



## References on the Administration of Cholinergic Agents Using ALZET® Osmotic Pumps

### 1. Acetylcholine

**P6643:** A. E. Reyes, *et al.* Acetylcholinesterase-A beta complexes are more toxic than A beta fibrils in rat hippocampus - Effect on rat beta-amyloid aggregation, laminin expression, reactive astrocytosis, and neuronal cell loss. *American Journal of Pathology* 2004;164(6):2163-2174

**ALZET Comments:** Amyloid protein, beta (1-40); acetylcholinesterase; PBS; CSF/CNS (dorsal hippocampus); Rat; 2002; 4 weeks; 14 days; Comparison of acute injections vs. mp; brain tissue distribution; peptides; neurodegenerative (Alzheimer's disease).

**P1926:** C. Touvay, *et al.* Effect of long-term infusion of platelet-activating factor on pulmonary responsiveness and morphology in the guinea-pig. *Pulmon. Pharm* 1991;4(43-51)

**ALZET Comments:** Acetylcholine; Platelet activating factor; Albumin, bovine serum; Saline; IV (jugular); Guinea pig; 2002; 15 days; Cholinergic agent; stability verified by measuring biological activity of residual solution from pumps after 12 days, no loss of activity observed.

**P0812:** T. Shimazu, *et al.* Chronic infusion of norepinephrine into the ventromedial hypothalamus induces obesity in rats. *Brain Research* 1986;369(1/2):215-223

**ALZET Comments:** Acetylcholine chloride; Cefalotin; Cholecystokinin tetrapeptide; Epinephrine HCl; Bombesin; Endorphin, B-; Enkephalin, methionine-; Norepinephrine HCl; Saline; Sodium bisulfite; CSF/CNS (hypothalamus); Rat; 2002; 5-20 weeks; Cholinergic agent; pumps replaced periodically; mp connected to perm. steel cannula in hypothalamus; cannula fitted w/removable protector; (see p.217); agents infused sep. (cefalotin infused w/each agent); long-term study; peptides.

**P0439:** B. Costall, *et al.* Locomotor hyperactivity caused by dopamine infusion into the nucleus accumbens of rat brain: specificity of action. *Psychopharmacology* 1984;82(174-180)

**ALZET Comments:** Acetylcholine HCl; Aminobutyric acid, Y-; Serotonin bimaleinate; Dopamine HCl; Norepinephrine bitartrate; Nitrogen; Sodium metabisulfite; CSF/CNS (nucleus accumbens); Rat; 2002; 13 days; Cholinergic agent; comparison of agents effects; no stress p. 175; stability of substances remaining in pump after 13 days was verified.

### 2. Atropine

**Q4725:** T. Kashihara, *et al.* beta(2)-Adrenergic and M(2)-muscarinic receptors decrease basal t-tubular L-type Ca(2+) channel activity and suppress ventricular contractility in heart failure. *EUROPEAN JOURNAL OF PHARMACOLOGY* 2014;724(1):122-131

**ALZET Comments:** Atropine; ICI-118,551; Saline; DMSO; Mice; 1004; 21 days; Animal info (male, C57BL6, 8-10 weeks old); cardiovascular;.

**Q4399:** M. Demion, *et al.* Trpm4 Gene Invalidation Leads to Cardiac Hypertrophy and Electrophysiological Alterations. *PLoS One* 2014;9(U821-U848)

**ALZET Comments:** Atropine; Mice; 2001; 6 hours; Animal info (male, Trpm4 -/-, 12-32 weeks old); cardiovascular;.

**Q0436:** G. Vrbova, *et al.* Chemical communication between regenerating motor axons and Schwann cells in the growth pathway. *European Journal of Neuroscience* 2009;30(3):366-375

**ALZET Comments:** Gallamine triethiodide; tubocurarine; atropine; suramin; CSF/CNS (sciatic nerve); Rat; 2ML4; 2-4 weeks; Controls received mp w/saline; animal info (female, adult, Sprague Dawley, 200-220 g); schematic illustration of pump with silastic catheter, Fig 1b.

**P8761:** C. M. Hildreth, *et al.* Impaired serotonergic regulation of heart rate may underlie reduced baroreflex sensitivity in an animal model of depression. *American Journal of Physiology-Heart and Circulatory Physiology* 2008;294(1):H474-H480



**ALZET Comments:** Metoprolol; atropine methylnitrate; SC; Rat; 3 days; Cardiovascular; post op. care (carprofen, cephazolan); animal info (male, Sprague Dawley Flinders Resistive Line, Flinders Sensitive Line, 10-14 wks old).

**P5092:** E. Dupont, *et al.* Atropine prevents the changes in the hindlimb cortical area induced by hypodynamia-hypokinesia. *Brain Research* 2002;926(51-57)

**ALZET Comments:** Atropine sulfate; CSF, artificial; CSF/CNS (cortex); Rat; 2002; 14 days; controls received mp w/ vehicle; brain tissue distribution; atropine is a muscarinic antagonist; agent infused topically to cortex, crosses blood-brain barrier to reach and be absorbed in primary somatosensory cortex; "We used an ALZET pump because (i) administration was continuous and constant and (ii) atropine was delivered onto the cortical surface." (p. 55).

**P5328:** A. S. Basile, *et al.* Deletion of the M-5 muscarinic acetylcholine receptor attenuates morphine reinforcement and withdrawal but not morphine analgesia. *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA* 2002;99(17):11452-11457

**ALZET Comments:** Atropine sulfate; SC; Mice; 7 days; Muscarinic antagonist.

**P2824:** P. A. Witt-Enderby, *et al.* Regulation of airway muscarinic cholinergic receptor subtypes by chronic anticholinergic treatment. *Mol. Pharmacol* 1995;47(485-490)

**ALZET Comments:** Atropine sulfate; SC; rabbit; 2ML4; 7, 14 or 27 days; controls received mp with vehicle; functionality of mp verified by taking blood plasma levels.

**P2721:** P. A. Lapchak, *et al.* Cholinergic regulation of hippocampal brain-derived neurotrophic factor mRNA expression: evidence from lesion and chronic cholinergic drug treatment studies. *Neuroscience* 1993;52(3):575-585

**ALZET Comments:** Atropine sulfate; Nicotine bitartrate; Rat; 2002; 14 days; controls received mp w/ saline or were unlesioned.

**P2119:** S. J. Wall, *et al.* Differential regulation of subtypes M1-M5 of muscarinic receptors in forebrain by chronic atropine administration. *J. Pharmacol. Exp. Ther* 1992;262(2):584-588

**ALZET Comments:** Atropine; SC; Rat; 2ML2; 14 days; no comment posted.

**P3493:** J. Ellis, *et al.* Chronic lithium treatment prevents atropine-induced supersensitivity of the muscarinic phosphoinositide response in rat hippocampus. *Biol. Psychiatry* 1990;28(609-619)

**ALZET Comments:** Atropine sulfate; Saline; SC; Rat; 6 days; controls received mp w/ saline.

**P1751:** G. E. Watson, *et al.* The effect of chronic atropine treatment on salivary composition and caries in rats. *J. Dent. Res* 1989;68(12):1739-1745

**ALZET Comments:** Atropine; Saline; SC; Rat; 2ML4; 24 days; Functionality of mp verified by measuring blood levels; stability verified at 7 days in vitro.

**P1359:** R. M. Levin, *et al.* Effect of chronic atropine administration on the rat urinary bladder. *J. Urol* 1988;139(1347-1349)

**ALZET Comments:** Atropine; Saline; SC; Rat; 2ML2; 1, 2, 4, 7, 11, 14 days and 6 hours; dose-response (text); functionality of mp verified by serum levels.

**P0683:** N. W. Pedigo Jr, *et al.* Reduced muscarinic receptor plasticity in frontal cortex of aged rats after chronic administration of cholinergic drugs. *Life Sci* 1985;37(15):1443-1449

**ALZET Comments:** Methylatropine; Oxotremorine; Saline; CSF/CNS; Rat; 2ML4; 3 weeks; comparison of agents effects in young and old rats; stability of drugs at 37C determined at weekly intervals for 5 wks by bioassay; delivery into lateral cerebroventricle.

**P0908:** P. Frey. Changes in cholecystokinin content in rat brain after subchronic treatment with neuroleptics. *Ann. N. Y. Acad. Sci* 1985;448(601-603)



**ALZET Comments:** Flupenthixol, cis-; Flupenthixol, trans-; Amitriptyline; Amphetamine; Atropine; Chlorpromazine; Clozapine; Fluphenazine; Haloperidol; Morphine; Prazosin; SC; Rat; 2 weeks; mp model not stated; comparison of sc injections vs. mp infusion; antihypertensive.

**P0423:** Y. Y. Wu, *et al.* Mechanisms underlying the pressor responses to acute and chronic intraventricular administration of carbachol in the rat. *J. Pharmacol. Exp. Ther* 1984;228(2):354-363

**ALZET Comments:** Atropine methyl nitrate; Hexamethonium bromide; Carbachol; Saline; CSF/CNS; SC; Rat; 2001; 2002; 1-12 days; comparison of agents effects; pumps primed in saline before implant; carbachol admin. sc in one exp., other exp. deliv. Car., Hex., & Atr. icv; antihypertensive.

### 3. Carbachol

**Q4121:** Y. Suzuki, *et al.* Vagal Hyperactivity Due to Ventromedial Hypothalamic Lesions Increases Adiponectin Production and Release. *Diabetes* 2014;63(16):1637-1648

**ALZET Comments:** Carbachol; Saline; SC; Rat; 5 days; Controls received mp w/ vehicle; animal info (female, Sprague-Dawley, 13 weeks old); carbachol is a parasympathetic stimulator; obesity;.

**Q1999:** A. Osaki, *et al.* Enhanced expression of nesfatin/nucleobindin-2 in white adipose tissue of ventromedial hypothalamus-lesioned rats. *Neuroscience Letters* 2012;521(1):46-51

**ALZET Comments:** Carbachol; Saline; SC; Rat; 5 days; Controls received mp w/ vehicle; animal info (Sprague Dawley, female, 13 wks old).

**Q0242:** J. M. Van Kampen, *et al.* Agonist-induced restoration of hippocampal neurogenesis and cognitive improvement in a model of cholinergic denervation. *Neuropharmacology* 2010;58(6):921-929

**ALZET Comments:** Physostigmine; carbachol; nicotine; pirenzepine; oxotremorine; mecamylamine; Saline; CSF/CNS; Rat; 2002; 2004; Controls received mp w/ vehicle; animal info (female, Sprague Dawley, 250 g.); neurodegenerative (Alzheimer's Disease).

**P9643:** K. Lorenz, *et al.* A new type of ERK1/2 autophosphorylation causes cardiac hypertrophy. *Nature Medicine* 2009;15(1):75-83

**ALZET Comments:** Angiotensin II; carbachol; SC; Mice (transgenic); 14 days; Animal info (wt, ERK2<sup>T188</sup>); peptides.

**P0998:** P. J. Shiromani, *et al.* Continuous pontine cholinergic microinfusion via mini-pump induces sustained alterations in rapid eye movement (REM) sleep. *Pharmacol. Biochem. Behav* 1986;25(6):1253-1261

**ALZET Comments:** Carbachol; Scopolamine; Saline; CSF/CNS; CSF/CNS (medulla); CSF/CNS (pons); Rat; 2001; 7 days; Cholinergic agent; mp w/vehicle; mp connected to cann. in brain sites; MP failed to deliver drugs after 5 days possibly due to extended length of tubing.

**P0628:** D. A. Fitts, *et al.* Fluid intake, distribution, and excretion during lateral ventricular infusions of carbachol in rats. *Brain Research* 1985;332(2):237-245

**ALZET Comments:** Carbachol; Saline; CSF/CNS; Rat; 2001; 6 days; comparison of icv injec. (acute infusion) vs. mp infusion; stability of residual carbachol verified by dipsogenic effect on 2 bioassay rats.

**P0423:** Y. Y. Wu, *et al.* Mechanisms underlying the pressor responses to acute and chronic intraventricular administration of carbachol in the rat. *J. Pharmacol. Exp. Ther* 1984;228(2):354-363

**ALZET Comments:** Atropine methyl nitrate; Hexamethonium bromide; Carbachol; Saline; CSF/CNS; SC; Rat; 2001; 2002; 1-12 days; comparison of agents effects; pumps primed in saline before implant; carbachol admin. sc in one exp., other exp. deliv. Car., Hex., & Atr. icv; antihypertensive.

**P0199:** Y. Y. Wu, *et al.* Infusions of chemicals into the brain and the development of sustained elevations of blood pressure in the rat. *Life Sci* 1982;30(15):1537-1545



**ALZET Comments:** Carbachol chloride; Echothiophate iodide; Histamine dihydrochloride; Prostaglandin E2; Thyrotropin-rel. factor; Saline; CSF/CNS; Rat; 1701; 2001; no duration posted; 2001 w/carbachol & echothiophate, 1701 w/histamine, PGE2, & TRH, 7 days; comparison of agents effects.

**P0056:** D. B. Avrith, *et al.* Increased sodium appetite in the rat induced by intracranial administration of components of the renin-angiotensin system. *J. Physiol* 1980;301(349-364

**ALZET Comments:** Carbachol; Saline; CSF/CNS; Rat; no duration posted; Sage pump also used; comparison of injection vs. infusion.

#### 4. Oxotremorin

**Q0242:** J. M. Van Kampen, *et al.* Agonist-induced restoration of hippocampal neurogenesis and cognitive improvement in a model of cholinergic denervation. *Neuropharmacology* 2010;58(6):921-929

**ALZET Comments:** Physostigmine; carbachol; nicotine; pirenzepine; oxotremorine; mecamylamine; Saline; CSF/CNS; Rat; 2002; 2004; Controls received mp w/ vehicle; animal info (female, Sprague Dawley, 250 g.); neurodegenerative (Alzheimer's Disease).

**P1408:** M. Miyamoto, *et al.* Effects of continuous infusion of cholinergic drugs on memory impairment in rats with basal forebrain lesions. *J. Pharmacol. Exp. Ther* 1989;248(2):825-835

**ALZET Comments:** Oxotremorine; Physostigmine sulfate; Saline; SC; Rat; 2002; 3 weeks; no comment posted.

**P0683:** N. W. Pedigo Jr, *et al.* Reduced muscarinic receptor plasticity in frontal cortex of aged rats after chronic administration of cholinergic drugs. *Life Sci* 1985;37(15):1443-1449

**ALZET Comments:** Methylatropine; Oxotremorine; Saline; CSF/CNS; Rat; 2ML4; 3 weeks; comparison of agents effects in young and old rats; stability of drugs at 37C determined at weekly intervals for 5 wks by bioassay; delivery into lateral cerebroventricle.

**P0663:** J. C. R. Fernando, *et al.* Rapid induction of supersensitivity to muscarinic antagonists-induced motor excitation by continuous stimulation of cholinergic receptors. *Life Sci* 1985;37(9):883-892

**ALZET Comments:** Oxotremorine; Physostigmine sulfate; Saline; SC; Rat; 2002; 2 weeks; comparison of single sc injec vs. daily injec vs. mp infusion of agents effects.

#### 5. Physostigmine

**Q5056:** D. P. Holschneider, *et al.* Remote brain network changes after unilateral cortical impact injury and their modulation by acetylcholinesterase inhibition. *J Neurotrauma* 2013;30(11):907-19

**ALZET Comments:** physostigmine; water; SC; Rat; 2ML4; 3 weeks; controls received mp w/ saline; animal info: sprague-dawley, male, 250-300g; functionality of mp verified by residual volume; enzyme inhibitor (Acetylcholine); neurodegenerative (Traumatic brain injury); except for model number, paper does not mention ALZET much; dose: 1.6 micromoles/kg/day.

**Q2076:** R. Miyazaki, *et al.* Acetylcholinesterase inhibitors attenuate angiogenesis. *Clinical Science* 2012;123(3-4):241-249

**ALZET Comments:** Physostigmine; Mice; 2 weeks; Animal info (C57BL/6, 9 wks old); enzyme inhibitor (acetylcholinesterase); hindlimb ischemia.

**R0292:** H. P. M. Van Helden, *et al.* Non-enzymatic pretreatment of nerve agent (soman) poisoning: A brief state-of-the-art review. *TOXICOLOGY LETTERS* 2011;206(1):35-40

**ALZET Comments:** Physostigmine; scopolamine; pyridostigmine bromide; SC; Guinea pig; 12 days;



**Q0242:** J. M. Van Kampen, *et al.* Agonist-induced restoration of hippocampal neurogenesis and cognitive improvement in a model of cholinergic denervation. *Neuropharmacology* 2010;58(6):921-929

**ALZET Comments:** Physostigmine; carbachol; nicotine; pirenzepine; oxotremorine; mecamlamine; Saline; CSF/CNS; Rat; 2002; 2004; Controls received mp w/ vehicle; animal info (female, Sprague Dawley, 250 g.); neurodegenerative (Alzheimer's Disease).

**Q0425:** B. Mauck, *et al.* Cholinesterase inhibitors and stress: Effects on brain muscarinic receptor density in mice. *Neurotoxicology* 2010;31(5):461-467

**ALZET Comments:** Pyridostigmine bromide; physostigmine; SC; Mice; 30 days; Controls received mp w/saline; animal info (male, C57BL6, 25 g); enzyme inhibitor (cholinesterase).

**P7570:** I. H. C. H. Philippens, *et al.* Stress adversely affects efficacy of physostigmine-scopolamine pretreatment against soman in guinea pigs. *Pharmacology Biochemistry and Behavior* 2005;82(1):125-132

**ALZET Comments:** Physostigmine; scopolamine bromide; Water, distilled; propylene glycol; acetic acid, glacial; ethanol; SC; Guinea pig; 2002; 2 weeks; Controls received mp w/ vehicle; post op. care (nobecutane); animal info (male, dunkin-hartley albino, 400-450 g); 10% ETOH; wound clips used.

**P6417:** R. J. Langley, *et al.* Central but not the peripheral action of cholinergic compounds suppresses the immune system. *Journal of Neuroimmunology* 2004;148(1-2):140-145

**ALZET Comments:** Physostigmine; pyridostigmine bromide; edrophonium; Saline; CSF, artificial; SC; CSF/CNS; Rat; 2ML4; 3 weeks; Controls received mp w/ vehicle; enzyme inhibitor (acetylcholinesterase); immunology; ALZET brain infusion kit.

**P6802:** E. K. Choi, *et al.* Protection by sustained release of physostigmine and procyclidine of soman poisoning in rats. *European Journal of Pharmacology* 2004;505(1-3):83-91

**ALZET Comments:** Physostigmine salicylate; procyclidine hydrochloride; Propylene glycol; acetic acid, glacial; ethanol; water; SC; Rat; 2001; 3 days; Functionality of mp verified by plasma levels; dose-response (table 1); enzyme inhibitor (cholinesterase); procyclidine is an NMDA antagonist.

**P5707:** N. G. Muggleton, *et al.* Assessment of a combination of physostigmine and scopolamine as pretreatment against the behavioral effects of organophosphates in the common marmoset (*Callithrix jacchus*). *Psychopharmacology* 2003;166(3):212-220

**ALZET Comments:** Physostigmine salicylate; scopolamine hydrobromide; Saline; SC; Monkey (marmoset); 2002; 14 days; Controls received mp w/ vehicle; behavioral testing; agents infused via same pumps; toxicology.

**P5352:** J. Wetherell, *et al.* Physostigmine and hyoscine improves protection against the lethal and incapacitating effects of nerve agent poisoning in the guinea-pig. *Neurotoxicology* 2002;23(3):341-349

**ALZET Comments:** Physostigmine salicylate; Hyoscine hydrobromide; Pyridostigmine; Saline; SC; Guinea pig; 2001; 7 days; Physostigmine and hyoscine infused together; toxicology.

**P5145:** Y. Meshulam, *et al.* Prophylaxis against organophosphate poisoning by sustained release of scopolamine and physostigmine. *Journal of Applied Toxicology* 2001;21(S75-S78)

**ALZET Comments:** Scopolamine; Physostigmine; Propylene glycol; Ethanol; Water; Acetic acid, glacial; SC; Dog; 2001; 24 or 48 hours; functionality of mp verified by plasma scopolamine & physostigmine levels; dose-response (table, p. S77); toxicology; vehicle was 10% ethanol, 20% PG, 70% water, 0.0035% AA; mentions benefits of infusion via pump (p. S77).

**P4806:** G. Lallement, *et al.* Subchronic administration of various pretreatments of nerve agent poisoning. II. Compared efficacy against soman toxicity. *Drug and Chemical Toxicology* 2001;24(2):165-180

**ALZET Comments:** Pyridostigmine; Huperzine; Physostigmine; Scopolamine;; SC;; Guinea pig;; 6 days;; Controls received sham operation; enzyme inhibitor; these are poisons known to be acetylcholinesterase inhibitors; doses inhibited 30% of AChE activity; Physostigmine was infused alone or together with Scopolamine; toxicology.



**P4925:** J. M. Daniel, *et al.* Acetylcholine mediates the estrogen-induced increase in NMDA receptor binding in CA1 of the hippocampus and the associated improvement in working memory. *Journal of Neuroscience* 2001;21(17):6949-6956

**ALZET Comments:** Physostigmine hemisulfate; Ethanol; Propylene glycol; Water, distilled;; SC; Rat; 3 days; controls received mp w/ vehicle; replacement therapy (ovariectomy); brain tissue distribution; enzyme inhibitor; physostigmine is an acetylcholinesterase inhibitor; 10% ethanol and 40% propylene glycol vehicle used.

**P4935:** T. G. Beach, *et al.* Reduction of cortical amyloid beta levels in guinea pig brain after systemic administration of physostigmine. *Neuroscience Letters* 2001;310(21-24)

**ALZET Comments:** Physostigmine salicylate; Saline, sterile; SC; Guinea pig; 2ML2; 10 days; controls received mp w/ vehicle; peptides; neurodegenerative (Alzheimer's disease); peptide amyloid beta; physostigmine is an acetylcholinesterase enzyme inhibitor;.

**Q5041:** Aas P, *et al.* The effect of stress on the medical treatment of soman poisoning in the brain. *Researchgate* 2001;

**ALZET Comments:** Pyridostigmine; physostigmine; Saline; SC; Guinea pig; 2001; 5 days; Dose (pyridostigmine: 0.02 mg/hr; physostigmine: 0.0063 mg/hr); Controls received mp w/ vehicle; animal info (male guinea pigs weighing 250-300g); behavioral testing (swimming);.

## 6. Pyridostigmine

**Q4881:** B. C. Halil Sayin, Philippe Chevalier, Christian Barrès, Claude Julien. Assessment of cardiac autonomic tone in conscious rats. *Autonomic Neuroscience-Basic & Clinical* 2016;194(26-31)

**ALZET Comments:** Pyridostigmine bromide; SC; Rat; 2ML4; 3 weeks; animal info (male, SHR, 46 weeks old); cardiovascular; bp measured using radiotelemetry; Dose (15 mg/kg/day);.

**Q5005:** R. M. Lataro, *et al.* Acetylcholinesterase Inhibition Attenuates the Development of Hypertension and Inflammation in Spontaneously Hypertensive Rats. *Am J Hypertens* 2015;28(10):1201-8

**ALZET Comments:** Pyridostigmine bromide; donepezil; SC; Rat; 2004; 16 weeks; animal info (male, Wistar-Kyoto or SHR); pumps replaced every 4 weeks; long-term study; cardiovascular; bp measured using tail cuff; Dose (Pyridostigmine bromide 1.5 mg/kg/day; donepezil 1.4 mg/kg/day);.

**Q3860:** M. T. Durand, *et al.* Pyridostigmine Restores Cardiac Autonomic Balance after Small Myocardial Infarction in Mice. *PLoS One* 2014;9(U327-U335)

**ALZET Comments:** Pyridostigmine; Saline, sterile; SC; Mice; 1004; 4 weeks; Controls received mp w/ vehicle; animal info (male, C57BL6, 10-15 weeks old, 25-30g); ischemia (cardiac); cardiovascular; pyridostigmine is an acetylcholinesterase inhibitor; pyridostigmine aka PYR; bp measured using radiotelemetry; pumps primed at 37C saline for 48 hours;.

**Q3265:** M. Richtsfeld, *et al.* Prolonged Administration of Pyridostigmine Impairs Neuromuscular Function with and without Downregulation of Acetylcholine Receptors. *Anesthesiology* 2013;119(2):412-421

**ALZET Comments:** Pyridostigmine; Saline; SC; Rat; 2ML4; 14 days; 28 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 220-260g); dose-response (p.416, 418); post op. care (antibiotic ointment); incision closed with (4-0) suture;.

**R0292:** H. P. M. Van Helden, *et al.* Non-enzymatic pretreatment of nerve agent (soman) poisoning: A brief state-of-the-art review. *TOXICOLOGY LETTERS* 2011;206(1):35-40

**ALZET Comments:** Physostigmine; scopolamine; pyridostigmine bromide; SC; Guinea pig; 12 days;

**Q0425:** B. Mauck, *et al.* Cholinesterase inhibitors and stress: Effects on brain muscarinic receptor density in mice. *Neurotoxicology* 2010;31(5):461-467

**ALZET Comments:** Pyridostigmine bromide; physostigmine; SC; Mice; 30 days; Controls received mp w/saline; animal info (male, C57BL6, 25 g); enzyme inhibitor (cholinesterase).



- P8259:** M. Dubovicky, *et al.* Effects of combined exposure to pyridostigmine bromide and shaker stress on acoustic startle response, pre-pulse inhibition and open field behavior in mice. *Journal of Applied Toxicology* 2007;27(3):276-283  
**ALZET Comments:** Pyridostigmine bromide; SC; Mice; 1007D; 7 days; Controls received mp w/ vehicle, or isotonic saline; no stress (see pg. 278, 280); enzyme inhibitor (acetylcholinesterase); animal info (male, C57BL/6J, 24-26g., 2 months old).
- P8082:** R. J. Hornby, *et al.* Multiple vaccine and pyridostigmine bromide interactions in the common marmoset *Callithrix jacchus*: Immunological and endocrinological effects. *INTERNATIONAL IMMUNOPHARMACOLOGY* 2006;6(12):1765-1779  
**ALZET Comments:** Pyridostigmine bromide; Saline, sterile isotonic; SC; Marmoset; 2004; 28 days; Controls received mp w/ vehicle; no stress (see p.1776); immunology; animal info (female, vasectomized male, 331-565g. 2-5.5 yrs. old); mp primed 40 hours.
- P8143:** G. D. Griffiths, *et al.* Development of methods to measure humoral immune responses against selected antigens in the common marmoset (*Callithrix jacchus*) and the effect of pyridostigmine bromide administration. *INTERNATIONAL IMMUNOPHARMACOLOGY* 2006;6(12):1755-1764  
**ALZET Comments:** Pyridostigmine bromide; Saline, sterile isotonic; SC; Marmoset; 28 days; Controls received mp w/ vehicle; no stress (see p.1759,1762); immunology; animal info (male, female, 300-500g.); mp primed 40 hours; "delivery by pump ensured the animals would receive an appropriate dose of the drug over the desired time period.", oral delivery "would introduce unacceptable stress into the experiment and presentation in food was discounted because of difficulties in estimating the dose administered." (p.1757).
- P8345:** I. Bernatova, *et al.* Acetylcholinesterase inhibition affects cardiovascular structure in mice. *PHYSIOLOGICAL RESEARCH* 2006;55(S89-S97)  
**ALZET Comments:** Pyridostigmine bromide; SC; Mice; 1007D; 7 days; Controls received mp w/ isotonic saline; enzyme inhibitor (acetylcholinesterase); cardiovascular; animal info (male, C57BL/6J, 10-12 weeks old, 25 grams).
- P7217:** G. D. Griffiths, *et al.* A T-cell-dependent humoral immune response is preserved during the administration of the nerve agent pre-treatment pyridostigmine bromide in a murine model. *INTERNATIONAL IMMUNOPHARMACOLOGY* 2005;5(3):525-540  
**ALZET Comments:** Pyridostigmine bromide; Saline, sterile isotonic; SC; Mice; 2004; 28 days; Controls received mp w/ vehicle; enzyme inhibitor (cholinesterase); immunology; mp primed in saline at 37 degrees celsius for 48 hours; "PB administration was achieved by 28-day mini-osmotic pumps thus removing the requirement for multiple oral dosing and the associated stress this may have caused." (p. 536).
- P6741:** H. P. M. Van Helden, *et al.* Low levels of Sarin affect the EEG in marmoset monkeys: a pilot study. *Journal of Applied Toxicology* 2004;24(6):475-483  
**ALZET Comments:** Pyridostigmine bromide; Propylene glycol: ethanol; acidic acid, glacial; water, distilled; SC; Marmoset; 2002; Controls received mp w/ vehicle; toxicology; sarin vapor.
- P6551:** H. P. M. Van Helden, *et al.* Low-level exposure of guinea pigs and marmosets to sarin vapour in air: Lowest-observable-adverse-effect level (LOAEL) for miosis. *Journal of Applied Toxicology* 2004;24(1):59-68  
**ALZET Comments:** Pyridostigmine bromide; Propylene glycol; ethanol; water; acetic acid, glacial; SC; Guinea pig; marmoset; 2002; 4 days; Controls received mp w/ vehicle; toxicology.
- P6417:** R. J. Langley, *et al.* Central but not the peripheral action of cholinergic compounds suppresses the immune system. *Journal of Neuroimmunology* 2004;148(1-2):140-145  
**ALZET Comments:** Physostigmine; pyridostigmine bromide; edrophonium; Saline; CSF, artificial; SC; CSF/CNS; Rat; 2ML4; 3 weeks; Controls received mp w/ vehicle; enzyme inhibitor (acetylcholinesterase); immunology; ALZET brain infusion kit.
- P7030:** L. F. Joaquim, *et al.* Enhanced heart rate variability and baroreflex index after stress and cholinesterase inhibition in mice. *American Journal of Physiology-Heart and Circulatory Physiology* 2004;287(1):H251-H257  
**ALZET Comments:** Pyridostigmine; SC; Mice; 1007D; 3 days; Controls received mp w/ saline; enzyme inhibitor (acetylcholinesterase); cardiovascular.



**P5638:** I. Bernatova, *et al.* Effect of chronic pyridostigmine bromide treatment on cardiovascular and behavioral parameters in mice. *Pharmacology Biochemistry and Behavior* 2003;74(4):901-907

**ALZET Comments:** Pyridostigmine bromide; Saline; SC; Mice; 1007D; 7 days; Controls received mp w/ vehicle; pyridostigmine blood levels checked; enzyme inhibitor (acetylcholinesterase).

**P5352:** J. Wetherell, *et al.* Physostigmine and hyoscine improves protection against the lethal and incapacitating effects of nerve agent poisoning in the guinea-pig. *Neurotoxicology* 2002;23(3):341-349

**ALZET Comments:** Physostigmine salicylate; Hyoscine hydrobromide; Pyridostigmine; Saline; SC; Guinea pig; 2001; 7 days; Physostigmine and hyoscine infused together; toxicology.

**P5528:** G. Lallement, *et al.* Subchronic administration of pyridostigmine or huperzine to primates: Compared efficacy against soman toxicity. *Drug and Chemical Toxicology* 2002;25(3):309-320

**ALZET Comments:** Pyridostigmine; huperzine; SC; Monkey; 2ML1; 6 days; Enzyme inhibitor (acetylcholinesterase); toxicology.

**P4806:** G. Lallement, *et al.* Subchronic administration of various pretreatments of nerve agent poisoning. II. Compared efficacy against soman toxicity. *Drug and Chemical Toxicology* 2001;24(2):165-180

**ALZET Comments:** Pyridostigmine; Huperzine; Physostigmine; Scopolamine;; SC;; Guinea pig;; 6 days;; Controls received sham operation; enzyme inhibitor; these are poisons known to be acetylcholinesterase inhibitors; doses inhibited 30% of AChE activity; Physostigmine was infused alone or together with Scopolamine; toxicology.

**P4817:** G. D. Griffiths, *et al.* Biological consequences of multiple vaccine and pyridostigmine pretreatment in the guinea pig. *Journal of Applied Toxicology* 2001;21(59-68)

**ALZET Comments:** Pyridostigmine bromide;; Saline;; SC;; Guinea pig;; 28 days;; Controls received mp w/ vehicle; functionality of mp verified by AChE levels via assay p. 60; immunology; enzyme inhibitor; PB is an acetylcholinesterase inhibitor; toxicology.

**Q5041:** Aas P, *et al.* The effect of stress on the medical treatment of soman poisoning in the brain. *Researchgate* 2001;

**ALZET Comments:** Pyridostigmine; physostigmine; Saline; SC; Guinea pig; 2001; 5 days; Dose (pyridostigmine: 0.02 mg/hr; physostigmine: 0.0063 mg/hr); Controls received mp w/ vehicle; animal info (male guinea pigs weighing 250-300g); behavioral testing (swimming);.

## 7. Scopolamine

**Q6743:** H. Pierce, *et al.* Cholinergic Signals from the CNS Regulate G-CSF-Mediated HSC Mobilization from Bone Marrow via a Glucocorticoid Signaling Relay. *Cell Stem Cell* 2017;20(5):648-658 e4

**ALZET Comments:** Pirenzepine; Scopolamine hydrobromide; Metyrapone; luteinizing hormone; ACTH; PBS; CSF/CNS (Third ventricle); Mice (knockout); 1002; Dose (0.6 mg/kg/day Pirenzepine; 1.0 mg/kg Scopolamine hydrobromide; 100mg/kg/day Metyrapone; 2.8 mg/kg/day ACTH; 16ug/day LH); Controls received mp w/ vehicle; animal info (wild-type and *Chrm1*<sup>-/-</sup>); luteinizing hormone aka LH and adrenocorticotrophic hormone aka ACTH; peptides; Brain coordinates (*A/P* 0.6 mm posterior to bregma, *D/V* -4.7 mm);.

**Q6369:** U. Gehlsen, *et al.* A semifluorinated alkane (F4H5) as novel carrier for cyclosporine A: a promising therapeutic and prophylactic option for topical treatment of dry eye. *Graefes Arch Clin Exp Ophthalmol* 2017;255(4):767-775

**ALZET Comments:** Scopolamine; SC; Mice; 1002; 2 weeks; Dose (0.1 mg/day); animal info (10–12-week-old female C57BL/6 mice); Therapeutic indication (experimental dry eye);.

**Q4293:** H. Saijo, *et al.* Microangiopathy triggers, and inducible nitric oxide synthase exacerbates dextran sulfate sodium-induced colitis. *LABORATORY INVESTIGATION* 2015;95(728-748)





**ALZET Comments:** Butylscopolamine; PBS; SC; Mice; 1007D; 3 days; 5 days; 7 days;; Animal info (male, C57BL6J, 9-10 weeks old); ischemia (colitis);.

**Q3274:** W. W. Chen, *et al.* Lycium barbarum Polysaccharides Prevent Memory and Neurogenesis Impairments in Scopolamine-Treated Rats. PLoS One 2014;9(2):U1116-U1128

**ALZET Comments:** Scopolamine; SC; Rat; 2ML4; 28 days; Control animals received mp w/ saline; animal info (male, Sprague Dawley, 200-220 g, adult);.

**Q5958:** D. Y. Yoo, *et al.* Effects of luteolin on spatial memory, cell proliferation, and neuroblast differentiation in the hippocampal dentate gyrus in a scopolamine-induced amnesia model. Neurol Res 2013;35(8):813-20

**ALZET Comments:** Scopolamine; Saline; SC; Rat; 2ML4; 28 days; Controls received mp w/ vehicle; Dose (44 mg/ml delivered at 2.5 ml/h); functionality of mp verified (The release of SCO was confirmed by the increase of locomotor activity and mydriasis);.

**Q2091:** E. R. Gross, *et al.* Neuronal Serotonin Regulates Growth of the Intestinal Mucosa in Mice. Gastroenterology 2012;143(2):408-U430

**ALZET Comments:** Scopolamine; Saline; IP; Mice; 3, 7, 14 days; Controls received mp w/ vehicle; animal info (SERTKO, TPH1KO, wt).

**Q1530:** D. Y. Yoo, *et al.* Effects of a new synthetic butyrylcholinesterase inhibitor, HBU-39, on cell proliferation and neuroblast differentiation in the hippocampal dentate gyrus in a scopolamine-induced amnesia animal model. NEUROCHEMISTRY INTERNATIONAL 2011;59(5):722-728

**ALZET Comments:** Scopolamine; Saline, physiological; SC; Rat; 2ML4; 28 days; Controls received mp w/ vehicle; animal info (Wistar, male).

**Q1417:** D. Y. Yoo, *et al.* Effects of Nelumbo nucifera Rhizome Extract on Cell Proliferation and Neuroblast Differentiation in the Hippocampal Dentate Gyrus in a Scopolamine-induced Amnesia Animal Model. PHYTOTHERAPY RESEARCH 2011;25(6):809-815

**ALZET Comments:** Scopolamine; Saline; SC; Rat; 28 days; Controls received mp w/ vehicle; animal info (male, Wistar, 5 wks old).

**Q1379:** S. Viau, *et al.* No consequences of dietary n-3 polyunsaturated fatty acid deficiency on the severity of scopolamine-induced dry eye. Graefes Archive for Clinical and Experimental Ophthalmology 2011;249(4):547-557

**ALZET Comments:** Scopolamine; SC; Rat; 2ML2; 10 days; Animal info (Lewis, female, 6 wks old).

**R0292:** H. P. M. Van Helden, *et al.* Non-enzymatic pretreatment of nerve agent (soman) poisoning: A brief state-of-the-art review. TOXICOLOGY LETTERS 2011;206(1):35-40

**ALZET Comments:** Physostigmine; scopolamine; pyridostigmine bromide; SC; Guinea pig; 12 days;

**Q2214:** J. P. Raufman, *et al.* Muscarinic receptor subtype-3 gene ablation and scopolamine butylbromide treatment attenuate small intestinal neoplasia in Apc(min/+) mice. Carcinogenesis 2011;32(9):1396-1402

**ALZET Comments:** Scopolamine butylbromide; PBS; SC; Mice; 2004; 8 weeks; Controls received mp w/ vehicle; animal info (6 wks old, male, APC min/+); pumps replaced after 4 weeks; post op. care (betadine).

**Q1500:** P. Jain, *et al.* An NGF mimetic, MIM-D3, stimulates conjunctival cell glycoconjugate secretion and demonstrates therapeutic efficacy in a rat model of dry eye. Experimental Eye Research 2011;93(4):503-512

**ALZET Comments:** Scopolamine hydrobromide; SC; Rat; 2ML2; 2ML4; 14, 28 days; Controls did not receive any scopolamine; animal info (male, Sprague Dawley, 6-8 wks old).

**P9610:** C. H. K. West, *et al.* Antidepressant drugs with differing pharmacological actions decrease activity of locus coeruleus neurons. INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY 2009;12(5):627-641



**ALZET Comments:** Desipramine; mirtazapine; chlorpheniramine; Paroxetine; scopolamine; amphetamine; escitalopram; chlordiazepoxide; SC; IP; Rat; 2ML2; 14, 21 days; 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.

**P9638:** S. Viau, *et al.* Efficacy of a 2-month dietary supplementation with polyunsaturated fatty acids in dry eye induced by scopolamine in a rat model. *Graefes Archive for Clinical and Experimental Ophthalmology* 2009;247(8):1039-1050

**ALZET Comments:** Scopolamine; Rat; 2ML2; 2ML4; 2, 10, 28 days; Controls received mp w/saline; animal info (female, Lewis, 6 wks old).

**P8200:** S. Kotani, *et al.* Pharmacological evidence of cholinergic involvement in adult hippocampal neurogenesis in rats. *Neuroscience* 2006;142(2):505-514

**ALZET Comments:** Scopolamine; Water, distilled; SC; Rat; 2ML4; 4 weeks; Controls received mp w/ vehicle; dose-response (fig.6); animal info (male, Sprague-Dawley, 200-250g., 5wks old).

**P7514:** C. H. K. West, *et al.* A selective test for antidepressant treatments using rats bred for stress-induced reduction of motor activity in the swim test. *Psychopharmacology* 2005;182(1):9-23

**ALZET Comments:** Amitriptyline HCl; venlafaxine HCl; clordiazepoxide HCl; imipramine HCl; phenelzine sulfate; scopolamine HBr; desipramine HCl; bupropion HCl; chlorpheniramine maleate; fluoxetine HCl; sertraline; amphetamine sulfate, D-; Water, sterile distilled; PEG; SC; Rat; 2ML2; 6,14 days; Controls received mp w/ vehicle; functionality of mp verified by agent blood levels; dose-response (fig. 5); animal info (male, female, susceptible, selectively bred); some animals had saline-filled catheter attached to mp to delay drug infusion by 5 days; "The most notable advantage of minipump delivery is that it eliminates stress resulting from daily injection of drug....minipumps also provide constant infusion of drug" (pg. 22).

**P7570:** I. H. C. H. Philippens, *et al.* Stress adversely affects efficacy of physostigmine-scopolamine pretreatment against soman in guinea pigs. *Pharmacology Biochemistry and Behavior* 2005;82(1):125-132

**ALZET Comments:** Physostigmine; scopolamine bromide; Water, distilled; propylene glycol; acetic acid, glacial; ethanol; SC; Guinea pig; 2002; 2 weeks; Controls received mp w/ vehicle; post op. care (nobecutane); animal info (male, dunkin-hartley albino, 400-450 g); 10% ETOH; wound clips used.

**P7259:** H. A. A. Pereira, *et al.* Plastic changes and disease-modifying effects of scopolamine in the pilocarpine model of epilepsy in rats. *Epilepsia* 2005;46(118-124)

**ALZET Comments:** Scopolamine hydrobromide; Saline, sterile; SC; Rat; 2002; 14 days; Controls received mp w/ vehicle, or no treatment; dose-response no stress (see pg. 120); epilepsy.

**P5707:** N. G. Muggleton, *et al.* Assessment of a combination of physostigmine and scopolamine as pretreatment against the behavioral effects of organophosphates in the common marmoset (*Callithrix jacchus*). *Psychopharmacology* 2003;166(3):212-220

**ALZET Comments:** Physostigmine salicylate; scopolamine hydrobromide; Saline; SC; Monkey (marmoset); 2002; 14 days; Controls received mp w/ vehicle; behavioral testing; agents infused via same pumps; toxicology.

**P5145:** Y. Meshulam, *et al.* Prophylaxis against organophosphate poisoning by sustained release of scopolamine and physostigmine. *Journal of Applied Toxicology* 2001;21(S75-S78)

**ALZET Comments:** Scopolamine; Physostigmine; Propylene glycol; Ethanol; Water; Acetic acid, glacial; SC; Dog; 2001; 24 or 48 hours; functionality of mp verified by plasma scopolamine & physostigmine levels; dose-response (table, p. S77); toxicology; vehicle was 10% ethanol, 20% PG, 70% water, 0.0035% AA; mentions benefits of infusion via pump (p. S77).

**P4806:** G. Lallement, *et al.* Subchronic administration of various pretreatments of nerve agent poisoning. II. Compared efficacy against soman toxicity. *Drug and Chemical Toxicology* 2001;24(2):165-180



**ALZET Comments:** Pyridostigmine; Huperzine; Physostigmine; Scopolamine;; SC;; Guinea pig;; 6 days;; Controls received sham operation; enzyme inhibitor; these are poisons known to be acetylcholinesterase inhibitors; doses inhibited 30% of AChE activity; Physostigmine was infused alone or together with Scopolamine; toxicology.