



References on the Administration of Epinephrine
Using ALZET® Osmotic Pumps

- 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 µg/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/6); 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 beta₂-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 Otolaryngology* 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