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


**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);


**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 37°C 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);


**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


**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


**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 (rentamcin, buprenex)

**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)


**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


**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


**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


**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


**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)


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

**ALZET Comments:** pulsed delivery described; detailed surgical methods


**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

**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


**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


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


**Agents:** Methoxypsoralen, 8-; Radio-isotopes; Sorbinil  
**Vehicle:** 3H tracer;  
**Route:** Eye;  
**Species:** rabbit;  
**Pump:** 2ML1;  
**Duration:** 7 days;  
**ALZET Comments:** comparison of 3H-Leucine injec vs. mp infusion; stress/no stress p. 276; surgical methods; tissue perfusion


**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


**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


**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 - analagous to injection/ infusion comparison; mp primed overnight in saline


**Agents:** Cannabinol, tetrahydro-; Nantradol, 1-  
**Vehicle:** PEG 400;  
**Route:** Eye;  
**Species:** cat;  
**Pump:** 2001;  
**Duration:** 9 days;  
**ALZET Comments:** topical application; tissue perfusion


**Agents:** Fluorescein sodium  
**Vehicle:** Saline;  
**Route:** Eye;  
**Species:** rabbit;  
**Pump:** 2001;  
**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

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

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

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

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

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