

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

**Q9836:** Z. Zhao, *et al.* Attenuation of atrial remodeling by aliskiren via affecting oxidative stress, inflammation and PI3K/Akt signaling pathway. Cardiovascular Drugs and Therapy 2021;35(3):587-598

Agents: Wortmannin Vehicle: Not Stated; Route: IV; Species: Dog; Pump: Not Stated; Duration: 2 weeks;

**ALZET Comments:** Dose (70 ug/kg/day); animal info (mongrel dogs of either sex, weighing from 11 to 17 kg); 131.71 mmHg - 117.29 mmHg; Wortmannin aka WM, PI3K antagonist; cardiovascular;

**Q7574:** G. Z. Liu, *et al.* Aldosterone stimulation mediates cardiac metabolism remodeling via Sirt1/AMPK signaling in canine model. Naunyn Schmiedebergs Arch Pharmacol 2019;392(7):851-863

Agents: Aldosterone Vehicle: Saline; Route: SC; Species: Dog (Beagle); Pump: 2ML4; Duration: 4 weeks;

**ALZET Comments:** Dose (12 ug/kg/day); Controls received mp w/ vehicle; animal info (male adult purebred beagle dogs (8.0–8.5 kg)); cardiovascular;

**Q7838:** X. Wang, et al. Angiotensin-(1-7) prevents atrial tachycardia induced-heat shock protein 27 expression. J Electrocardiol 2018;51(1):117-120

**Agents:** Angiotensin(1–7) **Vehicle:** Not Stated; **Route:** IV (jugular); **Species:** Dog; **Pump:** Not Stated; **Duration:** 2 weeks; **ALZET Comments:** Dose (6 μg/kg/h); Controls did not receive mp; animal info (Mongrel, 11-15 kg); cardiovascular; Therapeutic indication (intravenously administered Ang-(1–7) may be responsible for inhibiting atrial remodeling induced by rapid atrial pacing, which in turn decreases HSP27 gene and protein expression.);

**Q7841:** Z. H. Dailiana, *et al.* Vascular endothelial growth factor for the treatment of femoral head osteonecrosis: An experimental study in canines. World J Orthop 2018;9(9):120-129

**Agents:** Vascular Endothelial Growth Factor **Vehicle:** Saline; **Route:** SC; **Species:** Dog; **Pump:** Not Stated; **Duration:** Duration; **ALZET Comments:** Dose (500 ng); 0.9% Saline used; Controls received mp w/ vehicle; animal info (Beagle); Vascular endothelial Growth Factor aka VEGF;

**Q10082:** H. K. Ananthula, et al. Preclinical pharmacokinetic evaluation to facilitate repurposing of tyrosine kinase inhibitors nilotinib and imatinib as antiviral agents. BMC Pharmacology and Toxicology 2018;19(1):80

**Agents:** Nilotinib; Imatinib **Vehicle:** Ethanol; PEG300; Cremophor EL; Water, sterile; **Route:** IV injection; Gavage; **Species:** Mice; Guinea pigs; Prairie Dogs; Cynomolgus monkeys; **Pump:** Not Stated; **Duration:** Not Stated;

**ALZET Comments:** Nilotinib 1.5:4.5:20 (ethanol:PEG300:Cremophor) in 3.7% dextrose solution used; animal info (Mice C57BL/6, 20g both genders; Prairie dogs wild caught male black tailed, 1-2 years; Guinea pigs male hartley 450-650g); half-life (p.1,8); Resultant plasma level (Figure 1 nilotinib, Figure 2 imatinib); enzyme inhibitor (tyrosine kinase (TKI)); good methods (elimination half-lives were quite short (1–2 h). Thus, further testing of these agents in C57BL/6 mice is feasible but may require a continuous delivery system such as an Alzet® mini pump.); didn't use Alzet pmup, but recommends using it in future studies of these agents in mice or guinea pigs;

**Q5980:** W. Shangguan, *et al.* Angiotensin-(1-7) attenuates atrial tachycardia-induced sympathetic nerve remodeling. J Renin Angiotensin Aldosterone Syst 2017;18(3):1470320317729281

**Agents:** Ang (1-7) **Vehicle:** Not Stated; **Route:** IV (jugular); **Species:** Dog; **Pump:** Not Stated; **Duration:** 14 days; **ALZET Comments:** Controls received mp w/ vehicle; animal info (12-14 kg); cardiovascular; Pacemaker also implanted; Therapeutic indication (Atrial tachycardia); Dose (6 ug/kg/h);

**Q5112:** J. Zhao, et al. The potential role of atrial natriuretic peptide in the effects of Angiotensin-(1-7) in a chronic atrial tachycardia canine model. J Renin Angiotensin Aldosterone Syst 2016;17(1):1470320315627409

**Agents:** Angiotensin (1-7); A-71915 **Vehicle:** Not Stated; **Route:** IV (jugular); **Species:** Dog; **Pump:** Not Stated; **Duration:** 14 days;

**ALZET Comments:** 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  $\mu$ g/kg/h is verified as the highest dose that wouldn't affect blood pressure in our preliminary study" pg 2;





**Q3960:** J. Y. Lee, *et al.* Simultaneous Inferior Alveolar Nerve Regeneration and Osseointegration With a Nerve Growth Factor-Supplying Implant: A Preliminary Study. Journal of Oral and Maxillofacial Surgery 2015;73(410-423

**Agents:** Nerve growth factor, human B- **Vehicle:** PBS; **Route:** CSF/CNS (inferior alveolar nerve); **Species:** Dog (beagle); **Pump:** 2ML2; **Duration:** 6 weeks;

**ALZET Comments:** 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;

**Q5012:** J. K. a. M.-S. Kim. The Evaluation of Osmotic Pump as Glaucoma Drug Delivery System in Normal Dogs. Pakistan Veterinary Journal 2015;35(2):239-241

**Agents:** Dorzolamide; timolol **Vehicle:** Not Stated; **Route:** SC (Eye); **Species:** Dog; **Pump:** 2004; **Duration:** 24 days; **ALZET Comments:** 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);

**Q3753:** X. W. Wang, et al. Angiotensin-(1-7) Prevent Atrial Tachycardia Induced Sodium Channel Remodeling. PACE-PACING AND CLINICAL ELECTROPHYSIOLOGY 2014;37(1349-1356

**Agents:** Angiotensin (1-7) **Vehicle:** Not Stated; **Route:** IV (jugular); **Species:** Dog (mongrel); **Pump:** Not Stated; **Duration:** Not Stated;

ALZET Comments: Animal info (male, female, 11-15 kg); peptides

**Q3534:** M. Klarica, et al. "COMPENSATED HYPEROSMOLARITY" OF CEREBROSPINAL FLUID AND THE DEVELOPMENT OF HYDROCEPHALUS. Neuroscience 2013;248(;):278-289

Agents: Sucrose Vehicle: Not Stated; Route: CSF/CNS; Species: Dog; Pump: 2ML1; Duration: 7 days;

**ALZET Comments:** 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 acrylate to fix cannula; hydrocephalus;

**Q2331:** M. Harada, *et al.* Transient Receptor Potential Canonical-3 Channel-Dependent Fibroblast Regulation in Atrial Fibrillation. Circulation 2012;126(17):2051-U112

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

**R0267:** P. W. Coneannon, *et al.* Endocrine control of ovarian function in dogs and other carnivores. Animal Reproduction Science 2009;6(1):172-193

**Agents:** Nafarelin, aza-gly **Vehicle:** Not Stated; **Route:** SC; **Species:** Dog (beagle); **Pump:** Not Stated; **Duration:** Not Stated; **ALZET Comments:** Animal info (ovariectomized); Aza-gly Nafarelin is a GnRH agonist

**P9505:** P. W. Concannon, *et al.* Effects of dose and duration of continuous GnRH-agonist treatment on induction of estrus in beagle dogs: Competing and concurrent up-regulation and down-regulation of LH release. Theriogenology 2009;66(1488-1496 **Agents:** Wy-40972 **Vehicle:** Not Stated; **Route:** SC; **Species:** Dog (beagle); **Pump:** 2ML1; 2ML2; 2ML4; **Duration:** 7, 8, 12, 14 days:

**ALZET Comments:** 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

**Q5571:** M. Guarnieri, et al. Catheters for chronic administration of drugs into brain tissue. Methods in molecular research 2008:437(109-117

**Agents:** Carboplatin **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Monkey; Rat; dog; **Pump:** Not Stated; **Duration:** 7 days; **ALZET Comments:** functionality of mp verified by residual volume; Carboplatin brain tissue distribution;





**P8480:** A. Levy, *et al.* Extrapolating from animal studies to the efficacy in humans of a pretreatment combination against organophosphate poisoning. Archives of Toxicology 2007;81(5):353-359

**Agents:** Caramiphen **Vehicle:** Not Stated; **Route:** SC; **Species:** Dog; **Pump:** 2001; 2ML1; **Duration:** 48 hours; **ALZET Comments:** Animal info (beagle, male, 14-16 kg); Functionality of mp verified by plasma levels; toxicology; pharmacokinetics

**P9013:** M. S. Ruggieri, et al. Functional reinnervation of the canine bladder after spinal root transection and immediate end-on-end repair. Journal of Neurotrauma 2006;23(7):1125-1136

**Agents:** Brain-derived neurotrophic factor **Vehicle:** Not Stated; **Route:** CSF/CNS (intrathecal); **Species:** Dog; **Pump:** 2002; **Duration:** 14 days;

**ALZET Comments:** 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)

**P7144:** M. Miyauchi, *et al.* Chronic nicotine in hearts with healed ventricular myocardial infarction promotes atrial flutter that resembles typical human atrial flutter. American Journal of Physiology Heart and Circulatory Physiology 2005;288(6):H2878-H2886

**Agents:** Nicotine **Vehicle:** Not Stated; **Route:** SC; **Species:** Dog (mongrel); **Pump:** 2ML4; **Duration:** 28 days; **ALZET Comments:** Functionality of mp verified by nicotine plasma levels; MRI; multiple pumps per animal (2)

**P7601:** M. R. Batista, *et al.* Chronic estradiol and progesterone treatment in conscious dogs: effects on insulin sensitivity and response to hypoglycemia. American Journal of Physiology Regulatory, Integrative, and Comparable Physiology 2005;289(4):R1064-R1073

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

**P6259:** T. Yokota, *et al.* Functional and anatomical effects of hormonally induced experimental prostate growth: A urodynamic model of benign prostatic hyperplasia (BPH) in the beagle. PROSTATE 2004;58(2):156-163

**Agents:** Dihydrotestosterone, 5 alpha-; Estradiol, 17B- **Vehicle:** Not Stated; **Route:** SC; **Species:** Dog; **Pump:** 2ML4; **Duration:** 28 days;

ALZET Comments: Animal info (Beagle, 3.5-7.2 yrs); testosterone induced BPH animal model

**P6756:** T. Sasaki, et al. Role of p38 mitogen-activated protein kinase on cerebral vasospasm after subarachnoid hemorrhage. Stroke 2004;35(6):1466-1470

Agents: FR167653 Vehicle: Not Stated; Route: IV (jugular); Species: Dog; Pump: Not Stated; Duration: 7 days;

**ALZET Comments:** 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)

**P6627:** K. Doh-ura, *et al.* Treatment of transmissible spongiform encephalopathy by intraventricular drug infusion in animal models. JOURNAL OF VIROLOGY 2004;78(10):4999-5006

**Agents:** Quinacrine; chloroquine; amphotericin B; E-64d; pentosan polysulfate **Vehicle:** PBS; water, distilled; DMSO; **Route:** SC; CSF/CNS; **Species:** Rat; mice; dog (mongrel); **Pump:** Not Stated; **Duration:** 2 months; 4 weeks;

**ALZET Comments:** 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







**P5417:** G. Weckbecker, et al. SOM230: A new somatostatin peptidomimetic with potent inhibitory effects on the growth hormone/insulin-like growth factor-I axis in rats, primates, and dogs. Endocrinology 2002;143(10):4123-4130

**Agents:** Octreotide; SOM230 **Vehicle:** Water, sterile; **Route:** SC; **Species:** Rat; Monkey; Dog; **Pump:** 2002; 2ML1; 2ML2; **Duration:** 7,14, 56 days;

**ALZET Comments:** 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

**P7118:** D. B. Gilberto, *et al.* Use of three infusion pumps for postoperative administration of buprenorphine or morphine in dogs. JAVMA 2002;220(11):1655-1660

Agents: Buprenorphine Vehicle: Not Stated; Route: SC; Species: Dog; Pump: 2ML1; Duration: 48 hours;

**ALZET Comments:** 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.* Modulation of QT interval by cardiac sympathetic nerve sprouting and the mechanisms of ventricular arrhythmia in a canine model of sudden cardiac death. Journal of Cardiovascular Electrophysiology 2001;12(1068-1073 **Agents:** Nerve growth factor **Vehicle:** Saline; Albumin, bovine serum; **Route:** CSF/CNS (stellate ganglion); **Species:** Dog; **Pump:** 

2ML4; Duration: 5 weeks;

**ALZET Comments:** Controls received mp w/ vehicle; tissue perfusion (left and right stellate ganglion); cardiovascular; peptides; vehicle was saline with 0.1% bovine serum albumin

**P5145:** Y. Meshulam, *et al.* Prophylaxis against organophosphate poisoning by sustained release of scopolamine and physostigmine. Journal of Applied Toxicology 2001;21(S75-S78

**Agents:** Scopolamine; Physostigmine **Vehicle:** Propylene glycol; Ethanol; Water; Acetic acid, glacial; **Route:** SC; **Species:** Dog; **Pump:** 2001; **Duration:** 24,48 hours;

**ALZET Comments:** Functionality of mp verified by plasma scopolamine & physostigmine levels; dose-response (table, p. S77); toxicology; vehicle was 10% ethanol, 20% PG, 70% water, 0.0035% AA; mentions benefits of infusion via pump (p. S77)

**Q6821:** P.-S. Chena, *et al.* Sympathetic nerve sprouting, electrical remodeling and the mechanisms of sudden cardiac death. Cardiovascular Research 2001;50(409-416

Agents: Nerve Growth Factor Vehicle: Not Stated; Route: CSF/CNS (left stellate ganglion); Species: Dog; Pump: Not Stated;

**Duration:** 2 weeks;

**ALZET Comments:** cardiovascular;

**P5557:** H. Senzaki, *et al.* B-blockade prevents sustained metalloproteinase activation and diastolic stiffening induced by angiotensin II combined with evolving cardiac dysfunction. Circulation Research 2000;86(807-815

Agents: Angiotensin II Vehicle: Acetic acid; Route: IV; Species: Dog; Pump: 2ML1; Duration: 6,7 days;

**ALZET Comments:** Cardiovascular; peptides

**P4763:** S. Meier, *et al.* The induction of parturition in the bitch using sodium cloprostenol. Theriogenology 2000;54(457-465 **Agents:** Cloprostenol, sodium **Vehicle:** Not Stated; **Route:** SC; **Species:** Dog (pregnant); **Pump:** 2001; **Duration:** Not Stated; **ALZET Comments:** Dose-response (graph p. 460); varying doses (0.875 - 4.5 *ug*/kg - day); higher doses caused polydipsia.

**P4480:** Y. Ueda, et al. Glycoprotein IIb/IIIa antagonist FK633 could not prevent neointimal thickening in stent implantation model of canine coronary artery. Arteriosclerosis, Thrombosis, and Vascular Biology 1999;19(343-347

Agents: FK-633 Vehicle: Not Stated; Route: SC; Species: Dog; Pump: 2ML4; Duration: 3 months;

**ALZET Comments:** Controls received mp w/ vehicle; long-term study, pump replaced after 1 and 2 months; no stress (p. 344); cardiovascular



**R0210:** J. M. Meythaler. Intrathecally delivered medications for spasticity and dystonia. Spinal Drug Delivery 1999;513-529 **Agents:** Baclofen **Vehicle:** Not Stated; **Route:** SC; **Species:** Dog; **Pump:** Not Stated; **Duration:** 28 days; **ALZET Comments:** 

**P4590:** H. Senzaki, et al. Synergistic exacerbation of diastolic stiffness from short-term tachycardia-induced cardiodepression and angiotensin II. Circulation Research 1998;82(503-512

**Agents:** Angiotensin II **Vehicle:** Acetic acid; **Route:** Not Stated; **Species:** Dog; **Pump:** Not Stated; **Duration:** 4,7 days; **ALZET Comments:** Controls received mp w/angiotensin II only; functionality of mp verified by plasma levels; stability verified by HPLC; peptides, cardiovascular

**P3779:** J. R. Watts, *et al.* Calcium cloprostenol administered at a continuous low dosage induces luteolysis and abortion in bitches. Theriogenology 1997;48(1313-1328

**Agents:** Cloprostenol, calcium **Vehicle:** Water, sterile; **Route:** SC; **Species:** Dog; **Pump:** 2001; **Duration:** 7 days; **ALZET Comments:** 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)

**P3898:** T. Mori, *et al.* An improved canine model of subarachnoid hemorrhage using intrathecal indwelling catheters. J. Vet. Med. Sci 1997;59(9):825-828

**Agents:** Dye, toluidine blue; Saline **Vehicle:** Not Stated; **Route:** CSF/CNS (subarachnoid space, intrathecal); **Species:** Dog; **Pump:** 2ML1; **Duration:** 7 days;

**ALZET Comments:** No stress (see pg. 826); controls received mp w/saline; comparison of injections vs. mp; brain tissue distribution

**P4511:** S. M. Fitzgerald, *et al.* Systemic hemodynamic responses to chronic angiotensin II infusion into the renal artery of dogs. American Journal of Physiology Regulatory, Integrative, and Comparable Physiology 1997;273(R1980-R1989

**Agents:** Angiotensin II **Vehicle:** Not Stated; **Route:** IV (inferior vena cava); **Species:** Dog; **Pump:** 2ML4; **Duration:** 28 days; **ALZET Comments:** Peptides

**P3740:** C. Chen, et al. Boundary layer infusion of nitric oxide reduces early smooth muscle cell proliferation in the endarterectomized canine artery. J. Surg. Res 1997;67(26-32

**Agents:** Proline, I-; Proline, nitric oxide- **Vehicle:** NaOH; **Route:** IA (femoral); **Species:** Dog; **Pump:** 2ML2; **Duration:** 7 days; **ALZET Comments:** 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

**P4428:** S. G. Mattar, *et al.* Local infusion of FGF-Saporin reduces intimal hyperplasia. Journal of Surgical Research 1996;60(339-344

**Agents:** Fibroblast growth factor; saporin **Vehicle:** Sodium citrate; NaCl; EDTA; **Route:** IA (carotid); **Species:** Dog; **Pump:** 2002; **Duration:** 14 days;

**ALZET Comments:** 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.

**P4646:** C. Chen, et al. Transgraft infusion of heparin to prevent early thrombosis of expanded PTFE grafts in canine femoral veins. Annals of Vascular Surgery 1996;10(147-155

Agents: Heparin Vehicle: PBS; Route: IV (femoral); Species: Dog; Pump: 2ML2; Duration: 14 days;

**ALZET Comments:** Controls received mp w/ vehicle; functionality of mp verified by pump residual volume & reservoir tubing patency; infusion to a vascular graft

**P3388:** K. Sundquist, *et al.* Altering tooth eruption by blocking bone resorption - the local delivery of bafilomycin A1. Connective Tissue Research 1995;32(1-4):159-163

Agents: Bafilomycin A1 Vehicle: DMSO; Saline; Route: Bone; Species: Dog; Pump: 2002; Duration: Not Stated;

**ALZET Comments:** Contralateral controls received mp w/vehicle; tissue perfusion (bone crypts of mandibular fourth molar)







**P3359:** S. C. Marks Jr, et al. Bafilomycin A1 in bone resorption and tooth eruption in dogs. European Journal of Oral Sciences 1995;103(231-235

Agents: Bafilomycin A1 Vehicle: DMSO; Saline; Route: Bone; Species: Dog; Pump: Not Stated; Duration: 1, 3, 4 weeks;

ALZET Comments: Tissue perfusion (bone crypts of mandibular fourth molar); pumps replaced at 2 weeks

**P3095:** R. N. Willette, et al. Nonpeptide endothelin antagonist. Cerebrovascular characterization and effects on delayed cerebral vasospasm. Stroke 1994;25(12):2450-2456

**Agents:** SB-209670 **Vehicle:** Not Stated; **Route:** CSF/CNS (cisterna); **Species:** Dog; **Pump:** 2ML1; **Duration:** 7 days; **ALZET Comments:** Controls received mp with 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(571-575

Agents: Aldosterone Vehicle: Saline; Route: SC; Species: Dog; Pump: 2ML2; Duration: 10 days;

ALZET Comments: Controls received mp w/ saline

**P2976:** K. T. Sundquist, *et al.* Bafilomycin A1 inhibits bone resorption and tooth eruption in vivo. J. Bone and Min. Res 1994;9(10):1575-1582

**Agents:** Bafilomycin A1 **Vehicle:** DMSO; Saline; **Route:** Bone; **Species:** Dog; **Pump:** Not Stated; **Duration:** Not Stated; **ALZET Comments:** 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

**P3232:** J. A. Leal, et al. A-75998 and other GnRH antagonists suppress testosterone in male beagle dogs. A comparison of single injection, multiple injections and infusion administration. Endocrine 1994;2(921-927

**Agents:** A-75998; RS-26306 **Vehicle:** Propylene glycol; Saline; Sodium acetate buffer; **Route:** SC; **Species:** Dog; **Pump:** 1003D; **Duration:** 3 days;

**ALZET Comments:** Comparison of single and 5x daily injections vs. mp; infusion dose was four-fold lower than daily injection for same results

**P3059:** K. Yoshimura, *et al.* Physical dependence on morphine induced in dogs via the use of miniosmotic pumps. J. Pharm. & Tox. Meth 1993;30(2):85-95

Agents: Morphine HCl Vehicle: Saline; Route: SC; Species: Dog; Pump: 2ML1; Duration: 8 days;

**ALZET Comments:** 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

**P2527:** S. C. Miller, et al. Local stimulation of new bone formation by prostaglandin E1: quantitative histomorphometry and comparison of delivery by minipumps and controlled-release pellets. Bone 1993;14(143-151

**Agents:** Prostaglandin E1 **Vehicle:** Emulphor; Ethanol; **Route:** Bone (mandible); **Species:** Dog; **Pump:** Not Stated; **Duration:** 3 weeks;

**ALZET Comments:** 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

**P3203:** W. T. Johnson, et al. Effects of systemic and topical nicotine on pulpal blood flow in dogs. Dental Traumatology 1993;9(71-74

Agents: Nicotine Vehicle: Not Stated; Route: SC; Species: Dog; Pump: Not Stated; Duration: 28 days;

**ALZET Comments:** Controls received mp with saline; comparison of topical nicotine vs. mp

**P3192:** Y. Himura, *et al.* Cardiac noradrenergic nerve terminal abnormalities in dogs with experimental congestive heart failure. Circulation 1993;88(1299-1309

**Agents:** Norepinephrine **Vehicle:** Not Stated; **Route:** SC; **Species:** Dog; **Pump:** 2ML4; **Duration:** 8 weeks; **ALZET Comments:** Controls received mp with saline; long-term study, pumps replaced after 3-4 weeks







**P2110:** A. Yonezawa, et al. Chronic clonidine treatment and its termination: effects on penile erection and ejaculation in the dog. Life Sci 1992;51(1999-2007

Agents: Clonidine HCI Vehicle: Saline; Route: SC; Species: Dog; Pump: 2ML4; Duration: 4 weeks;

**ALZET Comments:** Tolerance; antihypertensive

**P2035:** J. M. Stewart, et al. Chronic elevation of norepinephrine in conscious dogs produces hypertrophy with no loss of LV reserve. American Journal of Physiology Heart and Circulatory Physiology 1992;262(31):H331-H339

Agents: Norepinephrine Vehicle: Not Stated; Route: SC; Species: Dog; Pump: 2ML4; Duration: 28 days;

ALZET Comments: an additional pump was implanted sc on day 10 to maintain plasma levels of norepinephrine p. 332

**P3071:** A. J. Nichols, *et al.* Effect of fenoldopam on the acute and subacute nephrotoxicity produced by amphotericin B in the dog. J. Pharmacol. Exp. Ther 1992;260(1):269-274

Agents: Fenoldopam mesylate Vehicle: Water, distilled; Citric acid; Propylene glycol; Sodium metabisulfate; Route: IV (jugular);

Species: Dog; Pump: 2ML2; Duration: Not Stated;

ALZET Comments: Controls received mp with vehicle; multiple pumps per animal (2)

**P3311:** S. C. Marks Jr, *et al.* Local induction of alveolar bone in adult dogs by infusion of prostaglandin E1. Biological Mechanisms of Tooth Movement and Craniofacial Adaptation 1992;137-143

**Agents:** Prostaglandin E1 **Vehicle:** Emulphor; Ethanol; **Route:** Bone (mandible); **Species:** Dog; **Pump:** Not Stated; **Duration:** 3 weeks:

**ALZET Comments:** 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)

**P2342:** K. Kiuchi, et al. Mechanisms of alpha-adrenergic vascular desensitization in conscious dogs. Circulation Research 1992;71(5):1185-1199

**Agents:** Amidephrine mesylate **Vehicle:** Saline; **Route:** SC; **Species:** Dog; **Pump:** Not Stated; **Duration:** 3,4 weeks; **ALZET Comments:** pumps replaced weekly; multiple pumps per animal (2 or 3) to elevate AMD levels (pg.1186)

**P2409:** M. B. Patel, *et al.* Altered function and structure of the heart in dogs with chronic elevation in plasma norepinephrine. Circulation 1991;84(5):2091-2100

**Agents:** Norepinephrine **Vehicle:** Not Stated; **Route:** SC; **Species:** Dog; **Pump:** 2ML4; **Duration:** 28 days; **ALZET Comments:** no comment posted

P1940: H. Kobayashi, et al. Cerebral vasospasm and vasoconstriction caused by endothelin. Neurosurgery 1991;28(5):673-679

Agents: Endothelin-1 Vehicle: Water; Route: CSF/CNS (intrathecal); Species: Dog; Pump: 2001; Duration: 7 days;

**ALZET Comments:** Controls received sham op or mp w/ water; peptides

**P1853:** G. K. Johnson, *et al.* Effects of topical and systemic nicotine on gingival blood flow in dogs. J. Dent. Res 1991;70(5):906-909

**Agents:** Nicotine sulfate **Vehicle:** Not Stated; **Route:** SC; **Species:** Dog; **Pump:** Not Stated; **Duration:** 28 days; **ALZET Comments:** no comment posted

**P3140:** S. C. Marks, *et al.* Site-directed formation of new lamellar bone in adult dogs by infusion of prostaglandin E1. In 'Fundamentals of bone growth: methodology and applications', A. D. Dixon, B. G. Sarnat and D. A. N. Hoyte (eds), CRC Press, Boca Raton 1990;Chp. 37):375-381

**Agents:** Prostaglandin E1 **Vehicle:** Emulphor; Ethanol; **Route:** Bone (mandible); **Species:** Dog; **Pump:** Not Stated; **Duration:** 5 weeks;

**ALZET Comments:** 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



**P1601:** M. Doursout, et al. Effect of gender on centrally induced angiotensin II hypertension in dogs. Hypertension 1990;15(2):117-120

Agents: Angiotensin II Vehicle: Not Stated; Route: CSF/CNS; Species: Dog; Pump: 2ML4; Duration: 4 weeks;

**ALZET Comments: Peptides** 

**P1727:** A. Albino-Teixeira, et al. Purine agonists prevent trophic changes caused by sympathetic denervation. European Journal of Pharmacology 1990;179(141-149

**Agents:** Adenosine; Adenosine, N-ethylcarboxamido-; Inosine; Norepinephrine **Vehicle:** Not Stated; **Route:** IV (saphenous); **Species:** Dog; **Pump:** 2ML1; **Duration:** Not Stated;

**ALZET Comments:** functionality of mp verified by inspecting catheter for clots, observing collapsed pump reservoir, and measuring residual drug solution

**P1476:** A. A. Teixeira, et al. Sympathetic denervation caused by long-term noradrenaline infusions; prevention by desipramine and superoxide dismutase. British Journal of Pharmacology 1989;97(95-102

**Agents:** Desipramine HCl; Norepinephrine; tempol **Vehicle:** EDTA; Heparin; Saline; **Route:** IV (saphenous); **Species:** Dog; **Pump:** 2ML1; **Duration:** 5 days;

**ALZET Comments:** 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

**P1453:** K. Fogh, *et al.* 15-Hydroxy-eicosatetraenoic acid (15-HETE) inhibits carragheenan-induced experimental arthritis and reduces synovial fluid leukotriene B4 (LTB4). Prostaglandins 1989;37(2):213-228

**Agents:** HETE, 15- **Vehicle:** Saline; **Route:** Knee (articular cavity); **Species:** Dog; **Pump:** 2ML2; 2ML4; **Duration:** 10 days; **ALZET Comments:** Tissue perfusion (knee joint)

**P3028:** S. C. Marks Jr, et al. Local infusion of prostaglandin E1 stimulates mandibular bone formation in vivo. J. Oral Pathol 1988;17(500-505

**Agents:** Prostaglandin E1 **Vehicle:** Emulphor; Ethanol; **Route:** Bone (mandible); **Species:** Dog; **Pump:** Not Stated; **Duration:** 3 weeks;

**ALZET Comments:** 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

**P1415:** R. A. Guilmette, et al. Reducing the radiation dose from inhaled americium-241 using continuously administered DTPA therapy. International Journal of Radiation Biology 1988;53(2):261-271

Agents: ZnDTPA Vehicle: Saline; Route: SC; Species: Dog; Pump: 2ML4; Duration: 64 days;

**ALZET Comments:** 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

**P0994:** H. H. Malluche, et al. Calcitriol, parathyroid hormone, and accumulation of aluminum in bone in dogs with renal failure. Journal of Clinical Investigation 1987;79(754-761

**Agents:** Parathyroid hormone, bovine 1-34 **Vehicle:** Albumin; HCl; Saline; **Route:** SC; **Species:** Dog; **Pump:** 2001; **Duration:** 8 months;

**ALZET Comments:** Controls received mp w/vehicle; pumps replaced every 12 days; replacement therapy (thyroparathyroidectomy); no stress (see pg. 755); long-term study

**P1056:** B. D. King, *et al.* Absence of hypertension despite chronic marked elevations in plasma norepinephrine in conscious dogs. Hypertension 1987;9(582-590

Agents: Norepinephrine Vehicle: Not Stated; Route: SC; Species: Dog; Pump: 2ML4; Duration: 28 days;

**ALZET Comments:** Dose-response; functionality of mp verified

**P1027:** M. Ader, et al. Recombinant deoxyribonucleic acid-derived 22K- and 20K-human growth hormone generate equivalent diabetogenic effects during chronic infusion in dogs. Endocrinology 1987;120(2):725-731

Agents: Growth hormone, human Vehicle: Not Stated; Route: SC; Species: Dog; Pump: 2ML2; Duration: 12 days;

ALZET Comments: pumps primed in sterile water overnight before implantation; functionality of mp verified upon removal



**P0866:** H. H. Malluche, et al. 1,25-Dihydroxyvitamin D maintains bone cell activity, and parathyroid hormone modulates bone cell number in dogs. Endocrinology 1986;119(3):1298-1304

**Agents:** Parathyroid hormone, bovine 1-34 **Vehicle:** Albumin; HCl; Saline; **Route:** SC; **Species:** Dog; **Pump:** 2002; **Duration:** 8 months;

**ALZET Comments:** 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

**P3090:** T. P. Wright, et al. Comparison of indium 111-labeled platelets v leukocytes in a pyogenic abscess. Arch Surg 1985:120(137-141

**Agents:** Morphine sulfate **Vehicle:** Not Stated; **Route:** SC; **Species:** Dog; **Pump:** 2ML1; **Duration:** Not Stated; **ALZET Comments:** Immunology; multiple pumps per animal (2)

**P0752:** G. I. McRae, et al. Long-term reversible suppression of oestrus in bitches with nafarelin acetate, a potent LHRH agonist. Journal of Reproduction and Fertility 1985;74(2):389-397

**Agents:** Nafarelin acetate **Vehicle:** Propylene glycol; Water; **Route:** SC; **Species:** Dog; **Pump:** 2002; 2ML4; **Duration:** 18 months;

**ALZET Comments:** Comparison of injection vs. infusion; pump replaced after 2 or 4 weeks; long-term study; dose-response data; contraception in dogs; peptides

**P0674:** T. Liu, *et al.* Effect of a cyclic hexapeptide analog (L363,586) of somatostatin on the function of pancreas grafts in dogs. Journal of Surgical Research 1985;39(1):39-45

Agents: L-363586 Vehicle: Saline; Route: SC; Species: Dog; Pump: 2ML1; Duration: 1 week;

**ALZET Comments:** 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

**P0717:** R. J. Kemppainen, et al. Effects of continuous a(1-24)ACTH infusion in the dog. Hormone and Metabolic Research 1985;17(58-62

**Agents:** ACTH (1-24), a- **Vehicle:** Not Stated; **Route:** IV (jugular); **Species:** Dog; **Pump:** 2ML1; **Duration:** 2 weeks; **ALZET Comments:** mp replaced on day 7; dose-response data; controls received empty mp; mp attached to silastic rubber catheter in jugular vein; peptides

**R0059:** J. W. Fara. Physiological limitations: gastric emptying and transit of dosage forms. In 'Rate Control in Drug Therapy,' L. F. Prescott and W. S. Nimmo (eds.), Churchill Livingstone, New York 1985;144-150

Agents: Not Stated Vehicle: Not Stated; Route: PO; Species: Dog; Pump: Not Stated; Duration: Not Stated;

**ALZET Comments:** ALZA-authored; pump swallowed empty: gastric transit comparison of objects varying in size, swallowed w/ or w/o a meal

**P0759:** A. Beck, *et al.* Angiotensin-induced hypertension in conscious dogs: biochemical parameters and baroreceptor reflex. Cardiovascular Research 1985;19(11):721-726

**Agents:** Angiotensin II; Isoproterenol **Vehicle:** Ascorbic acid; Water; **Route:** IV (jugular); **Species:** Dog; **Pump:** 2ML4; **Duration:** 28 days;

**ALZET Comments:** mp connected to tygon catheter in jugular vein; mp implanted sc; dose-response data (plasma levels and blood pressure); agents infused simultaneously; hypertension; peptides

**P0455:** T. Oshima, *et al.* Pharmacological manipulation of canine cyclooxygenase and thromboxane synthetase in vivo: differential renal and platelet recovery rates. The Journal of Pharmacology and Experimental Therapeutics 1984;229(2):598-602 **Agents:** Acetylsalicylic acid **Vehicle:** DMSO; Saline; **Route:** IV (superficial cervical vein); **Species:** Dog; **Pump:** 2ML1; **Duration:** 3 days;

**ALZET Comments:** 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

## **Bibliography**





P0524: M. Levy, et al. Subacute endotoxemia in dogs with experimental cirrhosis and ascites: effects on kidney function. Canadian Journal of Physiology and Pharmacology 1984;32(6):673-677

Agents: Endotoxin, E. coli Vehicle: Saline; Route: IV (jugular); Species: Dog; Pump: 2001; 2ML1; Duration: 1 week; ALZET Comments: 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

P0545: J. Holtz, et al. Development of specific tolerance to nicotine infusions in dogs on chronic nicotine treatment. Klinische Wochenschrift 1984;62(2):51-57

Agents: Nicotine salicylate Vehicle: Saline; Sodium salicylate; Route: SC; Species: Dog; Pump: Not Stated; Duration: 5, 8 weeks;

ALZET Comments: 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

P0501: M. Chvapil, et al. Development of topical BAPN delivery system for acute spinal cord injury in dogs. Journal of Biomedical Materials Research 1984;18(757-769

Agents: Aminopropionitrile fumarate, B- Vehicle: Not Stated; Route: CSF/CNS (intrathecal); Species: Dog; Pump: 2ML2;

**Duration:** Not Stated;

ALZET Comments: 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

P0400: R. W. Stevenson, et al. Changes in plasma calcium and in radiocalcium kinetics after termination of 5-week infusions of synthetic parathyroid peptide in dogs. European Journal of Endocrinology 1983;104(462-467

Agents: Parathyroid hormone, human 1-34 Vehicle: Caproic acid, E-amino-; Route: SC; Species: Dog; Pump: Not Stated; **Duration:** 4 weeks:

ALZET Comments: Pump replaced every week; mp used to avoid infection associated with 4 wk. iv cannula; no stress (infection) see p. 463; peptides

P0325: R. Podbesek, et al. Effects of two treatment regimes with synthetic human parathyroid hormone fragment on bone formation and the tissue balance of trabecular bone in greyhounds. Endocrinology 1983;112(3):1000-1006

Agents: Parathyroid hormone, human 1-34 Vehicle: Not Stated; Route: SC; Species: Dog; Pump: Not Stated; Duration: 5, 6

ALZET Comments: Omparison 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

Agents: Parathyroid hormone, human 1-34 Vehicle: Not Stated; Route: SC; Species: Dog; Pump: Not Stated; Duration: 6, 8 months;

ALZET Comments: Pumps replaced; long-term study; comparison of intermittent injections vs. infusion; peptides

P0089: B. H. Vickery, et al. Manipulation of duration of action of a synthetic prostaglandin analogue (TPT) assessed in the pregnant beagle bitch. Prostaglandins and Medicine 1980;5(2):93-100

Agents: Prostaglandin analog (TPT) Vehicle: Ethanol; Sodium phosphate; Route: SC; Species: Dog; Pump: Not Stated; **Duration:** 1, 2 days;

**ALZET Comments:** Comparison of injections sc vs. infusion