References on the In Vitro or In Situ Use of ALZET® Osmotic Pumps


Agents: Florfenicol, voriconazole; amikacin Vehicle: Not Stated; Route: SC; in vitro; Species: Rat; Snake (corn, rattle); Iguana; Cat; Hamster; Gelada; Pudu; Wallaby; Monkey; Quail; Hen; Pump: Not Stated; Duration: Not Stated;

ALZET Comments: "animal info (Eastern massasauga rattlesnakes (Sistrurus catenatus); timber rattle (Crotalus horridus); puda (Pudu puda); wallaby (Macropus rufogriseus); iguanas (Iguana iguana); Mojave rattlesnakes (Crotalus scutulatus); corn snakes (Elaphe guttata guttata); Japanese quails (Coturnix coturnix japonica); hens (Gallus domesticus)); Finally, the use of intracoelomic osmotic pumps was reported in iguanas (Iguana iguana) in a study of reproductive behavior. No complication due to the pump placement was reported in that study." pg. 508; Advantages: Can be extracted in case of drug overdose or toxicity, Is not altered by its biological environment, Release the drug at a constant rate, Low cost, Commercially available, Release rate and operation time can be chosen; Drawbacks: Necessitate 2 light surgical procedures under anesthesia to be implanted and explanted, Can sometimes migrate in unwanted location (especially if implanted accidently in air sacs during intracoelomic implantation)"


ALZET Comments: Ultra-high molecular weight polyethylene particles; oligodeoxynucleotide, decoy; oligodeoxynucleotide, scrambled; Endotoxin, LPS; Brain-derived neurotropic factor; Saline; In Vitro (cell culture); Bone (Femur); Mice (nude); 2006; 4 weeks; Controls received mp w/ vehicle; animal info (Male athymic nude mice, 10-15 weeks old); stability verified by (in vitro experiment); dose-response (pg. 277); good methods (pg. 276); tissue perfusion (bone); Dose (15 mg/ml UHMWPE, 50uM decoy, 1 ug/ml LPS); Therapeutic indication (Bone loss, chronic inflammation);


ALZET Comments: Interleukin-4, mouse recombinant; BSA; PBS; In vitro (cell culture); Cell culture; 2006; 4 weeks; 1% BSA used; immunology; "Osmotic pumps delivered IL-4 at a rate that closely followed the expected delivery rate." pg 1343; used vinyl tubing; pumps lead into mouse bone marrow macrophage augmented media; incubated at 37C.


ALZET Comments: In situ (marine environment); 2ML1 (osmosampler); 9 months; “This technique allows for continued and unsupervised deployment of a sampler for weeks to months, representing a cost-efficient formof chemical monitoring.” pg 112;


ALZET Comments: Nettle powder; Water, spring; In vitro; Toad (tadpole); 2ML2; 12 days; Animal info (Xenopus laevis); teratology; spaceflight;


ALZET Comments: Naproxen; PBS; In vitro; 1002; Naproxen is anono- steroidal anti-inflammatory agent; This paper reports the characterization of an electrochemical biosensor for the continuous monitoring of Naproxen delivered by alzet pumps.

ALZET Comments: Naproxen; Methanol; In Vitro; 1002; 16 hours; Functionality of mp verified by naproxen levels measured with sensors.

Q2848: D. Sabater, et al. The use of Transwells(TM) improves the rates of differentiation and growth of cultured 3T3L1 cells. ANALYTICAL AND BIOANALYTICAL CHEMISTRY 2013;405(16):5605-5610
ALZET Comments: Spermine nitric oxide complex; DMEM-GlutaMAX-I; In vitro (cell culture); 1003D; 3 days; Spermine nitric oxide complex is a nitric oxide donor; polyethylene capillary tube used; image of ALZET pump inside Transwells(TM); pumps were placed in wells containing sterile water.

ALZET Comments: Sodium sulfite; In Vitro; 1003D;

ALZET Comments: In situ (marine environment); 2ML1 (osmosampler); In situ CH4 concentrations were measured on water samples collected with a Mini-Pore Fluid Array (mPFA), which is a modified version of an existing sample collection tool that collects and maintains samples at in situ pressure. The mPFA is a polyvinyl chloride box that contains three OsmoSamplers, a high-pressure valve submerged in oil to reduce corrosion, and three 300 m long coils of copper tubing (Figure 3). Each OsmoSampler has eight 2ML1 semi-permeable membranes that separate a saturated salt solution from deionized water, creating an osmotic potential, which creates the pump. Sampler pumping rates were calibrated in the laboratory prior to deployment and found to be ~0.5 mL/d at 4oC.

ALZET Comments: Compound A, nanosuspension; Acetonitrile; water; SC; in vitro; Mice; 1007D; 7 days; Animal info (Crl NMRI, 27-32.5 g, female); comparison of SC mp versus bolus injections; “Subcutaneously implanted osmotic pumps prove to be a valuable delivery system for nanosuspensions in pharmacokinetic studies by consideration of the key parameter viscosity in release kinetics.”; good methods.

ALZET Comments: Verapamil; Saline; In vitro (egg); Bird (chicken embryo); 2001; Controls received mp w/ (saline); Dose (1 ng/μl);

ALZET Comments: FITC; In vitro (cell migration); 2ML2; 24, 72 hours; Controls received mp w/ PBS; “we show that by powering our chemotaxis platform with two ALZET osmotic pumps, our chemotaxis platform can achieve both exquisite control and long-term stability over the gradient." pg 2.

ALZET Comments: Fenofibrate nanosuspension; captopril; methylene blue; Hydroxypropylmethylcellulose; dioctyl sulfosuccinate sodium salt; hydroxyethylcellulose; In vitro; 1007D; 7 days; Functionality of mp verified; effect of different osmolalities, viscosities, particle size, and pump orientation on release rate kinetics.

ALZET Comments: In situ (marine environment); 2ML1 (osmosampler); 1 month; Comparison of osmotic pump in situ water osmosampler versus manual sampling; 12 Model 2ML1 pumps; maximum depth of 180 cm; “The Alzet pump specification states that there is a ±10% uncertainty in flow rate for each pump element in the absence of any calibration. By comparison, the maximum error in the laboratory determination of flow rate was ±5%, and the error using the dye marker..."
was ±1 cm and does not change with sample age." pg 7297; "The key modification that we have made to osmosampler technology to enable use and evaluation in dynamic environments is implementation of time stamping using a tracer/dye. This enables comparison of performance with laboratory characterization of flow rate as a function of temperature." pg 7298.


**ALZET Comments:** Olanzapine; Acetic acid, glacial; water, sterile; In vitro; 2ML4; Controls received vehicle; drug levels verified using a liquid-liquid extraction and liquid chromatography; "We suggest that olanzapine administration via (ALZET pumps) represents a viable option for (sub)chronic exposure with the caveats that a) duration be confined to 2 weeks..., and b) consideration be given to strategies in dissolving olanzapine that diminish the risk of oxidation." pg 89; "we strongly agree with van der Zwaal and colleagues (2008) that the issue of drug degradation is not specific to olanzapine, and that it is imperative to establish whether compounds being considered for minipump administration are capable of remaining stable in solution at body temperature."


**ALZET Comments:** Sodium sulfide; In situ (marine environment); "A new species, Tisbe dahmsi, sp. nov., is described from the Eiffel Tower edifice located in the Lucky Strike vent field"; pump at depth of 1698 m.

**P9959:** C. H. Vinkers, et al. The rapid hydrolysis of chlordiazepoxide to demoxepam may affect the outcome of chronic osmotic minipump studies. Psychopharmacology 2010;208(4):555-562

**ALZET Comments:** Chlordiazepoxide; In vitro; "When the cumulative CDP concentration over time was corrected for its hydrolysis, drug release from the minipumps followed the theoretical release profile over time (white symbols), suggesting that CDP hydrolysis completely accounted for the declined CDP release over time." pg 558; "In general, the use of osmotic minipumps presents a valid and attractive alternative to the labor-intensive daily injections. However, the issue of drug stability and release should always be carefully investigated before initiating chronic minipump experiments." pg 562.


**ALZET Comments:** Monocyte chemoattractant protein-1; CSF, artificial; BSA; CSF/CNS (striatum); in vitro (cell culture); Rat; 1003D; 2001; 3, 7 days; Controls received sham operation; peptides; cardiovascular; animal info (SHR, 270-300g); ischemia (cerebral); dose-response (fig. 5); in vitro MCP-1 administration to neurospheres in a culture plate was performed by submerging mp in normal saline in an adjacent well in the culture plate, connected via catheter (see fig. 5D).

**P7395:** H. W. Jannasch, et al. Continuous chemical monitoring with osmotically pumped water samplers: OsmoSampler design and applications. LIMNOLOGY AND OCEANOGRAPHY-METHODS 2004;2(102-113

**ALZET Comments:** In situ (marine environment); 2ML1 (osmosampler); >3 years; Novel use of ALZET Osmotic Pumps to sample seawater (osmosampler); "the inherent simplicity of osmotic pumps makes them an excellent replacement for electromechanical pumps, especially for extended sampling periods in harsh aquatic environments." p. 103; device diagram, p. 103, fig 1; flow rate is 4 ul/hr at 20 Celsius; membranes have successfully been used for more than 3 years; pumps have operated at depths up to 4,000 m.


**ALZET Comments:** Dye, methylene blue; in vitro; 2002; 3 days;

ALZET Comments: Mannitol; Radio-isotopes; Pyrrolidone, N-methyl-2-; Propylene glycol; PEG; 14C tracer; Water; Dimethylacetamide; in vitro; 2ML1; 8 days; Functionality of mp verified by in vitro testing; ALZAI chemical compatibility kit used; various solvents employed to find compatibility with drug reservoir.

ALZET Comments: Octreotide; NaCl; SC; in vitro (cell culture); Mice (SCID); 1002; 7 days; Cancer; animal info (AR4-2J tumor-bearing, CB17).

ALZET Comments: Verapamil; Saline; In vitro (egg); extraembryonic vascular bed; Bird (chicken embryo); 2001; 24, 48, 72 hours; controls received mp w/vehicle; pump immersed in saline; teratology; cardiovascular.

ALZET Comments: Diazepam; Clonazepam; flumazenil; DMSO; Propylene glycol; Tetraglycol; 3H tracer; Radio-isotopes; in vitro (egg); 2ML4; no duration posted; no comment posted.

ALZET Comments: In vitro; 2ML1; 2ML4; no duration posted; "Our sample pumps, therefore, usually contain at least four 2ML1 membranes for a total flow rate of at least 12 ul/h at 20C."

ALZET Comments: NaHCO3; Glucose; HEPES; DMEM; Serum, fetal calf; Gentamicin; in vitro (cell culture); 2001; no duration posted; mp connected to cell culture chamber; "...the osmotic pump delivered sufficient fresh medium to support cell growth in the perfusion chambers." p. 37; spaceflight.

ALZET Comments: Medium, astrocyte conditioned-; In vitro (egg); chorioallantoic membrane; Bird (chicken embryo); 2002; 5 days; controls received mp with PBS; gelfoam placed on chorioallantoic membrane; mp connected to gelfoam with PE tubing; mp kept in saline.

ALZET Comments: Rapamycin; Dimethylacetamide; Tween 80; PEG 400; in vitro; 2002; 2 weeks; stability verified by in vitro testing and HPLC for 14 days; in vitro validation of functionality and rapamycin stability.

Q0611: J. A. Lobrinus, et al. Induction of the blood-brain barrier specific HT7 and neurothelin epitopes in endothelial cells of the chick chorioallantoic vessels by a soluble factor derived from astrocytes. DEVELOPMENTAL BRAIN RESEARCH 1992;70(207-211
ALZET Comments: Medium, astrocyte conditioned-; In vitro (egg); chorioallantoic membrane; Bird (chicken embryo); 2004; 5 days; Schematic diagram of the experiment with ALZET pump, fig. 1; mp connected to gelfoam with PE tubing; mp kept in saline.

ALZET Comments: Verapamil; In vitro (egg); Bird (chicken embryo, extraembryonic vascular bed); no duration posted; en ovo, schematic p. H167.
P4504: O. Rasmussen, *et al.* Plant protoplast development on "Biokosmos 9". ESA 1990;307(527-530

**ALZET Comments:** Growth medium; *in vitro* (cell culture); 14 days; mp used to deliver growth medium to protoplasts during spaceflight.


**ALZET Comments:** Nerve growth factor; CSF, artificial; *in vitro*; CSF/CNS; Rat; 2002; 3, 7, or 14 days; no stress-see page 236; stress/adverse reaction: pages 232,236; previous experiments by investigators brought about evidence that mp were introducing cytotoxic substances into infusion fluid. This paper documents creation of coiled (Lynch coil) tubing method w/air/oil spacer whereby the fluid infused is insulated from mp while still propelled by its advance; paraffin dipping of pump utilized to reduce release rate; residual flow rate was slower in in vivo pumps than in in vitro pumps; with the modified pump fewer than 10% of rats had infusion-induced lesions; tracing air-oil space movement allows a precise measurement of volume of infusate.


**ALZET Comments:** Methazolamide; Tyrode's solution; Eye; *in vitro* (egg, eye); Bird (chicken embryo); 2001; 3 days; comparison of topical dosing vs. mp infusion; tissue perfusion.


**ALZET Comments:** Culture media; Glucose; Fetal calf serum; HEPES buffer; Gentamycin,; *in vitro* (cell culture); 2001; 2002; diagram of dynamic cell culture system on page 123; *in vitro*; spaceflight.


**ALZET Comments:** Methadol, N-desmethyl-1-acetyl; Methadone; Radio-isotopes; 3H tracer; Propylene glycol; Saline; Water; *in vitro* (egg); Bird (chicken embryo); 2001; 7 days; pump delivered to chicken egg via catheter; pump extracorporeal; comparison of a single injection vs. mp infusion.


**ALZET Comments:** Culture media, DMEM; HEPES; Serum, fetal calf; Gentamicin; Glucose; *in vitro* (cell culture); 2001; 7 days; Mp connected to cell culture chamber; cytotoxicity described; spaceflight.


**ALZET Comments:** GdDTPA; Water; *in vitro*; 2ML1; 220 hours; GdDTPA is gadolinium diethylenetriamine pentaacetic acid; MRI.

P0773: M. D. Lifschitz. Prostaglandins may mediate chloride concentration gradient across domes formed by MDCK1 cells. Am. J. Physiol 1986;250(F525-F531

**ALZET Comments:** Prostaglandin E2; Glycine; *in vitro* (cell culture); 2002; 5 hours; mp infusion in culture dish to continually add PGE2 to MDCK cell culture.


**ALZET Comments:** Radio-isotopes; Thymidine; 3H tracer; Saline; *in vitro* (cell culture); 2001; no duration posted; pumps immersed in tissue culture dish for thymidine experiments.

**ALZET Comments:** Parathyroid hormone, bovine 1-84; Culture medium, BGI; Cysteine; HCl; Saline; Serum, rat; bone (parietal); in vitro; Rat; no duration posted; in vitro: pump immersed in Ringer's solution 2-6 days; in vivo: tubing from mp wired to supraorbital ridges w/outlet cut in tubing overlying parietal bone for 2 days; peptides; tissue perfusion.


**ALZET Comments:** Thyroxine, l-; In vitro (egg); chorioallantoic membrane; Bird (chicken embryo); 2001; 7 days; mp placed in small test tube filled w/ water and then sealed w/ parafilm; mp connected to catheter that bathed the chorioallantoic membrane.