References on the Administration of Agents to Dogs
Using ALZET® Osmotic Pumps

ALZET Comments: Ang (1-7); IV (jugular); Dog; 14 days; Controls received mp w/ vehicle; animal info (12-14 kg); cardiovascular; Pacemaker also implanted; Therapeutic indication (Atrial tachycardia); Dose (6 ug/kg/h);

ALZET Comments: Angiotensin (1-7); A-71915; IV (jugular); Dog; 14 days; animal info (mongrel, 13-17 kg); cardiovascular; peptides; A-71915 is an ANP receptor antagonist; Dose (Ang (1-7) 6 ug/kg/hr; A-71915 0.3 ug/kg/hr); “Ang-(1–7) dose was selected because 6 μg/kg/h is verified as the highest dose that wouldn’t affect blood pressure in our preliminary study” pg 2;

ALZET Comments: Nerve growth factor, human B-; PBS; CSF/CNS (inferior alveolar nerve); Dog (beagle); 2ML2; 6 weeks; Controls received mp w/ vehicle; animal info (male, beagle, 18 weeks old, 10-12 kg); good methods (picture of implant pg 413); Multiple pumps per animal (2; one pump delivered NGF other delivered PBS); used rat jugular catheter, 15 cm long; pump body placed into retromandibular area; long-term study;

ALZET Comments: Dorzolamide; timolol; SC (Eye); Dog; 2004; 24 days; Controls received no mp; Controls received no mp; "Osmotic pump, as one of the constant drug delivery systems, can be placed in the subcutaneous pocket with minimal surgical skills, and continuously administer the wanted drugs into the target regions" pg 241; picture of implantation pg 240; Interesting (use of pump in veterinary application);

ALZET Comments: Angiotensin (1-7); IV (jugular); Dog (mongrel); Animal info (male, female, 11-15 kg); peptides.

ALZET Comments: Sucrose; CSF/CNS; Dog; 2ML1; 7 days; Controls received mp w/ isomolar solution; animal info (adult, 11.0-25.0 kg); Cannula placement verified via visual inspection using trypan blue dye; used 25g cannula; used two stainless steel screws and dental acrylic to fix cannula; hydrocephalus;

ALZET Comments: Pyrazole-3; DMSO; polyethylene glycol; IV; Dog; 2ML1; 7 days; Control animals received mp w/ vehicle; animal info (mongrel, 20-36 kg, atrial fibrilation).

ALZET Comments: Nafarelin, aza-gly; SC; Dog (beagle); Animal info (ovariectomized); Aza-gly Nafarelin is a GnRH agonist.

ALZET Comments: Wy-40972; SC; Dog (beagle); 2ML1; 2ML2; 2ML4; 7, 8, 12, 14 days; Controls received mp w/ saline; animal info (1.2-6 years old; 9-16 kg, ovario-hysterectomy); Wy-40972 is a LHRH agonist; also known as lutrelin.

ALZET Comments: Carboplatin; CSF/CNS; Monkey; Rat; dog; 7 days; functionality of mp verified by residual volume; Carboplatin brain tissue distribution.

ALZET Comments: Caramiphen; SC; Dog; 2001; 2ML1; 48 hours; Animal info (beagle, male, 14-16 kg); Functionality of mp verified by plasma levels; toxicology; pharmacokinetics.

ALZET Comments: Brain-derived neurotrophic factor; CSF/CNS (intrathecal); Dog; 2002; 14 days; Controls received mp w/ saline; dose-response; peptides; post io. care (ketoprofen); animal info (female, mongrel hound, 6-12 months old, 18-22 kg., bladder denervation); mp connected to silicone cuff surrounding spinal cord root bundles (2).

ALZET Comments: Nicotine; SC; Dog (mongrel); 2ML4; 28 days; Functionality of mp verified by nicotine plasma levels; MRI; multiple pumps per animal (2).

ALZET Comments: Estradiol; Saline; SC; Dog; 2ML4; 3 weeks; Controls received mp w/ vehicle; no stress (see pg. R1065); animal info (female, mongrel, 1 yr, hypoglycemia).

ALZET Comments: Dihydrotestosterone, 5 alpha-; Estradiol, 17B-; SC; Dog; 2ML4; 28 days; Animal info (Beagle, 3.5-7.2 yrs); testosterone induced BPH animal model.

ALZET Comments: FR167653; IV (jugular); Dog; 7 days; Animal info (7.5-17 kg); controls received mp w/ physiological saline; functionality of mp verified by serum FR167653 levels; enzyme inhibitor (p38MAPKinase); cardiovascular; ischemia (cerebral).

ALZET Comments: Quinacrine; chloroquine; amphotericin B; E-64d; pentosan polysulfate; PBS; water, distilled; DMSO; SC; CSF/CNS; Rat; mice; dog (mongrel); 2 months; 4 weeks; Controls received mp w/ vehicle; dose-response (fig. 2); no stress (see pg. 5004); stress/adverse reaction: (see pg. 5002) PPS at highest dose (20mg/kg/day) showed hemorrhage in the SC area surrounding the mp; enzyme inhibitor (cysteine protease [E-64d]); long-term study.

ALZET Comments: Octreotide; SOM230; Water, sterile; SC; Rat; monkey; dog; 2002; 2ML1; 2ML2; 7, 14, or 56 days; Controls received mp w/ vehicle; functionality of mp verified by IGF-I plasma levels; long-term study, pumps replaced every 2 weeks; peptides; Somatostatin analogs; 2002 pumps used in rats; 2ML2 used in monkeys; 2ML1 pumps used in dogs; octreotide also called SMS 201-995.

ALZET Comments: Buprenorphine; SC; Dog; 2ML1; 48 hours; Animal info (young adult, beagle or mixed breed, 8.4-12.8 kg); Functionality of mp verified by residual volume and serum buprenorphine levels; comparison of infudisk, pegasus vs. ALZET vs. mp; multiple pumps per animal (3,4); mp primed overnight in sterile saline; paper provides list of most possible negative outcomes. Upon pump removal the incisions were closed with tissue glue; ALZET pump was the most cost effective method; wound clips used.

P4992: S. M. Zhou, et al. Use of three infusion pumps for postoperative administration of buprenorphine or morphine in dogs. JAVMA 2002;220(11):1655-1660
ALZET Comments: Nerve growth factor; Saline; Albumin, bovine serum; CSF/CNS (stellate ganglion); dog; 2ML4; 5 weeks; controls received mp w/ vehicle; tissue perfusion (left and right stellate ganglion); cardiovascular; peptides; vehicle was saline with 0.1% bovine serum albumin.

ALZET Comments: Cloprostenol, sodium;; SC;; dog (pregnant);; 2001;; Dose-response (graph p. 460); varying doses (0.875 - 4.5 ug/kg - day); higher doses caused polydipsia.

ALZET Comments: FK-633; SC;; dog;; 2ML4;; 3 months;; controls received mp w/ vehicle; long-term study, pump replaced after 1 and 2 months; no stress (p. 344); cardiovascular;.

ALZET Comments: Angiotensin II; Acetic acid; dog;; 4-7 days;; controls received mp w/angiotensin II only; functionality of mp verified by plasma levels; stability verified by HPLC; peptides, cardiovascular;.

ALZET Comments: Cloprostenol, calcium; Water, sterile; SC; dog; 2001; 7 days; controls received mp w/vehicle; dose-response; no stress (see pg. 1318); toxicology; "The miniosmotic pump was well tolerated..and its insertion and removal were easy." (pg. 1318).


ALZET Comments: Dye, toluidine blue; Saline; CSF/CNS (subarachnoid space, intrathecal); dog; 2ML1; 7 days; no stress (see pg. 826); controls received mp w/saline; comparison of injections vs. mp; brain tissue distribution.


ALZET Comments: Angiotensin II; IV (inferior vena cava); dog; 2ML4; 28 days; peptides.


ALZET Comments: Proline, l-; Proline, nitric oxide-; NaOH; IA (femoral); dog; 2ML2; 7 days; controls received mp w/ proline to contralateral vessel; stability verified by in vitro assay; half-life (pg. 27); cardiovascular; constructed local infusion device and attached to mp via catheter.


ALZET Comments: Fibroblast growth factor; saporin; Sodium citrate; NaCl; EDTA; IA (carotid); dog; 2002; 14 days; controls received mp w/ vehicle; stability verified for 14 days by cellular assay; peptides; Saporin- FGF2 conjugate was infused; pump placed externally; Saporin is a potent ribosome-inactivating protein.


ALZET Comments: Heparin; PBS; IV (femoral); dog; 2ML2; 14 days; controls received mp w/ vehicle; functionality of mp verified by pump residual volume & reservoir tubing patency; infusion to a vascular graft.


ALZET Comments: Bafilomycin A1; DMSO; Saline; bone; dog; 2002; no duration posted; contralateral controls received mp w/ vehicle; tissue perfusion (bone crypts of mandibular fourth molar).


ALZET Comments: Bafilomycin A1; DMSO; Saline; bone; dog; 1, 3, 4 weeks; tissue perfusion (bone crypts of mandibular fourth molar); pumps replaced at 2 weeks.


ALZET Comments: SB-209670; CSF/CNS (cisterna); dog; 2ML1; 7 days; controls received mp w/ vehicle; +/- SB-209670 is a non-peptide endothelin antagonist.

P2777: W. Wang. Chronic administration of aldosterone depresses baroreceptor reflex function in the dog. Hypertension 1994;24(577-577

ALZET Comments: Aldosterone; Saline; SC; dog; 2ML2; 10 days; controls received mp w/ saline.

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Bibliography

ALZET Comments: Bafilomycin A1; DMSO; Saline; bone; dog; no duration posted; controls received mp w/ vehicle or no treatment; tissue perfusion (bone crypts of mandibular fourth molar); stability verified in vitro for 2 weeks at 37 degrees C; enzyme inhibitor; dogs given prophylactic im penicillin for first postoperative week; local infusion used because systemic delivery may cause lethal side effects; bafilomycin A1 is a specific inhibitor of vacuolar H+-ATPases.

ALZET Comments: A-75998; RS-26306; Propylene glycol; Saline; Sodium acetate buffer; SC; dog; 1003D; 3 days; comparison of single and 5x daily injections vs. mp; infusion dose was four-fold lower than daily injection for same results.

ALZET Comments: Morphine HCl; Saline; SC; dog; 2ML1; 8 days; functionality of mp verified by plasma levels; comparison of injections vs. mp; dependence; infusion plasma levels were 1/5 the maximal concentration of injected animals, and were far more stable.

ALZET Comments: Prostaglandin E1; Emulphor; Ethanol; bone (mandible); dog; 3 weeks; controls received undiluted vehicle which was 1:1 mixture of Emulphor:80% ETOH; tissue perfusion (bone); comparison of pellets vs. mp; pumps replaced weekly; authors state that subperiosteal bone formation was greater for comparable doses when PGE1 was delivered by minipumps as compared to pellets.

ALZET Comments: Nicotine; SC; dog; 28 days; controls received mp with saline; comparison of topical nicotine vs. mp.

ALZET Comments: Norepinephrine; SC; dog; 2ML4; 8 weeks; controls received mp with saline; long-term study, pumps replaced after 3-4 weeks.

ALZET Comments: Clonidine HCl; Saline; SC; dog; 2ML4; 4 weeks; tolerance; antihypertensive.

ALZET Comments: Norepinephrine; SC; dog; 2ML4; 28 days; an additional pump was implanted sc on day 10 to maintain plasma levels of norepinephrine p. 332.

ALZET Comments: Fenoldopam mesylate; Water, distilled; Citric acid; Propylene glycol; Sodium metabisulfate; IV (jugular); dog; 2ML2; no duration posted; controls received mp with vehicle; multiple pumps per animal (2).

ALZET Comments: Prostaglandin E1; Emulphor; Ethanol; bone (mandible); dog; 3 weeks; controls received mp w/vehicle; tissue perfusion (bone); comparison of pellets vs. mp; pumps replaced weekly; "...we estimated that PGE delivered by minipump produces 25 to 30% more bone than the same amount of starting material delivered by pellet." (p.139).

ALZET Comments: Amidephrine mesylate; Saline; SC; dog; 3,4 weeks; pumps replaced weekly; multiple pumps per animal (2 or 3) to elevate AMD levels (pg.1186).


ALZET Comments: Norepinephrine; SC; dog; 2ML4; 28 days; no comment posted.


ALZET Comments: Endothelin-1; Water; CSF/CNS (intrathecal); dog; 2001; 7 days; controls received sham op or mp w/ water; peptides.


ALZET Comments: Nicotine sulfate; SC; dog; 28 days; no comment posted.


ALZET Comments: Prostaglandin E1; Emulphor; Ethanol; bone (mandible); dog; 5 weeks; control side of mandible received mp with vehicle; tissue perfusion (bone); long-term study, pumps replaced weekly; each dog served as its own control -- one mp with PGE1 to one side and one with vehicle to the other side of mandible; pump implanted in superficial neck tissues; dogs given penicillin orally (100,000 U/d) for first post-operative week.


ALZET Comments: Angiotensin II; CSF/CNS; dog; 2ML4; 4 weeks; peptides.


ALZET Comments: Adenosine; Adenosine, N-ethylcarboxamido-; Inosine; Norepinephrine; IV (saphenous); dog; 2ML1; no duration posted; functionality of mp verified by inspecting catheter for clots, observing collapsed pump reservoir, and measuring residual drug solution.


ALZET Comments: Desipramine HCl; Norepinephrine; tempol; EDTA; Heparin; Saline; IV (saphenous); dog; 2ML1; 5 days; dose-response; implanted sc above the knee; functionality of mp verified by visual inspection of sectioned pump and by serum levels; tissue perfusion; animal info (m, 9-15 kg); 5000 Units of heparin.


ALZET Comments: HETE, 15-; Saline; knee (articular cavity); dog; 2ML2; 2ML4; 10 days; tissue perfusion (knee joint).


ALZET Comments: Prostaglandin E1; Emulphor; Ethanol; bone (mandible); dog; 3 weeks; controls received mp with vehicle; tissue perfusion (bone); pumps replaced weekly; stability: 70% of original activity after 1 week at 37 degrees C; penicillin given for 1 week post-surgery.
**ALZET Comments:** ZnDTPA; Saline; SC; dog; 2ML4; 64 days; comparison of iv injections vs. mp infusion; functionality of mp verified in vitro; pump replaced at day 28 and 50; ZnDTPA is a chelating agent; long-term study.

**ALZET Comments:** Parathyroid hormone, bovine 1-34; Albumin; HCl; Saline; SC; dog; 2001; 8 months; controls received mp w/vehicle; pumps replaced every 12 days; replacement therapy (thyroparathyroidectomy); no stress (see pg. 755); long-term study.

**ALZET Comments:** Norepinephrine; SC; dog; 2ML4; 28 days; dose-response; functionality of mp verified.

**ALZET Comments:** Growth hormone, human; SC; dog; 2ML2; 12 days; pumps primed in sterile water overnight before implantation; functionality of mp verified upon removal.

**ALZET Comments:** Parathyroid hormone, bovine 1-34; Albumin; HCl; Saline; SC; dog; 2002; 8 months; controls rec’d mp w/vehicle; pumps replaced every 12 days; mp infusion of PTH in comb. with vit. D treatment; replacement therapy (thyroparathyroidectomy); no stress or infection (see p.1299); long-term study; peptides.

**ALZET Comments:** Morphine sulfate; SC; dog; 2ML1; no duration posted; Immunology; multiple pumps per animal (2).

**ALZET Comments:** Nafarelin acetate; Propylene glycol; Water; SC; dog; 2002; 2ML4; 18 months; comparison of injection vs. infusion; pump replaced after 2 or 4 weeks; long-term study; dose-response data; contraception in dogs; peptides.

**ALZET Comments:** L-363586; Saline; SC; dog; 2ML1; 1 week; exocrine inhibition promotes transplant acceptance; comparison of timing of drug delivery and grafting; L-363586 is a cyclic hexapeptide somatostatin analog; transplantation; half-life in dogs is 40 min. and in human is 1 hour.

**ALZET Comments:** ACTH (1-24), a-; IV (jugular); dog; 2ML1; 2 weeks; controls received empty mp; mp attached to silastic rubber catheter in jugular vein; peptides.

**ALZET Comments:** PO; dog; no duration posted; ALZA-authored; pump swallowed empty: gastric transit comparison of objects varying in size, swallowed w/ or w/o a meal.

ALZET Comments: Angiotensin II; Isoproterenol; Ascorbic acid; Water; IV (jugular); dog; 2ML4; 28 days; mp connected to tygon catheter in jugular vein; mp implanted sc; dose-response data (plasma levels and blood pressure); agents infused simultaneously; hypertension; peptides.

ALZET Comments: Acetylsalicylic acid; DMSO; Saline; IV (superficial cervical vein); dog; 2001; 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.

ALZET Comments: Endotoxin, E. coli; Saline; IV (jugular); dog; 1 week; used diff. pumps in same animal to deliv. variable dosage; solubility of endotoxin in mp max. of 12-15 mg/ml; functionality of mp verified.

ALZET Comments: Nicotine salicylate; Saline; Sodium salicylate; SC; dog; 5-8 weeks; comparison of acute iv infusion/ injec vs. chronic mp infusion; pump replaced every week; long-term study; no stress p. 53; pumping rate verified at 38C; infection at implant site in 1 dog.

ALZET Comments: Aminopropionitrile fumarate, B-; CSF/CNS (intrathecal); dog; 2ML2; no duration posted; Author states use of 2ML2 pump w/ delivery rate of 10ul/h - this is an error; delivery rate verified - possibly a 2ML1 mp was used; advantages of mp p. 768; spinal cord injury.

ALZET Comments: Parathyroid hormone, human 1-34; Caproic acid, E-amino-; SC; dog; 4 weeks; pump replaced every week; mp used to avoid infection associated with 4 wk. iv cannula; no stress (infection) see p. 463; peptides.

ALZET Comments: Parathyroid hormone, human 1-34; SC; dog; 5-6 months; comparison of pulsatile injec. vs. mp infusion; pump replaced weekly; comparison of human clinical data vs. animal; long-term study; peptides.

P0179: R. D. Podbesek, et al. Treatment with human parathyroid hormone fragment (hPTH 1-34) stimulates bone formation and intestinal calcium absorption in the greyhound: comparison with data from the osteoporosis trial. 7th Int'l. Conf. on Calcium Regulating Hormones, Estes Park, Colorado, Sept. 5-9, 1980. In 'Hormonal Control of Calcium Metabolism,' D. V. Cohn and R. V. Talmage (eds.), Excerpta Medica, Amsterdam 1981:118-123
ALZET Comments: Parathyroid hormone, human 1-34; SC; dog; 6-8 months; pumps replaced; long-term study; comparison of intermittent injections vs. infusion; peptides.

ALZET Comments: Prostaglandin analog (TPT); Ethanol; Sodium phosphate; SC; dog; 1-2 days; comparison of injections sc vs. infusion.