US EPA ARCHIVE DOCUMENT

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PESTICIDES AND TOXIC SUBSTA

114AA

MEMORANDUM

DATE: JUL 7 1981

SUBJECT: A One Month Anticoagulant Antidote Study in Beagle Dog
FINAL REPORT

FROM: Salvatore F. Biscardi
Review Section #1
Toxicology Branch/HED (TS-769)

TO: Mr. William Miller, PM 16
Registration Division (TS-767)

THRU: Christine F. Chaisson, Acting Chief
Toxicology Branch/HED (TS-769)

LAB. - Bio/Dynamics
East Millstone, N.J. 08873

Sponsor: ICI Americas Inc.
Wilmington, Delaware 19897

Method:

Vitamin K1 was administered to beagle dogs, 2/sex/group at 2.0 mg/kg following a single oral dose of anticoagulant of either Brodifacoum (1.0 mg/kg) or Warfarin (300 mg/kg). One male and one female received Vitamin K1 6 hours after a single oral dose of anticoagulant on day 1, then twice daily for 4 days and then once daily for 3 days following. The other dogs received the antidote 24 hours after the anticoagulant (day 2), a second injection 31 hours after the anticoagulant (day 2), then twice daily for 3 days and then once daily for the next 3 days. Prothrombin and partial thromboplastin times were determined twice pretest and then only once on day 30. Body weights, food consumption were monitored. All survivors were sacrificed on day 31 followed by gross post mortem examinations. All tissues were then discarded.

Results:

There would appear to be no significant differences between prothrombin and partial thromboplastin times between the two pre-test periods and at the final 30 day post treatment period.

Conclusions:

These data would infer that Vitamin K1 is effective (i.m.) in the restoration of prothrombin and partial thromboplastin times after a single oral dose of either warfarin (300 mg/kg) or of Brodifacoum (1.0 mg/kg).

Validation:

This study is invalid. No test control animals were used to demonstrate the actual existance of blood coagulation problems that might be imposed by one single oral dose of either of the two anticoagulants administered orally. Prothrombin and partial thromboplastin times may indeed have returned to normal thirty day after the single oral administration of anticoagulant. There is no evidence that one single oral dose was effective in producing an anticoagulant effect. This study design is therefore considered to be invalid.

Attachments

2

TEXTBOOK OF PATHOLOGY - BOYD

ous epithelium. In the female the ovaries do not appear to be injured, fertilization of the ovum occurs, and gestation commences, but about the eighth day in the rat pathological changes develop in the placenta and the fetus dies and is absorbed. In addition to its effect on the reproductive function, vitamin E is a necessary factor for the preservation of the integrity of skeletal muscle. When female mice are maintained on a vitamin E low diet but are given a single dose of vitamin to ensure the birth of living young, the offspring show marked necrosis of skeletal muscle in 20 per cent of cases with early calcification (Pappenheimer).

VITAMIN K

Physiology.—This, the fourth of the fat-soluble vitamins, is of very much greater clinical significance than vitamin E on account of its relationship to bleeding. In 1930 Dam, of Copenhagen, noticed that chicks fed on a deficient diet developed hemorrhages owing to the loss of coagulating power of the blood, and that this was prevented by giving alfalfa. The coagulation factor in the alfalfa was extracted, crystallized and finally synthesized. It was called Koagulations-vitamin or vitamin K. The vitamin is necessary for the manufacture of prothrombin, so that when the vitamin is deficient the prothrombin in the blood is low, a condition of *hypoprothrombinemia*. Estimation of the plasma prothrombin thus affords a simple method of determining if there is a deficiency of vitamin K. Such deficiency in man is probably never due to lack of the vitamin in the food. In addition to the supply in the food, the vitamin is also manufactured by the normal bacteria of the bowel. As we have already seen in the case of fat-soluble vitamins A and D, it is a conditioned deficiency rather than a deficient supply of the vitamin which is the threat.

Pathology.—The three groups of conditions which may bring about vitamin K deficiency are: (1) biliary obstruction; (2) malabsorption of fat in celiac disease, pancreatic disease, sprue, hypermotility of the bowel, *etc.*; (3) failure of bacterial synthesis of the vitamin due to the action of antibiotics. The two major clinical conditions in which there is a dangerous degree of vitamin K deficiency are obstructive jaundice and hemorrhagic disease of the newborn. Unless bile is present in the bowel vitamin K is not absorbed, prothrombin is not formed in sufficient amount, and hemorrhage occurs. In *obstructive jaundice* bile is prevented from entering the bowel. This explains the marked tendency to bleeding after operations on jaundiced patients. The bleeding can be prevented by the administration of bile and vitamin K, or by giving the synthetic vitamin by mouth (the synthetic product is absorbed without the assistance of bile), or intravenously. If the liver is severely damaged (cirrhosis, amyloid, *etc.*) the administration of vitamin K is of no avail, because it is in the liver that the prothrombin is produced which is essential to coagulation. The explanation of *bleeding in the newborn* is that vitamin K is produced by the action of intestinal bacteria, and these are absent during the first few days of life. A contributing factor is the failure of the liver to produce bile during this period. At birth the baby has sufficient prothrombin from the maternal blood, but this rapidly falls, and there may be severe and even fatal hemorrhage, particularly intracranial. This is now prevented by giving the mother vitamin K before delivery. Bleeding due to vitamin K deficiency is of particular importance following operations for the relief of obstructive jaundice. In addition to bleeding from severed vessels, there may be hemorrhages in the skin and mucous membranes, particularly that of the bowel.

VITAMIN C. ASCORBIC ACID

We come now to the *water-soluble vitamins*, namely vitamin C and the B complex. Being soluble in water they are rapidly and readily absorbed from the small intestine, but for the same reason they are largely removed from food by the ordinary methods of cooking. The vitamin deficiency will therefore be of the primary type due to lack of the vitamin in the food, and not secondary to or conditioned by loss of power of absorption or storage of the vitamin.

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lation. The narcotic antagonists, naloxone, nalorphine, and levallorphan, are specific antidotes against the respiratory depression produced by propoxyphene. An appropriate dose of one of these antagonists should be administered, preferably by the intravenous route, simultaneously with efforts at respiratory resuscitation, and the antagonist should be repeated as necessary until the patient's condition remains satisfactory. In addition to the use of a narcotic antagonist, the patient may require careful titration with an anticonvulsant to control convulsions. Analeptic drugs (for example, caffeine or amphetamine) should not be used because of their tendency to precipitate convulsions.

Oxygen, intravenous fluids, vasopressors, and other supportive measures should be employed as indicated.

Gastric lavage may be helpful. Activated charcoal can absorb a significant amount of ingested propoxyphene. Dialysis is of little value in poisoning by propoxyphene alone.

How Supplied: (B) *Pulvules Darvon® (Propoxyphene Hydrochloride Capsules, USP): No. 364, H02,*® 32 mg. (No. 4, Light-Pink Opaque), in bottles of 100 (BPak) and 500 and in 10 strips of 10 individually labeled blisters each containing 1 Pulvule (ID100); *No. 365, H03,*® 65 mg. (No. 3, Light-Pink Opaque), in bottles of 100 (BPak) and 500, in 10 strips of 10 individually labeled blisters each containing 1 Pulvule (ID100), in 500 single-cut individually labeled blisters each containing 1 Pulvule (ID500), and in BPaks (prescription packages, Lilly) in 25 packages of 30 and 20 packages of 50. All BPaks have safety closures.
65 mg.—500's—6505-00-958-2364

(B) *Darvon Compound, Pulvules No. 368, H05*® (No. 0, Light-Pink Opaque Body, Light-Gray Opaque Cap), in bottles of 100 (BPak) and 500 and in 10 strips of 10 individually labeled blisters each containing 1 Pulvule (ID100). Each Pulvule contains 32 mg. propoxyphene hydrochloride, 227 mg. aspirin, 162 mg. phenacetin, and 32.4 mg. caffeine. All BPaks have safety closures.

(B) *Darvon Compound-65, Pulvules No. 369, H06*® (No. 0, Red Opaque Body, Light-Gray Opaque Cap), in bottles of 100 (BPak) and 500, in 10 strips of 10 individually labeled blisters each containing 1 Pulvule (ID100), in 500 single-cut individually labeled blisters each containing 1 Pulvule (ID500), and in BPaks in 25 packages of 30 and 20 packages of 50. Each Pulvule contains 65 mg. propoxyphene hydrochloride, 227 mg. aspirin, 162 mg. phenacetin, and 32.4 mg. caffeine. All BPaks have safety closures.

(B) *Darvon with A.S.A., Pulvules No. 366, H04*® (No. 0, Red Opaque Body, Light-Pink Opaque Cap), in bottles of 100 (BPak) and 500 and in 10 strips of 10 individually labeled blisters each containing 1 Pulvule (ID100). Each Pulvule contains 65 mg. propoxyphene hydrochloride and 325 mg. aspirin. All BPaks have safety closures. [052274B]

[Shown in Product Identification Section]

DICUMAROL

Capsules, USP B

Description: Chemically, dicumarol is bis-hydroxycoumarin (3,3'-methylenebis [4-hydroxycoumarin]), $C_{19}H_{12}O_6$.

Actions: Dicumarol reduces the concentration of prothrombin in blood and increases the prothrombin time by inhibiting the formation of prothrombin in the liver. Since the drug also interferes with the production of factors VII, IX, and X, their concentration in the blood is lowered during therapy. The inhibition of prothrombin involves interference with the action of vitamin K, and it has been postulated that dicumarol competes with vitamin K for an enzyme essential to prothrombin synthesis.

After oral administration of dicumarol, maximum plasma concentrations are reached in two to eight hours. Greatest effect on prothrombin time is achieved in thirty-six to seventy-two hours. Following a single therapeutic dose of the drug, its effect on prothrombin time persists for four to five days.

Indications: Dicumarol is indicated for the prophylaxis and treatment of pulmonary embolism and of venous thrombosis and its extension, for therapy of atrial fibrillation with embolization, and as an adjunct in the treatment of coronary occlusion.

Contraindications: Dicumarol is contraindicated in patients who have active bleeding or subacute bacterial endocarditis.

Warnings: Dicumarol is a potent drug, and its effects tend to be cumulative and prolonged. Caution should be used when dicumarol is administered in any situation in which the risk of hemorrhage is present. The drug should be withdrawn at the earliest sign of bleeding. It cannot be emphasized too strongly that treatment of each patient is a highly individualized matter. Dosage can be controlled only by periodic determination of prothrombin time. Clotting and bleeding times are not effective measures for control of therapy.

It is important to bear in mind that heparin sodium prolongs the one-stage prothrombin time. Accordingly, when heparin sodium is given with dicumarol, a period of four to five hours after the last intravenous dose and of twelve to twenty-four hours after the last subcutaneous dose of heparin sodium should elapse before blood is drawn if a valid prothrombin time is to be obtained.

During pregnancy, both mother and fetus are subject to the risks of anticoagulant therapy with dicumarol; fetal hemorrhage and intrauterine death have occurred. Pregnant women who are candidates for anticoagulant therapy with dicumarol should be carefully evaluated and the indications critically reviewed. The risk of withholding the drug should be weighed against the possible dangers entailed in administering it. Since the drug appears in the mother's milk, the nursing infant should be observed for evidence of unexpected bleeding.

Precautions: Several factors may alter the activity of dicumarol (*see also* Factors Influencing Activity of Dicumarol): any change in the intake of vitamin K, fat, or leafy green vegetables; vitamin K deficiency of the newborn; fever; alcoholism; vitamin C deficiency; x-ray therapy; and diarrhea, which causes increased loss in the stool and/or decreased absorption from the gut.

Many drugs can increase or decrease the effect of dicumarol on the prothrombin time. No other agent should be administered with dicumarol unless its potentialities for interacting with an oral anticoagulant are fully appreciated. If a drug is added to or withdrawn from a patient's therapeutic regimen, it is essential that his prothrombin time be carefully monitored. Fatalities have been reported from interactions that affected the metabolism of coumarin anticoagulants or their binding to plasma proteins.

Care in patient selection is desirable to insure cooperation, particularly from alcoholic, emotionally unstable, psychotic, or senile patients. Bleeding during oral anticoagulant therapy may not always correlate with the prothrombin time.

Factors Influencing Activity of Dicumarol: Factors which enhance the anticoagulant effect of dicumarol include decreased dietary intake or absorption of vitamin K, infancy, cachexia, liver impairment, renal insufficiency, fever, scurvy, congestive heart failure, salicylates, sulfas, chloramphenicol, tetracycline, neomycin (and possibly other antibiot-

Continued on next page

*Identi-Code ® symbol.

4.

Lilly—Cont.

ics which suppress intestinal bacterial flora), phenylbutazone, oxyphenbutazone, phenyramidol hydrochloride, diphenylhydantoin sodium, pyrazoline drugs, quinine, quinidine, thyroxine, clofibrate, anabolic steroids, ACTH, adrenocorticosteroids, alcoholism, methylthiouracil, x-ray, and radioactive compounds.

Factors which reduce the anticoagulant effect of dicumarol include vitamin K, barbiturates, chloral hydrate, glutethimide, meprobamate, griseofulvin, and haloperidol.

Adverse Reactions: Hemorrhage is the principal adverse reaction to overdosage with dicumarol. Hemorrhagic tendency may be manifested by hematuria, petechiae in the skin, hemorrhage into or from a wound or ulcerating lesion, or petechial and purpuric hemorrhages throughout the body. Patients receiving dicumarol should be examined daily for evidence of these complications, and the urine should be tested daily to detect hematuria. When an ulcerative lesion of the gastrointestinal tract is suspected to be present or when dicumarol is administered in the postoperative period to patients who have had an operative procedure upon the gastrointestinal tract, the stools should be examined frequently for evidence of hemorrhage into the bowel.

The occurrence of significant gastrointestinal or urinary tract bleeding during anticoagulant therapy may indicate the presence of an underlying occult lesion.

Paralytic ileus and intestinal obstruction have been reported from submucosal or intramural hemorrhage.

Nonhemorrhagic adverse reactions have been noted. These include dermatitis, urticaria, alopecia, fever, anorexia, nausea, vomiting, cramps, diarrhea, leukopenia, agranulocytosis, mouth ulcers, nephropathy, and red-orange urine.

Administration and Dosage: Dicumarol is given by mouth. The dosage must be individualized and adjusted according to the prothrombin time. Probably the best method of reporting of prothrombin time is to give the patient's prothrombin time together with that of the control, both expressed in seconds. Many laboratories still report prothrombin time in percent of normal, on the basis of a prothrombin dilution curve; if this is done, it is essential for the laboratory to state what type of diluent was used.

There is no general agreement as to the minimum prothrombin time that accomplishes effective anticoagulation. The following schedule serves only as a guide. On the average, the dose for the first day in adults with normal prothrombin activity is 200 to 300 mg. On subsequent days, the dose may range from 25 to 200 mg. When expressed in seconds, the prothrombin time should be maintained, in general, at one and one-half to three times the control value; this ratio varies with the different types of tissue thromboplastin used in performing the prothrombin time test.

Combined Use with Heparin—Because dicumarol has a slow onset of action, heparin should be used when a rapid anticoagulant effect is desired. Both drugs can be given together at the start of therapy, and heparin administration may be continued for twenty-four to seventy-two hours or until a satisfactory effect from dicumarol is obtained as determined by prothrombin time studies.

Management of Overdosage: Usually, an overly prolonged prothrombin time or minor hemorrhage will respond satisfactorily to withdrawal of the drug alone, but whole-blood transfusion may also be desirable in some cases.

If prothrombin activity falls below the therapeutic range or if hemorrhage occurs, dicumarol should be temporarily withdrawn.

If warranted by the clinical situation, phytonadione (vitamin K_1) may be administered by slow intravenous injection—1 to 5 mg. in cases of mild overdosage and 20 to 40 mg. in cases of severe overdosage. Such use of vitamin K_1 complicates subsequent anticoagulant therapy; therefore, caution must be used in determining the need for this vitamin. It has been reported that a hypercoagulable state occurs following the rapid reversal of a prolonged prothrombin time.

How Supplied: (B) *Pulvules® Dicumarol, Capsules, USP No. 314, F71,* ° 25 mg. (No. 4, Clear), and *No. 291, F54,* ° 50 mg. (No. 3, Clear), in bottles of 100 and 1,000.

[070775]

DICURIN® PROCAINE (B)
(merethoxylline procaine)

Description: Dicurin® Procaine (merethoxylline procaine, Lilly) is an organic mercurial combined with procaine and theophylline (for stabilization of the solution).

Each ml. contains—

2-N - (3'-Hydroxy-mercuri-2'-methoxy-ethoxy)-propyl-carbamyl Phenoxyacetic Acid, as the Procaine Salt of the Anhydro Acid ..... 100 mg.
(Equivalent to 39.3 mg. mercury and 45 mg. procaine base)

Theophylline, Anhydrous ..... 50 mg.

Contains 0.5 percent chlorobutanol (chloroform derivative) as a preservative. Sodium hydroxide and/or hydrochloric acid may have been added during manufacture to adjust the *pH*.

Prolonged exposure to direct sunlight should be avoided, since it causes darkening of the solution. Freezing is harmless. Refrigeration storage is recommended.

Actions: Like other mercurial diuretics, Dicurin® Procaine (merethoxylline procaine, Lilly) inhibits the tubular reabsorption of sodium and chloride and, secondarily, water. Mercurial diuretics have a dual action on potassium secretion. Urinary potassium is increased or decreased, depending upon whether the initial secretory rate is low or high. In the treatment of edema, mercurial diuretics usually increase potassium secretion slightly.

Indications: Dicurin® Procaine (merethoxylline procaine, Lilly) is indicated for the treatment of edema secondary to congestive heart failure, the nephrotic syndrome, the nephrotic stage of glomerulonephritis, and hepatic cirrhosis or portal obstruction.

Contraindications: Dicurin® Procaine (merethoxylline procaine, Lilly) is contraindicated for intravenous use.

It should not be given when the patient is hypersensitive to mercury, procaine, or theophylline. In addition, because of the possibility of cross-sensitization, Dicurin Procaine should not be administered to patients who are sensitive to other drugs containing the *para*-aminobenzoic acid group, such as benzocaine, tetracaine, butacaine, etc. It is also contraindicated in patients with acute glomerulonephritis, ulcerative colitis, or gouty diathesis.

Warnings: A few instances of anaphylactic reactions have been reported.

Use in Pregnancy—Since the safety of this preparation in pregnancy, during lactation, or in women of childbearing age has not been established, use of the drug in such patients requires that the potential benefits be weighed against the possible hazards to the mother and child.

Precautions: Diuresis of any kind should be induced with great caution in the presence of benign prostatic hypertrophy; distention of the bladder may precipitate obstruction. If the blood urea nitrogen is more than 60 mg. per 100 ml., mercurial diuretics should be used with caution. If defi... ria, or oliguria appears, a mercurial diuretic ... continued.

Lack of the anticipated ... patient previously re... physician's attention ... insufficient restriction ... inadequate dosage of ... lying renal disease ...

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Adverse Reactions: As ... rial diuretic, Dicurin ° ... line procaine, Lilly) ...

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Gastrointestinal reac... diarrhea, and ulce...

Bone-marrow depres... tropenia and agran...

Mercurialism arising ... teral therapy or ... renal disease ... marginal gingivitis ... and proteinuria.

Local reactions: ...

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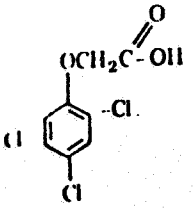


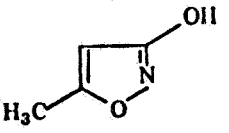
2,4,5-T

... Agrangesellschaft (Federal Republic of Ger-... *U 46 Brushkiller LV*, U 46 Brush-... HV*)*
... GmbH & Co. KG (West Germany) ...
... Chemical Co. (*Esteron* 245, Esteron* ... Killer*)
... & Co., Ltd. (Great Britain)
... Ltd. (Great Britain) (*Spontox**)
... Hayward Chemical Co. (*Ded-Weed**)
... (*Brush-Rhap*, Transamine**)
... Protection Division (Great Britain) ...
... Agricultural Div. (*Visko-Rhap* Low ... Ester*)
... (France) (*Debroussaillant Con-... Debrousaillant Super Concentre**)

... Di *n*-butylsuccinate.
... *Labatrex* (earlier spelling).
... repellent.
... oral LD_{50} (rat), about 8000 mg/kg.
... ACTION.
... To repel biting flies of cattle, and cock-... around houses and barns.
... to be used on livestock or in dairy barns or ...
... Chemical Co., Inc.

... Labatrex*.

... 3-Hydroxy-5-methylisoxazole.
... *hymexazol.*
... *F-319, SF-6505.*
... fungicide for damping off caused by ... *Pythium, Corticium*, etc. Agent ... and cold resistance of crop seedling.
... PROPERTIES: Colorless crystals, m.p. 86-... mm Hg (25° C). Soluble in water 8.5% ... soluble in most organic solvents.
... oral LD_{50} (male rat), 4678 mg/kg; (fe-... (male mouse), 2148 mg/kg; (female) ... dermal LD_{50} (rat or mouse), greater than ... level on rat and mouse, 5000-2500 ...
... as a soil drench, soil incorporation, ... in Japan for use on paddy rice, ... and forest tree seedlings.
... liquid, 4% dust, 70% dust for seed



Hymexazol

BP: Sankyo Co., Ltd. (Japan) (*F-319*)

Tack Trap * — see Sticky Trapping Materials.

Taeniacide
An anthelmintic intended especially for the control of tapeworms (taenia species).

Tag * — see PMA.

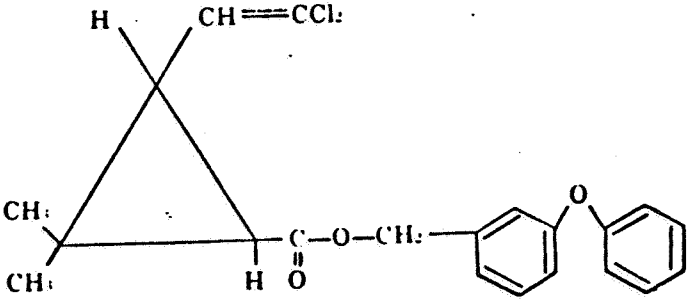
Tako * — see Dusts, Kaolin.

Talan * — see Dinobuton.

Talbot * — see Lead Arsenate.

Talc
CHEMICAL NAME: Hydrous magnesium silicate: $Mg_3(SiO_{10})(OH)_2$.
APPLICATION: Inert carrier and diluent in pesticides. When the ultra fine grinds are used (Mistron grades), they contribute to large surface areas and are non-reactive with sensitive toxicants and can be used in wettable powders.
BP: Cyprus Industrial Minerals Co., Talc Div.

Talcord *
CHEMICAL NAME: 3-phenoxybenzyl 2-(2, 2-dichlorovinyl)-3,3-dimethyl cyclopropane-1-carboxylate.
COMMON NAME: *permethrin*.
ACTION: Insecticide.
CHEMICAL PROPERTIES: More stable in acidic than in alkaline solution. Moderately soluble in a range of organic solvents. High thermal stability. Brown semi-solid mass. Relatively non-volatile.
TOXICITY: Acute oral LD_{50} to rats ranges from 430 mg/kg (male) to 470 mg/kg (female); acute dermal LD_{50} to rats (undiluted material) > 2500 mg/kg.
APPLICATION: Used for control of insects in a wide range of crops. Also used for control of nuisance flies in animal health.
FORMULATION: Emulsifiable concentrate.



Talcord *

BP: Shell International Chemical Co. (Great Britain)

Talon * Rodenticide
CHEMICAL NAME: 3-[3-(4′-bromo[1-1′-biphenyl]-4-yl)-1, 2, 3, 4-tetrahydro-1-napthalenyl]-4-hydroxy-2H-1-benzopyran-2-one.

* - Indicates trade name. BP - Basic Producer. F - Formulator.
♦ - Indicates common name officially designated by USDA.
SLN - Special Local Need

Talon ® Rodenticide (Cont.)

COMMON NAME: *brodifacoum*.

OTHER NAMES: *PP581, WBA8119*.

ACTION: anticoagulant rodenticide.

CHEMICAL PROPERTIES: Off-white powder. Soluble in benzene + chloroform. Insoluble in water and petroleum ether. Stable as a solid under normal storage conditions.

TOXICITY: Acute oral LD_{50} (rat), 0.27 mg kg. Acute dermal (dust) LD_{50} (rat), 50 mg kg.

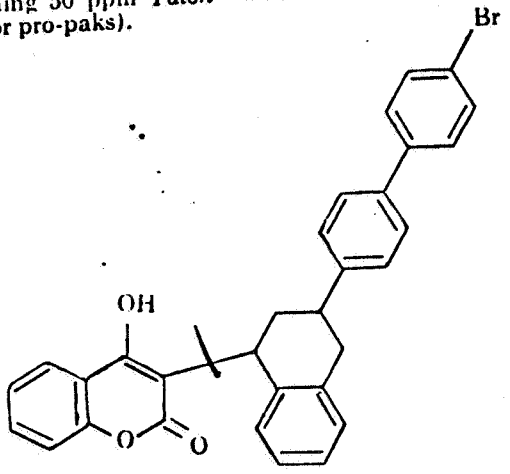
SIGNAL WORD: CAUTION — U.S. (DANGER, POISON).

ANTIDOTE: Vitamin K_1.

HANDLING AND STORAGE PRECAUTIONS: Keep away from children, domestic animals and wildlife. Wash hands after handling bait. Avoid all contact by mouth. Do not allow to contaminate food, feed or water supplies. After treatment, remove and bury uneaten bait and rodent bodies. Keep container closed to maintain freshness of bait. Do not re-use empty container.

APPLICATIONS: A new rodenticide of exceptional activity against a variety of pest rodents. Effective against rodents which are resistant to conventional anticoagulants. Single feeding only necessary for rodent death to occur.

FORMULATIONS: Ready-to-use grain-base bait containing 50 ppm *Talon* ® rodenticide in form of pellets (loose or pro-paks).



Brodifacoum

BP: ICI Americas Inc., Agricultural Chemicals Div.
ICI Plant Protection Div. (Great Britain)

Tamaron ® — see Monitor ®.

Tamol ®

ACTION: A series of surfactants for formulation of wettable powders.

BP: BASF India Limited.

Tanalith ® — see Wolman Salts ®; Fluor Chrome Arsenate Phenol.

Tandex ® (Product discontinued by FMC Corp., Agricultural Div.)

CHEMICAL NAME: *m*-(3,3-Dimethylureido)phenyl-*tert*-butylcarbamate.

COMMON NAME: *karbutilate*.

OTHER NAMES: *NIA 11092, FMC 11092*.

ACTION: Broad spectrum weed and brush killer for use on noncropland.

CHEMICAL PROPERTIES: White crystalline solid, melting at 176-176.5°C. Water solubility, 325 ppm at room temperature.

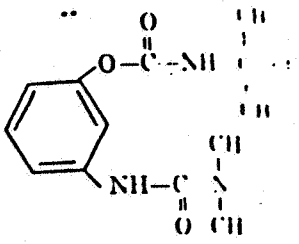
TOXICITY: Acute oral LD_{50} (rat), 3000 mg kg (tech. material in propylene glycol suspension).

SIGNAL WORD: CAUTION

CAUTION: Do not apply, or dr... near desirable trees or other ... chemical may be washed or ... roots. Care should be taken to pr... spray to desirable plants. *Tand...* and once the spray has been d... vaporization exists.

APPLICATIONS: Control of ann... leaf weeds and grasses, brush and ... utility and pipeline rights of w... industrial plant sites and noncrop...

FORMULATIONS: Granules, F... 80%.



Karbutilate

Tank Mix

A tank mix is a mixture of two or ... spray tank at the time of applicat... cleared by EPA requiring a new ... aspects of the mixture as though ... otherwise such a mixture should ... should be used with caution until ... ibility of the ingredients.

The application of soluble con... present some problems when u... used alone as a spray there is no ... in the tank, but when mixed with ... that the pesticide is soluble in wat... an undesirable chemical reaction ta... tank.

See *Adjuvant, Serial Application*.

Tanone ® — see Phenthoate.

Tantizon ®

CHEMICAL NAME: 6-*tert*-butyl-... 3-methylthio-1,2,4- triazin-5(4H)-one

COMMON NAME: *Isomethiozin* (ISO...

OTHER NAME: *DIC 1577*.

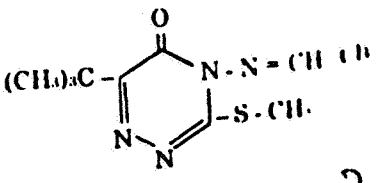
ACTION: Herbicide.

CHEMICAL PROPERTIES: Colorless ... pound, m.p. 159.3°C, v.p. $3.5 \times 10^{-...}$ ... tically insoluble in water. Solubility ... hexanone: 10.3%.

TOXICITY: Acute oral LD_{50} (rat), ... dermal LD_{50} (rat), > 1000 mg kg

APPLICATIONS: Used for control of ... weeds in winter barley; in combina... spring barley and spring wheat.

FORMULATIONS: Wettable powder; ... combination products with *2,4-DP* (WP



Tantizon ®

?

Warbex * — see Famphur ♦.

Warfarin ♦

CHEMICAL NAME: 3(α-Acetonylbenzyl)-4-hydroxycoumarin.

COMMON NAMES: *warfarin* (BSI, ISO); *coumafene* (France), *zoocoumarin* (Netherlands and USSR).

OTHER NAMES: *Kypfarin* *, *RAX* *, *Warfarin Plus*.

ACTION: Rodenticide (anticoagulant).

TOXICITY: There has been no development of tolerance in rodents after ingestion and apparently neither sex nor age of the rat or mouse causes any difference in effectiveness.

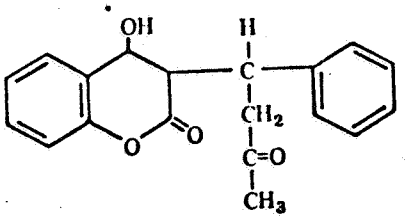
SIGNAL WORD: WARNING - CAUTION.

APPLICATIONS: An anticoagulant that is highly effective in controlling Norway rats and house mice. 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 effected.

Warfarin has found very ready acceptance because rodents do not tend to become bait shy after once tasting the material. They continue to consume it until its anti-clotting properties have produced death through internal hemorrhaging.

A "rodent drink" is made with water containing 0.54% *warfarin* sodium coated on sugar *(Dethmor * Water Soluble)*; a similar "rodent drink" containing 0.54% *warfarin* coated on sand (silica) *(Rax * Water Soluble)*.

FORMULATION: It is formulated in ready-to-use baits and as concentrates in corn starch for mixing at a 1:19 ratio with cornmeal or other materials. Baits should be used only in protected stations that prevent access to larger animals. *RAX* powder, .50% concentrate.



Warfarin ♦

BP: All India Medical Corp. (India) (*Warfarin 0.5% Dust*)
Prentiss Drug & Chemical Co. (*RAX* *)
Velsicol Chemical Corp. (*Warfarin, Warfarin Plus*)

Warfarin Plus — see Warfarin ♦.

Warning — see Signal Words (under Toxicity-Human).

Warning Agent — see Chloropicrin, Tritox *.

Watathion * — see Surecide *.

Water Dispersible Liquid

A formulation made to mix with water, usually for use as a spray. It may be a wettable powder (WP), and emulsifiable concentrate (EC), or similar formulation requiring surfactants.

Water Dispersible Slurry

A two-phase concentrate that contains solid pesticide suspended in liquid which is capable of suspension in water.

Water Modifier

The AAPCO has adopted this definition:

"A substance which is used to change the pH or the chemical composition of dissolved or suspended material in the spray water in order to prevent undesirable behavior."

See *Safener*.

WBA 8107 — see Ratak.

WBA 8119 — see Talon *.

Weecon * — see Sodium Cyanate.

Weed

The AAPCO has adopted this definition

"Any plant which grows where not wanted

Weed-Ag-Bar * — see 2,4-D.

Weedar * — see 2,4-D; 2,4,5-T; MCPA.

Weedazol * — see Amitrole ♦.

Weedazol TL * — see Amitrole ♦.

Weedbeads * — see Sodium Pentachlorophenate.

Weed-B-Gon * — see 2,4-D, Silvex.

Weed Broom * (Product discontinued by [illegible]

COMPOSITION: *DSMA, Bromacil* and [illegible]

ACTION: Herbicide.

APPLICATION: Industrial weed control.

Weed-E-Rad * — see DSMA, MSMA.

Weed-E-Rad * DMA Powder — see DSMA.

Weed-E-Rad * 360 — see DSMA.

Weedez Wonder Bar * — see 2,4-D.

Weed-Hoe * — see DSMA; MSMA.

Weedmaster *

COMPOSITION: *Dicamba* 1 pound [illegible] pounds gallon, a registered pre-mix.

ACTION: Herbicide.

TOXICITY: Acute oral LD_{50} *DMA* salt [illegible] mg kg. Acute oral LD_{50} of the *DMA* salt [illegible] mg kg.

SIGNAL WORD: CAUTION.

APPLICATION: For control of annual and [illegible] leaf weeds on pasture and rangeland [illegible] land areas such as fencerows, roadways, [illegible] farm buildings.

Weedmaster * is currently cleared for [illegible] Arkansas, Louisiana, and Mississippi.

FORMULATION: Liquid.

F: Velsicol Chemical Corp.

Weedol * — see Diquat; Paraquat.

Weedone * — see 2,4-D; 2,4,5-T; Dichlorp[illegible]

Weed-Rhap * — see 2,4-D; MCPA.

Weed Rhap 2,4-D 2-Ethyl Hexyl Ester — see [illegible]

Weedtrine *

COMBINATION: *Cutrine* * plus *diquat*

ACTION: Aquatic herbicide.

APPLICATION: Registered for control of [illegible] aquatic weeds. May be sprayed on the [illegible] only in depths no greater than 3 feet [illegible] Florida.

Weedtrine-D *

COMPOSITION: 6,7-Dihydrodipyridol [illegible] razidinium dibromide.

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