References on the Administration of Nonsteroidal Anti-Inflammatory Drugs
Using ALZET® Osmotic Pumps

1. Acetylsalicylic


**ALZET Comments:** CI-988; chlordiazepoxide; Acetylsalicylic acid; DMSO; saline; SC; CSF/CNS (intrathecal); Rat; 2ML1; 2001; 2002; 14 days; Controls received mp w/ vehicle; animal info (Male, Sprague-Dawley, 300-325 g, 8 wks old; ALZET intrathecal catheter used (0007740); behavioral testing (elevated plus-maze).

**P8555:** A. Adamek, *et al.* High dose aspirin and left ventricular remodeling after myocardial infarction. Basic Research In Cardiology 2007;102(4):334-340

**ALZET Comments:** Acetylsalicylic acid, lysine; Saline; SC; Mice; 2002; 4 weeks; Controls received mp w/ placebo; functionality of mp verified by serum salicylate concentrations; pumps replaced after 2 weeks; cardiovascular; ischemia (cardiac); animal info (female, C57BL/6, 8-12 weeks old, 20-25 grams); MI induced by coronary artery ligation.

**P4829:** M. Yuan, *et al.* Reversal of obesity- and diet-induced insulin resistance with salicylates or targeted disruption of Ikkb. Science 2001;293(1673-1677

**ALZET Comments:** Acetylsalicylic acid; salicylate, sodium; SC; Rat; mice; 2002; 2ML2; 3-4 weeks; Controls received mp w/ vehicle; 2ML2 used in rats, 2002 used in mice; acetylsalicylic acid also called aspirin: dose was 120 mg/kg/day; diabetes (type II).


**ALZET Comments:** Acetylsalicylic acid; DMSO; Saline; IV (superficial cervical vein); dog; 2ML1; 3 days; pumps primed for 4 hrs. before implant; used prefilled catheter in vein; greater solubility of ASA in DMSO allowed greater concentration in smaller total volume.

2. Diclofenac


**ALZET Comments:** Vasopressin, 1-desamino-8-D arginine; L-NAME; diclofenac; ranitidine; Saline; DMSO; SC; Rat; 2001; 2002; 5 days; Vasopressin, 1-desamino-8-D arginine was infused in the 2002 pump; L-NAME was dissolved in saline and diclofenac was dissolved in 50% DMSO; both were infused from a 2001 pump.

**P3383:** O. Risto, *et al.* The effect of low dose diclofenac sodium administered locally on heterotopic bone formation in rats. Int. Orthopaedics (SICOT) 1995;19(392-395

**ALZET Comments:** Diclofenac; NaCl; bone; Rat; 2001; < or = 2 weeks; controls received mp w/saline; tissue perfusion (demineralized bone implant); functionality of mp verified by residual volume; diclofenac is an NSAID.

3. Flurbiprofen


**ALZET Comments:** Flurbiprofen; PEG 400; IP; Rat; 2002; 7 days; Comparison of IP injections vs. mp; stability verified in vitro test for 14 days; animal info (male, Sprague Dawley, adult, 300-350 g,); "There was no significant difference between the two i.p. groups in the post-mortem plasma R or S-flurbiprofen concentration or in the percent of the dose excreted as glucuronidated flurbiprofen in urine on days 1 and 7" pg 207.

ALZET Comments: Flurbiprofen analogues; flurbiprofen; SC; Rat; 2001; 4-7 days; Dose-response; neurodegenerative (Alzheimer’s disease); cassette dosing technology: 2-6 different analog compounds administered simultaneously to one animal.


ALZET Comments: Flurbiprofen; SC; monkey; 2ML2; 2ML4; 6, 12 months; controls received no drugs or sham pumps; multiple pumps per animal (2) (simultaneously); pumps replaced every 2 weeks or monthly; long-term study; one animal removed from study due to a 'secondary infection caused by a cage-pressure abrasion at the site of the s.c.


ALZET Comments: Flurbiprofen; Tris buffer; SC; monkey; 2ML2; 2ML4; 6 months; controls received mp w/ tris buffer; dose-response (table); 2 doses of agent infused; high dosage group received 2 pumps (2ML2); pumps replaced every 4 weeks for 2ML4, 2 weeks for 2ML2; long-term study.

4. Ibuprofen


ALZET Comments: Chloridotetrakis(ibuprofenato)diruthenium-(II,III); Rat; cancer (glioma);


ALZET Comments: Ibuprofen; PBS; SC; Rat; Controls received mp w/ vehicle; animal info (male Sprague-Dawley rats, 278-315 g); spinal cord injury; behavioral testing (grooming test, cylinder rearing test, Montoya staircase test, horizontal ladder test); Healing/recovery after spinal cord injury study; Dose (2.5 mL/hour);


ALZET Comments: Ibuprofen; PEG; DMSO; SC; Mice; 2004; 8 weeks; Animal info (male, nfkb1 -/-, 24 weeks old); pumps replaced every 28 days; 50% DMSO used; 50% PEG used; behavioral testing (tightrope test); used 7mm wound clips;


ALZET Comments: Diruthenium-ibuprofen; Ethanol; CSF, artificial; CSF/CNS (intratumoral); Rat; 2002; 14 days; Animal info (female, Wistar, 250-350g); ALZET brain infusion kit used; 15% ethanol used; comparison of injection vs mp; cancer (glioma); tissue perfusion (intratumoral, glioma); “Using the orthotopic C6 model the effects of either chronic 14-day treatment by intra-peritoneal injection of chronic 14-day intra-tumour infusion by an Alzet osmotic pump attached to a brain infusion cannula were tested. Tumour growth was reduced by both routes of administration with the osmotic pump appearing to be the less harmful route in terms of haematological responses.” pg 1033; Diruthenium-Ibuprofen aka RuIbp;


ALZET Comments: Ibuprofen; Saline; SC; Rat; 2ML4; 4 weeks; Controls received mp w/ vehicle; animal info (female, Sprague-Dawley, 9-10 weeks old); spinal cord injury; post op. care (bladders expressed BID); behavioral testing (hindlimb
5. **Indomethacin**

- **Q4542:** Y. R. Na, *et al.* Consistent Inhibition of Cyclooxygenase Drives Macrophages towards the Inflammatory Phenotype. *PloS One* 2015;10(U1730-U1742)

- **P4819:** M. C. Babin, *et al.* Systemic administration of candidate antivesicants to protect against topically applied suitor mustard in the mouse ear vesicant model (MEVM ). *Journal of Applied Toxicology* 2000;20(S141 -S144)


**ALZET Comments**: Antibody, anti-interferon gamma; Antibody, indomethacin; Antibody, anti-TNFα; Antibody, interleukin 1 alpha; PBS, sterile; ETHANOL; Indomethacin; SC; mice; 1007D; 7 days; immunology; pump implanted next to Dacron graft; peptides.
ALZET Comments: Indomethacin; Antibody, anti-IL-1a; Antibody, anti-TNFa; PBS; ETHANOL; SC; Mice; 7 days; Controls received mp w/ vehicle; immunology.

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

ALZET Comments: Indomethacin; Sodium carbonate; SC; Rat; 2ML2; 7 days; sonication used to suspend indomethacin.

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: Indomethacin; Prostaglandin F2a; HCl; Sodium hydroxide; Saline; intrauterine; rabbit; 2002; 11 days; controls received mp w/ vehicle; separate and simultaneous infusion of agents; comparison of agents effects; NaOH, HCl and saline were used in combination as the vehicle for indomethacin; many different exp.; tissue perfusion (cornua of uterus).

ALZET Comments: Indomethacin; Prostaglandin E2; Prostaglandin E2; Ethanol; Gelatin; PBS; intrauterine; Rat; 2001; 5 days; replacement therapy (ovariectomy); controls received mp w/ vehicle; estradiol and progesterone injected sc w/ mp PG infusion; vehicle contained indomethacin to reduce PG synthesis; tissue perfusion (uterus).

ALZET Comments: Indomethacin; Prostaglandin E1; Prostaglandin E2; Ethanol; Gelatin; PBS; intrauterine; Rat; 2001; 5 days; mp w/vehicle; dose-response; indomethacin infused with prostaglandin E1 in one group and with prostaglandin E2 in another group; tissue perfusion (uterus).

P0739: T. G. Kennedy. Evidence for the involvement of prostaglandins throughout the decidual cell reaction in the rat. Biol. Reprod 1985;33(140-146
ALZET Comments: Indomethacin; Prostaglandin E2; Prostaglandin F2a; Ethanol; PBS; intrauterine; Rat; 2001; 5 days; replacement therapy (ovariectomy); pumps primed overnight in saline; sc adminis. of agents in comb. w/mp infusion; separate and simultaneous infusion of agents; tissue perfusion (uterus).

6. Ketorolac
ALZET Comments: Ketonolac; Saline; sterile; SC; Mice; 1007D; 2 days; Controls received mp w/ vehicle; animal info (male, C57BL/6J, 4-5 wks old).

ALZET Comments: Ketonolac tromethamine; Saline; CSF/CNS (intrathecal); Rat; 2001; 48 hours; controls received mp w/ vehicle; ketorolac is an NSAID sold as Toradol; cannula patency verified by saline injection.

ALZET Comments: Ketonolac; IV (jugular); rabbit; 2ML1; 7 days; controls received mp w/saline; functionality of mp verified by residual volume; comparison of i.m. injections vs. mp; ketorolac also called Toradol; NSAID.

7. Meclofenamate

ALZET Comments: Meclofenamate, sodium; Saline; Water; intraovarian (corpus luteum); IV (jugular); monkey; 2ML1; 7 days; stress/adverse reaction (cortisol and progesterone levels); tissue perfusion.

8. Naproxen

ALZET Comments: JNJ7777120; naproxen; SC; Mice; 1004; Control animals received mp w/ vehicle; animal info (male, C57BL/6, ~2 mo old, 25-30 g); infusion rate listed as 0.11 ul/hr; JNJ7777120 also known as (1-[(5-chloro-1H-indol-2-yl)carbonyl]-4-methylpiperazine), is a selective H4R antagonist; one group received combination of JNJ7777120 and naproxen.

ALZET Comments: Naproxen; PBS; In vitro; 1002; Naproxen is an non-steroidal anti-inflammatory agent; This paper reports the characterization of an electrochemical biosensor for the continuous monitoring of Naproxen delivered by alzet pumps.

ALZET Comments: Naproxen; Methanol; In Vitro; 1002; 16 hours; Functionality of mp verified by naproxen levels measured with sensors.

ALZET Comments: Ibuprofen; naproxen; PBS; SC; Rat; mice; 2004; 2ML4; 4 weeks; Controls received mp w/ vehicle; animal info (female, Sprague Dawley, 11-12 wks old, 250-270 g., female, C57BL/6, 8-9 wks old, 20 g.); spinal cord injury; behavioral testing (BBB locomotor scale, Basso mouse scale).

ALZET Comments: Naproxen, sodium; Saline; SC; Rat (pregnant); 2001; 3 days; no comment posted.

9. Sup Dismut-PEG

ALZET Comments: Collagenase inhibitor A; Collagenase inhibitor B; Collagenase inhibitor C; tempol; Superoxide dismutase-PEG; Cytochalasin B; Pepstatin; APMSF; TLCK; SBTI; Leupeptin; E-64; Methylamine; SC; Rat; 2001; 2ML1; 7 days; controls received mp w/vehicle; no stress (see pg. 39); immunology; pumps connected with catheter tubing to 14C-collagen-gelled cotton buds.

ALZET Comments: Superoxide dismutase-PEG; Saline; CSF/CNS; gerbil; 1007D; 6 days; controls received mp with vehicle; ischemia (cerebral).

10. Tempol or Sup Dismutase

Q4181: K. L. H. Wu, et al. Role of Nitric Oxide Synthase Uncoupling at Rostral Ventrolateral Medulla in Redox-Sensitive Hypertension Associated With Metabolic Syndrome. Hypertension 2014;64(815-+)
ALZET Comments: Tempol; coenzyme Q10; CSF, artificial; CSF/CNS (cisterna magna); Rat; 1007D; 2 weeks; Controls received mp w/vehicle; animal info (male, Sprague Dawley 8 weeks old, 235-296g); post op. care (1000 IU IM); tissue perfusion (cisterna magna); cardiovascular; diabetes; used PE-10 catheter;.

Q3661: Q. Su, et al. Inhibition of reactive oxygen species in hypothalamic paraventricular nucleus attenuates the renin-angiotensin system and proinflammatory cytokines in hypertension. TOXICOLOGY AND APPLIED PHARMACOLOGY 2014;276(115-120)
ALZET Comments: Tempol; angiotensin II; CSF, artificial; saline, sterile; CSF/CNS (paraventricular nuclei); Rat; 1004; 4 weeks; Controls received mp w/vehicle; animal info (male, Sprague Dawley, adult, 250-275g); functionality of mp verified by increase bp; tissue perfusion (paraventricular nucleus); immunology; “The success rate of bilateral microinjection and vein infusion is respectively 65% and 78%.” pg 116; bp measured using tail-cuff;.

ALZET Comments: Superoxide dismutase; Saline; IP; Rat; 3 weeks; Controls received mp w/ vehicle; animal info (female, Sprague Dawley);.

ALZET Comments: Enalapril maleate, Losartan, Tempol; CSF, artificial; CSF/CNS (ventricle); Rat; 1003D; 14 days; Controls received mp w/ aCSF; ALZET brain infusion kit 2 used; Enalapril is an ACE inhibitor; Losartan is an ANG II AT1 receptor antagonist; tempol is a SOD mimetic; Therapeutic indication (erectile dysfunction); Dose: Enalapril (0.5 mg/m), losartan (2 mg/mL), tempol (50 mg/mL);.

Q2125: K. Ozumi, et al. Role of Copper Transport Protein Antioxidant 1 in Angiotensin II-Induced Hypertension A Key Regulator of Extracellular Superoxide Dismutase. Hypertension 2012;60(2):476-U487
ALZET Comments: Angiotensin II; Tempol; Saline; SC; Mice; 2002; 7 days; Controls received mp w/ vehicle; animal info (Atox1 -/-, 3 mo old); blood pressure measured via tail cuff.
ALZET Comments: Tempol; Mice; 2002; Controls received mp w/ saline; animal info (CHOP-10 deficient, wt, 28 g, 8 wks old); ischemia.

ALZET Comments: Tempol; Saline; folate; IV (jugular); Mice; 48 hours; Controls received mp w/ vehicle; animal info (male, C57BL/6, 11 wks old); ischemia (renal); 7-day pump used; post op. care (buprenorphine in saline).

ALZET Comments: Tempol; CSF, artificial; CSF/CNS; IP; Rat; 2002; 4 weeks; Controls received mp w/ vehicle; animal info (Sprague Dawley, male, 3 wks old); pumps replaced after 2 week; cannula placement verified by ICV injection of Evans Blue dye after euthanization.

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: Tempol; SC; Rat; 2ML2; 8 days; Animal info (male, Wistar, Kyoto, 280-300 g).

ALZET Comments: Methylisothiourea, S-; PTIO, carboxy-; Coenzyme Q10; tempol; FeTMPyP; furosemide; PJ-34; CSF, artificial; sesame oil; CSF/CNS (spinal cord); Rat; 1003D; 3 days; Controls received mp w/ vehicle; multiple pumps per animal (2); post op. care (procaine penicillin); adult, male, specific pathogen free, 200-250 g.; spinal cord injury; PE-10 catheter used; PTIO is a NO trapping agent; enzyme inhibitor PJ-34 is poly(ADP-ribose) polymerase PARP inhibitor.

ALZET Comments: Angiotensin II; losartan; pyrrolidine dithiocarbamate; tempol; Saline; CSF/CNS; Rat; 4 weeks; Controls received mp w/vehicle; peptides; multiple pumps per animal (2); animal info (adult, male, Sprague-Dawley, 275-300g); bilateral cannula used for multiple drug infusions; bilateral infusion.

ALZET Comments: Aldosterone; RU-28318; Tempol; Losartan; CSF, artificial; CSF/CNS; Rat; 2002; 1 week; Controls received mp w/ vehicle; post op. care (buprenorphine); animal info (male, Sprague-Dawley, 250-300 g.); silastic tubing used; dental cement used.

ALZET Comments: Tempol; estradiol, 17B-; ICI-182780; SC; CSF/CNS; Mice; 1002; 7, 14 days; ALZET brain infusion kit used; peptides; animal info (male, C57BL/6, 12-16 wks old); location of cannula was verified histologically post mortem.

*ALZET Comments:* Angiotensin II; norepinephrine; tempol; Saline; SC; Mice; 2002; 14 days; Controls received sham surgery with no mp or empty mp; functionality of mp verified by blood pressure; cardiovascular; peptides; multiple pumps per animal (2); animal info (female, C57BL/6J blotchy MNK mut, 8-12 wks old).

*ALZET Comments:* Tempol; CSF, artificial; CSF/CNS; Rabbit; 2001; 7 days; Controls received mp w/ vehicle; animal info (New Zealand, White, 3.5-4.3 kg.); 19 gauge cannula used.

*ALZET Comments:* Losartan; SN50; tempol; CSF, artificial; CSF/CNS; Rat; 4 weeks; Controls received mp w/ vehicle; peptides; animal info (male, Sprague Dawley, 250-275 g.); pumps were primed in 0.9% saline for 24 hours; SN50 is a synthetic protein.

P9759: N. N. Ge, et al. Long-Term Hearing Loss in Gerbils With Bacterial Meningitis Treated With Superoxide Dismutase. OTOTOLOGY & NEUROTOLOGY 2008;29(8):1061-1067
*ALZET Comments:* Superoxide dismutase; CSF, artificial; CSF/CNS (intrathecal); Gerbil; 2002; 14 days; Controls received IM injections of SOD; half-life (p.1065) 40 hours; animal info (8 wks old, male, Mongolian); dental cement used to hold tubing in place; silastic tubing used; image of surgical placement of pumps fig.2., fig. 4.

11. Tolmetin

*ALZET Comments:* Doxorubicin HCl; Mitoxantrone; Tolmetin sodium; Bleomycin; Cisplatin; Methotrexate; PBS; IP; Rat; 2ML1; 7 days; Antibiotic; cancer; no stress (see p249).