References on the Administration of Naloxone and Naltrexone Using ALZET® Osmotic Pumps

Naloxone


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: Naloxone HCl Vehicle: Saline; Route: SC; Species: Mice; Pump: 1007D; Duration: 1 week;
ALZET Comments: Dose (1 mg/100 uL); 0.9% NaCl used; animal info (four-week-old male ddY-strain mice, 24 g); behavioral testing (double activity monitoring system; Von Frey Test); spinal cord injury;

Q7026: P. M. Grace, et al. Protraction of neuropathic pain by morphine is mediated by spinal damage associated molecular patterns (DAMPs) in male rats. Brain, Behavior, and Immunity 2018;72(45-50

Agents: naloxone; A438079; YVAD-cmk, Ac- Vehicle: Not Stated; Route: CSF/CNS (intrathecal); Species: Rat; Pump: 2001;
ALZET Comments: Dose (naloxone: 60 ug/h; A438079: 30 ng/h; ac-YVAD-cmk: 1 ug/h); animal info (10-12 week old male Fischer 344 rats); enzyme inhibitor (caspase-1);


Agents: Naloxone Vehicle: Water, ultrapure; Route: CSF/CNS (left ventricle); Species: Rat; Pump: 2002; Duration: 12 days;
ALZET Comments: Dose (96 mg/ml, 0.5 ul/h); Controls received mp w/ vehicle; animal info (Adult male Sprague-Dawley rats, 200–250 g); behavioral testing (locomotor activity); half-life (1.57 +/- 0.784 h); ischemia (ischemia stroke);


Agents: Naloxone Vehicle: Not Stated; Route: SC; Species: Mice; Pump: Not Stated; Duration: 5 days;
ALZET Comments: Dose (3 mg/kg/d); Controls received mp w/ vehicle;

Q6094: L. Deng, et al. Prophylactic treatment with the tricyclic antidepressant desipramine prevents development of paclitaxel-induced neuropathic pain through activation of endogenous analgesic systems. Pharmacol Res 2016;114(75-89

Agents: Desipramine, naloxone, AM251, AM630 Vehicle: Water, saline, PEG 400, DMSO; Route: SC; Species: Rat; Pump: 2ML4; Duration: 28 days;
ALZET Comments: Dose: Desipramine (10 mg/kg/d), Naloxone (12 mg/kg/d), AM251 (3 mg/kg/d), AM630 (3 mg/kg/day); Desipramine dissolved distilled water, naloxone dissolved in saline, AM251 and AM630 dissolved in 50% PEG400 and 50% DMSO; Controls received mp w/ vehicle; animal info (Sprague-Dawley rats weighing 275–350 g); Multiple pumps per animal (2 when given the treatment of 2 different agents), Desipramine,vehicle, all antagonists delivered in separate osmotic pumps;


Agents: Naloxone Vehicle: Saline, normal; Route: SC; Species: Mice; Pump: 1007D; Duration: 7 days;
ALZET Comments: Controls received mp w/ vehicle; animal info: obesity induced, C57black/6J male mice, 6 wks old; functionality of mp verified by behavioral test; dose-response (pg 13, 14); dose-response (pg 13, 14); behavioral testing (Porsolt forced swim, Elevated Plus Maze, Dowel Gnawing); delayed delivery (24 hours via a 1.5 cm vinyl catheter); Isoflurane anesthesia used; minipump combined with a dose of 1 mg/kg/day of rimonabant (rim nal) injected IP; Dose: 0.5 mg/mouse/day


Agents: Naloxone methiodide; naloxone Vehicle: Saline; Route: SC; Species: Rat; Pump: 2002; Duration: 10 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (SD, 280-300g); behavioral testing (von Frey filament);

Agents: Naloxone; Naltrexone Vehicle: Saline; Route: SC; Species: Rat; Pump: 1007D; Duration: Not Stated;
ALZET Comments: Control animals received mp w/ vehicle; animal info (Sprague Dawley, 250-350 g)


Agents: Morphine; naloxone Vehicle: Saline; Route: CSF/CNS (intrathecal); Species: Rat; Pump: Not Stated; Duration: 5 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Wistar, 350-400 g); behavioral testing (tail-flick); dependence; IT catheter created from PE tube joined with silastic tube with epoxy resin and silicon rubber;


Agents: Naloxone hydrochloride; naloxone methiodide; morphine sulfate Route: SC; Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: Animal info (Sprague Dawley, 200-250 g, P7, P14, P21, P28)


Agents: Naloxone; BW373U86; U50,488H; morphine-6-glucuronide; morphine-3-glucuronide; wortmannin; PKI-(14-22)-amide Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 1007D; Duration: 5 days;
ALZET Comments: Animal info (7-12 wks old, C57/BL6, male); BW373U86 also known as (R)-4-[(2S,5R)-4-allyl-2,5-dimethyl-1-piperazinyl]-3-hydroxy-hydroxybenzyl]-N,N-diethylbenzamide is a delta opioid receptor selective agonist; U50,488H also known as trans-(R)-3,4-dichloro-N-methyl-N-2-(1-pyrrolidin)cyclohexyl)-benzeneacetamide methane sulfonate hydrate is a kappa opioid selective receptor agonist;


Agents: Naloxone; binaltorphimine, nor Vehicle: Not Stated; Route: CSF/CNS; Species: Mice; Pump: 1007D; Duration: 7 days;
ALZET Comments: Animal info (129/SvEv, lacking MOR, KOR, DOR); ALZET brain infusion kit 3 used; cyanoacrylate adhesive used; post op. care (meloxicam); cannula placement verified at end of experiment by methylene blue staining; half-life “Naloxone... has a short half-life in vivo”; “NorBNI has... an extremely long half-life" pg 3662


Agents: Naloxone; morphine Vehicle: Not Stated; Route: CSF/CNS (intrathecal); Species: Rat; Duration: 5 days;
ALZET Comments: Controls received mp w/ saline; animal info (male, Wistar, 350-400 g); two intrathecal catheters implanted


Agents: Morphine; Naloxone Route: CSF/CNS (intrathecal); Species: Rat; Duration: 5 days;
ALZET Comments: Controls received mp w/ saline; animal info (pathogen-free, male, Wistar, 350-400 g); infusion rate of 1 ul/hr; two catheters inserted intrathecally

Q0909: M. R. Hutchinson, et al. Evidence that opioids may have toll-like receptor 4 and MD-2 effects. Brain, Behavior, and Immunology 2010;24(1):83-95

Agents: Morphine; Naloxone Vehicle: Not Stated; Route: SC; Species: Rat; Pump: Not Stated; Duration: Not Stated;
ALZET Comments: Controls received mp w/ saline; animal info (adult, male, Sprague Dawley, 300-375 g); multiple pumps per animal (2)
Q0746: R. J. Horvath, et al. Inhibition of microglial P2X(4) receptors attenuates morphine tolerance, Iba1, GFAP and &mu; opioid receptor protein expression while enhancing perivascular microglial ED2. Pain 2010;150(3):401-413

**Agents:** Morphine sulfate; naloxone **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 1, 4, 7 days;

**ALZET Comments:** Controls received mp w/ saline; animal info (male, Sprague-Dawley, 175-200 g); one pump contained morphine plus naloxone; “All morphine pumps were filled with 0.833 mg/kg/hr morphine to deliver the equivalent of twice daily 10 mg/kg injections over the course of 24 h” pg 402; tolerance


**Agents:** Naloxone **Vehicle:** Saline, sterile; **Route:** SC, CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2001; **Duration:** 4 days;

**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, Sprague-Dawley, 300-375 g.); sciatic nerve injury


**Agents:** Naltrexol HCl, 6B-; Naloxone HCl **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 7 days;

**ALZET Comments:** Controls received placebo pellets; dose-response (fig 3, 5); comparison of pellets, SC injections vs. mp; animal info (male, Swiss-Webster, 22-30g)


**Agents:** Morphine; Naloxone **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;

**ALZET Comments:** Controls received mp w/ vehicle; dose-response (p. 157, 159); no stress (see pg. 155); cancer (bone); multiple pumps per animal (2); animal info (20-25g, male, adult, C3H/HeJ); pain


**Agents:** Morphine sulfate; Naloxone hydrochloride; Ketorlac **Route:** SC; CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2001; **Duration:** 4 days;

**ALZET Comments:** Controls received mp w/ saline; tolerance; animal info (adult, male, Sprague Dawley, 350 g.)


**Agents:** Naloxone; Naloxone methiodide **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 1007D; **Duration:** 3 days;

**ALZET Comments:** Controls received mp w/ saline; animal info (male, Sprague-Dawley, 175-200 g); sciatic constrictive injury of the left infraorbital nerve


**Agents:** Naloxone; Etophine hcl; Morphine sulfate **Vehicle:** Saline, normal; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 7 days;

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


**Agents:** Buprenorphine; naloxone; methadone **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat (pregnant); **Pump:** 2ML4;

**ALZET Comments:** Controls received mp w/ water; dose-response (fig. 3); teratology


**Agents:** Naloxone HCL **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 7 days;

**ALZET Comments:** Controls received placebo pellets; dose-response (fig.2)
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<td>P7207:</td>
<td>A. Ogawa, et al.</td>
<td>Hard-food mastication suppresses complete Freund’s adjuvant-induced nociception.</td>
<td>Naloxone</td>
<td>Vehicle: Not Stated</td>
<td>Route: IV (jugular)</td>
<td>Species: Rat</td>
<td>Pump: Not Stated</td>
<td>Duration: 3, 6 days</td>
<td>Controls received mp w/ saline; functionality of mp verified by measuring residual volume</td>
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<td>P6250:</td>
<td>J. Froehlich, et al.</td>
<td>Preclinical and clinical studies on naltrexone: What have they taught each other?</td>
<td>Naloxone</td>
<td>Vehicle: Not Stated</td>
<td>Route: Not Stated</td>
<td>Species: Rat</td>
<td>Pump: Not Stated</td>
<td>Duration: Not Stated</td>
<td>Dose-response (p.5); dependence</td>
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<td>Q1495:</td>
<td>R. T. Rahim, et al.</td>
<td>Administration of mu-, kappa- or delta-receptor agonists via 2 osmotic minipumps suppresses murine splenic antibody responses.</td>
<td>Morphine sulfate; U50,488H; DPDPE; naltriben methanesulfonate; deltorphin II</td>
<td>Vehicle: Sodium chloride; DMSO; saline; sterile</td>
<td>Route: SC</td>
<td>Species: Mice</td>
<td>Pump: 1003D</td>
<td>Duration: 48 hours</td>
<td>Controls received mp w/ saline; animal info (6 wks old, pathogen free, C3HeBrFeJ); comparison of pellets vs. mp; multiple pumps per animal (2); &quot;Minipumps have two advantages, (1) a variety of agonists and antagonists can be used that are not available in slow-release pellet form, and (2) full dose-response curves can be generated.&quot; pg 2002; &quot;Minipumps have an advantage over slow-release pellets in that they do not result in splenic atrophy. Thus, drugs administered by the minipumps appear to be less potent, but also to have fewer side effects, than morphine given by slow-release pellets.&quot; pg 2007; &quot;The use of osmotic minipumps should permit more extensive and definitive testing of the pharmacokinetics and pharmacodynamic action of a variety of opioids for their effects on immune cell function.&quot; pg 2008; 10% DMSO used</td>
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<td>P4800:</td>
<td>X. Li, et al.</td>
<td>Opioid-induced hyperalgesia and incisional pain.</td>
<td>Morphine sulfate; Naloxone</td>
<td>Vehicle: Saline</td>
<td>Route: SC</td>
<td>Species: Rat</td>
<td>Pump: 2ML1</td>
<td>Duration: 6 days</td>
<td>Controls received mp w/ vehicle; tolerance; dependence</td>
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<td>Q6819:</td>
<td>J. Braz, et al.</td>
<td>Therapeutic Efficacy in Experimental Polyarthritis of Viral-Driven Enkephalin Overproduction in Sensory Neurons.</td>
<td>Naloxone; Naloxone methiodide</td>
<td>Vehicle: Saline</td>
<td>Route: SC</td>
<td>Species: Rat</td>
<td>Pump: 2001</td>
<td>Duration: 3 days</td>
<td>Dose (3 mg/kg/day); Controls received mp w/ vehicle; animal info (polynarthritic male sprawg dawley rats, 6 weeks old); behavioral testing (foot withdrawal (pain)); Therapeutic indication (Rheumatoid arthritis);</td>
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<tr>
<td>P4965:</td>
<td>Z. Vertes, et al.</td>
<td>Epidermal growth factor influenced by opioid peptides in immature rat uterus.</td>
<td>Enkephalin analog; Naloxone</td>
<td>Vehicle: Saline</td>
<td>Route: IP</td>
<td>Species: Rat</td>
<td>Pump: 1003D</td>
<td>Duration: 1,3 days</td>
<td>Controls received mp w/ vehicle; functionality of mp verified by aspirating remaining contents; peptides; Enkephalin analog ENK was (D-Met2-Pro5)enkephalinamide, inhibits epidermal growth factor.</td>
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<td>P5212:</td>
<td>X. Lu, et al.</td>
<td>Naloxone prevents microglia-induced degeneration of dopaminergic substantia nigra neurons in adult rats.</td>
<td>Naloxone</td>
<td>Vehicle: PBS; ethanol</td>
<td>Route: SC</td>
<td>Species: Rat</td>
<td>Pump: 2002</td>
<td>Duration: 14 days</td>
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**Agents:** Naloxone  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2ML1;  
**Duration:** 8 days;

**ALZET Comments:** Controls received mp w/vehicle; functionality of mp verified by residual volume


**Agents:** Naloxone  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2001;  
**Duration:** 7 days;

**ALZET Comments:** Controls received mp w/saline; dependence


**Agents:** Naloxone HCl  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2ML2;  
**Duration:** 7 days;

**ALZET Comments:** Controls received mp w/saline; no stress (see pg. 337)


**Agents:** Naloxone; Fentanyl citrate; Etorphine HCl  
**Vehicle:** NaCl;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** 2001; 2002;  
**Duration:** 7, 8 days;

**ALZET Comments:** Controls received placebo pellets


**Agents:** Naloxone HCl  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2002;  
**Duration:** 14 days;

**ALZET Comments:** Controls received mp w/saline; functionality of pump verified with pump emptying


**Agents:** Naloxone HCl; Morphine sulfate; Meperidine HCl; Fentanyl citrate  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2ML1;  
**Duration:** 7 days;

**ALZET Comments:** Controls received sham pumps; tolerance


**Agents:** Etorphine HCl; Fentanyl citrate; Naloxone HCl  
**Vehicle:** NaCl;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** 2001; 2002;  
**Duration:** 7, 8 days;

**ALZET Comments:** Controls received placebo pellets; dose-response; comparison of sc fentanyl injections vs. mp; good methods; tolerance
Agents: Naloxone HCl Vehicle: Saline; Route: SC; Species: Rat; Pump: 2002; Duration: 14 days;
ALZET Comments: controls received mp with saline; functionality of pump verified with pump emptying

P3247: D. Levesque, et al. The potentiating effects of restraint stress and continuous naloxone infusion on the analgesic potency of morphine are additive. Brain Research 1993;617(176-180
Agents: Naloxone HCl Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2ML1; Duration: 7 days;
ALZET Comments: controls received empty mp; stress/adverse reaction (pg. 179); possible surgical stress of pump removal may have affected results

Agents: Morphine; Naloxone Vehicle: Saline; Route: CSF/CNS (intrathecal); Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: controls received mp w/saline; tolerance; medical category:pain/analgesia;skc

Agents: Naloxone Vehicle: Water; Route: SC; Species: Rat; Pump: 2ML1; Duration: 7 days;
ALZET Comments: controls received mp w/water

Agents: Naloxone Vehicle: Water, distilled; Route: SC; Species: Rat; Pump: 2ML1; Duration: 7 days;
ALZET Comments: controls received mp w/water

P2047: C. A. Paronis, et al. Apparent pA2 value of naltrexone is not changed in rats following continuous exposure to morphine or naloxone. Life Sci 1992;50(1407-1416
Agents: Morphine sulfate; Naloxone HCl Vehicle: Saline; Route: SC; Species: Rat; Pump: 2ML1; Duration: 7 days;
ALZET Comments: controls received empty pumps previously used, which is not recommended by the manufacturer

Agents: Naloxone Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2002; Duration: 28 days;
ALZET Comments: controls received sham operation; pumps replaced at 2 weeks

Agents: Naloxone Vehicle: Saline; Route: SC; Species: Rat; Pump: Not Stated; Duration: 4 days;
ALZET Comments: neuroscience; multiple pumps per animal (2)

Agents: Naloxone Vehicle: Saline; Route: SC; Species: Rat; Pump: 2ML1; Duration: 7 days;
ALZET Comments: no comment posted

Agents: Naloxone Vehicle: Water, sterile; Route: SC; Species: Rat; Pump: 2ML1; Duration: 7 days;
ALZET Comments: controls received mp with vehicle; mp placed on flank
Agents: Naloxone HCl Vehicle: Water; Route: SC; Species: Rat; Pump: 2ML1; Duration: 6 days;
ALZET Comments: no comment posted

Agents: Naloxone Vehicle: Saline; Route: SC; Species: Squirrel; Pump: 2ML4; Duration: 35 days;
ALZET Comments: no comment posted

Agents: Naloxone Vehicle: Water; Route: SC; Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: no comment posted

Agents: Naloxone Vehicle: Water; Route: SC; Species: Rat; Pump: 2001; 2ML1; Duration: 1 week;
ALZET Comments: no comment posted

Agents: Bremazocine; MR-2266; MR-2267; Naloxone; Sufentanil Vehicle: DMSO; HCl; Sodium hydroxide; Propylene glycol; Water; Route: SC; Species: Rat; Pump: 2001; 2ML1; Duration: 3, 6, 7 days;
ALZET Comments: mp malfunction -- pump plugged at 4 days due to propylene glycol; water was vehicle for naloxone; propylene glycol, HCl, NaOH was vehicle for MR-2200; pump replaced at 3 days

Agents: Naloxone Vehicle: Saline; Route: Abdomen; Species: Rat; Pump: 2ML2; Duration: 14 days;
ALZET Comments: Mp connected to catheter; tissue perfusion

Agents: Naloxone Vehicle: Water; Route: SC; Species: Rat; Pump: 2001; Duration: 6 hours;
ALZET Comments: controls received mp w/water; concomitant CRF ICV infusion; 3 exp., only 1 used mp

Agents: Naloxone HCl; Naltrexone HCl Vehicle: Saline; Route: CSF/CNS (intrathecal); Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: mp connected to a ‘Y’ catheter; half-life; morphine administered intrathecally via the external arm of the ‘Y’ catheter; concomitant infusion of agents; comparison of bolus injections vs. mp infusion

Agents: Naloxone Vehicle: Water; Route: SC; Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: controls received mp w/ vehicle; concomitant administration of morphine; stimulation of midbrain

Agents: Morphin; Naloxone Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2ML1; Duration: 12 days;
ALZET Comments: controls received spent mp; agents infused separately

Agents: Apomorphine; FK-33824; Haloperidol; Naloxone
Vehicle: Ethanol; Tartaric acid; Water
Route: SC
Species: Rat
Pump: Not Stated
Duration: 5, 9 days

ALZET Comments: mp model not stated; controls received mp w/unspecified vehicle or were sham-operated; agents infused separately w/appropriate vehicle; comparison of sc inject. vs. mp infusion

P1156: D. S. Bruce, et al. Opioids and hibernation. I. effects of naloxone on bear hit's depression of guinea pig ileum contractility and on induction of summer hibernation in the ground squirrel. Life Sciences 1987;41(18):2107-2113

Agents: Naloxone
Vehicle: Saline
Route: SC
Species: Squirrel
Pump: 2ML4
Duration: 28 days

ALZET Comments: Controls received mp w/ saline; concomitant administration of winter bear plasma or its albumin fraction


Agents: Naloxone HCl
Vehicle: Saline
Route: SC
Species: Rat
Pump: 2001
Duration: 3 days

ALZET Comments: controls received mp w/saline; toxicology; multiple pumps per animal (3); comparison of single icv injection vs. mp infusion


Agents: Naloxone
Vehicle: Water
Route: SC
Species: Rat
Pump: 2001
Duration: 52 hours

ALZET Comments: comparison of injec of 3 naloxone doses vs. mp infusion; multiple pumps per animal (2)


Agents: Diprenorphine; Naloxone; Naltrexone
Vehicle: Saline
Route: SC
Species: Cat
Pump: 2ML1
Duration: 7 days

ALZET Comments: mp functionality and accuracy of delivery verified; acute ip adminis. of agents w/mp infusion; ischemia


Agents: Naloxone Vehicle: Water
Route: SC
Species: Rat
Pump: 2001
Duration: 52 hours

ALZET Comments: comparison of injec of 3 naloxone doses vs. mp infusion; multiple pumps per animal (2)


Agents: Naloxone HCl
Vehicle: Saline
Route: SC
Species: Rat (pregnant)
Pump: 2002
Duration: Not Stated

ALZET Comments: Controls received mp w/saline


Agents: Morphine; Naloxone
Vehicle: Not Stated
Route: CSF/CNS
Species: Rat
Pump: 1701
Duration: 14 days

ALZET Comments: controls received mp w/Naloxone; mp connected to cannula; water infused for 6 days before being replaced w/agent filled mp; 2 pumps/animal; comparison of 3 morphine pellets vs. mp infusion; pump replaced


Agents: Naloxone HCl
Vehicle: Saline
Route: CSF/CNS
Species: Squirrel
Pump: 2001
Duration: 2, 7 days

ALZET Comments: Dose-response data
Agents: Endorphin, α-; Endorphin, ovine β-; Enkephalin, methionine-; Naloxone HCl Vehicle: Saline; Route: CSF/CNS; Species: Rat; Pump: 2001; Duration: 1, 2 days;
ALZET Comments: Comparison of agents effects; peptides

Agents: Naloxone HCl Vehicle: Water; Route: SC; Species: Rat; Pump: 2001; Duration: 8 weeks;
ALZET Comments: pump replaced weekly; long-term study; 1-2 pumps of naloxone/test animal; controls got 1 pump w/ water

Agents: Naloxone Vehicle: Saline; Route: SC; Species: Rat; Pump: 2ML2; Duration: 4 weeks;
ALZET Comments: controls received mp w/ saline; pumps replaced after 2 weeks

Agents: Naloxone HCl Vehicle: Saline; Route: SC; Species: Rat; Pump: 2001; 2ML1; Duration: 2, 5 weeks;
ALZET Comments: Pumps replaced weekly; stress/adverse reaction (fibrous tissue growth, mp malfunction)

Agents: Enkephalin agonist DADL; Naloxone Vehicle: Saline; Route: CSF/CNS (intrathecal); Species: Rat; Pump: 2001; Duration: 5 days;
ALZET Comments: agents infused alone and/or concomitantly; peptides

Agents: Naloxone HCl Vehicle: Water; Route: SC; Species: Rat; Pump: 2001; Duration: 8 days;
ALZET Comments: Exp. 1-2) morphine or naloxone injections 3) 2001, 8 days naloxone; morphine injec. on last day, 4) naloxone injec; comparison of injec vs. mp infusion

Agents: Naloxone Vehicle: Saline; Route: SC; Species: Rat; Pump: Not Stated; Duration: 7 days;
ALZET Comments: no comment posted

Naltrexone

Agents: Naltrexone Vehicle: Saline; Route: SC; Species: Rat; Pump: 2ML4; Duration: 28 days;
ALZET Comments: Dose (10 mg/kg/h); Controls received mp w/ vehicle; animal info (male Wistar rats, 280–300 g); 163 mmHg - 142 mmHg;cardiovascular;

Q9503: E. A. Townsend, et al. Evaluation of a Dual Fentanyl/Heroin Vaccine on the Antinociceptive and Reinforcing Effects of a Fentanyl/Heroin Mixture in Male and Female Rats. ACS Chemical Neuroscience 2020;11(9):1300-1310
Agents: Naltrexone Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2ML2; Duration: 2 weeks;
ALZET Comments: Dose (0.032 mg/kg/h); animal info (SDawley, 10 weeks); behavioral testing (tail withdrawal test);

Agents: Naltrexone; Clonidine
Vehicle: Saline; Route: SC; Species: Rat; Pump: 2001; Duration: 1 week;
ALZET Comments: Dose (Naltrexone- 0.01, 0.032, or 0.1 mg/kg/hr or 3.2, 10 ug/kg/hr); Controls received mp w/ vehicle; animal info (19 Sprague Dawley, 10 weeks old); behavioral testing (Tail Withdrawal Test); dependence;


Agents: Naltrexone Hydrochloride
Vehicle: Saline; Route: SC; Species: Mice; Pump: 1007D; Duration: 7 days;
ALZET Comments: Dose (20 mg/kg/day); Controls received mp w/ vehicle; animal info (Male, C57BL/6J, 3 months old);

Q7421: bioRxiv. Effectiveness and selectivity of a heroin conjugate vaccine to attenuate heroin, 6-acetylmorphine, and morphine antinociception in rats: Comparison with naltrexone. bioRxiv 2019;577494

Agents: Naltrexone
Vehicle: Saline; Route: SC; Species: Rat; Pump: 2ML2; Duration: 14 days;
ALZET Comments: Dose (0.01 mg/kg/h); Controls received mp w/ vehicle; animal info (Adult male and female Sprague Dawley rats); pumps were aseptically removed on day 15; Therapeutic indication (opioid use disorder treatment);


Agents: Bupropion hydrochloride, naltrexone hydrochloride
Vehicle: Saline; Route: SC; Species: Rat; Pump: 2ML2; Duration: 12 days;
ALZET Comments: Dose (40 mg/kg/day BUP, 4 mg/kgiday NTX); Controls received sham surgery; animal info (Adult male Sprague-Dawley rats weighing 200-250 g); behavioral testing (locomotion tests); Drugs administered together or in separate pumps; Contrave® is an adjunct pharmacotherapy for obesity that contains bupropion and naltrexone.; Therapeutic indication (Obesity);

Q4836: L. S. Hwa, et al. Dissociation of u-opioid receptor and CRF-R1 antagonist effects on escalated ethanol consumption and mPFC serotonin in C57BL/6J mice. Addiction Biology 2016;21(11);112-124

Agents: CP154526; naltrexone
Vehicle: DMSO; CSF, artificial; Route: CSF/CNS; Species: Mice; Pump: 1002; Duration: 14 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, C58BL/6J, 8 weeks old); functionality of mp verified by IAA drinking test or morphine-sensitive tail withdrawal; ALZET brain infusion kit 3 used; 4% DMSO used; Cannula placement verified via Nissl staining;


Agents: Naltrexone Vehicle: Water, sterile; Route: SC; Species: Rat; Pump: Not Stated; Duration: 14 days;
ALZET Comments: Control animals received mp w/ vehicle; 14-day pump used


Agents: Naltrexone HCl
Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 1007D; Duration: 7 days;
ALZET Comments: Animal info (male, Sprague Dawley, albino, 160-180g); ALZET brain infusion kit used; post op. care (ampicillin 100 mg/kg IM; meloxicam 2.0 mg/kg IM); behavioral testing (flexion reflex, flinch response, mechanical threshold pressure); Incision closed with wound clip


Agents: Naltrexone Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: Controls received mp w/ saline; animal info (Sprague Dawley, male, 250-300 g)
Agents: Naltrexone Vehicle: Saline; Route: SC; Species: Rat; Pump: 2006; Duration: 5 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 250-380 g); wound clips used; neuropathic pain

Agents: Naltrexone, methyl Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 1002; Duration: 12 days;
ALZET Comments: Controls received mp w/ PBS; animal info (MOR KO, C57BL/6 wt); cancer (lung); Methylnaltrexone (also known as MNTX) is a mu opioid receptor inhibitor

Agents: Naltrexone HCI Vehicle: Saline, physiological; Route: SC; Species: Rat; Pump: 2ML4; Duration: 2 weeks;
ALZET Comments: Controls received mp w/vehicle; Dependence; Animal info (male, Long-Evans, 250 g); Dose-response (fig. 1)

Agents: Naltrexone Vehicle: DMSO; saline, sterile; Route: SC; Species: Mice; Pump: 1007D; Duration: 7 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (HIV-1, TAT, adult, 2-6 mo old); 50% DMSO used

Agents: L-NAME; naltrexone Vehicle: Saline, physiological; Route: CSF/CNS; Species: Mice; Pump: 2001; Duration: Not Stated;
ALZET Comments: Controls received mp w/ vehicle; animal info (NIH, Swiss, 18-22 g); ALZET brain infusion kit used; hyperbaric oxygen

Agents: Naltrexone Vehicle: DMSO; saline, sterile; Route: SC; Species (transgenic); Pump: 1007D; Duration: 7 days;
ALZET Comments: Animal info (TAT); 50% DMSO used

Agents: Naltrexone Vehicle: DMSO; Saline, sterile; Route: SC; Species (transgenic); Pump: 1007D; Duration: 2, 5, 10 days;
ALZET Comments: Controls received mp w/ vehicle; pumps replaced after 5 days; animal info (male, female, C3H x C57BL/6, Tat (+), Tat (-), 2-6 months old); 50% DMSO used

Agents: Naltrexone Vehicle: Saline; Route: SC; Species (knockout); Pump: 1002; Duration: 21 days;
ALZET Comments: Pumps replaced at day 13; behavioral study

Agents: Naltrexone Vehicle: Water; sterile; Route: SC; Species: Hamster; Pump: 2001; Duration: 7 days;
ALZET Comments: Controls received mp w/ vehicle; comparison of acute injections vs. chronic mp; naltrexone is a nonselective opioid antagonist; behavioral study

**Agents:** Naltrexone  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** 1007D;  
**Duration:** 7 days;  
**ALZET Comments:** Controls received mp w/ vehicle

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**Agents:** Naltrexone  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 1007D;  
**Duration:** 20 days;  
**ALZET Comments:** Pumps replaced once; post op. care (topical antibiotic)

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**Agents:** Naltrexone  
**Vehicle:** CSF, artificial;  
**Route:** CSF/CNS (nucleus of solitary tract);  
**Species:** Rat;  
**Pump:** 1007D;  
**Duration:** 13 days;  
**ALZET Comments:** Controls received mp w/ vehicle; ALZET brain infusion kit used; 7-day recovery period; cannula placement verified by histological examination

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**Agents:** Naltrexone  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Hamster;  
**Pump:** 1003D;  
**Duration:** 48 hours;  
**ALZET Comments:** Controls received mp w/ vehicle

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**Agents:** Naltrexone  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** Not Stated;  
**Duration:** 4 weeks;  
**ALZET Comments:** controls received mp w/ vehicle; tolerance; dependence

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**Agents:** β-endorphin; naltrexone  
**Vehicle:** CSF, artificial;  
**Route:** CSF/CNS (bilateral paraventricular nuclei);  
**Species:** Rat;  
**Pump:** 2002;  
**Duration:** 4 hours;  
**ALZET Comments:** Dose (100 ng of β-EP/0.5 µl/h); Controls received mp w/ vehicle; animal info (Male Fischer-344 rats of 150–175 g body weight); naltrexone is an opiate antagonist; Brain coordinates (1.8 mm behind bregma, 1.5 mm lateral to the midline, and 7.7 mm below the skull surface); bilateral cannula used: The osmotic pump was implanted was connected with two infusion cannulae (bilateral guide cannula) using a Y-connector;

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**Agents:** Endorphin, B-; Naltrexone  
**Vehicle:** CSF, artificial;  
**Route:** CSF/CNS (paraventricular nucleus);  
**Species:** Rat;  
**Pump:** 2002;  
**Duration:** 4,16 hours;  
**ALZET Comments:** Controls received mp w/ vehicle; bilateral infusion;

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**Agents:** Naltrexone  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** 2001;  
**Duration:** 7 days;  
**ALZET Comments:** Controls received mp w/ vehicle; dose-response (graph p. 324); comparison of SC injections vs. mp; good methods priming p. 322; tolerance; Naltrexone is an opioid antagonist; injected naltrexone reduced drinking behavior, infused naltrexone did not; repeated injections and infusion increased ethanol consumption; recovery period

**Agents:** Naltrexone  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** Not Stated;  
**Duration:** 4 weeks;  
**ALZET Comments:** Controls received mp w/vehicle; tolerance; dependence


**Agents:** Naltrexone HCl  
**Vehicle:** Saline, sterile;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2001;  
**Duration:** 7 days;  
**ALZET Comments:** controls received mp w/vehicle


**Agents:** Cocaine; Naltrexone HCl; Morphine sulfate  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2001;  
**Duration:** 7 days;  
**ALZET Comments:** controls received mp w/vehicle; functionality of mp verified by plasma levels; dose-response (p. 279-280); tolerance


**Agents:** Naltrexone  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 1003D;  
**Duration:** Not Stated;  
**ALZET Comments:** controls received mp w/saline; functionality of mp verified by residual volume; no stress (see pg. 260)


**Agents:** Naltrexone  
**Vehicle:** Not Stated;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2001;  
**Duration:** 48 hours;  
**ALZET Comments:** no comment posted


**Agents:** Naltrexone  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 1003D;  
**Duration:** 48 hours;  
**ALZET Comments:** controls received vehicle infusion; functionality of mp verified by measuring residual volume


**Agents:** Naltrexone  
**Vehicle:** Not Stated;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2001;  
**Duration:** 7 days;  
**ALZET Comments:** controls received mp w/saline


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


**Agents:** Ascorbic acid; Naltrexone  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Rat (pregnant);  
**Pump:** Not Stated;  
**Duration:** 7 days;  
**ALZET Comments:** controls received mp w/vehicle


**Agents:** Naltrexone; DAGO; Enkephalin analog DADLE; DPDPE; U-50,488H  
**Vehicle:** Not Stated;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2001;  
**Duration:** 7 days;  
**ALZET Comments:** DAGO is a mu-opioid agonist; DPDPE is a delta-opioid agonist

**Agents:** Naltrexone HCl  
**Vehicle:** Lactic acid  
**Route:** SC  
**Species:** Rat  
**Pump:** Not Stated  
**Duration:** 7 days  
**ALZET Comments:** controls received empty silastic implants


**Agents:** Naltrexone HCl  
**Vehicle:** Water, distilled; Cyclodextrin  
**Route:** SC  
**Species:** Rat  
**Pump:** Not Stated  
**Duration:** 8,15 days  
**ALZET Comments:** controls received mp w/ vehicle


**Agents:** Naltrexone  
**Vehicle:** Not Stated  
**Route:** SC  
**Species:** Mice  
**Pump:** Not Stated  
**Duration:** Not Stated  
**ALZET Comments:** Immunology; dependence; pumps used to evaluate naltrexone’s ability administered via Alzet mini-osmotic pumps to block morphine actions on the thymocytes; main study used morphine pellets


**Agents:** Naltrexone  
**Vehicle:** Not Stated  
**Route:** SC  
**Species:** Rat  
**Pump:** Not Stated  
**Duration:** 14 days  
**ALZET Comments:** controls received mp w/ saline


**Agents:** Naltrexone  
**Vehicle:** Not Stated  
**Route:** SC  
**Species:** Rat  
**Pump:** Not Stated  
**Duration:** 8 days  
**ALZET Comments:** controls received mp with saline

P2371: C. E. Markowitz, et al. Effect of opioid receptor antagonism on proopiomelanocortin peptide levels and gene expression in the hypothalamus. Mol. and Cellular Neurosciences 1992;3(184-190

**Agents:** Naltrexone  
**Vehicle:** Lactic acid  
**Route:** SC  
**Species:** Rat  
**Pump:** Not Stated  
**Duration:** 1, 3 weeks  
**ALZET Comments:** no comment posted


**Agents:** Levorphanol tartrate; Naltrexone HCl; U-50,488H; ICI-154,129  
**Vehicle:** Saline  
**Route:** IP  
**Species:** Mice  
**Pump:** Not Stated  
**Duration:** 7 days  
**ALZET Comments:** Functionality of mp verified by measuring residual pump volume; tolerance


**Agents:** Naltrexone HCl  
**Vehicle:** Saline  
**Route:** SC  
**Species:** Rat  
**Pump:** Not Stated  
**Duration:** 7 days  
**ALZET Comments:** no comment posted
<table>
<thead>
<tr>
<th>Study ID</th>
<th>Authors</th>
<th>Title</th>
<th>Journal</th>
<th>Agents</th>
<th>Vehicle</th>
<th>Route</th>
<th>Species</th>
<th>Pump</th>
<th>Duration</th>
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</thead>
<tbody>
<tr>
<td>P1164</td>
<td>C. W. Stevens, et al.</td>
<td>Chronic antagonist infusion does not increase morphine antinociception in rat spinal cord.</td>
<td>Brain Research</td>
<td>Naloxone HCl; Naltrexone HCl</td>
<td>Saline;</td>
<td>Route: CSF/CNS (intrathecal);</td>
<td>Species: Rat;</td>
<td>Pump: 2001;</td>
<td>Duration: 7 days;</td>
</tr>
<tr>
<td>P1205</td>
<td>L. Steinberg, et al.</td>
<td>The influence of chronic naltrexone infusions on energy metabolism in pregnant rats.</td>
<td>Nutr. Rep. Int</td>
<td>Naltrexone HCl</td>
<td>Saline;</td>
<td>SC;</td>
<td>Rat; Rat (pregnant);</td>
<td>Pump: 2002;</td>
<td>Duration: 14 days;</td>
</tr>
<tr>
<td>P0742</td>
<td>D. S. Baskin, et al.</td>
<td>Treatment of experimental stroke with opiate antagonists, effects on neurological function, infarct size, and survival.</td>
<td>Journal of Neurosurgery</td>
<td>Diprenorphine; Naloxone; Naltrexone</td>
<td>Saline;</td>
<td>SC;</td>
<td>Cat;</td>
<td>Pump: 2ML1;</td>
<td>Duration: 7 days;</td>
</tr>
<tr>
<td>P0564</td>
<td>A. Tempel, et al.</td>
<td>Neurochemical and functional correlates of naltrexone-induced opiate receptor up-regulation.</td>
<td>Journal of Pharmacology and Experimental Therapeutics</td>
<td>Naltrexone HCl</td>
<td>Saline;</td>
<td>SC;</td>
<td>Species: Rat;</td>
<td>Pump: 2001;</td>
<td>Duration: 8 days;</td>
</tr>
<tr>
<td>P0749</td>
<td>A. M. Moudy, et al.</td>
<td>Differential up-regulation of microsomal and synaptic membrane mu opioid receptors.</td>
<td>Biochemical and Biophysical Research Communications</td>
<td>Naltrexone HCl</td>
<td>Saline;</td>
<td>SC;</td>
<td>Species: Rat;</td>
<td>Pump: 2002;</td>
<td>Duration: 2 weeks;</td>
</tr>
<tr>
<td>P0239</td>
<td>R. S. Zukin, et al.</td>
<td>Naltrexone-induced opiate receptor supersensitivity.</td>
<td>Brain Research</td>
<td>Naltrexone HCl</td>
<td>Saline;</td>
<td>SC;</td>
<td>Species: Rat;</td>
<td>Pump: 2001;</td>
<td>Duration: 1 week;</td>
</tr>
<tr>
<td>P0242</td>
<td>G. L. Nieder, et al.</td>
<td>Effects of opiate antagonists on early pregnancy and pseudopregnancy in mice.</td>
<td>Journals of Reproduction Fertility</td>
<td>Naltrexone</td>
<td>Saline;</td>
<td>SC;</td>
<td>Species: Mice (pregnant);</td>
<td>Pump: 2001;</td>
<td>Duration: 9 days;</td>
</tr>
<tr>
<td>P0412</td>
<td>I. M. Lang, et al.</td>
<td>Investigations of the preferential reduction in drinking behavior of opiate antagonists.</td>
<td>Proceedings of the Western Pharmacology Society</td>
<td>Naltrexone</td>
<td>Not Stated;</td>
<td>SC;</td>
<td>Species: Rat;</td>
<td>Pump: Not Stated;</td>
<td>Duration: 16 days;</td>
</tr>
</tbody>
</table>

**ALZET Comments:**
- P1665: controls received a smooth, hollow glass capsule of the same size and weight as pumps.
- P1164: mp connected to a 'Y' catheter; half-life; morphine administered intrathecally via the external arm of the 'Y' catheter; concomitant infusion of agents; comparison of bolus injections vs. mp infusion.
- P1205: controls received mp w/ saline; mp implanted in pregnant rats on day 3 of exp. (7 days sperm positive).
- P0742: mp functionality and accuracy of delivery verified; acute ip adminis. of agents w/mp infusion; ischemia (cerebral).
- P0564: comparison of ip injec vs. mp infusion vs. pellets.
- P0749: Comparison of agents.
- P0239: sterilized Tygon tubing used as a control; poly E-caprolactone capsules used to admin. N for 52 days.