



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

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);

Q4316: J. H. Bae, *et al.* Continuous ophthalmic treatment using an osmotic pump in a bull calf following surgical removal of an ocular dermoid: a case report. VETERINARNI MEDICINA 2015;60(282-287

Agents: Ciprofloxacin **Vehicle:** Not Stated; **Route:** Eye; **Species:** Cattle (bull); **Pump:** Not Stated; **Duration:** 4 weeks;
ALZET Comments: Animal info (male, Hanwoo bull calf, 6 months old); functionality of mp verified by drug levels in aqueous humor and residual volume; good methods (pg. 284); no stress (see pg. 285); "As the owner could not apply topical medications regularly, a drug-filled osmotic pump (Alzet; Alza, Palo Alto, CA) was implanted subconjunctivally under the upper eyelid and connected to a catheter at the lateral limbus." pg 282; "... it is clear that the osmotic infusion pump maintained the aqueous concentration of ciprofloxacin at a reasonable steady state until its removal four weeks after implantation. The amount of drug remaining in the pump was about 17 µg/ml after four weeks. This also demonstrates the reliability of the pump. " pg. 286; picture of pump pg 283; pumps primed for 40 hours in 37C saline; pumps removed after 4 weeks;

Q0959: Z. Aktas, *et al.* Matrix metalloproteinase-9 expression in retinal ganglion cell layer and effect of topically applied brimonidine tartrate 0.2% therapy on this expression in an endothelin-1-induced optic nerve ischemia model. International Ophthalmology 2010;30(3):253-259

Agents: Endothelin-1, human, porcine **Vehicle:** Not Stated; **Route:** Eye (optic nerve); **Species:** Rabbit; **Pump:** 2002; **Duration:** 2 weeks;
ALZET Comments: Animal info (New Zealand, albino); vinyl tubing used; image of pump and tubing through the upper eyelid (Fig.1, Fig 2b);

P7650: K. Okabe, *et al.* Effect of benzalkonium chloride on transscleral drug delivery. INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE 2005;46(703-708

Agents: Betamethasone, phosphate 21-; benzalkonium chloride **Vehicle:** Not Stated; **Route:** Eye (intrasclera); **Species:** Rabbit; **Pump:** 1002; **Duration:** 1 week;
ALZET Comments: Animal info (albino, 2.0-2.5 kg); diagram of pump position and cannulation (p.704); silicone tube used to connect mp

P6277: C. A. Leamey, *et al.* Disruption of Retinogeniculate Pattern Formation by Inhibition of Soluble Guanylyl Cyclase. The Journal of Neuroscience 2004;21(11):3871-3880

Agents: KT5823; Oxadiazolo quinoxalin-1-one, 1H-[1,2,4], [4,3-a] **Vehicle:** DMSO; saline; **Route:** Eye; **Species:** Ferret; **Pump:** Not Stated; **Duration:** 1-2 weeks;
ALZET Comments: Controls received mp w/ vehicle; dose-response (p.3875); enzyme inhibitor (guanylyl cyclase; protein Kinase G); DMSO at 50%; OD1; KT5832 added to vehicle control

P6550: B. C. Chauhan, *et al.* Model of endothelin-1 - Induced chronic optic neuropathy in rat. INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE 2004;45(1):144-152

Agents: Endothelin-1 **Vehicle:** Balanced salt solution; **Route:** Eye (retrobulbar optic nerve); **Species:** Rat; **Pump:** 2004; **Duration:** 21,42,84 days;
ALZET Comments: Controls received mp w/ vehicle and fellow eye w/ no treatment; dose-response (fig.5); long-term study; pumps replaced every 28 days; peptides; post op. care (rentamicin, buprenex)



P7940: J. Ambati, *et al.* Transscleral delivery of bioactive protein to the choroid and retina. *Invest Ophthalmol. Vis. Sci* 2000;41(5):1186-1191

Agents: Immunoglobulin G, FITC-, rabbit; antibody, monoclonal mouse anti-ICAM-1; immunoglobulin, mouse IgG2a **Vehicle:** Not Stated; **Route:** Eye (superotemporal scleral surface, transscleral); **Species:** Rabbit; **Pump:** 2001D; 2ML4; **Duration:** 3,5,13,20,28 days; 24 hours;

ALZET Comments: Controls received mp w/ control Ab; functionality of mp verified by fluorescence in ocular tissues and plasma mAb levels; stability verified by efficacy experiments, FITC linkage timing; half-life (p. 1188), 3 days; ALZET brain infusion kit used; animal info (dutch-belted, pigmented); "We have developed a minimally invasive transscleral drug delivery modality that can deliver therapeutic concentrations of bioactive proteins to the choroid and retina without significant systemic absorption or tissue damage." (P. 1186-87)

P4259: D. B. Clarke, *et al.* Prolonged administration of NT-4/5 fails to rescue most axotomized retinal ganglion cells in adult rats. *Vision Research* 1998;38(1517-1524

Agents: NT-4/5 **Vehicle:** PBS; **Route:** Eye (vitreous chamber); **Species:** Rat; **Pump:** 2002; **Duration:** 14,28 days;

ALZET Comments: controls received mp w/vehicle; comparison of injections vs. mp; peptides

P3483: H. Sawai, *et al.* Brain-derived neurotrophic factor and neurotrophin-4/5 stimulate growth of axonal branches from regenerating retinal ganglion cells. *J. Neurosci* 1996;16(12):3887-3894

Agents: NT-4/5 **Vehicle:** PBS; **Route:** Eye (vitreous chamber); **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;

ALZET Comments: comparison of intraocular injections vs. mp

P2852: T. Sakamoto, *et al.* Effect of intravitreal administration of indomethacin on experimental subretinal neovascularization in the subhuman primate. *Arch Ophthalmol* 1995;113(222-226

Agents: Indomethacin **Vehicle:** GBR buffer; Cyclodextrin, B-; **Route:** Eye (vitreous); **Species:** monkey; **Pump:** 2ML2; **Duration:** 14 days;

ALZET Comments: control eyes received mp with vehicles; enzyme inhibitor; indomethacin is a cyclooxygenase (COX) inhibitor; detailed description of vitreal cannula implantation; empty pump implanted at time of cannula implantation to allow 1-month recovery period; beta-cyclodextrin used as a carrier molecule; some monkeys served both as control and drug treatment group (different treatment in each eye); a vitreous opacity appeared in some eyes during infusion but disappeared after the pump was disconnected

P2490: G. Soubrane, *et al.* Basic fibroblast growth factor experimentally induced choroidal angiogenesis in the minipig. *Current Eye Research* 1994;13(183-195

Agents: Fibroblast growth factor **Vehicle:** PBS; **Route:** Eye (suprachoroidal space); **Species:** Pig (mini); **Pump:** 2001; **Duration:** no duration posted;

ALZET Comments: stability verified by biological activity assay (p 185-6) after 4 days; peptides; spatial distribution of exogenous FGF examined (p 188); basic FGF used

R0095: D. C. Metrikin, *et al.* Intravitreal drug administration with depot devices. *Current Opinion in Ophthalmology* 1994;5(111):21-29

Agents: Not Stated **Vehicle:** Not Stated; **Route:** Eye; **Species:** Not Stated; **Pump:** Not Stated; **Duration:** no duration posted;

ALZET Comments: comparison of drug delivery systems vs. mp; tissue perfusion (p. 26)

P1978: S. Lerman, *et al.* Miniosmotic pumps for liposomal drug delivery. *Liposome Technol* 1993;1(429-438

Agents: Liposomes **Vehicle:** Not Stated; **Route:** Eye (lens); **Species:** rabbit; **Pump:** 2ML1; **Duration:** no duration posted;

ALZET Comments: pulsed delivery described; detailed surgical methods

P2491: B. K. Colasanti. A comparison of the ocular and central effects of delta-9 tetrahydrocannabinol and cannabigerol. *J. Ocular Pharmacol* 1990;6(4):259-269

Agents: Cannabinol, delta-9-tetrahydro-; Cannabigerol **Vehicle:** PEG 400; **Route:** Eye (cornea); **Species:** cat; **Pump:** Not Stated; **Duration:** 9 days;

ALZET Comments: controls received mp w/ vehicle; dose-response (p.262); unilateral delivery



P1552: P. J. Linser, *et al.* A role for carbonic anhydrase in early eye morphogenesis. *Invest. Ophthalmol. Vis. Sci* 1989;30(4):783-785

Agents: Methazolamide **Vehicle:** Tyrode's solution; **Route:** Eye; in vitro (egg, eye); **Species:** Bird (chicken embryo); **Pump:** 2001; **Duration:** 3 days;

ALZET Comments: comparison of topical dosing vs. mp infusion; tissue perfusion

P1722: S. Lerman. Test models to determine potential ocular drug induced side effects. *Lens Eye Toxic. Res* 1989;6(1/2):1-36

Agents: 8-MOP; Chromophore; Sorbinil; Liposomes **Vehicle:** Radio-isotopes; **Route:** Eye (lens); **Species:** rabbit; **Pump:** 2ML1; **Duration:** 7 days;

ALZET Comments: tissue perfusion (ocular lens); liposome-encapsulated agents

P4548: D. W. Sretavan, *et al.* Modification of retinal ganglion cell axon morphology by prenatal infusion of tetrodotoxin. *Nature* 1988;336(1):468-471

Agents: Tetrodotoxin; **Vehicle:** Citrate buffer;; **Route:** Eye;; **Species:** cat (fetus);; **Pump:** 2002;; **Duration:** 16 days;;

ALZET Comments: teratology;

P1112: J. M. Megaw, *et al.* Application of miniosmotic pumps for liposomal drug delivery to the ocular lens. *Invest. Ophthalmol. Vis. Sci* 1987;28(14):29-1433

Agents: Methoxypsoralen, 8-; Radio-isotopes; Sorbinil **Vehicle:** 3H tracer; **Route:** Eye; **Species:** rabbit; **Pump:** 2ML1; **Duration:** 7 days;

ALZET Comments: mp connected to PE 60 tubing in eye; tissue perfusion

P0665: K. Miki, *et al.* An indwelling cannula system for the primate eye. *J. Neurosci. Methods* 1985;13(3/4):267-279

Agents: Leucine; Radio-isotopes **Vehicle:** 3H tracer; Balanced salt solution; **Route:** Eye (vitreous); **Species:** monkey; **Pump:** 2001; **Duration:** 1 week;

ALZET Comments: comparison of 3H-Leucine injec vs. mp infusion; stress/no stress p. 276; surgical methods; tissue perfusion

P0644: K. Miki, *et al.* Intraocular cannula for continuous, chronic drug delivery: histopathologic observations and function. *Arch. Ophthalmol* 1985;103(5):712-717

Agents: Fluorescein sodium; Leucine; Radio-isotopes **Vehicle:** 3H tracer; **Route:** Eye (vitreous); **Species:** rabbit; **Pump:** 2001; **Duration:** 1 week;

ALZET Comments: agents admin. in combination; tissue perfusion

P0691: D. M. Maurice, *et al.* The absence of corneal toxicity with low-level topical anesthesia. *American Journal of Ophthalmology* 1985;93(6):691-696

Agents: Proparacaine **Vehicle:** Not Stated; **Route:** Eye (corneal stroma); **Species:** rabbit; **Pump:** 1701; **Duration:** no duration posted;

ALZET Comments: tissue perfusion (central stroma of cornea); comparison of intermittent admin of eye drops vs. mp infusion - analogous to injection/ infusion comparison; mp primed overnight in saline

P1511: B. K. Colasanti. Intraocular pressure, ocular toxicity and neurotoxicity in response to 11-hydroxy-delta9-tetrahydrocannabinol and 1-nantradol. *J. Ocular Pharmacol* 1985;1(2):123-135

Agents: Cannabinol, tetrahydro-; Nantradol, 1- **Vehicle:** PEG 400; **Route:** Eye; **Species:** cat; **Pump:** 2001; **Duration:** 9 days;

ALZET Comments: topical application; tissue perfusion

P0561: K. Miki, *et al.* A method for chronic drug infusion into the eye. *Jpn. J. Ophthalmol* 1984;28(2):140-146

Agents: Fluorescein sodium **Vehicle:** Saline; **Route:** Eye; **Species:** rabbit; **Pump:** 2001; 2002; **Duration:** no duration posted;

ALZET Comments: detailed account of materials, surgical procedures & complications; stress/adverse reaction (infection at implantation site) see p. 144-145; tissue perfusion



P0466: B. K. Colasanti, *et al.* Intraocular pressure, ocular toxicity and neurotoxicity after administration of delta9-tetrahydrocannabinol or cannabichromene. *Experimental Eye Research* 1984;38(63-71

Agents: Cannabichromene; Cannabinol, delta-9-tetrahydro- **Vehicle:** PEG 400; **Route:** Eye (cornea); **Species:** cat; **Pump:** 2001; **Duration:** 9 days;

ALZET Comments: comparison of agents effects; pump implanted sc and connected via sc tubing to cornea; tissue perfusion

P0577: B. K. Colasanti, *et al.* Intraocular pressure, ocular toxicity and neurotoxicity after administration of cannabinol or cannabigerol. *Experimental Eye Research* 1984;39(3):251-259

Agents: Cannabigerol; Cannabinol **Vehicle:** PEG 400; **Route:** Eye; **Species:** cat; **Pump:** Not Stated; **Duration:** 9 days;

ALZET Comments: mp model not stated; comparison of agents effects; intermittent eye drop admin. vs. mp infusion; tissue perfusion

P0652: B. K. Colasanti, *et al.* Ocular hypotension, ocular toxicity, and neurotoxicity in response to marihuana extract and cannabidiol. *Gen. Pharmacol* 1984;15(6):479-484

Agents: Cannabidiol; Marihuana extract; Cannabinol, delta-9-tetrahydro- **Vehicle:** PEG; **Route:** Eye (cornea); **Species:** cat; **Pump:** Not Stated; **Duration:** 9 days;

ALZET Comments: mp model not stated; comparison of acute topical admin/ injec vs. mp infusion; comparison of agents effects; agents admin. topically to cat corneas; tissue perfusion

P0044: J. A. Eliason, *et al.* An ocular perfusion system. *Invest. Ophthalmol. Vis. Sci* 1980;19(1):102-105

Agents: Fluorescein sodium **Vehicle:** Saline; **Route:** Eye (cornea); **Species:** rabbit; **Pump:** Not Stated; **Duration:** 12 days;

ALZET Comments: tissue perfusion (cornea)

P0032: J. B. Michelson, *et al.* Experimental endophthalmitis treated with an implantable osmotic minipump. *JAMA Ophthalmology* 1979;97(7):1345-1346

Agents: Gentamicin sulfate **Vehicle:** Not Stated; **Route:** Eye (vitreous); **Species:** rabbit; **Pump:** Not Stated; **Duration:** 4.5 days;

ALZET Comments: mp model not stated; comparison of intravitreal injection vs. infusion; antibiotic; tissue perfusion

P0004: M. G. Falcon, *et al.* Antivirals for the therapy of herpetic eye disease. *Trans. Ophthal. Soc. UK* 1977;97(330-332

Agents: Ara-AMP **Vehicle:** Not Stated; **Route:** Eye; **Species:** Rabbit; **Pump:** Not Stated; **Duration:** 45 hours;

ALZET Comments: Ara-AMP (Adenine arabinoside 5' monophosphate) is an antiviral