IPCS INTERNATIONAL PROGRAMME ON CHEMICAL SAFETY

Health and Safety Guide No. 93

BRODIFACOUM HEALTH AND SAFETY GUIDE

UNITED NATIONS
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Health and Safety Guide No. 93

BRODIFACOUM HEALTH AND SAFETY GUIDE

This is a companion volume to
Environmental Health Criteria 175: Anticoagulant Rodenticides

Published by the World Health Organization for the International Programme on Chemical Safety (a collaborative programme of the United Nations Environment Programme, the International Labour Organisation, and the World Health Organization)

WORLD HEALTH ORGANIZATION, GENEVA 1995

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INTRODUCTION

The Environmental Health Criteria (EHC) monographs produced by the International Programme on Chemical Safety include an assessment of the effects on the environment and on human health of exposure to a chemical or combination of chemicals, or physical or biological agents. They also provide guidelines for setting exposure limits.

The purpose of a Health and Safety Guide is to facilitate the application of these guidelines in national chemical safety programmes. The first three sections of a Health and Safety Guide highlight the relevant technical information in the corresponding EHC. Section 4 includes advice on preventive and protective measures and emergency action; health workers should be thoroughly familiar with the medical information to ensure that they can act efficiently in an emergency. Within the Guide is a Summary of Chemical Safety Information which should be readily available, and should be clearly explained, to all who could come into contact with the chemical. The section on regulatory information has been extracted from the legal file of the International Register of Potentially Toxic Chemicals (IRPTC) and from other United Nations sources.

The target readership includes occupational health services, those in ministries, governmental agencies, industry, and trade unions who are involved in the safe use of chemicals and the avoidance of environmental health hazards, and those wanting more information on this topic. An attempt has been made to use only terms that will be familiar to the intended user. However, sections 1 and 2 inevitably contain some technical terms. A bibliography has been included for readers who require further background information.

Revision of the information in this Guide will take place in due course, and the eventual aim is to use standardized terminology. Comments on any difficulties encountered in using the Guide would be very helpful and should be addressed to:

The Director
International Programme on Chemical Safety
World Health Organization
1211 Geneva 27
Switzerland

THE INFORMATION IN THIS GUIDE SHOULD BE CONSIDERED AS A STARTING POINT TO A COMPREHENSIVE HEALTH AND SAFETY PROGRAMME

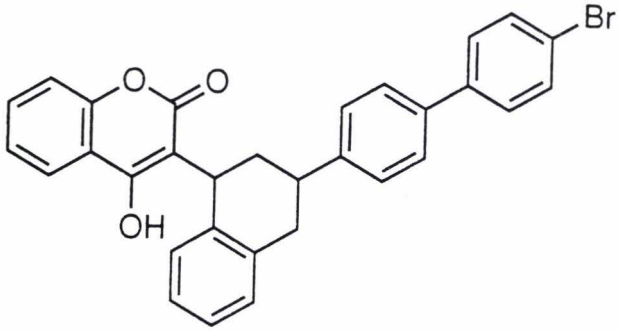
1. PRODUCT IDENTITY AND USES

1.1 Identity

Common name: brodifacoum

Chemical formula: $C_{31}H_{23}BrO_3$

Chemical structure:



Common synonyms: Super-warfarin, bromfenacoum, BFC, PP-581, WBA 8119, ICI-581

Trade names: Finale, Folgorat, Havoc, Klerat, Matikus, Mouser, Ratak +, Rodend, Talon, Volak, Volid

CAS chemical name: 3-[3-(4'-bromo-[1,1'-biphenyl]-4-yl)-1,2,3,4-tetrahydro-1-naphthalenyl]-4-hydroxy-2H-1-benzopyran-2-one

IUPAC chemical name: 3-[3-(4'-bromobiphenyl 4-yl)-1,2,3,4-tetrahydro-1-naphtyl]-4-hydroxy coumarin

CAS registry number: 56073-10-0

RTECS registry number: GN4934750

1.2 Physical and Chemical Properties

Brodifacoum is an off-white powder, which is stable in the solid form. Its solubility in water is very low (less than 10 mg/litre at 20 °C and pH 7); it is slightly soluble in benzene and soluble in acetone.

Further physical and chemical properties of brodifacoum are given in the "Summary of Chemical Safety Information" (section 6).

1.3 Analytical Methods

Analytical methods for the determination of brodifacoum include liquid chromatography with fluorescence detection and high-performance liquid chromatography, with detection limits of 0.001 mg/litre and 0.002 mg/kg, respectively.

1.4 Production and Uses

The rodenticidal properties of brodifacoum were described in 1976. It is an anticoagulant that is effective against rats and mice, including warfarin-resistant strains. It is used in agriculture and urban rodent control as ready-to-use baits of low concentration (usually 0.005% brodifacoum).

2. SUMMARY AND EVALUATION

2.1 Identity, Physical and Chemical Properties, and Analytical Methods

Brodifacoum is an off-white to fawn powder, which is stable at room temperature in the solid form and has a melting point of 228-232 °C. Its solubility in water is very low; it is slightly soluble in benzene and chloroform and soluble in acetone. Determination of brodifacoum is based on high-performance liquid chromatography.

2.2 Sources of Human and Environmental Exposure

Brodifacoum does not occur naturally. It is used as a rodenticide against pest rodents and acts by preventing the production of essential blood-clotting factors.

2.3 Environmental Transport, Distribution, and Transformation

Brodifacoum does not enter the atmosphere, because of its low volatility. It is practically insoluble in water. Brodifacoum is strongly bound on soil particles and is not taken up by plants. The rate of degradation is relatively slow and depends on soil type. Residues in crops have never been detected in field studies.

2.4 Environmental Levels and Human Exposure

Brodifacoum is not intended for direct application to growing crops or for use as a food additive.

No information is available on concentrations in air, water, and soil.

Residues of brodifacoum were detected in dead barn owls in the United Kingdom at levels of 0.019-0.515 mg/kg. Brodifacoum residues were also found in the liver, muscle, and fatty tissues of rabbits, intentionally poisoned during field trials with baits containing 0.005% active ingredient, at concentrations of 4.4, 0.26, and 0.86 mg/kg, respectively.

2.5 Kinetics and Metabolism in Laboratory Animals and Humans

Brodifacoum is absorbed through the gastrointestinal tract, skin, and respiratory system. The major route of elimination in different species after

oral administration is through the faeces. The liver is the main organ of accumulation and storage. Brodifacoum has mainly been found as an unchanged compound. After a single oral dose to rats, liver concentrations remained high and relatively constant for 96 h. Elimination from the liver is slow and biphasic with an initial rapid phase lasting from 2 to 8 days after dosing and a slower terminal phase with an elimination half-life of 130 days. In accidentally poisoned patients, the plasma half-life was found to be approximately 16-36 days.

2.6 Effects on Laboratory Mammals and *in vitro* Test Systems

Brodifacoum has a high acute oral toxicity (LD_{50} less than 1 mg/kg) for various species, including rodents and non-rodents. The dermal and inhalation toxicities are also high. Signs of poisoning are similar for all routes of administration and are those associated with an increased tendency to bleeding.

Brodifacoum is a slight irritant for the skin and a mild eye irritant.

In feeding studies on rats, the only effect was that associated with anti-coagulant action. No long-term studies have been reported. Mutagenicity and teratogenicity studies did not show any mutagenic, embryotoxic, or teratogenic effects.

2.7 Effects on Humans

Symptoms of acute intoxication by brodifacoum vary from an increased tendency to bleed in less severe poisonings to massive haemorrhage in more severe cases. The signs of poisoning develop with a delay of one to several days after ingestion.

Both intentional and unintentional poisoning incidents have been reported.

2.8 Effects on Other Organisms in the Laboratory and Field

Brodifacoum was highly toxic for fish when tested as a technical material.

Bird species varied in their susceptibility to brodifacoum, oral LD_{50}s ranging from less than 1 mg/kg body weight to more than 20 mg/kg body weight.

The possible effects of brodifacoum on non-target organisms can be considered in two categories, i.e., primary (direct poisoning) and secondary (through consumption of poisoned rodents).

Cases of abortion and haemorrhage in sheep and goats caused by the misuse of brodifacoum have been reported.

Secondary poisoning through the consumption of rats and mice killed with brodifacoum may occur in dogs and cats in urban situations, but are more likely in farm situations.

2.9 Evaluation of Human Health Risks and Effects on the Environment

2.9.1 *Evaluation of human health risks*

Brodifacoum is widely used in urban rodent control and against rodent pests in agriculture. As it is used as low-concentration baits, increased levels in air are unlikely. Being slightly soluble in water, its use cannot be a significant source of water contamination. Brodifacoum is not intended for direct application to growing crops and no residues are expected in plant foodstuffs. Occupational exposure may occur during manufacture, formulation, and bait application, but data indicating the levels of exposure are not available.

Brodifacoum may be absorbed through the gastrointestinal tract, skin, and respiratory system. The major route of elimination in different species, after oral administration, is through the faeces. The urine is a very minor route of elimination. The liver is the major organ for the accumulation and storage of brodifacoum, which has mainly been found as the unchanged parent compound. Its elimination from the liver is slow.

As a technical material, brodifacoum is extremely toxic for mammalian species. Signs of poisoning in all species, including humans, are associated with an increased bleeding tendency.

Both intentional and unintentional poisoning incidents have been reported.

Prothrombin time is a satisfactory guide to the severity of acute intoxication, and also for the effectiveness and duration of the therapy.

Vitamin K_1 is a specific antidote for both animals and humans (see section 4.1.1).

2.9.2 *Evaluation of effects on the environment*

Brodifacoum is applied to discrete sites in the form of low-concentration baits and is stable under normal conditions. The solubility of brodifacoum in water is low and, in bait formulation, its use is unlikely to be a source of water pollution. As a technical material, it is highly toxic for fish.

Brodifacoum appears to bind rapidly in the soil with very slow desorption and without leaching.

Non-target organisms are potentially at risk in two ways: from direct consumption of baits (primary hazard) and through eating poisoned rodents (secondary hazard).

Small pellets and whole grain baits are highly attractive to birds. Wax-block formulations appear to decrease the attractiveness to the birds and this reduces the possibility of poisoning incidents. Bird species vary in their susceptibility to brodifacoum.

The main reason for the poisoning of domestic animals is direct consumption of brodifacoum baits.

Brodifacoum shows a similar range of acute toxicity for non-target and target mammals. The primary hazard is usually expressed by the amount of finished bait that must be consumed to approach the lethal dose. To reach the toxic or lethal dose, the non-target animals must consume comparatively large amounts of bait with a concentration of 0.005 % active ingredient.

Some secondary toxicity laboratory studies on wildlife have shown that captive predators could be intoxicated by the no-choice feeding of brodifacoum-poisoned or dosed prey. The significance of these results in terms of hazard under field conditions is difficult to assess, because the predators would not be expected to eat only poisoned animals. However, predators may take poisoned, but not dead, small mammals preferentially. In areas close to baiting, poisoned rodents may represent a high proportion of the diet for individual birds. However, only few individuals will be affected, unless there has been very widespread and constant use of the baits.

3. CONCLUSIONS AND RECOMMENDATIONS

3.1 Conclusions

Exposure of the general population to brodifacoum through air, drinking-water, or food is unlikely and does not constitute a significant health hazard. Poisoning incidents may occur in cases of massive intentional or unintentional ingestion or prolonged skin contact during manufacture and formulation.

Brodifacoum is relatively persistent in the environment, but its specific use in the form of low-concentration bait formulations cannot be a significant source of air, water, soil or food contamination. Direct and secondary poisoning of birds, domestic and farm animals, and wildlife has been observed.

3.2 Recommendations for the Protection of Human Health and the Environment

Potentially exposed workers should receive appropriate biomonitoring and health evaluation.

To prevent primary poisonings, baits should be placed where they cannot be readily available to non-target species, e.g., in bait stations.

Killed rodents should be burned or buried to prevent secondary poisoning in predators.

4. HUMAN HEALTH HAZARDS, PREVENTION AND PROTECTION, EMERGENCY ACTION

4.1 Human Health Hazards, Prevention and Protection, First Aid

The oral, dermal, and inhalation toxicities of brodifacoum for mammals are extremely high (rat oral LD_{50} 0.3 mg/kg; rat inhalation LC_{50} 0.005 mg/litre). The ingestion of 1 mg of brodifacoum by an adult person was reported to produce bleeding that persisted for more than two months. The average fatal dose for an adult man (60 kg) is estimated to be approximately 15 mg brodifacoum or 300 g of 0.005% bait.

The main features in less severe cases of brodifacoum poisoning are excessive bruising, nose and gum bleeding, and blood in the urine and faeces. Bleeding from several organs within the body leading to shock and possibly death is seen in more severe cases. The onset of the signs of poisoning may not be evident until a few days after absorption.

Brodifacoum is a mild eye irritant and a slight skin irritant, but it is not a skin sensitizer.

It is slowly metabolized by mammals and, following prolonged exposure, may accumulate in the liver reaching toxic levels.

Full air-fed protection and an impervious suit, suitable for wash-down, are necessary when handling technical material or powder concentrates. In operations involving liquid concentrates, it is necessary to wear PVC or nitrile-rubber gloves, armlets, and an apron, together with a face shield and rubber boots.

All persons who are bleeding must obtain medical attention.

4.1.1 *Advice to physicians*

If poisoning following ingestion has occurred recently (within a few hours), treatment involving gastric lavage and the administration of charcoal in repeated doses is recommended.

A venous blood sample should be taken for measurement of the haemoglobin level, prothrombin time, blood grouping, and cross-matching.

If a patient is bleeding severely, give 25 mg of vitamin K_1 (phytomenadione) by slow intravenous injection. Transfuse patient with whole blood or

plasma. Fresh, frozen plasma may be given. Check prothrombin time at 3-h intervals and repeat injections of vitamin K_1 if no improvement occurs. Administration of factor concentrate may be considered to avoid volume overload.

In less severe cases of poisoning, vitamin K_1 may be given in lower doses and also fresh, frozen plasma to rapidly restore the blood clotting factors. Check prothrombin time after 8-10 h and repeat vitamin K_1 administration, if necessary.

Once the prothrombin time has stabilized, continue treatment with oral vitamin K_1, giving 10 mg four times daily.

Oral treatment may be sufficient in mild cases.

Keep the patient in hospital until the prothrombin time has remained normal for three days.

Discharge the patient from hospital with the following treatment: vitamin K_1, 10 mg to be taken orally, twice daily, for up to 60 days, with close monitoring of the prothrombin time. It may be possible to reduce the length of treatment.

4.1.2 *Health surveillance advice*

Workers handling concentrates must have periodic determination of the potential disturbances of the clotting mechanisms by the most appropriate method, such as, circulating descarboxyprothrombin, prothrombin concentration, or prothrombin time.

4.2 Explosion and Fire Hazards

Brodifacoum is a combustible solid. Most industrial operations involve the solution concentrates with flash point of solvents higher than 90 °C.

Heating of containers will cause a pressure rise, with the risk of bursting and subsequent ignition. Fire-exposed containers should be kept cool by spraying with water.

High temperature decomposition or burning in air will lead to the formation of toxic gases, which may include carbon monoxide as well as fumes of unchanged rodenticide; breathing apparatus must be worn in fire-fighting.

Carbon dioxide or dry powders are recommended for extinguishing small fires, and foam or water fog for larger fires. A water jet should not be used.

Run-off water from the fire should be prevented from entering surface-water drains or water sources.

4.3 Storage

Technical brodifacoum and formulations should be stored in sealed containers in locked, well-ventilated, dry areas away from frost, direct sunlight, and sources of heat and ignition. Keep products out of reach of children and unauthorized personnel. Do not store near food and animal feed.

4.4 Transport

Comply with any local regulations regarding the movement of hazardous goods. Before despatch, ensure that the containers are sound and that labels are securely fixed and undamaged.

4.5 Spillage

During decontamination, the operator must wear protective clothing, PVC gloves, face shield, and rubber boots.

Dry spillages should be collected at once, by suction, and disposed of as toxic waste, according to local legislation.

Liquid spillages should be adsorbed onto vermiculite or other inert adsorbent and treated similarly.

Contaminated areas should be washed down with cold water containing surfactant; the washings must be prevented from entering surface-water drains.

4.6 Disposal

Disposal should be carried out according to national regulations.

5. HAZARDS FOR THE ENVIRONMENT AND THEIR PREVENTION

Brodifacoum is stable, but is rapidly bound to the soil, with very slow desorption and without leaching. It is only slightly soluble in water and, in the form of bait formulations, it is unlikely to be a source of water contamination.

Do not place baits where domestic or farm animals and birds can reach them. Burn or bury any uneaten bait. Do not dump it in water. Look for dead rats and mice and burn or bury them.

6. SUMMARY OF CHEMICAL SAFETY INFORMATION

This summary should be easily available to all health workers concerned with, and users of, brodifacoum. It should be displayed at, or near, entrances to areas where there is potential exposure to brodifacoum, and on processing equipment and containers. The summary should be translated into the appropriate language(s). All persons potentially exposed to the chemical should also have the instructions in the summary clearly explained.

Space is available for insertion of the National Occupational Exposure Limit, the address and telephone number of the National Poison Control Centre, and local trade names.

SUMMARY OF CHEMICAL SAFETY INFORMATION

BRODIFACOUM

Chemical formula: $C_{31}H_{23}BrO_3$

CAS chemical name:
3-[3-(4'-bromo-[1,1'-biphenyl]-4-yl)-1,2,3,4-tetrahydro-1-naphthalenyl]-4-hydroxy-2H-1-benzopyran-2-one

IUPAC chemical name: 3-[3-(4'-bromobiphenyl 4-yl)-1,2,3,4-tetrahydro-1-naphtyl]-4-hydroxycoumarin

CAS registry number: 56073-10-0

RTECS number: GN4934750

PHYSICAL PROPERTIES

Physical state	powder
Colour	off-white
Relative molecular mass	523.4
Melting point (°C)	228-232
Vapour pressure (25 °C)	less than 0.13 mPa
Solubility in water at 20 °C, pH 7	less than 0.01 g/litre
Solubility	
in acetone	6-20 g/litre
in benzene	< 0.6 mg/litre
in chloroform	3 g/litre

OTHER CHARACTERISTICS

Brodifcoum is an anticoagulant rodenticide; it is formulated as low-concentration baits (usually 0.005% active ingredient)

HAZARD SYMPTOMS	PREVENTION AND PROTECTION	FIRST AID
GENERAL: Readily absorbed following ingestion, inhalation or through the skin; if absorbed, may cause increased bleeding tendency to massive haemorrhage	Avoid exposure	Obtain medical attention; antidote - vitamin K_1
SKIN: Slight irritant; significant skin absorption occurs with liquid concentrates; the baits are not irritant	Wear gloves when handling concentrate	Wash with soap and water; seek medical advice
EYES: Mild irritant	Use face shield when handling concentrates	Flush eyes with water for at least 15 min
INHALATION: Significant vapour exposure unlikely	Avoid inhaling concentrate aerosols or bait dust	Obtain immediate medical attention
INGESTION: Nausea/vomiting acute anticoagulant poisoning in several hours or days may occur	Wash hands before eating, drinking, or smoking	Rinse out the mouth with water; transfer to hospital immediately

SUMMARY OF CHEMICAL SAFETY INFORMATION

SPILLAGE	STORAGE	FIRE/EXPLOSION
Wear protective clothing during decontamination; dry spillage - collect by suction and dispose of as toxic waste; liquid spillage - absorb onto vermiculite or other inert absorbent and treat similarly; do not contaminate surface-water drains	Store in sealed containers in a dry, ventilated, and locked storeroom, away from children, unauthorized persons, domestic animals, food, and animal feed	Combustible solid; burning in air will lead to the formation of toxic gases; for small fires use carbon dioxide, halons, or dry powder; for larger fires, use foam or water fog; keep containers cool by spraying with water

WASTE DISPOSAL	NATIONAL INFORMATION
Proper incineration is the method of choice	

7. CURRENT REGULATIONS, GUIDELINES, AND STANDARDS

7.1 Previous Evaluations by International Bodies

Technical brodifacoum has been classified by WHO in Class Ia - Extremely Hazardous, based on acute oral LD_{50} of 0.3 mg/kg for rats.

A *Poisons Information Monograph* for brodifacoum has been issued by IPCS.

7.2 Exposure Limit Values

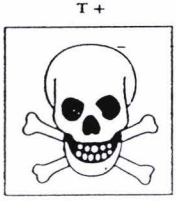
No information is available.

7.3 Specific Restrictions

Brodifacoum has been officially approved for use as a rodenticide in many countries. In some countries, specific uses are defined, as well as limitations and precautions.

7.4 Labelling, Packaging, and Transport

The European Community legislation requires labelling of technical brodifacoum as very toxic with a hazard symbol T+ and the following pictogram:



VERY TOXIC

The United Nations in its Recommendations on the Transport of Dangerous Goods classified brodifacoum in category 6.1, as a poisonous substance (No. 3027).

7.5 Waste Disposal

No specific information is available.

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