



### References on the Administration of Epinephrine Using ALZET® Osmotic Pumps

**Q10345:** L. Staurengo-Ferrari, *et al.* Sexual dimorphism in the contribution of neuroendocrine stress axes to oxaliplatin-induced painful peripheral neuropathy. *Pain* 2021;162(3):907-918

**Agents:** Epinephrine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2004; **Duration:** Not Stated;

**ALZET Comments:** Dose: Epinephrine (5.4 mg/0.25 mL/h); Controls received mp w/ vehicle; animal info: adults, male and female Sprague-Dawley rats 8 weeks old; neurodegenerative (Peripheral neuropathy);

**Q9574:** L. M. de Souza Cordeiro, *et al.* Hypothalamic MC4R regulates glucose homeostasis through adrenaline-mediated control of glucose reabsorption via renal GLUT2 in mice. *Diabetologia* 2021;64(1):181-194

**Agents:** Adrenaline **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** Not Stated;

**ALZET Comments:** Dose (1 ug/day); 0.9% Saline used; Controls received mp w/ vehicle; animal info (MC4R deficient, C57BL/6J);

**Q10138:** R. Cetin-Atalay, *et al.* Intermittent Hypoxia-Induced Activation of Endothelial Cells Is Mediated via Sympathetic Activation-Dependent Catecholamine Release. *Frontiers in Physiology* 2021;12(701995)

**Agents:** Epinephrine **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 10 days;

**ALZET Comments:** Dose: Epinephrine (5 mg/kg/24 h; Controls received mp w/ vehicle; animal info: (6- to 8-week-old C57BL/6J); Blood pressure measured via tail-cuff method; Obstructive sleep apnea (OSA)

**Q8158:** P. Alvarez, *et al.* Unpredictable stress delays recovery from exercise-induced muscle pain: contribution of the sympathoadrenal axis. *Pain Rep* 2019;4(5):e782

**Agents:** Epinephrine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2004; **Duration:** 2 weeks;

**ALZET Comments:** Dose (5.4 mg/0.25 mL/h); Controls received mp w/ vehicle; animal info (adult male Sprague-Dawley rats, weighing 250 to 400 g (approximatel 8-12 weeks old)); antisense (intrathecal b2-adrenergic receptor antisense);

**Q4766:** Mohan R Dasu, *et al.* Crosstalk Between Adrenergic and Toll-Like Receptors in Human Mesenchymal Stem Cells and Keratinocytes: A Recipe for Impaired Wound Healing. *STEM CELLS TRANSLATIONAL MEDICINE* 2014;3):745-759

**Agents:** epinephrine, macrophage-activating lipopeptide-2; **Route:** SC; **Species:** mice; **Pump:** 1002; **Duration:** 7,11 days

**ALZET Comments:** animal info (Jax Mice, male, 8-10 weeks of age); peptides; macrophage-activating lipopeptide-2 aka MALP-2; Dose (7mg/kg body weight/day EPI; .7 mg/kg body weight/day ICI);

**Q3234:** M. H. Kim, *et al.* Catecholamine Stress Alters Neutrophil Trafficking and Impairs Wound Healing by beta(2)-Adrenergic Receptor-Mediated Upregulation of IL-6. *Journal of Investigative Dermatology* 2014;134(3):809-817

**Agents:** Epinephrine; antagonist, beta adrenergic receptor **Vehicle:** Saline; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 1002; **Duration:** 8 days;

**ALZET Comments:** Controls received mp w/ vehicle; animal info (female, EGFP-lys); functionality of mp verified by plasma levels; dose-response (pg. 810); immunology;

**Q4819:** M. R. DASU, *et al.* Crosstalk Between Adrenergic and Toll-Like Receptors in Human Mesenchymal Stem Cells and Keratinocytes: A Recipe for Impaired Wound Healing. *STEM CELLS TRANSLATIONAL MEDICINE* 2014;3):745-759

**Agents:** Epinephrine; macrophage-activating lipopeptide-2; ICI-118,551 **Vehicle:** Not Stated; **Route:** SC; **Species:** mice; **Pump:** 1002; **Duration:** 7 days; 11 days;

**ALZET Comments:** animal info (Jax Mice, male, 8-10 weeks of age); peptides; macrophage-activating lipopeptide-2 aka MALP-2; Dose (7mg/kg body weight/day EPI; .7 mg/kg body weight/day ICI);

**Q1759:** F. C. Beasley, *et al.* Staphylococcus aureus Transporters Hts, Sir, and Sst Capture Iron Liberated from Human Transferrin by Staphyloferrin A, Staphyloferrin B, and Catecholamine Stress Hormones, Respectively, and Contribute to Virulence. *Infection and Immunity* 2011;79(6):2345-2355

**Agents:** Epinephrine **Vehicle:** Saline, buffered; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 4 days;

**ALZET Comments:** Controls received mp w/ vehicle; animal info (BALB/c)



**Q0775:** S. G. Khasar, *et al.* Sound Stress-Induced Long-Term Enhancement of Mechanical Hyperalgesia in Rats Is Maintained by Sympathoadrenal Catecholamines. JOURNAL OF PAIN 2009;10(10):1073-1077

**Agents:** Epinephrine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2004; **Duration:** 14 days;

**ALZET Comments:** Animal info (adrenal medullectomy, adult, male, Sprague Dawley, 300-400 g); functionality of mp verified by plasma drug levels

**P8857:** C. von Montfort, *et al.* Contribution of the sympathetic hormone epinephrine to the sensitizing effect of ethanol on LPS-induced liver damage in mice. American Journal of Physiology Gastrointestinal and Liver Physiology 2008;294(5):G1227-G1234

**Agents:** Epinephrine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 5 days;

**ALZET Comments:** Half-life (p. G1227) "very short"; animal info (male, C57BL/6, 4-6 wks old); "Owing to the very short half-life of epinephrine, the hormone was infused instead of injected to maintain a low-grade elevated plasma level over a prolonged period which better mimics the effect of ethanol." pg. G1227

**P8832:** O. A. Dina, *et al.* Alcohol-induced stress in painful alcoholic neuropathy. European Journal of Neuroscience 2008;27(1):83-92

**Agents:** Epinephrine **Vehicle:** Saline; Ascorbic acid; **Route:** SC; **Species:** Rat; **Pump:** 2004; **Duration:** 3 weeks;

**ALZET Comments:** Replacement therapy (adrenal medullectomy); animal info (male, Sprague Dawley, 250-450g.)

**P9158:** O. A. Dina, *et al.* Neurotoxic catecholamine metabolite in nociceptors contributes to painful peripheral neuropathy. European Journal of Neuroscience 2008;28(6):1180-1190

**Agents:** Epinephrine **Vehicle:** Saline; Ascorbic acid; **Route:** Not Stated; **Species:** Rat; **Pump:** Not Stated; **Duration:** Not Stated;

**ALZET Comments:** Animal info (male, Sprague Dawley, 270-450 g.)

**P7594:** S. G. Khasar, *et al.* Repeated sound stress enhances inflammatory pain in the rat. Pain 2005;116(1-2):79-86

**Agents:** Epinephrine bitartrate **Vehicle:** Saline; Ascorbic acid; **Route:** SC; **Species:** Rat; **Pump:** 1007D; **Duration:** 7 days;

**ALZET Comments:** Controls received no treatment; animal info (male, Sprague-Dawley 250-380 g); pain

**P7253:** S. G. Khasar, *et al.* Estrogen regulates adrenal medullary function producing sexual dimorphism in nociceptive threshold and beta<sub>2</sub>-adrenergic receptor-mediated hyperalgesia in the rat. European Journal of Neuroscience 2005;21(12):3379-3386

**Agents:** Epinephrine **Vehicle:** Saline; Ascorbic acid; **Route:** SC; **Species:** Rat; **Pump:** 1007D; 2002; **Duration:** 7, 14 days;

**ALZET Comments:** Functionality of mp verified by plasma epinephrine levels; replacement therapy (adrenal medullectomy, adrenal gland denervation); dose-response (Fig 3)

**P7157:** J. Jensen, *et al.* Improved insulin-stimulated glucose uptake and glycogen synthase activation in rat skeletal muscles after adrenaline infusion: role of glycogen content and PKB phosphorylation. Acta Physiologica Scandinavica 2005;184(2):121-130

**Agents:** Adrenaline **Vehicle:** Water, sterile; Ascorbic acid; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 1, 12 days;

**ALZET Comments:** Controls received mp w/ vehicle

**P5984:** Y. Kitano, *et al.* Epinephrine inhibits tracheal occlusion induced lung growth in fetal sheep. Fetal Diagnosis and Therapy 2003;18(5):333-337

**Agents:** Epinephrine **Vehicle:** Saline; Ascorbic acid; **Route:** SC; **Species:** Sheep (fetus); **Pump:** 2ML1; **Duration:** 4 days;

**ALZET Comments:** Teratology

**P5711:** S. G. Khasar, *et al.* Vagal modulation of nociception is mediated by adrenomedullary epinephrine in the rat. European Journal of Neuroscience 2003;17(4):909-915

**Agents:** ICI-118,551; epinephrine **Vehicle:** Saline; Ascorbic acid; ethanol; **Route:** SC; **Species:** Rat; **Pump:** 1007D; 2004; **Duration:** 3, 7, 14 days;

**ALZET Comments:** Controls received mp w/ vehicle; dose-response (p. 911); ICI-118, 55 dissolved in ethanol and saline and infused for 7 days via 1007D pumps; epinephrine dissolved in saline and ascorbic acid and delivered for 3, 7, or 14 days via 2004 pumps.



**P5744:** G. V. R. Born, *et al.* Factors influencing the uptake of atherogenic plasma proteins by artery walls. *Biorheology* 2003;40(1-3):13-22

**Agents:** Epinephrine; Angiotensin II **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 6 days;  
**ALZET Comments:** Controls received mp w/ saline; plasma levels reported; cardiovascular; pump rate 0.5 ul hr (p.15)

**R0161:** G. V. Born, *et al.* Endothelial factors in the flux of atherogenic plasma proteins into artery walls. *Clinical Hemorheology and Microcirculation* 2002;26(2):107-116

**Agents:** Epinephrine; Angiotensin II **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 1007D; **Duration:** 6 days;  
**ALZET Comments:** Controls received mp w/ vehicle; functionality of mp verified by epinephrine plasma levels; cardiovascular; peptides; various methods of inducing hypertension explored

**P4994:** S. K. Juhn, *et al.* Effect of stress-related hormones on inner ear fluid homeostasis and function. *American Journal of Otology* 1999;20(800-806

**Agents:** Epinephrine **Vehicle:** Saline; **Route:** SC; **Species:** Chinchilla; **Pump:** Not Stated; **Duration:** 1,2,3, or 4 weeks;  
**ALZET Comments:** controls received mp w/ vehicle;

**P3714:** E.-L. Sainio. The role of adrenal hormones in the activation of tryptophan 2,3-dioxygenase by nicotinic acid in rat liver. *Meth. Find Exp. Clin. Pharmacol* 1997;19(7):465-470

**Agents:** Epinephrine; Corticosterone **Vehicle:** Ethanol; NaCl; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 6 days;  
**ALZET Comments:** controls received mp w/vehicle; replacement therapy (adrenalectomy)

**P3530:** L. E. Cardona-Sanclemente, *et al.* Increase by adrenaline or angiotensin II of the accumulation of low density lipoprotein and fibrinogen by aortic walls in unrestrained conscious rats. *British Journal of Pharmacology* 1996;117(1089-1094

**Agents:** Epinephrine; Angiotensin II **Vehicle:** Ascorbic acid; **Route:** SC; IA (carotid); **Species:** Rat; **Pump:** 2ML4; 1007D;  
**Duration:** 6 days;

**ALZET Comments:** controls received saline infusion; functionality of mp verified by plasma levels; stability verified by analyzing residual solution

**P3704:** F. Brandao, *et al.* Homogeneous or heterogeneous distribution of systemically administered adrenaline: organ dependence. *Naunyn-Schmiedeberg's Arch. Pharmacol* 1996;353(579-583

**Agents:** Epinephrine **Vehicle:** Water, distilled; **Route:** IP; **Species:** Rat; **Pump:** Not Stated; **Duration:** 6 days;  
**ALZET Comments:** comparison of short-term iv infusion vs. mp

**P3221:** L. T. Jablonskis, *et al.* Lack of influence of circulating adrenaline on blood pressure in normotensive and hypertensive rats. *Blood* 1994;3(112-119

**Agents:** Epinephrine bitartrate **Vehicle:** Saline; Ascorbic acid; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 5-6 weeks;  
**ALZET Comments:** long-term study, pumps replaced every 2 weeks; mp implanted in flank region

**P2640:** S. C. Birnbaum, *et al.* Nicotine- or epinephrine-induced uteroplacental vasoconstriction and fetal growth in the rat. *Toxicology* 1994;94(69-80

**Agents:** Nicotine free base; Epinephrine acid tartrate **Vehicle:** Saline; Ascorbic acid; Water, distilled; **Route:** SC; **Species:** Rat (pregnant); **Pump:** 2ML1; **Duration:** no duration posted;  
**ALZET Comments:** controls received mp w/ saline; toxicology; teratology

**P2391:** T. A. Deisher, *et al.* Protective effect of clentiazem against epinephrine-induced cardiac injury in rats. *J. Pharmacol. Exp. Ther* 1993;266(1):262-269

**Agents:** Epinephrine bitartrate; Clentiazem **Vehicle:** Saline; Ethanol; DMSO; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 2 weeks;  
**ALZET Comments:** no comment posted



**P2425:** H. M. Sadeghi, *et al.* Chronic epinephrine treatment fails to alter prejunctional adrenoceptor modulation of sympathetic neurotransmission in the rat mesentery. *J. Pharmacol. Exp. Ther* 1992;261(3):924-930

**Agents:** Epinephrine **Vehicle:** Saline; Ascorbic acid; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 6 days;  
**ALZET Comments:** no comment posted

**P1979:** R. Dehner, *et al.* Adrenaline in cardiovascular diseases - effect of B-adrenoceptor antagonists. *Z. Kardiol* 1990;79(3):79-88

**Agents:** Epinephrine **Vehicle:** Ascorbic acid; **Route:** Not Stated; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;  
**ALZET Comments:** English with German summary

**P1486:** S. G. Trend, *et al.* Resistance of the rat embryo to elevated maternal epinephrine concentrations. *American Journal of Obstetrics & Gynecology* 1989;160(4):498-501

**Agents:** Epinephrine **Vehicle:** Ascorbic acid; Saline; Water; **Route:** IV (jugular); **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;  
**ALZET Comments:** dose-response; functionality of mp verified by plasma levels; no stress

**P1584:** W. Terres, *et al.* Effects of chronic treatment with adrenaline or propranolol on platelet function and c-AMP levels in the rat. *Cardiovascular Research* 1989;23(1):112-116

**Agents:** Epinephrine **Vehicle:** Ascorbic acid; Saline; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 8 weeks;  
**ALZET Comments:** long-term study, pump replaced every 14 days

**P1176:** D. D. Schwartz, *et al.* Enhanced endogenous neurotransmitter overflow in the isolated perfused rat kidney after chronic epinephrine administration: lack of a prejunctional beta adrenoceptor influence. *J. Pharmacol. Exp. Ther* 1988;244(1):11-18

**Agents:** Epinephrine **Vehicle:** Ascorbic acid; Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 6 days;  
**ALZET Comments:** controls received mp w/ vehicle; propranolol used to examine influence of beta adrenoceptors and phentolamine for alpha adrenoceptors

**P1554:** N. M. Deighton, *et al.* The effects of chronic administration of adrenaline on the function and number of adrenoceptors in the rabbit. *J. Cardiovasc. Pharmacol* 1988;12(3):332-337

**Agents:** Epinephrine **Vehicle:** Ascorbic acid; Water; **Route:** IV (femoral); **Species:** rabbit; **Pump:** 2002; **Duration:** 10 days;  
**ALZET Comments:** dose-response; pump embedded in thigh muscle; functionality of mp verified by plasma levels

**P1412:** B. F. Becker, *et al.* Blood platelet function after chronic treatment of rats and guinea pigs with nicotine. *Klin. Wochenschr* 1988;66(11):28-36

**Agents:** Nicotine base; Epinephrine bitartrate **Vehicle:** Ascorbic acid; Saline; Water; **Route:** SC; **Species:** Guinea pig; Rat; **Pump:** 2002; **Duration:** 2, 8 weeks;  
**ALZET Comments:** dose-response; functionality of mp verified by plasma levels; long-term study; pump replaced every 2 week

**P0861:** D. D. Schwartz, *et al.* Cardiovascular responsiveness to sympathetic activation after chronic epinephrine administration. *J. Pharmacol. Exp. Ther* 1986;238(1):148-154

**Agents:** Epinephrine bitartrate **Vehicle:** Ascorbic acid; Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 6 days;  
**ALZET Comments:** controls received mp w/vehicle; hypertension

**P0713:** M. E. Upsher, *et al.* Beta-adrenergic receptors in rat myocardium during the development and reversal of hypertrophy and following chronic infusions of angiotensin 11 and epinephrine. *Archives Internationales de Pharmacodynamie* 1985;274(65-79)

**Agents:** Angiotensin II; Epinephrine **Vehicle:** Water; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 6 and 12 days;  
**ALZET Comments:** mp primed in distilled water 24 hours prior to implant; peptides

**P0651:** G. Tsujimoto, *et al.* Desensitization of B-adrenergic receptor-mediated vascular smooth muscle relaxation. *Mol. Pharmacol* 1985;27(2):210-217

**Agents:** Epinephrine HCl, I- **Vehicle:** HCl; Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 1 week;  
**ALZET Comments:** states in error that mp will deliver up to 10 days; mp primed 3 hr prior to implant; bioavailability of EPI determined by plasma level increase



**P0607:** W. B. Jeffries, *et al.* Withdrawal syndrome follows abrupt cessation of intracerebroventricular infusion of epinephrine in spontaneously hypertensive rats. *Life Sci* 1985;36(14):1331-1337

**Agents:** Epinephrine bitartrate **Vehicle:** Ascorbic acid; Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2001; **Duration:** 5 days;  
**ALZET Comments:** 2 day delay of mp Epi achieved by filling connecting tubing with vehicle; some tubing externalized to allow immediate cutoff of infusion; dose-response data; delayed delivery;

**P0600:** K. Kumano, *et al.* Adenylate cyclase activity in rat myocardium following chronic infusions of angiotensin II and epinephrine. *J. Cardiovasc. Pharmacol* 1984;6(5):756-761

**Agents:** Angiotensin II; Epinephrine, I- **Vehicle:** Ascorbic acid; HCl; Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; 2002;  
**Duration:** 6 or 13 days, or 4 weeks;

**ALZET Comments:** comparison of agents effects; 2002 mp replaced after 2 weeks; saline used as vehicle w/ AngII, HCl & ascorbic acid w/Epi; controls received vehicle; mp primed in saline before use; peptides