References on the Administration of Opioids Using ALZET® Osmotic Pumps

1. Apomorphine


Agents: Apomorphine Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 1002; Duration: 4 weeks;

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


Agents: MK-801; apomorphine HCL hemihydrate Vehicle: Saline; Ascorbic acid; Route: CSF/CNS (nucleus accumbens); Species: Rat; Pump: 2002; Duration: Not Stated;

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


Agents: MPTP; L-dopa; apomorphine Vehicle: Not Stated; Route: IP; SC; Species: Mice; Pump: 2004; Duration: 1-28 days;

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


Agents: Apomorphine Vehicle: Saline; Route: SC; Species: Mice; Pump: Not Stated; Duration: 28 days;

ALZET Comments: Dose (3.15 mg/kg/day); Controls received mp w/ vehicle; animal info (10 week old, C57, black); ischemia (Brain);

2. Buprenorphine


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

ALZET Comments: Dose (Buprenorphine- 1 mg/kg/day or ); Controls received mp w/ vehicle; animal info (Female); post op. care (Metacam); dependence;
Agents: Norbuprenorphine; Morphine Vehicle: Saline; Route: SC; Species: Rat; Pump: 2ML2; Duration: 14 days;
ALZET Comments: Dose (1, 3 or 10 mg/kg/day); Controls received mp w/ vehicle; animal info (Long-Evans); dependence;

Agents: Morphine; buprenorphine; methadone Vehicle: Saline; Route: SC; Species: Mice; Pump: Not Stated; Duration: 6 days;
ALZET Comments: Dose (45 mg/kg/d; 5 mg/kg/day; 60 mg/kg/day); Controls received mp w/ vehicle; animal info (Male CD-1 mice, approximately 30g); comparison of morphine alkaloid pellet vs mp;

Agents: Buprenorphine; methadone Vehicle: Saline; Route: SC; Species: Mice; Pump: Not Stated; Duration: 6 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, CD-1, 30g); behavioral testing (tail flick latencies, mouse locomotion); dependence; Dose (Buprenorphine 5 mg/kg/day; methadone 60 mg/kg/day);

Agents: Buprenorphine Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 1007D; 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; Pharmacokinetics; Dose: 247 ug/kg/h); Resultant plasma level ((mean, 106.4 ug/L; range, 61.8 to 133.0 ug/L)); Industry authored (Wildlife Conservation Society); Interesting (Plasma concentrations of butorphanol in common peafowl were maintained at or above reported efficacious analgesic concentrations; Use of these osmotic pumps may provide options for avian analgesia) pg. 1070

3. Butorphanol

Q5136: M. Meredith M. Clancy DVM, et al. Pharmacokinetics of butorphanol delivered with an osmotic pump during a seven-day period in common peafowl (Pavo cristatus). American Journal of Veterinary Research 2015;76(12):1070-1076
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)); Industry authored (Wildlife Conservation Society); Interesting (Plasma concentrations of butorphanol in common peafowl were maintained at or above reported efficacious analgesic concentrations; Use of these osmotic pumps may provide options for avian analgesia) pg. 1070

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 the pumps took less than 1 min per rat, and the length of the anesthesia was approximately 5 min per rat." pg 576; functionality of mp verified via residual volume

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

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

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

4. Dynorphin

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

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

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

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

ALZET Comments: Dynorphin A; Calcium chloride; Magnesium chloride; Potassium chloride; Saline; CSF/CNS (intrathecal); Rat; 2001; 1 week; peptides.

5. Endorphin

Agents: Endorphin, beta, (1-31)  
Vehicle: Saline, sterile  
Route: CSF/CNS  
Species: Rat  
Pump: 2001; 1003D  
Duration: 3, 7 days  

ALZET Comments: Animal info (Sprague Dawley, male, 200-250 g); pumps replaced  


Agents: Endorphin, B; corticotropin releasing hormone  
Vehicle: CSF, artificial  
Route: CSF/CNS (paraventricular nucleus of hypothalamus)  
Species: Rat  
Pump: 2002  
Duration: 16 hours  

ALZET Comments: Controls received mp w/ vehicle; peptides; animal info (male, Fischer, 160-175g.)  


Agents: Endorphin, B  
Vehicle: Not Stated  
Route: CSF/CNS (paraventricular nucleus)  
Species: Rat  
Pump: 2002  
Duration: 18 hours  

ALZET Comments: Controls received mp w/ aCSF; immunology; peptides  


Agents: Endorphin, beta  
Vehicle: CSF, artificial  
Route: CSF/CNS (paraventricular nucleus)  
Species: Rat  
Pump: 2002  
Duration: 6 days  

ALZET Comments: Plastics One bilateral guide cannula used with a Y-connector; bilateral infusion  


Agents: Endorphin, B  
Vehicle: CSF, artificial  
Route: CSF/CNS  
Species: Rat; Mice  
Pump: Not Stated  
Duration: 12 days  

ALZET Comments: Cardiovascular  

6. Enkephalin  


Agents: [D-Ala2, N-Me-Phe4, Gly5-ol]-enkephalin  
Vehicle: Not Stated  
Route: CSF/CNS (intrathecal)  
Species: Rat; mouse  
Pump: Not Stated  
Duration: Not Stated  

ALZET Comments: animal info (rat - male, adult, Sprague Dawley, 250-300g; good methods (intrathecal catheter placement pg. 11704); mice - male, adult, C57BL/6, 20-25g); No pump used, catheter only for lumbar catherization  


Agents: Morphine sulfate; enkephalin analog DPDPE; U50,488H; deltorphin II, D-ala2-  
Vehicle: Saline, pyrogen free  
Route: SC  
Species: Mice  
Pump: 1003D  
Duration: 48 hours  

ALZET Comments: Controls received mp w/ vehicle; dose-response (fig 1); comparison of pellets vs. mp; immunology; animal info (female, 6 wk old); mp primed 4 hours in 37 C saline; "morphine pellet potently exacerbated oral salmonella infection, but morphine given by pump, at doses which were immunosuppresive had a substantially lesser effect (of infection)." (p. 251). "Further, we and others have found that morphine pellets induce sepsis in mice." (p. 251)  


Agents: Enkephalin  
Vehicle: Saline  
Route: SC  
Species: Mice (nude)  
Pump: 2004  
Duration: 28 days
ALZET Comments: Controls received mp w/ vehicle; OGF plasma levels taken; comparison of IP and intratumoral injections vs. SC mp; adverse reaction: (see pg. 229) "within 2 days...3 minipumps containing saline were spontaneously dislodged." [possible pocket too small]; cancer (carcinoma); peptides; enkephalin was met-^5 and termed OGF or opioid growth factor

Agents: Morphine sulfate; Enkephalin analog DAMGO; Dermorphin-derived tetrapeptide (TAPS) Vehicle: CSF, artificial; Route: CSF/CNS; Species: Rat; Pump: 2001; Duration: 6 days;
ALZET Comments: Controls received mp w/ vehicle; comparison of bolus injections vs. chronic mp; pumps replaced on day 4 to achieve 6 days due to dead space in catheter; ALZET brain infusion kit used; tolerance; dependence; peptides; second hole with guide cannula & stylet used for bolus injections; (ALZET) cannula placement confirmed by fast green dye & the guide cannula confirmed by methylene blue; TAPS is a potent mu-opioid receptor agonist

Agents: Enkephalin Vehicle: Saline; Route: SC; Species: Rabbit; Pump: 2ML1; Duration: 24 hours;
ALZET Comments: Controls received mp w/ vehicle; cardiovascular; peptides; enkephalin was met-^5

7. Etorphine

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

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

Agents: Naloxone; etorphine 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: Etorphine HCl; morphine sulfate Vehicle: Saline; Route: SC; Species: Mice; Pump: Not Stated; Duration: 3 days;
ALZET Comments: Tolerance

Agents: Etorphine hydrochloride; Morphine sulfate  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** mice;  
**Pump:** 2001;  
**Duration:** 7 days;  

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

8. Fentanyl


**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);  


**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, Sprague-Dawley); comparison of oxycodone and morphine injection vs mp; opioids administered 1 hour, 10 days, or 28 days post-CCI (chronic constriction injury) surgery;


**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 puda); wallaby (Macropus rufogriseus); iguanas (Iguana iguana); Mojave rattlesnakes (Crotalus scutulatus); corn snakes (Elaphe guttata guttata); Japanese quails (Coturnix coturnix japonica); hens (Gallus domesticus)); “ Finally, the use of intracoelomic osmotic pumps was reported in iguanas (Iguana iguana) in a study of reproductive behavior.26 No complication due to the pump placement was reported in that study.” pg. 508; Advantages: Can be extracted in case of 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 accidently in air sacs during intracoelomic implantation)"

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

**Agents:** Fentanyl  
**Vehicle:** Not Stated;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** Pump model not stated;  
**Duration:** 5 days;  

**ALZET Comments:** Dose (0.01mg/kg/hr); Controls received mp w/ vehicle; animal info (Male, Sprague-dawley); dependence;
9. Morphine

Agents: Morphine Hydrochloride Vehicle: Saline; Route: SC; Species: Mice; Pump: 2001; Duration: 7 days;
ALZET Comments: Dose (5 mL/kg); 0.9% Saline used; Controls received mp w/ vehicle; animal info (C57BL/6J, Oprm1 KO, ); dependence;

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

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

Q7533: C. R. Leibrand, et al. HIV-1 Tat and opioids act independently to limit antiretroviral brain concentrations and reduce blood-brain barrier integrity. J Neurovirol 2019;
Agents: Dolutegravir, Abacavir, Lamivudine; Morphine Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 2001; Duration: 5 days;
ALZET Comments: Dose (abacavir 2.5 mg/day (123.5 mg/kg/day), dolutegravir 0.2 mg/day (10.3 mg/kg/day), and lamivudine 1.2 mg/day (61.7 mg/kg/day); Morphine (2 mg/day)); Controls received mp w/ vehicle; animal info (Adult female mice, 70 days of age); post op. care (Bupivacaine);

Agents: DMT-DALDA; morphine sulfate Vehicle: Saline; Route: CSF/CNS (intrathecal); Species: Rat; Pump: 2001, 2002; Duration: 7 days, 14 days;
ALZET Comments: Dose ((DMT-DALDA 0.3, 1, 3, or 10 pmol/μL/hour), (MS 37.5 nmol/hour)); dose-response (Figure 1a graph on page 4); Controls received mp w/ vehicle; animal info (adult, male, Sprague-Dawley rats, 220–240 g); 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);

10. Pentazocine

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

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

ALZET Comments: Ethylketocyclazocine; Heroin; Meperidine; Oxymorphone; Pentazocine; Propoxyphene; Bremaazocine; 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.

11. Sufentanil


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)); dependence;


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

ALZET Comments: Controls received mp w/ vehicle; tolerance; Group 1 received sufentanil, Group 2 received sufentanil & nimodipine, Group 3 received nimodipine, Group 4 received vehicle; Nimodipine is a Ca channel blocker; sufentanil was diluted in saline; nimodipine was diluted in 10% ethanol / 20% propylene glycol / 70% water;


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

ALZET Comments: Controls received mp w/ vehicle; tolerance; Group 1 received vehicle alone, Group 2 received chronic sufentanil, Group 3 received sufentanil & nimodipine, Group 4 received nimodipine alone; Nimodipine is a CA2+ antagonist opioid; sufentanil citrate was diluted in saline; nimodipine was diluted in 10% ethanol / 20% propylene glycol / 70% water;


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

ALZET Comments: controls received mp w/saline; tolerance

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 Vehicle: Not Stated; Route: CSF/CNS (intrathecal); Species: Rat; Pump: Not Stated; Duration: 7 days;

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