References on the Administration of Antioxidants
Using ALZET® Osmotic Pumps

1. AEOL10150


ALZET Comments: AEOL 10150; SC; Rat; 2002; 10 weeks; 8 days; Controls received mp w/ vehicle; functionality of mp verified by plasma AEOL 10150 concentrations; dose-response (fig. 4); long-term study; pumps replaced every 2 weeks; half-life (p. 574), short; cancer; animal info (female, Fisher-344, 150-170 grams); "Osmotic mini-pumps provided consistent and dose-dependent delivery of AEOL 10150," "a continuous availability of antioxidant via osmotic infusion pumps throughout the study." (p. 575).


ALZET Comments: AEOL 10150; PBS; IV (jugular); Mice; 1003D; 6 hours; Controls received mp w/ vehicle; AEOL 10150 is a catalytic antioxidant metalloporphyrin; ischemia (cerebral); MCAO.


ALZET Comments: AEOL 10150; PBS; IV (jugular); Mice; 1003D; 3 days; Controls received mp w/ vehicle; plasma levels of AEOL 10150 determined by HPLC; ischemia (cerebral); MCAO.

2. Ascorbic Acid


ALZET Comments: Trolox; neomycin; ascorbic acid; Perilymph, artificial; sodium bicarbonate; Ear (cochlea); Guinea pig; 2002; 26 days; Controls received mp w/ vehicle; pumps replaced after 14 days; post op. care (doxycycline); animal info (male, pigmented, 250-400g., neomycin deafening); cannula primed with 10% neomycin solution followed by a small air bubble spacer to allow neomycin infusion for first 2 days; trolox, a vitamin F analogue, and ascorbic acid delivered together in 1 mp; tissue perfusion (cochlea).


ALZET Comments: Ascorbic acid; Naltrexone; Saline; SC; Rat (pregnant); Rat; 7 days; controls received mp w/ vehicle.

3. Catalase


Agents: Peptide, Nox2ds-tat; polyethylene glycol-conjugated catalase Vehicle: Not Stated; Route: SC; Species: Rat; mice; Pump: 2ML1; 1002; Duration: 7 days;

ALZET Comments: Controls received mp w/ scramble ds-tat or vehicle; animal info (Rat male, Wister-Kyoto, 2-3 months; mice male, C57Bl6j and p47 phox -/-, 4.5-6 months old; cardiovascular; peptides; polyethylene glycol-conjugated catalase aka PEG-CAT; arterial ligation; NOX2 is NADPH oxidase;

Agents: Catalase; Dimethyl sulfoxide; Dexamethasone; Indomethacin; Pyrilamine maleate; AA-861; Cimetidine; Phenidone
Vehicle: Ethanol; saline; Route: SC; Species: mice; Pump: 1007D; Duration: 72 hours;
ALZET Comments: all agents infused concomitantly in the same pump; preliminary study conducted to test solubility and toxicity for 5 days; enzyme inhibitors; toxicology

Agents: Tempol; catalase Vehicle: Not Stated; Route: CSF/CNS; Species: Gerbil; Pump: 1007D; Duration: 7 days;
ALZET Comments: Controls received mp with saline; agents given separately and together; ischemia (cerebral)

Agents: Catalase; tempol Vehicle: Not Stated; Route: CSF/CNS (intrathecal); Species: monkey; Pump: 2ML1; Duration: 7 days;
ALZET Comments: controls received inactivated SOD and BSA; functionality of mp verified by measuring enzyme levels in CSF during infusion and testing agent released from pump in vitro for 7 days; stability verified by measuring activity of enzymes released from pumps in vitro over 7 days; daily CSF sampling performed using a subcutaneous Ommaya reservoir; authors report no cases of catheter blockage or dislodgement

Agents: Glutathione peroxidase; Catalase; tempol Vehicle: Not Stated; Route: Not Stated; Species: Rat; Pump: Not Stated; Duration: no duration posted;
ALZET Comments: Japanese with English abstract

4. Dimethylthiourea

Agents: Dimethylthiourea Vehicle: Not stated; Route: SC; Species: Mice; Pump: Not stated; Duration: 8 weeks;
ALZET Comments: Dose (100 mg/kg/day); animal info (Male, C57BL/6J); Blood pressure measured via Tail Cuff Method; Dimethylthiourea aka DMTU; cardiovascular;

ALZET Comments: Angiotensin II; Dimethylthiourea; PBS; IP; Rat; 2002; 7 days; Controls received mp w/ vehicle; cardiovascular; peptides; Dimethylthiourea, also called DMTU, is an antioxidant; some animals received 2 pumps (IP): one pump for ANG II infusion and one for DMTU infusion;

5. Ebselen

ALZET Comments: Ebselen; DMSO; saline; SC; Rat; 2ML4; 1 week; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 200g); 80% DMSO used; cardiovascular; bp measured with radiotelemetry; Dose (10 mg/kg/day);

ALZET Comments: Ebselen; DMSO; SC; Mice; 2004; Controls received mp w/ vehicle; animal info (8 wks old, Prdx -/-, ApoE -/-); 80% DMSO used.
**ALZET Comments:** Tempol; ebselen; DMSO; saline; SC; IV (jugular); Mice; 2ML1; 1007D; 4 days; Animal info (male, 11-13 wks old, C57BL/6, P47 phox -/-); 50% DMSO used.

**ALZET Comments:** Ebselen; DMSO; SC; Mice (transgenic); 14 days; Controls received mp w/ vehicle; cardiovascular; 50% DMSO; ebselen is a glutathione peroxidase-mimetic antioxidant (a.k.a Harmokisane).

6. EUK-189

**Agents:** EUK-189 **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Not Stated; **Pump:** Not Stated; **Duration:** Not Stated; **ALZET Comments:**

**Agents:** EUK-189 **Vehicle:** Mannitol; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 2004; **Duration:** 7 days; **ALZET Comments:** Controls received mp w/ vehicle; animal info (alpha synuclein A53T Tg)

**Agents:** EUK-189; EUK-207 **Vehicle:** Mannitol; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 6 months; **ALZET Comments:** Controls received mp w/ vehicle; long-term study; pumps replaced every 28 days; animal info (C57BL/6N Sim, 27-36 g, 17 months old)

**Agents:** EUK-189 **Vehicle:** Mannitol; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 28 days; **ALZET Comments:** Controls received mp w/vehicle; animal info (C57BL/6, 2-12 months old); neurodegenerative (Parkinson's disease)

**Agents:** EUK-189 **Vehicle:** Water, distilled; **Route:** SC; **Species:** Rat; **Pump:** 2004; **Duration:** 30 days; **ALZET Comments:** Controls received mp w/vehicle; functionality of mp verified by residual volume; animal info (male, Fischer 344, 6 month old, 300-400g., 24 month old, 350-450g.)

7. Genistein

**ALZET Comments:** Genistein; DMSO; water, distilled; **Route:** SC; **Species:** Rat; **Pump:** 1002; **Duration:** 14 days; Controls received mp w/ vehicle; animal info (female, ovariectomized); 50% DMSO used; ischemia (cerebral); cardiovascular.

ALZET Comments: Genistein; Cyclodextrin, hydroxypropyl beta; IP; Rat; 2ML1; 3 days; Control animals received mp w/ vehicle; animal info (Wistar, male, 300-350 g).

P6396: I. F. Benter, et al. Inhibition of Ras-GTPase, but not tyrosine kinases or Ca\(^{2+}\)/calmodulin-dependent protein kinase II, improves recovery of cardiac function in the globally ischemic heart. MOLECULAR AND CELLULAR BIOCHEMISTRY 2004;259(1-2):35-42
ALZET Comments: FPT III; KN-93; Genistein; Saline; IP; Rat; 2ML1; 6 days; Controls received mp w/ vehicle; enzyme inhibitor (tyrosine kinase, CaMKII); cardiovascular; ischemia (cardiac).

ALZET Comments: Genistein; Estradiol, 17B-; DMSO; PEG 300; SC; Mice; 2002; 4 weeks; Replacement therapy (orchidectomy); dose-response (p.336); 20% DMSO used in vehicle.

ALZET Comments: Genistein; DMSO; ethanol; water; IV (superior vena cava); Rat; 2ML2; 14 days; Controls received mp w/ vehicle; comparison of IP injections vs IV mp; immunology; transplantation; Genistein is a soybean isoflavone; antioxidant; Vehicle composition: DMSO, ethanol; water (50/20/30).

8. Glutathione

Agents: S-nitrosogluthathione; insulin; glutathione Vehicle: Not Stated; Route: CSF/CNS (third ventricle); Species: Rat; mice; Pump: 1002; Duration: 1 week;
ALZET Comments: Dose (GSNO (50 μM)/insulin (0.033 UI/μL) and GSH (50 μM)/insulin (0.033 UI/μL)); animal info (Male 4-week-old Wistar rats, Swiss, C57BL/6 and iNOS-null (iNOS\(^{-/-}\)) mice); S-nitrosogluthathione is an NO donor; Brain coordinates (rats DV: −8.5 mm and AP: - 0.5 mm; mice DV: −5 mm and AP: −1.8 mm);

Agents: S-nitrosogluthathione Vehicle: PBS; Route: SC; Species: Mice; Pump: Not Stated; Duration: 24 hours; 7 days;
ALZET Comments: Dose (10 mg/kg/day); Controls received mp w/ vehicle; animal info (GRK2-C340S mice); cardiovascular

Agents: Ascorbate; glutathione; tocopherol, alpha- Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 1007D; Duration: Not Stated;
ALZET Comments: Controls received mp w/saline; animal info (male, C57BL/6J, 25-30g, 10-12 weeks old); compounds were mixed and infused together as an antioxidant cocktail

Agents: Amyloid protein, beta (1-42), human oligomeric; lipoprotein, high density; glutathione ethyl ester Vehicle: HEPES; Route: CSF/CNS; Species: Mice (transgenic); Pump: 1004; Duration: 28 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (Tg-SREBP-2, NPC1-/-, Tg-APP/PS1); neurodegenerative (Alzheimer’s Disease)
Agents: Glutathione Vehicle: Not Stated; Route: CSF/CNS (third ventricle); Species: Rat; Pump: 1003D; Duration: 3 days;
ALZET Comments: Controls received mp w/PBS-HEPES; animal info (obese, lean, male, Zucker, 7 wks old); cannula placement verified by angiojensin II dipsogenic effect; Plastics One cannula used; no stress (see pg 2193) "Well being of the animals (weight gain and food intake) was preserved during the infusion"; good methods

9. Magnolol

ALZET Comments: Magnolol; Alcohol; SC; Rat; 2001; 2 weeks; Dose-response (p. 129); pumps replaced every 7 days; magnolol, an active component purified from magnolia officinalis, is a commonly used Chinese medicinal herb, with reported anti-inflammatory and antioxidant effects.

10. Mannitol

ALZET Comments: Aminobutyric acid, Y-; mannitol; Saline; CSF/CNS (amygdala); Rat; 2001; 7 days; Controls received mp w/mannitol; functionality of mp verified by cutting open & visual inspection; dose-response (table 1); no stress (see pg. 25).

ALZET Comments: Mannitol; Inulin;; Radio-isotopes; 3H tracer; saline; ethanol; Ear (round window); Guinea pig; 1007D; 7 days; Tissue perfusion (round window).

ALZET Comments: Mannitol; Radio-isotopes; Pyrrolidone, N-methyl-2-; Propylene glycol; PEG; 14C tracer; Water; Dimethylacetamide; in vitro; 2ML1; 8 days; Functionality of mp verified by in vitro testing; ALZAID chemical compatibility kit used; various solvents employed to find compatibility with drug reservoir.

ALZET Comments: Cerebrospinal fluid, artificial; Mannitol; CSF/CNS; Rat; 2002; no duration posted; controls were sham operated and received mixed-concentration aCSF, received no infusions, or received aCSF w/normal physiological balance of sodium and potassium; experimental groups consisted of varying the ratio of potassium to sodium in the aCSF; mannitol added to infusate in one high-potassium group to maintain isosmolality.

ALZET Comments: Potassium Chloride, hypertonic; Sodium chloride, hypertonic; Mannitol, hypertonic; Saline, isotonic; Water; CSF/CNS (preoptic area); Rat; 2002; 2 weeks; bilateral infusion to brain.

11. Melatonin

Agents: Melatonin  
Vehicle: Not Stated  
Route: Not Stated  
Species: Rat  
Pump: Not Stated  
Duration: Not Stated  

ALZET Comments: animal info (Sprague-Dawley rats); comparison of infusion pump, pellets, transdermal, beads, sponge, iPRECIO vs mp; Lynch coil;

Agents: Melatonin  
Vehicle: Not Stated  
Route: Intrauterine  
Species: Sheep (pregnant)  
Pump: Not Stated  
Duration: Not Stated  

ALZET Comments:

Agents: Melatonin  
Vehicle: Saline  
Route: CSF/CNS (lateral ventricle)  
Species: Rat  
Pump: Not Stated  
Duration: 7 days  

ALZET Comments: Dose (1 mg•kg body wt•day•1); Controls received mp w/ vehicle; animal info (Male Fischer 344 rats weighing 175–200 g); Brain coordinates (_0.80 mm, ML: _1.50 mm, DV: _4.00 mm from Bregma);

Agents: Melatonin; luzindole  
Vehicle: DMSO; water  
Route: Intrauterine (uterine horn)  
Species: Sheep (ewe)  
Pump: 2ML4  
Duration: 28 days  

ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified by serum levels; 45% DMSO used; stress/adverse reaction: (see pg.2); post op. care (For two days: flunixin meglumine 50 mg/ml IM twice a day; Penicillin G procain 300,000 u/ml once per day); tissue perfusion (uterus mesometrium); cardiovascular;  

12. Resveratrol  

Agents: Resveratrol  
Vehicle: PEG 300; DMSO  
Route: SC  
Species: Rat  
Pump: Not stated  
Duration: 3 days  

ALZET Comments: Dose (4 mg/kg/day); Controls received mp w/ vehicle; animal info (Sprague-Dawley rats, 400-450 g); Blood pressure measured via tail-cuff method;Resveratrol aka RSV; cardiovascular;

Agents: Resveratrol; Nicotinamide  
Vehicle: Cyclodextrin, 2-hydroxypropyl-b; Saline  
Route: SC  
Species: Mice  
Pump: Not Stated  
Duration: 28 days  

ALZET Comments: Dose (resveratrol 1 mg/kg/day; nicotinamide 250 mg/kg/day); Controls received mp w/ vehicle; animal info (9-month-old YAC128 transgenic mice and age-matched WT controls); neurodegenerative (Huntington’s Disease);

Agents: Resveratrol; EX-527  
Vehicle: DMSO  
Route: SC  
Species: Mice  
Pump: 1002  
Duration: 14 days
ALZET Comments: Controls received mp w/ vehicle; animal info (7-9 weeks; C57BL/6J); Multiple pumps per animal (2); behavioral testing (open field, elevated-plus maze, forced swim test, sucrose preference test); Plastics One guide cannula used; bilateral cannulae (one pump for each pedestal); Loctite adhesive used; EX-527 is a SIRT1 antagonist; Therapeutic indication (Depression); Dose (0.1 or 0.2 ug/day, EX-527: 0.5 or 1.0 ug/day);


Agents: Resveratrol Vehicle: DMSO; Route: SC; Species: mice; Pump: 1004; Duration: 4 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info: Male, 6-week-old C57BL/6J mice; 50% of DMSO; dose-response (pg. 1257-1259); Resveratrol aka RSV; Animals fed high-fat diets concurrently; Dose: 8 mg/kg/day


Agents: Resveratrol Vehicle: DMSO; Route: SC; Species: Mice; Pump: 1004; Duration: 4 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, C57BL6); 50% DMSO used; no stress (see pg. 697); diabetes; "Resveratrol was administered via an osmotic pump, which is a safe and standard delivery system for rodents" "no side effects were observed by monitoring weight change, behavior and inflammatory response around the implantation area." pg 697;


Agents: Resveratrol Vehicle: DMSO; ethanol; Route: SC; Species: Mice; Pump: 2002; Duration: 14 days;

ALZET Comments: Control animals received mp w/ vehicle; animal info (6 wks old, female, C57BL/6J); 50% DMSO used; 15% ethanol used; "Owing to the limited compatibility of the osmotic pumps with DMSO and/or ethanol, as well as the limited solubility of resveratrol in aqueous solutions, it wasn't possible to achieve higher doses of resveratrol using osmotic pumps" pg 17585

13. Retinoic Acid


ALZET Comments: Retinoic acid, 13-cis-; Ethanol; SC; Mice (transgenic); 1007D; 5 weeks; Controls received mp w/ vehicle; dose-response (fig. 1); no stress (see pg. 312-13); cancer (neuroblastoma).


ALZET Comments: Retinoic acid; uridine, bromodeoxy-; SC; Mice; 1, 3, 6 days; Controls received mp w/ vehicle; comparison of SC injections vs. mp; cancer (gastric); multiple pumps per animal (2).


ALZET Comments: Transforming growth factor; insulin-like growth factor I; retinoic acid; brain-derived neurotrophic factor;; PBS; BSA;; Ear (vestibule); Guinea pig; 2002; 4 weeks; Controls received mp w/ vehicle; pumps replaced after 2 weeks; peptides; IntraEAR catheter used; GFI group pumps filled with TGF, IGF and Retinoic acid; GFII group pumps filled with TGF, IGF, BDNF and retinoic acid; tissue perfusion (vestibule).


ALZET Comments: Dipyridamole; Lazaroids; Retinoic acid; Review of adhesion formation and prevention; mentions the use of mini-osmotic pumps to evaluate new agents to reduce experimental pelvic adhesions (p. 125).
14. Tempol

Q8077: T. Li, et al. Elevated Oxidative Stress and Inflammation in Hypothalamic Paraventricular Nucleus Are Associated With Sympathetic Excitation and Hypertension in Rats Exposed to Chronic Intermittent Hypoxia. Front Physiol 2018;9(840

Agents: Tempol Vehicle: Not stated; Route: SC; Species: Rat; Pump: 2002; Duration: 7 days;
ALZET Comments: Dose (5 ug/min); Controls received mp w/ vehicle; animal info (Male, Sprague Dawley, 10 weeks old, 300-325 g); Tempol aka superoxide scavenger ; bilateral cannula used; cardiovascular;


Agents: Porphyrin-based superoxide dismutase mimetic (MnHex) Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 1004; Duration: 8 weeks;
ALZET Comments: Dose (450 ug/kg/day); pumps replaced every 4 weeks; Porphyrin-based potent superoxide dismutase mimetic aka (Mn(III) meso-tetrakis-(n-hexylpyridinium-2-yl) porphyrinx (MnTnHex-2-PyP5+ ); neurodegenerative (Ionizing radiation);


Agents: mitochondrial superoxide dismutase mimetic (Hexyl) Vehicle: Saline; Route: SC; Species: Monkey; Pump: Not Stated; Duration: 6 weeks;
ALZET Comments: Dose (0.1 mg/kg/day); Controls received mp w/ vehicle; animal info (Rhesus monkeys); MnTnHex-2-PyP5+ aka hexyl; cardiovascular;


Agents: Losartan; Tempol; Clonidine Vehicle: CSF, artificial; Route: CSF/CNS (lateral ventricle); Species: Rat; Pump: Not Stated; Duration: Not Stated;
ALZET Comments: Dose (1 mg/kg/day losartan; 4.5 ug/kg/day tempol; 5.76 ug/kg/day clonidine); Controls received mp w/ vehicle; animal info (Five-week-old male Sprague-Dawley rats); Therapeutic indication (5/6 nephrectomy);


Agents: Tempol Vehicle: Saline; Route: CSF/CNS (cisterna magna); Species: Rat; Pump: 1002; Duration: 14 days;
ALZET Comments: Dose (10 mM); Controls received mp w/ vehicle; animal info (Male, adult spontaneously hypertensive rats and Wistar–Kyoto rats); ALZET brain infusion kit 2 used;

15. Thioredoxin


ALZET Comments: Thioredoxin-interacting protein DNAzyme; SC; Rat; 2006; 12 weeks; Controls received mp w/ scrambled TXNIP DNAzyme; animal info (female, heterozygous (mRen-2)27, 6 weeks old); pumps replaced every 6 weeks; cardiovascular; diabetes; Thioredoxin-interacting protein aka TXNIP;


ALZET Comments: Thioredoxin, human recomb.; SC; Mice (nude); 2002; 2 weeks; Controls received mp w/ PBS; plasma levels taken; cancer (colon, carcinoma); peptides; animal info (female, 6 weeks old, nude); xenograft.
**ALZET Comments:** Thioredoxin; IP; Rat; 2002; 4 weeks; controls received mp w/saline; pumps replaced after 2 weeks; immunology; peptides; thioredoxin is an endogenous antioxidant protein.

16. Vitamin E

**Q1590:** C. Y. Hsieh, *et al.* Inhibition of vascular smooth muscle cell proliferation by the vitamin E derivative pentamethylhydroxychromane in an in vitro and in vivo study: pivotal role of hydroxyl radical-mediated PLC-gamma-1 and JAK2 phosphorylation. Free Radical Biology and Medicine 2010;49(5):881-893
**ALZET Comments:** PMC; tocopherol, alpha; SC; Rat; 14 days; Controls received mp w/ normal saline; animal info (Wistar, male, 350-400 g); PMC, also known as (2,2,5,7,8-pentamethyl-6-hydroxchromane, is a vitamin E derivative; tocopherol also known as vitamin E.

**ALZET Comments:** Ascorbate; glutathione; tocopherol, alpha-; SC; Mice; 1007D; Controls received mp w/saline; animal info (male, C57BL/6J, 25-30g, 10-12 weeks old); compounds were mixed and infused together as an antioxidant cocktail.

**ALZET Comments:** Vitamin E; IP; Rat; 2001; 7 days; functionality of mp verified by measuring EPC-K1 plasma levels; immunology; EPC-K1 is a diester of a-tocopherol and ascorbic acid; agent also called D-alpha-tocopherol.

**ALZET Comments:** Phosphatidylcholine; vitamin E; Liposomes; CSF/CNS (cortex); Rat; 2001; 7 days; Multiple pumps per animal (2); agent also called D-alpha-tocopherol.