1. Apomorphine

**Q4660:** T. T. Yan, et al. Daily Injection But Not Continuous Infusion of Apomorphine Inhibits Form-Deprivation Myopia in Mice. INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE 2015;56(2475-2485)

**ALZET Comments:** Apomorphine; SC; Mice; 1002; 4 weeks; Controls received mp w/ vehicle; animal info (male, C57Bl6, 4 weeks old); functionality of mp verified by residual volume; pumps replaced every 2 weeks; comparison of injection vs mp;.

**Q0779:** R. Sarkis, et al. Chronic dizocilpine or apomorphine and development of neuropathy in two rat models I: Behavioral effects and role of nucleus accumbens. Experimental Neurology 2011;228(1):19-29

**ALZET Comments:** MK-801; apomorphine HCL hemihydrate; Saline; Ascorbic acid; CSF/CNS (nucleus accumbens); Rat; 2002; Controls received mp w/ vehicle; animal info (adult, female, Sprague Dawley, 200-300 g); post op. care (dexamethasone injections to prevent brain edema); behavioral testing (mechanical allodynia, Paw withdrawal latency, cold allodynia, hotplate test, spontaneous motor activity); cannula placement verified by picomicrograph of brain section; CCI, chronic constriction injury; SNI, spared nerve injury.


**ALZET Comments:** MPTP; L-dopa; apomorphine; IP; SC; Mice; 2004; 1-28 days; Controls received mp w/ saline; comparison of IP injections vs. mp; neurodegenerative (Parkinson’s disease); L-dopa and apomorphine group had SC implanted pumps; route is unclear for the MPTP group; "Continuous MPTP infusions thus recreate a disease state that mimics human PD better than acute MPTP bolus injections." (p. 3417); MPTP group received IP pumps (2004 model), verified by e-mailing author.


**ALZET Comments:** Apomorphine; Saline; SC; Mice; 28 days; Controls received mp w/ vehicle; comparison of sc bolus injections vs. mp; 20-day stability verified by HPLC (p.368); neurodegenerative (Parkinson’s disease); "The neurorescue effect of continuous subcutaneous infusion of apomorphine is particularly promising from a clinical standpoint." (p.372).


**ALZET Comments:** Apomorphine; L-DOPA methyl ester; Benserazide; Tetrabenazine; Ascorbic acid; Propylene glycol; SC; Rat; 2ML2; 2 weeks; controls received mp with propylene glycol; 2 mps used to deliver apomorphine.


**ALZET Comments:** Apomorphine; Haloperidol; Methamphetamine; SC; Rat; 2 weeks; japanese with english abstract.

**P1339:** M. A. Lyerly, et al. The deafferentation syndrome in the rat: effects of intraventricular apomorphine. Exp. Neurol 1988;100(188-202

**ALZET Comments:** Apomorphine; Ascorbic acid; water; CSF/CNS; Rat; 2002; 2 weeks; mp connected to cannula; stress/adverse reaction (pg 198).

**P1291:** C. A. Altar, et al. Dopamine release and metabolism after chronic delivery of selective or nonselective dopamine autoreceptor agonists. Mol. Pharmacol 1988;33(690-695

**ALZET Comments:** CGS-15855A; Apomorphine; Dopamine, antagonists; Ascorbic acid; Saline; SC; Rat; 2ML2; 2, 14 days; comparison of ip injections vs. mp infusion; functionality of mp verified by serum, brain levels; stability verified at 14 days by HPLC.
**ALZET Comments:** Apomorphine; FK-33824; Haloperidol; Naloxone; Ethanol; Tartaric acid; Water; SC; Rat; 5, 9 days; mp model not stated; controls received mp w/unspecified vehicle or were sham-operated; agents infused separately w/appropriate vehicle; comparison of sc inject. vs. mp infusion.

**ALZET Comments:** Apomorphine; Ascorbic acid; DMSO; SC; mice; 2002; 8-10 days; controls rec'd mp w/ vehicle; 6-OHDA unilateral lesions of the nigrostriatal dopaminergic neurons; no stress (see p. 243).

**ALZET Comments:** Apomorphine HCl; Ascorbic acid; Water; SC; Rat; 2ML1; 5 and 15 days; pump replaced on 8th day; pumps replaced w/ pumps previously incubated in saline.

**ALZET Comments:** Apomorphine HCl; Saline; SC; Rat; 2001; no duration posted; comparison of agents effects.

2. Buprenorphine

**ALZET Comments:** Morphine; buprenorphine; methadone; Saline; SC; Mice; 6 days; Dose (45 mg/kg/d; 5 mg/kg/day; 60 mg/kg/day); Controls received mp w/ vehicle; animal info (Male CD-1 mice, approximately 30g); comparison of morphine alkaloid pellet vs mp.;

**ALZET Comments:** Buprenorphine; methadone; Saline; SC; Mice; 6 days; Controls received mp w/ vehicle; animal info (male, CD-1, 30g); behavioral testing (tail flick latencies, mouse locomotion); dependence; Dose (Buprenorphine 5 mg/kg/day; methadone 60 mg/kg/day);.

**ALZET Comments:** Buprenorphine; SC; Mice; 1007D; 7 days; Controls received mp w/ PBS; animal info (female, C57BL6, 8 weeks old); behavioral testing (pain score); “we used subcutaneously implanted ALZET® osmotic pumps to apply the analgesic buprenorphine. We ob-served strongly reduced pain scores in diseased mice receiving analgesics, whereas the immune response was not altered in these mice. Hence, our study offers a new treatment option to improve wellbeing of mice used to study LCMV-induced meningitis without grossly altering immune parameters “ pg 184; “In this study, we subcutane¬ously implanted ALZET® osmotic pumps releasing the anal¬gesic agent buprenorphine. Continuous delivery with osmotic pumps ensures constant compound levels for maximized therapeutically efficacy and reduced adverse effects. Additionally, un¬necessary stressful animal handling due to repeated injection is not required. ” pg 188; Dose (0.15 mg/kg/day);.

ALZET Comments: Fentanyl propionanilide; buprenorphine hydrochloride; Saline, isotonic; CSF/CNS (intrathecal); Rat; 96 hours; Controls received mp w/ vehicle; animal info (male Wistar, 200-250 g); pain.

ALZET Comments: Buprenorphine; DMSO; water; Rat; 2ML1; Controls received mp w/ vehicle; functionality of mp verified by plasma drug levels; animal info (male, Sprague Dawley, 150-200 g.); 40% DMSO used; “the osmotic minipump delivered buprenorphine efficiently and predictably” pg. 7342.

ALZET Comments: Buprenorphine; SC; Rat; 2ML2; Controls received sham surgery; animal info (male, Long-Evans, 350-375 g.).

ALZET Comments: Buprenorphine HCL; SC; Rat; 2ML2; 14, 28 days; Controls received sham surgery; dose-response (fig. 2); pumps replaced after 14 days; half-life (pg. 300) long half-life; tolerance; animal info (male, Long-Evans, 325-350g.).

ALZET Comments: Buprenorphine; SC; Rat; 2ML2; 28 days; Controls received sham surgery; functionality of mp verified by plasma buprenorphine levels; dose-response (fig. 1); pumps replaced after 14 days; no stress (see pg. 29); dependence; animal info (male, Long-Evans, 300-350g.).

ALZET Comments: Buprenorphine; CSF/CNS (nucleus accumbens); Rat; 2ML2; Controls received incision and pocket, no pump; dependence; post op. care (antibiotic injection); animal info (male, long-evans, 350-375 g); Plastics One 20G cannula used.

ALZET Comments: Buprenorphine; Mice; 1,5,10 days;

ALZET Comments: Buprenorphine; SC; Mice; 12 hours; Pain treatment.

3. Butorphanol

Q5136: M. Meredith M. Clancy DVM, et al. Pharmacokinetics of butorphanol delivered with an osmotic pump during a seven-day period in common peafowl (Pavo cristatus). American Journal of Veterinary Research 2015;76(12):1070-1076
ALZET Comments: Butorphanol; SC; Bird (peafowl); 2ML1; 7 days; animal info: 14 healthy adult male common peafowl; functionality of mp verified by plasma levels; good methods (pg. 1071-1072); “Use of these osmotic pumps may provide options for avian analgesia.” pg 1070; analgesic administration to avian species; Pharmacokinetics; Dose: 247 ug/kg/h; Resultant plasma level ((mean, 106.4 ug/L; range, 61.8 to 133.0 ug/L)); Industry authored (Wildlife Conservation Society); Interesting (Plasma concentrations of butorphanol in common peafowl were maintained at or above reported efficacious analgesic concentrations; Use of these osmotic pumps may provide options for avian analgesia) pg. 1070.

**ALZET Comments:** Butorphanol tartrate; SC; Rat; 2ML1; 48 hours; Controls received mp w/ saline; animal info (Sprague Dawley, male, 302 g); “Implantation of the pumps took less than 1 min per rat, and the length of the anesthesia was approximately 5 min per rat.” pg 576; functionality of mp verified via residual volume.


**ALZET Comments:** Butorphanol tartrate; nitroindazole, 7-; Saline; DMSO; CSF/CNS; Rat; 2001; 72 hours; Enzyme inhibitor (nitric oxide synthase, NOS); animal info (male, Sprague Dawley, 250-275 g.); pump connected to catheter after 1 week recovery period; 10% DMSO used; PE60 tubing used.


**ALZET Comments:** Butorphanol tartrate; Saline, physiological; CSF/CNS; Rat; 2001; 3 days; Controls received mp w/ vehicle; dependence; post op. care (procaine penicillin G; animal info (male, Sprague-Dawley, 250-275 g).


**ALZET Comments:** Butorphanol tartrate; CSF/CNS; Rat; 2001; 3 days; Controls received mp w/ saline; dependence; animal info (male, Sprague-Dawley 230-250 g).


**ALZET Comments:** Butorphanol tartrate; CSF/CNS; Rat; 2001; 72 hours; Controls received mp w/ saline; functionality of mp verified by residual drug volume; dependence; post op. care (procaine penicillin G); stadol; mp primed overnight at 35 degree C in sterile saline.


**ALZET Comments:** Butorphanol; Saline; CSF/CNS; Rat; 2001; 72 hours; Controls received mp w/ vehicle; tolerance; guide cannula used (10mm); solution was filter sterilized.


**ALZET Comments:** Butorphanol; morphine; Saline, sterile; CSF/CNS; Rat; 2001; 72 hours; Controls received mp w/ vehicle; dependence; post op. care (penicillin, 0.5% sensorcaine in wound site); guide cannula with stylet was used; dental cement used to adhere cannula to skull; protective aluminum cap was placed around the cannula; tygon tubing was used; solutions were filter sterilized during filling of the pumps; brain diagram (p. 1066).


**ALZET Comments:** Morphine sulfate; butorphanol trtartrate; CSF/CNS; Rat; 2001; 3 days; Controls received mp w/ saline; dependence; minipumps were inserted 6-10 days after guide cannula implantation; stylet used.


**ALZET Comments:** Butorphanol; CSF/CNS; Rat; 2001; 3 days; Controls received mp w/ saline; tolerance; dependence.

4. Dynorphin

ALZET Comments: Endorphin, B-; Enkephalin, leucine-; Enkephalin, methionine-; Dynorphin A; SC; CSF/CNS; Rat; 2001; 2ML1; 6 days; controls received saline infusion; peptides; ALZET brain infusion kit used.

ALZET Comments: Dynorphin A (1-13); U-50,488; DuP E3800; SC; cat; 2ML1; 7 days; controls received mp w/ saline; no stress (see pg. 2048); ischemia (cerebral).

ALZET Comments: Dynorphin A (1-13); ICI-174,864; DMSO; CSF/CNS (intrathecal); Rat; 2001; 7 days; controls received mp w/saline; mp connected to catheter i.t.; DMSO is vehicle for ICI-174864; functionality of mp verified; comparison of ICV vs. i.t. injections vs. mp infusion; stability.

ALZET Comments: Dynorphin; Saline; Rat; 2002; 7 days; controls received mp w/saline; food consumption; comparison of injections vs. mp infusion; peptides.

ALZET Comments: Dynorphin A; Calcium chloride; Magnesium chloride; Potassium chloride; Saline; CSF/CNS (intrathecal); Rat; 2001; 1 week; peptides.
ALZET Comments: Dynorphin A(1-8); Bestatin; Captopril; Dynorphin A; Enkephalin agonist DADL; Fentanyl; Thiorphan; Saline; SC; vas deferens; Mice; 2003; 2ML1; no duration posted; Comparison of agents effects; 2ML1 pump used w/ captopril, thiorphan, and bestatin; DADL & FEN admin. sc; peptides; antihypertensive.

ALZET Comments: Dynorphin (1-13); Morphine sulfate; SC; Rat; 2001; 2 days; comparison of agents effects; agents given by mp alone and in combination; peptides.

ALZET Comments: Enkephalin, Leu-; dynorphin; dynorphin (3-13); Saline; SC; Cat; 2ML1; 7 days; Controls received mp w/ vehicle; peptides; post op. care (penicillin E, lactated ringer's solution); ischemia (cerebral); animal info (adult, male, MCAO).

ALZET Comments: Endorphin, a-neo-; DsThr; Dynorphin; Enkephalin analog DADLE; FK-33824; MR-2034; MRZ; Normorphine; Sufentanil; Water; SC; mice; 2001; 6 days; peptides; MRZ is 5,9-dimethyl,2'S-5,9-dimethyl-2'-hydroxy-2-(2-methoxy-propyl)-6,7-benzomorphan, a kappa opioid agonist.

5. Endorphin

ALZET Comments: Endorphin, beta, (1-31); Saline, sterile; CSF/CNS; Rat; 2001; 1003D; 3, 7 days; Animal info (Sprague Dawley, male, 200-250 g); pumps replaced.

ALZET Comments: Endorphin, B; corticotropin releasing hormone; CSF, artificial; CSF/CNS (paraventricular nucleus of hypothalamus); Rat; 2002; 16 hours; Controls received mp w/ vehicle; peptides; animal info (male, Fischer, 160-175g.).

ALZET Comments: Endorphin, B-; CSF/CNS (paraventricular nucleus); Rat; 2002; 18 hours; Controls received mp w/ aCSF; immunology; peptides.

ALZET Comments: Endorphin, beta; CSF, artificial; CSF/CNS (paraventricular nucleus); Rat; 2002; 6 days; Plastics One bilateral guide cannula used with a Y-connector; bilateral infusion.;

ALZET Comments: Endorphin, B-; CSF, artificial; CSF/CNS; Rat; 12 days; Cardiovascular.
6. Enkephalin


**ALZET Comments:** [D-Ala2, N-Me-Phe4, Gly5-ol]-enkephalin; CSF/CNS (intrathecal); Rat; mice; animal info (rat - male, adult, Sprague Dawley, 250-300g; good methods (intrathecal catheter placement pg.11704); mice - male, adult, C57BL/6, 20-25g); No pump used, catheter only for lumbar catherization.

P7610: P. Feng, *et al.* Effects of mu, kappa or delta opioids administered by pellet or pump on oral Salmonella infection and gastrointestinal transit. European Journal of Pharmacology 2006;534(1-3):250-257

**ALZET Comments:** Morphine sulfate; enkephalin analog DPDPE; U50,488H; deltorphin II, D-alal2; Saline, pyrogen free; SC; Mice; 1003D; 48 hours; Controls received mp w/ vehicle; dose-response (fig 1); comparison of pellets vs. mp; immunology; animal info (female, 6 wk old); mp primed 4 hours in 37 C saline; "morphine pellet potently exacerbated oral salmonella infection, but morphine given by pump, at doses which were immunosuppressive had a substantially lesser effect (of infection)." (p. 251). "Further, we and others have found that morphine pellets induce sepsis in mice." (p. 251).


**ALZET Comments:** Enkephalin; Saline; SC; Mice (nude); 2004; 28 days; Controls received mp w/ vehicle; OGF plasma levels taken; comparison of IP and intratumoral injections vs. SC mp; adverse reaction: (see pg. 229) "within 2 days...3 minipumps containing saline were spontaneously dislodged." [possible pocket too small]; cancer (carcinoma); peptides; enkephalin was met-5 and termed OGF or opioid growth factor.
ALZET Comments: Morphine sulfate; Enkephalin analog DAMGO; Dermorphin-derived tetrapeptide (TAPS); CSF, artificial; CSF/CNS; Rat; 2001; 6 days; Controls received mp w/ vehicle; comparison of bolus injections vs. chronic mp; pumps replaced on day 4 to achieve 6 days due to dead space in catheter; ALZET brain infusion kit used; tolerance; dependence; peptides; second hole with guide cannula & stylet used for bolus injections; (ALZET) cannula placement confirmed by fast green dye & the guide cannula confirmed by methylene blue; TAPS is a potent mu-opioid receptor agonist.

ALZET Comments: Enkephalin; Saline; SC; Rabbit; 2ML1; 24 hours; Controls received mp w/ vehicle; cardiovascular; peptides; enkephalin was met-5.

ALZET Comments: Enkephalin analog; Naloxone; Saline; IP; Rat; 1003D; 1-3 days; controls received mp w/ vehicle; functionality of mp verified by aspirating remaining contents; peptides; Enkephalin analog ENK was (D-Met2-Pro5)enkephalinamide, inhibits epidermal growth factor.

ALZET Comments: Endorphin, B-; Enkephalin, leucine-; Enkephalin, methionine-; Dynorphin A; SC; CSF/CNS; Rat; 2001; 2ML1; 6 days; controls received saline infusion; peptides; ALZET brain infusion kit used.

ALZET Comments: Morphine sulfate; Naltrexone; Enkephalin; U-50,488H; Saline; CSF/CNS (intrathecal); Rat; 2001; 7 days; DAGO is a mu-opioid agonist; DPDPE is a delta-opioid agonist.

ALZET Comments: Naltrexone; DAGO; Enkephalin analog DADLE; DPDPE; U-50,488H; SC; CSF/CNS; Rat; 2001; 7 days; DAGO is a mu-opioid agonist; DPDPE is a delta-opioid agonist.

ALZET Comments: Enkephalin; PBS; mice; 1003D; no duration posted; no stress (see pg. 207); immunology; agents are met-enkepalin, DTLET, FK 33-824; pump implantation has no significant effect on humoral immune response as compared with sham-op and untreated animals (p. 208).

ALZET Comments: Dexmedetomidine; Clonidine; Enkephalin analog ST-91; Saline; CSF/CNS (intrathecal); Rat; 2001; 7 days; controls received mp with vehicle; tolerance; externalized loop of tubing allowed cessation of flow; dose-response (pg. 330); antihypertensive.

ALZET Comments: Morphine sulfate; Enkephalin analog DADLE; Saline; CSF/CNS (intrathecal); Rat; 2001; 7 days; controls received mp w/ vehicle; dose-response (pg.600); stability of morphine in spinal cord assessed; tolerance; "cont. spinal
infusion, in contrast to...avoids the peak and trough or exponentially decreasing concentration of tolerogen and the receptor during exposure period"; y-catheter used for intrathecal infusion.

ALZET Comments: Morphone; Sufentanil; Enkephalin; Saline; IV; CSF/CNS (intrathecal); CSF/CNS; Rat; 7 days; controls received mp w/vehicle; dose-response (p. 163); tolerance; pain; reference of mp pump study on pp. 162-164.

7. Etorphine

ALZET Comments: Etorphine; oxycodone; hydrocodone; methadone; Saline; DMSO; SC; Mice; 2001; 7 days; Controls received placebo pellets wrapped in nylon mesh; animal info (Male, Swiss Webster, 23-30 g); tolerance; comparison of SC injections vs mp; "Higher doses of hydrocodone, oxycodone, and methadone could not be infused due to solubility issues." pg 415; 20% DMSO used; "infusion with hydrocodone or methadone produced greater tolerance than acute or intermittent treatment" pg 417.

ALZET Comments: Etorphine; Saline; SC; Mice; 2001; 7 days; Controls received placebo pellet; dose-response (p. 125, 126).

ALZET Comments: Naloxone; etorphine hcl; morphine sulfate; Saline, normal; SC; Mice; 2001; 7 days; Controls received inert, placebo pellets or saline injections; comparison of SC injections vs. pellets vs. mp; tolerance; "Intermittent naloxone and etorphine treatment did not regulate u-opioid receptor or dynamin-2, despite the fact that the total amount of drug administered was the same as continuous treatment." (pg. 94); animal info (m, 22-30 grams).

ALZET Comments: Etorphine hydrochloride; Morphine sulfate; Saline; SC; Mice; 3 days; Tolerance.

ALZET Comments: Etorphine; Morphine sulfate; Saline; SC; mice; 2001; 7 days; controls received placebo pellet; functionality of mp verified by analgesia "tail-flick" dose-response test; comparison of morphine pellets vs. mp; tolerance; receptor downregulation; animal info (male, swiss webster, 22-40 grams).

ALZET Comments: Etorphine; Morphine; SC;; mice;; 2001;; 2, 3 days;; Controls received inert placebo pellet; opioid agonists; etorphine infused for 2 days; morphine infused for 3 days; morphine pellets also used in mp/morphine implanted mice.

ALZET Comments: Etorphine HCl; Saline; SC; mice; 2001; 7 days; controls received inert placebo pellet; dose-response (p. 35-38); tolerance.

ALZET Comments: Morphine sulfate; Fentanyl; Etorphine; Saline; SC; mice; 2001; 2002; 7 days; 72 hrs; controls received inert placebos; comparison of SC injections vs. mp; tolerance; "Intrinsic efficacy appears to induce tolerance more significantly after continuous administration than after intermittent administration." p.1235.

ALZET Comments: Naloxone; Fentanyl citrate; Etorphine HCl; NaCl; SC; mice; 2001; 2002; 7-8 days; controls received placebo pellets.

ALZET Comments: Etorphine HCl; Fentanyl citrate; Naloxone HCl; NaCl; SC; mice; 2001; 2002; 7 -8 Days; controls received placebo pellets; dose-response; comparison of sc fentanyl injections vs. mp; good methods; tolerance.

8. Fentanyl

ALZET Comments: Fentanyl citrate; morphine sulphate salt pentahydrate; PBS; water, sterile; SC; Mice (transgenic); 1007D; 7 days; Dose (Fentanyl (2mg/kg/day); Morphine (17 mg/kg/day)); animal info (knock-in mice with 11S/T-A mutations (Oprm1tm3.1Shlz, MGI:6117673, 11S/T-A)); behavioral testing (hot plate test; open field locomotion test); dependence; “...we used subcutaneously implanted osmotic pumps to deliver opioids at a constant rate. This approach is a powerful means of assessing both tolerance and dependence in rodents” (p.5).

ALZET Comments: VRP26, Fentanyl; Saline; SC; mice; 7 days; Controls received mp w/ vehicle; animal info (Male, female C57BL/6 wild-type, homozygous MOR knockout; 20-30 g, 8-16 wks); functionality of mp verified by in vitro testing (pg. 2481); dose-response (pg 2481); good methods (pg 2481); behavioral testing (tail suspension test, conditioned place preference and locomotor activities); peptides; Primed for 4 hours, 37 degree Saline; antinociceptive peptide; Dose (0.3 mg/kg/day fentanyl or 10 mg/kg/day VRP26).

ALZET Comments: Fentanyl; Saline; SC; Rat; 2ML4; 28 days; Controls received mp w/ vehicle; animal info (male, Fischer 344 x Brown Norway, 16, 20 and 24 months old); behavioral testing (temperature preference/heat and cold sensitivity, locomotor activity); Pumps removed after 4 weeks;

ALZET Comments: Fentanyl propionanilide; buprenorphine hydrochloride; Saline, isotonic; CSF/CNS (intrathecal); Rat; 96 hours; Controls received mp w/ vehicle; animal info (male Wistar, 200-250 g); pain.

ALZET Comments: Morphine; methadone; fentanyl; oxycodone; Water, sterile, distilled; SC; Mice; 7 days; Animal info (male, WT, barr2-KO); dependence; wound clips used.

ALZET Comments: Fentanyl; SC; Rat; 2ML4; 4 weeks; Controls received mp w/ saline; animal info (male, Fisher 344 x Brown Norway, 12, 24, 30 mo old); behavioral testing (open field activity, grip strength, rotarod).

ALZET Comments: Morphine; fentanyl; Mice; 1003D; 3 days; Controls received mp w/ saline; animal info (adult, male, CD-1); comparison of SC injections vs. mp; "Although acute fentanyl injection (0.25 mg/kg) caused hyperalgesia within 15 min, hyperalgesia was not similarly evident on infusion Day 1 even though pumps were filled with a fentanyl dose (10mg/kg/24 h) that dispenses ~0.42 mg/kg/h, almost double the dose given by bolus injection."

ALZET Comments: Fentanyl; Saline, sterile; SC; Cat (felid); 2ML1; 96 hours; Animal info (spayed, female, 56 months old, 4.5 kg); functionality of mp verified by residual volume; comparison of transdermal patch vs. SC mp; "if fentanyl is “to be used for nondomestic cats, then the faster elimination of fentanyl after removal of a delivery device is an important advantage of the osmotic pump versus the transdermal patch" pg 953; "Compared with a transdermal patch, an osmotic pump provides several pharmacokinetic advantages for fentanyl administration in cats."

ALZET Comments: Fentanyl; SC; Mice; 7 days; Dependence; animal info (Swiss Webster, 25-33g).

ALZET Comments: Fentanyl citrate; Saline, physiological; SC; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; functionality of mp verified by plasma fentanyl levels; dose-responses (fig. 1); dependence; animal info (male, Wistar, 300-350 g.).

ALZET Comments: Fentanyl hydrochloride; Saline; SC; Mice; 7 days; Controls received placebo pellets; dose-response (fig. 3); comparison of SC injections vs. mp; tolerance; animal info (male, Swiss Webster, 23-35 g.).

9. Morphine

ALZET Comments: Morphine; Trimethoxy cinnamic acid, 3, 4, 5-; Saline; CSF/CNS (lateral ventricle); Rat; 2ML1; 7 days; Dose (26 nmol/10μ l/hr); Controls received mp w/ vehicle; animal info (male Sprague–Dawley rats, 220–240 g)); behavioral testing (Conditioned Place Preference Test); dependence;.

ALZET Comments: Fentanyl citrate; morphine sulphate salt pentahydrate; PBS; water, sterile; SC; Mice (transgenic); 1007D; 7 days; Dose (Fentanyl (2mg/kg/day); Morphine (17 mg/kg/day)); animal info (knock-in mice with 11S/T-A mutations (Oprm1tm3.1Shlz, MGI:6117673, 11S/T-A)); behavioral testing (hot plate test; open field locomotion test); dependence; “...we used subcutaneously implanted osmotic pumps to deliver opioids at a constant rate. This approach is a powerful means of assessing both tolerance and dependence in rodents” (p.5).

ALZET Comments: Morphine sulfate, Nicotine bitartrate; Saline, isotonic; SC; Rat; 2ML1; 7 days; Dose (morphine at 0.3 and 0.6 mg/kg/hr, nicotine at 9 mg/kg/day); Controls received mp w/ vehicle; animal info (Male Sprague-Dawley rats averaging 234 g); dependence;.

ALZET Comments: Morphine, oxycodone; Sterile water; SC; Rats; 2ML1; 7 days; Dose (oxycodone 3.6 mg day-1); (morphine 40 mg ml-1);animal info (Male Sprague-Dawley rats); behavioral testing (tail-flick, hot-plate tests); Toxicology (tolerance);.

ALZET Comments: Morphine; Saline; CSF/CNS (intrathecal); Rat; 7 days; Dose (15 μg/h); Controls received mp w/ vehicle; animal info (27 Male Wistar rats (350 400 g), each rat (with 12 weeks of age)); neurodegenerative ( ).;

Q7171: S. Arttamangkul, et al. Cellular tolerance at the micro-opioid receptor is phosphorylation dependent. Elife 2018;7(ALZET Comments: Morphine sulfate; Water; SC; Rat; 2ML1; 7 days; Dose (80mg/kg/day); animal info (5-6 Weeks); tolerance;,

ALZET Comments: Morphine; buprenorphine; methadone; Saline; SC; Mice; 6 days; Dose (45 mg/kg/d; 5 mg/kg/day; 60 mg/kg/day); Controls received mp w/ vehicle; animal info (Male Sprague-Dawley rats, approximately 30g); comparison of morphine alkaloid pellet vs mp;

ALZET Comments: Morphine; PD168,077; DMSO; NACL; SC; Rat; 2ML1; 6 days; animal info (male, Sprague Dawley, 225-250g); 2% DMSO used; behavioral testing (withdrawal behavior; tail-flick test);  dependence; Dose (Morphine 20 mg/kg/day; PD168,077 1 or 3 mg/kg/day);

ALZET Comments: Morphine; Saline; SC; Mice; 2001; 7 days; Dose (64 mg/mL); animal info (8 week old C57BL/6NCr mice); comparison of pellets vs mp; Resultant plasma level (Fig. 1, Pg 3); dependence;,

Q6212: A. Lyndon, et al. Risk to heroin users of polydrug use of pregabalin or gabapentin. Addiction 2017;112(9):1580-1589
ALZET Comments: Morphine; SC; Mice; 6 days; Dose (45 mg/kg/day); animal info (Male CD-1 mice weighing 30 g); comparison of sc pellet vs mp; tolerance;.

**ALZET Comments:** Morphine hydrochloride; SC; Rat; 2ML1; 5 days; Dose (41–48 mg/kg/day); animal info (8-week-old male Wistar rats weighing 200–240 g); Therapeutic indication (Knee arthritis).


**ALZET Comments:** Morphine; Saline; SC; Rat, Mice; 2ML1, 1007D; 7 days; Controls received mp w/ vehicle; animal info (180-200 g) ; functionality of mp verified by residual volume; behavioral testing (Cold plate assay); Therapeutic indication (Analgesic, Opioid).


**ALZET Comments:** JNJ63955918, Morphine; Saline; CSF/CNS (intrathecal); Rat; 2001; 7 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 180-200g); behavioral testing (Hargreaves test, hotplate test, tail-flick test, formalin flinching); JNJ63955918 is a tarantula venom-derived peptide (a potent, highly selective, closed-state Nav1.7 blocking peptide); Therapeutic indication (Pain, analgesia, electrophysiology).


**ALZET Comments:** Morphine; Saline; SC; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 180-200g); behavioral testing (von Frey testing; hind paw withdrawal); dependence; Dose (2 mg/kg/day).


**ALZET Comments:** Morphine; endomorphine analog; Saline; CSF/CNS (intrathecal); Rat; 2001; 7 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 250-400g); half-life (p. 219); behavioral testing (tail flick test; rotarod testing); stability verified by (internal testing; stability >1 year at 37C); pumps primed in 37C saline for 16 hours; used PE-8 IT catheter; Dose (2 ug/hr morphine; 0.056-0.075 ug/hr analog).


**ALZET Comments:** Ginsenoside, Rg3; ginsenoside, Rh; compound K; morphine; Saline; CSF/CNS (intrathecal); Rat; 2001; 7 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 220-240g); behavioral testing (conditioned place preference; escaping behavior); dependence; cyanoacrylate wound closure; Dose (morphine 26nmol/10ul/hr, ginsenoside 10 ug/ul/h); Brain coordinates (L: 1.3 mm; AeP: e0.5 mm; and DeV: e4.3 mm).


**ALZET Comments:** Morphine; CSF/CNS (intrathecal); Rat; 120 hours; Controls received mp w/ saline; animal info (male, Wistar); behavioral testing (tail-flick); Dose (15 ug/h).

Q5165: P. Nardelli, et al. Reduced motor neuron excitability is an important contributor to weakness in a rat model of sepsis. Exp Neurol 2016;282(1-8)

**ALZET Comments:** Oxymorphine; IP; Rat; 5 days; post op. care (buprenorphine SC 0.12 mg/kg; 5 ml SC saline; Baytril SC 10 mg/kg Q12H); used 2ML size; pumps used for continuous pain relief in rat sepsis model; Dose (30 ug/kg/h).

ALZET Comments: Morphine; Saline; Rat; 2002; 10.1210/en.2016-1374; Dose (10 mg/kg/day); Controls received mp w/ vehicle; animal info (Female adult freely-cycling Sprague-Dawley rats weighing ~280 g); dependence.


ALZET Comments: Morphine; Ro 25-6981; Saline; SC; Rat; 2ML1; 1 week; Controls received mp w/ vehicle; animal info (Male Sprague-dawley rats, 220-250 g); functionality of mp verified by behavioral tests; good methods (pg. 148); post op. care (opiate administration using pumps); behavioral testing (Hargreaves plantar test); Dependence/tolerance induced; Opiate use; Dose ( 15 mg/ml Morphine, 5 mg/kg Ro 25-6981).


ALZET Comments: Morphine; Saline; SC; Guinea pig; 2002; 14 days, 2 weeks; Controls received mp w/ vehicle; good methods (catheter construction pg. 379);

stress/adverse reaction: Note that these animals were receiving infusion through in-house/Non-Alzet catheters (see pg. 385 Therapeutic indication (Granuloma); Dose (0.25, 2.5, 8, or 25 mg/ml)).

10. Pentazocine


ALZET Comments: Haloperidol; JO-1784; Pentazocine; DTG; SC; Rat; 2-21 days; controls received mp w/saline; DTG is di(2-tolyl)guanidin.


ALZET Comments: Pentazocine, d-; Saline; SC; Rat; 2ML4; 4 weeks; no comment posted.


ALZET Comments: Ethylketocyclazocine; Heroin; Meperidine; Oxyphorphone; Pentazocine; Propoxyphene; Bremazocine; Buprenorphine; Butorphanol; Methadone; Morp hine; Nalbuphine; U-50,488H; SC; mice; 3 days; comparison of sc morphine pellets vs. mp infusion; comparison of agents effects; controls received unspecified placebo infusion.

11. Sufentanil


ALZET Comments: Sufentanil citrate; Nimodipine; Saline; Ethanol; Propylene glycol; Water; SC; Rat; 2001; 7 days; Controls received mp w/ vehicle; tolerance; Group 1 received sufentanil, Group 2 received sufentanil & nimodipine, Group 3 received nimodipine, Group 4 received vehicle; Nimodipine is a Ca channel blocker; sufentanil was diluted in saline; nimodipine was diluted in 10% ethanol / 20% propylene glycol / 70% water.


ALZET Comments: Sufentanil citrate; Nimodipine; Saline; Ethanol; Propylene glycol; Water; SC; Rat; 2001; 7 days; Controls received mp w/ vehicle; tolerance; Group 1 received vehicle alone, Group 2 received chronic sufentanil, Group 3 received sufentanil & nimodipine, Group 4 received nimodipine alone; Nimodipine is a Ca antagonist opioid; sufentanil citrate was diluted in saline; nimodipine was diluted in 10% ethanol / 20% propylene glycol / 70% water.
ALZET Comments: Sufentanil; Nimodipine; Bay K 8644; Saline; SC; Guinea pig; 2001; 7 days; controls received mp w/saline; tolerance.

R0117: C. W. Stevens. Perspectives on opioid tolerance from basic research: behavioural studies after spinal administration in rodents. Cancer Surveys 1994;21(25-47)
ALZET Comments: Morphine; DADLE; ST-91; Sufentanil; DAMGO; CSF/CNS (intrathecal); Rat; 7 days; controls received mp w/ saline; cancer; peptides; tolerance; comprehensive review of mp infusion methods using y-catheter.

ALZET Comments: Sufentanil; Saline, sterile; SC; Guinea pig; 2001; 7 days; controls received mp w/vehicle; tolerance.

ALZET Comments: Morphine; Sufentanil; Enkephalin; Saline; IV; CSF/CNS (intrathecal); CSF/CNS; Rat; 7 days; controls received mp w/vehicle; dose-response (p. 163); tolerance; pain; reference of mp pump study on pp. 162-164.

ALZET Comments: Morphine sulfate; Sufentanil citrate; Saline; CSF/CNS (intrathecal); Rat; 2001; 7 days; dose-response; tolerance; PE10 heat fused to PE60; externalized loop of catheter permitted cessation of infusion without pump removal.

ALZET Comments: Enkephalin analog ST-91; Enkephalin analog DADLE; Enkephalin analog DAMGO; Morphine; Sufentanil; Saline; CSF/CNS (intrathecal); Rat; 2001; 7 days; no comment posted.

ALZET Comments: Sufentanil citrate; Enkephalin analog DADLE; Enkephalin analog DAMGO; Morphine; Saline; CSF/CNS (intrathecal); Rat; 2001; 7 days; tissue infusion; dose-response; peptides; tolerance, dependence.

ALZET Comments: Enkephalin analog DADLE; Enkephalin analog DAMGO; Enkephalin analog ST-91; Morphine sulfate; Sufentanil citrate; Saline; CSF/CNS (intrathecal); Rat; 2001; 7 days; mp connected to Y-catheter; dose-response; peptides.

ALZET Comments: Sufentanil citrate;; Saline; SC; Rat; 2001; 7 days; controls received mp w/ saline; comparison of sc, iv & icv injections; tolerance; agent mu opioid receptor agonist; pumps left in longer than 7 days; "possibility that the minipump implanting process could influence the results was eliminated . . . no difference . . . in nonimplanted and implanted rats." (p. 372).