Adinazolam


**Agents:** Adinazolam; Diazepam

**Vehicle:** Benzyl alcohol; Ethanol; Propylene glycol; Sodium benzoate; Water

**Route:** IP

**Species:** Rat

**Pump:** 2002

**Duration:** 5 and 14 days

**ALZET Comments:** comparison of adinazolam. iv injec vs. mp infusion; comparison of agents effects; adinazolam. used with water vehicle, Diaz. with combination vehicle

Alprazolam


**Agents:** Alprazolam

**Vehicle:** Saline

**Route:** SC

**Species:** Mice

**Pump:** Not Stated

**Duration:** 1 day

**ALZET Comments:** Controls received mp w/ vehicle; animal info (female C57BL/6 mice); toxicology;


**Agents:** Alprazolam

**Vehicle:** Saline

**Route:** SC

**Species:** Mice

**Pump:** Not stated

**Duration:** 1 day

**ALZET Comments:** Controls received mp w/ vehicle; animal info (female C57BL/6 mice); toxicology;


**Agents:** acetaminophen, cephalothin sodium salt, clindamycin hydrochloride, disopyramide phosphate salt, labetalol hydrochloride, nitrofurantoin + -propranolol hydrochloride, terbutaline hemisulfate salt, verapamil hydrochloride, Acyclovir, alprazolam, atenolol, anhydrous caffeine, cefotaxime sodium salt, cephalin sodium salt, diltiazem hydrochloride, metronidazole, nitrazepam, prednisolone, 6-propyl-2-thiouracil, trazodone hydrochloride, chloramphenicol, cimetidine, theophylline, fluconazole, metoprolol, mirtazapine, praziquantel, quetiapine fumarate, triprolidine hydrochloride, metformin, moclobemide.

**Vehicle:** DMSO; water

**Route:** IP

**Species:** mice

**Pump:** 1003D

**Duration:** Not Stated

**ALZET Comments:** animal info: lactating mice, postnatal age of 14 days; functionality of mp verified by measurement of drug concentration in milk and plasma; mp were used to infuse study lactational drug transfer.


**Agents:** Phenezine; alprazolam; imipramine; buspirone

**Vehicle:** Water, sterile; DMSO; propylene glycol

**Route:** SC

**Species:** Rat

**Pump:** Not Stated

**Duration:** 21 days

**ALZET Comments:** Antidepressant; controls received mp w/ vehicle; pumps were turned in subcutaneous pocket to avoid fibrous tissue outgrowth


**Agents:** Alprazolam; Lorazepam

**Vehicle:** PEG 400

**Route:** SC

**Species:** mice

**Pump:** 2001; 2002

**Duration:** 7, 8, or 14 days

**ALZET Comments:** controls received vehicle; tolerance


**Agents:** Alprazolam; Lorazepam

**Vehicle:** PEG 400

**Route:** IP

**Species:** mice

**Pump:** 2001

**Duration:** 6 days

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

Agents: Triazolam; Alprazolam; Diazepam Vehicle: Propylene glycol; Route: SC; Species: mice; Pump: 2001; Duration: 7 days;
ALZET Comments: controls received mp with vehicle; functionality of mp verified by receptor binding study; comparison of oral alprazolam vs. mp; “. . .the use of implantable minipumps. . .permitted. . .development of behavioral tolerance associated with downregulation of benzodiazepine receptor binding and GABA receptor function. . .”; dependence


Agents: Alprazolam Vehicle: PEG 400; Route: SC; Species: mice; Pump: 2001; 2002; Duration: 14 days;
ALZET Comments: functionality of mp verified by measuring plasma levels; tolerance


Agents: Alprazolam; Lorazepam Vehicle: Ethanol; Propylene glycol; Saline; Route: SC; Species: Rat; Pump: 2ML2; Duration: 12 days;
ALZET Comments: no comment posted

Chlordiazepoxide


Agents: Chlordiazepoxide Vehicle: Saline; Route: SC; Species: Rat; Pump: 2ML1; Duration: 5 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (weight: 290-310g); behavioral testing (Social defeat); chlordiazepoxide is a benzodiazepine receptor agonist; Days infused (D5 – D+10) (Housing: individual cages post. Op.); Therapeutic indication (Anxiety); Dose (10 mg/kg*day);


Agents: Chlordiazepoxide Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2ML1; Duration: 6 days;
ALZET Comments: Control animals received mp w/ vehicle; animal info (Sprague Dawley, male, 250-300 g)


Agents: Chlordiazepoxide Vehicle: Not Stated; Route: SC; Species: Mice; Pump: Not Stated; Duration: 1 week;
ALZET Comments: Animal info (C57BL/6J)

P9959: C. H. Vinkers, et al. The rapid hydrolysis of chlordiazepoxide to demoxepam may affect the outcome of chronic osmotic minipump studies. Psychopharmacology 2010;208(4):555-562

Agents: Chlordiazepoxide Vehicle: Not Stated; Route: In vitro; Species: Not Stated; Pump: Not Stated; Duration: Not Stated;
ALZET Comments: “When the cumulative CDP concentration over time was corrected for its hydrolysis, drug release from the minipumps followed the theoretical release profile over time (white symbols), suggesting that CDP hydrolysis completely accounted for the declined CDP release over time.” pg 558; “In general, the use of osmotic minipumps presents a valid and attractive alternative to the labor-intensive daily injections. However, the issue of drug stability and release should always be carefully investigated before initiating chronic minipump experiments.” pg 562


Agents: CI-988; chlordiazepoxide; Acetylsalicylic acid Vehicle: DMSO; saline; Route: SC; CSF/CNS (intrathecal); Species: Rat; Pump: 2ML1; 2001; 2002; Duration: 14 days;
ALZET Comments: 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)
Agents: Desipramine; mirtazapine; chlorphenteramine; Paroxetine; scopolamine; amphetamine; escitalopram; chlordiazepoxide
Vehicle: Not Stated; Route: SC; IP; Species: Rat; Pump: 2ML2; Duration: 14, 21 days;
ALZET Comments: Controls received mp w/vehicle; dose-response (Fig 2-5); pumps replaced on day 14; good methods pg 629; animal info (male, Sprague Dawley, 5-7 mo old, 550-700g); "Importantly, use of minipumps also eliminates the need for repeated handling and injection of animals to administer the drug chronically." pg. 628; IP catheter used

Agents: Chlordiazepoxide
Vehicle: Saline; Route: SC; Species: Mice; Pump: 1007D; Duration: 7 days;
ALZET Comments: Controls received mp w/ saline; animal info (C57BL/6J, male); chlordiazepoxide is an anxiolytic

Agents: Chlordiazepoxide
Vehicle: Water, distilled; Route: SC; Species: Rat; Pump: 2ML1; Duration: 4-7 days;
ALZET Comments: Controls received mp w/ saline

Clonazepam
Agents: Diazepam; Clonazepam; flumazenil
Vehicle: DMSO; Propylene glycol; Tetraglycol; 3H tracer; Radio-isotopes; Route: in vitro (egg); Species: Not Stated; Pump: 2ML4; Duration: no duration posted;
ALZET Comments: no comment posted

Agents: Clonazepam
Vehicle: PEG; Route: CSF/CNS (dorsal raphe nucleus); Species: Rat; Pump: Not Stated; Duration: 10 days;
ALZET Comments: comparison of IP injections vs. mp

Agents: Nortriptyline; Amitriptyline; Clomipramine; Alaproclate; Clonazepam
Vehicle: Alcohol; Saline; Route: SC; Species: Rat; Pump: 2ML2; Duration: 14 days;
ALZET Comments: antidepressant; controls received mp w/ vehicle; functionality of mp verified by plasma levels; dose-response (Table 1; pg. 177); enzyme inhibitor; clonazepam is a benzodiazepene; the others are monoamine uptake inhibitors

Agents: Clonazepam; RO-16-6028
Vehicle: PEG 400; Route: SC; Species: mice; Pump: Not Stated; Duration: 14 days;
ALZET Comments: functionality of mp verified by tissue levels; dose-response (graph); tolerance/dependence
Diazepam Inhibits Post-Traumatic Neurogenesis and Blocks Aberrant Dendritic Development. J Neurotrauma 2019;36(16):2454-2467

**Agents:** Diazepam  
**Vehicle:** DMSO, Propylene Glycol  
**Route:** SC  
**Species:** Mice  
**Pump:** 2001  
**Duration:** 7 days

**ALZET Comments:** Dose (15 mg/kg/day); 1:1 DMSO:Propylene glycol used; Controls received mp w/ vehicle; animal info (Male and female C57Bl/6J wild-type mice); Therapeutic indication (traumatic brain injury);

Two distinct mechanisms for experience-dependent homeostasis. Nat Neurosci 2018;21(6):843-850

**Agents:** Diazepam; Ro 25-6981  
**Vehicle:** Saline; Propylene Glycol; DMSO  
**Route:** CSF/CNS (left lateral ventricle); SC  
**Species:** Mice  
**Pump:** 1007D  
**Duration:** 7 days

**ALZET Comments:** Dose (2 mg/mL Diazepam; 30mg/kg/day Ro 25-6981); 50% Propylene glycol, 50% saline used for Diazepam and 20% DMSO, 80% Saline for Ro 25-6981; Controls received mp w/ vehicle; animal info (C57BL/6, Pv-cre); post op. care (Meloxicam); enzyme inhibitor (Ro 25-6981 is a GluN2B-specific antagonist); Dental cement used; dependence;


**Agents:** Diazepam; zolpidem; TPA023; bretazenil  
**Vehicle:** PEG 400; alcohol; water, distilled  
**Route:** SC  
**Species:** Mice  
**Pump:** 2004  
**Duration:** 4 weeks

**ALZET Comments:** Controls received mp w/ vehicle; animal info (129 Sv/Ev Tac, 10-12 wks old); 95% PEG 400 used; 2.5% alcohol used; stress/adverse effects "severe hypothermia likely explains the death of seven animal's postsurgically..." pg 9; TPA023 is an alpha 2/3 selective GABAa receptor positive allosteric modulator

Food restriction enhances visual cortex plasticity in adulthood. Nature Communications 2011;2(;):U210-U217

**Agents:** Diazepam; mercaptopropionic acid  
**Vehicle:** Propylene glycol  
**Route:** CSF/CNS (visual cortex)  
**Species:** Rat  
**Pump:** 2002  
**Duration:** Not Stated

**ALZET Comments:** Animal info (Long Evans hooded, P60-P90, male, female); 50% propylene glycol used


**Agents:** Imipramine HCl, desmethyl; diazepam; fluoxetine; haloperidol  
**Vehicle:** Saline; DMSO; water  
**Route:** SC  
**Species:** Mice; Mice (neonate)  
**Pump:** 1002; 2002  
**Duration:** 14 days

**ALZET Comments:** Controls received mp w/either saline, 25, 50% or 100% DMSO; half-life (p. 191); animal info (male, Swiss Webster, 8-10 wks old); behavioral testing (swimming behavior, tail-suspension test, sucrose suspension test); "since drugs have relatively short half-lives in mice, to more closely mimic the human condition in which blood levels are maintained for prolonged periods, all agents were administered by osmotic minipump." (p. 191); all mice were housed singly for the duration of the experiment (3 weeks). Dose: desmethylimipramine in saline (10–11.5 mg/kg/d) in a 35–40 g mouse, fluoxetine dissolved at the same concentration in 50% DMSO; haloperidol dissolved in 25%DMSO at 0.3–0.34 mg/kg/day (2 mg/ml) and diazepam in 100% DMSO at 1–1.1 mg/kg/day (6.66 mg/ml).

GABA homeostasis contributes to the developmental programming of anxiety-related behavior. Brain Research 2008;1210(189-199

**Agents:** Diazepam  
**Vehicle:** Propylene glycol  
**Route:** SC  
**Species:** Mice; Mice (neonate)  
**Pump:** 1002; 2002  
**Duration:** 14 days

**ALZET Comments:** Controls received mp w/ vehicle; dose-response (Fig. 1); no stress (see pg. 193); post op. care (flumazenil); animal info (C57BL/6 x 129/SvJ, male, 14 days old, 60 days old); 50% DMSO used; behavioral testing (maze); wound clips used; 50% propylene glycol used

GABA homeostasis contributes to the developmental programming of anxiety-related behavior. Science 2004;303(5664):1678-1681

**Agents:** Diazepam  
**Vehicle:** Propylene Glycol  
**Route:** CSF/CNS (visual cortex)  
**Species:** Cat (kitten)  
**Pump:** 2004; 2ML4  
**Duration:** 4 weeks

**ALZET Comments:** Diazepam is a benzodiazepine agonist
Q7335: M. I. Arnot, et al. GABA A Receptor Gene Expression in Rat Cortex: Differential Effects of Two Chronic Diazepam Treatment Regimes. Journal of Neuroscience Research 2001;64(617-625)

**Agents:** Diazepam  
**Vehicle:** DMSO, propylene glycol;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** Not Stated;  
**Duration:** 14 days;  
**ALZET Comments:** Dose (15 mg/kg/day); 50% DMSO, 50% PG used; Controls received mp w/ vehicle; animal info (Male, Sprague-Dawley, 180–200 g); comparison of single daily injection vs mp; "Osmotic minipumps in vitro deliver diazepam at a relatively constant rate when 50% DMSO/50% PG is used as the vehicle (Arnot et al.,1996). Further, HPLC analysis of cortical tissue obtained from animals receiving diazepam via osmotic minipumps indicates that steady-state levels are achieved at 48 hr post implantation (159.2 +/- 14.7 ng/g) with the concentration (n = 3) at the 24-hr time point being 92.2 +/- 8.1 ng/g. A single daily sc injection (15 mg/kg diazepam; n = 3) resulted in an initial increase in diazepam levels in the cortex to a maximum concentration occurring 2 hr after injection (398.2 +/- 30.6 ng/g), followed by a decline to the limit of detection 24-hr post injection (33.8 +/- 2.4 ng/g)." pg.620; "Recently, we performed a behavioral comparison of animals receiving diazepam via daily injection demonstrating increased anxiety levels in the social interaction test relative to diazepam pump infused animals (Fernandes et al.,1999)." pg.624; “pumps were turned every second day” p.618


**Agents:** Diazepam  
**Vehicle:** Propylene glycol;  
**Route:** CSF/CNS (visual cortex);  
**Species:** Mice;  
**Pump:** 1007D;  
**Duration:** 4 days;  
**ALZET Comments:** Controls received mp w/ vehicle; comparison of icv injections vs. mp; 50% propylene glycol used


**Agents:** Tetrodotoxin; diazepam  
**Vehicle:** Propylene glycol;  
**Route:** CSF/CNS (visual cortex);  
**Species:** Mice;  
**Pump:** 1007D;  
**Duration:** 1 week;  
**ALZET Comments:** Controls received mp w/ vehicle; half-life (p. 1508), rapid breakdown (diazepam); monocular deprivation, localization of cannula delivery confirmed with dye


**Agents:** Diazepam; Clonazepam; flumazenil  
**Vehicle:** DMSO; Propylene glycol; Tetraglycol; 3H tracer; Radio-isotopes;  
**Route:** in vitro (egg);  
**Species:** Not Stated;  
**Pump:** 2ML4;  
**Duration:** no duration posted;  
**ALZET Comments:** no comment posted

P3118: C. D. Torchin, et al. A system for testing the development and reversal of anticonvulsant tolerance to benzodiazepines in mice. Epilepsy Research 1993;16(27-35

**Agents:** Diazepam; flumazenil; flunitrazepam; ZK-93426  
**Vehicle:** Tetraglycol;  
**Route:** SC;  
**Species:** mice;  
**Pump:** 2001;  
**Duration:** no duration posted;  
**ALZET Comments:** controls received mp with vehicle; tolerance; tetraglycol chosen as solvent because PEG, propylene glycol, tween, DMSO, saline, molecusol, and methyl cellulose did not maintain benzodiazepines in solution or proconvulsant activity was seen (see pg. 30); flumazenil is RO-15-1788; infusion delayed in some animals by using saline-filled catheter tubing; some animals received benzodiazepine + antagonist concomitantly


**Agents:** Diazepam  
**Vehicle:** Water; Tween 80;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2ML2;  
**Duration:** 12 days;  
**ALZET Comments:** no comment posted


**Agents:** Triazolam; Alprazolam; Diazepam  
**Vehicle:** Propylene glycol;  
**Route:** SC;  
**Species:** mice;  
**Pump:** 2001;  
**Duration:** 7 days;  
**ALZET Comments:** controls received mp with vehicle; functionality of mp verified by receptor binding study; comparison of oral alprozolam vs. mp; “. . .the use of implantable minipumps . . .permitted . . .development of behavioral tolerance associated with downregulation of benzodiazepine receptor binding and GABA receptor function. . .”; dependence

**Agents:** Diazepam  
**Vehicle:** Propylene glycol; Water;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2ML1;  
**Duration:** 7 days;  
**ALZET Comments:** functionality of mp verified by sectioning; neuroscience


**Agents:** Aminobutyric acid, Y-acetylenic Y-; Aminooxyacetic acid; Diazepam; THIP; Valproic acid  
**Vehicle:** Saline;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2ML2;  
**Duration:** 2 weeks;  
**ALZET Comments:** controls received mp w/saline; diazepam too unstable to be used in mp; epilepsy; functionality of mp verified after 14 day exper. period - all 50 mps worked accurately; stability of VPA, THIP, GAG and AOAA


**Agents:** Adinazolam; Diazepam  
**Vehicle:** Benzyl alcohol; Ethanol; Propylene glycol; Sodium benzoate; Water;  
**Route:** IP;  
**Species:** Rat;  
**Pump:** 2002;  
**Duration:** 5 and 14 days;  
**ALZET Comments:** comparison of adinazolam. iv injec vs. mp infusion; comparison of agents effects; adinazolam. used with water vehicle, Diaz. with combination vehicle

**Lorazepam**


**Agents:** Lorazepam  
**Vehicle:** PEG 400;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** Not Stated;  
**Duration:** 1, 14 days;  
**ALZET Comments:** Controls received mp w/ vehicle; functionality of mp verified by lorazepam plasma concentrations; tolerance; animal info (male, CD-1, 2-3 months old, 10-12 months old, 22-24 months old)


**Agents:** Lorazepam  
**Vehicle:** PEG 400;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** Not Stated;  
**Duration:** 1,14 days;  
**ALZET Comments:** Controls received mp w/ vehicle; plasma lorazepam levels; brains examined postmortem for membrane binding; lorazepam is a benzodiazepine with anxiolytic and anti-insomnia properties;


**Agents:** Lorazepam  
**Vehicle:** PEG 400;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** Not Stated;  
**Duration:** 7 days;  
**ALZET Comments:** Controls received mp w/vehicle; tolerance


**Agents:** Lorazepam  
**Vehicle:** PEG 400;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** Not Stated;  
**Duration:** 7 days;  
**ALZET Comments:** Tolerance


**Agents:** Alprazolam; Lorazepam  
**Vehicle:** PEG 400;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** Not Stated;  
**Duration:** 7, 8, or 14 days;  
**ALZET Comments:** Controls received vehicle; tolerance


**Agents:** Lorazepam; PK 11195  
**Vehicle:** Not Stated;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** Not Stated;  
**Duration:** Not Stated;  
**ALZET Comments:** Controls received mp w/ vehicle; tolerance; Lorazepam and PK11195 infused separately and together; PK11195 is a peripheral-type site ligand; pumps chosen because they produce “constant plasma and brain concentrations".

**Agents:** Alprazolam; Lorazepam  
**Vehicle:** PEG 400  
**Route:** IP; Species: Mice; **Pump:** 2001; **Duration:** 6 days;  
**ALZET Comments:** Controls received mp w/ vehicle


**Agents:** Lorazepam  
**Vehicle:** PEG 400; **Route:** SC; Species: Mice; **Pump:** Not Stated; **Duration:** 7 days;  
**ALZET Comments:** Tolerance


**Agents:** Lorazepam  
**Vehicle:** PEG 400; **Route:** SC; Species: Mice; **Pump:** Not Stated; **Duration:** 7 days;  
**ALZET Comments:** Tolerance


**Agents:** Lorazepam  
**Vehicle:** PEG 400; **Route:** SC; Species: Mice (pregnant); **Pump:** 2001; **Duration:** 7 days;  
**ALZET Comments:** Teratology


**Agents:** Lorazepam  
**Vehicle:** PEG 400; **Route:** SC; Species: Mice; **Pump:** 2001; 2002; **Duration:** 7 days;  
**ALZET Comments:** no comment posted


**Agents:** Lorazepam  
**Vehicle:** PEG 400; **Route:** SC; Species: Mice; **Pump:** 2001; **Duration:** 7 days;  
**ALZET Comments:** tolerance; functionality of mp verified by plasma, brain levels


**Agents:** Lorazepam  
**Vehicle:** PEG 400; **Route:** SC; Species: Mice; **Pump:** 2001; 2002; **Duration:** 14 days;  
**ALZET Comments:** Dose-response (graph, text); tolerance; functionality of mp verified by plasma levels


**Agents:** Alprazolam; Lorazepam  
**Vehicle:** Ethanol; PEG; Saline; **Route:** SC; Species: Rat; **Pump:** 2ML2; **Duration:** 12 days;  
**ALZET Comments:** no comment posted

**Triazolam**


**Agents:** Triazolam  
**Vehicle:** Propylene glycol; **Route:** SC; Species: Rat; **Pump:** 2ML2; **Duration:** 14 days;  
**ALZET Comments:** controls received mp w/ vehicle; tolerance; dependence

P2115: L.-W. Zhou, et al. Triazolam blocks the initial rotational effects of quinpirole but permits the later developing reduction of dopamine D2-mediated rotational behavior and dopamine D2 receptors. European Journal of Pharmacology 1992;218(219-227

**Agents:** Quinpirole HCl; Sulpiride; Triazolam  
**Vehicle:** Ascorbic acid; DMSO; **Route:** SC; Species: mice; **Pump:** 2001; **Duration:** 6 days;  
**ALZET Comments:** Quinpirole is a dopamine agonist, antidepressant; stability verified in vitro for 7 days

**Agents:** Triazolam; Alprazolam; Diazepam  
**Vehicle:** Propylene glycol  
**Route:** SC  
**Species:** mice  
**Pump:** 2001  
**Duration:** 7 days  
**ALZET Comments:** controls received mp with vehicle; functionality of mp verified by receptor binding study; comparison of oral alprozolam vs. mp; "...the use of implantable minipumps...permitted...development of behavioral tolerance associated with downregulation of benzodiazepine receptor binding and GABA receptor function..."; dependence