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POISONING BY RODENTICIDE

WHAT TO DO ABOUT POISONING BY RODENTICIDE?

There are many rodenticides on the market, the vast majority of them belonging to the anticoagulant class of chemical compounds.

Warfarin was the only anticoagulant used for this purpose for many years, but the evolution of warfarin-resistant rats led to the evolution of "second-generation", much more potent compounds. Not only are they more potent but they also have a longer duration of activity. In some circumstances, one exposure can lead to a fatality.

Veterinarians all over the world get to see the consequences of the free availability of these powerful new rodenticides, and often have to make quick decisions to ensure the survival of their patients. This isn't easy when the necessary information isn't readily available. So, we thought it would be useful to give you some facts about rodenticide poisoning and about the best way to treat cases of such poisoning.

The article below, "Poisoning by Rodenticide" provides background information, and help you identify the poison, and list rodenticide anticoagulants on the SA market (indicating the active ingredients).

The standard and now well-documented antidotal treatment is VITAMIN K1, which up to now has been expensive and awkward to obtain. The article discusses the question of oral treatment vs. parenteral and highlights that tablets may even be the preferred method of administration.

Vitamin K1 (phytomenadione) tablets are available from Kyron Laboratories.

These tablets are 25mg strength and packed in 25's, and should be used in both suspect and confirmed cases of rodenticide toxicity. For second-generation anticoagulants, treatment needs to be continued for 2 to 4 weeks. Phytomenadione is an expensive material, but these tablets have been reasonably priced to ensure that your clients won't be bankrupted by the lengthy treatment needed. Every veterinary practice should keep a bottle or two handy for:

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SUMMARY

Rodenticide poisoning of companion animals is a world-wide problem. The most widely-used rodenticides today are potent anticoagulants. This article discusses the mechanisms and clinical features of poisoning by these agents.*

The important role of Vitamin K_1 (phytomenadione) in the treatment of poisoning by anticoagulants is identified. A table is provided which will help the veterinarian identify the anticoagulant poison involved.

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In the early 20th century, *bis*-hydroxycoumarin was discovered after livestock had eaten spoiled sweet clover and died of a haemorrhagic condition. Today, coumarin derivatives are used therapeutically as anticoagulants and commercially as rodenticides. Warfarin (*4-hydroxy-3[3-oxo-1-phenylbutyl] coumarin*) was the original oral anticoagulant used both for medicinal purposes and to poison rats and mice, but the evolution of warfarin-resistant rats has led to the development of more potent compounds.

While warfarin remains the standard anticoagulant treatment for humans, today the new, powerful coumarin derivatives – second generation so-called "superwarfarins" – dominate the rodenticide field.

Unfortunately, international data indicates that these rodenticides are also the cause of accidental or deliberate poisoning of dogs, cats, birds and wildlife all over the world. Not all rodenticides are anticoagulant-based – some are organophosphates or other organic compounds and some are toxic inorganic substances like zinc phosphide.

Efekto Eco Rat™ active ingredient, cholecalciferol, is a natural compound (vitamin D3) which plays a vital part in the body but at excessive doses, it has a toxic effect in mammals. This characteristic is used in Eco Rat™ to control rodents as their tolerance for cholecalciferol is much less than that of dogs, cats and human beings. Cholecalciferol has a dual action: it rapidly induces appetite loss in rodents (after as little as one meal) and deposits high calcium loads (hypercalcaemia) in intestines and blood vessels. Rodents stop feeding within 2 days after the first ingestion of cholecalciferol.

Rats and mice die within 4 to 7 days. Eco-Rat™ is a green colourband pesticide and therefore falls within the least hazardous class of pesticides. Because of the unique characteristics of the active ingredient, the product has a reduced risk of secondary poisoning to pets like dogs and cats and very little risk of secondary poisoning to raptors like owls.

That said, the product can never be described as "safe" as it is still a pesticide and is designed to kill rats and mice and therefore can still pose a risk to children, uninformed persons and pets if not used in a responsible way. It is therefore very important that the label instructions are followed and the bait is put out in bait boxes or where it is secured and out of reach of pets and children.

Bait boxes are available to purchase at stores like Builders Warehouse and are always recommended for the use of rodenticides.

https://efekto.co.za/wp-content/uploads/2018/11/Efekto_Eco_Rat_FAQs.pdf

In South Africa about 60 different anticoagulant rodenticide products are available, the vast majority of them being superwarfarins (see Table 3); with their easy availability, many veterinary practices get to see poisoning cases on a more or less regular basis.

Second generation agents – superwarfarins - are highly potent. Their oral bioavailability (and that of warfarin) is nearly 100%. They are generally effective after a single exposure. They are highly bound (up to 97%) to plasma protein, and so, because they are retained in the body for extended periods they have a long duration of action.

After a single dose of warfarin the duration of anticoagulant effect is usually 5-7 days in humans – but superwarfarin products can continue to produce significant anticoagulation for *weeks to months after a single ingestion*.

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For instance, in dogs, approximately 8% of an oral dose of flocoumafen remains in the liver 43 weeks post-ingestion. The elimination of superwarfarins from the liver is typically biphasic, with a rapid elimination phase lasting 2 to 8 days followed by a slow release phase lasting about 100 to 200 days. Other sites of significant accumulation include the kidneys and pancreas. The toxicity of superwarfarins is also greatly increased by repeated low-level consumption. Even dermal absorption of anticoagulants has been associated with lethal toxicity in humans.

A consequence of the long duration of action of these compounds is that, after poisoning, a prolonged period of treatment is necessary.

Cats metabolise many substances differently to dogs. This is equally true of anticoagulants: in general the feline LD_{50} for superwarfarins is higher than the equivalent canine LD_{50} – so felines have better prospects for successful treatment than canines.

MECHANISM OF ACTION

Anticoagulant rodenticides interfere with the vitamin K-dependent carboxylation of factors II, VII, IX and X. Depletion of factors II, VII, IX and X inhibits the intrinsic, extrinsic and common clotting pathways, death is usually associated with the effects of haemorrhage.

The epoxide-reduction enzyme necessary for the recycling of vitamin K is inhibited, resulting in a rapid depletion of body stores of vitamin K. As vitamin K recycling is reduced or completely halted, a continuous source of vitamin K is essential for production of the above factors and prevention of a coagulopathy.

CLINICAL FEATURES

These can vary and include:

- lethargy
- respiratory distress
- lameness
- petechial and ecchymotic haemorrhages
- epistaxis and haemoptysis

The animal can occasionally die without external evidence of bleeding. When intrapulmonary haemorrhage occurs, a secondary bacterial pneumonia can develop.

DIAGNOSTIC LABORATORY TESTS

Interference with coagulation factors results in prolonged active coagulation time (ACT), prothrombin time (PT), and activated partial thromboplastin time (APTT). To assay for these factors a blood sample collected into a correctly-filled citrate tube should be obtained prior to commencement of any therapy.

An EDTA tube should be submitted at the same time to assist in determining the extent of haemorrhage and the platelet status. A marked thrombocytopaenia can lead to haemorrhage and similar presenting signs. In anticoagulant rodenticide toxicity there is generally no change or a mild increase or decrease in platelet count.

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TREATMENT

The objectives of treatment are to stabilize and decontaminate the patient, provide functional clotting factors, antagonize the effects of anticoagulant on vitamin K_1 metabolism and, if necessary, compensate for the blood loss that has occurred. Animals presenting with an acute haemorrhagic crisis require administration of whole blood at a rate of 10-20ml/kg. The animal should be placed under close observation and be kept warm and quiet. Unnecessary manipulation and trauma should be avoided.

Vitamin K_1 is the specific antidote. Vitamin K_1 treatment stops bleeding and causes APTT and PT to return to normal or near normal within 24 hours. If it is possible to ascertain whether a first-generation or second-generation rodenticide has been ingested, this should be done as this will determine the dose rate of vitamin K_1.

Intravenous vitamin K_1 can be administered initially but it can give rise to an anaphylactoid reaction, and therefore should be used only where there is a possibility of fatal haemorrhage. Under most clinical circumstances, oral vitamin K_1 administration is the preferred route – absorption can be enhanced by concomitant administration of fatty foods. For first-generation compounds (warfarin) the oral dose rate is 0,5 to 2,0 mg per kg per day, administered for 4-6 days.

Superwarfarins require higher dose rates – as high as 5 mg/kg initially, with a lower dose for most of the duration of treatment. Treatment for 2 to 4 weeks is desirable. High dose vitamin K_1 therapy can lead to Heinz body haemolytic anaemia in dogs, so caution is advised. The use of vitamin K_3 (menadione) is not advisable as it has poor efficacy and may have toxic side-effects.

Active ingredient	*Acute oral LD50*	*Vitamin K_1 therapy*		
	Canine	*Feline*	*Dose*	*Treatment duration*
WARFARIN	20-300 mg/kg	5-30 mg/kg	0,5-2	4-6 days
BRODIFACOUM	04-4 mg/kg	25 mg/kg	2,5-5 mg/kg	2 – 4 weeks
BROMADIOLONE	11-15 mg/kg	>25 mg/kg	2,5-5	2 – 4 weeks
COUMATETRALYL	Not available	Not available	2,5-5 mg/kg	2 – 4 weeks
FLOCOUMAFEN	0,5-0,75 mg/kg	>10 mg/kg	2,5-5	2 – 4 weeks

Human case reports have demonstrated coagulopathies lasting for six months or longer which required prolonged periods of treatment with large amounts of vitamin K_1 following poisoning with as little as 10mg of orally administered brodifacoum.

In animals, with appropriate treatment and care the prognosis is relatively good: survival rates of 80-100% have been reported. In humans, the literature shows that successful outcomes have been attained even in the face of massive brodifacoum overdose.

This article is largely a summary of a paper by Rhian B Cope, of the College of Veterinary Medicine, Oregon State University, Corvallis, Oregon, USA. It appeared in the journal, the Australian Veterinary Practitioner, in June 2004.

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Strength: 25mg, packed in 25's.

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ANTICOAGULANT RODENTICIDES AVAILABLE IN SOUTH AFRICA

(as at February 2021)

Anticoagulant name	*Trade name*	*Concentration*	*Manufacturer/marketer*
Brodifacoum	Broditop pasta	0.05 g/kg	Henchem/ Pathogen and Enviromental solutions
	Eradirat wedges	0.05 g/kg	Agrivet Business
	Eradirat liquid	0.5 g/L	Agrivet Business
	Eradirat pellets	0.02 g/kg	Agrivet Business
	Jaguar	0.05 g/kg	Pathogen ES/ MC Pharma (Pty) Ltd
	Klerat 20g wax blocks	0,05 g/kg	Syngenta SA
	Kill-all liquid	0.5 g/L	Protek SA/Almond Agrochemicals
	Kill-all pellets	0.02 g/kg	Protek SA/Almond Agrochemicals
	Kill-all wax blocks	0.05 g/kg	Protek SA
	Kill-all wedges	0.05 g/kg	Almond Agrochemicals
	Kill-all grain bait	0.02 g/kg	Almond Agrochemicals
	Kombat rat & mouse blocks	0,05 g/kg	Kombat Chemicals
	Kombat rat & mouse pellets	0,05 g/kg	Kombat Chemicals
	Liquid concentrate rat & mouse bait for PCO's only	2.5 g/L	Scientific Supa-kill
	Mortein Target rat kill	0.05 g/kg	Reckitt Benckiser SA
	Piff Paf rat kill	0.05 g/kg	Reckitt Benckiser SA
	Pulse wax blocks	0.05 g/kg	Synvita/Lifeguard Sciences (Pty) Ltd
	Pulse pellets	0.05 g/kg	Synvita/Lifeguard Sciences (Pty) Ltd
	Pulse liquid	0.75 g/kg	Synvita/Lifegaurd Sciences (Pty) Ltd
	Rat bait blocks	0.05 g/kg	Degesch SA
	Rat and mice blocks	0.05 g/kg	Kombat
	Rat and mice pellets	0.05 g/kg	Kombat
	Rattack	0.025 g/kg	BAS Delaney
	Rattex	0,05 g/kg	Tiger Brands
	Rodex liquid concentrate	2.5 g/L	Innovative Pest Management
	Rodex liquid bait	0.5 g/L	Henchem
	Rodex liquid concentrate	0.75 g/L	Henchem/Innovative Pest mngmt
	Rodex bait blocks	0.05 g/kg	Avima/Henchem
	Rodex grain bait	0.05 g/kg	Henchem/Protek SA
	Rodex paste bait	0.05 g/kg	Protek SA
	Rodex rat & mouse pellets	0.05 g/kg	Henchem
	Rodex wax blocks	0.05 g/kg	Henchem
	Rondenthor wax blocks	0.05 g/kg	Ensystex
	Rodenthor pasta	0.05 g/kg	Ensystex SA
	Stop Kill wax blocks	0.05 g/kg	Makhro
	Stop Kill rodent blocks	0.05 g/kg	Henchem
	Stop Kill rats and mice	0.02 g/kg	Volcano Agroscience (Pty) Ltd
	Stops Kills wax blocks	0.05 g/kg	Reckitt Benckiser SA
	Supa-Kill liquid concentrate rat & mouse	0.75 g/L	Scientific Supa-Kill
	Supa-Kill rat & mouse blocks	0.05 g/kg	Scientific Supa-Kill
Bromadiolone	Bromard (with Bitrex) paste	0.1 g/kg	Rentokil Initial
	Bromatrol contact dust (with Bitrex)	1.5 g/kg	Rentokil Initial
	Supa Kill grain bait	0.05 g/kg	Scientific Supakill
	Tomcat	0.05 g/kg	Pathogen ES/ MC Pharma (Pty) Ltd

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Coumatetralyl	Muti-Ingundane	0.0375 g/kg	Growing Manufr
	Mirron grain bait	0.375 g/kg	Villa Crop protection
	Racumin liquid rat poison	8 g/L	Bayer SA
	Racumin paste	0.375 g/kg	Bayer ES
	Racumin rat bait	0.375 g/kg	Bayer (Pty) Ltd
	Racumin rat & mouse bait blocks	0.375 g/kg	Bayer ES
	Racumin wax blocks	0.375 g/kg	Bayer (Pty) Ltd
	Racumin tracking powder	7.5 g/kg	Bayer ES
	Rumour grain bait	0.375 g/kg	Universal crop protection
Difenacoum	Advanced Paste	0.05 g/kg	Coopers ES
	Alpha-Rat liquid concentrate	0.8 g/l	Novartis
	Alpha-Rat rat & mouse bait	0.05 g/kg	Novartis
	Fentrol gel	1 g/kg	Rentokil
	Neosorexa liquid concentrate	0.8 g/L	Detekto International
	Neosorexa liquid concentrate P	2.67 g/L	Detekto International
	Neosorexa rat & mouse bait	0.05 g/kg	Detekto International
	Ridak bait block	0.05 g/kg	BASF SA (Pty) Ltd
	Ridak Gold	0.05 g/kg	BASF SA (Pty) Ltd
	Ridax pasta	0.05 g/kg	BASF SA (Pty) Ltd
	Rodex	0.1 g/kg	Small Pack Solution
	Tornado bait blocks	0.1 g/kg	Henchem
	Ultrakill rat and mouse liquid bait	0.8 g/kg	Coopers ES
Difethialone	Difethialone rodent grain bait	0.05 g/kg	Rentokil Initial
	Finale gel rat & mouse bait	0,025 g/kg	Bayer
	Finale rat and mouse grain bait	0.025g/kg	Bayer
	Finale liquid concentrate rat poison	1.25 g/L	Bayer
	Finale paste rat and mouse bait	0.025 g/kg	Bayer
	Finale rat & mouse pellets	0.025 g/kg	Bayer
	Finale liquid rat and mouse bait	0.5 g/l	Bayer (Pty) Ltd
	Kombat rats & mice	0.025 g/kg	Kombat
	Rat & Mouse Killer	0.025 g/kg	Bayer (Pty) Ltd
	Rats and Mice	0.025 g/kg	Kombat
	Rattex deadly wedges	0.025 g/kg	Adcock Ingram
	Rattex Kill It	0.025 g/kg	Adcock Ingram
	Rattex	0.025 g/kg	Adcock Ingram
	Rodilin rat and mouse wax blocks	0.025 g/kg	Bayer
Diphacinone	Ramik green bait pack	0.05 g/kg	Nutribasics
	Ramik mini bars	0.05 g/kg	Nutribasics
	Ramik mouser prebaited box	0.05 g/k	Nutribasics
	Tomcat rat & mouse bait	0.05 g/kg	Antec
Flocoumafen	Storm Secure	0.05 g/kg	BASF
	Rat & Mouse wax blocks	0.05 g/kg	Coopers ES
	Ultrakill rat and mouse grain bait	0.05 g/kg	Coopers ES
	Ultrakill rat and mouse pellets	0.05 g/kg	Coopers ES
Warfarin	Killit rat & mouse killer	0,375 g/kg	Adcock Ingram

Health and beauty for all animals®

Kyron Laboratories
a division of Kyron Group (Pty) Ltd. | Co.Reg.No. 1997/016380/07
29 Barney Road, Benrose, 2094, South Africa
Tel +27 11 618 1544 | info@kyronlaboratories.com | www.kyronlabs.co.za