References on the Administration of Epinephrine Using ALZET® Osmotic Pumps


**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);


**Agents:** Epinephrine  
**Vehicle:** Not Stated;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** Not Stated;  
**Duration:** 10 days;  
**ALZET Comments:** Dose: Epinehrine (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)


**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);


**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);


**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;


**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);


**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)


**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
**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

**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.)

**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.)

**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

**Agents:** Epinephrine **Vehicle:** Saline; Ascorbic acid; **Route:** SC; **Species:** Rat; **Pump:** 1007D; **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)

**Agents:** Adrenaline **Vehicle:** Water, sterile; Ascorbic acid; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 1, 12 days;
**ALZET Comments:** Controls received mp w/ vehicle

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

**Agents:** ICI-118,551; epinephrine **Vehicle:** Saline; Ascorbic acid; ethanol; **Route:** SC; **Species:** Rat; **Pump:** 1007D; **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.

**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)
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

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;

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)

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

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

Agents: Epinephrine Vehicle: Saline; Route: SC; Species: Rat; Pump: 2ML1; Duration: no duration posted;
ALZET Comments: no comment posted

Agents: Nicotine free base; Epinephrine acid tartrate Vehicle: Saline; Ascorbic acid; Water, distilled; Route: SC; Species: Rat; Pump: 2ML1; Duration: 5-6 weeks;
ALZET Comments: long-term study, pumps replaced every 2 weeks; mp implanted in flank region

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

Agents: Epinephrine Vehicle: Saline; Ascorbic acid; Route: SC; Species: Rat; Pump: Not Stated; Duration: 6 days;
ALZET Comments: no comment posted
<table>
<thead>
<tr>
<th>Reference</th>
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<th>Agents</th>
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<th>ALZET Comments</th>
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</thead>
<tbody>
<tr>
<td>P1486</td>
<td>S. G. Trend, et al.</td>
<td>Resistance of the rat embryo to elevated maternal epinephrine concentrations. American Journal of Obstetrics &amp; Gynecology</td>
<td>Epinephrine</td>
<td>Ascorbic acid</td>
<td>IV (jugular)</td>
<td>Rat</td>
<td>2001</td>
<td>7 days</td>
<td>dose-response; functionality of mp verified by plasma levels; no stress</td>
</tr>
<tr>
<td>P1584</td>
<td>W. Terres, et al.</td>
<td>Effects of chronic treatment with adrenaline or propranolol on platelet function and c-AMP levels in the rat. Cardiovascular Research</td>
<td>Epinephrine</td>
<td>Ascorbic acid</td>
<td>SC</td>
<td>Rat</td>
<td>2002</td>
<td>8 weeks</td>
<td>long-term study, pump replaced every 14 days</td>
</tr>
<tr>
<td>P1176</td>
<td>D. D. Schwartz, et al.</td>
<td>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</td>
<td>Epinephrine</td>
<td>Ascorbic acid</td>
<td>SC</td>
<td>Rat</td>
<td>2001</td>
<td>6 days</td>
<td>controls received mp w/ vehicle; propranolol used to examine influence of beta adrenoceptors and phentolamine for alpha adrenoceptors</td>
</tr>
<tr>
<td>P1554</td>
<td>N. M. Deighton, et al.</td>
<td>The effects of chronic administration of adrenaline on the function and number of adrenoceptors in the rabbit. J. Cardiovasc. Pharmacol</td>
<td>Epinephrine</td>
<td>Ascorbic acid</td>
<td>IV (femoral)</td>
<td>Rabbit</td>
<td>2002</td>
<td>10 days</td>
<td>dose-response; pump embedded in thigh muscle; functionality of mp verified by plasma levels</td>
</tr>
<tr>
<td>P0861</td>
<td>D. D. Schwartz, et al.</td>
<td>Cardiovascular responsiveness to sympathetic activation after chronic epinephrine administration. J. Pharmacol. Exp. Ther</td>
<td>Epinephrine bitartrate</td>
<td>Ascorbic acid</td>
<td>SC</td>
<td>Rat</td>
<td>2001</td>
<td>6 days</td>
<td>controls received mp w/vehicle; hypertension</td>
</tr>
<tr>
<td>P0713</td>
<td>M. E. Upsher, et al.</td>
<td>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</td>
<td>Angiotensin II; Epinephrine</td>
<td>Water</td>
<td>SC</td>
<td>Rat</td>
<td>2001</td>
<td>6 and 12 days</td>
<td>mp primed in distilled water 24 hours prior to implant; peptides</td>
</tr>
<tr>
<td>P0651</td>
<td>G. Tsujimoto, et al.</td>
<td>Desensitization of B-adrenergic receptor-mediated vascular smooth muscle relaxation. Mol. Pharmacol</td>
<td>Epinephrine HCl</td>
<td>HCl</td>
<td>SC</td>
<td>Rat</td>
<td>2001</td>
<td>1 week</td>
<td>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</td>
</tr>
</tbody>
</table>
**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;  

**Agents:** Angiotensin II; Epinephrine, l-  
**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