

E X T O X N E T

Extension Toxicology Network

A Pesticide Information Project of Cooperative Extension Offices of Cornell University, Michigan State University, Oregon State University, and University of California at Davis. Major support and funding was provided by the USDA/Extension Service/National Agricultural Pesticide Impact Assessment Program.

Pesticide
Information
Profile

Warfarin

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TRADE OR OTHER NAMES

The active ingredient warfarin is found in a variety of commercial rodenticides. Some trade names for products containing warfarin include Cov-R- Tox, Co-Rax, d-Con, Dethmor, Mar-Fin, Rattunal, Rax, Rodex, Rodex Blox, Rosex, Solfarin, Tox-Hid, Warf, and Warfarat ([3](#), [4](#), [11](#)). Warfarin is called coumafene in France, zoocoumarin in the Netherlands and Russia, and coumarin in Japan ([1](#), [3](#), [8](#)).

REGULATORY STATUS

Warfarin is a general use pesticide (GUP). Check with specific state regulations for local restrictions which may apply. The Signal Word for technical and high concentrations of warfarin is "Danger". The Signal Word "Caution" is used for low concentrations and ready-to-use baits ([3](#)).

INTRODUCTION

Warfarin was the first anticoagulant rodenticide introduced and was first registered for use in the United States in 1952 ([4](#), [13](#)). Warfarin is used for controlling rats and house mice in and around homes, animal and agricultural premises, and commercial and industrial sites. It is odorless and tasteless and effective in very low dosages. Action is not rapid; usually about a week is required before a marked reduction in the rodent population is noticeable. Rodents do not tend to become bait-shy after once tasting warfarin; they continue to consume it until its anti-clotting properties have produced death through internal hemorrhaging. The prothrombin content of the blood is reduced and internal bleeding is induced. Repeated ingestion is needed to produce toxic symptoms. This rodenticide can be used year-after-year wherever a rodent problem exists. Mice are harder to control than rats, and complete control may take a longer period. Recently, resistant strains of rats and mice are developing ([3](#), [4](#), [11](#), [13](#)).

Warfarin comes in water soluble, ready-to-use bait, concentrate, powder, liquid concentrate, nylon pouch, coated talc and dust formulations. The compound also comes in mixed formulations with pindone, calciferol, and sulphaquinoxaline. It is considered compatible with other rodenticides ([1](#), [2](#), [3](#)).

Warfarin is only slightly dangerous to humans and domestic animals when used as directed, but care must be taken with young pigs, which are especially susceptible ([1](#)).

TOXICOLOGICAL EFFECTS

ACUTE TOXICITY

The amount of Warfarin that is lethal to one-half (50%) of experimental animals fed the material is referred to as its acute oral lethal dose fifty, or LD50. The acute oral toxicity for warfarin in rats is variously reported to be 3 mg/kg ([3](#), [4](#), [6](#), [7](#), [11](#), [12](#)); 1,600 ug/kg ([5](#)); 186 mg/kg (Hartley and Kidd, 1987) ([7](#), [11](#)); 58 mg/kg in female rats ([9](#), [12](#)). The acute oral LD50 for rats over 4-5 days is 1 mg/kg/day ([1](#), [2](#)). There was no development of ingestion tolerance indicated regardless of rodent sex or age ([3](#)).

The acute oral LD50 for technical sodium warfarin in rats was 323 mg/kg for males and 58 mg/kg for females ([12](#)). A single, large dose of warfarin is about as toxic as a single, small dose. On a multiple-dose basis, the reported LD100 for rats is 0.2 mg/kg/day for 5 days ([4](#), [11](#)).

The dermal LD50 for rats was 1,400 mg/kg; 420 mg/kg intraperitoneal LDlo (Lethal Dose, Low. The lowest dose which causes death in test animals.); and 320 mg/m³ inhalation LC50 ([5](#)). The same source indicated the acute oral LD50 for mice was 60 mg/kg; 800 mg/kg subcutaneous LDlo; and 165 mg/kg intravenous LD50 ([5](#)).

Toxicity values for warfarin in other animals are: an oral LD50 for cats of 2.5-20 mg/kg ([6](#), [12](#)); an acute oral LD50 of 35 mg/kg for a single dose or 3 mg/day for 5 days ([1](#), [2](#)); and 12 mg/kg oral LDlo ([5](#)). The acute oral LD50 for dogs exposed to warfarin was 3 mg/kg/day for 5 days ([1](#)). Technical sodium warfarin in dogs had an LD50 of 200-300 mg/kg ([12](#)). The acute oral LD50 for warfarin in cattle was 200 mg/kg/day for 5 days ([1](#)). The LD50 for technical sodium warfarin in guinea pigs was 182 mg/kg ([12](#)). The oral LDlo for warfarin in pigs was reported to be 1,200 ug/kg ([5](#)). Death followed 5 daily doses of 1 mg/kg for pigs ([2](#), [11](#)).

Studies done on rabbits indicated the dermal LD50 of warfarin to be greater than 8 g/kg ([6](#), [12](#)). Technical sodium warfarin in rabbits had an LD50 of 800 mg/kg. Rabbits exhibited mild to slight conjunctival irritation in response to technical warfarin ([12](#)).

Toxicity values for humans exposed to warfarin indicated an oral-woman TDlo of 15 mg/kg/21 weeks intermittent; 10,200 ug/kg oral-man TDlo; and 6,667 mg/kg oral-human LDlo. Average or large doses of warfarin in humans may cause hemorrhage ([9](#)). Warfarin is not known to be an eye irritant. It has produced hemorrhages in the retina, however, through its systemic toxicity ([11](#)). The compound is considered highly toxic by inhalation and ingestion and moderately toxic by dermal absorption. A dose of warfarin at 200 mg/m³ is considered highly toxic and immediately dangerous to life or health ([5](#)).

CHRONIC TOXICITY

A farmer whose hands were intermittently wetted with a 0.5% solution of warfarin over a period of 24 days developed gross hematuria two days after the last contact with the solution; the following day, spontaneous hematomas appeared on the arms and legs. Within four days, there were also epistaxis, punctate hemorrhages of the palate and mouth, and bleeding from the lower lip. The bleeding time was over 30 minutes; the clotting time was 11 minutes and 30 seconds; the prothrombin index was 17; and the prothrombin percentage (thrombotest) was 5. Four days later, after treatment for two days with phytonadione, the values were in the normal range ([11](#)).

Another source indicated that two human fatalities occurred after ingesting 0.25% warfarin on corn meal over 15 days ([12](#)).

Reproductive Effects

No information currently available.

Teratogenic Effects

Warfarin has been established as a human teratogen, because it causes birth defects in the offspring of women receiving clinical doses of the compound during any trimester of pregnancy. Therapeutic use by pregnant women has resulted in fatal hemorrhaging of the fetus and malformations and mental retardation in infants. However, the amount of warfarin contained in the rodenticide bait is very low. A single ingestion of warfarin-treated bait by an adult female would not be likely to cause teratogenic effects ([5](#), [13](#), [12](#)).

Other studies also indicated fetal abnormalities in humans exposed to clinical sodium warfarin ([12](#)).

Mutagenic Effects

No information currently available.

Carcinogenic Effects

No information currently available.

Organ Toxicity

Warfarin causes organ damage by inhibiting blood coagulation ([1](#)). Absorption by the lungs may result in hemorrhagic effects ([5](#)).

Animals killed by warfarin exhibit extreme pallor of the skin, muscles, and all the viscera. In addition, evidence of hemorrhage may be found in any part of the body but usually only in one location in a single autopsy. Such blood as remains in the heart and vessels is grossly thin and forms a poor clot or no clot ([8](#), [10](#)). Rats injected intraperitoneally with ¹⁴C-warfarin excreted approximately 90% of the activity in 14 days, about half in the urine and half in the feces ([8](#)).

Symptoms of human exposure to warfarin include hematuria, back pain, hematoma in arms and legs, bleeding lips, mucous membrane hemorrhage, abdominal pain, vomiting, and fecal blood.

One source stated that serious illness was induced by the ingestion of 1.7 mg of warfarin/kg/day for 6 consecutive days with suicidal intent. This would correspond to eating almost 1 pound of bait (0.025% warfarin) each day for 6 days. All signs and symptoms were caused by hemorrhage and, following multiple transfusions and massive doses of vitamin K, recovery was complete ([10](#)).

Fate in Humans and Animals

When 9 normal men and 5 normal women were given a single oral dose of 1.5 mg/kg warfarin, maximal concentration in plasma was reached in 2 to 12 hours. Maximal depression of prothrombin activity was between 36 and 72 hours. Their individual increases in prothrombin time were proportional to their half-times for disappearance of the warfarin from plasma. In other words, the pharmacological effect was greatest in those with slower excretion. The half- times for disappearance from the plasma varied from 15 to 58 hours with an average of 42 hours. Absorption of warfarin from the gastrointestinal tract was apparently complete; no warfarin was

found in the stool even after massive doses, and plasma levels and prothrombin activity responses were virtually identical following oral and intravenous administration at the same rates ([8](#)).

Warfarin is readily absorbed by the gastrointestinal tract; absorption in man requires about 3 hours as indicated by a comparison of the rate of action of oral and intravenous doses ([10](#)).

Another study indicated that 96 hours after intraperitoneal injection of warfarin, the concentrations of activity in the kidney, liver, and pancreas were 3, 12, and 15 times, respectively, greater than that in the blood ([8](#)).

Metabolites in animals include 4-, 6-, 7- and 8-hydroxycoumarin ([1](#), [8](#)).

ECOLOGICAL EFFECTS

Effects on Birds

The acute avian toxicity of warfarin indicates that it is practically non-toxic to game birds. In subacute studies, warfarin ranged from moderately toxic to practically non-toxic to upland game birds and waterfowl ([13](#)). Another source indicated that an acute oral mallard duck study was performed with a 10% formulation of warfarin. This formulation of warfarin was considered moderately toxic to mallard ducks (LC50 greater than 120 mg/kg) when administered as a single dose. However, when exposed to 60 mg/kg for a period of 14 days, 4 out of 5 ducks died ([12](#)).

Chickens are relatively resistant to warfarin ([4](#)).

Effects on Aquatic Organisms

The toxicity of warfarin to aquatic organisms is felt to be of low potential due to the fact that warfarin is insoluble in water. A long field experience shows no potential hazards to aquatic organisms ([13](#)).

A 96-hour rainbow trout study was performed using a 0.54% formulation of warfarin sodium salt. With a 96-hour LC50 of greater than 10,000 ppm, this formulation is considered non-toxic to rainbow trout ([12](#)).

Effects on Other Animals (Nontarget species)

Warfarin used as a prepared bait (0.13%) is considered non-toxic to bees when used as prescribed ([1](#), [3](#)).

The use of warfarin as a hand-placed bait limits the potential for any secondary exposure of nontarget animals. However, because of its high degree of mammalian toxicity and its use patterns, warfarin could adversely affect endangered or threatened species ([13](#)). One study exists on a 50/50 percent formulation of warfarin-sulfaquinoxaline technical. The warfarin-sulfaquinoxaline caused secondary poisoning in mammalian carnivores such as mink and dogs when ingesting prey killed after they were provided with treated bait (carrots containing 0.025% by weight of the test material). The first death occurred after 8 days of continuous exposure to treated nutria ([12](#)).

A study by Bucklew et al. investigated the short-term influence of warfarin on the growth of the gram-positive spore-forming soil microorganism, *Bacillus megaterium*. Impregnation of paper disks and subsequent measurement of the zones of growth inhibition showed that spore

germination for this bacterium was not affected by the presence of warfarin for 15-21 hours at 21 degrees C and at concentrations as high as 1 mg/ml (about 1,000 ppm) ([12](#)).

ENVIRONMENTAL FATE

Breakdown of Chemical in Soil and Groundwater

No information currently available.

Breakdown of Chemical in Surface Water

No information currently available.

PHYSICAL PROPERTIES AND GUIDELINES

Exposure Guidelines:

TLV-TWA: 0.1 mg/m³ (OSHA) ([3](#), [7](#), [11](#))

STEL: 0.3 mg/m³ ([11](#))

Physical Properties:

CAS No.: 81-81-2

Chemical name: 4-hydroxy-3-(3-oxo-1-phenylbutyl)coumarin; 4-hydroxy-3-(3-oxo-1-phenylbutyl)-2H-1-benzopyran-2-one ([1](#), [2](#))

Chemical Class/Use: Rodenticide, anticoagulant

Specific gravity: greater than 1 ([5](#))

Solubility in water: Practically insoluble (1.7 mg/100 ml at 20 degrees C) ([1](#), [5](#), [9](#))

Solubility in other solvents: Soluble to very slightly soluble in acetone, benzene, ethanol, ether, toluene, xylene, methyl ethyl ketone and cyclohexane.

Moderately soluble in methanol, ethanol, and isopropanol.

In acetone 6.5, chloroform 5.6, dioxane 10.0 (all in g/100 ml at 20 degrees C).

Dissolves in aqueous alkalis with the formation of water-soluble salts ([1](#), [2](#), [7](#), [8](#), [9](#))

Melting point: 161-162 degrees C ([1](#), [7](#)); 159-165 degrees C ([3](#)); 318-322 degrees F ([5](#))

Boiling point: decomposes ([7](#), [11](#))

Vapor pressure: 9 x 10 to the minus 2 mbar at 21.5 degrees C

Koc: 2.96 (calculated) ([7](#))

Kow: 3.20 (calculated) ([7](#))

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