References on the Administration of Endothelins Using ALZET® Osmotic Pumps


Agents: Selective endothelin subtype-A receptor agonist Vehicle: Saline; Route: SC; Species: Mice; Pump: Not stated;
Duration: Not stated;
ALZET Comments: Dose (200 nmol/kg/day); Selective endothelin subtype-A receptor agonist aka cyclic peptide BQ-123; peptides; cardiovascular;


Agents: Endothelin A antagonist aka BQ-123 and Endothelin B antagonist aka BQ-788; Vehicle: Saline; Route: CSF/CNS (Hippocampus CA1); Species: Mice; Pump: 1007D; Duration: 4 days;
ALZET Comments: Dose (M1-EV 1.5 μg/μl, M2-EV 0.5 μl/h); Controls received mp w/ vehicle; animal info (4-month-old C57BL6 male mice); Brain coordinates (anteroposterior: 1.8 mm relative to bregma; mediolateral: +1 mm; dorsoventral: 1.5 mm relative to the dura); neurodegenerative (Multiple sclerosis);

Q7254: J. Polak, et al. Blockade of Endothelin-1 Receptor Type B Ameliorates Glucose Intolerance and Insulin Resistance in a Mouse Model of Obstructive Sleep Apnea. Front Endocrinol (Lausanne) 2018;9(280

Agents: Endothelin-1 antagonist Vehicle: Saline, PEG; Route: SC; Species: Mice; Pump: 1002; Duration: 14 days;
ALZET Comments: Dose (ET(A) antagonist; 200 nmol/kg/day, ET(B) antagonist; 200 nmol/kg/day); Controls received mp w/ vehicle; animal info (Adult male C57BL6/J mice aged 6-8 weeks); Endothelin A antagonist aka BQ-123 and Endothelin B antagonist aka BQ-788;


Agents: Transforming growth factor-B1; endothelin-1 Vehicle: Saline; Route: Not Stated; Species: Mice; Pump: Not Stated; Duration: 3 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (FVB/N, 4 weeks old); used 28 day model pump;


Agents: Endothelin-1; PD142,893; DAPT; Jagged1 Fc, recombinant rat Vehicle: Saline; Route: CSF/CNS; Species: Mice; Pump: 1007D; 1002; Duration: 2 days; 7 days; 8 days; 15 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (TNR, C57BL6N, 8-12 weeks old); ALZET brain infusion kit 3 used; cyanoacrylate adhesive; DAPT aka N-[(3,5-Difluorophenyl)acetyl]-L-alanyl-2-phenylglycine-1,1-dimethyl ester; DAPT is a gamma secretase inhibitor

Q2397: M. A. Saleh, et al. Chronic endothelin-1 infusion elevates glomerular sieving coefficient and proximal tubular albumin reuptake in the rat. LIFE SCIENCES 2012;91(13-14):634-637

Agents: Endothelin-1 Vehicle: NaCl; Route: SC; Species: Rat; Pump: Not Stated; Duration: 2 weeks;
ALZET Comments: Control animals received mp w/ vehicle; animal info (Munich-Wistar, male, 200-250 g);

Q1784: F. Li, et al. eNOS Deficiency Acts through Endothelin to Aggravate sFlt-1-Induced Pre-Eclampsia-Like Phenotype. Journal of the American Society of Nephrology 2012;23(4):652-660

Agents: Preproendothelin-1 Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 1002; Duration: Not Stated;
ALZET Comments: Controls received mp w/ saline; animal info (wt, female, nonpregnant, 3-5 mo old)

Agents: Endothelin-1 Vehicle: Not Stated; Route: CSF/CNS (optic nerve, perineural region); Species: Rabbit; Pump: Not Stated; Duration: 2, 4, 8 weeks;

ALZET Comments: Animal info (New Zealand, 2.5-3.5 kg); long-term study; PE tubing used

Q1214: F. Ljuca, et al. Contribution of Ras farnesyl transferase, MAP kinase and cytochrome P-450 metabolites to endothelin-1 induced hypertension. BJMS 2011;11(2):84-86

Agents: Endothelin 1; FPT III; PD-98059; baicalein; ODYA, 17- Vehicle: Not Stated; Route: IV (jugal); Species: Rat; Pump: Not Stated; Duration: 9 days;

ALZET Comments: Controls received no pump; animal info (male, Sprague Dawley); peptides; enzyme inhibitor (Ras farnesyl transferase, MAP kinase, COX); 17-ODYA is a CYP450 inhibitor; PE-60 tubing used


Agents: Endothelin-1 Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2001; Duration: 7 days;

ALZET Comments: Controls received mp w/ saline; animal info (Male, Sprague-Dawley, 250 g)


Agents: Endothelin-1 Vehicle: Saline; Route: IV (jugal); Species: Rat; Pump: 2ML2; Duration: 14 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 225-250 g); peptides


Agents: Endothelin-1 Vehicle: Sodium chloride; Route: IV (jugal); Species: Rat; Pump: Not Stated; Duration: 14 days;

ALZET Comments: Controls received mp w/ sodium chloride; animal info (male, Wistar, 8-10 wks old, 230-250 g.); 0.9% sodium chloride used


Agents: Endothelin-1, ala-1, 3, 11, 15- Vehicle: CSF, artificial; Route: CSF/CNS; Species: Rat; Pump: 2002; Duration: 3, 7 days;

ALZET Comments: Controls received mp w/ vehicle; ALZET brain infusion kit used; animal info (male, Wistar, 250-300 g.)


Agents: Endothelin-1, ala-1, 3, 11, 15- Vehicle: CSF, artificial; Route: CSF/CNS, Species: Rat; Pump: 2002; Duration: 7 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, Wistar, 250-300 g); artificial CSF recipe listed; ALZET brain infusion kit used; ala-1, 3, 11, 15-ET-1 is an ETB-receptor agonist

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: Endothelin-1 Vehicle: Not Stated; Route: CSF/CNS (optic nerve); Species: Rat; Pump: 2004; Duration: 28 days;

ALZET Comments: Post op. care (buprenorphine); animal info (adult, male, Brown Norway, 250-300g); fellow eye served as untreated control; silastic tubing used; brain tissue distribution

**Agents:** Endothelin-1  **Vehicle:** Saline;  **Route:** SC;  **Species:** Rat;  **Pump:** 2001;  **Duration:** 7 days;

**ALZET Comments:** Controls received mp w/ saline; animal info (male, Sprague-Dawley, 250 g)


**Agents:** Endothelin-1  **Vehicle:** Not Stated;  **Route:** CSF/CNS (optic nerve);  **Species:** Monkey (Rhesus);  **Pump:** 2004;  **Duration:** 8 months;

**ALZET Comments:** Controls received mp w/ vehicle; long-term study; pumps replaced every 4 weeks; peptides; animal info (young, male, Rhesus); glaucoma


**Agents:** Endothelin-1  **Vehicle:** Water;  **Route:** IV (jugular);  **Species:** Rat;  **Pump:** Not Stated;  **Duration:** 7, 20 days;

**ALZET Comments:** Controls received sham surgery; functionality of mp verified by plasma E7-1 levels; stability verified by 7 and 28 day incubation at 37 degrees celsius and HPLC; cardiovascular; peptides


**Agents:** Endothelin-1, Ala-1, 3, 11, 15  **Vehicle:** CSF, artificial;  **Route:** CSF/CNS;  **Species:** Rat;  **Pump:** 2002;  **Duration:** 3, 7 days;

**ALZET Comments:** Controls received mp w/ vehicle; ALZET brain infusion kit used; peptides; endothelin B receptor agonist


**Agents:** Endothelin-1, Ala-1, 3, 11, 15  **Vehicle:** CSF, artificial;  **Route:** CSF/CNS;  **Species:** Rat;  **Pump:** 2002;  **Duration:** 3, 7 days;

**ALZET Comments:** Controls received mp w/ vehicle; ALZET brain infusion kit used; peptides; endothelin B receptor agonist


**Agents:** Endothelin-1  **Vehicle:** Saline;  **Route:** IV (jugular);  **Species:** Rat;  **Pump:** 2ML2;  **Duration:** 14 days;

**ALZET Comments:** Controls received mp w/ vehicle; cardiovascular; peptides


**Agents:** Endothelin-1  **Vehicle:** Saline, normal;  **Route:** IV (external jugular);  **Species:** Rat;  **Pump:** 2001;  **Duration:** 7 days;

**ALZET Comments:** Controls received mp w/ vehicle; functionality of mp verified by confirming mp was empty and correct catheter position; cardiovascular; peptides


**Agents:** Endothelin-1  **Vehicle:** Saline;  **Route:** IV (femoral);  **Species:** Rat;  **Pump:** 2002;  **Duration:** 2 weeks;

**ALZET Comments:** Controls received mp w/ vehicle; ET-1 plasma levels taken
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)

Agents: Endothelin Vehicle: Saline; acetic acid; Route: CSF/CNS (optic nerve); Species: Monkey; Pump: Not Stated; Duration: 18 months;
ALZET Comments: Controls received mp w/ vehicle; long-term study; pumps replaced every 6 weeks; no stress (see pg. 1833); peptides; "The osmotic minipumps were well tolerated by the monkeys for the length (1.5 years) of the experiment." The long exposure time was used to "mimic more closely the prolonged human glaucomatous condition." p. 1838; pump model not listed; ischemia

Agents: Endothelin-1 Vehicle: Not Stated; Route: IV; Species: Rat; Pump: Not Stated; Duration: 5 days;
ALZET Comments: Controls received mp w/ saline

Agents: Endothelin-1; tempol Vehicle: Not Stated; Route: IV (jugular); Species: Rat; Pump: 2002; Duration: 9 days;
ALZET Comments: Peptides

P5747: S. D. Rogers, et al. Endothelin B receptors are expressed by astrocytes and regulate astrocyte hypertrophy in the normal and injured CNS. Glia 2003;41(2):180-190
Agents: Endothelin-1; Bosentan; Dye, Evans blue Vehicle: CSF, artificial; Route: CSF/CNS (optic nerve); Species: Rabbit; Pump: 2ML2; Duration: 14 days;
ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified by Evans Blue Dye; good methods p.182, 181; antihypertensive; Bosentan (commercial drug name is tracleer) is an endothelin receptor antagonist (ERA); Vialon catheter with holes used; pump/catheter schematic (p.182); pump is described as advantageous for optic nerve infusion (p.182)

Agents: Endothelin-1 Vehicle: Saline; Route: IV (femoral); Species: Rat; Pump: 2002; Duration: 2 weeks;
ALZET Comments: Funcionality of mp verified by pump assessment; 2-week stability verified by previous studies by other groups; ET-1 plasma levels measured

Agents: Endothelin-1 Vehicle: Saline; Route: IV (superior vena cava); Species: Rat; Pump: 2ML4; Duration: 3 weeks;
ALZET Comments: controls received mp w/ vehicle; functionality of mp verified by ET-1 levels; cardiovascular; peptides

Agents: Endothelin-1 Vehicle: Saline; Route: Perivascular (femoral artery adventitia); Species: Rat; Pump: Not Stated; Duration: 3 or 5 days;
ALZET Comments: controls received mp w/ vehicle; tissue perfusion (adventitia); cardiovascular; peptides; ET-1 is a vasoconstrictor peptide; Arteries perfused via a custom silastic artery cuff attached to catheter tube; pump placed sc

Agents: Endothelin-1 Vehicle: Not Stated; Route: SC; IP; Species: Rat; Pump: 2002; Duration: 3 or 28 days;
ALZET Comments: ET-1 infused at a subpressor dose of 2 pmol/kg/min; ischemia (hind-limb); cardiovascular


Agents: Cyclosporin A; Endothelin-1; Endothelin-3; Vehicle: Saline; propylene glycol; Route: SC;; Species: Rat;; Pump: 2ML4;; Duration: 56 days;;
ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified by whole blood CsA levels; long-term study, pumps replaced after 28 days; antihypertensive; cardiovascular; secretion in nephrotoxicity, relationship with Angiotensin II in renal expression propylene glycol used as vehicle for CsA.


Agents: Endothelin-1; Vehicle: Saline;; Route: IV (femoral);; Species: Rat;; Pump: 2002;; Duration: 2 weeks;;
ALZET Comments: controls received mp w/vehicle; peptides;


Agents: Endothelin-1; Vehicle: Saline;; Route: SC;; Species: Rat;; Pump: 2002;; Duration: 2 weeks;;
ALZET Comments: controls received mp w/vehicle; peptides;


Agents: Endothelin-I Vehicle: Not Stated; Route: CSF/CNS (optic nerve); Species: monkey; Pump: Not Stated; Duration: 2-6 months;
ALZET Comments: long-term study, pumps replaced after 4 weeks; peptides; abstract states pump implanted in rabbits also but no mention of rabbits throughout paper; ischemia


Agents: Endothelin-1 Vehicle: Saline; Route: IV (jugular); Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: functionality of mp verified by plasma levels; cardiovascular


Agents: Endothelin-1 Vehicle: BSA; Route: IV (jugular); Species: Rat; Pump: Not Stated; Duration: 7 days;
ALZET Comments: functionality of mp verified by plasma levels; cardiovascular


Agents: Endothelin-1 Vehicle: Not Stated; Route: CSF/CNS (optic nerve); Species: rabbit; Pump: Not Stated; Duration: 2, 8 weeks;
ALZET Comments: controls received mp w/ balanced salt solution; tissue perfusion (perineural region of optic nerve); long-term study, pumps replaced every 2 weeks; peptides; pump implanted above the eye; ischemia (optic nerve)


Agents: Endothelin-1 Vehicle: Not Stated; Route: CSF/CNS (optic nerve); Species: monkey; Pump: 2002; Duration: 7 days;
ALZET Comments: controls received saline infusion; good methods; peptides; ischemia (optic nerve)

**Agents:** Endothelin-3  **Vehicle:** Water, distilled;  **Route:** IV (jugular);  **Species:** Rat;  **Pump:** Not Stated;  **Duration:** 3 days;

**ALZET Comments:** controls received mp w/ vehicle; stability verified by injection of ET-3 from minipump; stable for 3 days - lost biological activity thereafter; peptides


**Agents:** Endothelin-1  **Vehicle:** Balanced salt solution;  **Route:** CSF/CNS (optic nerve);  **Species:** rabbit;  **Pump:** Not Stated;  **Duration:** 4 weeks, 3 days;

**ALZET Comments:** controls received mp w/ vehicle; peptides; pumps implanted above the eye; ischemia (optic nerve)


**Agents:** Endothelin-1  **Vehicle:** Balanced salt solution;  **Route:** CSF/CNS (optic nerve);  **Species:** rabbit;  **Pump:** Not Stated;  **Duration:** no duration posted;

**ALZET Comments:** controls received mp w/ vehicle; comparison of intravitreal injections vs. mp; peptides; pumps implanted above upper eyelid


**Agents:** Endothelin-1  **Vehicle:** Albumin, bovine serum; Saline;  **Route:** IV (inferior vena cava);  **Species:** Rat;  **Pump:** 2ML2;  **Duration:** 2 weeks;

**ALZET Comments:** peptides; pump implanted in groin; transmitter catheters implanted in suprarenal aorta to measure blood pressure and heart rate continuously


**Agents:** Endothelin-1  **Vehicle:** Saline;  **Route:** IV (jugular);  **Species:** Rat;  **Pump:** 2ML1; 2ML4;  **Duration:** 4 weeks;

**ALZET Comments:** controls received mp with vehicle; functionality of mp verified by plasma levels; stability verified by examining pressor activity after 4 weeks at 37 degrees; peptides


**Agents:** Norepinephrine; Angiotensin II; Endothelin  **Vehicle:** Acetic acid; Saline;  **Route:** IP; IV (jugular);  **Species:** Rat;  **Pump:** Not Stated;  **Duration:** 6 days;

**ALZET Comments:** controls received mp w/ vehicle; functionality of mp verified upon removal; peptides


**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


**Agents:** Endothelin  **Vehicle:** Saline;  **Route:** IV (jugular);  **Species:** Rat;  **Pump:** Not Stated;  **Duration:** 6 days;

**ALZET Comments:** stability assessed by monitoring elevated blood pressure throughout infusion period; peptides


**Agents:** Endothelin  **Vehicle:** Saline;  **Route:** IV (jugular);  **Species:** Rat;  **Pump:** Not Stated;  **Duration:** 6 days;

**ALZET Comments:** stability assessed by comparing BP elevating activity of solution recovered from pump with fresh solution; peptides