



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

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Narcotic

Alfentanil

P1206: M. Fujinaga, R. I. Mazze, E. C. Jackson and J. M. Baden. Reproductive and teratogenic effects of sufentanil and alfentanil in sprague-dawley rats. *Anesth. Analg* 1988;67(166-169)

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)

Q9504: E. A. Townsend, *et al.* A drug-vs-food "choice" self-administration procedure in rats to investigate pharmacological and environmental mechanisms of substance use disorders. *Journal of Neuroscience Methods* 2021;354(109110)

Agents: Buprenorphine **Vehicle:** Ethanol; DMSO; Sterile water; **Route:** SC; **Species:** Rat; **Pump:** 2001; 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;

Q9318: H. J. Kulbeth, *et al.* Automated quantification of opioid withdrawal in neonatal rat pups using Ethovision(R) XT software. *Neurotoxicology and Teratology* 2021;84(106959)

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;

Q9147: A. Bakhti-Suroosh, *et al.* A buprenorphine-validated rat model of opioid use disorder optimized to study sex differences in vulnerability to relapse. *Psychopharmacology (Berl)* 2021;238(4):1029-1046

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;

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;

Q8226: M. Kongstorp, *et al.* High Accumulation of Methadone Compared with Buprenorphine in Fetal Rat Brain after Maternal Exposure. *J Pharmacol Exp Ther* 2019;371(1):130-137

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;

Q8013: B. A. Griffin, *et al.* In Utero Exposure to Norbuprenorphine, a Major Metabolite of Buprenorphine, Induces Fetal Opioid Dependence and Leads to Neonatal Opioid Withdrawal Syndrome. *J Pharmacol Exp Ther* 2019;370(1):9-17

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;



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; 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;

Q4834: R. Hill, *et al.* Ethanol Reversal of Tolerance to the Respiratory Depressant Effects of Morphine. *Neuropsychopharmacology* 2016;41(762-773)

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));

Q1826: A. Mitra, *et al.* Effects of butorphanol on feeding and neuropeptide Y in the rat. *Pharmacology Biochemistry and Behavior* 2012;100(3):575-580

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

P9327: Y. H. Tian, *et al.* 7-nitroindazole, nitric oxide synthase inhibitor, attenuates physical dependence on Butorphanol in rat. *Synapse* 2008;62(8):582-589

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

P7624: S. Tanaka, *et al.* Butorphanol dependence increases hippocampal kappa-opioid receptor gene expression. *Journal of Neuroscience Research* 2005;82(2):255-263

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)

P7657: S. Y. Lee, *et al.* Increases in 3H-alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid AMPA receptor binding and mRNA expression of AMPA-sensitive glutamate receptor A GluR-A subunits in rats withdrawn from butorphanol. *Journal of Toxicology and Environmental Health-Part A-Current Issues* 2005;68(23-24):2163-2174

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](#)

P4917: M. Chew, J. M. White, A. A. Somogyi, F. Bochner and R. J. Irvine. Precipitated withdrawal following codeine administration is dependent on CYP genotype. *European Journal of Pharmacology* 2001;425(159-164

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.



Fentanyl (2016-Present) [Back to top](#)

Q7581: E. Nguyen, *et al.* (353) Cell-Type Specific Modulation of RBM Neurons in Nociceptive Behaviors. *The Journal of Pain* 2019;20(4):S62-S63

Agents: Fentanyl **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 28 days;
ALZET Comments: Dose (0.01 mg/kg/hr); animal info (Male, Sprague Dawley); neurodegenerative (Chronic pain);

Q6131: A. Kliewer, *et al.* Phosphorylation-deficient G-protein-biased mu-opioid receptors improve analgesia and diminish tolerance but worsen opioid side effects. *Nat Commun* 2019;10(1):367

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 and 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;

Q8735: S. M. Green-Fulgham, *et al.* Oxycodone, fentanyl, and morphine amplify established neuropathic pain in male rats. *Pain* 2019;160(11):2634-2640

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);

R0391: T. Coutant, *et al.* Advances in Therapeutics and Delayed Drug Release. *Vet Clin North Am Exot Anim Pract* 2019;22(3):501-520

Agents: Florfenicol voriconazole; fentanyl; amikacin **Vehicle:** Not Stated; **Route:** SC; in vitro; **Species:** Rat; Snake (corn, rattle); Iguana; Cat; Hamster; 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 pudu*); 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 drug overdose or toxicity, Is not altered by its biological environment, Release the drug at a constant rate, Low cost, Commercially available, Release rate and operation time can be chosen; Drawbacks: Necessitate 2 light surgical procedures under anesthesia to be implanted and explanted, Can sometimes migrate in unwanted location (especially if implanted accidentally 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;

Q5277: J. P. Anand, *et al.* The behavioral effects of a mixed efficacy antinociceptive peptide, VRP26, following chronic administration in mice. *Psychopharmacology (Berl)* 2016;233(13):2479-87

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; Primed for 4 hours, 37 degree Saline; antinociceptive peptide; Dose (0.3 mg/kg/day fentanyl or 10 mg/kg/day VRP26);



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;

P9162: P. Kumar, S. Sunkaraneni, S. Sirohi, S. V. Dighe, E. A. Walker and B. C. Yoburn. Hydromorphone efficacy and treatment protocol impact on tolerance and mu-opioid receptor regulation. European Journal of Pharmacology 2008;597(1-3):39-45

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.

P3843: G. J. Lesser, S. A. Grossman, K. W. Leong, H. Lo and S. Eller. In vitro and in vivo studies of subcutaneous hydromorphone implants designed for the treatment of cancer pain. Pain 1996;65(265-272)

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;.

P2556: W. Kowalski, R. T. Chatterton, R. R. Kazer and A. C. Wentz. The impact of subchronic hypercortisolemia on progesterone metabolism and the luteinizing hormone-progesterone axis in the cynomolgus monkey. J. Clin. Endocrinol. Metab 1993;77(6):1597-1604

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.

P0770: M. C. Behm, M. V. Stout-Caputi, M. P. Mahalik and R. F. Gautieri. Evaluation of the teratogenic potential of hydromorphone administered via a miniature implantable pump in mice. Res. Commun. Substance Abuse 1985;6(3):165-177

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](#)

P2440: G. C. Teskey and M. Kavaliers. Modifications of social conflict-induced analgesic and activity responses in male mice receiving chronic opioid agonist and antagonist treatments. Pharmacol. Biochem. Behav 1991;38(485-493)

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](#)

P3555: C. A. Paronis and S. G. Holtzman. Sensitization and tolerance to the discriminative stimulus effects of mu-opioid agonists. Psychopharmacology 1994;114(601-610)

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

P2408: C. A. Paronis and S. G. Holtzman. Development of tolerance to the analgesic activity of mu agonists after continuous infusion of morphine, meperidine or fentanyl in rats. J. Pharmacol. Exp. Ther 1992;262(1):1-9

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

P0588: W. K. Schmidt, S. W. Tam, G. S. Sholtzberger, D. H. Smith Jr, R. Clark and V. G. Vernier. Nalbuphine. Drug Alcohol Depend 1985;14(339-362)

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;

Q8214: L. L. Jantzie, *et al.* Prenatal opioid exposure: The next neonatal neuroinflammatory disease. *Brain Behav Immun* 2020;84(45-58)

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);

Q8226: M. Kongstorp, *et al.* High Accumulation of Methadone Compared with Buprenorphine in Fetal Rat Brain after Maternal Exposure. *J Pharmacol Exp Ther* 2019;371(1):130-137

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;

Q7797: S. Daniels, *et al.* Effect of steady-state methadone on high fructose corn syrup consumption in rats. *J Psychopharmacol* 2018;32(2):215-222

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; 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;

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



Q4834: R. Hill, *et al.* Ethanol Reversal of Tolerance to the Respiratory Depressant Effects of Morphine. *Neuropsychopharmacology* 2016;41(762-773)

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);

Q4151: A. A. Vestal-Laborde, *et al.* The Opioid System and Brain Development: Effects of Methadone on the Oligodendrocyte Lineage and the Early Stages of Myelination. *Developmental Neuroscience* 2014;36(409-421)

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;

Q3624: S. Schreiber, *et al.* Interaction of Different Antidepressants with Acute and Chronic Methadone in Mice, and Possible Clinical Implications. *Journal of Molecular Neuroscience* 2014;52(4):598-604

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](#)

Q9368: F. Meng, *et al.* Naloxone Facilitates Contextual Learning and Memory in a Receptor-Independent and Tet1-Dependent Manner. *Cellular and Molecular Neurobiology* 2021;41(5):1031-1038

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;

Q9318: H. J. Kulbeth, *et al.* Automated quantification of opioid withdrawal in neonatal rat pups using Ethovision(R) XT software. *Neurotoxicology and Teratology* 2021;84(106959)

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; SCH 39166; Pramipexole **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 1002; 2002; **Duration:** 14 days;
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;

Q9796: E. M. Lefevre, *et al.* Interruption of continuous opioid exposure exacerbates drug-evoked adaptations in the mesolimbic dopamine system. *Neuropsychopharmacology* 2020;45(11):1781-1792

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;

Q8250: E. M. Lefevre, *et al.* Interruption of continuous opioid exposure exacerbates drug-evoked adaptations in the mesolimbic dopamine system. *Neuropsychopharmacology* 2020;

Agents: Morphine Hydrochloride **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2001; **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;

Q8759: T. W. Grim, *et al.* A G protein signaling-biased agonist at the mu-opioid receptor reverses morphine tolerance while preventing morphine withdrawal. *Neuropsychopharmacology* 2020;45(2):416-425

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;



Q8430: W. D. Cornwell, *et al.* Tobacco smoke and morphine alter peripheral and CNS inflammation following HIV infection in a humanized mouse model. *Sci Rep* 2020;10(1):13977

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;

Q7580: J. V. Negrete-Diaz, *et al.* Pharmacological activation of dopamine D4 receptor modulates morphine-induced changes in the expression of GAD65/67 and GABAB receptors in the basal ganglia. *Neuropharmacology* 2019;152(22-29)

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;

Q7004: S. Moon, *et al.* Morphine Dependence is Attenuated by Treatment of 3,4,5-Trimethoxy Cinnamic Acid in Mice and Rats. *Neurochem Res* 2019;

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/10 μ 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);

Q7622: S. Kokubu, *et al.* Characterization of Analgesic Actions of the Chronic Intrathecal Infusion of H-Dmt-D-Arg-Phe-Lys-NH₂ in Rat. *Neuromodulation* 2019;

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/ μ L/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);

Q6131: A. Kliewer, *et al.* Phosphorylation-deficient G-protein-biased mu-opioid receptors improve analgesia and diminish tolerance but worsen opioid side effects. *Nat Commun* 2019;10(1):367

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)



Nalbuphine [Back to top](#)

P8971: S. Jang, H. Kim, D. Kim, M. W. Jeong, T. Ma, S. Kim, I. K. Ho and S. Oh. Attenuation of morphine tolerance and withdrawal syndrome by coadministration of nalbuphine. ARCHIVES OF PHARMACAL RESEARCH 2006;29(8):677-684

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.).

P0588: W. K. Schmidt, S. W. Tam, G. S. Sholtzberger, D. H. Smith Jr, R. Clark and V. G. Vernier. Nalbuphine. Drug Alcohol Depend 1985;14(339-362)

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.

Normorphine [Back to top](#)

P0170: R. Schulz, M. Wuster, P. Rubini and A. Herz. Functional opiate receptors in the guinea-pig ileum: their differentiation by means of selective tolerance development. J. Pharmacol. Exp. Ther 1981;219(2):547-550

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

P0173: R. Schulz and M. Wuster. Are there subtypes (isoreceptors) of multiple opiate receptors in the mouse vas deferens. Eur. J. Pharmacol 1981;76(61-66)

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.

Oxymorphone [Back to top](#)

P9615: K. R. Novak, P. Nardelli, T. C. Cope, G. Filatov, J. D. Glass, J. Khan and M. M. Rich. Inactivation of sodium channels underlies reversible neuropathy during critical illness in rats. Journal of Clinical Investigation 2009;119(5):1150-1158

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

P4892: M. B. Gillingham, M. D. Clark, E. M. Dahly, L. A. Krugner-Higby and D. M. Ney. A comparison of two opioid analgesics for relief of visceral pain induced by intestinal resection in rats. CONTEMPORARY TOPICS IN LABORATORY ANIMAL SCIENCE 2001;40(1):21-26

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.

P0588: W. K. Schmidt, S. W. Tam, G. S. Sholtzberger, D. H. Smith Jr, R. Clark and V. G. Vernier. Nalbuphine. Drug Alcohol Depend 1985;14(339-362)

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.

Pentazocine [Back to top](#)

P3459: R. Bergeron, C. de Montigny and G. Debonnel. Effect of short-term and long-term treatments with sigma ligands on the N-methyl-D-aspartate response in the CA(3) region of the rat dorsal hippocampus. Br. J. Pharmacol 1997;120(1351-1359)

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



P1911: A. D. Weissman and E. B. De Souza. Chronic treatment of rats with the specific sigma ligand D-pentazocine fails to modulate dopamine D2 and sigma binding in brain. *Eur. J. Pharmacol* 1991;195(163-165)

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

P0588: W. K. Schmidt, S. W. Tam, G. S. Sholtzberger, D. H. Smith Jr, R. Clark and V. G. Vernier. Nalbuphine. *Drug Alcohol Depend* 1985;14(339-362)

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.

Propoxyphene [Back to top](#)

P0588: W. K. Schmidt, S. W. Tam, G. S. Sholtzberger, D. H. Smith Jr, R. Clark and V. G. Vernier. Nalbuphine. *Drug Alcohol Depend* 1985;14(339-362)

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](#)

Q7464: M. A. Hurlle. Changes in the expression of G protein-coupled receptor kinases and beta-arrestin 2 in rat brain during opioid tolerance and supersensitivity. *J Neurochem* 2001;77(2):486-92

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));

P4727: A. Diaz, *et al.* Autoradiographic mapping of m-opioid receptors during opiate tolerance and supersensitivity in the rat central nervous system. *Nauyn-Schmiedeberg's Arch Pharmacol* 2000;362(101-109)

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;

P4728: A. Diaz, *et al.* Opioid tolerance and supersensitivity induce regional changes in the autoradiographic density of dihydropyridine-sensitive calcium channels in the rat central nervous system. *Pain* 2000;86(227-235)

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

P3361: J. V. Garaulet, *et al.* Effect of chronic administration of dihydropyridine Ca²⁺ channel ligands on sufentanil-induced tolerance to u- and k- opioid agonists in the guinea pig ileum myenteric plexus. *Regul. Pept* 1996;63(1-8)

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

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](#)

Q0421: C. Rivat, C. Becker, A. Blugeot, B. Zeau, A. Mauborgne, M. Pohl and J. J. Benoliel. Chronic stress induces transient spinal neuroinflammation, triggering sensory hypersensitivity and long-lasting anxiety-induced hyperalgesia. *Pain* 2010;150(2):358-368

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).

P8555: A. Adamek, K. Hu, B. Bayer, H. Wagner, G. Ertl, J. Bauersachs and S. Frantz. High dose aspirin and left ventricular remodeling after myocardial infarction. *Basic Research In Cardiology* 2007;102(4):334-340

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).

P0455: T. Oshima, E. R. McCluskey, A. Honda and P. Needleman. Pharmacological manipulation of canine cyclooxygenase and thromboxane synthetase in vivo: differential renal and platelet recovery rates. *J. Pharmacol. Exp. Ther* 1984;229(2):598-602

ALZET Comments: Acetylsalicylic acid; DMSO; Saline; IV (superficial cervical vein); dog; 2ML1; 3 days; pumps primed for 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](#)

P3395: S. K. Kuwahara, T. J. Shinn, B. D. Schreider, M. L. Phan and A. N. Kotake. Aminopyrine infusion breath test for the determination of changes in P450 metabolism in vivo. *Xenobiotica* 1995;25(9):973-980

ALZET Comments: Aminopyrine; Formate, sodium; radio-isotopes; ¹⁴C tracer; water, acidified; NaOH; SC; Rat; 2001; no duration posted; stability of [N-dimethyl-¹⁴C] aminopyrine verified by radiochromatographic analysis- no decomposition observed.

P1268: S. Azri and K. W. Renton. Depression of murine hepatic mixed function oxidase during infection with listeria monocytogenes. *J. Pharmacol. Exp. Ther* 1987;234(3):1089-1093

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

Antipyrene [Back to top](#)

R0077: N. Ray and F. Theeuwes. Implantable osmotically powered drug delivery systems. In 'Drug Delivery Systems: Fundamentals and Techniques,' P. Johnson and J. G. Lloyd-Jones (eds.), Ellis Horwood Ltd. , Chichester, England and VCH Verlagsgesellschaft mbH, Weinheim, Federal Republic of Germany 1987;Ch. 7):120-138

ALZET Comments: Antipyrene; 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; ALZA-authored; synoptic review of mp; post op. care (antibiotic); comparison of sc injections vs. mp infusion; pulsed delivery.

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

ALZET Comments: Antipyrene; 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) [Back to top](#)

Q8543: Y. H. Hsieh, *et al.* Brainstem inflammation modulates the ventilatory pattern and its variability after acute lung injury in rodents. *J Physiol* 2020;598(13):2791-2811

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;

Q7826: L. Hao, *et al.* Indomethacin Enhances Brown Fat Activity. *J Pharmacol Exp Ther* 2018;365(3):467-475

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.);

Q4542: Y. R. Na, *et al.* Consistent Inhibition of Cyclooxygenase Drives Macrophages towards the Inflammatory Phenotype. *PLoS One* 2015;10(U1730-U1742)

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;

Q7687: S. D. Hursting, *et al.* Diet and cancer prevention studies in p53-deficient mice. *J Nutr* 2001;131(11 Suppl):3092s-4s

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);

P4819: M. C. Babin, *et al.* Systemic administration of candidate antivesicants to protect against topically applied suitor mustard in the mouse ear vesicant model (MEVM). *Journal of Applied Toxicology* 2000;20(S141-S144)

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 [Back to top](#)

Q10325: D. R. Seeger, *et al.* Blood-Brain Barrier Is the Major Site for a Rapid and Dramatic Prostanoid Increase upon Brain Global Ischemia. *Lipids* 2020;55(1):79-85

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);

Q9450: D. R. Seeger, *et al.* Blood-Brain Barrier Is the Major Site for a Rapid and Dramatic Prostanoid Increase upon Brain Global Ischemia. *Lipids* 2020;55(1):79-85

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), 4–6 months of age); Resultant plasma level (2.03% Ketorolac concentration); ischemia (cerebral);

P8822: J. M. Scarlett, E. E. Jobst, P. J. Enriori, D. D. Bowie, A. K. Batra, W. F. Grant, M. A. Cowley and D. L. Marks. Regulation of central melanocortin signaling by interleukin-1beta. *Endocrinology* 2007;148(9):4217-4225

ALZET Comments: Ketorolac; Saline, sterile; SC; Mice; 1007D; 2 days; Controls received mp w/ vehicle; animal info (male, C57BL/6J, 4-5 wks old).



P5091: M. D. Southall, L. A. Bolyard and M. R. Vasko. Twenty-four hour exposure to prostaglandin downregulates prostanoid receptor binding but does not alter PGE(2)-mediated sensitization of rat sensory neurons. *Pain* 2002;96(285-296

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.

P4204: J. V. Shufflebarger, J. Doyle, T. Roth, K. Maguire and D. M. Rothkopf. The effect of ketorolac on microvascular thrombosis in an experimental rabbit model. *Plast. Reconstr. Surg* 1996;98(140-145

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](#)

Q3710: A. C. Rosa, A. Pini, L. Lucarini, C. Lanzi, E. Veglia, R. L. Thurmond, H. Stark, E. Masini and E. Masini. Prevention of Bleomycin-Induced Lung Inflammation and Fibrosis in Mice by Naproxen and JNJ7777120 Treatment. *Journal of Pharmacology and Experimental Therapeutics* 2014;351(308-316

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.

P8571: C. Baj-Rossi, T. Rezzonico Jost, A. Cavallini, F. Grassi, G. De Micheli and S. Carrara. Continuous monitoring of Naproxen by a cytochrome P450-based electrochemical sensor. *Biosens Bioelectron* 2014;53(283-7

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

Q4700: C. Baj-Rossi, T. R. Jost, A. Cavallini, F. Grassi, G. De Micheli and S. Carrara. Continuous monitoring of Naproxen by a cytochrome P450-based electrochemical sensor. *BIOSENSORS & BIOELECTRONICS* 2014;53(;):283-287

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

P9697: X. X. Wang, S. Budel, K. Baughman, G. Gould, K. H. Song and S. M. Strittmatter. Ibuprofen Enhances Recovery from Spinal Cord Injury by Limiting Tissue Loss and Stimulating Axonal Growth. *Journal of Neurotrauma* 2009;26(1):81-95

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).

P1504: W. Y. Chan, *et al.* Effects of inhibition of prostaglandin synthesis on uterine oxytocin receptor concentration and myometrial gap junction density in parturient rats. *Biology of Reproduction* 1988;39(1117-1128

Agents: Naproxen, sodium **Vehicle:** Saline; **Route:** SC; **Species:** Rat (pregnant); **Pump:** 2001; **Duration:** 3 days;

ALZET Comments: no comment posted

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Q7348: P. S. Khansari, *et al.* Mechanisms Underlying Neuroprotection by the NSAID Mefenamic Acid in an Experimental Model of Stroke. *Front Neurosci* 2019;13(64

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);



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).

P3550: C. J. Gordon. Pharmacological analysis of diisopropyl fluorophosphate: effects on core temperature, heart rate, and motor activity in the unrestrained rat. *Pharmacol. Biochem. Behav* 1996;55(2):185-194

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

P1664: K. Bergman, E. Cekan, P. Slanina, J. Gabrielsson and K.-E. Hellenas. Effects of dietary sodium selenite supplementation on salicylate-induced embryo- and fetotoxicity in the rat. *Toxicology* 1990;61(135-146)

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

P0826: J. Gabrielsson, *et al.* Constant rate of infusion - improvement of tests for teratogenicity and embryotoxicity. *Life Sci* 1985;37(24):2275-2282

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

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P4849: Y. C. Tsai and S. J. Won. Effects of tramadol on T lymphocyte proliferation and natural killer cell activity in rats with sciatic constriction injury. *Pain* 2001;92(63-69)

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.

P4947: Y. C. Tsai, Y. H. Sung, P. J. Chang, F. C. Kang and K. S. Chu. Tramadol relieves thermal hyperalgesia in rats with chronic constriction injury of the sciatic nerve. *FUNDAMENTAL & CLINICAL PHARMACOLOGY* 2000;14(335-340)

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.

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P8923: K. Deseure, S. Breand and F. C. Colpaert. Curative-like analgesia in a neuropathic pain model: Parametric analysis of the dose and the duration of treatment with a high-efficacy 5-HT_{1A} receptor agonist. *European Journal of Pharmacology* 2007;568(1-3):134-141

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).

P7681: F. C. Colpaert, K. Deseure, L. Stinus and H. Adriaensen. High-efficacy 5-hydroxytryptamine 1A receptor activation counteracts opioid hyperalldynia and affective conditioning. *Journal of Pharmacology and Experimental Therapeutics* 2006;316(2):892-899

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.



P6803: F. C. Colpaert, W. P. Wu, J. X. Hao, I. Royer, F. Sautel, Z. Wiesenfeld-Hallin and X. J. Xu. High-efficacy 5-HT_{1A} receptor activation causes a curative-like action on allodynia in rats with spinal cord injury. *European Journal of Pharmacology* 2004;497(1):29-33

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-HT_{1A} receptor agonist; spinal cord injury; pain.

P6234: W. P. Wu, J. X. Hao, X. J. Xu, Z. Wiesenfeld-Hallin, W. Koek and F. C. Colpaert. The very-high-efficacy 5-HT_{1A} receptor agonist, F 13640, preempts the development of allodynia-like behaviors in rats with spinal cord injury. *European Journal of Pharmacology* 2003;478(2-3):131-137

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).

P5716: L. A. B. Slot, W. Koek, J. P. Tarayre and F. C. Colpaert. Tolerance and inverse tolerance to the hyperalgesic and analgesic actions, respectively, of the novel analgesic, F 13640. *European Journal of Pharmacology* 2003;466(3):271-279

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).

P5902: K. Deseure, W. Koek, H. Adriaensen and F. C. Colpaert. Continuous administration of the 5-hydroxytryptamine 1A agonist (3-chloro-4-fluoro-phenyl)-[4-fluoro-4-[[5-methyl-pyridin-2-ylmethyl]-amino]-methyl]piperidin-1-yl]-methadone (F 13640) attenuates allodynia-like behavior in a rat model of trigeminal neuropathic pain. *Journal of Pharmacology and Experimental Therapeutics* 2003;306(2):505-514

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-HT_{1A} receptor agonist; behavioral study; F13640, F13714 & morphine were infused in one pump; baclofen infused in two pumps due to limited solubility.

P6585: F. C. Colpaert, J. P. Tarayre, W. Koek, P. J. Pauwels, L. Bardin, X. J. Xu, Z. Wiesenfeld-Hallin, C. Cosi, E. Carilla-Durand, M. B. Assie and B. Vacher. Large-amplitude 5-HT_{1A} receptor activation: a new mechanism of profound, central analgesia. *Neuropharmacology* 2002;43(6):945-958

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).