References on the Administration of Nitric Oxide Synthase Inhibitors Using ALZET® Osmotic Pumps

1. **1400W**


- **Agents:** 1400W dihydrochloride
- **Vehicle:** Not Stated
- **Route:** SC
- **Species:** Mice (nude)
- **Pump:** 1002
- **Duration:** Not Stated

**ALZET Comments:** Animal info (female, nu/nu, 6-8 weeks old); cancer (breast); enzyme inhibitor (nitric oxide synthase); immunology;

**Q3098:** F. Klug, *et al.* Low-Dose Irradiation Programs Macrophage Differentiation to an iNOS(+)/M1 Phenotype that Orchestrates Effective T Cell Immunotherapy. Cancer Cell 2013;24(5):589-602

- **Agents:** 1400W
- **Vehicle:** PBS
- **Route:** SC
- **Species:** Mice
- **Pump:** Not Stated
- **Duration:** 2 weeks

**ALZET Comments:** Controls received mp w/ vehicle; animal info (RT5); cancer (cancer immunotherapy); immunology; iNOS inhibitor

**Q1253:** M. Nishida, *et al.* Heterologous down-regulation of angiotensin type 1 receptors by purinergic P2Y(2) receptor stimulation through S-nitrosylation of NF-kappaB. PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA 2011;108(16):6662-6667

- **Agents:** 1400W; suramin
- **Vehicle:** Saline
- **Route:** Not Stated
- **Species:** Mice
- **Pump:** Not Stated
- **Duration:** Not Stated

**ALZET Comments:** Controls received mp w/ vehicle; animal info (C57BL/6J, 6 wks old, male); enzyme inhibitor (NO synthase, iNOS)


- **Agents:** 1400W
- **Vehicle:** Isoproterenol bitartrate
- **Route:** SC
- **Species:** Mice
- **Pump:** 2002
- **Duration:** 14 days

**ALZET Comments:** Controls received mp w/ vehicle; enzyme inhibitor (iNOS); animal info (C57BL/6, 3, 20 months old); ischemia (myocardial)

**P8870:** Y. I. Chirino, *et al.* Selective iNOS inhibition reduces renal damage induced by cisplatin. TOXICOLOGY LETTERS 2008;176(1):48-57

- **Agents:** 1400W; cisplatin
- **Vehicle:** Saline
- **Route:** SC
- **Species:** Rat
- **Pump:** 2001
- **Duration:** 3 days

**ALZET Comments:** Controls received mp w/ vehicle; enzyme inhibitor (iNOS); animal info (male, Wistar, 230-275g.)

2. **L-NAME**

**Q7443:** H. E. Chen, *et al.* Resveratrol prevents combined prenatal N(G)-nitro-L-arginine-methyl ester (L-NAME) treatment plus postnatal high-fat diet induced programmed hypertension in adult rat offspring: interplay between nutrient-sensing signals, oxidative stress and gut microbiota. J Nutr Biochem 2019;70(28-37

- **Agents:** L-NAME
- **Vehicle:** Not Stated
- **Route:** SC
- **Species:** Rat
- **Pump:** Not stated
- **Duration:** 6 weeks

**ALZET Comments:** Dose (60 mg/kg/day); Controls received mp w/ vehicle; animal info (12-16 weeks old, male); L-NAME aka NG-nitro-L-arginine-methyl ester; cardiovascular;

**Q7412:** H. E. Chen, *et al.* Resveratrol prevents combined prenatal N(G)-nitro-L-arginine-methyl ester (L-NAME) treatment plus postnatal high-fat diet induced programmed hypertension in adult rat offspring: interplay between nutrient-sensing signals, oxidative stress and gut microbiota. J Nutr Biochem 2019;70(28-37

- **Agents:** L-NAME
- **Vehicle:** Not Stated
- **Route:** SC
- **Species:** Rat
- **Pump:** Not Stated
- **Duration:** 6 weeks

**ALZET Comments:** Dose (60 mg/kg/day); Controls received mp w/ vehicle; animal info (12-16 weeks old, male); L-NAME aka NG-nitro-L-arginine-methyl ester; cardiovascular;

Agents: L-NAME Vehicle: Saline; Route: SC; Species: Rat (pregnant); Pump: 2ML1; Duration: 3 days;
ALZET Comments: Dose (50 mg/day); Controls received mp w/ vehicle; animal info (Pregnant female Sprague-Dawley rats on embryonic day 16); L-NAME aka Nω-nitro-L-arginine methyl ester;

Q7151: D. S. Lee, et al. PDI-mediated S-nitrosylation of DRP1 facilitates DRP1-S616 phosphorylation and mitochondrial fission in CA1 neurons. Cell Death & Disease 2018;9(9):869

Agents: RNA, small interfering (protein disulfide isomerase), L-NAME Vehicle: Saline; Route: CSF/CNS (right lateral ventricle); Species: Rats; Pump: 1007D; Duration: Not Stated;
ALZET Comments: Dose (15 μg/μl L-NAME); animal info (7-week-old male Sprague-Dawley rats); Nω-nitro-L-arginine methyl ester hydrochloride aka L-name; enzyme inhibitor (protein disulfide isomerase); ALZET brain infusion kit 1 used; Brain coordinates (right lateral ventricle, 1mm posterior; 1.5 mm lateral; 3.5 mm depth from bregma);


Agents: RNA, small interfering; L-NAME; PACMA31 Vehicle: Saline; Route: CSF/CNS (Right lateral ventricle); Species: Rat; Pump: 1007D; Duration: 1 week;
ALZET Comments: Controls received mp w/ vehicle; animal info (7 week old male Sprague-Dawley rats); enzyme inhibitor (PACMA31 is a selective PDI inhibitor); ALZET brain infusion kit 1 used; Brain coordinates (1 mm posterior; 1.5 mm lateral; 3.5 mm depth from bregma); Therapeutic indication (seizure);

3. L-NMA

ALZET Comments: L-NMA; IP; Rat; 1003D; 72 hours; Controls received mp w/ vehicle; enzyme inhibitor; nitric oxide synthase inhibitors; L-NMA also called N-monomethyl-L-arginine.

ALZET Comments: Aminoguanidine; Lysine, L-N6-(1-imino-ethyl)-; V-PYRRO/NO; L-NAME; L-NMA; Saline; IV (jugular); IV (gastric); Rat; 2001D; 16 hours; controls received mp w/vehicle; good methods (p. 406); nitric oxide synthase inhibitors; PE10 catheter tubing inserted in gastric vein; some animals implanted with one pump for gastric vein and one for jugular vein; NMA is NG-monomethyl-L-arginine.

4. L-NMMA

ALZET Comments: L-NMMA; IP; CSF/CNS; Rat; 2ML4; 4 weeks; Controls received mp w/ saline; replacement therapy (nephrectomy); dose-response (fig. 1); enzyme inhibitor (no synthase); cardiovascular; animal info (male, Wistar, 7 wk. old, 240g.); cannula location confirmed by methylene blue staining.

ALZET Comments: L-NMMA; D-NMMA; SC; Mice; mice (SCID); 1002; 8, 21 days; Controls received mp w/ D-NMMA; pumps replaced at day 14; enzyme inhibitor (NO synthase); cancer (melanoma); cardiovascular; eNOS -/- mice; iNOS -/- mice.

ALZET Comments: L-NMMA; IP; Rat; 2 weeks; Controls received mp w/ saline; enzyme inhibitor (no synthase).


ALZET Comments: L-NMMA; D-NMMA; SC; Mice; 3 days; Controls received mp w/ D-NMMA; enzyme inhibitor (NO synthase); cardiovascular.


ALZET Comments: L-NMMA; Aminoguanidine hemisulphate; MITU;; PBS;; IP;; mice;; 10 days;; control received mp w/vehicle; comparison of IP injections vs. mp; wound healing study; MITU is S-methyl isothiouronium, a competitive NO synthase inhibitor.

5. L-NNA


ALZET Comments: L-NNA; Saline; CSF/CNS (lateral geniculate nucleus); Ferret; 2002; 12 days; Controls received mp with saline; animals received antibiotics prophylactically.


ALZET Comments: L-NNA; Heparin; Saline; IV (jugular); Rat; 2ML1; 6 days; heparin added for anticoagulation; NNA stable for at least 6 days (p. 85).


ALZET Comments: L-NNA; Saline; SC; Rat; 2ML1; 8 days; controls received mp w/ saline; comparison of ip injections vs mp; Injected L-NNA "was more effective than continuous infusion"; L-NNA is L-N-nitroarginine and is a NOS inhibitor.

6. Methylisothiourea


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 (propraine 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: Methylisothiourea, S-; adenovirus vector; gene, mouse iNOS cDNA sequence; Saline; Dye, methylene blue; Dye, India black ink; PBS; SC (wound healing site); Rat;; 2001; 2ML1;; 7 days;; Controls received mp w/ saline; functionality of mp verified by dye infusion; gene therapy; enzyme inhibitor; methylisothiourea,S- is an inducible nitric oxide synthase inhibitor (iNOS inhibitor); wound healing; SC-implanted pumps infused 2 hydroxyproline sponges via catheter; initial studies used 2ML1 pumps to infuse dyes in order to assess the feasibility of direct infusion with pumps; iNOS inhibitor infusion was with 2001 pumps; pumps were designed to infuse directly into SC implanted polyvinyl sponges at the wound site; Adenovirus vector was dissolved in PBS; iNOS inhibitor was delivered in saline; diagram of pump-catheter
assembly and location (p. 18); "Dye infusion demonstrated both grossly and microscopically excellent delivery of the infusate to wound sponges" (p. 18);

7. MITU

ALZET Comments: L-NMMA; Aminoguanidine hemisulphate; MITU;; PBS;; IP;; mice;; 10 days;; control received mp w/vehicle; comparison of IP injections vs. mp; wound healing study; MITU is S-methyl isothiouronium, a competitive NO synthase inhibitor.

ALZET Comments: MITU; IP; mice; 10 days; controls received mp w/ PBS; immunology; MITU is S-methyl isothiouronium, a competitive NO synthase inhibitor; wound healing.

8. MLA

ALZET Comments: Nicotine ditartrate; MLA; erythroidine, dihydro-beta; Saline, sterile; CSF, artificial; SC; CSF/CNS (ventral hippocampus); Rat; 2004; 2ML4; 4 weeks; Controls received mp w/ vehicle; multiple pumps per animal (2); animal info (female, Sprague-Dawley, 200-300g.); neurodegenerative (Alzheimer’s disease); methyllycaconitine; cannula placement confirmed w/ Chicago sky-blue dye; schizophrenia.

ALZET Comments: MLA; IP; Mice (nude); 1007D; 7 days; Cancer (head, neck); MLA is NW-monomethyl-L-arginine.

ALZET Comments: MLA; SC; mice; 2001; no duration posted; controls received sham implantation; MLA is n-monomethyl-L-arginine, an NOS inhibitor; cancer; immunology.

ALZET Comments: MLA; SC; mice; 2001; 8 days; controls received sham surgery; pumps replaced after 8 days; cancer; MLA is N-monomethyl-L-arginine, an NOS inhibitor.

ALZET Comments: MLA; SC; mice; 2001; 1007D; no duration posted; controls received sham implantation or no treatments; immunology; toxicology.

9. Nitroindazole

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ALZET Comments: Butorphanol tartrate; nitroindazole, 7-; Saline; DMSO; CSF/CNS; Rat; 2001; 72 hours; Enzyme inhibitor (nitric oxide synthase, NOS); animal info (male, Sprague Dawley, 250-275 g.); pump connected to catheter after 1 week recovery period; 10% DMSO used; PE60 tubing used.

P8379: T. Thippeswamy, et al. NO-cGMP mediated galanin expression in NGF-deprived or axotomized sensory neurons. Journal of Neurochemistry 2007;100(3):790-801
ALZET Comments: Nitroindazole, 7-; DMSO; IP; Rat; 2ML1; 7 days; Controls received mp w/ vehicle; animal info (male, Wistar, Albino, 250-280g.); 20% DMSO.

ALZET Comments: Nitroindazole, 7-, sodium salt; thiocitrulline dihydrochloride, methyl-; PBS; CSF/CNS (striatum); Rat; 2002; no duration posted; dose-response; microdialysis; quinolinic acid administered alone or w/1 other agent in same pump; enzyme inhibitor (nitric oxide synthase); cyanoacrylate adhesive.

P3492: T. Bazzett, et al. The neuronal NOS inhibitor L-MIN, but not 7-NINA, reduces neurotoxic effects of chronic intrastratal administration of quinolinic acid. Brain Research 1997;775(229-232)
ALZET Comments: Quinolinic acid; Nitroindazole, 7-, sodium salt; thiocitrulline dihydrochloride, methyl-; PBS; CSF/CNS (striatum); Rat; 2002; no duration posted; dose-response; microdialysis; quinolinic acid administered alone or w/1 other agent in same pump; enzyme inhibitor; nitric oxide synthase inhibitor.

ALZET Comments: Nitroindazole, 7-, sodium salt; IP; gerbil; 1003D; 72 hours; comparison of ip injections vs. mp; 2 pumps implanted in each animal; 7-nitroindazole is a neuronal nitric oxide synthase inhibitor; neuroprotection seen when 7-nitroindazole was infused via mp, but not when injected 12X after occlusion.

10. Thiocitrulline

ALZET Comments: S-Methyl-L-thiocitrulline; Saline; SC; Rat; 1007D; 7 days; Dose (0.5 ± 0.1 μL/hr/day); 0.9% saline used; animal info (male Sprague Dawley); post op. care (Ampicillin, meloxicam); enzyme inhibitor (S-Methyl-L-thiocitrulline is a neuronal nitric oxide synthase (nNOS) inhibitor); Brain coordinates (AP –1.0 mm, ML –2.0 mm, DV –3.5mm from bregma); bilateral cannula used; dependence.

P3492: T. Bazzett, et al. The neuronal NOS inhibitor L-MIN, but not 7-NINA, reduces neurotoxic effects of chronic intrastratal administration of quinolinic acid. Brain Research 1997;775(229-232
ALZET Comments: Quinolinic acid; Nitroindazole, 7-, sodium salt; thiocitrulline dihydrochloride, methyl-; PBS; CSF/CNS (striatum); Rat; 2002; no duration posted; dose-response; microdialysis; quinolinic acid administered alone or w/1 other agent in same pump; enzyme inhibitor; nitric oxide synthase inhibitor.