



## References on the Administration of Barbituates Using ALZET® Osmotic Pumps

### 1. 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

**ALZET Comments:** Pentobarbital; Saline; CSF/CNS; Rat; 2001; 7 days; Controls received mp w/ vehicle; tolerance; dependence; one week recovery period after cannula placement.

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

**ALZET Comments:** Pentobarbital; Saline; CSF/CNS; Rat; 2ML1; 6 days; 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

**ALZET Comments:** Pentobarbital; CSF/CNS; Rat; 2ML1; 7 days; 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

**ALZET Comments:** Pentobarbital; Saline; CSF/CNS; Rat; 2ML1; 6 days; 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

**ALZET Comments:** Pentobarbital; Saline; CSF/CNS; Rat; 2ML1; 7 days; 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. *Eur. J. Pharmacol* 1996;295(169-179)

**ALZET Comments:** Pentobarbital; Saline; CSF/CNS; Rat; 2ML1; 6 days; 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)

**ALZET Comments:** Pentobarbital; CSF/CNS; Rat; 2ML1; 6 days; 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

**ALZET Comments:** Pentobarbital; CSF/CNS; Rat; 2ML1; 6 days; 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 a1- and B3-subunit mRNAs. *J. Neurochem* 1994;63(301-309)

**ALZET Comments:** Pentobarbital; CSF/CNS; Rat; 2ML1; 6 days; tolerance.

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

**ALZET Comments:** Pentobarbital; CSF/CNS; Rat; 2ML1; 6 days; controls received mp with saline; animals allowed 1 week recovery after cannula placement.



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

**ALZET Comments:** Pentobarbital; CSF/CNS; Rat; no duration posted; tolerance.

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

**ALZET Comments:** Pentobarbital; Saline; CSF/CNS; Rat; 2ML1; 6,7 days; 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

**ALZET Comments:** Pentobarbital; Saline; CSF/CNS; Rat; 2ML1; 6 days; 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

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

## 2. Phenobarbital

**R0242:** W. Loeschler. 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.

**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

**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.

**P0447:** T. P. Davis, *et al.* Centrally acting drugs alter in vitro B-endorphin processing in the rat. *Eur. J. Pharmacol* 1984;100(249-251)

**ALZET Comments:** Chlorpromazine; haloperidol; phenobarbital; promethazine; SC; Rat; 2001; 8 days; 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. *Arzneimittelforschung* 1983;33(11):1579-1582

**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.

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

**ALZET Comments:** Phenobarbital; Water; IP; Rat; 5 days; 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 Research* 1979;176(327-336)

**ALZET Comments:** Phenobarbital, sodium; Propylene glycol; Water; CSF/CNS; Rat; 3 days; some groups given 6-OHDA or vehicle of ascorbic acid in Artificial CSF prior to infusion.