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

1. Acetylsalicylic Acid


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).


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.


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.


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 glucoronicicated 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

**Agents:** Chloridotetrakis (ibuprofenato)diruthenium-(II,III) **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Rat; **Pump:** Not Stated; **Duration:** Not Stated;
**ALZET Comments:** cancer (glioma);

**Agents:** ibuprofen **Vehicle:** Saline; **Route:** CSF/CNS (sciatic nerve); **Species:** Rat; **Pump:** 1004; **Duration:** 21 days;
**ALZET Comments:** Dose (7 μg/day); Controls received mp w/ vehicle; animal info (male, Wistar, 220-250g); pump was implanted locally parallel to re-connected nerve (p.1631);

**Agents:** Ibuprofen **Vehicle:** PBS; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** Not Stated;
**ALZET Comments:** 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);

**Agents:** Ibuprofen **Vehicle:** PEG; DMSO; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 8 weeks;
**ALZET Comments:** 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;

**Agents:** Diruthenium-ibuprofen **Vehicle:** Ethanol; CSF, artificial; **Route:** CSF/CNS (intratumoral); **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: 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;

5. Indomethacin

Agents: indomethacin Vehicle: saline, Kolliphor HS15 buffered; Route: SC; Species: Mice; Pump: 2006; Duration: 4 weeks;
ALZET Comments: Dose (10 mg/ml at 0.15 ml/h); saline with 18.75% Kolliphor HS15 used; Controls received mp w/ vehicle; animal info (6 weeks, male, C57BL/6J); good methods ("We connected a piece of silicon tubing at the end of each pump, and sutured the tubing on the mouse back muscle to ensure that the opening of the tubing was on the iBAT of the mouse during pump implantation." p.469); controls split into three groups (saline, Kolliphor HS15, saline + Kolliphor HS15); Therapeutic indication (expression of genes involved in thermogenesis in iBAT (interscapular brown adipose tissue) and improved hyperglycemia found in DIO (diet-induced obesity) mice along with promoting mouse brown adipocyte differentiation.);

Agents: NA-398; SC-560; indomethacin Vehicle: DMSO; Route: SC; Species: Mice; Pump: Not Stated; Duration: 30 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (female, BALB/c); immunology;

Agents: fenretinide; indomethacin Vehicle: Not Stated; Route: Not Stated; Species: Mice; Pump: Not Stated; Duration: 24 weeks;
ALZET Comments: animal info (6 weeks, male, p53+/-); comparison of caloric restriction vs mp; long-term study; fenretinide is a synthetic retinoid. indomethacin is a nonsteroidal anti-inflammatory drug; cancer (bladder); citation for study listed as (Hursting, S.D. and Perkins, S.N., unpublished observations, 2001);

Agents: Hydrocortisone; indomethacin; olvanil Vehicle: PEG 200; Route: SC; Species: mice; Pump: Not Stated; Duration: 2 days;
ALZET Comments: Controls received mp w/ vehicle; toxicology

Agents: Iloprost; Cicaprost; L-NAME; Indomethacin Vehicle: Saline; Route: SC; Species: Rat (pregnant); Pump: 2ML2; Duration: 2 weeks;
ALZET Comments: controls received mp w/vehicle; comparison of SC injections vs. mp; cardiovascular; L-NAME is a synthase inhibitor;

6. Ketorolac

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

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;
11. Tolmetin


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