RODENTICIDES

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Contents

Summary

A rodenticide is defined as any compound used to kill rodents or other small animals. They are widely used, and as a class encompass a disparate group of compounds with differing structures and mechanisms of action.

Rodenticides can be subdivided into inorganic and organic compounds. Inorganic rodenticides include agents such as arsenic salts, thallium, phosphorus, zinc phosphide and barium salts. They are considered highly toxic, exhibiting single-dose oral LD_{50}

values for rats of 50 mg kg^{-1} or less, based on the ingestion of the commercially available product and including both active and inert ingredients. The estimated lethal dose for inorganic rodenticides ranges from 1 mg kg^{-1} for elemental phosphorus, 3-7 mg kg^{-1} for sodium monofluoroacetate, to 13-14 mg kg^{-1} for sodium fluoroacetamide and thallium. The mechanisms of toxicity for the inorganic rodenticides is as variable as the agents. Thallium interacts with sulfhydryl moieties within mitochondria, interfering with oxidative phosphorylation. Likewise, arsenic inhibits the activity of a variety of enzymes through binding to sulfhydryl groups. Fluoroacetate derivatives disrupt the Kreb's cycle by serving as competitive substrates. Both barium and strychnine act, directly or indirectly, to block motor neuron activity, and phosphorus causes severe local irritation and burns followed by gastrointestinal, hepatic and renal dysfunction.

Organic rodenticides include fluoroacetate derivatives, thiourea-based agents, derivatives of vitamin D, short- and long-acting anticoagulants, red squill, norbormide and strychnine. Of these, pyriminil is designated as being highly toxic, with an estimated fatal dose of 5 mg kg^{-1}. Its primary mechanism of toxicity appears to be interference with nicotinamide metabolism, resulting in dysfunction in a number of tissues including the central and peripheral nervous systems, the heart and the pancreas. α-Naphthylthiourea, which causes acute pulmonary toxicity, and vitamin D-based rodenticides, which cause hypercalcemia with predictable sequelae, are considered moderately toxic; oral LD_{50} values for commercially available preparations range between 50-500 mg kg^{-1}. Some other organic rodenticides are designated as having low toxicity with LD_{50} values in excess of 500 mg kg^{-1}. Norbormide appears to be selectively toxic to rats. It causes vasoconstriction through a norbormide-specific receptor on rat vascular smooth muscle, and there have been no reported cases of systemic toxicity to norbormide in humans. Red squill is a glycoside and, as such, causes both cardiotoxicity and convulsant effects. Bromethalin uncouples oxidative phosphorylation. Concomitant depletion of cellular ATP has functional consequences on all cell types, but effects within the central and peripheral nervous systems are most pronounced. Although bromethalin has a reported LD_{50} in rats of 2 mg kg^{-1}, the potential for bromethalin poisoning in humans is considered to be low. Warfarin and its more-long acting counterparts are anticoagulants, and death ultimately results from internal hemorrhage.

In the light of the mechanisms of action of many of the rodenticides, it is of no surprise that they are not selectively toxic to rodents. Variable toxicities to humans and other non-target species have been described. In relation to toxicity to humans, some groups of people are at greater risk than others from exposure to rodenticides. Exposure to rodenticides, particularly the more toxic agents, is an occupational hazard for pest control applicators. Intentional poisoning with rodenticides in cases of suicide (attempted or otherwise) or homicide have been reported. Individuals who abuse alcohol or other drugs, as well as people who suffer psychological disorders may be more prone to unintentionally ingest rodenticides for one reason or another. Likewise, children and the elderly may be more susceptible to the adverse effects of intentional or unintentional exposure to rodenticides.

In the United States, most human toxicities involve accidental poisoning of children, typically children younger than 6 years old. There are relatively few deaths, however,

and the deaths that do occur as a result of poisoning with known rodenticides are attributable to strychnine or the long-acting anticoagulants. Although the latter are considered to have only a low potential for toxicity in humans, they are available commercially for residential use. Thus, children are more likely to be exposed to the long-acting anticoagulant rodenticides than they are to more toxic agents with a more restricted use. Also repeated ingestion, in combination with their prolonged action, can be problematic in children.

The rodenticides have been described extensively in the scientific literature. Although limited in some cases, information regarding their physical properties, practical considerations in relation to their use as bait, mechanisms of action, and appropriate therapeutic intervention in cases of human toxicity is available. This review represents a compilation of that material. However, it should not be considered complete in and of itself. The reader is encouraged to consult the primary references as well as other reports for greater detail. Additional information can also be obtained from any number of textbooks on the principles of toxicology and the medical management of the poisoned patient.

1. Introduction

Rats and mice, when unchecked, can have a significant socioeconomic impact on humans. The control of rodent populations comprises an important component of post-harvest food protection, notably of grain and cereal crops. The ability of rats as well as other rodents to serve as vectors for human disease also brings the animals into the realm of public health. In settings in which sanitation is compromised and rats and humans are in close contact, reduction (if not complete eradication) of rodent populations is obligatory for effective prevention and containment of disease.

A variety of products have been designed specifically to kill rats and mice. These products, or rodenticides, consist of a wide range of inorganic and organic chemicals with diverse structures, mechanisms of action, effectiveness, and toxicities to non-target species including humans. Some rodenticides occur naturally in plants, whereas others are derived synthetically. In some cases, a metabolic process or a biochemical characteristic unique to the rat is targeted in an effort to diminish toxicity to other animals. For most rodenticides, however, the site and mechanisms of action are common across animal phyla and between species. Thus, with the use of most rodenticides, secondary poisoning to non-target species can be significant. Such non-specific toxicity associated with some agents has led to their application in the control of other small animal pests; for example, opossum, squirrels, moles, gophers, birds, bats, as well as small mammalian carnivores such as coyotes and foxes. It also increases the concern about potential toxicity to humans.

For any rodenticide to be effective, it must be accepted by the target species. Ideally, the rodenticide is lethal in a single dose and has a high lethal efficiency within the population. Long-term control also requires that the rodent population as a whole does not develop resistance to the poison. Characteristics of the ideal poison are only partially met by most rodenticides. The first is often achieved by mixing the rodenticide with food. Unfortunately, this tactic makes the poison attractive to other animals and, in

domestic settings, to children. Learned avoidance and development of tolerance continue to drive the development of rodenticides with different mechanisms of action to maintain effective control of commensal rodent populations. For the most part, complete eradication of rodents or other pests is impractical. The best that can be hoped for is stabilization of an acceptable population through the use of a combination of methods, often utilizing a number of different rodenticides.

The potential hazard associated with the use some rodenticides can be offset to some extent by application strategy (location, presentation), and the relative dosages at which toxicity develops between target and non-target species. In some cases, the immediate physiological response (e.g., regurgitation) to ingestion of the chemical or an adjuvant in the formulation can minimize poisoning to non-target species while maintaining effectiveness in rats. In the case of humans, restrictions on the use of highly toxic rodenticides to licensed applicators or appropriate government officials figure prominently in reducing the frequency of unintentional poisoning. For those rodenticides that are readily available "over-the-counter", knowledge about proper handling and potential toxicities are equally important.

2. Fluoroacetate Derivatives

2.2. Sodium Monofluoroacetate

Sodium monofluoroacetate (SMFA or compound 1080) is a highly toxic single dose rodenticide. It is the sodium salt of fluoroacetate, a compound which occurs naturally in a number of poisonous plants throughout the world (e.g., *Acacia* and *Leguminosae* (Australia), *Dichapetalaceae* (South Africa), and *Palicourea* (South America). Sodium monofluoroacetate is highly effective against all types of rodents, and is used in some countries for the control of exotic vertebrate pests such as cats, opossums, rabbits and foxes. It is applied as single-lethal-dose baits or as a toxic collar on the prey of targeted pest. Oral LD_{50} values in mice and rats are 2-3 mg kg^{-1}, and those in other mammals are between 0.03 mg kg^{-1} and 1 mg kg^{-1}. The oral LD_{50} for sodium monofluoroacetate in humans is estimated at 0.7-5 mg kg^{-1}. Poultry, with an LD_{50} of 10-30 mg kg^{-1}, are less sensitive to sodium monofluoroacetate than are mammals. Due to its toxicity, sodium monofluoroacetate is best used in settings where the potential for secondary poisoning of non-pest species is minimal or where public access can be controlled. In some countries, including the U.S., the application of sodium monofluoroacetate is strictly controlled, and its use is restricted to licensed exterminators or Public Health officials.

Because of its chemical stability, water solubility and high toxicity, there is concern for the potential of sodium monofluoroacetate to contaminate ground water and to persist in the environment. In addition, sodium monofluoroacetate that leaches into soil from bait can be taken up and accumulated by plants, posing a risk of secondary poisoning to herbivores. However, in biologically active systems, the window for toxicity to sodium monofluoroacetate is relatively narrow. Fluoroacetate was rapidly absorbed by grass with peak levels being achieved within 3 days. However, it was just as rapidly degraded or otherwise eliminated from the plant. Absorption and elimination of fluoroacetate by broadleaf plants was somewhat slower; plant levels of fluoroacetate were maximal after 10 days, and elimination was complete by 24 days. The half-life of fluoroacetate in

biologically active water has been estimated at 1 day or less to as long as 6 days, depending on temperature and specific conditions. Fluoroacetate can undergo microbial metabolism in water and soil to glycolate or fluorocitrate. Glycolate is relatively nontoxic (oral LD_{50} in rats is about 2g kg^{-1}), whereas fluorocitrate is thought to mediate the toxicity to sodium monofluoroacetate in mammals. In comparison to fluoroacetate, fluorocitrate has a comparable half-life in aquatic systems and a lower oral toxicity. Fluoroacetate in uneaten bait is degraded through microbial action.

Sodium monofluoroacetate is readily absorbed if ingested or inhaled. It can also be absorbed through broken skin, but it is not absorbed through intact skin. Clearance of fluoroacetate varies between species. Studies in rats indicate that fluoroacetate is retained in tissues for several days. The half-live of sodium monofluoroacetate in sheep and goats, respectively, is 10.8 and 5.4 hours, whereas its half-life is less than 2 hours in mice and 1.1 hours in rabbits. The concentrations of fluoroacetate in tissues are only 25-50% of those in plasma, and fluoroacetate appears to be cleared somewhat faster from tissue than from plasma. In studies using sodium [2-^{14}C]fluoroacetate, distribution of the isotope was accompanied, at least in liver and kidney, by accumulation of fluorocitrate.

The primary mechanism of toxicity to sodium monofluoroacetate is inhibition of the Krebs cycle and depletion of energy stores. In mammalian cells, fluoroacetate is converted to fluoroacetyl-CoA and then to fluorocitrate. Fluorocitrate, in turn, can inhibit aconitase, preventing the conversion of citrate to isocitrate. It can also inhibit the translocation of citrate across the mitochondrial membrane. Although only about 3% of a dose of sodium monofluoroacetate appears to be converted to fluorocitrate, these actions account for the depletion of energy stores – especially in heart, liver, kidney and brain – as well as the accumulation of citrate associated with sodium monofluoroacetate poisoning. Fluorocitrate mimics sodium monofluoroacetate in precipitating hypocalcemia as well as toxicity within the central nervous and cardiovascular systems. Although fluoroacetate is metabolized to products other than fluorocitrate, there is little evidence that other metabolites contribute to sodium monofluoroacetate toxicity. Similarly, fluoroacetate can undergo defluorination in the liver, but its toxicity is independent of its fluoride content or the concentrations of free fluoride obtained.

Symptoms often present within 30-180 minutes after the ingestion of sodium monofluoroacetate. The delay is attributed to the time required for fluoroacetate to be converted to fluorocitrate. Once symptoms begin, they are severe and widespread, presenting as respiratory, neurologic, gastrointestinal, cardiovascular and electrolyte disturbances. Manifestations of toxicity in the central nervous system and cardiovascular system, however, may be most apparent. The general response to sodium monofluoroacetate poisoning includes nausea, vomiting and abdominal pain initially, followed by respiratory distress and then signs of central toxicity. Toxicity within the central nervous system is reflected in agitation, apprehension, loss of consciousness, seizures, coma and respiratory failure. Muscle spasms and stupor are also common, and animals that die of monofluoroacetate poisoning show a characteristic hyperextension of the extremities. Cardiovascular symptoms commonly consist of hypotension and sinus tachycardia. The hypotension is associated with decreased peripheral vascular resistance, which is unresponsive to inotropic therapy and volume expansion,

suggesting a direct toxic effect of fluoroacetate on the vasculature. Tachycardia may progress to dysrhythmia marked by nonspecific T-wave and ST-T segment irregularities, then to supraventricular or ventricular tachycardia and, finally, to ventricular fibrillation and sudden cardiac arrest. Metabolic acidosis, hypocalcemia and hypokalemia are common, and acute renal failure with frank uremia can occur. Hypotension, increased plasma creatinine and metabolic acidosis were the most predictive indicators of poor prognosis and mortality in sodium monofluoroacetate poisoning.

There is no known antidote for sodium monofluoroacetate poisoning, but some therapeutic steps have been advocated on the basis of studies in experimental animals. In general, treatment is nonspecific and supportive. Repeated gastric lavage and catharsis seem empirically useful because of enterohepatic recycling of fluoroacetate, but there is no evidence of their effectiveness. Evidence to support the use of activated charcoal as an initial step to remove unabsorbed fluoroacetate is also lacking. Attempts to identify a substrate that would compete with, or by-pass, the inhibition of citrate metabolism caused by fluoroacetate indicated that glycerol monoacetate was the most beneficial in mice, rats, rabbits, dogs and monkeys. Glycerol monoacetate was also less acutely toxic than was either glycerol diacetate or glycerol triacetate. Ethanol, alone or in combination with glycerol monoacetate, was effective against fluoroacetate poisoning in mice and rats. But, the usefulness of ethanol as an antidote to fluoroacetate poisoning in humans is questionable, since it had no beneficial effect in monkeys. A combination of calcium gluconate and sodium succinate decreased mortality to sodium monofluoroacetate in mice, although neither was effective alone. Hypocalcemia contributes to the neural and cardiovascular effects caused by fluoroacetate, and administration of calcium chloride to sodium monofluoroacetate-poisoned cats prolonged survival. In contrast, calcium chloride augmented toxicity to sodium monofluoroacetate in monkeys. Sodium acetate, digoxin, sodium chloride and potassium chloride also enhanced sodium monofluoroacetate toxicity, presumably by exacerbating existing hypernatremia, hyperkalemia or metabolic acidosis. General recommendations for the management of a sodium monofluoroacetate-poisoned patient following these observations consist of intramuscular administration of glycerol monoacetate at hourly intervals, continued monitoring of cardiac function, control of seizures with an anticonvulsant such as diazepam or pentobarbital, and avoidance of cardiac glycosides, calcium, potassium, sodium, bicarbonate and excess acetate. It is important to note that these recommendations have not been evaluated in controlled clinical settings.

2.3. Fluoroacetamide

Fluoroacetamide (compound 1081) is a fluoroacetate derivative that is slightly less toxic and somewhat slower in onset than is sodium monofluoroacetate. Its intraperitoneal LD_{50} in mice is 85 mg kg^{-1} compared to 18 mg kg^{-1} for fluoroacetate. The mechanism of action of fluoroacetamide appears to be identical to that of sodium monofluoroacetate. That premise is based on the observations that fluoroacetamide undergoes deamination to fluoroacetate *in vivo* and that whole body citrate levels increase subsequent to fluoroacetamide administration. Not surprisingly, the symptoms of fluoroacetamide poisoning mimic those of fluoroacetate poisoning. Thus, interventions appropriate for

the management of the sodium fluoroacetate-poisoned patient apply equally to the management of fluoroacetamide poisoning. Regulations for the use of fluoroacetamide parallel those governing the use of sodium monofluoroacetate.

2.3. 1,3-Difluoro-2-propanol

1,3-Difluoro-2-propanol (DFP) is the major (70%) active component of the pesticide gliftor; the remainder is 1-chloro-3-fluoro-2-propanol. Gliftor is used widely as a rodenticide in some countries and is being evaluated in others as a potential replacement for sodium monofluoroacetate. The oral LD_{50} for gliftor in rats is about 46 mg kg^{-1}. Although 1,3-difluoro-2-propanol is not strictly a derivative of fluoroacetate, the signs of its toxicity and its apparent mechanism of action are similar to those caused by sodium monofluoroacetate.

1,3-Difluoro-2-propanol can undergo conversion to fluorocitrate *in vivo* and *in vitro* through a series of reactions initiated by an NAD^+-dependent alcohol dehydrogenase. The resulting product, 1,3-difluoroacetone, undergoes a cytochrome P450-mediated defluorination and an acetyl-CoA-mediated decarboxylation to fluoroacetyl CoA. Finally, fluoroacetyl CoA is converted to fluorocitrate. Following administration of 1,3-difluoro-2-propanol to rats, citrate concentrations in the kidney increased coincident with fluoride and fluorocitrate concentrations. Increases in citrate and fluorocitrate concentrations caused by 1,3-difluoro-2-propanol were comparable to, but slower in onset than, the increases caused by sodium monofluoroacetate.

Increases in renal citrate and fluorocitrate concentrations caused by administration of 1,3-difluoro-2-propanol, but not those caused by sodium monofluoroacetate, were markedly attenuated by pretreatment of rats with 4-methylpyrazole. The protective effect of 4-methylpyrazole may reflect an inhibition of malate dehydrogenase. In any event, these observations raise the possibility of 4-methylpyrazole being an effective antidote for 1,3-difluoro-2-propanol poisoning without the introduction of significant additional toxicity. In that light, 1,3-difluoro-2-propanol may be a useful alternative for sodium monofluoroacetate in the control of rodents and other vertebrate pests.

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Bibliography

Fluoroacetate Derivatives

Blomstrand R, Ellin A, Lof A, Ostling-Wintzell H 1980 Biological effects and metabolic interactions after chronic and acute administration of 4-methylpyrazole and ethanol to rats. Arch Biochem Biophys 199:591-605

Booth LH, Ogilvie SC, Wright GR, Eason CT 1999 Degradation of sodium monofluoroacetate (1080) and fluorocitrate in water. Bull Environ Contam Toxicol 62:34-39

Bosakowski T, Levin AA 1987 Comparative acute toxicity of chlorocitrate and fluorocitrate in dogs. Toxicol Appl Pharmacol 89:97-104

Buck WB 1978 Clinical toxicosis induced by pesticides in livestock. Vet Med Small Anim Clin 73:810-819

Buffa P, Peters RA 1949 Formation of citrate *in vivo* induced by fluoroacetate poisoning. Nature 163:914

Buffa P, Peters RA 1950 The in vivo formation of fluorocitrate induced by fluoroacetate and its significance. J Physiol 110:488-500

Chenoweth MB, Kandel A, Johnson LB, Bennett DR 1951 Factors influencing fluoroacetate poisoning: practice treatment with glycerol monoacetate. J Pharm Exp Therap 102:31-49

Chi CH, Chen KW, Chan SH, Wu MH, Huang JJ 1996 Clinical presentation and prognostic factors in sodium monofluoroacetate intoxication. J Toxicol Clin Toxicol 34:707-712

Chi CH, Lin TK, Chen KW 1999 Hemodynamic abnormalities in sodium monofluoroacetate intoxication. Hum Exp Toxicol 18:351-353

Chung HM 1984 Acute renal failure caused by acute monofluoroacetate poisoning. Vet Hum Toxicol 26 Suppl 2:29-32:29-32

Dipalma JR 1981 Human toxicity from rat poisons. Am Fam Physician 24:186-189

Eason CT, Gooneratne R, Fitzgerald H, Wright G, Frampton C 1994 Persistence of sodium monofluoroacetate in livestock animals and risk to humans. Hum Exp Toxicol 13:119-122

Eason CT, Gooneratne R, Wright GR, Pierce R, Frampton CM 1993 The fate of sodium monofluoroacetate (1080) in water, mammals, and invertebrates. Proc 46th NZ Plant Protection Conf 297-301

Egekeze JO, Oehme FW 1979 Inorganic and organic fluoride concentrations in tissues after the oral administration of sodium monofluoroacetate (Compound 1080) to rats. Toxicology 15:43-53

Feldwick MG, Noakes PS, Prause U, Mead RJ, Kostyniak PJ 1998 The biochemical toxicology of 1,3-difluoro-2-propanol, the major ingredient of the pesticide gliftor: the potential of 4-methylpyrazole as an antidote [published erratum appears in J Biochem Mol Toxicol 1998;12(2):133]. J Biochem Mol Toxicol 12:41-52

Gal EM, Drewes PA, Taylor NF 1961 Metabolism of fluoroacetic acid - 2 C^{14} in the intact rat. Arch Biochem Biophys 93:1-4

Gooneratne SR, Eason CT, Dickson CJ, Fitzgerald H, Wright G 1995 Persistence of sodium monofluoroacetate in rabbits and risk to non-target species. Hum Exp Toxicol 14:212-216

Gribble GW 1973 Fluoroacetate toxicity. J Chem Educ 50:460-462

Hagan RC, Ramsey LL, Woodward G 1950 Absorption, distribution and excretion of sodium monofluoroacetate (compound 1080) in rats. J Pharm Exp Therap 99:426-441

Kirsten E, Sharma ML, Kun E 1978 Molecular toxicology of (-)-erythro-fluorocitrate: selective inhibition of citrate transport in mitochondria and the binding of fluorocitrate to mitochondrial proteins. Mol Pharmacol 14:172-184

Li RC, Sah PPT, Anderson HH 1941 Acute toxicity of monacetin, diacetin and triacetin. Proc Soc Exp Biol Med 46:26-28

Magnusson G, Nyberg J-A, Bodin N-O, Hanson E 1972 Toxicity of pyrazole and 4-methylpyrazole in mice and rats. Experentia 28:1198-1200

Matsumura F, O'Brien RD 1963 A comparative study of the modes of action of fluoroacetamide and fluoroacetate in the mouse and American cockroach. Biochem Pharmacol 12:1201-1205

McTaggart DR 1970 Poisoning due to sodium fluoroacetate ("1080"). Med J Aust 2:641-642

Morrison JF, Peters RA 1954 Biochemistry of fluoroacetate poisoning. The effects of fluorocitrate on purified aconitase. Biochem J 58:473-479

Ogilvie SC, Booth LH, Eason CT 1998 Uptake and persistence of sodium monofluoroacetate (1080) in plants. Bull Environ Contam Toxicol 60:745-749

Ogilvie SC, Hetzel F, Eason CT 1996 Effect of temperature on the biodegradation of sodium monofluoroacetate (1080) in water and in Elodea canadensis. Bull Environ Contam Toxicol 56:942-947

Omara F, Sisodia CS 1990 Evaluation of potential antidotes for sodium fluoroacetate in mice. Vet Hum Toxicol 32:427-431

Parfitt RL, Eason CT, Morgan AJ, Wright GR, Burke CM 1994 The fate of sodium monofluoroacetate (1080) in soil and water. In: Seawright, A.A.; Eason, C.T. (eds) Proceedings of the science workshop on 1080. The Royal Society of New Zealand, Miscellaneous Series 28:59-66

Parkin PJ, McGiven AR, Bailey RR 1977 Chronic sodium monofluoroacetate (Compound 1080) intoxication in a rabbit. N Z Med J 85:93-96

Peters RA, Spencer H, Bidstrup PL 1981 Subacute fluoroacetate poisoning. J Occup Med 23:112-113

Reigart JR, Brueggeman JL, Keil JE 1975 Sodium fluoroacetate poisoning. Am J Dis Child 129:1224-1226

Shapira AR, Taitelman U, Bursztein S 1980 Evaluation of the role of ionized calcium in sodium fluoroacetate ("1080") poisoning. Toxicol Appl Pharmacol 56:216-220

Smith FA, Gardner DE, Yuile CL 1977 Defluorination of fluoroacetate in the rat. Life Sci 20:1131-1138

Soiefer AI, Kostyniak PJ 1984 Purification of a fluoroacetate-specific defluorinase from mouse liver cytosol. J Biol Chem 259:10787-10792

Sykes TR, Ruth TJ, Adam MJ 1986 Synthesis and murine tissue uptake of sodium [18F]fluoroacetate. Int J Rad Appl Instrum B 13:497-500

Tkach NZ 1969 Toxicology of gliftor to rats after single oral administration. Tr Inst Kraev Patol Min Zdravookhr Kaz SSR 16:146-149

Tkach NZ, Milovanova VI, Knysh VS 1971 Change in the morphological composition of the peripheral blood during gliftor poisoning. Tr Nauchno-Issled Inst Kraev Patol Alma-Ata 22:12-16

Wong DH, Kirkpatrick WE, Kinnear JE, King DR 1991 Defluorination of sodium monofluoroacetate (1080) by microorganisms isolated from Western Australian soils. Soil Biol Biochem 24:9-14

Thiourea Rodenticides

Ahn JS, Lee TH, Lee MC 1998 Ultrastructure of neuromuscular junction in Vacor-induced diabetic rats. Korean J Intern Med 13:47-50

Allison RC, Rippe B, Prasad VR, Parker JC, Taylor AE 1989 Pulmonary vascular permeability and resistance measurements in control and ANTU-injured dog lungs. Am J Physiol 256:H1711-H1718

Bakhle YS 1982 Decreased inactivation of prostaglandin E2 in isolated lungs from rats with alpha-naphthyl thiourea-induced pulmonary oedema. Biochem Pharmacol 31:3395-3401

Barton CC, Bucci TJ, Lomax LG, Warbritton AG, Mehendale HM 2000 Stimulated pulmonary cell hyperplasia underlies resistance to alpha-naphthylthiourea. Toxicology 143:167-181

Benowitz NL, Byrd R, Schambelan M, Rosenberg J, Roizen MF 1980 Dihydroergotamine treatment for orthostatic hypotension from Vacor rodenticide. Ann Intern Med 92:387-388

Bohm GM 1972 Changes in lung arterioles in pulmonary oedema induced in rats by alpha-naphthylthiourea. J Path 110:343-345

Boyd MR, Neal RA 1976 Studies on the mechanism of toxicity and of development of tolerance to the pulmonary toxin, alpha-naphthylthiourea (ANTU). Drug Metab Dispos 4:314-322

Chanutin A, Gjessing EC, Ludewig S 1947 α-Naphthylthiourea in dogs. Electrophoretic and cholesterol studies on blood plasma and pleural effusion. Proc Soc Exp Biol Med 64:174-179

Cunningham AL, Hurley JV 1972 Alpha-naphthyl-thiourea-induced pulmonary oedema in the rat: a topographical and electron-microscope study. J Pathol 106:25-35

Deckert FW 1979 Selected examples of biochemical-toxicological problems. Drug Metab Rev 10:285-298

Deckert FW, Godfrey WJ, Lisk DC, Steigerwalt RB, Udinsky JR 1978 Metabolic interactions with RH-787 (Vacor rodenticide). Fed Proc 37:424

Deckert FW, Hagerman LM, Lisk DC, Steigerwalt RB, Udinsky JR 1978 The disposition of [14C]RH-7878 (Vacor Rodenticide) in rodents and dogs. Toxicol Appl Pharmacol 45:313

Deckert FW, Moss JN, Sambuca AS, Seidel MC, Steigerwalt RB 1977 Nutritional and drug interactions with vacor rodenticide in rats. Fed Proc 36:990

Devi SV, Krishnamoorthy RV 1979 Non-competitive inhibition of serum acetylcholinesterase (E.C.3.1.1.7) by Vacor (N-3-pyridyl methyl-N'-P-nitrophenyl urea) in bandicoot rats. Indian J Physiol Pharmacol 23:285-290

Dieke SH 1947 Pigmentation and hair growth in black rats, as modified by the chronic administration of thiourea, phenyl thiourea and alpha-naphthylthiourea. Endocrinology 40:123-136

Dieke SH, Richter CP 1946 Age and species variations in the acute toxicity of alpha-naphthyl thiourea. Proc Soc Exp Biol Med 62:22-25

Dieke SH, Richter CP 1946 Comparative assays of rodenticides on wild Norway rats. I. Toxicity. Public Health Rep 61:672-679

DuBois KP, Herman RG, Erway WF 1947 Mechanism of action of thiourea and related compounds. III. Effect of poisoning on carbohydrate metabolism. J Pharm Exp Ther 89:186-195

Ercan ZS, Eren S, Zengil H, Turker RK 1993 Possible involvement of eicosanoids in alpha-naphthylthiourea-induced pulmonary oedema and alteration of angiotensin-converting enzyme activity. Pharmacology 46:274-280

Esposti MD, Ngo A, Myers MA 1996 Inhibition of mitochondrial complex I may account for IDDM induced by intoxication with the rodenticide vacor. Diabetes 45:1531-1534

Fantone JC, Kunkel RG, Kinnes DA 1984 Potentiation of alpha-naphthyl thiourea-induced lung injury by prostaglandin E1 and platelet depletion. Lab Invest 50:703-710

Fears WB 1980 The rat poison Vacor [letter]. N Engl J Med 302:1147

Feingold KR, Lee TH, Chung MY, Siperstein MD 1986 Muscle capillary basement membrane width in patients with vacor-induced diabetes mellitus. J Clin Invest 78:102-107

Fisslthaler B, Fleming I, Busse R 2000 EDHF: a cytochrome P450 metabolite in coronary arteries. Semin Perinatol 24:15-19

Fitzhugh OG, Nelson AA 1947 Chronic oral toxicity of alpha-napthyl thiourea. Proc Soc Exp Biol Med 64:305-310

Fretthold D, Sunshine I, Udinsky JR, Deckert FW 1980 Postmortem findings for a Vacor poisoning case. Clin Toxicol 16:175-180

Gallanosa AG, Spyker DA, Curnow RT 1981 Diabetes mellitus associated with autonomic and peripheral neuropathy after Vacor rodenticide poisoning: a review. Clin Toxicol 18:441-449

Gunnarson R 1975 Inhibition of insulin biosynthesis by alloxan, streptozotocin, and N-nitrosomethylurea. Mol Pharmacol 11:759-765

Hardwick SJ, Skamarauskas JT, Smith LL, Upshall DG, Cohen GM 1991 Protection of rats against the effects of alpha-naphthylthiourea (ANTU) by elevation of non-protein sulphydryl levels. Biochem Pharmacol 42:1203-1208

Hill NS, O'Brien RF, Rounds S 1984 Repeated lung injury due to alpha-naphthylthiourea causes right ventricular hypertrophy in rats. J Appl Physiol 56:388-396

Innes JR, Ulland BM, Valerio MG, Petrucelli L, Fishbein L, Hart ER, Pallotta AJ, Bates RR, Falk HL, Gart JJ, Klein M, Mitchell I, Peters J 1969 Bioassay of pesticides and industrial chemicals for tumorigenicity in mice: a preliminary note. J Natl Cancer Inst 42:1101-1114

Johnson D, Kubic P, Levitt C 1980 Accidental ingestion of Vacor rodenticide: the symptoms and sequelae in a 25-month-old child. Am J Dis Child 134:161-164

Karam JH, Lewitt PA, Young CW, Nowlain RE, Frankel BJ, Fujiya H, Freedman ZR, Grodsky GM 1980 Insulinopenic diabetes after rodenticide (Vacor) ingestion: a unique model of acquired diabetes in man. Diabetes 29:971-978

Kawalek JC, Andrews AW, Pienta RJ 1979 1-Naphthylthiourea: a mutagenic rodenticide that transforms hamster embryo cells. Mol Pharmacol 15:678-684

Kenney RM, Michaels IA, Flomenbaum NE, Yu GS 1981 Poisoning with N-3-pyridylmethyl-N'-p-nitrophenylurea (Vacor). Immunoperoxidase demonstration of beta-cell destruction. Arch Pathol Lab Med 105:367-370

King J, Deboisblanc BP, Mason CM, Onofrio JM, Lipscomb G, Mercante DE, Summer WR, Nelson S 1995 Effect of granulocyte colony-stimulating factor on acute lung injury in the rat. Am J Respir Crit Care Med 151:302-309

Latta H 1947 Pulmonary edema and pleural effusion produced by acute ANTU poisoning in rats and dogs. Bull John Hopkins Hosp 80:197

Lee PW, Arnau T, Neal RA 1980 Metabolism of alpha-naphthylthiourea by rat liver and rat lung microsomes. Toxicol Appl Pharmacol 53:164-173

Lee S, Kim JG 1982 [Burning feet caused by the rodenticide RH-787]. Hautarzt 33:649-650

Lee TH, Choi KC, Park YK, Choi JK 1985 Thickening of the capillary basement membrane of the quadriceps muscle in Vacor-induced diabetic patients. Diabetes Res Clin Pract 1:155-159

Lee TH, Doi K, Yoshida M, Baba S 1988 Morphological study of nervous system in Vacor-induced diabetic rats. Diabetes Res Clin Pract 4:275-279

Lee TH, Kang JC, Han MD, Kim JS, Roh JW, Chung MY, Choi BJ 1977 A clinical analysis of rodenticide RH-787 (Vacor) intoxication. J Korean Diabet Assoc 4:43

LeWitt P 1980 PNU intoxication [letter]. Am J Dis Child 134:1178

Lewitt PA 1980 The neurotoxicity of the rat poison vacor. A clinical study of 12 cases. N Engl J Med 302:73-77

Litovitz TL, Felberg L, Soloway RA, Ford M, Geller R 1995 1994 annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. Am J Emerg Med 13:551-597

Litovitz TL, Felberg L, White S, Klein-Schwartz W 1996 1995 annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. Am J Emerg Med 14:487-537

Litovitz TL, Klein-Schwartz W, Caravati EM, Youniss J, Crouch B, Lee S 1999 1998 annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. Am J Emerg Med 17:435-487

Litovitz TL, Klein-Schwartz W, Dyer KS, Shannon M, Lee S, Powers M 1998 1997 annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. Am J Emerg Med 16:443-497

Litovitz TL, Smilkstein M, Felberg L, Klein-Schwartz W, Berlin R, Morgan JL 1997 1996 annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. Am J Emerg Med 15:447-500

Mais DE, Bosin TR 1984 A role for serotonin in alpha-naphthylthiourea-induced pulmonary edema. Toxicol Appl Pharmacol 74:185-194

Martin D, Korthuis RJ, Perry M, Townsley MI, Taylor AE 1986 Oxygen radical-mediated lung damage associated with alpha-naphthylthiourea. Acta Physiol Scand Suppl 548:119-25:119-125

Mason CM, Guery BP, Summer WR, Nelson S 1996 Keratinocyte growth factor attenuates lung leak induced by alpha-naphthylthiourea in rats [see comments]. Crit Care Med 24:925-931

McClosky WT, Smith MI 1945 Studies on the pharmacologic action and the pathology of alpha-naphthylthiourea (ANTU). I. Pharmacology. Public Health Rep 60:1101-1113

Meyrick B, Miller J, Reid L 1972 Pulmonary oedema induced by ANTU, or by high or low oxygen concentrations in rat--an electron microscopic study. Br J Exp Pathol 53:347-358

Miller LV, Stokes JD, Silpipat C 1978 Diabetes mellitus and autonomic dysfunction after vacor rodenticide ingestion. Diabetes Care 1:73-76

Mindel JS, Kharlamb AB, Friedman AH, Karam JH, Stone RD, Siegel IM 1988 N-3-pyridylmethyl-N'-p-nitrophenylurea ocular toxicity in man and rabbits. Br J Ophthalmol 72:584-590

Mindel JS, Rubenstein AE, Franklin B 1981 Ocular ergotamine tartrate toxicity during treatment of Vacor-induced orthostatic hypotension. Am J Ophthalmol 92:492-496

Minty BD, Scudder CM, Grantham CJ, Jones JG, Bakhle YS 1987 Sequential changes in lung metabolism, permeability, and edema after ANTU. J Appl Physiol 62:491-496

Olson JW, Gebb SA, Orlinska U, Gillespie MN 1989 Polyamine synthesis in rat lungs injured with alpha-naphthylthiourea. Toxicology 55:317-326

Osterman J, Zmyslinski RW, Hopkins CB, Cartee W, Lin T, Nankin HR 1981 Full recovery from severe orthostatic hypotension after vacor rodenticide ingestion. Arch Intern Med 141:1505-1507

Papasozomenos S 1980 The rat poison Vacor [letter]. N Engl J Med 302:1146-1147

Patil TN, Radhakrishnamurty R 1978 Biochemical changes induced by -naphthylthiourea in albino rats. Pest Biochem Physiol 8:217-227

Peardon DL 1974 RH-787, a new selective rodenticide. Pest Control 42:14,16,18,27

Peoples SA, Maddy KT 1979 Poisoning of man and animals due to ingestion of the rodent poison, VACOR. Vet Hum Toxicol 21:266-268

Peters KS, Tong TG, Kutz K, Benowitz NL 1981 Diabetes mellitus and orthostatic hypotension resulting from ingestion of Vacor rat poison: endocrine and autonomic function studies. West J Med 134:65-68

Pont A, Rubino JM, Bishop D, Peal R 1979 Diabetes mellitus and neuropathy following Vacor ingestion in man. Arch Intern Med 139:185-187

Raunio H, Hakkola J, Hukkanen J, Lassila A, Paivarinta K, Pelkonen O, Anttila S, Piipari R, Boobis A, Edwards RJ 1999 Expression of xenobiotic-metabolizing CYPs in human pulmonary tissue. Exp Toxicol Pathol 51:412-417

Richter CP 1945 The development and use of alpha-naphthyl thiourea (ANTU) as a rat poison. J A M A 129:927-931

Richter CP 1952 Physiology and cytology of pulmonary edema and pleural effusion produced in rats by ANTU. J Thor Surg 23:66-91

Roth RA, Ball TM 1986 Technical grade but not recrystallized alpha-naphthylthiourea potentiates superoxide release by rat neutrophils stimulated in vitro by phorbol myristate acetate. Fundam Appl Toxicol 7:324-328

Rutili G, Kvietys P, Martin D, Parker JC, Taylor AE 1982 Increased pulmonary microvascular permeability induced by alpha-naphthylthiourea. J Appl Physiol 52:1316-1323

Rutili G, Parker JC, Taylor AE 1984 Fluid balance in ANTU-injured lungs during crystalloid and colloid infusions. J Appl Physiol 56:993-998

Schein PS, Rakieten N, Cooney DA, Davis R, Vernon ML 1973 Streptozotocin diabetes in monkeys and dogs, and its prevention by nicotinamide. Proc Soc Exp Biol Med 143:514-518

Seiler JP 1977 Nitrosation *in vitro* and *in vivo* by sodium nitrite, and mutagenicity of nitrogenous pesticides. Mutat Res 48:225-236

Seon YD, Lee TH, Lee MC 1999 Changes of glomerular basement membrane components in Vacor-induced diabetic nephropathy. Korean J Intern Med 14:77-84

Sipahi E, Hodoglugil U, Ercan ZS, Turker RK 1996 Acute effect of endothelin-1 on lung oedema induced by alpha-naphthylthiourea (ANTU). Pharmacol Res 33:375-378

Sipahi E, Hodoglugil U, Ustun H, Zengil H, Turker RK, Ercan ZS 1997 An unexpected interaction between NG-nitro-L-arginine methyl ester and L-arginine in alpha-naphthylthiourea-induced pulmonary oedema in rats. Eur J Pharmacol 321:45-51

Smith BR, Brian WR 1991 The role of metabolism in chemical-induced pulmonary toxicity. Toxicol Pathol 19:470-481

Stauffacher W, Burr I, Gutzeit A, Beaven D, Veleminsky J, Renold AE 1969 Streptozotocin diabetes: time course of irreversible B-cell damage; further observations on prevention by nicotinamide. Proc Soc Exp Biol Med 133:194-200

Tutor JD, Mason CM, Dobard E, Beckerman RC, Summer WR, Nelson S 1994 Loss of compartmentalization of alveolar tumor necrosis factor after lung injury. Am J Respir Crit Care Med 149:1107-1111

van den Brenk HA, Kelly H, Stone MG 1976 Innate and drug-induced resistance to acute lung damage caused in rats by alpha-naphthyl thiourea (ANTU) and related compounds. Br J Exp Pathol 57:621-636

Vogel RP 1982 Poisoning with vacor rodenticide [letter]. Arch Pathol Lab Med 106:153

Watson DF, Griffin JW 1987 Vacor neuropathy: ultrastructural and axonal transport studies. J Neuropathol Exp Neurol 46:96-108

Widdicombe JG, Pack RJ 1982 The Clara cell. Eur J Respir Dis 63:202-220

Wilson GL, Gaines KL 1983 Effects of the rodenticide Vacor on cultured rat pancreatic beta cells. Toxicol Appl Pharmacol 68:375-379

Bromethalin

Buller G, Heard J, Gorman S 1996 Possible bromethalin-induced toxicity in a human. A case report. J Toxicol Clin Toxicol 34:572-573

Carson TL 1989 Bromethalin poisoning. In: Kirk RW (ed). Current Veterinary Therapy WB Saunders, Philadelphia. 147-148

Cherry LD, Gunnoe MD, van Lier RBL 1982 The metabolism of bromethalin and its effects on oxidative phosphorylation and cerebrospinal fluid pressure. Toxicologist 2:108

Dorman DC 1989 Neurotoxicology of new and emerging pesticides. Proceedings, 7th Am Coll Vet Intern Med Forum 969-972

Dorman DC 1990 Toxicology of selected pesticides, drugs, and chemicals. Anticoagulant, cholecalciferol, and bromethalin-based rodenticides. Vet Clin North Am Small Anim Pract 20:339-352

Dorman DC, Cote LM, Buck WB 1992 Effects of an extract of Ginkgo biloba on bromethalin-induced cerebral lipid peroxidation and edema in rats. Am J Vet Res 53:138-142

Dorman DC, Parker AJ, Buck WB 1991 Electroencephalographic changes associated with bromethalin toxicosis in the dog. Vet Hum Toxicol 33:9-11

Dorman DC, Simon J, Harlin KA, Buck WB 1990 Diagnosis of bromethalin toxicosis in the dog. J Vet Diagn Invest 2:123-128

Dorman DC, Zachary JF, Buck WB 1992 Neuropathologic findings of bromethalin toxicosis in the cat. Vet Pathol 29:139-144

Dreikorn BA, O'Doherty GOP, Clinton AJ, Krammer KE 1979 EL-614, a novel acute rodenticide. Proc Brit Crop Protect Conf 491-498

Grolleau G 1988 Susceptibility of three synanthropic rodent species to bromethalin under laboratory conditions. Bull OEPP (Organ Eur Mediterr Prot Plant) 18:469-474

Kesiakova S, Nikiforov I 1983 [Toxic action and deratization effect of acute rodenticide]. Vet Med Nauki 20:72-80

Khan AA, Ahmad M 1991 Field efficacy of the second generation anticoagulants, zinc phosphide and bromethalin against *Meriones hurrianae Jerdon*. Ind J Plant Prot 19:43-48

Marsh RE 1988 Current (1987) and future rodenticides for commensal rodent control. Bull Soc Vector Ecol 13:102-107

Martin T, Johnson B 1989 A suspected case of bromethalin toxicity in a domestic cat. Vet Hum Toxicol 31:239-240

van Lier RB, Cherry LD 1988 The toxicity and mechanism of action of bromethalin: a new single-feeding rodenticide. Fundam Appl Toxicol 11:664-672

van Lier RBL, Ottosen LD 1981 Studies on the mechanism of toxicity of bromethalin: A new rodenticide. Toxicologist 1:114

Vitamin D-based Rodenticides

Brown DL, Robbins R 1999 Developments in the therapeutic applications of bisphosphonates. J Clin Pharmacol 39:651-660

Byers RE, Carbaugh DH 1989 Vole population shifts related to rodenticide usage. Hortscience 24:783-785

DeCristofaro JD, Tsang RC 1986 Calcium. Emerg Med Clin North Am 4:207-221

DeLuca HF 1988 The vitamin D story: a collaborative effort of basic science and clinical medicine. FASEB J 2:224-236

DeLuca HF 1992 Remembrance: discovery of the vitamin D endocrine system. Endocrinology 130:1763

Dougherty SA, Center SA, Dzanis DA 1990 Salmon calcitonin as adjunct treatment for vitamin D toxicosis in a dog. J Am Vet Med Assoc 196:1269-1272

Fooshee SK, Forrester SD 1990 Hypercalcemia secondary to cholecalciferol rodenticide toxicosis in two dogs. J Am Vet Med Assoc 196:1265-1268

Gunther R, Felice LJ, Nelson RK, Franson AM 1988 Toxicity of vitamin D-3 rodenticides to dogs. J Am Vet Med Assoc 193:211-214

Jibani M, Hodges NH 1986 Prolonged hypercalcemia after industrial exposure to vitamin D_3. Br Med J 290:748-749

Jolly SE, Eason CT, Frampton C 1993 Serum calcium levels in response to cholecalciferol and calcium carbonate in the Australian brushtail possum. Pest Biochem Physiol 47:159-164

Jolly SE, Henderson RJ, Frampton C, Eason CT 1995 Cholecalciferol toxicity and its enhancement by calcium carbonate in the common brushtail possum. Wildlife Res 22:579-583

Livezey KL, Hooser SB, Dorman DC, Buck WB 1991 Hypercalcemia induced by vitamin D3 toxicosis in two dogs. Canine Pract 16:26-32

Lund M 1974 Calciferol as a rodenticide. Intern Pest Control 16:10-11

Moore FM, Kudisch M, Richter K, Faggella A 1988 Hypercalcemia associated with rodenticide poisoning in three cats. J Am Vet Med Assoc 193:1099-1100

Peterson EN, Kirby R, Sommer M, Bovee KC 1991 Cholecalciferol rodenticide intoxication in a cat. J Am Vet Med Assoc 199:904-906

Pineau X, Kammerer M 1995 Intoxications by rodenticides containing vitamin D3 in domestic carnivores. Rec Med Vet L'ecole D'alfort 171:121-126

Rennison BD 1974 Field trials of calciferol against warfarin resistant infestations of the Norway rat

(*Rattus norvegicus* Berk.). J Hyg 73:361-367

Scheftel J, Setzer S, Walser M, Pertile T, Hegstad RL, Felice LJ, Murphy MJ 1991 Elevated 25 hydroxycholecalciferol and normal 1 25 dihydroxycholecalciferol serum concentrations in a successfully-treated case of vitamin D-3 toxicosis in a dog. Vet Hum Toxicol 33:345-348

Sexton PM, Findlay DM, Martin TJ 1999 Calcitonin. Curr Med Chem 6:1067-1093

Talcott PA, Mather GG, Kowitz EH 1991 Accidental ingestion of a cholecalciferol-containing rodent bait in a dog. Vet Hum Toxicol 33:252-256

Thomas JB, Hood JC, Gaschk F 1990 Cholecalciferol rodenticide toxicity in a domestic cat. Aust Vet J 67:274-275

Witmer GW, Matschke GH, Campbell DL 1995 Field trials of pocket gopher control with cholecalciferol. Crop Prot 14:307-309

Norbormide

Bova S, Cargnelli G, D'Amato E, Forti S, Yang Q, Trevisi L, Debetto P, Cima L, Luciani S, Padrini R 1997 Calcium-antagonist effects of norbormide on isolated perfused heart and cardiac myocytes of guinea-pig: a comparison with verapamil. Br J Pharmacol 120:19-24

Bova S, Trevis L, Debetto P, Cima L, Furnari M, Luciani S, Padrini R, Cargnelli G 1996 Vasorelaxant properties of norbormide, a selective vasoconstrictor agent for the rat microvasculature. Br J Pharmacol 117:1041-1046

Niu M, Jr. 1970 Pharmacological action of norbormide. Nippon Yakurigaku Zasshi 66:224-236

Patil TN, Radhakrishnamurty R 1973 Effect of norbormide on blood glucose levels in albino rats. Indian J Biochem Biophys 10:206-208

Patil TN, Radhakrishnamurty R 1977 Influence of norbormide on properties of rat liver mitochondria. Indian J Biochem Biophys 14:68-71

Patil TN, Radhakrishnamurty R 1979 Studies on norbormide toxicity in albino rats. Pest Biochem Physiol 11:74-82

Roszkowski AP 1965 The pharmacological properties of norbormide, a selective rat toxicant. J Pharmacol Exp Ther 149:288-299

Roszkowski AP, Poos GI, Mohrbacher RJ 1964 Selective Rat Toxicant. Science 144:412-413

Tsyrkunov LP 1989 [Skin lesions caused by exposure to a pesticide norbormide. Gig Tr Prof Zabol 46-47

Yelnosky J, Lawlor R 1971 Cardiovascular effects of norbormide. Eur J Pharmacol 16:117-119

Scilliroside

Azoyan P, Garnier R, Poitrineau H, Taboulet P 1991 Acute poisoning by scilliroside. J Toxicol Clin Exp 11:3-4

Brooks JE, Htun PT 1980 Laboratory evaluation of scilliroside used as a rodenticide against lesser bandicoot rat, *Bandicota bengalensis*. J Hyg 85:227-234

Chen KK 1970 Newer cardiac glycosides and aglycones. J Med Chem 13:1029-1034

Crabtree DG, Ward JC, Welch JF 1939 Sex differences in albino rats to toxic doses of powdered red squill. Endocrinology 25:629-632

Cummins RO, Haulman J, Quan L, Graves JR, Peterson D, Horan S 1990 Near-fatal yew berry intoxication treated with external cardiac pacing and digoxin-specific FAB antibody fragments. Ann Emerg Med 19:38-43

Dybing F, Dybing O, Stormorken H 1952 The toxicity of red squill and scilliroside to rats and mice. Acta Pharmacol et Toxicol 8:391-399

Gold H, Cattell M, Modell W, Greiner T, Guevara R 1950 Local emetic activity of glycosides of the digitalis series. J Pharm Exp Ther 98:337-345

Gold H, Modell W, Cattell M, Benton JG, Cotlove EW 1947 Actions of digitalis glycosides on the central nervous system with special reference to the convulsant action of red squill. J Pharm Exp Therap 91:15-30

Grollman A, Suki W, Ghavamian M 1962 The direct action of squill on the kidney as compared to certain other digitalis bodies. Arch Int Pharmacodyn 140:55-60

Lam YM 1993 Toxicity and palatability of scilliroside to *Rattus argentiventer*. Mardi Res J 21:113-120

Rich SA, Libera JM, Locke RJ 1993 Treatment of foxglove extract poisoning with digoxin-specific Fab fragments. Ann Emerg Med 22:1904-1907

Rothlin VE, Schalch WR 1952 Zur pharmakologie und toxikologie des scillirosids und des scillirosidins. Helv Physiol Acta 10:427-437

Sabouraud A, Urtizberea M, Cano N, Garnier R, Scherrmann JM 1990 Specific anti-digoxin Fab fragments: an available antidote for proscillaridin and scilliroside poisoning? Hum Exp Toxicol 9:191-193

Shapiro VW, Podrazik P 1993 Undiagnosed hypothyroidism: a risk factor for digoxin toxicity. Am J Emerg Med 11:670-671

Stoll A, Renz J 1942 Über scillirosid, ein gegen nager spezifisch wirksames gift der roten meerzwiebel. Helv Chim Acta 25:43-64

Stoll A, Renz J 1951 Spaltung von herzglykosiden mit enzympräparaten aus tierishen organen. Helv Chim Acta 34:782-786

Thurston D, Taylor K 1984 Gee's linctus. Pharm J 233:63

Tuncok Y, Kozan O, Cavdar C, Guven H, Fowler J 1995 *Urginea maritima* (Squill) toxicity. Clin Toxicol 33:83-86

Verbiscar AJ, Banigan TF, Marsh RE, Tunberg AD 1989 Red squill modified by *Lactobacillus acidophilus* for rodenticide use. J Agric Food Sci 37:1005-1009

Verbiscar AJ, Banigan TF, Schatz RA 1987 Modification of red squill by *Aspergillus niger*. J Agric Food Sci 35:365-368

Verbiscar AJ, Patel J, Banigan TF, Schatz RA 1986 Scilliroside and other scilla compounds in red squill. J Agric Food Chem 34:973-979

von Wartburg A 1966 Die herzglykoside der roten meerswiebel (*Scilla maritima*): Scillirubrosid. Helv Chim Acta 49:30-42

von Wartburg A, Renz J 1959 Die konstitution des scillirosidins. Helv Chim Acta 42:1620-1642

Winton FR 1927 A contrast between the actions of red and white squills. J Pharm Exp Therap 31:137-144

Winton FR 1927 The rat poisoning substance in red squills. J Pharm Exp Ther 31:123-136

Wolff JR, Schieweck C, Emmenegger H, Meier-Ruge W 1975 Cerebrovascular ultrastructural alterations after intra-arterial infusions of ouabain, scilla-glycosides, heparin and histamine. Acta Neuropathol 31:45-58

Alpha-chlorohydrin

Aire TA, Olusanya SK 1980 The response of the male domestic fowl (Gallus domesticus) to alpha-chlorohydrin treatment. Int J Androl 3:188-192

Andrews RV, Belknap RW 1975 An effective application of U-5897 to the control of established, feral rats. Part I. Nebraska Med J 60:46-48

Andrews RV, Belknap RW 1975 An effective application of U-5897 to the control of established, Feral rats. Part II. Nebr Med J 60:77-82

Andrews RV, Belknap RW 1983 Efficacy of alpha-chlorhydrin in sewer rat control. J Hyg (Lond) 91:359-366

Back DJ, Glover TD, Shenton JC, Boyd GP 1975 The effects of alpha-chlorohydrin on the composition of rat and rabbit epididymal plasma: a possible explanation of species difference. J Reprod Fertil 45:117-128

Ban Y, Asanabe U, Inagaki S, Sasaki M, Nakatsuka T, Matsumoto H 1999 Effects of alpha-chlorohydrin on rat sperm motions in relation to male reproductive functions. J Toxicol Sci 24:407-413

Braz I, Shandilya LN, Ramaswami LS 1976 Effect of alpha-chlorohydrin on the male reproductive organs of the Indian langur. Andrologia 8:290-296

Brown-Woodman PD, Mohri H, Mohri T, Suter D, White IG 1978 Mode of action of α-chlorohydrin as a male anti-fertility agent. Inhibition of the metabolism of ram spermatozoa by α-chlorohydrin and location of block in glycolysis. Biochem J 170:23-37

Brown-Woodman PD, Sale D, White IG 1976 The glycerylphosphorylcholine content of the rat epididymis after injecting alpha-chlorohydrin and ligating the vasa efferentia. Acta Eur Fertil 7:155-162

Brown-Woodman PD, White IG 1976 Disruption of the metabolism, motility and morphology of spermatozoa by injection of alpha-chlorohydrin into rams. Aust J Biol Sci 29:545-555

Brown-Woodman PDC, Salamon S, White IG 1974 Effect of -chlorohydrin on the fertility of rams. Acta Europ Fert 5:193-197

Cavanagh JB, Nolan CC, Seville MP 1993 The neurotoxicity of alpha-chlorohydrin in rats and mice: I. Evolution of the cellular changes. Neuropathol Appl Neurobiol 19:240-252

Chulavatnatol M, Hasibuan I, Yindepit S, Eksittikul T 1977 Lack of effect of alpha-chlorohydrin on the ATP content of rat, mouse and human spermatozoa. J Reprod Fertil 50:137-139

Cooney SJ, Jones AR 1988 Inhibitory effects of (S)-3-chlorolactaldehyde on the metabolic activity of boar spermatozoa in vitro. J Reprod Fertil 82:309-317

Cooper ERA, Jones AR, Jackson H 1974 Effects of -chlorohydrin and related compounds on the reproductive organs and fertility of the male rat. J Reprod Fert 38:379-386

Coppola JA 1969 An extragonadal male antifertility agent. Life Sci 8:43-48

Crabo BG, Zimmerman KJ, Gustafson B, Holtman M, Koh TJ, Graham EF 1975 Effect of low doses of alpha-chlorohydrin on fertility and semen characteristics and binding of the drug of spermatozoa in swine. Int J Fertil 20:87-94

Dixit VP, Agrawal M 1980 Inhibition of spermatogenesis in house rat (*Rattus rattus Rufescens*) following the administration of alpha- chlorohydrin. Andrologia 12:513-520

Dixit VP, Lohiya NK 1975 Chemical sterilization: effects of a single high dose of 3-chloro-1,2-propanediol on the testes and epididymides of dog. Acta Eur Fertil 6:57-62

Dixit VP, Lohiya NK, Arya M, Agrawal M 1975 Reversible changes in the testes and epididymides of dog treated with alpha-chlorohydrin. Acta Biol Med Ger 34:1851-1856

Dixit VP, Lohiya NK, Jain HC 1974 Effects of alpha-chlorohydrin and gonadectomy on the adenohypophysial cells of male rats and gerbils. J Reprod Fertil 38:185-188

Edwards EM, Dacheux JL, Waites GM 1976 Effects of alpha-chlorohydrin on the metabolism of testicular and epididymal spermatozoa of rams. J Reprod Fertil 48:265-270

Edwards EM, Jones AR, Waites GM 1975 The entry of alpha-chlorohydrin into body fluids of male rats and its effect upon the incorporation of glycerol into lipids. J Reprod Fertil 43:225-232

Ericsson RJ 1970 Male antifertility compounds: U-5897 as a rat chemosterilant. J Reprod Fert 22:213-222

Ericsson RJ, Baker VF 1970 Male antifertility compounds: biological properties of U5897 and U-15,646. J Reprod Fert 21:267-273

Ericsson RJ, Samojlik E 1970 Male antifertility compounds: structure and activity relationships of U-5897, U-15,646 and related substances. J Reprod Fert 21:263-266

Ford SA, Jones AR 1983 The effect of -chlorohydrin on the oxidation of fructose by rabbit spermatozoa in vitro . Contraception 28:565-573

Ford WC, Harrison A 1980 Effect of alpha-chlorohydrin on glucose metabolism by spermatozoa from the cauda epididymidis of the rhesus monkey (Macaca mulatta). J Reprod Fertil 60:59-64

Ford WC, Harrison A 1986 The concerted effect of alpha-chlorohydrin and glucose on the ATP concentration in spermatozoa is associated with the accumulation of glycolytic intermediates. J Reprod Fertil 77:537-545

Ford WC, Harrison A 1987 Futile substrate cycles in the glycolytic pathway of boar and rat spermatozoa and the effect of alpha-chlorohydrin. J Reprod Fertil 79:21-32

Ford WC, Harrison A, Waites GM 1977 Effects of the optical isomers of -chlorohydrin on glycolysis by ram testicular spermatozoa and the fertility of male rats. J Reprod Fertil 51:105-109

Ford WCL, Harrison A 1985 The presence of glucose increases the lethal effect of -chlorohydrin on ram and boar spermatozoa *in vitro*. J Reprod Fert 73:197-206

Ford WCL, Waites GMH 1982 Activities of various 6-chloro-6-deoxysugars and (S) -chlorohydrin in producing spermatocoeles in rats and paralysis in mice and in inhibiting glucose metabolism in bull spermatozoa *in vitro.* J Reprod Fert 65:177-183

Frei H, Wurgler FE 1997 The vicinal chloroalcohols 1,3-dichloro-2-propanol (DC2P), 3-chloro-1,2-propanediol (3CPD) and 2-chloro-1,3-propanediol (2CPD) are not genotoxic in vivo in the wing spot test of Drosophila melanogaster. Mutat Res 394:59-68

Gunn SA, Gould TC, Anderson WAD 1969 Possible mechanism of post-testicular antifertility action of 3-chloro-1,2-propanediol. Proc Soc Exp Biol Med 132:656-659

Guraya SS, Gill SK 1978 Histochemical changes of the rat testis and epididymis after treatment of alpha-chlorohydrin-effects of a single low dose. Andrologia 10:278-284

Hinton BT, Hernandez H, Howards SS 1983 The male antifertility agents alpha chlorohydrin, 5-thio-D-glucose, and 6-chloro-6-deoxy-D-glucose interfere with sugar transport across the epithelium of the rat caput epididymidis. J Androl 4:216-221

Hoffer AP, Hamilton DW 1970 Effects of U-5897 on fine structure of the rat epididymis. Anat Rec 166:319

Homonnai T, Paz G, Sofer A, Yedwab GA, Kraicer PF 1975 A direct effect of -chlorohydrin on motility and metabolism of ejaculated human spermatozoa. Contraception 12:579-588

Hutton P, Dawson AG, Jones AR 1980 Inhibition of glycolysis in boar sperm by alpha-chlorohydrin. Contraception 22:505-512

Jackson H, Robinson B 1976 The antifertility effects of -chlorohydrins and their stereo-isomers in male rats. Chem Biol Interact 13:193-197

Jackson H, Rooney FR, Fitzpatrick RW, Gibson KH 1977 Characterization and antifertility activity in rats of S(+)alpha-chlorohydrin. Chem Biol Interact 17:117-120

Johnson LA, Pursel VG 1972 Reversible infertility in male swine fed -chlorohydrin. J Anim Sci 34:241

Jones AR 1978 The antifertility actions of alpha-chlorohydrin in the male. Life Sci 23:1625-1645

Jones AR, Davies P, Edwards K, Jackson H 1969 Antifertility effects and metabolism of and epi-chlorohydrins in the rat. Nature 224:83

Jones AR, du Toit JI 1985 The anti-glycolytic action of (S)-alpha-chlorohydrin on epididymal bovine spermatozoa in vitro. Int J Androl 8:119-127

Jones AR, Ford SA 1984 The action of (S)-alpha-chlorohydrin and 6-chloro-6-deoxyglucose on the metabolism of guinea pig spermatozoa. Contraception 30:261-269

Jones AR, Gadiel P, Murcott C 1979 The renal toxicity of the rodenticide alpha-chlorohydrin in the rat. Naturwissenschaften 66:425

Jones AR, Milton DH, Murcott C 1978 The oxidative metabolism of alpha-chlorohydrin in the male rat and the formation of spermatocoeles. Xenobiotica 8:573-582

Jones AR, Murcott C 1976 The oxidative metabolism of alpha-chlorohydrin and the chemical induction of spermatocoeles. Experientia 32:1135-1136

Jones AR, Stevenson D 1983 Formation of the active antifertility metabolite of (S)-alpha-chlorohydrin in boar sperm. Experientia 39:784-785

Jones P, Jackson H 1976 Antifertility and dominant lethal mutation studies in male rats with dl- -chlorohydrin and an amino-analogue. Contraception 13:639-646

Kakaria VK, Sood PP 1983 Correlative histochemical and biochemical studies on the adenosine triphosphatase, succinic dehydrogenase and acetylcholinesterase in the epididymis of mice after alpha-chlorohydrin treatment. Acta Eur Fertil 14:353-361

Kalla NR, Chohan KS 1980 Studies on the mechanism of action of alpha-monochlorohydrin. Exp Pathol (Jena) 18:430-437

Kaur S, Guraya SS 1981 Effect of low doses of alpha chlorohydrin on the enzymes of glycolytic and phosphogluconate pathways in the rat testis and epididymis. Int J Androl 4:196-207

Kaur S, Guraya SS 1981 Effects of low doses of alpha chlorohydrin on the dehydrogenases and oxidases of rat epididymal epithelium and sperms: a correlative histochemical and biochemical study. Andrologia 13:225-231

Kirton KT, Ericsson RJ, Ray JA, Forbes AD 1970 Male antifertility compounds: efficacy of U-5897 in primates (*Macaca mulatta*). J Reprod Fert 21:275-278

Kreider JL, Dutt DH 1972 Induction of temporary infertility in rams with orally administered chlorohydrin. J Anim Sci 31:95-98

Lohika NK, Arya M 1979 Antifertility activity of alpha-chlorohydrin (3-chloro-1, 2 propanediol, U-5897) on the female rats. Acta Eur Fertil 10:23-27

Lubicz-Nawrocki CM, Chang MC 1974 Effect of -chlorohydrin on the fertilizing ability of hamster epididymal spermatozoa. J Reprod Fert 38:65-71

Lubicz-Nawrocki CM, Chang MC 1974 The onset and duration of infertility in hamsters treated with alpha-chlorohydrin. J Reprod Fertil 39:291-295

Morris S, Brown-Woodman PD, White IG 1976 Decrease in the glycerylphosphorylcholine content of the epididymis after injecting -chlorohydrin into rats. J Reprod Fertil 46:506

Paz GF, Homonnai TZ 1982 A direct effect of alpha-chlorohydrin on rat epididymal spermatozoa. Int J Androl 5:308-316

Piasecki A, Ruge A, Marquardt H 1990 Malignant transformation of mouse M2-fibroblasts by glycerol chlorohydrines contained in protein hydrolysates and commercial food. Arzneimittelforschung 40:1054-1055

Porter KE, Jones AR 1982 The effect of the isomers of alpha-chlorohydrin and racemic beta-chlorolactate on the rat kidney. Chem Biol Interact 41:95-104

Romero IA, Rist RJ, Chan MW, Abbott NJ 1997 Acute energy deprivation syndromes: investigation of m-dinitrobenzene and alpha-chlorohydrin toxicity on immortalized rat brain microvessel endothelial cells. Neurotoxicology 18:781-791

Samojlik E, Chang MC 19701 Antifertility activity of 3-chloro-1,2-propanediol (U-5897) on male rats. Biol Reprod 2:299-304

Setty BB, Kar AB, Roy SK, Chowdhury SR 1970 Studies with sub-toxic doses of alpha-chlorohydrin in the male monkey (*Macaca mulatta*). Contraception 1:279

Shinha Hikim AP 1986 Effects of alpha-chlorohydrin on the reproductive organs of the male bandicoot rat (*Bandicota bengalensis*). Acta Eur Fertil 17:301-306

Stevenson D, Jones AR 1985 Production of (S)-3-chlorolactaldehyde from (S)-alpha-chlorohydrin by boar spermatozoa and the inhibition of glyceraldehyde 3-phosphate dehydrogenase in vitro. J Reprod Fertil 74:157-165

Tsunoda Y, Chang MC 1976 Fertilizing ability *in vivo* and *in vitro* of spermatozoa of rats and mice treated with -chlorohydrin. J Reprod Fertil 46:401-406

Vickery BH, Erickson GI, Bennett JP 1974 Mechanism of antifertility action of low doses of -chlorohydrin in the male rat. J Reprod Fert 38:1-10

Wagenfeld A, Yeung CH, Strupat K, Cooper TG 1998 Shedding of a rat epididymal sperm protein associated with infertility induced by ornidazole and alpha-chlorohydrin. Biol Reprod 58:1257-1265

Welsburger EK, Ulland BM, Nam J, Gart JJ, Welsburger JH 1981 Carcinogenicity tests of certain environmental and industrial chemicals. J Natl Canc Instit 67:75-88

Yang CH, Srivastava PN 1976 Inhibition of bull and rabbit sperm enzymes by -chlorohydrin. J Reprod Fertil 46:289-293

Thallium

Ali SF, Jairaj K, Newport GD, Lipe GW, Slikker W, Jr. 1990 Thallium intoxication produces neurochemical alterations in rat brain. Neurotoxicology 11:381-390

Aoyama H, Yoshida M, Yamamura Y 1988 Induction of lipid peroxidation in tissues of thallous malonate-treated hamster. Toxicology 53:11-18

Appenroth D, Gambaryan S, Winnefeld K, Leiterer M, Fleck C, Braunlich H 1995 Functional and morphological aspects of thallium-induced nephrotoxicity in rats. Toxicology 96:203-215

Atkins HL, Budinger TF, Lebowitz E, Ansari AN, Greene MW, Fairchild RG, Ellis KJ 1977 Thallium-201 for medical use. Part 3: Human distribution and physical imaging properties. J Nucl Med 18:133-140

Bank WJ, Pleasure DE, Suzuki K, Nigro M, Katz R 1972 Thallium poisoning. Arch Neurol 26:456-464

Barclay RK, Peacock WC, Karnofsky DA 1953 Distribution and excretion of radioactive thallium in the chick embryo, rant, and man. J Pharm Exp Therap 107:178-187

Burger A, Starke K 1969 [Influencing by thallium of the ATPase of amino-storing granules in adrenal medulla and splenic nerves]. Experientia 25:578-579

Cotton FA, Wilkinson G 1980 Advanced Inorganic Chemistry: A Comprehensive Text. John Wiley & Sons, New York, Fourth Edition

Davis LE, Standefer JC, Kornfeld M, Abercrombie DM, Butler C 1981 Acute thallium poisoning: toxicological and morphological studies of the nervous system. Ann Neurol 10:38-44

Dumitru D, Kalantri A 1990 Electrophysiologic investigation of thallium poisoning. Muscle Nerve 13:433-437

Gettler AO, Weiss L 1943 Thallium poisoning. III. Clinical toxicology of thallium Am J Clin Path 13:422-429

Grisham CM, Gupta RK, Barnett RE, Mildvan AS 1974 Thallium-205 nuclear relaxation and kinetic studies of sodium and potassium ion-activated adenosine triphosphatase. J Biol Chem 249:6738-6744

Hasan M, Ali SF, Tariq M 1978 Levels of dopamine, norepinephrine and 5-hydroxytryptamine in different regions of the rat brain in thallium toxicosis. Acta Pharmacol Toxicol 43:169-173

Heath A, Ahlmen J, Branegard B, Lindstedt S, Wickstrom I, Andersen O 1983 Thallium poisoning--toxin elimination and therapy in three cases. J Toxicol Clin Toxicol 20:451-463

Hologgitas J, Ullucci P, Driscoll J, Grauerholz J, Martin H 1980 Thallium elimination kinetics in acute thallotoxicosis. J Anal Toxicol 4:68-75

Innis R, Moses H, III 1978 Thallium poisoning. John Hopkins Med J 142:27-31

Kamerbeek HH, Rauws AG, Ham MT, Heijst AV 1971 Dangerous redistribution of thallium by treatment with sodium diethyldithiocarbamate. Acta Med Scand 189:149-154

Kennedy P, Cavanagh JB 1976 Spinal changes in the neuropathy of thallium poisoning. A case with

neuropathological studies. J Neurol Sci 29:295-301

Lindegren CC, Lindegren G 1971 Thallium as a vital stain for yeast mitochondria. Nature 234:297

Moeschlin S 1980 Thallium poisoning. Clin Toxicol 17:133-146

Nogue S, Mas A, Pares A, Nadal P, Bertran A, Milla J, Carrera M, To J, Pazos MR, Corbella J 1982 Acute thallium poisoning: an evaluation of different forms of treatment. J Toxicol Clin Toxicol 19:1015-1021

Papp JP, Gay PC, Dodson VN, Pollard HM 1969 Potassium chloride treatment in thallotoxicosis. Ann Int Med 71:119-123

Pedersen RS, Olesen AS, Freund LG, Solgaard P, Larsen E 1978 Thallium intoxication treated with long-term hemodialysis, forced diuresis and Prussian blue. Acta Med Scand 204:429-432

Schafer EW 1972 The acute oral toxicity of 369 pesticidal, pharmaceutical and other chemicals to wild birds. Toxicol Appl Pharmacol 21:315-330

Shaw PA 1933 Toxicity and deposition of thallium in certain game birds. J Pharm Exp Therap 48:478-487

Spencer PS, Peterson ER, Madrid R, Raine CS 1973 Effects of thallium salts on neuronal mitochondria in organotypic cord-ganglia-muscle combination cultures. J Cell Biol 58:79-95

van Kesteren RG, Rauws AG, de Groot G, van Heijst ANP 1980 Thallium intoxication. an evaluation of therapy. Intensivmed 17:293-297

Yoshida M, Igeta S, Kawashima R, Akama Y, Yoshida K 1997 Changes in adenosine triphosphate (ATP) concentration and its activity in murine tissue after thallium administration. Bull Environ Contam Toxicol 59:268-273

Yellow Phosphorus

Atkinson HV 1921 The treatment of acute phosphorus poisoning. J Lab Clin Med 7:148

Caley JP, Kellock IA 1955 Acute yellow phosphorus poisoning with recovery. Lancet 268:539-541

Dathe RA, Nathan DA 1945 Electrocardiographic changes resulting from phosphorus poisoning.`. Am Heart J 31:98-102

Diaz-Rivera RS, Collazo PJ, Pons ER, Torregrosa MV 1950 Acute phosphorus poisoning in man: a study of 56 cases. Medicine 29:269-298

Duerksen-Hughes P, Ingerman L, Ruoff W. Toxicological profile for white phosphorus and white phosphorus smoke. 1994. Atlanta, Georgia, USA, U.S. Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry.

Ehrentheil OF 1957 Acute phosphorus poisoning: a case with severe granulocytopenia and hypoprothrombinemia. Bull Tufts N Eng Med Center 3:201-206

Fernandez OU, Canizares LL 1995 Acute hepatotoxicity from ingestion of yellow phosphorus-containing fireworks. J Clin Gastroenterol 21:139-142

Greenberger NJ, Robinson WL, Isselbacher KJ 1964 Toxic hepatitis after the ingestion of phosphorus with subsequent recovery. Gastroenterology 47:179-183

LaDue JS, Schenken JR, Kuker LH 1944 Phosphorus poisoning: a report of sixteen cases with repeated liver biopsies in a recovered case. Am J M Sci 208:223

Marin GA, Montoya CA, Sierra JL, Senior JR 1971 Evaluation of corticosteroid and exchange-transfusion treatment of acute yellow-phosphorus intoxication. N Engl J Med 284:125-128

Matsumoto S, Kohri Y, Tanaka K, Tsuchiya G 1972 A case of acute phosphorus poisoning with various electrocardiographic changes. Jap Cir J 36:963-970

McCarron MM, Gaddis GP, Trotter AT 1981 Acute yellow phosphorus poisoning from pesticide pastes. Clin Toxicol 18:693-711

Nachman M, Hartley PL 1975 Role of illness in producing learned taste aversions in rats: a comparison of several rodenticides. J Comp Physiol Psychol 89:1010-1018

Pietras RJ, Stavrakos C, Gunnar RM, Tobin JR, Jr. 1968 Phosphorus poisoning simulating acute myocardial infarction. Arch Intern Med 122:430-434

Rubbitsky HJ, Myerson RM 1949 Acute phosphorus poisoning. Arch Intern Med 83:164-178

Salfelder K, Doehnert HR, Doehnert G, Sauerteig E, DeLiscano TR, Fabrega E 1972 Fatal phosphorus poisoning. a study of forty-five cases. Beitr Pathol 174:321

Simon FA, Pickering LK 1976 Acute yellow phosphorus poisoning. "Smoking stool syndrome". JAMA 235:1343-1344

Sontag LW 1938 Acute phosphorus poisoning in an infant resulting from an antirachitic preparation. Am J Dis Child 56:114-118

Talley RC, Linhart JW, Trevino AJ, Moore L, Beller BM 1972 Acute elemental phosphorus poisoning in man: cardiovascular toxicity. Am Heart J 84:139-140

Wellsa GH 1926 Case of chronic phosphorus poisoning. M Clin N Am 10:95

Whalen JP, O'Donohue N, Krook L, Nunez EA 1973 Pathogenesis of abnormal remodeling of bones: effects of yellow phosphorus in the growing rat. Anat Rec 177:15-22

Zinc Phosphide

Amr MM, Abbas EZ, El Samra M, El Batanuoni M, Osman AM 1997 Neuropsychiatric syndromes and occupational exposure to zinc phosphide in Egypt. Environ Res 73:200-206

Bai KM, Majumder SK 1982 Enhancement of mammalian safety by incorporation of antimony potassium tartrate in zinc phosphide baits. Bull Environ Contam Toxicol 29:107-114

Barbosa A, Rosinova E, Dempsey J, Bonin AM 1994 Determination of genotoxic and other effects in mice following short term repeated-dose and subchronic inhalation exposure to phosphine. Environ Mol Mutagen 24:81-88

Burgess JL, Morrissey B, Keifer MC, Robertson WO 2000 Fumigant-related illnesses: Washington State's five-year experience. J Toxicol Clin Toxicol 38:7-14

Cabrol Telle AM, de Saint BG, Derache R, Hollande E, Periquet B, Thouvenot JP 1985 Nutritional and toxicological effects of long-term ingestion of phosphine-fumigated diet by the rat. Food Chem Toxicol 23:1001-1009

Chefurka W, Kashi KP, Bond EJ 1976 The effect of phosphine on electron transport in mitochondria. Pest Biochem Physiol 6:65-84

Chin KL, Mai X, Meaklim J, Scollary GR, Leaver DD 1992 The interaction of phosphine with haemoglobin and erythrocytes. Xenobiotica 22:599-607

Chugh SN, Aggarwal HK, Mahajan SK 1998 Zinc phosphide intoxication symptoms: analysis of 20 cases. Int J Clin Pharmacol Ther 36:406-407

Garry VF, Griffith J, Danzl TJ, Nelson RL, Whorton EB, Krueger LA, Cervenka J 1989 Human genotoxicity: pesticide applicators and phosphine. Science 246:251-255

Garry VF, Nelson RL, Danzl TJ, Cervenka J, Krueger LA, Griffith J, Whorton E 1990 Human genotoxicity in phosphine-exposed fumigant applicators. Prog Clin Biol Res 340C:367-76:367-376

Hsu CH, Quistad GB, Casida JE 1998 Phosphine-induced oxidative stress in Hepa 1C1C7 cells. Toxicol Sci 46:204-210

Jain SM, Bhandari A, Sepaha GC, Sanghvi VC, Raman PG 1985 Electrocardiographic changes in aluminum phosphide poisoning. J Assoc Phys Ind 33:406-409

Khosla SN, Chugh SN, Nand N, Saini RS 1985 Systemic involvement in aluminum phosphide poisoning. J Assoc Phys Ind 34:227-228

Kligerman AD, Bishop JB, Erexson GL, Price HC, O'Connor RW, Morgan DL, Zeiger E 1994

Cytogenetic and germ cell effects of phosphine inhalation by rodents: II. Subacute exposures to rats and mice. Environ Mol Mutagen 24:301-306

Kligerman AD, Bryant MF, Doerr CL, Erexson GL, Kwanyuen P, McGee JK 1994 Cytogenetic effects of phosphine inhalation by rodents. I: Acute 6-hour exposure of mice. Environ Mol Mutagen 23:186-189

Krishnakumari MK, Bai KM, Majumder SK 1980 Toxicity and rodenticidal potency of zinc phosphide. Bull Environ Contam Toxicol 25:153-159

Misra UK, Bhargava SK, Nag D, Kidwai MM, Lal MM 1988 Occupational phosphine exposure in Indian workers. Toxicol Lett 42:257-263

Misra UK, Tripathi AK, Pandey R, Bhargwa B 1988 Acute phosphine poisoning following ingestion of aluminium phosphide. Hum Toxicol 7:343-345

Nakakita H, Katsumata Y, Ozawa T 1971 The effect of phosphine on respiration of rat liver mitochondria. J Biochem (Tokyo) 69:589-593

Newton PE, Hilaski RJ, Banas DA, Wilson NH, Busey WM, Shaheen DG 1999 A 2-year inhalation study of phosphine in rats [In Process Citation]. Inhal Toxicol 11:693-708

Pal BB, Bhunya SP 1995 Mutagenicity testing of a rodenticide, zinctox (zinc phosphide) in a mouse in vivo system. In Vivo 9:81-83

Patial RK, Bansal SK, Kashyap S, Sharma AK, Sharma B 1990 Hypoglycaemia following zinc phosphide poisoning. J Assoc Physicians India 38:306-307

Potter WT, Rong S, Griffith J, White J, Garry VF 1991 Phosphine-mediated Heinz body formation and hemoglobin oxidation in human erythrocytes. Toxicol Lett 57:37-45

Sangle SA, Thomas A, Verma S, Wadia RS 1987 Zinc phosphide poisoning. J Assoc Physicians India 35:591-594

Sarma PS, Narula J 1996 Acute pancreatitis due to zinc phosphide ingestion. Postgrad Med J 72:237-238

Shivanandappa T, Ramesh HP, Krishnakumari MK 1979 Rodenticidal poisoning of non-target animals: acute oral toxicity of zinc phosphide to poultry. Bull Environ Contam Toxicol 23:452-455

Siwach SB, Gupta A 1995 The profile of acute poisonings in Harayana-Rohtak Study. J Assoc Physicians India 43:756-759

Waritz RS, Brown RM 1975 Acute and subacute inhalation toxicities of phosphine, phenylphosphine and triphenylphosphine. Am Ind Hyg Assoc J 36:452-458

Strychnine

Andersen AH 1946 Experimental studies on the pharmacology of activated charcoal. I. Adsorption power of charcoal in aqueous solutions. Acta Pharmacol 2:69-78

Aprison MH, Lipkowitz KB, Simon JR 1987 Identification of a glycine-like fragment on the strychnine molecule. J Neurosci Res 17:209-213

Dieke SH, Richter CP 1946 Comparative assays of rodenticides on wild Norway rats. Public Health Rept U S 61:672-679

Dittrich K, Bayer MJ, Wanke LA 1984 A case of fatal strychnine poisoning. J Emerg Med 1:327-330

Edmunds M, Sheehan TM, Van't Hoff W 1986 Strychnine poisoning: clinical and toxicological observations on a non-fatal case [published erratum appears in J Toxicol Clin Toxicol 1986;24(5):461]. J Toxicol Clin Toxicol 24:245-255

Flood RG 1999 Strychnine poisoning. Pediatr Emerg Care 15:286-287

Garlough FE 1941 Poisons and their application in the control of rats and mice. Pests 9:15-19

Hatcher RA, Eggleston C 1918 The fate of strychnine in the body. J Pharm Exp Therap 10:281-319

Heidrich H, Ibe K, Klinge D 1969 Akute vergiftung mit strychnin N-oxydhydrochlorid und ihre behandlung mit diazepam. Arch Toxik 24:188

Heiser JM, Daya MR, Magnussen AR, Norton RL, Spyker DA, Allen DW, Krasselt W 1992 Massive strychnine intoxication: serial blood levels in a fatal case. J Toxicol Clin Toxicol 30:269-283

Howard WE, Palmateer SD, Nachman M 1968 Aversion to strychnine sulfate by Norway rats, roof rats, and pocket gophers. Toxicol Appl Pharmacol 12:229-241

Lambert JR, Byrick RJ, Hammeke MD 1981 Management of acute strychnine poisoning. Can Med Assoc J 124:1268-1270

Maron BJ, Krupp JR, Tune B 1971 Strychnine poisoning successfully treated with diazepam. J Pediatr 78:697-699

Palatnick W, Meatherall R, Sitar D, Tenenbein M 1997 Toxicokinetics of acute strychnine poisoning. J Toxicol Clin Toxicol 35:617-620

Smith BA 1990 Strychnine poisoning. J Emerg Med 8:321-325

Swissman N, Jacoby J 1964 Strychnine poisoning and its treatment. Clin Pharmacol Ther 5:136

Tucker RK, Haegele MA 1971 Comparative acute oral toxicity of pesticides to six species of birds. Toxicol Appl Pharmacol 20:57-65

Weiss S, Hatcher R 1922 Studies on strychnine. J Pharm Exp Therap 19:421-482

Anticoagulants

Babcock J, Hartman K Pedersen A, Murphy M, Alving B 1993 Rodenticide-induced coagulopathy in a young child: a case of Munchausen syndrome by proxy. Am J Pediatr Hematol Oncol 15:126-130

Bachman KA, Sullivan TJ 1983 Disposition and pharmacodynamic characteristics of brodifacoum in warfarin-sensitive rats. Pharmacology 27:281-288

Barlow AM, Gay AL, Park BK 1982 Difenacoum (neosorexa) poisoning. Brit Med J 285:541

Beasley VR, Buck WB 1983 Warfarin and other anticoagulant poisonings. In Kirk RW (ed): Current Veterinary Therapy VIII. Philadelphia, WB Saunders, pp 101-106

Bell RG 1978 Metabolism of vitamin K and prothrombin synthesis: anticoagulants and the vitamin K-epoxide cycle. Proc Soc Exp Biol Med 37:2599-2604

Bellah JR, Weigel JP 1983 Hemarthrosis secondary to suspected warfarin toxicosis in a dog. J Am Vet Med Assoc 182:1126-1127

Braithwaite GB 1982 Vitamin K and brodifacoum. J Am Vet Med Assoc 181:531-534

Breckenridge A, Leck JB, Serlin MJ, Wilson A 1987 Mechanisms of action of the anticoagulants warfarin, 2-chloro-3-phytylnaphthoquinone (CL-K), acenocoumarol, brodifacoum, and difenacoum in the rabbit. Br J Pharmacol 64:339

Bruno GR, Howland MA, MCMeeking A, Hoffman RS 2000 Long-acting anticoagulant overdose: brodifacoum kinetics and optimal vitamin K dosing. Ann Emerg Med 36:262-267

Burucoa C, Mura P, Robert R, Boinot C, Bouquet S, Piriou A 1989 Chlorophacinone intoxication: a biological and toxicological study. Clin Toxicol 27:79-89

Dorman DC 1990 Anticoagulant, cholecalciferol, and bromethalin-based rodenticides. Vet Clin North Am [Small Anim Pract] 20:339-351

Fristedt B, Sterner B 1965 Warfarin intoxication from percutaneous absorption. Arch Environ Health 11:205-208

Grand M 1976 Experimental data on a new anticoagulant raticide: bromadiolone. Phytiatrie-Phytopharmacie 25:69-88

Greaves JH, Shepherd DS, Gill JE 1982 An investigation of difenacoum resistance in Norway rat populations in Hampshire. Ann Appl Biol 100:581-587

Hadler MR, Shadbolt RS 1975 Novel 4-hydroxycoumarin anticoagulants active against resistant rats. Nature (London) 253:275-277

Hellemans J, Vorlat M, Verstraete M 1963 Survival time of prothrombin and factors VII, IX and X after complete synthesis of blocking doses of coumarin derivatives. Br J Haematol 9:506-512

Hoffman RS 1998 Anticoagulants. In: Goldfrank LR, Flomenbaum NE, Lewin NA, Weisman RS, Howland MA, Hoffman RS (ed), Goldfrank's Toxicological Emergencies. Stamford, CT, Appleton & Lange, pp 703-725

Hollinger BR, Pastoor TP 1993 Case management and plasma half-life in a case of brodifacoum poisoning. Arch Intern Med 153:1925-1928

Holms RW, Love J1952 Suicide attempt with warfarin, a bishydroxycoumarin-like rodenticide. JAMA 148:935-937

Jackson WB, Spear PJ, Wright CG 1971 Resistance of Norway rats to anticoagulant rodenticides confirmed in the United States. Pest Control 39:13-14

Leck JB, Park BK 1981 A comparative study of the effects of warfarin and brodifacoum on the relationship between vitamin K metabolism and clotting factor activity in warfarin-susceptible and warfarin-resistant rats. Biochem Pharmacol 30:123-128

Lund M 1981 Comparative effects of the three rodenticides warfarin, difenacoum, and brodifacoum on eight rodent species in short feeding periods. J Hyg 87:101-107

Marsh RE 1985 Anticoagulant rodenticides provide pet problems. Pest Control 53:26-28,31.

Marsh RE 1987 Current (1987) and future rodenticides for commensal rodent control. Bull Soc Vector Ecol 13:102-107

Mount ME 1988 Diagnosis and therapy of anticoagulant rodenticides intoxications. Vet Clin North Am [Small Anim Pract] 18:115-130

Mount ME, Feldman BF 1983 Mechanism of diphacinone rodenticide toxicosis in the dog, and its therapeutic implications. Am J Vet Res 44:2009-2017

Mount ME, Feldman BF, Buffington, T 1982 Vitamin K and its therapeutic importance. J Am Vet Med Assoc 180:1354

Mount ME, Woody bG, Murphy MDI 1986 The anticoagulant rodenticides, In Kirk RW (ed): Current Veterinary Therapy IX. Philadelphia, WB Saunders, pp 156-165

Murphy MDI, Jerkin FD 1989 The anticoagulant rodenticides, In Kirk RW (ed): Current Veterinary Therapy X. Philadelphia, WB Saunders, pp 143-146

Park BK, Leck JB 1982 A comparison of vitamin K antagonism by warfarin, difenacoum and brodifacoum in the rabbit. Biochem Pharmacol 31:3636-3639

Renee P, Stark PY, Johnson LR, Bell rG 1977 Mechanism of action of anticoagulants. J Pharmacol Exp Ther 201:541-546

Rowe FP, Brasfield A, Swinney T 1985 Pen and field trials of a new anticoagulant rodenticide flocoumafen against the house mouse (*Mus musculus L.*). J Hyg (Cab) 95:623-627

Schiff LB, Kern AB 1968 Cutaneous reactions to anticoagulants. Arch Dermatol 98:136-137

Watts rG, Casselberry RP, Sadowsky JA 1990 Accidental poisoning with a superwarfarin compound (brodifacoum) in a child. Pediatrics 86:883-887

Whilton DS, Sodowski JA, Suttie JW 1978 Mechanism of coumarin action: significance of vitamin K epoxide reductase inhibition. Biochemistry 17:1371-1377

Yu CC, Atallah YH, Whitacre DM 1982 Metabolism and disposition of diphacinone in rats and mice. Drug Metab Dispos 10:645-648

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Rodney C. Baker received a Master of Science Degree (nutrition) from Utah State University in 1970. His thesis addressed the interaction between diet protein quantity or quality and the metabolism of organochlorine pesticides. He received a Doctor of Philosophy Degree in 1974 from North Carolina State University (physiology/toxicology). His research project was directed toward elucidating the mechanism of piperonyl butoxide action. Dr Baker's postdoctoral training was in the area of lipid biochemistry. His research activities have centered on the interaction of various classes of drugs and xenobiotics on lipid metabolism and disruption of phospholipid dependent intracellular signal transduction processes. Dr. Baker is currently a Professor of Pharmacology and Toxicology at The University of Mississippi Medical Center, Jackson, Mississippi.