References on the Administration of Vitamins
Using ALZET® Osmotic Pumps

RO-23-7553

P3719: B. W. Light, *et al.* Potentiation of cisplatin antitumor activity using a vitamin D analogue in a murine squamous cell carcinoma model system. Cancer Res 1997;57(3759-3764
ALZET Comments: RO-23-7553; PBS; IP; mice; 1007D; 7 days; controls received sham mp; cancer.

Vitamin A

Q8858: C. Huang, *et al.* Chronic retinoic acid treatment induces affective disorders by impairing the synaptic plasticity of the hippocampus. Journal of Affective Disorders 2020;274(678-689
Agents: Retinoic acid **Vehicle:** Saline; DMSO; **Route:** CSF/CNS (lateral ventricle); **Species:** Rat; **Duration:** 21 days;
ALZET Comments: Dose (20 µg/day); Controls received mp w/ vehicle; animal info (Adult male Wistar rats, 220–240 g); behavioral testing (Sucrose Preference Test, Open Field Test, Elevated Plus Maze Test, Tail Suspension Test, Forced Swim Test); Retinoic acid aka RA; ALZET brain infusion kit used; Brain coordinates (AP: 0.8 mm, ML: 1.5 mm, DV: 4.0 mm);

Q7860: N. Y. Ru, *et al.* Glycosylated CD147 reduces myocardial collagen cross-linking in cardiac hypertrophy. J Cell Biochem 2018;119(10):8022-8034
Agents: retinoic acid **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Dose (5 mg/kg/day); Controls received mp w/ vehicle; animal info (male, Sprague-Dawley, 160-180g); Retinoic acid is an agonist of N-acetylglucosamine transferase V; cardiovascular;

P7250: T. Liu, *et al.* The retinoid anticancer signal: mechanisms of target gene regulation. British Journal of Cancer 2005;93(3):310-318
Agents: Retinoic acid, 13-cis- **Vehicle:** Ethanol; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 1007D; **Duration:** 5 weeks;
ALZET Comments: Controls received mp w/ vehicle; dose-response (fig. 1); no stress (see pg. 312-13); cancer (neuroblastoma)

P7232: S. M. Karam, *et al.* Retinoic acid stimulates the dynamics of mouse gastric epithelial progenitors. Stem Cells 2005;23(3):433-441
Agents: Retinoic acid; Uridine, bromodeoxy- **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Duration:** 1, 3, 6 days;
ALZET Comments: Controls received mp w/ vehicle; comparison of SC injections vs. mp; cancer (gastric); pumps per animal (2)

P4739: R. D. Kopke, *et al.* Growth factor treatment enhances vestibular hair cell renewal and results in improved vestibular function. PNAS 2001;98(10):5886-5891
Agents: Transforming growth factor; insulin-like growth factor I; retinoic acid; brain-derived neurotrophic factor; **Vehicle:** PBS; BSA;; **Route:** Ear (vestibule); **Species:** Guinea pig; **Pump:** 2002; **Duration:** 4 weeks;
ALZET Comments: Controls received mp w/ vehicle; pumps replaced after 2 weeks; peptides; IntraEAR catheter used; GFI group pumps filled with TGF, IGF and Retinoic acid; GFII group pumps filled with TGF, IGF, BDNF and retinoic acid;

R0148: D. Al Musawi, *et al.* Adhesion prevention: state of the art. GYNAECOLOGICAL ENDOSCOPY 2001;10(123-130
Agents: Dipyridamole; Lazaroids; Retinoic acid **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Not Stated;
ALZET Comments: Review of adhesion formation and prevention; used mp to evaluate new agents to reduce experimental pelvic adhesions (p. 125).

P4026: K. E. Rodgers, *et al.* Reduction of adhesion formation by intraperitoneal administration of various anti-inflammatory agents. J. Invest. Surgery 1998;11(327-339
Agents: Retinoic acid; Quinacrine; Dipyridamole **Vehicle:** PBS; Ethanol; **Route:** Injury site; **Species:** Rabbit; **Pump:** 2ML1; **Duration:** 1, 2, 3, 7 days;
ALZET Comments: Controls received mp w/vehicle; tissue perfusion (surgical injury site); animals given morphine i.m. for post-operative pain; catheter stabilized in sidewall w/suture; in some studies, catheter tubing was disconnected to halt flow at specific times; immunology

P3491: M. Kaya*, et al.* Chemical induction of fenestrae in vessels of the blood-brain barrier. Experimental Neurology 1996;142(6-13
Agents: Retinoic acid; Phorbol myristate acetate **Vehicle:** ETHANOL; Gibco BRL minimal essential medium; DMSO; Culture medium, serum-free; **Route:** CSF/CNS (cortex); **Species:** Rat; **Pump:** 2ML1; **Duration:** 21, 28 days;
ALZET Comments: controls received mp w/ vehicle; functionality of mp verified by residual volume; pumps replaced weekly

Vitamin B12

Q4348: E. Mutti*, et al.* 4-ethylphenyl-cobalamin impairs tissue uptake of vitamin B12 and causes vitamin B12 deficiency in mice. PLoS One 2013;8(9):e75312
ALZET Comments: Vitamin b12; Cobalamin, ethylphenyl-; saline; SC; mice; 2004; 4 weeks; controls received mp w saline; animal info: 7 wks old, female, strain 129.S6; mp used to infuse EtPhCbI in mice to see if it causes CbI (cobalamin) deficiency; EtPhCbI (3.5 nmol/24 h), CNCbI.

Q2430: D. L. Lildballe*, et al.* Maximal Load of the Vitamin B12 Transport System: A Study on Mice Treated for Four Weeks with High-Dose Vitamin B12 or Cobinamide. PLoS One 2012;7(10):U386-U392
ALZET Comments: Cobinamide; vitamin B12; Saline; SC; Mice; 2004; 27 days; Control animals received mp w/ vehicle; animal info (129.S6, 8 wks old, female); "To avoid wound biting between mice, the mice were housed in individual cages for 3 days after surgery."; post op. care (buprenorphine in the water); cobinamide is a vitamin B12 analogue.

P3776: T. Kiuchi*, et al.* Effect of vitamin B12 on the sleep-wake rhythm following an 8-hour advance of the light-dark cycle in the rat. Physiol. Behav 1997;61(4):551-554
ALZET Comments: Vitamin B12; IP; Rat; 2002; 15 days; controls received mp w/saline.

P1825: E. P. Brass*, et al.* Effect of hydroxycobalamin[c-lactam] on propionate and carnitine metabolism in the rat. Biochem. J 1990;226(809-815
ALZET Comments: Vitamin B12 analog; SC; Rat; 2002; controls received pumps with saline only; pumps replaced after 3 weeks;

Vitamin B12 analog

P1825: E. P. Brass*, et al.* Effect of hydroxycobalamin[c-lactam] on propionate and carnitine metabolism in the rat. Biochem. J 1990;226(809-815
ALZET Comments: Vitamin B12 analog; SC; Rat; 2002; no duration posted; controls received pumps with saline only; pumps replaced after three weeks; cobalamin analog.

Vitamin D

Q10596: R. H. Mak*, et al.* Differential Effects of 25-Hydroxyvitamin D3 versus 1 25-Dihydroxyvitamin D3 on Adipose Tissue Browning in CKD-Associated Cachexia. Cells 2021;
Agents: 25-Hydroxyvitamin D3; 1a25-Dihydroxyvitamin D3 **Vehicle:** Ethylene glycol; **Route:** SC; **Species:** Mice; **Pump:** 2006; **Duration:** 6 weeks;
ALZET Comments: Dose (75 ug/kg/day); animal info (CKD Male; 6 weeks of age; Housed in individual cages; Rodent diet);

Q8466: G. Fernandez Lahore*, et al.* Vitamin D3 receptor polymorphisms regulate T cells and T cell-dependent inflammatory diseases. Proceedings of the National Academy of Sciences of the United States of America 2020;117(40):24986-24997
Agents: Vitamin D3 **Vehicle:** Propylene, glycol; **Route:** SC; **Species:** Mice; **Pump:** Not stated; **Duration:** 1 day;
ALZET Comments: Dose (1000 IU/kg); Controls received mp w/ vehicle; animal info (QB Mice, 10 weeks old); immunology;

Q7891: I. Kaneko*, et al.* Eldecalcitol Causes FGF23 Resistance for Pi Reabsorption and Improves Rachitic Bone Phenotypes in the Male Hyp Mouse. Endocrinology 2018;159(7):2741-2758
Agents: 1a,25-dihydroxyvitamin D; **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 3 weeks;
ALZET Comments: animal info (137 day old, C57BL/6J); 1a,25-dihydroxyvitamin D; aka 1, 25D ; dependence;

Q5205: Stephanie R. Sisley, *et al.* Hypothalamic Vitamin D Improves Glucose Homeostasis and Reduces Weight. Diabetes 2016;1-35
Agents: Vitamin D3, 1,25-dyhydroxy **Vehicle:** Cyclodextrin; hydroxypropyl-B-; **Route:** CSF/CNS (third ventricle); **Species:** Rat; **Pump:** 1004; **Duration:** 28 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Long Evans, adult); dose-response (Supplementary Figure 3); obesity; Dose (-.264 ug/day); Brain coordinates (i3vt 2.2A/P, 7.8D/V);

Q5398: D. Ovejero, *et al.* 1,25-Dihydroxyvitamin D as Monotherapy for XLH: Back to the Future? J Bone Miner Res 2016;31(5):925-8
Agents: Vitamin D, 1,25-Dihydroxy- **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Pump:** Not Stated; **Duration:** 4 weeks;
ALZET Comments: animal info (Hyp mice); "In contrast, Alzet minipump infusion of 1,25D into Hyp mice for 4 weeks after weaning, along with a diet rich in phosphate, normalizes the growth plate and dramatically improves osteoid thickness" pg 936; Oral vs. minipump (pg. 936);

Q3925: M. L. Hyde, *et al.* In vivo measurement of the absorption of strontium in the rumen and small intestine of sheep as an index of calcium absorption capacity. British Journal of Oral and Maxillofacial Surgery 2014;112(718-724
Agents: Hydroxyvitamin D3, 1a- **Vehicle:** Not Stated; **Route:** SC; **Species:** Sheep (ewe); **Pump:** 2002; **Duration:** 6 days;
ALZET Comments: Animal info (merino, mature); functionality of mp verified by plasma 1,125-dihydroxycholecalciferol levels;

Q3900: S. K. Halder, *et al.* Paricalcitol, a Vitamin D Receptor Activator, Inhibits Tumor Formation in a Murine Model of Uterine Fibroids. REPRODUCTIVE SCIENCES 2014;21(1108-1119
Agents: Vitamin D3, 1,25-dihydroxy **Vehicle:** PEG; ethanol; **Route:** SC; **Species:** Mice (nude); **Duration:** 28 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (female, athymic, nude, 5-6 weeks old); 95% PEG used; 5% ethanol used; cancer (uterine fibroid tumor);

Q4711: T. Chaichanasakul, *et al.* Diverse Osteoclastogenesis of Bone Marrow From Mandible Versus Long Bone 1116. JOURNAL OF PERIODONTOLOGY 2014;85(829-836
Agents: Parathyroid hormone (1-34), human; vitamin D3, 1,25-dihydroxy **Route:** SC; **Species:** Rat; **Duration:** 3 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 3 months old);

Q2055: S. K. Halder, *et al.* 1,25-Dihydroxyvitamin D3 Treatment Shrinks Uterine Leiomyoma Tumors in the Eker Rat Model. Biology of Reproduction 2012;86(4):U41-U50
Agents: Vitamin D3, 1,25-dihydroxy **Vehicle:** Ethylene glycol; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 3 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (female, Eker, 14-16 wks old); functionality of mp verified via serum drug levels; cancer (uterine leiomyomas)

Q0314: M. S. K. Wong, *et al.* Chronic treatment with vitamin D lowers arterial blood pressure and reduces endothelium-dependent contractions in the aorta of the spontaneously hypertensive rat. American Journal of Physiology Heart and Circulatory Physiology 2010;299(4):H1226-H1234
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2006; **Duration:** 6 weeks;
ALZET Comments: Animal info (adult, SHR, WKY, 36 wk old); long-term study

Q1190: M. Lamblin, *et al.* Vitamin D receptor agonist/histone deacetylase inhibitor molecular hybrids. Biometals 2010;18(11):4119-4137
Agents: Vitamin D, 1 alpha 25-dihydroxy; Vitamin D hybrid, 1 alpha 25-dihydroxy **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Pump:** Not Stated; **Duration:** 6-7 days;
ALZET Comments: Animal info (female, virgin, FVB, 8 wks old); cancer; enzyme inhibitor (histone deacetylase, HDAC)

P8554: G. Mailhot, *et al.* Endocrine and bone consequences of cyclic nutritional changes in the calcium, phosphate and vitamin D status in the rat: An in vivo depletion-repletion-redepletion study. Bone 2007;41(3):422-436
Agents: Vitamin D3 **Vehicle:** Not Stated; **Route:** IP; **Species:** Rat; **Pump:** Not Stated; **Duration:** 14 days;
ALZET Comments: No stress (see pg. 425, 432); animal info (male, Sprague-Dawley, 7 weeks old)

P8289: W. Banach-Petrosky, *et al.* Vitamin D inhibits the formation of prostatic intraepithelial neoplasia in Nkx3.1; Pten mutant mice. Clinical Cancer Research 2006;12(19):5895-5901
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Propylene glycol; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 1,4 months;
ALZET Comments: Controls received mp w/ vehicle; long-term study; pumps replaced every 4 weeks; stability verified by serum calcium levels; cancer (prostate); animal info (4-7 months old, male)

P7307: K. Nakagawa, *et al.* 22-oxa-1alpha,25-dihydroxyvitamin D_3 inhibits metastasis and angiogenesis in lung cancer. Carcinogenesis: Integrative Cancer Research 2005;26(6):1044-1054
Agents: Vitamin D3, 1, 25-dihydroxy-; vitamin D3, 22-oxa-la, 25-dihydroxy- **Vehicle:** Tween 20; Ethanol; **Route:** SC; **Species:** Mice; **Pump:** 2ML4; **Duration:** 3 weeks; 10, 18 days;
ALZET Comments: Controls received mp w/ vehicle; dose-response; cancer (lung carcinoma); 10% ethanol;

P7170: G. Duque, *et al.* $1,25(OH)_2D_3$ acts as a bone-forming agent in the hormone-independent senescence-accelerated mouse (SAM-P/6). American Journal of Physiology Endocrinology and Metabolism 2005;288(4):E723-E730
Agents: Vitamin D3, 1, 25-dihydroxy- **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Duration:** 6 weeks;
ALZET Comments: Controls received mp w/ vehicle; pumps replaced after 3 weeks, no stress (see pg. E728)

P6832: R. Narayanan, *et al.* Differential skeletal responses of hindlimb unloaded rats on a vitamin D-deficient diet to 1,25-dihydroxyvitamin D_3 and its analog, seocalcitol (EB1089). Bone 2004;35(1):134-143
Agents: Vitamin D3, 1,25-dihydroxy; EB 1089 **Vehicle:** Polypropylene glycol; sodium phosphate; **Route:** SC; **Species:** Rat; **Duration:** 28 days;
ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified by plasma 25(OH)-D and 1,25-D levels; stress/adverse reaction: (see pg. 137) 5 animals died due to anesthesia complications and to tail irritation and diarrhea

P6206: G. Duque, *et al.* Vitamin D treatment of senescence accelerated mice (SAM-P/6) induces several regulators of stromal cell plasticity. Bioelectromagnetics 2004;5(6):421-429
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Pump:** 2004; **Duration:** 6 weeks;
ALZET Comments: Controls received mp w/ vehicle; pumps replaced after 3 weeks

P5867: C. Theodoropoulos, *et al.* High sensitivity of rat hepatic vitamin D-3-25 hydroxylase CYP27A to 1,25-dihydroxyvitamin D-3 administration. American Journal of Physiology Endocrinology and Metabolism 2003;284(1):E138-E147
Agents: Vitamin D3, 125-dihydroxy-; vitamin D3, 25-dihydroxy- **Route:** IP; **Species:** Rat; **Duration:** 1,3,5,7 days;
ALZET Comments: Functionality of mp verified by serum levels (p. E140); dose-response (p. E140); pump model not stated

P5121: M. Thierry-Palmer, *et al.* Plasma 24,25-dihydroxyvitamin D concentration of Dahl salt-sensitive rats decreases during high salt intake. Journal of Steroid Biochemistry and Molecular Biology 2002;80(315-321
Agents: Vitamin D3, 24,25-dihydroxy-; Vitamin D3, 25-hydroxy- **Vehicle:** Propylene glycol; Ethanol; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** Up to 28 days;
ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified by plasma levels; vehicle was 95% PG with 5% ETOH

P6248: K. Rummens, *et al.* Vitamin D deficiency in guinea pigs: Exacerbation of bone phenotype during pregnancy and disturbed fetal mineralization, with recovery by 1, 25(OH)(2)D-3 infusion or dietary calcium-phosphate supplementation. Calcified Tissue International 2002;71(4):364-375
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Not Stated; **Route:** SC; **Species:** Guinea pig; **Pump:** 2ML4; **Duration:** 4 weeks;
ALZET Comments:

P6660: D. C. Huang, *et al.* Targeted disruption of the 25-hydroxyvitamin D_3 1 alpha-hydroxylase gene in *ras*-transformed keratinocytes demonstrates that locally produce d 1 alpha,25-dihydroxyvitamin D_3 suppresses growth and induces differ entiation in an autocrine fashion. Molecular Cancer Research 2002;1(1):56-67
Agents: Vitamin D3, 25-hydroxy- **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice (SCID); **Duration:** 5.5 weeks;
ALZET Comments: Controls received mp w/ vehicle or agent with no tumor; functionality of mp verified by 25-OHD_3 plasma levels; no stress (see pg. 11 and fig.7); cancer (squamous carcinoma)

P5058: R. Gill, *et al.* Regulation of rat ileal NHE3 by 1,25(OH)(2)-vitamin D-3. Digestive Diseases and Sciences 2002;47(5):1169-1174
Agents: Vitamin D3, 1, 25-dihydroxy- **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: controls received mp w/ vehicle; functionality of mp verified by serum Vitamin D3 levels; streptozotocin induced diabetes, p. 1170

Q7708: V. Panichi, *et al.* Effects of 1,25(OH)2D3 in experimental mesangial proliferative nephritis in rats. Kidney Int 2001;60(1):87-95
Agents: 1,25-Dihydroxyvitamin D3 **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 14 days;
ALZET Comments: Dose (25 ng/100g wt/day); Controls received mp w/ vehicle; animal info (Female, 8 week old, Wistar, 160-200 g); 1,25-Dihydroxyvitamin D3 aka 1,25(OH)2D3; enzyme inhibitor (Monocyte-derived cytokine inhibitor); dependence;

P4614: I. V. Silva, *et al.* PTH regulates expression of ClC-5 chloride channel in the kidney. American Journal of Physiology Renal Physiology 2000;278(F238-F245
Agents: Vitamin D; Parathyroid hormone (1-34) **Vehicle:** Ringer's solution; **Route:** SC; **Species:** Rat (pregnant); **Pump:** 1003D;; **Duration:** 3 days;
ALZET Comments: Controls received mp w/vehicle + sham operation; replacement therapy (thyroparathyroidectomy); peptides

P4691: G. Mailhot, *et al.* Influence of the *in vivo* calcium status on cellular calcium homeostasis and the level of the calcium-binding protein calreticulin in rat hepatocytes. Endocrinology 2000;141(3):891-900
Agents: Vitamin D **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Rat; **Pump:** Not Stated; **Duration:** 1 week;
ALZET Comments:

P4476: L. Xue, *et al.* Influence of dietary calcium and vitamin D on diet-induced epithelial cell hyperproliferation in mice. J. Natl. Cancer Inst 1999;91(176-181
Agents: Vitamin D; uridine, bromodeoxy- **Vehicle:** Not Stated; **Route:** SC;; **Species:** Mice; **Pump:** 1003D; **Duration:** 3 days;
ALZET Comments: Cancer

P3992: A. W. Saxe, *et al.* Effect of chronic vitamin D infusion upon in vivo glucose disposal. Calcified Tissue International 1999;64(248-251
Agents: Vitamin D **Vehicle:** Propylene glycol; Ethanol; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 5 days;
ALZET Comments: controls received mp w/vehicle

P3929: M. G. Tordoff, *et al.* Calcium intake by rats: influence of parathyroid hormone, calcitonin, and 1,25-dihydroxyvitamin D. American Journal of Physiology Regulatory, Integrative, and Comparable Physiology 1998;274(43):R214-R231
Agents: Parathyroid hormone; Calcitonin; Vitamin D, 1,25-dihydroxy- **Vehicle:** NaCl; HCl; Cysteine; Saline, isotonic; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 13 days;
ALZET Comments: controls received sham tubing; functionality of mp verified by hormone assays; replacement therapy (thyroidectomy, thyroparathyroidectomy); dose-response; stress/adverse reaction: high doses led to animal death; peptides; agents given singly and in combination

P3994: A. Sela-Brown, *et al.* Calreticulin inhibits vitamin D's action on the PTH gene in vitro and may prevent vitamin D's effect in vivo in hypocalcemic rats. Molec. Endocrinol 1998;12(8):1193-1200
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Propylene glycol; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 7 days;
ALZET Comments: controls received mp w/vehicle

P3993: U. Schwarz, *et al.* Effect of 1,25 (OH)2 vitamin D3 on glomerulosclerosis in subtotally nephrectomized rats. Kidney Int 1998;53(1696-1705
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Ethanol; **Route:** Not Stated; **Species:** Rat; **Pump:** 2ML4; **Duration:** Not Stated;
ALZET Comments: Controls received mp w/vehicle

P3606: H. Tsuji, *et al.* Abnormal modulation of serum osteocalcin by dietary phosphate and 1,25-dihydroxyvitamin D3 in the hypophosphatemic mouse. J. Bone and Min. Res 1996;11(9):1234-1240
Agents: Parathyroid hormone; Vitamin D3, 1,25-dihydroxy- **Vehicle:** Propylene glycol; Saline; Cysteine; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 3,14 days;
ALZET Comments: Controls received mp w/ vehicle; peptides

P3621: J. R. Stabel, *et al.* Low calcium diet and 1,25-dihydroxyvitamin D(3) infusion modulate immune responses during mycobacterium paratuberculosis infection in beige mice. Vet. Immunology and Immnopathology 1996;50(127-143
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** Not Stated;
ALZET Comments: Functionality of mp verified by plasma levels; immunology

P3991: J. R. Stabel, *et al.* Influence of vitamin D3 infusion and dietary calcium on secretion of interleukin 1, interleukin 6 and tumor necrosis factor in mice infected with Mycobacterium paratuberculosis. American Journal of Veterinary Research 1996;57(6):825-829
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 14 days;
ALZET Comments: Immunology

P2853: K. V. Rogers, *et al.* Calcium receptor messenger ribonucleic acid levels in the parathyroid glands and kidney of vitamin D-deficient rats are not regulated by plasma calcium or 1,25-dihydroxyvitamin D3. Endocrinology 1995;136(2):499-504
Agents: Calcium chloride; Vitamin D3, 1,25-dihydroxy- **Vehicle:** Propylene glycol; Ethanol; **Route:** SC; IV (inferior vena cava);
Species: Rat; **Pump:** 2002; 2ML1; **Duration:** 7 days;
ALZET Comments: no comment posted

P3281: R. A. Meyer, *et al.* Response of jejunal phosphate absorption to 1,25-dihydroxyvitamin D3 stimulation in vivo in young X-linked hypophosphatemic (Hyp) mice. Endocrine 1995;3(209-214
Agents: Vitamin D3, 1,25-dihydroxy **Vehicle:** Propanediol, 1,2; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 4 days;
ALZET Comments: Normal and Hyp mice used

P3541: B. Ecarot, *et al.* Effect of 1,25-dihydroxyvitamin D3 treatment on bone formation by transplanted cells from normal and X-linked hypophosphatemic mice. J. Bone and Min. Res 1995;10(3):424-431
Agents: Vitamin D3, 1,25-dihydroxy-; Vitamin D3, 24,25-dihydroxy- **Vehicle:** Propylene glycol; **Route:** SC; **Species:** Mice;
Pump: 2001; 2002; **Duration:** 17 days;
ALZET Comments: Pumps replaced at day 6; vitamins given singly and together

P3198: D. C. Hatton, *et al.* 1,25(OH)2 Vitamin D3-induced alterations in vascular reactivity in the spontaneously hypertensive rat. Am. J. Med. Sci 1994;307(Sup 1):S154-S158
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: controls received mp with vehicle; comparison of daily sc injections vs. mp

P3142: A. Uhland-Smith, *et al.* The necessity for calcium for increased renal vitamin D receptor in response to 1,25-dihydroxyvitamin D. Biochimica et Biophysica Acta (BBA) - Molecular Cell Research 1993;1176(321-326
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 4,8 weeks;
ALZET Comments: comparison of oral vitamin D-3 vs. mp; long-term study, pumps replaced after 2 weeks

P3576: M. G. Tordoff, *et al.* Independence of salt intake from the hormones regulating calcium homeostasis. American Journal of Physiology Regulatory, Integrative, and Comparable Physiology 1993;264(R500-R512
Agents: Parathyroid hormone, bovine; Vitamin D3, 1,25-dihydroxy- **Vehicle:** Propylene glycol; **Route:** SC; **Species:** Rat; **Pump:** 2001; 2002; **Duration:** 1, 2 weeks;
ALZET Comments: replacement therapy (thyroparathyroidectomy)

P2142: T. Shimosawa*, et al.* Enhancement of vasoconstrictor response by a noncalcemic analogue of vitamin D3. Hypertension 1993;21(2):253-258
Agents: Oxacalcitriol, 22-; Vitamin D3, 24,25-dihydroxy-; Vitamin D3, 1,25-dihydroxy- **Vehicle:** Propylene glycol; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: no comment posted

P2886: H. Reichel*, et al.* Intermittent versus continuous administration of 1,25-dihydroxyvitamin D3 in experimental renal hyperparathyroidism. Kidney Int 1993;44(1259-1265
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Propylene glycol; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 6 days;
ALZET Comments: functionality of mp verified by residual volume, radioactive tracing and serum levels; comparison of i.p. injections vs. mp

P2664: A. J. Brown*, et al.* The mechanism for the disparate actions of calcitriol and 22-oxacalcitriol in the intestine. Endocrinology 1993;133(3):1158-1164
Agents: Oxacalcitriol, 22-; Vitamin D3, 1,25-dihydroxy- **Vehicle:** Propylene glycol; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 3 days;
ALZET Comments: controls received mp w/ vehicle; comparison of ip injections vs. mp; agent is 1,25-(OH)2D3

P2280: J. P. Goff*, et al.* Effect of dietary calcium or phosphorus restriction and 1,25-dihydroxyvitamin D administration on rat intestinal 24-hydroxylase. Endocrinology 1992;131(1):101-104
Agents: Vitamin D, 1,25-dihydroxy- **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 3,7 days;
ALZET Comments: comparison of ip injections vs mp

P2073: J. Fox*, et al.* Normal plasma calcium, phosphate, and parathyroid hormone levels during 1,25(OH)2D3 infusions in rats. American Journal of Physiology Endocrinology and Metabolism 1992;262(E126-E129
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Ethanol; Propylene glycol; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 10 days;
ALZET Comments: dose-response graphs (pp. E127-E128); infusion of D3 represents a better approach over injections for determining the physiology of tissue D3 responsiveness

P1759: B. Stein*, et al.* Cyclosporin-A increases synthesis of 1,25-dihydroxyvitamin D3 in the rat and mouse. Endocrinology 1991;128(3):1369-1373
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Radio-isotopes; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** Not Stated;
ALZET Comments: Not Stated

P1850: J. M. Lemire*, et al.* 1,25-dihydroxyvitamin D3 prevents the in vivo induction of murine experimental autoimmune encephalomyelitis. J. Clin. Invest 1991;87(1103-1107
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** Not Stated;
ALZET Comments: no comment posted

P1761: G. A. Davidai*, et al.* Variable phosphate-mediated regulation of vitamin D metabolism in the murine hypophosphatemic rachitic/osteomalacic disorders. Endocrinology 1991;128(3):1270-1276
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Propylene glycol; **Species:** Mice; **Pump:** 2001; **Duration:** 48 hours;
ALZET Comments: no comment posted

P1700: T. A. Reinhardt*, et al.* Parathyroid hormone down-regulates 1,25-dihydroxyvitamin D receptors (VDR) and VDR messenger ribonucleic acid in vitro and blocks homologous up-regulation of VDR in vivo. Endocrinology 1990;127(2):942-948
Agents: Parathyroid hormone; Vitamin D3, 1,25-dihydroxy- **Vehicle:** Cysteine; Ethanol; HCl; Propylene glycol; Saline; **Route:** Not Stated; **Species:** Rat; **Pump:** Not Stated; **Duration:** 5 days;
ALZET Comments: controls received pumps with saline only; peptides; PTH and vit. D infused separately and concurrently

P1393: H. Yamato, *et al.* Effect of 24,25-dihydroxyvitamin D3 on 1,25-dihydroxyvitamin D3 [1,25-(OH)2D3] metabolism in vitamin D-deficient rats infused with 1,25-(OH)2D3. Endocrinology 1989;124(1):511-517
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Propylene glycol; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 7, 10 days;
ALZET Comments: dose-response (serum levels); half-life; functionality of mp verified by serum levels

P1540: A. Szabo, *et al.* 1,25(OH)2 vitamin D3 inhibits parathyroid cell proliferation in experimental uremia. Kidney Int 1989;35(1049-1056
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Propanol; **Route:** IP; **Species:** Rat; **Pump:** Not Stated; **Duration:** Not Stated;
ALZET Comments: Comparison of IP injections vs. mp infusion

P1656: S. Patel, *et al.* Effect of vitamin D metabolites on calcitriol metabolism in experimental renal failure. Kidney Int 1989;36(234-239
Agents: Calcitriol; Vitamin D3, 1,25-dihydroxy- **Vehicle:** Ethanol; Propylene glycol; **Route:** SC; **Species:** Rat; **Pump:** 2001;
Duration: 1 week;
ALZET Comments: functionality of mp verified by measuring residual volume

P1576: Y. Naito, *et al.* Effects of continuous administration of 1,25-dihydroxyvitamin D3 on plasma minerals and unoccupied colon mucosal 1,25-dihydroxyvitamin D3 receptor concentrations. J. Dairy Sci 1989;72(2936-2941
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Propylene glycol; **Route:** SC; **Species:** Cattle; **Pump:** 2ML1; **Duration:** 7 days;
ALZET Comments: functionality of mp verified by measuring plasma vit. D levels; discusses comparison of IM injections vs. mp; states pump effectively maintained plasma conc. throughout (p. 2939), states conc. achieved via pump may improve vit. D3 therapy for preventing p

P1588: R. L. Horst, *et al.* Advancing age results in reduction of intestinal and bone 1,25-dihydroxyvitamin D receptor. Endocrinology 1989;126(2):1053-1057
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Ethanol; Propylene glycol; **Route:** Not Stated; **Species:** Rat; **Pump:** 2001;
Duration: 6 days;
ALZET Comments: no comment posted

P1515: M. H. Meyer, *et al.* Increased intestinal absorption of calcium in young and adult X-linked hypophosphatemic mice after the administration of 1,25-dihydroxyvitamin D3. J. Bone and Min. Res 1988;3(2):151-157
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Propanediol, 1,2-; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 3 days;
ALZET Comments: No comment posted

P1401: R. A. Meyer, *et al.* Evidence that low plasma 1,25-dihydroxyvitamin D causes intestinal malabsorption of calcium and phosphate in juvenile X-linked hypophosphatemic mice. J. Bone and Min. Res 1987;2(1):67-82
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Propanediol, 1,2-; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 3 days;
ALZET Comments: Dose-response; functionality of mp verified by plasma levels

P1089: P. Haddad, *et al.* Influence of the vitamin D hormonal status on the hepatic response to bromobenzene. J. Pharmacol. Exp. Ther 1987;242(1):354-363
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Ethanol; Propylene glycol; Saline; **Route:** IP; **Species:** Rat; **Pump:** 2001;
Duration: 8 days;
ALZET Comments: controls received mp w/vehicle

P8175: M. R. Clements, *et al.* A new mechanism for induced vitamin D deficiency in calcium deprivation. Letters to Nature 1987;325(6099):62-65
Agents: Vitamin D, 1,25-dihydroxy- **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** Not Stated;
ALZET Comments: Animal info (male, Norwegian hooded)

P1058: M. E. Bruns, *et al.* Vitamin D-dependent calcium binding proteins in the kidney and intestine of the X-linked hypophosphatemic mouse: Changes with age and responses to 1,25-dihydroxycholecalciferol. Endocrine Society 1987;121(1-6
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Propylene glycol; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 3 days;
ALZET Comments: Controls received mp w/vehicle; mice were hypophosphatemic

P0927: T. J. Wronski, *et al.* Chronic administration of 1,25-dihydroxyvitamin D3: Increased bone but impaired mineralization. Endocrinology 1986;119(6):2580-2585
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Ethanol; Propylene glycol; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 13 days;
ALZET Comments: controls received mp w/vehicle

P0779: J. Sonnenberg, *et al.* 1,25-dihydroxyvitamin d3 treatment results in increased choline acetyltransferase activity in specific brain nuclei. Endocrinology 1986;118(4):1433-1439
Agents: Calcium chloride; Vitamin D3, 1,25-dihydroxy- **Vehicle:** Propylene glycol; Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: mp connected to cannula in 3rd ventricle and implanted sc; vitamin d3 administered ip in combination w/mp infusion; controls received mp w/appropriate vehicle; agents administered separately

P2521: G. K. Potter, *et al.* Response to an active vitamin D3 metabolite of transplantable human myeloid leukemic cell lines in adult nude mice. In 'Experimental Hematology Today--1985,' S. J. Baum, D. H. Pluznick, and L. A. Rozenszajn (eds.), Springer-Verlag New York, Inc 1986;106-113
Agents: Vitamin D3 metabolites **Vehicle:** Propylene glycol; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** Not Stated;
ALZET Comments: Not Stated

P0781: T. Nesbitt, *et al.* Abnormal parathyroid hormone stimulation of 25-hydroxyvitamin d-1a-hydroxylase activity in the hypophosphatemic mouse. J. Clin. Invest 1986;77(1):181-187
Agents: Parathyroid hormone, bovine; Vitamin D3, 1,25-dihydroxy- **Vehicle:** Cysteine HCl; Propylene glycol; Saline; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 48 hours;
ALZET Comments: mp primed in saline 24 hrs prior to implant; controls received sham pumps; dose-response (plasma levels & kidney conc.); agents infused separately; advantages of mp infusion (see pg. 185); peptides

P0921: J. R. Jobin, *et al.* Compensatory renal growth: Modulation by calcium PTH and 1,25-(OH)2D3. Kidney Int 1986;29(1124-1130
Agents: Parathyroid hormone, bovine; Vitamin D3, 1,25-dihydroxy- **Vehicle:** Acetic acid; Albumin; Ethanol; Propylene glycol; Saline; **Route:** IP; **Species:** Rat; **Pump:** 2001; **Duration:** 3 days;
ALZET Comments: 4 doses of agents infused; replacement therapy (thyroparathyroidectomy); peptides

P0777: B. P. Halloran, *et al.* The role of 1,25-dihydroxyvitamin D in the inhibition of bone formation induced by skeletal unloading. Endocrinology 1986;118(3):948-954
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Ethanol; Propylene glycol; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 2wks
ALZET Comments: dose-response (serum conc.)

P0893: B. P. Halloran, *et al.* Chronic 1,25-dyhydroxyvitamin D3 administration in the rat reduces the serum concentration of 25-hydroxyvitamin D by increasing metabolic clearance rate. J. Clin. Invest 1986;78(622-628
Agents: Radio-isotopes; Vitamin D3, 1,25-dihydroxy- **Vehicle:** 3H tracer; Ethanol; Propylene glycol; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 3, 7, 12 days;
ALZET Comments: metabolic clearance rate measured by mp infusion of labelled Vit. D3, see ref. 15 & 16

P0734: G. K. Potter, *et al.* Action of 1,25-(OH)2D3 in nude mice bearing transplantable human myelogenous leukemic cell lines. Experimental Hematology 1985;13(722-732
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Propylene glycol; **Route:** SC; **Species:** Mice (nude); **Pump:** 2001; **Duration:** 70 days;
ALZET Comments: mp replaced periodically; long-term study; comparison of various agents iv vs. mp infusion;

P0646: P. J. Marie, *et al.* Contrasting effects of 1,25-dihydroxyvitamin D3 on bone matrix and mineral appositional rates in the mouse. Metabolism 1985;34(8):777-783
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Propylene glycol; **Route:** SC; **Species:** Mice; **Duration:** 1 week;
ALZET Comments: 3 doses of Vit D3 given; dose-response data

P0434: R. Brommage, *et al.* 1,25-Dihydroxyvitamin D3 normalizes maternal food consumption and pup growth in rats. American Journal of Physiology Endocrinology and Metabolism 1984;246(E227-E231
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Ethanol; Propylene glycol; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 17d
ALZET Comments: comparison of single ip injection vs. mp infusion; mp coated w/ Panalog ointment to reduce risk of infection

P0357: P. J. Marie, *et al.* Continuous infusion of 1,25-dihydroxyvitamin D3 stimulates bone turnover in the normal young mouse. Calcified Tissue International 1983;35(418-425
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Propylene glycol; **Route:** SC; **Species:** Mice; **Duration:** 4 weeks;
ALZET Comments: 4 dose levels tested: 0.05, 0.10, 0.175, and 0.25 ug/kg/day

P0303: K. Jarnagin, *et al.* 1- But not 24-hydroxylation of vitamin D is required for growth and reproduction in rats. American Journal of Physiology Endocrinology and Metabolism 1983;244(E290-E297
Agents: Vitamin D3, 1,25-dihydroxy-; Vitamin D3, 25-hydroxy- **Vehicle:** Propylene glycol; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 20 weeks;
ALZET Comments: comparison of oral vs. sc infusion; mp replaced every 2 weeks; pumps coated w/ Panalog ointment; animals washed w/surg. scrub & not shaved; long-term study; no stress - p. E296

P0309: E. Hefti, *et al.* Nature of calcemic effect of 1,25-dihydroxyvitamin D3 in experimental hypoparathyroidism. American Journal of Physiology Endocrinology and Metabolism 1983;244(E313-E316
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Propylene glycol; **Route:** IP; **Species:** Rat; **Pump:** 1701; **Duration:** 1 week;
ALZET Comments: no comment posted

P0304: R. Brommage, *et al.* 1- But not 24-hydroxylation of vitamin D is required for skeletal mineralization in rats. American Journal of Physiology Endocrinology and Metabolism 1983;244(E298-E304
Agents: Vitamin D3, 1,25-dihydroxy-; Vitamin D3, 25-hydroxy- **Vehicle:** Propylene glycol; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** Not Stated;
ALZET Comments: Comparison of oral vs. sc infusion

P0234: P. J. Marie, *et al.* Healing of bone lesions with 1,25-dihydroxyvitamin D3 in the young X-linked hypophosphatemic male mouse. Endocrinology 1982;111(3):904-911
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Propylene glycol; **Route:** SC; **Species:** Mice; **Duration:** 4 weeks;
ALZET Comments: no comment posted

P0236: P. J. Marie, *et al.* Bone response to phosphate and vitamin D metabolites in the hypophosphatemic male mouse. Calcified Tissue International 1982;34(158-164
Agents: Vitamin D3, 24,25-dihydroxy-; Vitamin D3, 25-dihydroxy-; Vitamin D3, 1,25-dihydroxy- **Vehicle:** Propylene glycol; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 18 days;
ALZET Comments: Comparison of agents

P0149: H. S. Tenenhouse, *et al.* Effect of 1,25-dihydroxyvitamin D3 on phosphate homeostasis in the X-linked hypophosphatemic (Hyp) mouse. Endocrinology 1981;109(2):658-660
Agents: Vitamin D3, 1,25-dihydroxy- **Vehicle:** Propylene glycol; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 10 days;
ALZET Comments: Pumps replaced

Vitamin E

Q1590: C. Y. Hsieh*, et al.* Inhibition of vascular smooth muscle cell proliferation by the vitamin E derivative pentamethylhydroxychromane in an in vitro and in vivo study: pivotal role of hydroxyl radical-mediated PLC-gamma-1 and JAK2 phosphorylation. Free Radical Biology and Medicine 2010;49(5):881-893
Agents: PMC; tocopherol, alpha **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 14 days;
ALZET Comments: Controls received mp w/ normal saline; animal info (Wistar, male, 350-400 g); PMC, also known as (2,2,5,7,8-pentamethyl-6-hydroxychromane, is a vitamin E derivative; tocopherol also known as vitamin E

P9636: D. C. Irwin*, et al.* A potential role for reactive oxygen species and the HIF-1-alpha-VEGF pathway in hypoxia-induced pulmonary vascular leak. Free Radical Biology and Medicine 2009;47(1):55-61
Agents: Ascorbate; glutathione; tocopherol, alpha- **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1007D;
ALZET Comments: Controls received mp w/saline; animal info (male, C57BL/6J, 25-30g, 10-12 weeks old); compounds were mixed and infused together as an antioxidant cocktail
P3759: T. Udaka*, et al.* The effect of combination therapy with EPC-K1 and low-dose cyclosporine to pulmonary allograft after rat lung transplantation. J. Heart Lung Transplant 1997;16(839-845
Agents: Vitamin E **Vehicle:** Not Stated; **Route:** IP; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: functionality of mp verified by measuring EPC-K1 plasma levels; immunology; EPC-K1 is a diester of a-tocopherol and ascorbic acid; agent also called D-alpha-tocopherol

P2013: D. G. Stein*, et al.* Intracerebral administration of alpha-tocopherol-containing liposomes facilitates behavioral recovery in rats with bilateral lesions of the frontal cortex. J. Neurotrauma 1991;8(4):281-292
Agents: Phosphatidylcholine; vitamin E; Liposomes **Vehicle:** Not Stated; **Route:** CSF/CNS (cortex); **Species:** Rat; **Pump:** 2001;
Duration: 7 days;
ALZET Comments: Multiple pumps per animal (2); agent also called D-alpha-tocopherol