Recent References on the Administration of Analgesics Using the ALZET® Osmotic Pumps

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Narcotic

**Alfentanil**


**ALZET Comments:** Alfentanil; Sufentanil; Saline; SC; Rat (pregnant); 2ML2; 14 days; controls received mp w/ saline; dose-response (text); 3 doses of sufentanil infused; agents infused separately; author states 'in terms of experimental design, the cost of using sc implanted osmotic minipumps is small'; teratology.

**Buprenorphine (2016-Present)**


**Agents:** Buprenorphine  **Vehicle:** Ethanol; DMSO; Sterile water;  **Route:** SC;  **Species:** Rat;  **Pump:** 2ML1;  **Duration:** 1 week;

**ALZET Comments:** Dose (0.01; 0.032 mg/kg/h); 15% ethanol, 20% DMSO, 65% sterile water used; Controls received mp w/ vehicle; animal info (Sprague-Dawley female rats, 240– 260 g, ~12 weeks old and male rats, 290– 310 g, ~11 weeks old); dependence;


**Agents:** Buprenorphine, nor-; Morphine  **Vehicle:** DMSO; PEG 400; Saline, Sterile;  **Route:** SC;  **Species:** Rat;  **Pump:** 2ML2;

**ALZET Comments:** Dose (15 or 20 mg/kg/day Morphine; 0.3, 1.0, 3.0, or 10 mg/kg/day norbuprenorphine); Controls received mp w/ vehicle; animal info (timed-pregnant Long-Evans rats); norbuprenorphine aka NorBUP; dependence;


**Agents:** Buprenorphine  **Vehicle:** Water;  **Route:** SC;  **Species:** Rat;  **Pump:** 2ML4;  **Duration:** 14 days;

**ALZET Comments:** Dose (3 mg/kg/day); Controls received mp w/ vehicle; animal info (sexually mature male and female Sprague-Dawley rats, 370 g (male) and 270 g (female)); dependence;

Q8788: M. Kongstorp, et al. Prenatal exposure to methadone or buprenorphine impairs cognitive performance in young adult rats. Drug and Alcohol Dependence 2020;212(108008

**Agents:** Methadone HCl; Buprenorphine HCl  **Vehicle:** Water, Sterile;  **Route:** SC;  **Species:** Rat;  **Pump:** 2ML4;  **Duration:** 5 days;

**ALZET Comments:** Dose (8 mg/kg/day methadone; 0.8 mg/kg/day buprenorphine); Controls received mp w/ vehicle; animal info (Female (346.9 ± 8.1 g, n = 55) and male (12 weeks, n = 28) Sprague-Dawley rats); behavioral testing (novel object recognition test, simultaneous brightness discrimination test, Morris water maze test); dependence;


**Agents:** Methadone HCl; Buprenorphine HCl  **Vehicle:** Water, Sterile;  **Route:** SC;  **Species:** Rat;  **Pump:** 2ML4;  **Duration:** 28 days;

**ALZET Comments:** Dose (10 mg/kg/day Methadone HCl; 1 mg/kg/day Buprenorphine HCl); Controls received mp w/ vehicle; animal info (Female Sprague– Dawley Rat); dependence;


**Agents:** Methadone; Buprenorphine  **Vehicle:** Saline;  **Route:** CSF/CNS;  **Species:** Rat;  **Pump:** 2ML4;  **Duration:** 28 days;

**ALZET Comments:** Dose (Buprenorphine- 1 mg/kg/day or Methadone 10mg/kg/day); Controls received mp w/ vehicle; animal info (Female); post op. care (Metacam); dependence;


**Agents:** Norbuprenorphine; Morphine  **Vehicle:** Saline;  **Route:** SC;  **Species:** Rat;  **Pump:** 2ML2;  **Duration:** 14 days;

**ALZET Comments:** Dose (1.3 or 10 mg/kg/day); Controls received mp w/ vehicle; animal info (Long-Evans); dependence;
**Agents:** Morphine; buprenorphine; methadone **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 6 days;
**ALZET Comments:** 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;

**Agents:** Buprenorphine; methadone **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 6 days;
**ALZET Comments:** 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);

**Butorphanol (2005-Present)** Back to top
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
**Agents:** Butorphanol **Vehicle:** Not Stated; **Route:** SC; **Species:** Bird (peafowl); **Pump:** 2ML1; **Duration:** 7 days;
**ALZET Comments:** 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));

**Agents:** Butorphanol tartrate **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 48 hours;
**ALZET Comments:** Controls received mp w/ saline; animal info (Sprague Dawley, male, 302 g); “Implantation of pumps took less than 1 min per rat, the length of the anesthesia was 5 min per rat.” pg 576; functionality of mp verified via residual volume

**Agents:** Butorphanol tartrate; Nitroindazole, 7- **Vehicle:** Saline; DMSO; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2001; **Duration:** 72 hours;
**ALZET Comments:** 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

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

**Agents:** Butorphanol tartrate **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2001; **Duration:** 3 days;
**ALZET Comments:** Controls received mp w/ saline; dependence; animal info (male, Sprague-Dawley 230-250 g)

**Codeine** Back to top
**ALZET Comments:** Morphine tartrate; Codeine phosphate; Saline; SC; Rat; 2ML1; 7 days; functionality of mp verified by plasma drug levels; dose response (graphs p. 161); dependence.

Agents: Fentanyl citrate; morphine sulphate salt pentahydrate Vehicle: PBS; water, sterile; Route: SC; Species: Mice (transgenic); Pump: 1007D; Duration: 7 days;
ALZET Comments: 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)

Q7582: B. Hunter, et al. (352) Sex Differences in Sensory Processing: The Role of Stimulus Modality ad Psychological Factors. The Journal of Pain 2019;20(4);

Agents: Fentanyl Vehicle: Not Stated; Route: SC; Species: Rat; Pump: Not Stated; Duration: 5 days;
ALZET Comments: Dose (0.01mg/kg/hr); Controls received mp w/ vehicle; animal info (male, SD); comparison of oxycodone and morphine injection vs mp; opioids administered 1 hr, 10 days, or 28 days post-CCI (chronic constriction injury) surgery;


Agents: Fentanyl Vehicle: Saline; Route: SC; Species: Rat; Pump: 2001; Duration: 5 days;
ALZET Comments: Dose (0.01 mg/kg/hr); Controls received mp w/ vehicle; animal info (Male, Sprague Dawley, 10 weeks old);


Agents: Florfenicol voriconazole; fentanyl; amikacin Vehicle: Not Stated; Route: SC; in vitro; Species: Rat; Snake (corn, rattlesnake); Iguana; Cat; Hammer; Gelada; Pudu; Wallaby; Monkey; Quail; Hen; Pump: Not Stated; Duration: Not Stated;
ALZET Comments: animal info (Eastern massasauga rattlesnakes (Sistrurus catenatus); timber rattlesnake (Crotalus horridus); pudu (Pudu puda); wallaby (Macropus rufogriseus); iguanas (Iguana iguana); Mojave rattlesnakes (Crotalus scutulatus); corn snakes (Elaphe guttata guttata); Japanese quails (Coturnix coturnix japonica); hens (Gallus domesticus)); "Finally, the use of intracoelomic osmotic pumps was reported in iguanas (Iguana iguana) in a study of reproductive behavior.26 No complication due to the pump placement was reported in that study.” pg. 508; Advantages: Can be extracted in case of accidently in air sacs during intracoelomic implantation"

Q7369: J. Ball, et al. (351) The Opioids Oxycodone, Fentanyl, and Morphine Amplify Neuropathic when Given after Chronic Pain is Established. The Journal of Pain 2019;20(4);

Agents: Fentanyl Vehicle: Not Stated; Route: SC; Species: Rat; Pump: Pump model not stated; Duration: 5 days;
ALZET Comments: Dose (0.01mg/kg/hr); Controls received mp w/ vehicle; animal info (Male, Sprague-dawley); dependence;


Agents: VRP26, Fentanyl Vehicle: Saline; Route: SC; Species: mice; Pump: 1007D; Duration: 7 days;
ALZET Comments: 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); behavioral testing (tail suspension test, conditioned place preference and locomotor activities); peptides; Prime for 4 hours, 37 degree Saline; antinociceptive peptide; Dose (0.3 mg/kg/day fentanyl or 10 mg/kg/day VRP26);
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Bibliography

Hydromorphone Back to top

Q3537: A. Koesters, K. L. Engisch, M. M. Rich and M. M. Rich. Decreased cardiac excitability secondary to reduction of sodium current may be a significant contributor to reduced contractility in a rat model of sepsis. CRITICAL CARE 2014;18(U351-U357
ALZET Comments: Hydromorphone; IP; Rat; 24 hours; Animal info (female, Wistar, adult, 250-300g); post op. care (buprenorphine 0.12 mg/kg SC injection); used 2ML size pump; pain relief.

ALZET Comments: Hydromorphone; Saline; SC; Mice; 2001; 7 days; Controls received inert placebo pellet; tolerance; animal info (male, Swiss Webster, 22-30 g.); “There was substantially more tolerance with infusion treatment compared to injection treatment.” pg. 43.

ALZET Comments: Hydromorphone; SC; rabbit; 2ML4; 4 weeks; functionality of mp verified by blood sample assays; comparison of IV bolus administration vs. EVA polymer drug delivery vs. mp; pain; cancer.

ALZET Comments: Hydrocortisone phosphate; Hydromorphone; Saline; SC; monkey; 2 months; monkeys received both a mp w/ HP and a mp w/ saline on alternating menstrual cycles; long-term study.

ALZET Comments: Hydromorphone; Saline; Water; SC; mice (pregnant); 2001; 4 days; no stress or complications (see pg. 170-71); describes mp as ‘valuable tool...’ and discusses advantages of this type of delivery system (see pgs. 165, 176); toxicology.

Levorphanol Back to top

ALZET Comments: Levorphanol tartrate; Naltrexone HCl; U-50,488H; ICI-154,129; Saline; IP; mice; 2001; 7 days; functionality of mp verified by measuring residual pump volume; tolerance.

Meperidine Back to top

ALZET Comments: Naloxone HCl; Morphine sulfate; Meperidine HCl; Fentanyl citrate; Saline; SC; Rat; 2ML1; 7 days; controls received sham pumps; tolerance.

ALZET Comments: Morphine; Meperidine; Fentanyl; Saline; SC; Rat; 2ML1; 1 week; tolerance.

ALZET Comments: Ethylketocyclazocine; Heroin; Meperidine; Oxymorphone; Pentazocine; Propoxyphene; Bremazocine; Buprenorphine; Butorphanol; Methadone; Morphine; 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.
Methadone (2014-Present) [Back to top]

**Q8788:** M. Kongstorp, et al. Prenatal exposure to methadone or buprenorphine impairs cognitive performance in young adult rats. Drug and Alcohol Dependence 2020;212(108008

**Agents:** Methadone HCl; Buprenorphine HCl  **Vehicle:** Water, Sterile;  **Route:** SC;  **Species:** Rat;  **Pump:** 2ML4;  **Duration:** 5 days;

**ALZET Comments:** Dose (8 mg/kg/day methadone; 0.8 mg/kg/day buprenorphine); Controls received mp w/ vehicle; animal info (Female (346.9 ± 8.1 g, n = 55) and male (12 weeks, n = 28) Sprague-Dawley rats); behavioral testing (novel object recognition test, simultaneous brightness discrimination test, Morris water maze test); dependence;

**Q8789:** M. Kongstorp, et al. Prenatal exposure to methadone or buprenorphine alters micro-opioid receptor binding and downstream signaling in the rat brain. International Journal of Developmental Neuroscience 2020;

**Agents:** Methadone HCl; Buprenorphine HCl  **Vehicle:** Water, Sterile;  **Route:** SC;  **Species:** Rat;  **Pump:** 2ML4;  **Duration:** 28 days;

**ALZET Comments:** Dose (10 mg/kg/day Methadone HCl; 1 mg/kg/day Buprenorphine HCl); Controls received mp w/ vehicle; animal info (Female Sprague–Dawley Rat); dependence;


**Agents:** Methadone  **Vehicle:** Saline;  **Route:** SC;  **Species:** Rat;  **Pump:** Not stated;  **Duration:** 28 days;

**ALZET Comments:** Dose (8 mg/kg, 12 mg/kg or 16 mg/kg); Controls received mp w/ vehicle; animal info (male and female Sprague Dawley rat pups); dependence;

**Q8843:** F. J. Rubio, et al. Prelimbic cortex is a common brain area activated during cue-induced reinstatement of cocaine and heroin seeking in a polydrug self-administration rat model. European Journal of Neuroscience 2019;49(2):165-178

**Agents:** Methadone  **Vehicle:** Not Stated;  **Route:** SC;  **Species:** Rat;  **Pump:** Not Stated;  **Duration:** Not Stated;

**ALZET Comments:** Animal info (Long-Evans, Male, 300-350 g); post op. care (Ketoprofen); Methadone aka Opioid receptor agonist; neurodegenerative (Psychostimulants);


**Agents:** Methadone; Buprenorphine  **Vehicle:** Saline;  **Route:** CSF/CNS;  **Species:** Rat;  **Pump:** 2ML4;  **Duration:** 28 days;

**ALZET Comments:** Dose (Buprenorphine- 1 mg/kg/day or Methadone 10mg/kg/day); Controls received mp w/ vehicle; animal info (Female); post op. care (Metacam); dependence;


**Agents:** methadone  **Vehicle:** Saline;  **Route:** SC;  **Species:** Rat;  **Pump:** 2ML2;  **Duration:** 13 days;

**ALZET Comments:** Dose (0, 10, 30 mg/kg/day); Controls received mp w/ vehicle; animal info (male, Sprague-Dawley, 175-200g); post op. care (meloxicam, 2 mg/kg, SC); behavioral testing (Orofacial reaction, activity chamber); dependence; minipumps were removed [after 13 day infusion] and intake was monitored for an additional six days.;

**Q6540:** S. L. Withey, et al. Effect of Tamoxifen and Brain-Penetrant Protein Kinase C and c-Jun N-Terminal Kinase Inhibitors on Tolerance to Opioid-Induced Respiratory Depression in Mice. J Pharmacol Exp Ther 2017;361(1):51-59

**Agents:** Morphine; buprenorphine  **Vehicle:** Saline;  **Route:** SC;  **Species:** Mice;  **Pump:** Not Stated;  **Duration:** 6 days;

**ALZET Comments:** 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;

**Q6771:** S. Schreiber, et al. Interaction between methylphenidate, methadone and different antidepressant drugs on antinociception in mice, and possible clinical implications. World J Biol Psychiatry 2017;18(4):300-307

**Agents:** methadone; escitalopram; venlafaxine; desipramine; clomipramine  **Vehicle:** Not Stated;  **Route:** SC;  **Species:** Mice;  **Pump:** 2002;  **Duration:** 14 days;

**ALZET Comments:** Dose: methadone (0.5 mg/kg) venlafaxine (2.5 mg/kg); escitalopram (20mg/kg); desipramine (1mg/kg); clomipramine (0.5 mg/kg); animal info (Male ICR mice, 25-35g); dependence
Agents: Buprenorphine; methadone Vehicle: Saline; Route: SC; Species: Mice; Pump: Not Stated; Duration: 6 days;
ALZET Comments: 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);

Agents: Methadone Vehicle: Saline; Route: SC; Species: Rat (pregnant); Pump: 2ML4; Duration: 28 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (female, Pregnant, Sprague Dawley, GD7); teratology; dependence;

Agents: Methadone Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 1007D; Duration: 14 days;
ALZET Comments: Animal info (male, ICR, 25-35g); behavioral testing (hot plate); dependence;

Morphine (2019-Present) Back to top
Agents: Naloxone; Morphine Vehicle: Saline; Route: SC; Species: Mice; Pump: 2001; Duration: 7 days;
ALZET Comments: Dose (); animal info (Male mice, 2-3 months old); behavioral testing (Morris Water Maze Test); dependence;

Agents: Buprenorphine, nor-; Morphine Vehicle: DMSO; PEG 400; Saline, Sterile; Route: SC; Species: Rat; Pump: 2ML2; Duration: Not Stated;
ALZET Comments: Dose (15 or 20 mg/kg/day Morphine; 0.3, 1.0, 3.0, or 10 mg/kg/day norbuprenorphine); Controls received mp w/ vehicle; animal info (timed-pregnant Long-Evans rats); norbuprenorphine aka NorBUP; dependence;

Q9432: H. M. Rodgers, et al. Dopamine D1 or D3 receptor modulators prevent morphine tolerance and reduce opioid withdrawal symptoms. Pharmacology, Biochemistry and Behavior 2020;194(172935
Agents: Morphine hydrochloride Vehicle: Saline; Route: SC; Species: Mice; Pump: 2001; Duration: Not Stated;
ALZET Comments: Dose (2 mg/kg); Controls received mp w/ vehicle; animal info (female, Long- Evans rats, weighing 200–225 g); behavioral testing (Withdrawal testing); Multiple pumps per animal (2 or 3); dependence;

Agents: Morphine hydrochloride Vehicle: Saline; Route: SC; Species: Mice; Pump: Duration: 7 days;
ALZET Comments: Dose (5 mL/kg); 0.9% Saline used; Controls received mp w/ vehicle; animal info (C57BL/6J); dependence;

Agents: Morphine Hydrochloride Vehicle: Saline; Route: SC; Species: Mice; Pump: Duration: 7 days;
ALZET Comments: Dose (63.2mg/kg/day); 0.9% Saline used; Controls received mp w/vehicle; animal info (C57BL/6J, Oprm1 KO, ); dependence;

Agents: Morphine Vehicle: Saline; Route: SC; Species: Mice; Pump: 2001; Duration: Not Stated;
ALZET Comments: Dose (24 or 48 mg/kg/day); 0.9% Saline used; Controls received mp w/ vehicle; animal info (C57BL6, 10-20 weeks old); dependence;
Agents: Morphine Vehicle: Not stated; Route: Not stated; Species: Mice; Pump: Not stated; Duration: 28 days;
ALZET Comments: Dose (1 mg/kg/day); dependence;

Q8413: I. J. Chen, et al. The Circadian Hormone Melatonin Inhibits Morphine-Induced Tolerance and Inflammation via the Activation of Antioxidative Enzymes. Antioxidants (Basel) 2020;9(9);
Agents: Morphine Vehicle: DMSO; Saline; Route: CSF/CNS (intrathecal); Species: Rat; Pump: Not stated; Duration: 10 days;
ALZET Comments: 0.9% Saline used; Controls received mp w/ vehicle; animal info (adult male wistar rats, 300-350 g); behavioral testing (Nociceptive Test); dependence;

Agents: PD168,077; morphine Vehicle: DMSO; Route: SC; Species: Rat; Pump: 2ML1; Duration: 6 days;
ALZET Comments: Dose (20 mg/kg/day- morphine, 1 mg/kg/day- PD168,077); 2% DMSO used; animal info (Male, Sprague Dawley, 250-300g ); PD168,077 aka D4R agonist; dependence;

Agents: Morphine; Trimethoxy cinnamic acid, 3, 4, 5- Vehicle: Saline; Route: CSF/CNS (lateral ventricle); Species: Rat; Pump: 2ML1; Duration: 7 days;
ALZET Comments: 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;

Q7533: C. R. Leibrand, et al. HIV-1 Tat and opioids act independently to limit antiretroviral brain concentrations and reduce blood-brain barrier integrity. J Neurovirol 2019;
Agents: Dolutegravir, Abacavir, Lamivudine; Morphine Route: SC; Species: Mice; Pump: 2001; Duration: 5 days;
ALZET Comments: Dose (abacavir 2.5 mg/day (123.5 mg/kg/day), dolutegravir 0.2 mg/day (10.3 mg/kg/day), and lamivudine 1.2 mg/day (61.7 mg/kg/day); Morphine (2 mg/day)); Controls received mp w/ vehicle; animal info (Adult female mice, 70 days of age); post op. care (Bupivacaine);

Agents: DMT-DALDA; morphine sulfate Vehicle: Saline; Route: CSF/CNS (intrathecal); Species: Rat; Pump: 2001, 2002; Duration: 7 days, 14 days;
ALZET Comments: Dose ((DMT-DALDA 0.3, 1, 3, or 10 pmol/μL/hour), (MS 37.5 nmol/hour)); dose-response (Figure 1a graph on page 4); Controls received mp w/ vehicle; animal info (adult, male, Sprague–Dawley, 225-300g); behavioral testing (Hargreaves-type hind paw thermal stimulator, formalin-induced flinching); DMT-DALDA (H-Dmt-D-Arg-Phe-Lys-NH2; Dmt = 2',6'-dimethyltyrosine) is a dermorphin analogue and selective mu opioid agonist; dependence; good methods (surgical techniques and pump/catheter implantation on p.2);

Agents: Fentanyl citrate; morphine sulphate salt pentahydrate Vehicle: PBS; water, sterile; Route: SC; Species: Mice (transgenic); Pump: 1007D; Duration: 7 days;
ALZET Comments: 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 chloride; nalbuphine HCl; Saline; CSF/CNS; Rat; 2001; 3 days; Controls received mp w/ vehicle; comparison of IP injections vs. mp; tolerance; dependence; animal info (male, Sprague Dawley, 220-240 g.).


ALZET Comments: Ethylketocyclazocine; Heroin; Meperidine; Oxymorphone; Pentazocine; Propoxyphene; Bremazocine; Buprenorphine; Butorphanol; Methadone; Morphine; 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.


ALZET Comments: DsThr; Enkephalin agonist DADL; Fentanyl; FK-33824; MR-2034; MRZ; Normorphine; Water; SC; Guinea pig; 2001; 6 days; peptides.


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.


ALZET Comments: Oxymorphone; Intramuscular (abdominal); Rat; Post op. care (buprenorphine); animal info (female, Wistar, 250-300g).


ALZET Comments: Oxymorphone HCl; IP; Rat; 32 hours; functionality of mp verified by pain relief indicators - posture, physical condition, behavior; comparison of iv infusions vs mp; compared bolus iv infusion, continuous iv infusion, osmotic pump.


ALZET Comments: Ethylketocyclazocine; Heroin; Meperidine; Oxymorphone; Pentazocine; Propoxyphene; Bremazocine; Buprenorphine; Butorphanol; Methadone; Morphine; 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.


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


ALZET Comments: Pentazocine, d-; Saline; SC; Rat; 2Ml4; 4 weeks; no comment posted.


ALZET Comments: Ethylketocyclazocine; Heroin; Meperidine; Oxymorphone; Pentazocine; Propoxyphene; Bremazocine; Buprenorphine; Butorphanol; Methadone; Morphine; 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.

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ALZET Comments: Ethylketocyclazocine; Heroin; Meperidine; Oxymorphone; Pentazocine; Propoxyphene; Bremazocine; Buprenorphine; Butorphanol; Methadone; Morphine; 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.

Sufentanil (1994-Present) Back to top


Agents: sufentanil; nimodipine Vehicle: Saline; Route: SC; Species: Rat; Pump: 2001; Duration: 10.1046/j.1471-4159.2001.00268.x;

ALZET Comments: Dose ((2 μg/h sufentanil), (1 μg/h nimodipine)); Controls received mp w/ vehicle; animal info (Male, albino Wistar, 250-300g); enzyme inhibitor ((mu-opioid agonist for sufentanil), (Ca2+ channel blocker for nimodipine));


Agents: Sufentanil citrate; Nimodipine; Vehicle: Saline; Ethanol; Propylene glycol; Water;; Route: SC;; Species: Rat;; Pump: 2001;; Duration: 7 days;;

ALZET Comments: 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;


Agents: Sufentanil citrate; Nimodipine; Vehicle: Saline; Ethanol; Propylene glycol; Water;; Route: SC;; Species: Rat;; Pump: 2001;; Duration: 7 days;;

ALZET Comments: 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 CA2+ antagonist opioid; sufentanil citrate was diluted in saline; nimodipine was diluted in 10% ethanol / 20% propylene glycol / 70% water.


Agents: Sufentanil; Nimodipine; Bay K 8644 Vehicle: Saline; Route: SC; Species: Guinea pig; Pump: 2001; Duration: 7 days;

ALZET Comments: controls received mp w/saline; tolerance


Agents: Sufentanil citrate; Nimodipine; Vehicle: Saline; Ethanol; Propylene glycol; Water;; Route: SC;; Species: Rat;; Pump: 2001;; Duration: 7 days;;

ALZET Comments: 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 CA2+ antagonist opioid; sufentanil citrate was diluted in saline; nimodipine was diluted in 10% ethanol / 20% propylene glycol / 70% water;


Agents: Sufentanil citrate; Nimodipine; Vehicle: Saline; Ethanol; Propylene glycol; Water;; Route: SC;; Species: Rat;; Pump: 2001;; Duration: 7 days;;

ALZET Comments: 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 CA2+ antagonist opioid; sufentanil citrate was diluted in saline; nimodipine was diluted in 10% ethanol / 20% propylene glycol / 70% water.

R0117: C. W. Stevens. Perspectives on opioid tolerance from basic research: behavioural studies after spinal administration in rodents. Cancer Surveys 1994;21(25-47

Agents: Morphine; DADLE; ST-91; Sufentanil; DAMGO Route: CSF/CNS (intrathecal); Species: Rat; Duration: 7 days;

ALZET Comments: controls received mp w/ saline; cancer; peptides; tolerance; comprehensive review of mp infusion methods using y-catheter
Non-Narcotic

**Acetylsalicylic Acid** [Back to top]


**ALZET Comments:** CI-988; chlordiazepoxide; Acetylsalicylic acid; DMSO; saline; SC; CSF/CNS (intrathecal); Rat; 2ML1; 2001; 2002; 14 days; Controls received mp w/ vehicle; animal info (Male, Sprague-Dawley, 300-325 g, 8 wks old; ALZET intrathecal catheter used (0007740); behavioral testing (elevated plus-maze).


**ALZET Comments:** Acetylsalicylic acid, lysine; Saline; SC; Mice; 2002; 4 weeks; Controls received mp w/ placebo; functionality of mp verified by serum salicylate concentrations; pumps replaced after 2 weeks; cardiovascular; ischemia (cardiac); animal info (female, C57BL/6, 8-12 weeks old, 20-25 grams); MI induced by coronary artery ligation.

**P4829:** M. Yuan, N. Konstantopoulos, J. Lee, L. Hansen, Z.-W. Li, M. Karin and S. E. Shoelson. Reversal of obesity- and diet-induced insulin resistance with salicylates or targeted disruption of *Ikkb*. Science 2001;293(1673-1677

**ALZET Comments:** Acetylsalicylic acid; salicylate, sodium; SC; Rat; mice; 2002; 2ML2; 3-4 weeks; Controls received mp w/ vehicle; 2ML2 used in rats, 2002 used in mice; acetylsalicylic acid also called aspirin: dose was 120 mg/kg/day; diabetes (type II).


**ALZET Comments:** Acetylsalicylic acid; DMSO; Saline; IV (superficial cervical vein); dog; 2ML1; 3 days; pumps replaced after 4 hrs. before implant; used prefilled catheter in vein; greater solubility of ASA in DMSO allowed greater concentration in smaller total volume.

**Aminopyrine** [Back to top]


**ALZET Comments:** Aminopyrine; Formate, sodium; radio-isotopes; 14C tracer; Saline; SC; Rat, mouse; 2002; 7 days


**ALZET Comments:** Aminopyrine; Radio-isotopes; 14C tracer; Saline; SC; mice; 2002; 7 days

**Antipyrine** [Back to top]


**ALZET Comments:** Antipyrine; bleomycin; dopamine HCl; melatonin; methotrexate, sodium; nicotine; prednisolone; radio-isotopes; valproic acid; 14C tracer; 3H tracer; IA; IP; SC; Mice, rabbit, Rat; no duration posted; stability of [N-dimethyl-14C] aminopyrine verified by radiochromatographic analysis- no decomposition observed.

**P0592:** S. L. Sendelbeck and J. Urquhart. Spatial distribution of dopamine, methotrexate and antipyrine during continuous intracerebral microperfusion. Brain Research 1985;328(251-258

**ALZET Comments:** Antipyrine; Dopamine HCl; Methotrexate, sodium; Radio-isotopes; 14C tracer; 3H tracer; CSF, artificial; Sodium fluorescein; CSF/CNS (diencephalon); rabbit; 2001; 6 days; comparison of agents effects; mp primed in saline 16 hr. prior to implant; stability of labelled & unlabelled Dop. & MTX tested by paper chromat. after 7 days at 37C.
Indomethacin (2000-Present)

Agents: Indomethacin Vehicle: DMSO; Route: CSF/CNS (intracisternal); Species: Rat; Pump: Not stated; Duration: 14 days;
ALZET Comments: Dose (100 ug/day); 50% DMSO used; Controls received mp w/ vehicle; animal info (adult (150–175 g) rats);
Brain coordinates (0.8 mm posterior to bregma, 1.5 mm lateral to the midline and 3.5 mm ventral to the surface of the skull);
dependence;

Agents: indomethacin Vehicle: saline, Kolliphor HS15 buffered; Route: SC; Species: Mice; Pump: 2006; Duration: 4 weeks;
ALZET Comments: Dose (10 mg/ml at 0.15 ml/h); saline with 18.75% Kolliphor HS15 used; Controls received mp w/ vehicle;
animal info (6 weeks, male, C57BL/6J); good methods (“We connected a piece of silicon tubing at the end of each pump, and sutured the tubing on the mouse back muscle to ensure that the opening of the tubing was on the iBAT of the mouse during pump implantation.” p.469); controls split into three groups (saline, Kolliphor HS15, saline + Kolliphor HS15); Therapeutic indication (expression of genes involved in thermogenesis in iBAT (interscapular brown adipose tissue) and improved hyperglycemia found in DIO (diet-induced obesity) mice along with promoting mouse brown adipocyte differentiation);

Agents: NA-398; SC-560; indomethacin Vehicle: DMSO; Route: SC; Species: Mice; Pump: Not Stated; Duration: 30 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (female, BALB/c); immunology;

Agents: fenretinide; indomethacin Vehicle: Not Stated; Route: Not Stated; Species: Mice; Pump: Not Stated; Duration: 24 weeks;
ALZET Comments: animal info (6 weeks, male, p53+/-); comparison of caloric restriction vs mp; long-term study; fenretinide is a synthetic retinoid. indomethacin is a nonsteroidal anti-inflammatory drug; cancer (bladder); citation for study listed as (Hursting, S.D. and Perkins, S.N., unpublished observations, 2001);

Agents: Hydrocortisone; indomethacin; olvanil Vehicle: PEG 200; Route: SC; Species: Mice; Pump: Not Stated; Duration: 2 days;
ALZET Comments: Controls received mp w/ vehicle; toxicology

Ketorolac

Agents: Ketorolac Vehicle: Saline; Route: SC; Species: Mice; Pump: Not Stated; Duration: 12 hours;
ALZET Comments: Dose (0.625 mg/kg/h); Controls received mp w/ vehicle; animal info: Mice (C57BL/6 background) at 4–6 months; Resultant plasma level (2.03 in Ketorolac concentration); ischemia (cerebral);

Agents: Ketorolac Vehicle: Saline; Route: SC; Species: Mice; Pump: Not Stated; Duration: 12 hours;
ALZET Comments: Dose (0.625 mg/kg/h); Controls received mp w/ vehicle; animal info (Mice (C57BL/6 background) at 4–6 months of age); Resultant plasma level (2.03% Ketorolac concentration); ischemia (cerebral);

ALZET Comments: Ketorolac; Saline, sterile; SC; Mice; 1007D; 2 days; Controls received mp w/ vehicle; animal info (male, C57BL/6J, 4-5 wks old).
ALZET Comments: Ketorolac tromethamine; Saline; CSF/CNS (intrathecal); Rat; 2001; 48 hours; controls received mp w/ vehicle; ketorolac is an NSAID sold as Toradol; cannula patency verified by saline injection.

ALZET Comments: Ketorolac; IV (jugular); rabbit; 2ML1: 7 days; controls received mp w/saline; functionality of mp verified by residual volume; comparison of i.m. injections vs. mp; ketorolac also called Toradol; NSAID.

Naproxen Back to top
ALZET Comments: JNJ7777120; naproxen; SC; Mice; 1004; Control animals received mp w/ vehicle; animal info (male, C57BL/6, ~2 mo old, 25-30 g); infusion rate listed as 0.11 ul/hr; JNJ7777120 also known as (1-[(5-chloro-1H-indol-2-yl)carbonyl]-4-methylpiperazine), is a selective H4R antagonist; one group received combination of JNJ7777120 and naproxen.

ALZET Comments: Naproxen; PBS; In vitro; 1002; Naproxen is an non- steroidal anti-inflammatory agent; This paper reports the characterization of an electrochemical biosensor for the continuous monitoring of Naproxen delivered by alzet pumps.

ALZET Comments: Naproxen; Methanol; In Vitro; 1002; 16 hours; Functionality of mp verified by naproxen levels measured with sensors;

ALZET Comments: Ibuprofen; naproxen; PBS; SC; Rat; mice; 2004; 2ML4: 4 weeks; Controls received mp w/ vehicle; animal info (female, Sprague Dawley, 11-12 wks old, 250-270 g., female, C57BL/6, 8-9 wks old, 20 g.); spinal cord injury; behavioral testing (BBB locomotor scale, Basso mouse scale).

Agents: Naproxen, sodium Vehicle: Saline; Route: SC; Species: Rat (pregnant); Pump: 2001; Duration: 3 days;
ALZET Comments: no comment posted

Sodium Salicylate Back to top
Agents: Mefenamic Acid, Sodium Salicylate Vehicle: Not Stated; Route: CSF/CNS (Left Lateral Ventricle); Species: Rat; Pump: 2001D; Duration: 24 Hours;
ALZET Comments: Dose (MFA (0.5 or 1 mg/kg), sodium salicylate (1 mg/kg)); Controls received mp w/ vehicle; animal info (32 male Wistar rats weighing 300–350 g); animal info (32 male Wistar rats weighing 300–350 g); Brain coordinates (1.5 mm lateral and 2 mm posterior to the left of bregma); ischemia (ischemic stroke);

ALZET Comments: Acetylsalicylic acid; salicylate, sodium; SC; Rat; mice; 2002; 2ML2; 3-4 weeks; Controls received mp w/ vehicle; 2ML2 used in rats, 2002 used in mice; acetylsalicylic acid also called aspirin; dose was 120 mg/kg/day; diabetes (type II).


ALZET Comments: Scopolamine; Methylscopolamine nitrate; Salicylate, sodium; SC; Rat; 2002; 10 days; temperatures were taken with radiotelemetry.


ALZET Comments: Salicylate, sodium; Water; IV; Rat; 2ML1; no duration posted; teratology.


Agents: Salicylate, sodium Vehicle: Not Stated; Route: IV (jugular); Species: Rat (pregnant); Pump: 2ML1; Duration: 7 days;

ALZET Comments: comparison of iv bolus injection vs. mp infusion; controls received mp; mp infusion during two periods of gestation; dose-response; teratology; embryotoxicity; study to determine effects on offspring

Tramadol Back to top


ALZET Comments: Tramadol; Saline; SC; Rat; 2ML1; 7 days; Controls received mp w/ vehicle; comparison of sc injections vs. mp; immunology; multiple pumps per animal (2) used in high-dose groups; nociception; tramadol is a centrally acting analgesic.


ALZET Comments: Tramadol; Saline; SC; Rat; 2ML1; 7 days; controls received mp w/ vehicle; functionality of mp verified by paw withdrawal latency (analgesia index); dose-response (graph p. 337); comparison of sc injection vs. mp; analgesia.

F13640 Back to top


ALZET Comments: F13640; Acetate buffer; water, sterile; SC; Rat; 2ML1; 2ML2; 2ML4; 2, 4, 8 weeks; 1, 2, 4, 7 days; Controls received mp w/ vehicle; dose-response (fig. 2); long-term study; pumps replaced; half-life (p. 139) 2.5 hrs. in rat plasma; multiple pumps per animal (2); post op. care (Na ampicillin); animal info (male, Sprague Dawley, 220-240 g., intraorbital nerve ligation).


ALZET Comments: F13640; morphine, HCl; Saline; SC; Rat; 2ML2; 6 weeks; Controls received mp w/ vehicle; long-term study; pumps replaced every two weeks; multiple pumps per animal (2); animal info (male, Sprague-Dawley, 220-240 g); during pump replacement a new incision was made about 1 cm away from the previous incision.

**ALZET Comments:** F13640; SC; Rat; 2ML4; 56 days; Controls received mp w/ saline; functionality of mp verified by plasma levels; long-term study; pumps replaced at day 28; 5-HT1A receptor agonist; spinal cord injury; pain.


**ALZET Comments:** F13640; SC; Rat; 2ML4; 56 days; Controls received mp w/ saline; functionality of mp verified by F13640 plasma levels; long-term study; pumps replaced (after 28 days).


**ALZET Comments:** F13640; Water, distilled; SC; Rat; 2ML2; 5 weeks; Controls received mp w/ saline; dose-response (Fig.2; p.275); pumps replaced every week, F13640 is a novel analgesic; serotonin receptor agonist; post op. care (the site of pump emplacement was massaged daily to avoid tissue adherence).


**ALZET Comments:** F13640; F13714; morphine; baclofen; Saline; SC; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; Post Op. Care (aerosol bandage applied to protect against bacterial contamination); F13640 is a novel analgesic & 5-HT1A receptor agonist; behavioral study; F13640, F13714 & morphine were infused in one pump; baclofen infused in two pumps due to limited solubility.


**ALZET Comments:** F13640; morphine HCL; imipramine HCl; ketamine HCl; gabapentin; Water, double distilled; SC; Rat; 2ML2; 14 days; Controls received mp w/ saline; dose-response (fig. 3); comparison of IP & SC injections vs. mp; tolerance; dependence; "Continuous F 13640 infusion uniquely produced profound analgesia in this model of severe, chronic pain." (p. 955).