

Supplemental Table 2 References. Chemical Castration by Intratesticular Administration and Potential Sterilizing Effects in Male Animals

Target Organ	Admin ¹	Chemical	Trade Name ³	Species	Dosage	Original Use	Short-term Pathology	Long-term Pathology	Mechanisms of action	T Decreased ³	Inflammation	Side-Effects	Refs ⁴
Testis	Intra-testicular ⁴	Zinc compounds	Kastrin, Neutersol™, Zeuterin™, EsterilSol™, Testoblock®, Infertile®	Rat, Dog, Cat, Monkey, Bear, Pig	2.6-58 mg/ml	Dietary supplement; treatment of common cold	Multinucleated giant cells; acute inflammation; edema; testis swelling	Seminiferous tubule necrosis; atrophy;	Sertoli cell barrier damage; massive neutrophilic inflammation; necrosis; tubular fibrosis	Yes	Yes	Scrotal ulceration and dermatitis; necrotizing reactions	1
		4-allyl-2-methoxyphenol	Eugenol Clove oil	Dog	1 ml	Cosmetics; anti-anthelmintic; expectorant	Testis swelling	Seminiferous tubular fibrosis	Testicular necrosis; inflammation	Yes	Yes	Epididymal vacuolation	2
		CaCl ₂ +/- ethanol & hypertonic NaCl	Calchlorin™, Salts	Rat, Dog, Cat, Bull, Goat, Donkey, Ram, Guinea pig, Buffalo	20-50% in water or ethanol	Inorganic salt; food additive; deicing salt; desiccant	Testis swelling; inflammation	Testicular atrophy	Testicular dehydration; necrosis; coagulative fibrosis	Yes	Yes	Scrotal necrosis if leakage	3
		CdCl ₂	Metallic salt	Rat, Mouse, Dog, Rabbit, Hamster	150 µ/kg	Inorganic salt pigment	Hemorrhage; edema; inflammation	Testicular atrophy	Decreased blood flow; ischemia; oxidative stress	Yes	Yes	Toxic to numerous organs, if given oral	4
		1,2,3-trihydroxypropane	Glycerol	Rat, Dog, Cat, Monkey, Rabbit	10-70%	Food additive; soap; laxative	Seminiferous tubule disruption	Testicular atrophy	Hyperosmotic dehydration	Yes	Yes	None	5
		Lactic acid	Chem-Cast®	Rat, Dog, Bull	85-92%	Organic synthesis; food additive	Germ cell degeneration	Testicular atrophy	Sclerosing, caustic chemical; necrosis; fibrosis	Yes	Yes	Scrotal necrosis if leakage	6
		KMnO ₄	N/A	Pig	0.25 g/17 ml acetic acid	Inorganic oxidizing agent; water treatment	N/A	Seminiferous tubular atrophy; fibrosis efferent ducts	Sclerosing, caustic chemical	N/A	Yes	Leydig cell hypertrophy	7
		Metallic & rare earth salts	N/A	Rat, Mouse, Monkey	0.02-0.08 mM/kg	Salts	Focal necrosis	Testicular total necrosis for some salts	Cytolysis, ischemia, necrosis	N/A	Yes	Some Leydig cell loss; early effects on vas deferens sperm; some salts showed no effect	8
		Ethanol	Alcohol	Bull	100%; 10 ml	Organic solvent	Testis swelling; necrosis	Testicular atrophy	Necrosis; inflammation; edema; fibrosis	Yes	Yes	Only 50% became infertile	9
	Intra-Testicular; s.c or i.m	Inflammatory induction agents ²	N/A	Guinea pig, Monkey, Rat, Rabbit; Dog; Ram	N/A	Antibody stimulating	Inflammation; seminiferous tubular dilation; testis swelling	Granuloma; necrosis; testicular atrophy	Inflammation;	No	Yes	Injection outside testis required for azoospermia for some agents	10

¹ Administration of the chemical/drug by intra-testicular injection or with subcutaneous or cutaneous (s.c.), intramuscular (i.m.) injection

² Testicular antigens +/- killed bacteria; killed mycobacteria; Freund’s complete adjuvant injected into foot after intratesticular injection of turpentine; Freund’s complete adjuvant plus testis homogenate

³ N/A, not applicable; T, testosterone

⁴ Supplemental References:

- 1: Zinc compounds [1-41]
- 2: 4-allyl-2-methoxyphenol [42-47]
- 3: CaCl₂ +/- ethanol and hypertonic NaCl₂ [46, 48-84]

- 4: CdCl₂ [85-110]
- 5: 1,2,3-trihydroxypropane [111-119]
- 6: Lactic Acid [120-123]
- 7: Potassium permanganate [124, 125]
- 8: Metallic and rare earth salts [126, 127]
- 9: Ethanol [64]
- 10: Inflammatory induction agents [35, 128-134]

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