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.