, prevention
- Gastrointestinal cytoprotective effect

External

Capsaicin preparations

- Fibromyalgia
- Cluster headache
- Chronic rhinopathy

Pharmacological Actions

Protects stomach; protects against peptic ulcer; increases fibrinolytic activity; stimulates carbohydrate oxidation.

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Dosage and Administration

Internal

Dried fruit: 30–120 mg, 3 times daily. As a digestive aid, 120–450 mg, 2–3 times daily with meals.

Infusion: 240 ml boiling water poured over 0.5–1.0 teaspoon of cayenne, steeped for 10 minutes, 1 tablespoon drunk, diluted with hot water when needed.

Tincture: 0.3–1.0 ml, 3 times daily, or as needed [1:20 (*g/ml*), 60% ethanol].

Oleoresin (standardized): 1.2 mg.

External

Commission E recommends taking capsaicin for no longer than 2 days; 14 days must pass before a new application can be used on the same location. Longer use on the same area may cause damage to sensitive nerves. In a contradictory recommendation, the *Physicians Desk Reference* listing for Zostrix®, a cream that contains capsaicin, states that capsaicin-containing preparations must be used continuously for up to several weeks (i.e., 3 to 4 applications daily for 2–6 weeks may be required) to be effective.

Liniment: Hot oil emulsion containing dried cayenne powder or alcoholic tincture, applied locally by friction method.

Ointment or cream (standardized): Semiliquid preparation containing 0.02–0.05% capsaicinoids in an emulsion base, applied to affected area.

Oleoresin (standardized): 2.5% maximum strength.

Poultice (standardized): Semisolid paste or plaster which, when applied locally, produces 10–40 mcg capsaicinoids per cm^2.

TINCTURE (STANDARDIZED): 1:10 (*g/ml*), 90% ethanol, aqueous-alcoholic preparation containing 0.005–0.01% capsaicinoids, applied locally.

PURE CAPSAICIN CREAM OR OINTMENT: For diabetic neuropathy, 0.075% (pure) capsaicin cream or ointment is applied 4 times daily. For postherpetic neuralgia, 0.025% capsaicin cream or ointment is applied 4 times daily.

CONTRAINDICATIONS

Internal

Inhalation is contraindicated because capsaicin causes immediate bronchoconstriction. Ingestion is contraindicated in the following conditions: chronic irritable bowel (because capsaicin is a neural irritant and causes intestinal contractions), gastroduodenal ulcers (although there are conflicting results for duodenal ulcers), acute gastritis, pulmonary tuberculosis, and hemorrhoids.

External

Cayenne preparations are contraindicated for application on injured skin, for use near the eyes, and for individuals with allergies to cayenne preparations.

PREGNANCY AND LACTATION: No known restrictions.

ADVERSE EFFECTS

The German Commission E noted that in rare cases, a hypersensitivity rash (urticaria) could occur. Capsaicinoids are strongly irritating to mucosal membranes, and inhaling cayenne can produce a form of allergic alveolitis.

DRUG INTERACTIONS

External

Commission E reported no known drug interactions but warned: "No additional heat application." Angiotensin-converting enzyme (ACE) inhibitors can predispose patients to coughing with application of topical preparations containing capsaicin.

Internal

Dried powder can protect against aspirin-induced gastroduodenal mucosal injury when taken one-half hour before aspirin (although this is more of a pharmacological action, not a true interaction). Capsicum may interfere with monoamine oxidase inhibitors (MAOIs) and antihypertensive therapy due to its ability to increase catecholamine secretion. It also may increase hepatic metabolism of drugs (i.e., via elevated glucose-6-phosphate dehydrogenase and adipose lipoprotein lipase activity).

CLINICAL REVIEW

Internal

All but one of eight clinical studies involving a total of 1,405 participants demonstrated positive effects for indications including gastrointestinal and metabolic conditions. Five studies investigated gastrointestinal effects related to the regular dietary intake of cayenne powder vs. non-ingestion of cayenne**.** The gastrointestinal effects under examination included a protective effect against peptic ulcer, a gastroprotective effect following ingestion of aspirin, risk of gastric cancer, gastric or duodenal mucosal damage, and elevated metabolic rate. In addition, a hematology study investigated fibrinolytic activity.

External (Preparations Containing Pure Capsaicin)

Eighteen clinical studies on pure capsaicin preparations involving a total of 1,326 participants were reviewed. All but one of the studies demonstrated positive effects for indications including neuralgia, neuropathy, psoriasis, arthritis, and fibromyalgia**.** Of 14 double-blind, placebo-controlled (DB, PC) studies that included a total of 1,036 participants, two investigated topical capsaicin in painful diabetic neuropathy and showed statistically significant results related to pain status. Four DB, PC studies on osteoarthritis all yielded statistically significant results, thus confirming capsaicin's efficacy in pain reduction. Three DB, PC studies focused on the treatment of rheumatoid arthritis, with two studies reporting significant reduction in pain. One study reported a significant reduction in primary osteoarthritis pain, but no significant reduction in rheumatoid arthritis pain. Other conditions for which topical capsaicin was evaluated in DB, PC studies include notalgia paresthetica, fibromyalgia, psoriasis, and postherpetic neuralgia. Only one study, a 12-week, DB, PC study on chronic distal painful polyneuropathy, failed to demonstrate a trend in favor of treatment with capsaicin. In clinical trials, creams containing low concentrations (0.025–0.075%) of capsaicin have been shown to be effective in the treatment of postherpetic neuralgia and other pain syndromes, including cluster headache.

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[Fam. *Solanaceae*]

Overview

Cayenne consists of the dried fruits of various capsaicin-containing *Capsicum* species, including many cultivated peppers found in the home garden. Common names for cayenne include cayenne pepper, chili pepper, paprika, red pepper, tabasco pepper, bird pepper, African bird pepper, piquin, aji pepper, Brown's pepper, Peruvian pepper, piris, habañero pepper, and bonnet pepper. Preparations made from various parts of the pepper are used in creams and ointments, and are available in three strengths: 0.025%, 0.050%, and 0.075%. The dried fruits of cayenne are also used for treating various illnesses.

Uses

External

Neuralgia (nerve pain) caused by herpes infections; diabetic neuropathy; psoriasis; osteoarthritis.

Dosage

Internal

DRIED FRUIT: 30–120 mg, 3 times daily. As a digestive aid, 120–450 mg, 2–3 times daily with meals.

TINCTURE: 0.3–1.0 ml, 3 times daily, or as needed [1:20 (*g/ml*), 60% ethanol].

External

Commercial creams that contain capsaicin (in dilutions of 0.025-0.75%), may require 3–4 applications daily for 2–6 weeks to be effective.

LINIMENT: Hot-oil emulsion containing dried cayenne powder or alcoholic tincture, applied locally by friction method.

OINTMENT OR CREAM (STANDARDIZED): Semiliquid preparation containing 0.02–0.05% capsaicinoids in an emulsion base, applied to affected area.

OLEORESIN (STANDARDIZED OIL-BASE PREPARATIONS): 2.5% maximum strength.

PURE CAPSAICIN CREAM OR OINTMENT: For diabetic neuropathy, apply 0.075% capsaicin cream or ointment, 4 times daily. For postherpetic neuralgia, apply 0.025% capsaicin cream or ointment, 4 times daily.

Contraindications

Consult a healthcare provider before ingesting cayenne pepper in cases of chronic irritable bowel, gastroduodenal ulcer, acute gastritis, pulmonary tuberculosis, or hemorrhoids. Do not inhale cayenne-containing products because they are strongly irritating to mucous membranes. Cayenne preparations should not be applied to injured skin, used near the eyes, or taken by individuals allergic to cayenne preparations.

Adverse Effects

In rare cases, a hypersensitivity rash (urticaria) can occur.

Drug Interactions

Cayenne has been reported to interfere with monoamine oxidase (MAO) inhibitors and with blood pressure lowering medications (i.e., ACE inhibitors). It may increase the rate at which the liver metabolizes other drugs.

Comments

When using a dietary supplement, purchase it from a reliable source. For best results, use the same brand of product throughout the period of use. As with all medications and dietary supplements, please inform your healthcare provider of all herbs and medications you are taking. Interactions may occur between medications and herbs or even among different herbs when taken at the same time. Treat your herbal supplement with care by taking it as directed, storing it as advised on the label, and keeping it out of the reach of children and pets. Consult your healthcare provider with any questions.

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Description

Cayenne preparations consist of the dried, ripe fruit, usually removed from the calyx, of various capsaicin-rich *Capsicum* species, such as *C. annuum* L. [Fam. *Solanaceae*], including a large number of varieties (Blumenthal, *et al.*, 2000). In Germany, pharmacopeial grade cayenne must contain no less than 0.4% total capsaicinoids, as determined by liquid chromatography (DAB, 1999). [NOTE: This herb was described under the monograph heading "Paprika (Cayenne)" in the German Commission E monographs (Blumenthal *et al.,* 1998).]

Primary Uses

External

Capsaicin preparations

Neuralgia

- Significant reduction of postherpetic neuralgia (Watson *et al.*, 1993; Peikert *et al.,* 1991; Bernstein *et al.*, 1989)

Neuropathy

- Improved pain relief for diabetic neuropathy (Capsaicin Study Group, 1991, 1992; Chad *et al.,* 1990)

Psoriasis

- Improvement in global evaluation, pruritus relief and combined psoriasis severity scores (Krogstad *et al.*, 1999; Ellis *et al.,* 1993)

Osteoarthritis

- Significant reduction in pain and joint tenderness (Altman *et al.,*1994; Schnitzer *et al.,* 1994; Weisman *et al.,* 1994; McCarthy and McCarty, 1992; Deal *et al.*, 1991)

Other Potential Uses

Internal

Cayenne preparations

Gastrointestinal

- Cytoprotective effect (Yeoh *et al.*, 1995)
- Peptic ulcer, prevention (Kang *et al.*, 1995; Yeoh *et al.*, 1995)

External

Capsaicin preparations

- Fibromyalgia (McCarty *et al.*, 1994)
- Cluster headache (Marks *et al.*, 1993)
- Chronic rhinopathy (Eberle and Gluck, 1994)

Dosage

Internal

Crude Preparations

DRIED FRUIT: 30–120 mg, 3 times daily, (BHP, 1983). As a digestive aid, 120–450 mg, 2–3 times daily with meals (McKenna *et al.,* 1998). In a clinical study, 10 g powdered fruit was administered one time with meals to stimulate carbohydrate oxidation (Lim *et al.,* 1997). However, this dose is probably too high for regular consumption.

INFUSION: 240 ml boiling water is poured over 0.5–1.0 teaspoon of cayenne and steeped for 10 minutes; 1 tablespoon is drunk, diluted with hot water when needed (Hoffmann, 1992; Lust, 1974).

TINCTURE: 1:20 (*g/ml*), 60% ethanol: 0.3–1.0 ml, 3 times daily, or when needed (Boon and Smith, 1999; BPC, 1968; Hoffmann, 1992; Karnick, 1994).

Standardized Preparations

OLEORESIN: 1.2 mg (maximum dose) (MD), 1.8 mg (maximum daily dose) (MDD) (GSL, 1984–1994).

External

Crude Preparations

LINIMENT: Hot oil emulsion containing dried cayenne powder or alcoholic tincture is applied locally by friction method (Blumenthal *et al.*, 2000).

Standardized Preparations

OINTMENT OR CREAM: Semiliquid preparation containing 0.02–0.05% capsaicinoids in an emulsion base, is applied to affected area (Blumenthal *et al.*, 2000).

OLEORESIN: 2.5% maximum strength (GSL, 1984–1994 from Newall *et al.*, 1996) is applied locally.

POULTICE: Semisolid paste or plaster which, when applied locally, produces 10–40 mcg capsaicinoids per cm^2 (Blumenthal *et al.*, 2000).

TINCTURE: 1:10 (*g/ml*), 90% ethanol, aqueous-alcoholic preparation containing 0.005–0.01% capsaicinoids, is applied locally (Blumenthal *et al.,* 2000).

Pure Capsaicin Preparations

For diabetic neuropathy, 0.075% capsaicin cream or ointment is applied 4 times daily. For postherpetic neuralgia, 0.025% capsaicin cream or ointment is applied 4 times daily (Boon and Smith, 1999; Pizzorno and Murray, 1999).

DURATION OF ADMINISTRATION

External

Crude Preparations

Commission E recommends no longer than two days; 14 days must pass before a new application can be used in the same location. Longer use on the same area may cause damage to sensitive nerves (Blumenthal *et al.,* 1998).

Preparations Containing Pure Capsaicin

Three to four applications daily for 2–6 weeks may be required (Kruse and Eland, 1999).

WARNING: Preparations made from cayenne irritate the mucous membranes even in very low concentrations and cause a painful burning sensation. Patients should avoid the contact of cayenne preparations with mucous membranes, especially the eyes (Blumenthal *et al.*, 1998).

CHEMISTRY

Cayenne contains up to 1.5% pungent principles known as capsaicinoids (usually 0.1–1.0%), composed of 49–69% capsaicin, 22–36% dihydrocapsaicin, 7.0–7.4% nordihydrocapsaicin, 1–2% homodihydrocapsaicin, and 1–2% homocapsaicin (Bennet and Kirby, 1968; Duke, 1985; Wood, 1987). Other constituents of cayenne include carotenoids and ascorbic acid (vitamin C) (Bruneton, 1999).

PHARMACOLOGICAL ACTIONS

Internal

Human

Crude Preparations

Dried powder can protect against aspirin-induced gastroduodenal mucosal injury when taken 1/2 hour prior to aspirin (Brinker, 2001; Yeoh *et al.*, 1995); protects against peptic ulcer (Kang *et al.*, 1995); increases fibrinolytic activity (Visudhiphan *et al.*, 1982); stimulates carbohydrate oxidation (Lim *et al.,* 1997); gastrointestinal stimulant (Osol and Farrar, 1955).

Animal

Antigenotoxic and anticarcinogenic (Surh *et al.,* 1998).

External

Crude Preparations

Local hyperemic and local nerve-damaging activity (Blumenthal *et al.,* 1998); rubefacient and vasostimulant (BHP, 1996; Kapoor, 1990). Capsicum oleoresin does not uniformly induce neuropeptide activity as reliably as purified capsaicin. Clinical efficacy studies have shown purified capsaicin depletes the neuropeptide-active agent substance P, which is stored in sensory neurons, though no similar studies have been done on capsicum oleoresin. Capsascin also further blocks resynthesis of substance P (Cordell and Araujo, 1993).

Pure Capsaicin Preparations

Block pain neurotransmitter, substance P (Ellison *et al.,* 1997); dilate blood vessels, release histamine and reduce perfusion in lesional skin (Krogstad *et al.*, 1999); reduce and relieve pain; cause activation followed by desensitization of the sensory neurons on short- and long-term treatments (Ellison *et al.*, 1997; Munn *et al.*, 1997; Vickers *et al.,* 1998).

MECHANISM OF ACTION

Internal

- Intragastric capsaicin stimulates afferent nerve endings in animal tests, suggesting that its gastroprotective effects may be caused by increased mucosal blood flow rather than by prostaglandin production (Yeoh *et al.*, 1995).
- Cayenne affects the cardiovascular system, reducing triglyceride levels and platelet aggregation, and increasing fibrinolytic activity (Pizzorno and Murray, 1999).
- Reduces serum triglyceride levels without an alteration in serum cholesterol or pre-β-lipoproteins, and stimulates lipid mobilization from adipose tissue (Boon and Smith, 1999).
- Increases catecholamine (plasma epinephrine and norepinephrine concentration) levels (Barna and Sreter, 1986; Lim *et al.*, 1997).
- Inhibits lipid peroxidation and myeloperoxidase activity in ethanol-induced gastric mucosal lesions; thereby demonstrating gastroprotective activity, which may be useful in chemoprevention (Park *et al.*, 2000).
- Vanilloid (capsaicin) receptors act in nonspecific manner (not specifically as previously believed) to activate sensory neurons. Capsaicin and the protons lower the heat threshold of the receptor, while it is the heat (<48°C) that opens the channel pore of the vanilloid receptor neurons (Szallasi and Blumberg, 1999).

External

Capsaicin Preparations

- Activate nociceptive fibers, which induces the release of excitatory neurotransmitters (substance P, N-methyl-D-asparic acid), bind to specific vanilloid (capsaicin) receptors, and its effects are reversible (Szallasi and Blumberg, 1999; Fusco and Giacovazzo, 1997; Lotz, 1994).
- Induce a selective analgesic effect by depleting substance P, a neuropeptide of 11 amino acids that mediates the transmission and modulation of pain impulses from the peripheral nerves to the spinal column. Capsaicin initially stimulates substance P release from peripheral sensory, C-type nerve fibers, then prevents its reuptake, and also blocks its transport within the neuron, which causes its eventual depletion, resulting in analgesia. The depletion of substance P initially takes one to three days, though with continued use the analgesic effect may last for weeks (Boon and Smith, 1999; Fusco and Giacovazzo, 1997; Tyler, 1992).

Contraindications

Internal

Crude Preparations

Inhalation is contraindicated due to immediate bronchoconstriction caused by capsaicin (Fuller *et al.,* 1985). Ingestion is contraindicated in cases of chronic irritable bowel due to neural irritant and intestinal contraction properties of capsaicin (Buck and Burks, 1986), gastroduodenal ulcers, acute gastritis, pulmonary tuberculosis, and hemorrhoids (But *et al.*, 1997). However, a randomized, comparison clinical study did not find gastric mucosal damage in patients with duodenal ulcers who consumed cayenne (Kumar *et al.*, 1984).

External

Cayenne preparations are contraindicated for application on injured skin, allergies to cayenne preparations (Blumenthal *et al.*, 1998), or use near the eyes (Brinker, 2001).

Pregnancy and Lactation: No known restrictions (McGuffin *et al.,* 1997).

Adverse Effects

Commission E noted that in rare cases, a hypersensitivity reaction (urticaria) can occur (Blumenthal *et al.,* 1998). Capsaicinoids are strongly irritating to mucosal membranes and inhalation of cayenne can produce a form of allergic alveolitis.

Drug Interactions

External

Commission E reported no drug interactions are known, but included the following note: "No additional heat application" (Blumenthal *et al.*, 1998). Angiotensin-converting enzyme (ACE) inhibitors can predispose patients to coughing with application of topical preparations containing capsaicin according to human case reports (Brinker, 2001).

Internal

Crude herb: Capsicum may interfere with monoamine oxidase inhibitors (MAOIs) and antihypertensive therapy (increased catecholamine secretion), and may increase the hepatic metabolism of drugs (glucose-6-phosphate dehydrogenase and adipose lipoprotein lipase activity elevated) (Newall *et al.,* 1996). In an animal study (rabbits), theophylline absorption was enhanced when administered before or simultaneously with cayenne (Bouraoui *et al.*, 1988).

American Herbal Products Association (AHPA) Safety Rating

Class 2d: External: Contraindicated on injured skin or near eyes.

Class 1: Internal: Can be safely consumed when used appropriately. Note: Excessive doses may cause gastrointestinal irritation in sensitive individuals (McGuffin *et al.*, 1997).

Regulatory Status

Austria: Official in the *Austrian Pharmacopoeia*, ÖAB 1991 (Wichtl, 1997).

Canada: Topical liniments, lotions, and plasters containing capsicum oleoresin or purified capsaicin are schedule OTC (over-the-counter) drugs requiring pre-market authorization and assignment of a Drug Identification Number (DIN) (Health Canada, 2001).

France: Topical preparations are approved for relieving minor articular pain in *French Pharmacopoeia*, Ph.Fr. X (Bradley, 1992; Reynolds *et al.*, 1993).

Germany: Topical preparations are approved nonprescription drugs of the Commission E monographs (Blumenthal *et al.*, 1998). Dried ripe fruit is official in the *German Pharmacopoeia* (DAB, 1999). Dried ripe fruit for preparation of hydro-alcoholic mother tincture and liquid dilutions is an official drug of the *German Homoeopathic Pharmacopoeia* (GHP, 1993).

Italy: Official in *Italian Pharmacopoeia* (Newall *et al.*, 1996).

Japan: Dried fruit and powdered dried fruit are both official in the *Pharmacopoeia of Japan* (JSHM, 1993).

Sweden: Topical capsaicin cream is an approved non-prescription drug (MPA, 1997). No capsicum products are listed in the Medical Products Agency (MPA) "Authorized Natural Remedies" (MPA, 2001).

Switzerland: Official in *Swiss Pharmacopoeia,* Ph.Helv.VII (Wichtl, 1997). External-use plasters containing cayenne and cayenne extract are nonprescription drugs, with sale limited to pharmacies and drugstores (Morant and Ruppanner, 2001).

U.K.: Capsicum oleoresin and water-soluble capsicum oleoresin are herbal medicines specified in the *General Sale List*, Schedule 1 (medicinal products requiring a full product license), Table B (external use only) (GSL, 1995).

U.S.: Generally recognized as safe (GRAS) (US FDA, 1998). Dietary supplement (USC, 1994). Capsicum oleoresin and purified capsaicin are safe and effective for use as OTC external analgesics (US FDA, 1979; US FDA, 1983).

Clinical Review

A total of 26 clinical trials conducted on cayenne and capsaicin are summarized in the following tables, "Clinical Studies on Cayenne" and "Clinical Studies on Capsaicin Preparations." All but one of these studies (López-Carrillo *et al.*, 1994), demonstrated positive effects for indications including gastrointestinal and metabolic conditions. Five studies investigated gastrointestinal effects related to the regular dietary intake of cayenne powder vs. non-ingestion of cayenne including a protective effect against peptic ulcer (Kang *et al.*, 1995), a gastroprotective effect following ingestion of aspirin (Yeoh *et al.*, 1995), risk of gastric cancer (Lopez-Carrillo *et al.*, 1994), gastric or duodenal mucosal damage (Graham *et al.*, 1988; Kumar *et al.*, 1984), and elevated metabolic rate (Henry and Emery, 1986). A hematology study found significantly higher fibrinolytic activity in Thai subjects who con-

sumed cayenne regulary, compared with American subjects (Visudhiphan *et al.*, 1982).

Table 2, "Clinical Studies on Capsaicin Preparations," summarizes 18 studies involving a total of 1,326 participants, evaluating the external use of preparations containing pure capsaicin. All but one of the studies (Low *et al.*, 1995) demonstrated positive effects for indications including neuralgia, neuropathy, psoriasis, arthritis, and fibromyalgia. The table includes 14 double-blind, placebo-controlled (DB, PC) studies involving a total of 1,036 participants. Two DB, PC studies investigated topical capsaicin in painful diabetic neuropathy, with statistically significant results related to pain status (Capsaicin Study Group, 1992; Chad *et al.*, 1990). Osteoarthritis was the subject of four DB, PC studies, all with statistically significant results confirming capsaicin's efficacy in pain reduction (Altman *et al.*, 1994; Deal *et al.*, 1991; McCarthy and McCarty, 1992; Schnitzer *et al.*, 1994). Three DB, PC studies focused on the treatment of rheumatoid arthritis, with two studies reporting significant reduction in pain (Deal *et al.*, 1991; Weisman *et al.*, 1994). One study reported a significant reduction in primary osteoarthritis pain, but no significant reduction in rheumatoid arthritis pain (McCarthy and McCarty, 1992). Other topics investigated with topical capsaicin in DB, PC studies include notalgia paresthetica (Wallengren and Klinker, 1995), fibromyalgia (McCarty *et al.*, 1994), psoriasis (Ellis *et al.*, 1993), and postherpetic neuralgia (Watson *et al.*, 1993). Only one study did not demonstrate a trend in favor of treatment with capsaicin. This was a 12-week, DB, PC study investigating chronic distal painful polyneuropathy (Low *et al.*, 1995). Creams containing low concentrations (0.025–0.075%) of capsaicin have been shown in clinical trials to be effective in the treatment of postherpetic neuralgia (Bernstein *et al.,* 1987; Bernstein *et al.*, 1989; Menke and Heins, 1999; Peikert *et al.*, 1991; Watson *et al.*, 1988; Watson *et al.*, 1993), diabetic neuropathy (Basha and Whitehouse, 1991; Tandan *et al.*, 1992), and other pain syndromes, including cluster headache (Marks *et al.*, 1993).

Branded Products

Axsain®: GenDerm Corporation / 4343 East Camelback Road / Phoenix, Arizona 85012 / U.S.A. Cream product with 0.075% capsaicin. This product is no longer available.

Capsig®: Schering-Plough / 2000 Galloping Hill Road / Kenilworth, NJ 07033 / U.S.A. / Tel: (908) 298-4000 / www.sch-plough.com. Cream with 0.025% capsaicin. This product is no longer available.

Chili powder (no product name specified): KNP Trading Pte Ltd, 50 Senoko Drive / Singapore 758 232 / Tel: 65-257 6916 / Fax: 65-753 6916 / www.knp-housebrand.com. Chili powder containing 478 ppm capsaicin.

Saemaul Kongjang 1: No product information available.

Zostrix®-HP: GenDerm Corporation. Cream product with 0.075% capsaicin.

References

Altman R, Aven A, Holmberg C *et al*. Capsaicin cream 0.025% as monotherapy for osteoarthritis: a double-blind study. *Semin Arthritis Rheum* 1994;23(No. 6 Suppl 3):25–33.

Barna J, Sreter F. Effect of chronically administered large amount of "sweet" paprika on some muscle characteristics. *Acta Aliment* 1986;15:299–305.

Basha K, Whitehouse F. Capsaicin: a therapeutic option for painful diabetic neuropathy. *Henry Ford Hosp Med J* 1991; 39(2):138–40.

Bennet D, Kirby G. Constitution and biosynthesis of capsaicin. *J Chem Soc C* 1968;442–6.

Berger A, Henderson M, Nadoolman W, *et al*. Oral capsaicin provides temporary relief for oral mucositis pain secondary to chemotherapy/radiation therapy. *J Pain Symptom Manage* 1995;10(3):243–8.

Bernstein J, Bickers D, Dahl M, Roshal J. Treatment of chronic postherpetic neuralgia with topical capsaicin. A preliminary study. *J Am Acad Dermatol* 1987; 17(1):93–6.

Bernstein J, Korman N, Bickers D, Dahl M, Millikan L. Topical capsaicin treatment of chronic postherpetic neuralgia. *J Am Acad Dermatol* 1989; 21(2 Pt 1):265–70.

BHP. See: *British Herbal Pharmacopoeia*.

Blumenthal M, Busse WR, Goldberg A, Gruenwald J, Hall T, Riggins CW, Rister RS (eds.). Klein S, Rister RS (trans.). *The Complete German Commission E Monographs—Therapeutic Guide to Herbal Medicines*. Austin, TX: American Botanical Council; Boston: Integrative Medicine Communication; 1998; 178.

Blumenthal M, Goldberg A, Brinckmann J (eds.). *Herbal Medicine: Expanded Commission E Monographs.* Newton, MA: Integrative Medicine Communications; 2000; 52–6.

Boon H, Smith M. *The Botanical Pharmacy: The Pharmacology of 47 Common Herbs.* Kingston, Ontario, Canada: Quarry Health Books; 1999;56–61.

Bouraoui A, Toumi A, Mustapha H, Brazier J. Effects of capsicum fruit on theophylline absorption and bioavailability in rabbits. *Drug-Nutrient Interact* 1988;5:345–50.

BPC. See: *British Pharmaceutical Codex*.

Bradley P (ed.). *British Herbal Compendium*, Vol. 1. Dorset, UK: British Herbal Medicine Association 1992;174–6.

Brinker F. *Herb Contraindications and Drug Interactions,* 3rd ed. Sandy, OR: Eclectic Medical Publications; 2001;57–59.

British Herbal Pharmacopoeia (BHP). Cayenne monograph. Exeter, U.K.: British Herbal Medicine Association; 1996;55–6.

British Herbal Pharmacopoeia (BHP). Cayenne monograph. Keighley, UK: British Herbal Medicine Association; 1983.

British Pharmaceutical Codex (BPC). London, UK: The Pharmaceutical Press; 1968.

Bruneton, J. *Pharmacogonosy, Phytochemistry, Medicinal Plants*, 2nd ed. Hatton, C.K (trans.). Paris: Intercept, Ltd.; 1999.

Buck S, Burks T. The neuropharmacology of capsaicin: review of some recent observations. *Pharmacol Rev* 1986;38(3):179–226.

But P, Kimura T, Guo J, Sung C (eds.). *International Collation of Traditional and Folk Medicine*, Vol. 2, Northeast Asia, Part II. River Edge, NJ: World Scientific Publishing, Co; 1997;138–9.

Buzzanell P, Gray F. The spice market in the United States: Recent developments and prospects. Economic Research Service, U.S. Department of Agriculture; Agricultural Information Bulletin No. 709. 1999.

Capsaicin Study Group. Effect of treatment with capsaicin on daily activities of patients with painful diabetic neuropathy. *Diabetes Care* 1992;15(2):159–65.

Capsaicin Study Group. Treatment of painful diabetic neuropathy with topical capsaicin. *Arch Intern Med* 1991;151:2225–9.

Chad D, Aronin N, Lundstrom R *et al*. Does capsaicin relieve the pain of diabetic neuropathy? *Pain* 1990;42:387–8.

Cordell G, Araujo O. Capsaicin: identification, nomenclature, and pharmacotherapy. *Ann Pharmacother* 1993;27:330–6.

DAB. See: *Deutsches Arzneibuch*.

Deal C, Schnitzer T, Lipstein E, *et al.* Treatment of arthritis with topical capsaicin: a double-blind trial. *Clin Therapeut* 1991;13(3):383–395.

Desai H *et al*. Effect of red chilli powder on DNA content of gastric aspirates. *Gut* 1973;14:974–6.

Deutsches Arzneibuch (DAB). Stuttgart, Germany: Deutscher Apotheker Verlag. 1999.

Duke J. *CRC Handbook of Medicinal Herbs*. Boca Raton, FL: CRC Press, Inc; 1985;98–9.

Eberle L, Gluck U. Clinical experiences with local capsaicin treatment of chronic rhinopathy. [in German]. *HNO* 1994;42(11):665–9.

Ellis C, Berberian B, Sulica V, *et al*. A double-blind evaluation of topical capsaicin in pruritic psoriasis. *J Am Acad Dermat* 1993;29:438–42.

Ellison N, Loprini C, Kugler J, *et al*. Phase III placebo-controlled trial of capsaicin cream in the management of surgical neuropathic pain in cancer patients. *J Clin Oncol* 1997;15(8):2974–80.

Fuller R, Dixon C, Barnes P. Bronchoconstrictor response to inhaled capsaicin in humans. *J Appl Physiol* 1985;58(4):1080–4.

Fusco B, Alessandri M. Analgesic effect of capsaicin in idiopathic trigeminal neuralgia. *Anest Analg* 1992;74:375–377.

Fusco BM Giacovazzo M. Peppers and pain: The promise of capsaicin. *Drugs* 1997;53(6):909–14.

General Sale List (GSL). Statutory Instrument 1995 No. 3216 The Medicines (Products Other Than Veterinary Drugs) Amendment Order 1995. London, U.K.: Her Majesty's Stationery Office (HMSO). 1995.

General Sale List (GSL). Statutory Instrument (S.I.). The Medicines (Products other than Veterinary Drugs). London, UK: Her Majesty's Stationery Office; 1984; S.I. No. 769, as amended 1985; S.I. No. 1540, 1990; S.I. No. 1129, 1994; S.I. No. 2410.

German Homeopathic Pharmacopoeia (GHP), 1st ed. 1978 with 5 supplements through 1991. Translation of the German "*Homöopathisches Arzneibuch* (HAB 1) Amtliche

Ausgabe." Stuttgart, Germany: Deutscher Apotheker Verlag; 1993;275–7.
GHP. See: *German Homeopathic Pharmacopoeia*.
Graham D, Smith J, Opekum A. Spicy food and the stomach: Evaluation by videoendoscopy. *JAMA* 1988;260(23):3473–5.
GSL. See: *General Sale List*.
Health Canada. *Drug Product Database (DPD) Product Information*. Ottawa, Ontario: Health Canada Therapeutic Products Programme; 2001.
Henry C, Emery B. Effect of spiced food on metabolic rate. *Human Nutr Clin Nutr* 1986;40(2):165–8.
Hoffmann D. *The New Holistic Herbal*. Rockport, MA: Element, Inc;. 1992;189.
Japanese Standards for Herbal Medicines (JSHM). Tokyo, Japan: Yakuji Nippo, Ltd; 1993;59–60.
JSHM. See: *Japanese Standards for Herbal Medicines*.
Kang J, Yeoh K, Chia H, *et al*. Chili – protective factor against peptic ulcer? *Dig Dis Sci* 1995;40(3)576–9.
Kapoor L. *CRC Handbook of Ayurvedic Medicinal Plants*. Boca Raton, FL: CRC Press; 1990; 98.
Karnick C. *Pharmacopoeial Standards of Herbal Plants*, Vol. 1. Delhi, India: Sri Satguru Publications; 1994;79–80.
Krogstad A, Lönnroth P, Larson G, Wallin B. Capsaicin treatment induces histamine release and perfusion changes in psoriatic skin. *Brit J Derm* 1999;141:87–93.
Kruse L, Eland J. *Capsaicin (Axsain®, Capsaicin-P, Zostrix® HP, Dolorac): Healthcare Professional Version*. Iowa City, IA: The University of Iowa College of Nursing; 1999 available at: <http://www.nursing.uiowa.edu/sites/PedsPain/Topicals/CAPSAIte.htm>.
Kumar N, Vij C, Sarin S, Anand B. Do chilies influence healing of duodenal ulcer? *Br Med J* 1984;288:1803–1804.
Lim K, Yoshioka M, Kikuzato S, *et al*. Dietary red pepper ingestion increases carbohydrate oxidation at rest and during exercise in runners. *Med Sci Sports Exerc* 1997 March;29(3):355–61.
Locock R. Capsicum. *Can Pharm J* 1985;118:517–9.
López-Carrillo L, Avila M, Dubrow R. Chili pepper consumption and gastric cancer in Mexico: A case-control study. *Am J Epidem* 1994;139(3):264–71.
Lotz M. 1994. Experimental models of arthritis: Identification of substance P as a therapeutic target and use of capsaicin to manage joint pain and inflammation. *Semin Arthritis Rheum* 1994; 23(6)Suppl 3:10–17.
Low P, Opfer-Gehrking T, Dyck P, Litchy W, O'Brien P. Double-blind, placebo-controlled study of the application of capsaicin cream in chronic distal painful polyneuropathy. *Pain* 1995;62:163–8.
Lust J. *The Herb Book*. New York, NY: Bantam Books; 1974;151–2.
Marks D, Rapoport A, Padla D, *et al*. A double-blind placebo-controlled trial of intranasal capsaicin for cluster headache. *Cephalalgia* 1993;13(2):114–6.
McCarthy G, McCarty D. Effect of topical capsaicin in the therapy of painful osteoarthritis of the hands. *J Rheumatol* 1992;19:604–7.
McCarty D, Csuka M, McCarthy G, Trotter D. Treatment of pain due to fibromyalgia with topical capsaicin: a pilot study. *Semin Arthritis Rheum* 1994;23(No. 6, Suppl 3):41–7.
McGuffin M, Hobbs C, Upton R, Goldberg A (eds.). *American Herbal Products Association's Botanical Safety Handbook*. Boca Raton, FL: CRC Press; 1997;23.
McKenna D, Hughes K, Jones K (eds.). *Natural Dietary Supplements: A Desktop Reference*. Marine on St. Croix, MN: Institute for Natural Products Research; 1998.
Medical Products Agency (MPA). *Läkemedelsmonografi: Capsina (kapsaicin)*. Uppsala, Sweden: Medical Products Agency; 1997.
Medical Products Agency (MPA). *Naturläkemedel: Authorised Natural Remedies* (as of January 24, 2001). Uppsala, Sweden: Medical Products Agency; 2001.
Menke J, Heins J. Treatment of postherpetic neuralgia. *J Am Pharm Assoc (Wash)* 1999; 39(2):217–21.
Morant J, Ruppanner H (eds.). Patienteninformation: Democal Kreuz-Pflaster D. In: *Arzneimittel-Kompendium der Schweiz*® 2001. Basel, Switzerland: Documed AG. 2001.
MPA. See: Medical Products Agency.
Munn S, Burrows N, Abadia-Molina F. The effect of topical capsaicin on substance P immunoreactivity: a clinical trial and immunohistochemical analysis [letter]. *Acta Derm Venereol (Stockh)* 1997; 77(2):158–9.
Newall C, Anderson L, Phillipson J. *Herbal Medicines: A Guide for Health-care Professionals*. London, UK: The Pharmaceutical Press; 1996;60–61.
Osol A, Farrar G. *The Dispensatory of the United States of America*, 25th edition. Philadelphia, PA: Lippincott; 1955;239–42.
Paice J, Ferrans C, Lashley F, *et al.* Topical capsaicin in the management of HIV-associated peripheral neuropathy. *J Pain Symptom Manage* 2000;19(1):45–52.
Palevitch D, Craker L. Nutritional and medical importance of red peppers (*Capsicum* spp.). *J Herbs Spices Med Plants* 1995; 3(2):55–83.
Park JS, Choi MA, Kim BS, *et al*. Capsaicin protects against ethanol-induced oxidateive injury in the gastric mucosa of rats. *Life Sci* 2000;67: 3087–93.
Peikert A, Hentrich M, Ochs G. Topical 0.025% capsaicin in chronic post-herpetic neuralgia: efficacy, predictors of response and long-term course. *J Neurol* 1991; 238(8):452–6.
Pimparkar B *et al*. Effects of commonly used spices on human gastric secretion. *J Assoc Physicians India* 1972;20:901–10.
Pizzorno JE, Murray MT, editors. Capsicum frutescens. In: *Textbook of Natural Medicine*, Vol. 1, 2nd ed. New York: Churchill Livingstone; 1999;629–32.
Reynolds JEF, Pafitt K, Parsons AV, Sweetman SC (eds.). *Martindale: The Extra Pharmacopoeia*, 30th edition. London, U.K.: The Pharmaceutical Press. 1993;899.
Richman A, Witkowski J. 17th annual consumer survey. *Whole Foods* 1999 Aug;33–8.
Rosenstein E. Topical agents in the treatment of rheumatic disorders. *Complement Alternative Ther Rheum Dis J* 1999;25(4):899–918.
Schnitzer T, Morton C, Coker S. Topical capsaicin therapy for osteoarthritis pain: Achieving a maintenance regimen. *Semin Arthritis Rheum* 1994;23(No. 6 Suppl 3):34–40.
Surh Y, Lee E, Lee J. Chemoprotective properties of some pungent ingredients present in red pepper and ginger. *Mut Res* 1998;402:259–67.
Szallasi A, Blumberg, PM. Vanilloid (capsaicin) receptors and mechanisms. *Pharmacol Rev* 1999;51(2):159–95.
Tandan R, Lewis G, 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.
Turkoski B, Lance B, Janosik J. *Drug Information Handbook for Nursing.* Hudson, Ohio: Lexi-Comp Inc. 1998;1475.
Tyler, VE. *The Honest Herbal: A Sensible Guide to the Use of Herbs and Related Remedies*, 3rd ed. New York: Pharmaceutical Products Press; 1992;79–80.
United States Congress (USC). Public Law 103–417: Dietary Supplement Health and Education Act of 1994. Washington, DC: 103rd Congress of the United States; 1994.
United States Food and Drug Administration (U.S. FDA). *Code of Federal Regulations*, Title 21, Part 182 – Substances Generally Recognized as Safe. Washington, DC: Office of the Federal Register National Archives and Records Administration; 1998;427–33.
United States Food and Drug Administration (U.S. FDA). *Code of Federal Regulations 21* (CFR 21). Proposed monographs on analgesic drug products for over-the-counter (OTC) human use. Washington, D.C.: Office of the Federal Register National Archives and Records Administration; 1979;44:69804–5; 1983;48:5852–69.
US FDA. See: United States Food and Drug Administration.
USC. See: United States Congress.
Vickers E, Cousins M, Walker S, Chisolm K. Analysis of 50 patients with atypical odontalgia. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1998;85:24–32.
Visudhiphan S, Poolsuppasit S, Piboonnukarintro S, *et al.* The relationship between high fibrinolytic activity and daily capscium ingestion in Thais. *Am J Clin Nutr* 1982;35:1452–58.
Wallengren J, Klinker M. Successful treatment of notalgia paresthetica with topical capsaicin: Vehicle-controlled, double-blind, crossover study. *J Am Academy Dermatol* 1995;32(No. 2, Part 1)287–9.
Watson C, Tyler K, Bickers D *et al*. A randomized vehicle-controlled trial of topical capsaicin in the treatment of postherpetic neuralgia. *Clin Ther* 1993; 15(3):510–26.
Watson C, Evans R, Watt V. Post-herpetic neuralgia and topical capsaicin. *Pain* 1988;33(3):333–40.
Watson C, Evans R. The postmastectomy pain syndrome and topical capsaicin: a randomized trial. *Pain* 1992;51(3):375–9.
Weisman M, Hagaman C, Yaksh T, Lotz M. Preliminary findings on the role of neuropeptide suppression by topical agents in the management of rheumatoid arthritis. *Semin Arthritis Rheum* 1994;23(No 6, Suppl 3):18-24.
Westerman R, Roberts R, Kotzmann R, *et al*. Effects of topical capsaicin on normal skin and affected dermatomes in *Herpes zoster*. *Clin Exp Neurol* 1988;25:71–84.
Wichtl M (ed.). *Tea Derived Drugs and Phytopharmaceuticals,* 3rd Edition*: A pocket reference for the evidence-based clinical practice*. [in German]. Stuttgart, Germany: Wissenschaftliche Verlagsgesellschaft GmbH; 1997;123–5.
Willard T. *The Wild Rose Scientific Herbal*. Calgary, Alberta: Wild Rose College of Natural Healing; 1991;68–73.
Wood A. Determination of the pungent principles of chilies and ginger by reversed-phase high-performance liquid chromatography with use of a single standard substance. *Flavour Fragrance J* 1987;2:1–12.
Yeoh K, Kang J, Yap I, *et al.* Chili protects against aspirin-induced gastroduodenal mucosal injury in humans. *Dig Dis Sci* 1995;40(3):580–3.

Clinical Studies on Cayenne (*Capsicum* spp.)

Internal Use of Cayenne Crude Herb Preparations

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Lim *et al.*, 1997	Metabolic elevation of plasma catecholamine levels and alteration of energy substrate utilization	R n=8 male middle- and long-distance runners (mean age 20.8 years)	1 dose on 2 occasions, separated by 1 week, or placebo	Experimental meal with or without 1 dose of 10 g pepper	Dried hot red pepper powder (Saemaul Kongjang 1) containing 0.3% capsaicin	Capsicum increased carbohydrate oxidation for energy substrate more than meal without capsicum, at rest and during exercise. Subjects had meal (2,720 kilojoules) with or without 10 g capsicum. During rest (2.5 hours after meal) and exercise (pedaling for 1 hour), expired gasses and venous blood were collected. Capsicum significantly elevated respiratory quotient ($p<0.05$) and blood lactate levels ($p<0.05$) at rest and during exercise. Capsicum group had significantly higher plasma epinephrine and norepinephrine levels 30 minutes after meal, compared to patients without capsicum-containing meal.
Kang *et al.*, 1995	Gastrointestinal amount of chili in patients with peptic ulcer	Cm n=190: 103 peptic ulcer patients; 87 controls without peptic ulcer or dyspepsia	2 years prior to interviews with standard questionnaire	Peptic ulcer group, median amount 312 teaspoons per month; control group, median amount 834 teaspoons per month	Dietary intake of fresh chilis, dried chili powder, chili sauces and dips, curry powder, etc.	Compared to controls, ulcer patients ingested chili less frequently and in smaller portions during the 2 years before diagnosis. The odds ratio of having peptic ulcer disease was 0.47 (95% confidence intervals: 0.25–0.89) for subjects who ingested chili more frequently and in larger amounts. Chili use appears to have a protective effect against peptic ulcer disease.
Yeoh *et al.*, 1995	Gastrointestinal (protective effect of chili against acute gastroduodenal mucosal injury induced by aspirin)	R, SB n=18 volunteers without a history of dyspeptic symptoms (ages 21–26 years)	2 days, 4 weeks apart	20 g chili powder (containing 9.5 mg capsaicin), mixed with 200 ml water followed by 600 mg aspirin with 200 ml water vs. aspirin without chili	Chili powder containing 478 ppm capsaicin (KNP Trading Pte Ltd., Singapore)	Chili powder demonstrated a gastroprotective effect in human subjects as determined by endoscopy. Median gastric injury score after chili was 1.5 compared to 4 in control group ($p<0.05$).
López-Carrillo *et al.*, 1994	Gastric cancer risk	E n=972 (incident group n=220; control group n=752) (mean age 57.2 years)	286 days	Approximately 20 g peppers/day	Chili peppers	Chili pepper consumers had a 5.5-fold greater risk for gastric cancer than non-chili pepper consumers. Among consumers, there was a highly significant trend of increasing risk with increasing, self-rated level of consumption. The odds ratio for high-level consumers compared with non-consumers was 17.11 (95% CI 7.78–37.59). The authors could not conclude definite results because there was a lack of a dose-response relationship observed when chili pepper consumption was measured as a frequency of consumption per day.
Graham *et al.*, 1988	Gastrointestinal (effect of spiced food on gastric mucosa)	SB, R, CO n=12 (ages 24–43 years)	4 days	30 g jalapeño peppers with spicy meal vs. bland meal	Jalapeño peppers	Ingestion of highly spiced meals by normal individuals did not cause endoscopically demonstrable gastric or duodenal mucosal damage.
Henry and Emery, 1986	Gastrointestinal (effect of spiced food on metabolic rate)	OL, Cm n=12	2 days, 180 minutes each day	3 g mustard and chili sauce	1 meal with 3 g mustard and chili sauce vs. 1 non-spicy meal	A statistically significant increase of 25% in the post-spicy meal resting metabolic rate (RMR) was measured, peaking at around 75–90 minutes post-meal. The peak increase in the non-spicy meal rate was smaller and came earlier, at 60–75 minutes. After 180 minutes, the metabolic rate after the spicy meal was still relatively elevated.
Kumar *et al.*, 1984	Gastrointestinal (effect of chili on healing rate of duodenal ulcers)	Cm, R n=50 (mean age chili group 32.6 years; mean age control group 36.8 years)	1 month	1 g red chili powder 3x/day with meals vs. meals without chili powder	Capsicum powder added to food (both groups also took 15 ml liquid antacid 6x/day)	Red chilies were found not to influence the healing of duodenal ulcer. No gastric mucosal damage in the form of hyperemia or erosions was observed. The authors concluded that patients with duodenal ulcer may consume a normal diet and that bland food is unlikely to serve any useful purpose.

KEY: C – controlled, **CC** – case-control, **CH** – cohort, **CI** – confidence interval, **Cm** – comparison, **CO** – crossover, **CS** – cross-sectional, **DB** – double-blind, **E** – epidemiological, **LC** – longitudinal cohort, **MA** – meta-analysis, **MC** – multi-center, **n** – number of patients, **O** – open, **OB** – observational, **OL** – open label, **OR** – odds ratio, **P** – prospective, **PB** – patient-blind, **PC** – placebo-controlled, **PG** – parallel group, **PS** – pilot study, **R** – randomized, **RC** – reference-controlled, **RCS** – retrospective cross-sectional, **RS** - retrospective, **S** – surveillance, **SB** – single-blind, **SC** – single-center, **U** – uncontrolled, **UP** – unpublished, **VC** – vehicle-controlled.

Clinical Studies on Cayenne (*Capsicum* spp.) (cont.)

Internal Use of Cayenne Crude Herb Preparations (cont.)

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Visudhiphan *et al.*, 1982	Hematology (effect on fibrinolytic activity and blood coagulation)	Cm n=143: 88 Thai and 55 American subjects (ages 12–68 years)	1 day	Thai meals w/ capsicum vs. American meals without capsicum	Powder of *C. frutescens* added to food	Fibrinolytic activity measured in 88 Thai subjects (mean ± SD = 167 ± 66.84 minutes) was significantly higher than in 55 American whites (mean ± SD = 254 ± 126.70 minutes) residing in Thailand for a period of time ($p<0.001$), presumably due to Thai population's daily consumption of capsicum with their food compared to the absence of daily capsicum in the American diet. Additionally, the Thai population had lower plasma fibrinogen ($p<0.01$) and higher anti-thrombin III (statistics not reported) compared to Americans.

Clinical Studies on Capsaicin Preparations

Neuralgia

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Watson *et al.*, 1993	Postherpetic neuralgia	DB, PC, PG n=143 patients with chronic postherpetic neuralgia	6 weeks	0.075% capsaicin in cream base 4x/day	Zostrix®-HP	Statistically significant pain reduction. Average reduction in pain by visual analog scale (VAS) ~15% decrease for capsaicin and 5% increase for placebo.
Peikert *et al.*, 1991	Postherpetic neuralgia	OL n=39 patients with chronic post-herpetic neuralgia	2 months with follow-up after 10–12 months	0.025% capsaicin in cream base	Brand not stated	Of the patients, 48% experienced substantial improvement. Of the 48% who responded, 72% were still improved after 10–12 months. Topically applied capsaicin may be effective in relieving pain of postherpetic neuralgia.
Bernstein *et al.*, 1989	Chronic post-herpetic neuralgia	DB, PG n=32 elderly patients	6 weeks	0.075% capsaicin in cream base 4x/day	Zostrix®-HP	After 6 weeks, nearly 80% of capsaicin group experienced some pain relief. The investigators' global evaluation for symptom relief at end of treatment indicated capsaicin was better than placebo.

Neuropathy

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Ellison *et al.*, 1997	Surgical neuropathic pain for at least 3 months	R, PC n=99 (median age in first capsaicin group 66 years; median age in first placebo group 64 years)	2 months	Rubbing preparation in until it vanished 4x/day	Zostrix®-HP	Average pain reduction of 53% vs. 17% placebo ($p=0.0005$). Post-surgical neuropathic pain decreased significantly and, despite some toxicities, was preferred 3:1 over placebo.
Low *et al.*, 1995	Chronic distal painful polyneuropathy	DB, PC, R n=39 patients with bilateral symmetric painful peripheral neuropathy in distal lower extremities for at least 6 months (mean age 56 years)	3 months	0.075% capsaicin in cream base 4x/day	Brand not stated	This study did not demonstrate a trend in favor of capsaicin. No statistically significant difference was found.
Capsaicin Study Group, 1992, 1991	Diabetic neuropathy	R, DB, PC, MC n=277 patients with peripheral polyneuropathy or radiculopathy (ages 22–92 years)	8 weeks	0.075% capsaicin in cream base 4x/day	Axsain®	Of capsaicin group, 69.5% showed improvement in pain relief compared to 53.4% with vehicle cream ($p=0.012$); 18.3 vs. 9.2% showed improvement in working ($p=0.019$); 26.1 vs 14.6% showed improvement in walking ($p=0.029$); 29.5 vs. 20.3% showed improvement in sleeping ($p=0.036$). 22.8 vs. 12.1% had improved participation in recreational activities ($p=0.037$).

KEY: C – controlled, **CC** – case-control, **CH** – cohort, **CI** – confidence interval, **Cm** – comparison, **CO** – crossover, **CS** – cross-sectional, **DB** – double-blind, **E** – epidemiological, **LC** – longitudinal cohort, **MA** – meta-analysis, **MC** – multi-center, **n** – number of patients, **O** – open, **OB** – observational, **OL** – open label, **OR** – odds ratio, **P** – prospective, **PB** – patient-blind, **PC** – placebo-controlled, **PG** – parallel group, **PS** – pilot study, **R** – randomized, **RC** – reference-controlled, **RCS** – retrospective cross-sectional, **RS** - retrospective, **S** – surveillance, **SB** – single-blind, **SC** – single-center, **U** – uncontrolled, **UP** – unpublished, **VC** – vehicle-controlled.

Clinical Studies on Capsaicin Preparations (cont.)

Neuropathy (cont.)

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Chad *et al.*, 1990	Diabetic neuropathy	DB, R n=46 patients with painful distal, symmetrical polyneuropathy	1 month	0.075% capsaicin in cream base 4x/day	Axsain®	Assessed by physician's global evaluation scores, capsaicin group showed trend towards beneficial effect and greater improvement. However, a clear positive therapeutic conclusion was not determined in this study due to the difficulty in separating the salutary effects of capsaicin from vehicle.

Psoriasis

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Krogstad *et al.*, 1999	Psoriatic lesions	PC n=22 psoriatic patients (mean age 44 years)	24 hours	0.75–1.0%, 1x capsaicin epicutaneously to skin	Essex cream	Compared with placebo, 24-hour treatment caused 15% decrease in basal perfusion in lesional skin. After 50 minutes of capsaicin treatment, histamine release increased by 30% ($p<0.05$). After 50–60 minutes, capsaicin increased perfusion in lesional skin by 30% ($p<0.001$).
Ellis *et al.*, 1993	Psoriasis	DB, PC, MC, PG n=197 patients with stable, plaque-type psoriasis with pruritis, involving >5% body surface (mean age capsaicin group 47 years; mean age placebo group 45 years)	6 weeks	0.025% cream 4x/day	Brand not stated (0.025% capsaicin cream)	Capsaicin-treated patients demonstrated significantly greater improvement in global evaluation ($p=0.024$ at 4 weeks; $p=0.03$ at 6 weeks), pruritus relief ($p=0.002$ at 4 weeks; $p=0.06$ at 6 weeks) and combined psoriasis severity scores ($p=0.3$ at 4 weeks; $p=0.36$ at 6 weeks). The most frequently reported side effect was transient burning sensation at application sites.

Osteoarthritis (OA)/Rheumatoid Arthritis (RA)

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Altman *et al.*, 1994	OA	DB, R, PC, MC n=113 (ages 18–86 years)	3 months	0.025% cream 4x/day	Zostrix®	Significantly better pain and tenderness relief with topical capsaicin than with placebo. Significant improvement of physicians' and patients' global evaluations with capsaicin ($p=0.03$). Capsaicin-treated patients reported great reduction of pain on the visual analog scale (VAS) ($p=0.02$ at 12 weeks) and on passive range of motion ($p=0.03$), and of joint swelling and tenderness ($p=0.01$). Results support use of capsaicin 0.025% as first-line therapy for OA pain.
Schnitzer *et al.*, 1994	OA involving one or both hands	DB, R, PC, PG n=59 4x/day regimen vs. 2x/day regimen (mean age capsaicin 69.3 years; mean age placebo 66.8 years)	9 weeks	Phase I: 0.025% cream 4x/day, 3 weeks; Phase II: 0.025% cream 2x/day, 6 weeks	Zostrix®	Study confirmed that topical capsaicin 4 times per day is safe and effective adjunctive therapy for OA pain ($p=0.018$ at 3 weeks; $p=0.13$ capsaicin vs. placebo after 6 weeks) and once effective symptomatic relief is achieved, reducing dosage to 4 times per day appears to provide relief with continued application.
Weisman *et al.*, 1994	RA (effect of capsaicin on synovial fluid of knee)	DB, PC, R n=10 (mean age capsaicin group 47.1 years; mean age placebo group 50.9 years)	6 weeks	0.075% cream 4x/day	Brand not stated	Analysis of synovial fluid showed that topical capsaicin caused greater reductions of inflammatory mediators than placebo. Study suggests that in addition to its effects on afferent neurons, capsaicin might also provide additional anti-inflammatory activity.

KEY: C – controlled, **CC** – case-control, **CH** – cohort, **CI** – confidence interval, **Cm** – comparison, **CO** – crossover, **CS** – cross-sectional, **DB** – double-blind, **E** – epidemiological, **LC** – longitudinal cohort, **MA** – meta-analysis, **MC** – multi-center, **n** – number of patients, **O** – open, **OB** – observational, **OL** – open label, **OR** – odds ratio, **P** – prospective, **PB** – patient-blind, **PC** – placebo-controlled, **PG** – parallel group, **PS** – pilot study, **R** – randomized, **RC** – reference-controlled, **RCS** – retrospective cross-sectional, **RS** - retrospective, **S** – surveillance, **SB** – single-blind, **SC** – single-center, **U** – uncontrolled, **UP** – unpublished, **VC** – vehicle-controlled.

Clinical Studies on Capsaicin Preparations (cont.)

Osteoarthritis (OA)/Rheumatoid Arthritis (RA) (cont.)

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
McCarthy and McCarty, 1992	Primary OA and RA on the hand with at least moderate severity	DB, R, PC OA: n=14 RA: n=7 (mean age 61 years)	1 month	0.075% cream 4x/day vs. vehicle-only cream	Brand not stated	OA: Significant reduction in pain ($p<0.02$). RA: No significant reduction in pain. Capsaicin reduced tenderness and pain associated with osteoarthritis ($p<0.02$). Local burning sensation was only adverse effect noted.
Deal *et al.*, 1991	Primary OA and RA with moderate to severe knee pain	DB, R, PC, MC OA: n=70 RA: n=31 patients with primary OA or RA of 1 or both knees (mean ages with OA: capsaicin 62 years, placebo 60 years; mean ages with RA: capsaicin 52 years, placebo 56 years)	1 month	0.025% cream 4x/day	Zostrix®	OA: mean reduction in pain of 33% ($p=0.033$). RA: mean reduction in pain of 57% ($p=0.003$). With global evaluation, 80% of the capsaicin-treated patients reported reduction in pain after 2 weeks of treatment. Both OA and RA patients had significant reduction of knee pain severity (categorical scale and visual analog scale [VAS]).

Other

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Vickers *et al.*, 1998	Atypical odontalgia (AO)	O n=50 duration of pain from 3 months to 32 months (ages 21–82 years)	1 month	Topical anesthetic mouthwash (benzocaine 15%), application for 3 minutes 2x/day, follow-up for at least 3 months	Capsig® (0.025% capsaicin)	Of 30 subjects, 19 responded positively, with pain reduction ranging from 10–100% (mean=58 ± 25 [SD]; $p<0.01$) using visual analog scale (VAS).
Wallengren and Klinker, 1995	Notalgia paresthetica	R, DB, PC, C n=20 duration of symptoms 3 years (mean age 59 years)	10 weeks	0.025% capsaicin in cream base 5x/day for 1 week, then 3x daily for 3 weeks, followed by 2-week washout, then crossover repeat application for 4 weeks	Zostrix®	Of capsaicin group, 70% showed improvement vs. 30% placebo. Improvement in capsaicin group was long-lasting in some cases for several months.
McCarty et al., 1994	Fibromyalgia	DB, PC n=45 (ages 18–70 years)	1 month	0.025% capsaicin in cream base 4x/day	Zostrix®	Capsaicin group reported significantly less tenderness in the tender points than placebo at week 4. No statistically significant differences between groups on visual analog scale (VAS). Significant increase ($p = .02$) in grip strength was noted at week 2 for capsaicin group.
Marks *et al.*, 1993	Cluster headache	DB, PC, R n=13	7 days, then recorded severity of each headache for 15 days	0.025% capsaicin in cream base	Intranasal capsaicin ointment	Headaches were significantly less severe in capsaicin-treated group on days 8–15 and on days 1–7 compared to placebo. Results indicated that intranasal capsaicin may provide new therapeutic option for treatment of cluster headaches.

KEY: **C** – controlled, **CC** – case-control, **CH** – cohort, **CI** – confidence interval, **Cm** – comparison, **CO** – crossover, **CS** – cross-sectional, **DB** – double-blind, **E** – epidemiological, **LC** – longitudinal cohort, **MA** – meta-analysis, **MC** – multi-center, **n** – number of patients, **O** – open, **OB** – observational, **OL** – open label, **OR** – odds ratio, **P** – prospective, **PB** – patient-blind, **PC** – placebo-controlled, **PG** – parallel group, **PS** – pilot study, **R** – randomized, **RC** – reference-controlled, **RCS** – retrospective cross-sectional, **RS** - retrospective, **S** – surveillance, **SB** – single-blind, **SC** – single-center, **U** – uncontrolled, **UP** – unpublished, **VC** – vehicle-controlled.