References on the Administration of Cannabinoids Using ALZET® Osmotic Pumps

Q11126: J. A. Komorowska-Muller, *et al.* Chronic low-dose Delta(9)-tetrahydrocannabinol (THC) treatment stabilizes dendritic spines in 18-month-old mice. Scientific Reports 2023;13(1):1390
Agents: Tetrahydrocannabinol **Vehicle:** Ethanol; cremophor; saline; **Route:** SC; **Species:** Mice; **Strain:** Tg(Thy1-EGFP)MJrs/J (GFP-M); **Pump:** 1004; **Duration:** 28 days;
ALZET Comments: Dose (3 mg/kg/day); Controls received mp w/ vehicle; 1:1:18 ethanol, cremophor, saline; animal info (3 and 18 months old; Male);

Q11011: M. E. Turner, *et al.* Vascular calcification maladaptively participates in acute phosphate homeostasis. Cardiovascular Research 2023;119(4):1077-1091
Agents: Calcitriol **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Strain:** Sprague-Dawley; **Pump:** 2ML1; **Duration:** 8 days;
ALZET Comments: Dose (0.5 µg/kg/day); animal info: (15–16 weeks); cardiovascular; nephrology (chronic kidney disease, phosphate homeostasis)

R0402: E. Zamberletti, *et al.* Dos(e)Age: Role of Dose and Age in the Long-Term Effect of Cannabinoids on Cognition. Molecules 2022;27(4):
Agents: Cannabinol, delta9-tetrahydro-; Cannabidiol **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 28 days;
ALZET Comments: Dose (3 mg/kg/day; 1 mg/kg/day each; 1:1 1 mg/kg/day THC and CBD); animal info (Male C57BL/6J; 12 and 18 months old); behavioral testing (Morris water maze; Nobel object location recognition task; Partner recognition task); toxicology;

Q5966: P. Weydt. Mechanisms and Modifiers of Energy Metabolism in ALS and Huntington Disease. Open Access Repositorium der Universität Ulm 2016;
Agents: Cannabinol **Vehicle:** PEG 400; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 4 weeks;
ALZET Comments: animal info (SOD 1 transgenic); pumps replaced every 28 days; Therapeutic indication (amyotrophic lateral sclerosis); Dose (5 mg/kg);

Q3610: E. J. Rahn, *et al.* Prophylactic cannabinoid administration blocks the development of paclitaxel-induced neuropathic nociception during analgesic treatment and following cessation of drug delivery. Molecular Pain 2014;10(U1-U19
Agents: AM1710; Taxol-WIN-55212-2; AM251; AM630 **Vehicle:** DMSO; PEG 400; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 28 days;
ALZET Comments: Controls received mp w/ saline; animal info (male, Sprague Dawley, 300-400g); functionality of mp verified by residual volume; 50% PEG 400 used; 50% DMSO used; Multiple pumps per animal (2); stress/adverse reaction: (see pg.15); behavioral testing (mechanical threshold, cold withdrawal, locomotor activity); AM1710 is a cannabilactone CB2-selective agonist; pumps removed on day 22; WIN55,212-2 is a CB1/CB2 agonist;

Q4814: Heloísa Helena Vilela Costa, *et al.* Continuous central infusion of cannabinoid receptor agonist WIN 55,212-2 decreases maternal care in lactating rats: Consequences for fear conditioning in adulthood males. Behavioural Brain Research 2013;257(31-38
Agents: WIN-55212-2 **Vehicle:** NaCl; Tween, DMSO; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 1007D; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (female, Wistar, 9 weeks old); 10% DMSO used; dose-response (pg 34); behavioral testing (fear conditioning, maternal behavior); teratology; "The continuous infusion of WIN in the CNS using an osmotic minipump in lactating dams eliminates the possibility that WIN affects the behavior of the offspring when offered in the milk. Thus, any behavioral change in offspring could be attributed only to changes inmaternal behavior from the administration of WIN in the dams." pg 37; Cannula placement verified via Evans Blue dye postmortem; Dose (10 or 100 nmol/h);

Q0907: N. Saghafi, *et al.* Cannabinoids attenuate cancer pain and proliferation in a mouse model. Neuroscience Letters 2011;488(3):247-251
Agents: WIN-55212-2; ACEA; AM1241 **Vehicle:** DMSO; Water; **Route:** SC; **Species:** Mice (nude); **Pump:** 2002; **Duration:** 2 weeks;
ALZET Comments: Animal info (Foxn1 nu, athymic, 4-5 wks old, 20-25 g); cancer (oral); behavioral testing (mechanical allodynia); 50% DMSO used; wound clips used; pain

Q1709: R. E. Hampson, *et al.* Memory encoding in hippocampal ensembles is negatively influenced by cannabinoid CB1 receptors. Behavioural Pharmacology 2011;22(4):335-346
Agents: Rimonabant; WIN-55212-2 **Vehicle:** Ethanol; saline, pluronic; **Route:** CSF/CNS (hippocampus); **Species:** Rat; **Pump:** 2004; **Duration:** 4 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Long Evans, 4-12 mo old); pumps replaced after 16-22 days; post op. care (antibiotic, buprenorphine); behavioral testing (delayed nonmatch to sample (DNMS) task)

P9694: Y. Marchalant, *et al.* Cannabinoids attenuate the effects of aging upon neuroinflammation and neurogenesis. NEUROBIOLOGY OF DISEASE 2009;34(2):300-307
Agents: WIN-55212-2; SR141716A; SR144528; iodoresiniferatoxin, 5- **Vehicle:** DMSO; PEG; **Route:** SC; CSF/CNS (fourth ventricle); **Species:** Rat; **Pump:** 2004; 2ML4; **Duration:** 4 weeks, 21 days;
ALZET Comments: Controls received mp w/ vehicle; no stress pg. 303 "well tolerated"; animal info (23 months old, male, F-344); 50% DMSO used; SR144528 is a selective CB2 antagonist; 50% PEG used

P9281: Y. Marchalant, *et al.* Cannabinoid receptor stimulation is anti-inflammatory and improves memory in old rats. Neurobiology of Aging 2008;29(12):1894-Rat1901
Agents: WIN-55212-2 **Vehicle:** DMSO; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 21 days;
ALZET Comments: Controls received mp w/ vehicle; dose-response (fig. 1); no stress (see pg. 1897); animal info (male, F-344; 3 and 23 months old); neurodegenerative (Alzheimer's Disease); behavioral testing (water maze); "Chronic infusion of DMSO and WIN-55212-2 were well tolerated by all rats." (p. 1897); 100% DMSO used

P8518: I. J. Lever, *et al.* Continuous infusion of the cannabinoid WIN 55,212-2 to the site of a peripheral nerve injury reduces mechanical and cold hypersensitivity. British Journal of Pharmacology 2007;151(2):292-302
Agents: WIN-55212-2 mesylate salt; SR141716A; SR144528 **Vehicle:** Saline; Tween 20; albumin, rat serum; DMSO; **Route:** CSF/CNS (sciatic nerve); **Species:** Rat; **Pump:** 2001; **Duration:** 6, 7 days;
ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified after removal, as well as mp/catheter connection, catheter patency and position; dose-response (fig. 3); animal info (male, Wistar, 250-300 g, partial ligation injury); 4% DMSO; 14.5 % DMSO

Q5957: A. Witting, *et al.* Endocannabinoids accumulate in spinal cord of SOD1 G93A transgenic mice. J Neurochem 2004;89(6):1555-7
Agents: Cannabinol **Vehicle:** PEG 400; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 12 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (SOD1 transgenic; 6 week old; 25 grams); Dose (5 mg/kg/day); long-term study; pumps replaced every 4 weeks up to 2 times; neurodegenerative (ALS); no stress (see pg. 183): dose and the repeated pump replacements were well tolerated; cannabinol (CBN) is a nonpsychotropic cannabinoid; Therapeutic indication (amyotrophic lateral sclerosis);

P5515: M. L. Casanova, *et al.* Inhibition of skin tumor growth and angiogenesis in vivo by activation of cannabinoid receptors. J. Clin. Invest 2003;111(1):43-50
Agents: JWH-133; WIN-55212-2 **Vehicle:** PBS; BSA; **Route:** SC; **Species:** Mice (nude); **Pump:** 2002; **Duration:** 11 days;
ALZET Comments: Controls received mp w/ vehicle; cancer; cannabinoid agonists

Q7709: B. C. Paria, *et al.* Dysregulated cannabinoid signaling disrupts uterine receptivity for embryo implantation. J Biol Chem 2001;276(23):20523-8
Agents: Tetrahydrocannabinol (- or +) **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 3 days;
ALZET Comments: Dose (20 ug/hr/day); animal info (Female, pregnant); dependence;

P5754: I. Galve-Roperh, *et al.* Anti-tumoral action of cannabinoids: involvement of sustained ceramide accumulation and extracellular signal-regulated kinase activation. Nat Med 2000;6(3):313-319
Agents: WIN-55212-2; Cannabinol, delta-9-tetrahydro- **Vehicle:** PBS; BSA; **Route:** CSF/CNS (intratumoral); **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Tissue perfusion (tumor); cancer; WIN-55,212-2 is a potent synthetic cannabinol agonist

P7108: B. C. Paria, *et al.* Effects of cannabinoids on preimplantation mouse embryo development and implantation are mediated by brain-type cannabinoid receptors[1]. Biology of Reproduction 1998;58(1490-1495
Agents: Cannabinol, delta-9-tetrahydro-; SR141716A **Vehicle:** Propylene glycol; Ethanol; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 3,4 days;
ALZET Comments: Controls received mp w/ the less active (+)THC stereoisomer; functionality of mp verified by plasma THC levels

P2491: B. K. Colasanti. A comparison of the ocular and central effects of delta-9 tetrahydrocannabinol and cannabigerol. J. Ocular Pharmacol 1990;6(4):259-269
Agents: Cannabinol, delta-9-tetrahydro-; Cannabigerol **Vehicle:** PEG 400; **Route:** Eye (cornea); **Species:** Cat; **Pump:** Not Stated; **Duration:** 9 days;
ALZET Comments: Controls received mp w/ vehicle; dose-response (p.262); unilateral delivery

P1511: B. K. Colasanti. Intraocular pressure, ocular toxicity and neurotoxicity in response to 11-hydroxy-delta9-tetrahydrocannabinol and 1-nantradol. J. Ocular Pharmacol 1985;1(2):123-135
Agents: Cannabinol, tetrahydro-; Nantradol, 1- **Vehicle:** PEG 400; **Route:** Eye; **Species:** Cat; **Pump:** 2001; **Duration:** 9 days;
ALZET Comments: Topical application; tissue perfusion

P0466: B. K. Colasanti, *et al.* Intraocular pressure, ocular toxicity and neurotoxicity after administration of delta9-tetrahydrocannabinol or cannabichromene. Experimental Eye Research 1984;38(63-71
Agents: Cannabichromene; Cannabinol, delta-9-tetrahydro- **Vehicle:** PEG 400; **Route:** Eye (cornea); **Species:** Cat; **Pump:** 2001; **Duration:** 9 days;
ALZET Comments: Comparison of agents effects; pump implanted sc and connected via sc tubing to cornea; tissue perfusion

P0577: B. K. Colasanti, *et al.* Intraocular pressure, ocular toxicity and neurotoxicity after administration of cannabinol or cannabigerol. Experimental Eye Research 1984;39(3):251-259
Agents: Cannabigerol; Cannabinol **Vehicle:** PEG 400; **Route:** Eye; **Species:** Cat; **Pump:** Not Stated; **Duration:** 9 days;
ALZET Comments: mp model not stated; comparison of agents effects; intermittent eye drop admin. vs. mp infusion; tissue perfusion

P0652: B. K. Colasanti, *et al.* Ocular hypotension, ocular toxicity, and neurotoxicity in response to marihuana extract and cannabidiol. Gen. Pharmacol 1984;15(6):479-484
Agents: Cannabidiol; Marihuana extract; Cannabinol, delta-9-tetrahydro- **Vehicle:** PEG; **Route:** Eye (cornea); **Species:** Cat; **Pump:** Not Stated; **Duration:** 9 days;
ALZET Comments: mp model not stated; comparison of acute topical admin/ injec vs. mp infusion; comparison of agents effects; agents admin. topically to cat corneas; tissue perfusion