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


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: Ciprofloxacin; Eye; Cattle (bull); 4 weeks; 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

ALZET Comments: Endothelin-1, human, porcine; Eye (optic nerve); Rabbit; 2002; 2 weeks; Animal info (New Zealand, albino); vinyl tubing used; image of pump and tubing through the upper eyelid (Fig.1, Fig 2b);


ALZET Comments: Betamethasone, phosphate 21-; benzalkonium chloride; Eye (intrasclera); Rabbit; 1002; 1 week; Animal info (albino, 2.0-2.5 kg); diagram of pump position and cannulation (p.704); silicone tube used to connect mp.


ALZET Comments: KT5823; Oxadiazolo quinoxalin-1-one, 1H-[1,2,4], [4,3-a]; DMSO; saline; Eye; Ferret; 1-2 weeks; 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.


ALZET Comments: Endothelin-1; Balanced salt solution; Eye (retrobulbar optic nerve); Rat; 2004; 21,42,84 days; 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).


ALZET Comments: Immunoglobulin G, FITC-, rabbit; antibody, monoclonal mouse anti-ICAM-1; immunoglobulin, mouse IgG2a; Eye (superotemporal scleral surface, transscleral); Rabbit; 2001D; 2ML4; 3,5,13,20,28 days; 24 hours; 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).

**ALZET Comments:** NT-4/5; PBS; Eye (vitreous chamber); Rat; 2002; 14,28 days; 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
**ALZET Comments:** NT-4/5; PBS; Eye (vitreous chamber); Rat; 2002; 14 days; comparison of intraocular injections vs. mp.

**ALZET Comments:** Indomethacin; GBR buffer; Cyclodextrin, B-; Eye (vitreous); monkey; 2ML2; 14 days; 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.

**ALZET Comments:** Fibroblast growth factor; PBS; Eye (suprachoroidal space); Pig (mini); 2001; no duration posted; stability verified by biological activity assay (p 185-6) after 4 days; peptides; spatial distribution of exogenous FGF examined (p 188); basic FGF used.

**ALZET Comments:** Eye; no duration posted; comparison of drug delivery systems vs. mp; tissue perfusion (p. 26).

**ALZET Comments:** Liposomes; Eye (lens); rabbit; 2ML1; no duration posted; pulsed delivery described; detailed surgical methods.

**ALZET Comments:** Cannabinol, delta-9-tetrahydro-; Cannabigerol; PEG 400; Eye (cornea); cat; 9 days; controls received mp w/ vehicle; dose-response (p.262); unilateral delivery.

**ALZET Comments:** Methazolamide; Tyrode’s solution; Eye; in vitro (egg, eye); Bird (chicken embryo); 2001; 3 days; 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
**ALZET Comments:** 8-MOP; Chromophore; Sorbinil; Liposomes; Radio-isotopes; Eye (lens); rabbit; 2ML1; 7 days; tissue perfusion (ocular lens); liposome-encapsulated agents.

**ALZET Comments:** Tetrodotoxin; Citrate buffer; Eye; cat (fetus); 2002; 16 days; teratology.

**ALZET Comments:** Methoxypsoralen, 8-; Radio-isotopes; Sorbinil; 3H tracer; Eye; rabbit; 2ML1; 7 days; mp connected to PE 60 tubing in eye; tissue perfusion.


**ALZET Comments:** Leucine; Radio-isotopes; 3H tracer; Balanced salt solution; Eye (vitreous); monkey; 2001; 1 week; comparison of 3H-Leucine injec vs. mp infusion; stress/no stress p. 276; surgical methods; tissue perfusion.


**ALZET Comments:** Fluorescein sodium; Leucine; Radio-isotopes; 3H tracer; Eye (vitreous); rabbit; 2001; 1 week; agents admin. in combination; tissue perfusion.


**ALZET Comments:** Proparacaine; Eye (corneal stroma); rabbit; 1701; no duration posted; 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.


**ALZET Comments:** Cannabinol, tetrahydro-; Nantradol, 1-; PEG 400; Eye; cat; 2001; 9 days; topical application; tissue perfusion.


**ALZET Comments:** Fluorescein sodium; Saline; Eye; rabbit; 2001; 2002; no duration posted; detailed account of materials, surgical procedures & complications; stress/adverse reaction (infection at implantation site) see p. 144-145; tissue perfusion.


**ALZET Comments:** Cannabichromene; Cannabinol, delta-9-tetrahydro-; PEG 400; Eye (cornea); cat; 2001; 9 days; comparison of agents effects; pump implanted sc and connected via sc tubing to cornea; tissue perfusion.


**ALZET Comments:** Cannabigerol; Cannabinol; PEG 400; Eye; cat; 9 days; mp model not stated; comparison of agents effects; intermittent eye drop admin. vs. mp infusion; tissue perfusion.


**ALZET Comments:** Cannabidiol; Marihuana extract; Cannabinol, delta-9-tetrahydro-; PEG; Eye (cornea); cat; 9 days; 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.


**ALZET Comments:** Fluorescein sodium; Saline; Eye (cornea); rabbit; 12 days; tissue perfusion (cornea).

ALZET Comments: Gentamicin sulfate; Eye (vitreous); rabbit; 4.5 days; mp model not stated; comparison of intravitreal injection vs. infusion; antibiotic; tissue perfusion.

ALZET Comments: Ara-AMP; Eye; Rabbit; 45 hours; Ara-AMP (Adenine arabinoside 5’monophospate) is an antiviral.