References on the Administration of Anticonvulsive Agents
Using ALZET® Osmotic Pumps

1. Carbamazepine


ALZET Comments: Carbamazepine, baclofen, clomipramine; DMSO, PEG, Ethyl Alcohol, Acetone; SC; Rat; 2ML1; Controls received mp w/ vehicle; animal info (7 weeks old); dimethyl sulfoxide, propylene glycol, ethyl alcohol, and acetone at a ratio of 42:42:15:1; post op. care (morphine 5 mg/day); behavioral testing (Facial grooming); Therapeutic indication (Trigeminal neuralgia, neuropathic pain);
Dose (30 mg/day carbamazepine (the first-line drug treatment for trigeminal neuralgia), 1.06 mg/day baclofen, 4.18 mg/day clomipramine, and 5 mg/day morphine).


ALZET Comments: Carbamazepine; DMSO; propylene glycol; ethyl alcohol; acetone; SC; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; functionality of mp verified by serum drug levels; 42% DMSO used; identified 3 mg/kg/day as the highest dose that could be reliably administered via minipumps over a 14-day period at 37 degrees Celsius, pg. 1969.


ALZET Comments: Carbamazepine; levetiracetam; DMSO; Propylene glycol; ethanol, saline; IP; Rat; 7 days; Controls received mp/vehicle; functionality of mp verified by drug serum levels; dose-response (text p.1428); carbamazepine was dissolved in 42.5% DMSO/42% Propylene glycol/15% ethanol. Levitiracetam was dissolved in saline; 2-day recovery period given using coiled PE-40 tubing; epilepsy; anticonvulsant.

2. Deprenyl


ALZET Comments: Clorgyline; phenelzine; deprenyl; SC; Rat; 2, 21 days; Controls received mp w/ saline; enzyme inhibitor (MAO, monoamine oxidase); animal info (male, Sprague Dawley, 250-300 g.).


ALZET Comments: Clorgyline; Deprenyl; Saline; SC; Mice (pregnant); 2002; 2004; 6 weeks; Controls received mp w/ vehicle; teratology; enzyme inhibitors (monoamine oxidase inhibitors); 2002 pumps were replaced w/ 2004 pumps after 2 weeks to complete a 6 week infusion; agents infused singly or concomitant in the same pump.


ALZET Comments: Deprenyl, L-; Water, distilled; SC; mice; 2002; 2004; 2,4 weeks; controls received mp w/saline; functionality of mp verified by residual volume; comparison of daily i.p. injections vs. mp; good methods (p. 1588); anticonvulsant; also called selegiline.

P3400: M. C. Carrillo, et al. The optimal dosage of (-) deprenyl for increasing superoxide dismutase activities in several brain regions decreases with age in male Fischer 344 rats. Life Sci 1993;52(1925-1934

ALZET Comments: Deprenyl; Saline; SC; Rat; 3 weeks; controls received mp w/saline; dose-response.
ALZET Comments: Imipramine HCl; Desipramine HCl; Clomipramine HCl; Tranylcypromine HCl; Phenelzine sulfate; Clorgyline HCl; Deprenyl HCl; SC; Rat; 2002; 2ML4; 14,28 days; antidepressant; controls received mp with vehicle; drug concentrations determined from Greenshaw program.

3. Levetiracetam

Agents: Levetiracetam Vehicle: Saline; Route: SC; Species: Mice; Pump: 1004; Duration: 4 weeks;
ALZET Comments: Dose (75 mg/kg/day); Controls received mp w/ vehicle; animal info (); levetiracetam aka LEV; neurodegenerative (Alzheimer's);

Agents: Z944; levetiracetam Vehicle: saline, normal, propylene glycol and DMSO buffered; Route: SC; Species: Rat; Pump: 2ML1; Duration: 1, 4 weeks;
ALZET Comments: "Dose ((Z944 60 mg/kg/day), (levetiracetam 200 mg/kg/day)); 40% propylene glycol, 40% DMSO, and 20% normal saline solution used; Controls received mp w/ vehicle; animal info (11 weeks, male, Wistar); behavioral testing (Sucrose preference, Elevated plus maze, Open field, Morris water maze, Forced swim test); Z944 is a highly potent and selective T-type Ca2+ channel antagonist; neurodegenerative (Temporal lobe epilepsy); Therapeutic indication (continuous levetiracetam infusion significantly reduced the average number of seizures and the seizure severity in comparison to vehicle treated animals, but without affecting the latency to the first seizure. Z944 treatment after SE significantly prolonged the latency to develop the first spontaneous seizure and also reduced the average number of seizures in comparison to the vehicle treated counterparts); 

Agents: Levetiracetam Vehicle: Saline; Route: SC; Species: Rat; Pump: 2ML4; Duration: 28 days;
ALZET Comments: Dose (10 mg/kg/day); Controls received mp w/ vehicle; animal info (Aged, male Long-Evans rats);

Q4492: M. Levesque, et al. The anti-ictogenic effects of levetiracetam are mirrored by interictal spiking and high-frequency oscillation changes in a model of temporal lobe epilepsy. SEIZURE-EUROPEAN JOURNAL OF EPILEPSY 2015;25(18-25
Agents: Levetiracetam Vehicle: Saline; Route: SC; Species: Rat; Pump: 2ML2; Duration: 2 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 250-300g); cardiovascular; “These pumps deliver a continuous dosing over 2 weeks, circumventing the need for repetitive invasive blood sampling. “ pg 19;

Agents: Levetiracetam; SB202190; BQ788 Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 1003D; Duration: 3 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 7 days); pumps replaced between trials;

4. Phenobarbital

R0242: W. Loescher. The pharmacokinetics of antiepileptic drugs in rats: Consequences for maintaining effective drug levels during prolonged drug administration in rat models of epilepsy. Epilepsia 2007;48(7):1245-1258
ALZET® Bibliography

ALZET Comments: Levetiracetam; phenobarbital; phenytoin; valproic acid; vigabatrin; Water, distilled; PEG 300; glycerol; PEG 400; propylene glycol; SC; IP; Rat; mice; gerbils; 2ML1; 2ML2; 1-4,2 weeks; 7 days; Comparison of IV, IP injections vs. food or water delivery vs mp; pumps replaced (every week in one set of experiments); stress/adverse reaction: (see pg. 1255); peritoneal irritation, peritonitis in some of the IP experiments); half-life (p. 1247) table 1 (18 compounds); animal info (epileptic, Sprague-Dawley, Wistar); review; see p. 1254-1255; see table 4 for advantages + disadvantages of different application routes.

ALZET Comments: Phenobarbital; SC; Rat; 2002; 8 days; Comparison of phenobarb. consumed po in drinking water vs. mp infusion; author states advantages of mp use.

ALZET Comments: Chlorpromazine; haloperidol; phenobarbital; promethazine; SC; Rat; 2001; 8 days; Comparison of agents effects.

ALZET Comments: Phenobarbital, sodium; Valproate, sodium; Water; SC; mice (pregnant); 2001; 2002; 1 and 2 weeks; no stress see p. 1580, 1582; 1-2 pumps/animal; VPA and PB used singly and in combination in mp.

ALZET Comments: Phenobarbital; Water; IP; Rat; 5 days; bolus injec. vs. mp infusion.

5. Promethazine

ALZET Comments: Chlorpromazine; haloperidol; phenobarbital; promethazine; SC; Rat; 2001; 8 days; Comparison of agents effects.

6. Tiagabine

ALZET Comments: Vigabatrin; Tiagabine; SC; Rat; 2 months; Neuroprotection; pump use mentioned on p. 147 and 155; long-term study.

ALZET Comments: Tiagabine;; Saline;; IV (jugular);; Rat;; 2ML2;; 14 days;; Controls received mp w/ vehicle; functionality of mp verified by plasma levels; dose-response (graph p. 145); comparison of IV injections vs. mp; Tiagabine is a GABA uptake inhibitor; seizure prevention; Epilepsy;;

ALZET Comments: Tiagabine; Propylene glycol; SC; Rat; 2ML1; 7 days; functionality of mp verified by in vitro testing and residual volumes; dose-response; half-life (p. 70); compound stable for one week (see p. 78); stability.

7. Valproic Acid

ALZET Comments: Valproic acid; IR (intra-renal); Rat; 2ML2; 10 days; Dose (50mg/Kg/d); Controls received mp w/ vehicle; animal info (male Dahl salt-sensitive rats, SS-13BN).

ALZET Comments: Valproic acid; Saline; CSF/CNS (left midbrain); Mice (transgenic); 1002; 2 weeks; 4 weeks; Dose (0.25 mg/µl); Controls received mp w/ vehicle; animal info (NestinCreERT2 C57BL/6 mice; ALZET brain infusion kit 1 used; Brain coordinates (3.0 mm posterior to Bregma, 1.5 mm lateral to the midline, and 4.0 mm below the surface of the brain); neurodegenerative (Parkinson’s disease).

ALZET Comments: Valproic acid; PBS; Rat; 5 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 300-400g); ischemia (cerebral); dose-response (pg 4-6); behavioral testing (modified limb-placing test); cardiovascular; bp measured using tail cuff.

ALZET Comments: Valproic acid-PEG; CSF/CNS (caudate putamen); CSF/CNS (sagittal fissure); Rat; 2004; 25 days; Animal info (male, Sprague Dawley, 275-300g); ALZET brain infusion kit 1 used; behavioral testing (elevated plus maze, open field test); wound clips used.

ALZET Comments: Valproic acid; PBS; CSF/CNS (intrathecal); Rat; 1003D; 3 days; Dose (1.5 µg VPA); Controls received mp w/ vehicle; animal info (Female adult Sprague-Dawley rats (n =41; 250 +/-30 g)); post op. care (sodium ampicillin); behavioral testing (locomotor function); enzyme inhibitor (histone deacetylase (HDAC) inhibitor); ALZET brain infusion kit 3 used; spinal cord injury.

8. Vigabatrin

ALZET Comments: Vigabatrin; PBS; SC; Mice; 2002; 12 days; Dose (35, 70, and 140 mg/kg/d); Controls received mp w/ vehicle; animal info (Male C57BL/6J mice, 8-10 weeks old, 20.8-26.1 g ); post op. care (Carprofen); dependence.

Q5697: K. R. Vogel, et al. mTOR Inhibition Mitigates Molecular and Biochemical Alterations of Vigabatrin-Induced Visual Field Toxicity in Mice. Pediatr Neurol 2017;66(44-52 e1
ALZET Comments: Vigabatrin; PBS; SC; Mice; 2002; 14 days; Controls received mp w/ vehicle; animal info (C57BL6, 8 weeks old).
R0242: W. Loescher. The pharmacokinetics of antiepileptic drugs in rats: Consequences for maintaining effective drug levels during prolonged drug administration in rat models of epilepsy. Epilepsia 2007;48(7):1245-1258
ALZET Comments: Levetiracetam; phenobarbital; phenytoin; valproic acid; vigabatrin; Water, distilled; PEG 300; glycerol; PEG 400; propylene glycol; SC; IP; Rat; mice; gerbils; 2ML1; 2ML2; 1-4,2 weeks; 7 days; Comparison of IV, IP injections vs. food or water delivery vs mp; pumps replaced (every week in one set of experiments); stress/adverse reaction: (see pg. 1255); peritoneal irritation, peritonitis in some of the IP experiments); half-life (p. 1247) table 1 (18 compounds); animal info (epileptic, Sprague-Dawley, Wistar); review; see p. 1254-1255; see table 4 for advantages + disadvantages of different application routes.

ALZET Comments: Vigabatrin; Tiagabine; SC; Rat; 2 months; Neuroprotection; pump use mentioned on p. 147 and 155; long-term study.

ALZET Comments: Vigabatrin; Saline; SC; Rat; 2ML2; 10 weeks; controls received mp w/ vehicle; long-term study, pumps replaced every 2 weeks for 10 weeks; epilepsy; seizures.