



References on the Administration of Barbiturates Using ALZET® Osmotic Pumps

1. Barbital

P0010: C. Siew, *et al.* Osmotic minipumps for administration of barbital to mice: demonstration of functional tolerance and physical dependence. *J. Pharmacol. Exp. Ther* 1978;204(3):541-546

Agents: Barbital, sodium **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 192 hours;

ALZET Comments: Barbital plasma levels taken; pumps replaced every 96 hours; tolerance; dependence; multiple pumps per animal (2); "This convenient implantation procedure may be a useful model for quantitative study of barbiturate tolerance and dependence as well as various chronic effects of other drugs." p. 545

2. Pentobarbitol

P5450: Y. Kim, *et al.* Changes of the level of G protein alpha-subunit mRNA by tolerance to and withdrawal from pentobarbital in rats. *Neurochemical Research* 2002;27(6):527-533

Agents: Pentobarbital **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ vehicle; tolerance; dependence; one week recovery period after cannula placement

P4317: C.-G. Jang, *et al.* Autoradiography of [³H] glutamate binding during pentobarbital tolerance and withdrawal in the rat. *Brain Research Bulletin* 1999;48(1):99-102

Agents: Pentobarbital **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2ML1; **Duration:** 6 days;

ALZET Comments: Controls received mp with vehicle; tolerance; dependence; animals allowed one week recovery after cannula placement

P4177: S. Oh, *et al.* Changes in (3H)forskolin binding to adenylate cyclase and (3H)phorbol dibutyrate binding to protein kinase c in pentobarbital tolerant/dependent rats. *Neurochem. Res* 1998;23(4):463-467

Agents: Pentobarbital **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;

ALZET Comments: guide cannula implanted; rats were allowed 1 week recovery before implantation of pump; tolerance; dependence

P4188: C.-G. Jang, *et al.* Changes in NMDAR2 subunit mRNA levels during pentobarbital tolerance/withdrawal in the rat brain: an in situ hybridization study. *Neurochem. Res* 1998;23(11):1371-1377

Agents: Pentobarbital **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2ML1; **Duration:** 6 days;

ALZET Comments: controls received mp w/saline; tolerance

P3852: S. Oh, *et al.* Role of NMDA receptors in pentobarbital tolerance/dependence. *Neurochem. Res* 1997;22(7):767-774

Agents: Pentobarbital **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;

ALZET Comments: controls received mp w/saline; tolerance; dependence

P3421: T. Suzuki, *et al.* An autoradiographic study of [3H]flunitrazepam binding sites in the brain of rat made tolerant to and dependent on pentobarbital. *European Journal of Pharmacology* 1996;295(169-179

Agents: Pentobarbital **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2ML1; **Duration:** 6 days;

ALZET Comments: controls received vehicle infusion; tolerance; dependence; recipe for equithesin anesthesia provided on p. 170

P3422: T. Ito, *et al.* Chronic pentobarbital administration alters g-aminobutyric acid(A) receptor a(6)-subunit mRNA levels and diazepam-insensitive [3H]Ro15-4513 binding. *Synapse* 1996;22(106-113

Agents: Pentobarbital **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2ML1; **Duration:** 6 days;

ALZET Comments: tolerance; dependence



P3351: T. Suzuki, *et al.* Changes in [3H] Flunitrazepam binding in the brain of rats made tolerant to and dependent upon pentobarbital. *Life Sci* 1995;57(5):L-69

Agents: Pentobarbital **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2ML1; **Duration:** 6 days;
ALZET Comments: controls received mp w/saline; tolerance; dependence; animals allowed 1 week recovery after cannula placement

P3112: Y. T. Tseng, *et al.* In situ hybridization evidence of differential modulation by pentobarbital of GABAA receptor α 1- and β 3-subunit mRNAs. *J. Neurochem* 1994;63(301-309

Agents: Pentobarbital **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2ML1; **Duration:** 6 days;
ALZET Comments: tolerance

P3173: T. Miyaoka, *et al.* Binding characteristics of [3H]flunitrazepam in pentobarbital-withdrawal rats. *Neurochem. Res* 1994;19(1):37-42

Agents: Pentobarbital **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2ML1; **Duration:** 6 days;
ALZET Comments: controls received mp with saline; animals allowed 1 week recovery after cannula placement

P3111: Y. T. Tseng, *et al.* Differential effects on GABAA receptor γ 2-subunit messenger RNA by tolerance to and withdrawal from pentobarbital -- an in situ hybridization study. *Life Sci* 1993;53(L321-L326

Agents: Pentobarbital **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Rat; **Pump:** Not Stated; **Duration:** no duration posted;
ALZET Comments: tolerance

P3113: Y. T. Tseng, *et al.* Region-specific changes of GABAA receptors by tolerance to and dependence upon pentobarbital. *European Journal of Pharmacology* 1993;236(23-30

Agents: Pentobarbital **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2ML1; **Duration:** 6,7 days;
ALZET Comments: controls received mp with saline; tolerance; dependence; animals allowed 1 week recovery after cannula placement; brain and serum samples taken at 0, 2, 4, 7 days during infusion & 6, 24, 48 hrs. after withdrawal

P2338: K. Toshiyuki, *et al.* Induction of tolerance to and physical dependence on phentobarbital continuous intracerebroventricular administration. *J. Pharmacol. Exp. Ther* 1993;266(3):1300-1305

Agents: Pentobarbital **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2ML1; **Duration:** 6 days;
ALZET Comments: tolerance; dependence

P3675: T. Kimura, *et al.* Induction of tolerance to and physical dependence on pentobarbital continuous intracerebroventricular administration. *J. Pharmacol. Exp. Ther* 1993;266(3):1300-1305

Agents: Pentobarbital, sodium **Vehicle:** Saline, normal; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2ML1; **Duration:** 6 days;
ALZET Comments: controls received mp w/ filtered, normal saline; tolerance; dependence; good illustration of pump placement (p. 1301)



3. 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

Agents: Levetiracetam; phenobarbital; phenytoin; valproic acid; vigabatrin **Vehicle:** Water, distilled; PEG 300; glycerol; PEG 400; propylene glycol; **Route:** SC; IP; **Species:** Rat; mice; gerbils; **Pump:** 2ML1; 2ML2; **Duration:** 1-4,2 weeks; 7 days;

ALZET Comments: 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

P0494: F. J. Hock, *et al.* A novel method for the administration of the enzyme inducer phenobarbital to rats via an osmotic minipump. *IRSC Med. Sci. : Biochem* 1984;12(8):661

Agents: Phenobarbital **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 8 days;

ALZET Comments: Comparison of phenobarb. consumed po in drinking water vs. mp infusion; author states advantages of mp use

P0447: T. P. Davis, *et al.* Centrally acting drugs alter in vitro B-endorphin processing in the rat. *European Journal of Pharmacology* 1984;100(249-251

Agents: Chlorpromazine; haloperidol; phenobarbital; promethazine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 8 days;

ALZET Comments: Comparison of agents effects

P0401: W. Kuhn, *et al.* A new method for kinetic studies of drug interactions in experimental animals during steady state: controlled-rate application of valproic acid, phenobarbital and their combinations via implanted osmotic minipumps in the mouse. *Drug Research* 1983;33(11):1579-1582

Agents: Phenobarbital, sodium; Valproate, sodium **Vehicle:** Water; **Route:** SC; **Species:** mice (pregnant); **Pump:** 2001; 2002; **Duration:** 1 and 2 weeks;

ALZET Comments: no stress see p. 1580, 1582; 1-2 pumps/animal; VPA and PB used singly and in combination in mp

P0311: I. M. Kapetanovic, *et al.* Phenobarbital pharmacokinetics in rat as a function of age. *Drug Metabolism and Disposition* 1982;10(6):586-589

Agents: Phenobarbital **Vehicle:** Water; **Route:** IP; **Species:** Rat; **Pump:** Not Stated; **Duration:** 5 days;

ALZET Comments: bolus injec. vs. mp infusion

P0036: B. Tabakoff, *et al.* The effect of selective lesions of brain noradrenergic systems on the development of barbiturate tolerance in rats. *Brain Pathology* 1979;176(327-336

Agents: Phenobarbital, sodium **Vehicle:** Propylene glycol; Water; **Route:** CSF/CNS; **Species:** Rat; **Pump:** Not Stated; **Duration:** 3 days;

ALZET Comments: some groups given 6-OHDA or vehicle of ascorbic acid in Artificial CSF prior to infusion