Supplemental Table. Detailed Information on Clinical Trials Included in the Systematic Review

Reference	Agent/Dosage	Study Design	Indication	Number of Patients	Duration of Treatment	Principal Findings
Goldstein et al,[28] 2011	pimecrolimus cream 1% 2× daily; clobetasol cream 0.05% at bedtime	randomized, double-blind	vulvar lichen sclerosus	38	12 weeks	Both treatments significantly decreased inflammation (P<0.01). Significantly (P=0.015) greater decrease in inflammation with clobetasol than with pimecrolimus. No significant difference between groups in pruritus or burning/pain
Irving et al,[29] 2011	capsaicin dermal patches 8%, 640 μg/cm^2 or 0.04%, 3.2 μg/cm^2 (control); 1 application, both	randomized, double-blind	postherpetic neuralgia	418	One 60-minute application; 12-week posttreatment assessment	Significantly greater pain reduction with the 8% patch than with control treatment for weeks 2-12 (P<0.05). Significantly more patients achieved ≥30% pain reduction with 8% patch than with control treatment (P=0.02)
Costantino et al,[30] 2011	diclofenac epolamine (DHEP) 180 mg–heparin plaster; DHEP 180 mg plaster; once daily	randomized, double-blind, placebo-controlled	mild to moderate ankle sprain	430	7 days	Significantly greater reduction in pain with movement after 3 days' treatment with DHEP-heparin than with DHEP alone (P=0.002). Both treatments significantly more effective than placebo (P≤0.005). Significantly greater reduction in edema with DHEP-heparin than with placebo (P=0.012)
Tiso et al,[31] 2010	ibuprofen gel 4%, 80 mg 4× daily; oral ibuprofen 800 mg 3× daily	randomized, prospective, unblinded	chronic knee pain	20	2 weeks	Treatments comparable in efficacy. Improvement in patient satisfaction with topical but not with oral therapy
Coudreuse and de Vathaire,[32] 2010	DHEP 180 mg–heparin plaster; applied once each morning	randomized, double-blind, placebo-controlled	acute ankle sprain	233	7 days	Significantly greater reduction in joint swelling with DHEP-heparin than with placebo (P=0.005). Significantly greater pain relief within 3 hours of treatment with DHEP-heparin (P<0.05)

Reference	Agent/Dosage	Study Design	Indication	Number of Patients	Duration of Treatment	Principal Findings
Claeys et al,[33] 2011	lidocaine (≤250 mg)–prilocaine (≤250 mg) cream, 30 minutes before debridement; nitrous oxide–oxygen mixture (NOOM) inhalation, 3 minutes before debridement (9-12 L/min for ≤15min); each NOOM followed by oxygen inhalation of 3 L/min for 5 min	randomized, open-label	debridement of leg ulcers	41	up to 2 weeks (one debridement session per day)	Significantly less pain in the lidocaine-prilocaine group than in NOOM group ($P<0.001$)
Barton et al,[34] 2011	baclofen 10 mg, amitriptyline HCl 40 mg, and ketamine 20 mg in a pluronic lecithin organogel (BAK-PLO); application of 1 level spoonful 2× daily	randomized, double-blind, placebo-controlled	chemotherapy-induced peripheral neuropathy	208	4 weeks	Greater improvement in sensory ($P=0.053$) and motor ($P=0.021$) symptoms with BAK-PLO than with placebo
Cianchetti,[35] 2010	capsaicin jelly 0.1%, 0.05-0.10 mL per scalp artery; massaged onto scalp in randomized succession with placebo half hour after first application if ≤50% pain reduction; if <50% reduction, alternate jelly not applied	randomized, single-blind, placebo-controlled, crossover	migraine pain	23	pain relief measured within 30 minutes of application	In the absence of migraine attacks, >50% reduction in arterial pain in 17 patients with capsaicin vs 2 with placebo. During mild or moderate attacks, >50% improvement in 11/17 patients on capsaicin vs 1 on placebo

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Rehm et al,[36]2010	lidocaine plaster 5%, 700 mg/plaster, ≤3 plasters/day; oral pregabalin 150-600 mg/day; both drugs in combination (only received by nonresponders to monotherapy: numerical rating scale, 3 days' previous pain [NRS-3] >4) during the 8-week combination phase, dosed in the same way as during the monotherapy phase	randomized, open-label, noninferiority study	postherpetic neuralgia	98	12 weeks total; 4-week comparison of 5% lidocaine plaster with oral pregabalin; 8-week combination phase (patients insufficiently treated during the initial 4 weeks [NRS-3 >4] received both drugs in combination; patients with NRS-3 ≤4 continued monotherapy)	Lidocaine plaster at least as effective as oral pregabalin in reducing pain, with a faster onset of action and a favorable benefit-risk ratio; combination therapy also effective and well tolerated
Mueller et al,[37] 2010	diclofenac sodium patch 140 mg 2× daily	post hoc analysis of randomized, double-blind, placebo-controlled	acute traumatic sports (soft tissue) injury	120	7 days	Diclofenac sodium patch consistently more effective than placebo in relieving pain. Greatest group differences after 2 and 3days of treatment (P<0.001)
Backonja et al,[38] 2010	capsaicin dermal patch 8%, 640 μg/cm^2, single application; low-concentration capsaicin patch control 0.04%, 3.2 μg/cm^2, single application	randomized, double-blind, with open-label extension	postherpetic neuralgia	44	48 weeks total; 4 weeks double-blind period, up to 44 weeks open-label extension	Significantly (P=0.003) greater reduction in pain with capsaicin patch than with control during double-blind period. Efficacy (reduction in NRS scores) maintained during open-label extension (weeks 2-12 and subsequent re-treatment cycles during 48 weeks)
Hsieh et al,[39] 2010	diclofenac sodium patch 60 mg 3× daily; menthol (control) patch 3× daily	randomized, double-blind, placebo-controlled	myofascial pain syndrome	153	7 days	Significant reduction in pain, improvement in function with diclofenac sodium patch vs placebo (P<0.05)

Reference	Agent/Dosage	Study Design	Indication	Number of Patients	Duration of Treatment	Principal Findings
Baron et al,[40]2009	lidocaine plaster 5%, 700 mg/plaster, ≤4 plasters/day; oral pregabalin 150-600 mg/day	randomized, open-label, noninferiority study	postherpetic neuralgia, diabetic polyneuropathy	300 (96 post herpetic neuralgia, 204 diabetic polyneuropathy)	4 weeks	Postherpetic neuralgia: lidocaine plaster more effective than oral pregabalin. Diabetic polyneuropathy: both treatments comparable in efficacy
Binder et al,[41] 2009	lidocaine plaster 5%, 700 mg/plaster, ≤3 plasters/day	randomized, double-blind, placebo-controlled	postherpetic neuralgia	265 (71, double-blind phase)	8 weeks, open-label run-in phase; 2 weeks, double-blind phase	In intent-to-treat population, lidocaine comparable to placebo in the median time to exit from double-blind phase (due to lack of efficacy assessed on intent-to-treat basis). In per-protocol population, median time to exit from double-blind phase significantly longer with lidocaine vs placebo (P=0.04). Lidocaine improved pain, allodynia, quality of life, and sleep measures. Lidocaine associated with lower incidence of adverse events (AEs; mostly reversible skin reactions) and study withdrawal
Baron et al,[42] 2009	lidocaine plaster 5%, 700 mg/plaster, ≤4 plasters/day; oral pregabalin 150-600 mg/day	randomized, controlled, open-label	postherpetic neuralgia, diabetic polyneuropathy	146 (55 post herpetic neuralgia, 91 diabetic polyneuropathy)	4 weeks	Postherpetic neuralgia: greater reduction in pain scores with lidocaine than with pregabalin (63.0% vs 37.5%); diabetic polyneuropathy: group treatments were comparable
Kanai et al,[43] 2009	lidocaine pump spray 8%, optimal dose of ≤30 sprays (0.1 mL per spray, 30 times) individually determined	randomized, double-blind, placebo-controlled, crossover	posttraumatic peripheral neuropathy	31	14 days (7 days per treatment)	Significant reduction in pain and allodynia with lidocaine spray, compared with placebo (P<0.01)

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Paoloni et al,[44] 2009	glyceryl trinitrate patches 0.72, 1.44, or 3.6 mg/day	randomized, double-blind, placebo-controlled	chronic lateral epicondylosis	154	8 weeks	Significant decrease in elbow pain with 0.72-mg/day dose compared with placebo (P=0.04); no other significant differences
Dualé et al,[45] 2008	amitriptyline (25, 50, or 100 mmol/L) 82.4 mg/day; saline (0.9% sodium chloride; control); lidocaine-prilocaine cream 50 mg/50 mg per day (2.5%/2.5%; positive control)	randomized, double-blind, controlled	healthy volunteers	15	1 session; pain sensitivity measured up to 24 hours after administration	Significant decreases in heat and cold thresholds with amitriptyline (P=0.004, P=0.01, respectively) vs placebo. Mild and transient (<4 hours) increase in tactile and mechanical nociceptive thresholds with amitriptyline
D'Anchise et al,[46] 2007	diclofenac gel 1.16 g/6-cm 4× per day; comfrey extract 6-cm ointment layer 4× daily	randomized, single-blind	acute ankle sprain	164	1 week	Diclofenac gel inferior in efficacy to comfrey extract
Ho et al,[47]2008	amitriptyline 5% (50 mg/mL), 3-5 mL twice daily; lidocaine 5% (50 mg/mL), 3-5 mL twice daily	randomized, double-blind, placebo-controlled, crossover	neuropathic pain (postsurgical, postherpetic, or diabetic)	35	1 week each treatment	Decreased pain intensity scores (P=0.013), but minimal clinical improvement, with lidocaine vs amitriptyline. No significant effect with amitriptyline; no significant difference between lidocaine and placebo
Paoloni and Murrell,[48] 2007	glyceryl trinitrate patch 1.25-5 mg/day, application duration varied (8 hour/day to continuous)	randomized, double blind, placebo-controlled	chronic noninsertional Achilles tendinopathy	52	follow-up at 3 years of previous 6-month study	Significantly less Achilles tendon tenderness (P=0.03) and more improvement in symptoms (P=0.04) with glyceryl trinitrate vs placebo. More patients (88%) asymptomatic after glyceryl trinitrate than after rehabilitation alone (67%)
Gorouhi et al,[49] 2007	pimecrolimus cream 1% 4× daily; triamcinolone acetonide paste 0.1% 4× daily	randomized, single-blind	oral lichen planus	40	2 months	No significant difference in efficacy between pimecrolimus and triamcinolone acetonide; both showed significant improvement in all efficacy endpoints (P<0.05)

Reference	Agent/Dosage	Study Design	Indication	Number of Patients	Duration of Treatment	Principal Findings
Welling,[50] 2007	15 g IntraSite[b] gel plus 10 mg/mL morphine sulphate; 15 g IntraSite gel plus 1 mL sterile water; conventional Jelonet[c] dressing (control); 1 application, each	randomized, double-blind, placebo-controlled	minor superficial burns	49	1 application in emergency department; pain measured at 2, 6, and 12 hours after application	Topical morphine showed the greatest decrease in pain scores (>20 mm on a 100-mm scale) on 2 consecutive time assessments (2 and 6 hours). Patients on morphine gel required more supplementary analgesia than those receiving placebo gel or Jelonet dressings
Sibbald et al,[51] 2007	ibuprofen foam dressing 50 mg, 1 application	pilot, open, comparative and prospective block-randomized	painful venous leg ulcers	24	1 application; patients rated pain intensity during 1 week	Significant reduction in pain with ibuprofen foam dressing, compared with local best practice ($P<0.05$) (eg, moist healing/antimicrobial/anti-inflammatory dressings)
Gottrup et al,[52] 2007	adhesive ibuprofen foam dressing 112.5 mg; foam nonadhesive dressing alone; dressings were changed every 48 hours to ensure uniform absorption/retention	randomized, double-blind, placebo-controlled	painful venous leg ulcers	122	6 weeks	Significantly greater pain relief with ibuprofen foam than with control dressing ($P<0.05$) during the first 5 days (primary endpoint)
Lee et al,[53] 2007	capsaicin cream 0.075%, 40 μL (a 6-mm strip of capsaicin cream) 4× daily	open-label	healthy volunteers; experimental, evoked pain (mechanical, heat, cold)	20	2 weeks	Capsaicin decreased facial sensitization to mechanical, heat, and cold pain. No effect on normal, nonpainful stimuli. Burning sensation after capsaicin application to the face decreased with continuing treatment
Esparza et al,[54] 2007	diclofenac gel 2-4 g 3× daily; ketoprofen transdermal delivery system patch 100 mg once daily	randomized, open-label	sports-related soft tissue injuries	223	7-14 days	Ketoprofen comparable in efficacy (noninferior) to diclofenac in reduction of baseline pain during daily activities. Significantly higher cure rate with ketoprofen than with diclofenac ($P=0.004$). Significantly higher patient ratings on treatment comfort with ketoprofen ($P=0.001$)

Reference	Agent/Dosage	Study Design	Indication	Number of Patients	Duration of Treatment	Principal Findings
Jensen et al,[55]2006	lidocaine patch 5%, 700 mg/patch, ≤3 patches/day; single injection of 0.5 mL lidocaine 1% plus methylprednisolone 40 mg	randomized, open-label	carpal tunnel syndrome	40	4 weeks	Lidocaine patch (daily application) comparable in efficacy to single injection of lidocaine plus methylprednisolone
Pöyhiä and Vainio[56]2006	ketamine gel 50 mg/mL, 1 mL rubbed into forearm 10 minutes prior to capsaicin injection	randomized, double-blind, placebo-controlled, crossover	healthy volunteers; experimental pain	9	1 application/ injection; pain measured up to 1 hour after injection	No effect of ketamine on immediate burning pain after capsaicin administration. Significant (P<0.05) decrease in intensity and unpleasantness of mechanical hyperalgesia with ketamine, compared with placebo. No evidence of tactile allodynia or thermal hyperalgesia
Predel et al,[57] 2005	diclofenac gel with diethylamine salt 1.16 g 4× daily; comfrey extract 6-cm ointment layer 4× daily	randomized, single-blind, noninferiority	acute ankle sprain	164	7 days	Comfrey extract comparable in efficacy (noninferior) to diclofenac gel in decreasing pain upon pressure to injured joint
Baer et al,[58]2005	diclofenac solution ~1.3 mL (40 drops) 4× daily	randomized, double-blind, vehicle-controlled	osteoarthritis of the knee	216	6 weeks	Significant improvements in pain (P=0.003), physical function (P=0.001), and stiffness (P=0.002) with diclofenac topical solution vs control
Lynch et al,[59] 2005	amitriptyline 2% cream, 4 mL 3× daily; ketamine 1% cream, 4 mL 3× daily; both products in combination	randomized, double-blind, placebo-controlled	neuropathic pain (various etiologies)	92	3 weeks	No significant difference in efficacy between treatments
Vernassiere et al,[60] 2005	IntraSite[b]gel plus morphine HCl 10 mg once daily	randomized, double-blind, placebo-controlled	chronic skin ulcers	18	5 days	No significant difference in pain reduction between morphine and placebo gels
Di Rienzo et al,[61] 2004	diclofenac solution 16 mg/mL (10 drops) 4× daily; oral diclofenac 50 mg 2× daily	randomized, open-label	Temporo-mandibular joint dysfunction	36	2 weeks	No significant difference in efficacy between topical and oral diclofenac. Better tolerability with topical diclofenac (lack of systemic AEs)

Reference	Agent/Dosage	Study Design	Indication	Number of Patients	Duration of Treatment	Principal Findings
Myrer et al,[62] 2004	Joint-Ritis[d] ~2 mL 3× daily	randomized, double-blind, placebo-controlled	chronic knee pain	43	5 weeks	No significant difference in pain reduction between active treatment and placebo (both patient groups experienced pain reduction, significant for all 3 pain scale scores [$P<0.05$])
Predel et al,[63] 2004	diclofenac sodium patch 140 mg 2× daily	randomized, double-blind, placebo-controlled	traumatic blunt soft tissue injuries	120	7 days	Significant decrease in tenderness during first 3 days with diclofenac patch, compared with placebo ($P<0.001$). Significantly ($P < 0.001$) shorter time to resolution of pain with diclofenac, compared with placebo
Kucera et al,[64] 2003	Sportino Acute Spray[e] 200 μL; active components of Sportino separately: ethanol 70%, 200 μL; arnica 200 μL; hydroxyethyl salicylate 200 μL; all single dose	randomized, single-blind, placebo-controlled	healthy volunteers (experimental pain)	40	single dose of each treatment and placebo (8-day washout between 2 treatment periods)	Combination of active agents showed significantly greater analgesic effects than individual agents ($P<0.05$)
Meier et al,[65] 2003	lidocaine patch 5%, 700 mg/patch, ≤4 patches for 12 hours/day	randomized, placebo-controlled, 2-way crossover	focal peripheral neuropathic pain syndromes	40	2 weeks separated by a 1-week washout period (2-week washout for patients without returning pretreatment pain)	As add-on therapy to current medication, lidocaine produced significant reductions in continuous pain ($P=0.017$) and allodynia ($P=0.023$) within 8 hours of first application, with continued efficacy ($P=0.018$) during 7 days
Carneiro et al,[66] 2002	phenytoin (dosage not reported); silver sulfadiazine/chlorhexidine (dosage not reported)	randomized, controlled	superficial dermal burn injuries	64	≤2 weeks (until complete wound healing or granulation of tissue ready for grafting)	Significant decrease in wound pain with phenytoin, compared with silver sulfadiazine/chlorhexidine ($P<0.01$)

Reference	Agent/Dosage	Study Design	Indication	Number of Patients	Duration of Treatment	Principal Findings
Lynch et al,[67] 2003	amitriptyline cream 1%, 5 mL; ketamine cream 0.5%, 5 mL; both products in combination, 5 mL; placebo (vehicle)	randomized, double-blind, placebo-controlled, 4-way crossover for all treatments, with open-label extension treatment for combination	neuropathic pain	20	2 days for crossover phase followed by 7 days for open-label phase	Double-blind phase: no significant difference in pain relief between active treatments and placebo. Open-label phase: combination treatment showed significant improvement in all pain relief scores ($P<0.05$), except pain intensity ($P<0.08$), vs placebo
Gerner et al[68] 2003	amitriptyline 0, 50, or 100 mmol/mL, 1 application	randomized, double-blind, placebo-controlled	healthy volunteers (experimental pain)	14	1-hour application of medicated dressing; pain measured 1 hour after dressing removal and each hour for next 7 hours	Significantly greater analgesic effect with amitriptyline (50 or 100 mmol/L) vs placebo or 10 mmol/L (both, $P<0.05$); no significant difference between placebo and 10 mmol/L or between 50 and 100 mmol/L
Hwang et al,[69] 2003	glyceryl trinitrate ointment 0.2%, 20 g during 3-week treatment period	randomized, double-blind, placebo-controlled	Posthemorrhoid-ectomy pain	110	3 weeks	Significant reduction in pain scores ($P<0.001$) and increase in wound healing rates ($P=0.002$) with glyceryl trinitrate vs placebo
Carneiro and Nyawawa,[70] 2003	phenytoin (dosage not reported); Edinburgh University solution of lime (dosage not reported)	randomized, controlled	chronic leg ulcers	102	≤4 weeks (until complete wound healing or granulation of tissue ready for grafting)	Significant ($P<0.05$) reduction in pain with phenytoin on day 7 (in all patients) and on day 14 (in patients with severe pain) ($P<0.01$). Significant clearance of ulcer discharge with phenytoin on days 7 and 14 ($P<0.05$). Improved wound healing with phenytoin
Whitefield et al,[71] 2002	ibuprofen gel 5%, (amount not reported), 1x daily plus placebo tablet, 3x daily; placebo gel, 1x daily plus oral ibuprofen 400 mg, 3× daily	randomized, double-blind, double-dummy	acute soft tissue injuries	100	≥7 days	No significant differences between treatments in any efficacy measures

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Balakrishnan et al,[72] 2001	acetylsalicylic acid (ASA) 75 mg ASA/mL of moisturizer, 5-10 mL 3× daily; oral ASA 375-750 mg 3× daily	randomized, open-label	acute herpetic neuralgia	30	3 weeks	Topical ASA superior to oral ASA in relieving pain associated with acute herpetic neuralgia (P<0.001)
McCleane,[73] 2000	doxepin HCl 3.3% (dosage not reported); capsaicin 0.025% (dosage not reported); both products in combination; each cream applied equal to size of a grain of rice 3× daily	randomized, double-blind, placebo-controlled	chronic neuropathic pain	200	4 weeks	Each treatment significantly more effective than placebo in pain reduction (for all, P<0.001). No significant difference in efficacy among the 3 treatments, but fastest analgesia with the combination cream
Galer et al,[74] 2000	diclofenac epolamine 1.3% patch 2× daily	randomized, double-blind, placebo-controlled	minor sports injuries	222	2 weeks	Significantly greater pain relief with diclofenac patch than with placebo on days 3 (P=0.036) and 14 (P=0.048). No significant group differences in safety/tolerability
Paice et al,[75] 2000	capsaicin cream 0.075% 4× daily (amount of cream not reported)	randomized, double-blind, controlled	human immuno-deficiency virus–associated distal symmetrical peripheral neuropathy	26	4 weeks	Significantly higher pain scores with capsaicin than with placebo at week 1 (P=0.042). Significantly higher study discontinuation rate with capsaicin than with vehicle (P=0.014)
Sjölund et al,[76] 1999	adenosine 60 μg/kg/min; intravenous infusion for 60 or 120 minutes, starting 15 minutes before induction of chemical (forearm) or thermal (lower leg) burn, respectively	randomized, double-blind, placebo-controlled, crossover	healthy volunteers	10	1-2 weeks between experimental sessions (adenosine or placebo)	Adenosine significantly reduced area of secondary hyperalgesia vs placebo (P<0.05)
Hadley et al,[77] 1998	quaternary ammonium 27 emulsion (dose not reported) 4× daily	randomized, double-blind, placebo-controlled, crossover	chronic pain associated with arthritis, tendinitis, or bursitis	100	2 weeks per treatment; 1-week washout period between each 2-week session	Temporary pain relief with test compound

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Bareggi et al,[78]1998	ASA 750 mg crushed into powder in diethyl ether 20 mL (ADE) for topical application; oral ASA 500 mg; single dose, each	randomized, single-blind, crossover	acute herpetic neuralgia, postherpetic neuralgia	19	1-week washout between single doses of each agent; pain measured 1 hour after administration	Rapid analgesic effect after topical application, but not after oral dosing. Greater pain relief with ADE vs oral ASA (82.6% vs 15.4% decrease in visual analog scale scores). Skin concentrations of ASA 80- to 100-fold higher after topical administration than after oral treatment
Svensson et al,[79] 1997	ibuprofen gel 5%, 2 g 3× daily; oral ibuprofen 400 mg 3× daily	randomized, double-blind, placebo-controlled, crossover	postexercise jaw muscle stiffness	10	3 days postexercise period following each exercise bout (5-minute jaw exercise, 3 bouts separated by 2 weeks)	Significantly higher pressure pain thresholds after topical ibuprofen than after oral ibuprofen or placebo ($P<0.05$)
Burnham et al,[80] 1998	diclofenac 2% in pluronic lecithin liposomal organogel 3× daily	randomized, double-blind, placebo-controlled, crossover	lateral epicondylitis	14	1 week per treatment, 1-week washout between treatments	Significantly less pain ($P=0.007$) and greater wrist extension strength ($P=0.03$) with diclofenac than with placebo
Patel and Leswell,[81]1996	ketoprofen gel 2.5%, 4-5 g 3× daily; piroxicam gel 0.5%, 1 g 3× daily; diclofenac gel 1%, 2-4 g 3× daily	randomized, open-label	acute soft tissue injuries	1575	5 days	Ketoprofen gel significantly better than piroxicam gel in physician global assessment of treatment response ($P<0.001$), improvement in stiffness ($P=0.013$), restriction of mobility ($P=0.006$), and pain with pressure ($P=0.02$) or movement ($P=0.01$). Greater proportion of patients rated their injury “greatly improved” with ketoprofen vs diclofenac (38% vs 30%)

Reference	Agent/Dosage	Study Design	Indication	Number of Patients	Duration of Treatment	Principal Findings
De Benedittis and Lorenzetti,[82] 1996	ASA (median dose: 1000 mg) in diethyl ether; diclofenac (median dose: 100 mg) in diethyl ether; indomethacin (median dose: 75 mg) in diethyl ether; single dose, each	randomized, double-blind, placebo-controlled, crossover	acute herpetic neuralgia, postherpetic neuralgia	37	pain measured after single dose of each agent (total of 4 single sessions of each topical agent)	Only ASA superior to placebo in reduction ($P<0.05$) and duration ($P<0.01$) of pain relief
Rowbotham et al,[83] 1996	lidocaine patch 5%, 700 mg/patch, ≤3 patches/day; vehicle only (placebo)	randomized, double-blind, vehicle-controlled, crossover	postherpetic neuralgia	35	four 12-hour application sessions: 2 lidocaine, 1 vehicle, 1 no treatment	Significant pain relief with lidocaine patches from 30 minutes to 12 hours, compared with no treatment, and from 4–12 hours, compared with control patches
Roth,[84] 1995	diclofenac 3%/sodium hyaluronate 2.5% gel, 2 g 4× daily	randomized, placebo-controlled	osteoarthritis	119	2 weeks	Greater analgesic effect with diclofenac than with placebo, effect not significant ($P=0.057$)
Campbell and Dunn,[85] 1994	ibuprofen cream, 4 inches 4× daily	randomized, double-blind, placebo-controlled	acute ankle sprain	100	≤2 weeks	Significant reduction in pain scores during first 48 hours of treatment (days 2 and 3) with ibuprofen vs placebo ($P<0.05$)
Airaksinen et al,[86] 1993	ketoprofen gel 2.5%, 125 mg/dose, 5 g 2× daily	randomized, double-blind, placebo-controlled	acute soft tissue injuries	56	7 days	Significant reduction in pain at rest with ketoprofen compared with placebo ($P<0.05$)

Reference	Agent/Dosage	Study Design	Indication	Number of Patients	Duration of Treatment	Principal Findings
De Benedittis et al,[87] 1992	ASA (mean dose: 1030 mg) in diethyl ether 3× daily	open-label	acute herpetic neuralgia, postherpetic neuralgia	45	4 weeks	Topical ASA/diethyl ether promoted healing of herpetic lesions. In ASA treatment group, incidence of postherpetic neuralgia lower than that of disease natural history in publications
	ASA (median dose: 1000 mg) in diethyl ether, indomethacin (median dose: 75 mg) in diethyl ether, or diclofenac (median dose: 100 mg) in diethyl ether	pilot double-blind, placebo-controlled crossover		11	single session	ASA (but not indomethacin or diclofenac) was significantly superior to placebo in respect to pain relief (P<0.05)
Russell,[88]1991	piroxicam 0.5% gel, 5 mg 4× daily	randomized, double-blind, placebo-controlled	acute soft tissue injuries	200	7-21 days	Significantly greater reductions in pain, joint restriction, pressure threshold, and tenderness with piroxicam, compared with placebo (P<0.05)
Akermark and Forsskåhl,[89]1990	indomethacin in 1% alcoholic solution (3-5 × 0.5-1.5 mL spray) and 3 placebo capsules daily; placebo spray (3-5 × 0.5-1.5 mL) and 3 indomethacin capsules (25 mg) daily; placebo spray and 3 placebo capsules daily	randomized, double-blind, double-dummy	superficial overuse sports injuries	70	2 weeks	Per patient assessment, significantly greater pain reduction with topical indomethacin than with oral indomethacin on days 3 and 7 (P<0.05). No significant group differences during second week. Systemic AEs (mainly gastrointestinal and central nervous system) with oral indomethacin
Baixauli et al,[90] 1990	naproxen 10% gel, 3-5 g 2× daily; ketoprofen 10% gel, 3-5 g 2× daily	randomized, single-blind	acute soft tissue injury	30	7 days	Gels comparable in efficacy and tolerability, but naproxen showed significantly greater reduction in pain with deep palpation on day 3 (P=0.02)

Reference	Agent/Dosage	Study Design	Indication	Number of Patients	Duration of Treatment	Principal Findings
Bouchier-Hayes et al,[91] 1990	diclofenac gel 4 g 3× daily; felbinac gel 4 g 3× daily	randomized, single-blind	acute soft tissue injury	384	3 or 7 days	Greater efficacy with diclofenac than with felbinac on all measures. Significantly greater reduction of bruising and pain at rest on day 3 (P=0.03) and of pain with pressure on day 7 (P=0.009) with diclofenac than with felbinac
Ginsberg and Famaey, [92] 1987	Rado-Salil ointment[f] (dosage not reported)	randomized, double-blind, placebo-controlled	acute mechanical low-back pain	40	2 weeks	Significant improvement in pain and muscular contracture with test ointment, compared with placebo, at days 3 and 14 (P<0.001). Decreased use of oral analgesics with test ointment

[a]Abbreviations: ADE = acetylsalicylic acid in diethyl ether; AE = adverse event; ASA = acetylsalicylic acid; BAK-PLO = baclofen, amitriptyline, and ketamine in a pluronic lecithin organogel; DHEP = diclofenac epolamine; NOOM = nitrous oxide–oxygen mixture; NRS = numerical rating scale. [b]Smith and Nephew, Yorkshire, UK. [c]Smith and Nephew, Yorkshire, UK. [d]Menthol (active ingredient) plus essential oils of eucalyptus, copaiba, citrus, and lavender, with moisturizers (chondroitin sulfate, glucosamine sulfate, and lanolin); Naturopathic Labs Intl., Inc., St. Petersburg, Florida.[62] [e]Arnica plus hydroxyethyl salicylate in ethanolic solution; Harras Pharma Curarina Arznelmittel GmbH, Munich, Germany.[64] [f]Main ingredients: ethyl salicylate, methyl salicylate, glycol salicylate, salicylic acid, camphor, menthol, capsicum oleoresin; Will Pharma, Belgium.[92]