

US EPA ARCHIVE DOCUMENT

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To: William H. Miller
Product Manager 16
Registration Division (TS-767)

From: Dr. Willa Garner, Chief lll
Review Section No. 1
Environmental Fate Branch
Hazard Evaluation Division (TS-769)

Attached please find the environmental fate review of:

Reg./File No.: 10182-38, -39, -40 and -41

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

Type Product: Rodenticide

Product Name: Talon-G

Company Name: ICI Americas, Inc.

Submission Purpose: Label Amendment with Data

ZBB Code: 3(c)(7)

ACTION CODE: 310

Date In: 8/20/81

EFB # 919-922

Date Completed: 10/28/81

TAIS (level II) Days

60

5

Deferrals To:

 Ecological Effects Branch

 Residue Chemistry Branch

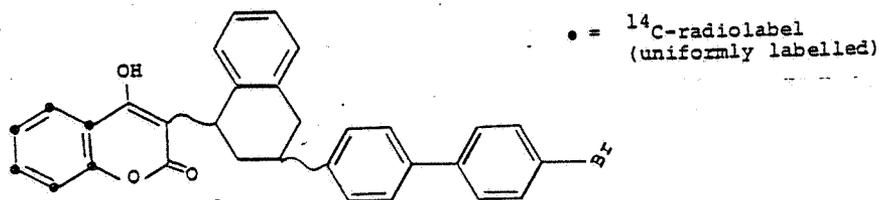
 Toxicology Branch

1.0 INTRODUCTION

On July 22, 1981, ICI Americas, Inc. submitted several studies for EFB review, in support of an application for an amended registration for TALON-G Rodenticide Pellets to add outdoor use against commensal rodents. The studies submitted (in PP# 245705) were as follows:

- 1.1.1 Arnold, D.J., J.H. Rapley and M.S. Weissler. BRODIFACOUM: Development of Methods to Study its Degradation in Soil. Report Series RJ 0064 B. 17 October 1979. ICI Plant Protection Division. (confidential).
 - 1.1.2 Newby, S.E. and B.G. White. BRODIFACOUM: Adsorption and Desorption in Soils Measured Under Laboratory Conditions. Report Series TMJ 1764 B. ICI Plant Protection Division. 17 July 1979. (confidential)
 - 1.1.3 Stevens, J.E.B. and I.R. Hill. BRODIFACOUM: Leaching on Soil Thick-Layer Chromatograms. Report Series RJ 0072 B. 8 October 1979. ICI Plant Protection Division. (confidential)
 - 1.1.4 Gowman, M.A. and D. Riley. Determination of the Physical and Chemical Properties of Soils. (Method in use at Jealott's Hill Research Station.) Report Series TMJ 1190A. 19 January 1976. ICI Plant Protection Division. (confidential)
- 1.2 Brodifacoum was known under the code numbers PP581 and WBA8119, prior to the adoption of a common chemical name. It has been the subject of two earlier reviews, both issued on 8/31/79.
- 1.3 TALON™ consists of 0.005% (50 ppm) 3-[3-(4'-bromo[1,1'-biphenyl]-4-yl)-1,2,3,4-tetrahydro-1-naphthalenyl]-4-hydroxy-2H-1-benzopyran-2-one, and 99.995% inert ingredients.

2.0 STRUCTURE



3.0 DIRECTIONS FOR USE

Norway and Roof Rats : Apply 4 to 16 ounces of bait (usually at intervals of 15-30 feet) per placement. Maintain an uninterrupted supply of fresh bait for 10 days or until signs of rat activity cease.

House Mice : Apply 1/4 to 1/2 ounce of bait at intervals of 8 to 12 feet per placement. Larger placements (up to 2 ounces) may be needed at points of very high mouse activity. Maintain an uninterrupted supply of fresh bait for 15 days or until signs of mouse activity cease.

Rats & Mice : Replace contaminated or spoiled bait immediately. Collect and dispose of all dead animals and unconsumed bait properly. Repeat treatment when infestation recurs. Where continuous source of infestation is present, establish permanent bait stations and replenish as needed.

4.0 REVIEW OF STUDIES

4.1 Arnold, D.J., J.H. Rapley and M.S. Weissler. BRODIFACOUM: Development of Methods to Study its Degradation in Soil. Report Series RJ 0064 B. 17 October 1979. ICI Plant Protection Division. (confidential).

4.1.1 Introduction

Utilizing a sandy clay loam treated with radiolabeled brodifacoum Arnold tested various extraction and elution (TLC) solvents to determine which, if any, would yield the highest recoveries/separations of the A.I. from background interferences. He found dichloromethane:methanol (80:20) to be the most efficient solvent system for removal of ¹⁴C-brodifacoum and its degradation products from soil, utilizing a "cold" extraction technique. On silica TLC, the best solvent system was found to be chloroform:methanol:ethyl acetate (60:30:10). Additionally, the best separation of the cis/trans isomers was achieved by use of a 30:70 dioxan:petroleum distillate (80-100°C) system.

The half-life of brodifacoum in this soil type under incubation conditions was found to be about 10 weeks. About 7% of the applied radioactivity was released as ¹⁴CO₂. None of the degradates identified exceeded 3% of the applied.

4.1.2 Methods and Materials

The sandy clay loam selected for this study was sieved to pass a 2mm mesh, homogenized and stored field-wet at 25°C in polythene until needed. Soil characteristics were as follows:

pH.....	7.3
% Organic Matter	7.1
Particle Size Analysis (%)	
Coarse Sand.....	34.0
Fine Sand.....	23.7
Silt.....	14.5
Clay.....	27.8
Cation Exchange Capacity (MEQ/100gm)...	14.8
Moisture Holding Capacity (1/3 bar)....	20.3
Available Nutrients (ppm)	
Phosphorus.....	101.
Potassium.....	240.
Magnesium.....	108.

B

In each experiment, a 29.5gm aliquot of soil was weighed into a glass pot, so that the addition of 0.5ml of pesticide solution would bring the final weight to 30 gm. All experiments were carried out only in the presence of indirect lighting, to minimize photolytic effects.

Positions 5,6,7,8,9, and 10 of the coumarin ring were ^{14}C -radio-labeled. Both cis and trans isomers of brodifacoum were prepared in dichloromethane, and labeled SM82 and SM83, respectively. Both had specific activity of 14.75 mCi/mM, and were, respectively, 97.6% and 95.6% pure.

As added to each soil sample, the radiolabelled pesticide was in a mixture of 60% acetone and 40% sterile distilled water, representing an application rate of 0.5 kg/ha. Treated soils were incubated in a stream of CO_2 -free air in the dark at $25^{\circ}\pm 1^{\circ}\text{C}$. Volatiles were trapped by sequentially washing the air stream through traps containing glass wool-0.05M H_2SO_4 -glass wool-2 methoxyethanol-glass wool-ethanolamine.

Radioactivity was quantitated using a Packard Automatic Tri-Carb Liquid Scintillation Spectrometer, Model 3390, in conjunction with a Model 544 Absolute Activity Analyser. Calibration was by external standardization. Suitable controls were included to correct for natural background activity.

Identification of the parent pesticide and of its degradative products was done by chromatographing with 20 different solvent systems of differing polarity, on silica 60 F254 TLC plates, and then visualizing all reference compounds by 254 nm uv.

Reference compounds used were:

- I. Brodifacoum
- II. 4-hydroxycoumarin
- III. cis Brodifacoum
- IV. trans Brodifacoum

Quantification of each chromatographed spot was done by scraping of the uv- or autoradiograph-visualized spots followed by combustion, and LSC counting.

4.1.3 Results and Discussion

Recovery of radiolabeled materials as a percentage of applied appeared to be reasonable. Recovery from unincubated (day 0) control samples ranged from 86 to 96%; from samples incubated for 3 week, from 69 to 122%; and from samples incubated for 10 weeks, 93-95%.

It was found that dichloromethane:methanol (80:20) consistently extracted more radioactivity from soil than any of the other solvents tested.

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Three TLC solvent systems were found to be suitable:

90:10	Dichloromethane:Ethylacetate	(DME)
60:30:10	Chloroform:Methanol:Ethylacetate	(CME)
30:70	Dioxan:(80°-100°C) Petroleum Spirits	(DP)

Solvent system CME was found early in the experiment to be superior to DME, and therefore was used for the remainder of the study. Solvent system DP most clearly separated the cis/trans isomers while leaving compound II. near the baseline of the TLC plate.

Identification of the degradative products indicated that, with the exception of the parent compound, no single degradate exceed 3% of the applied pesticide.

4.1.4 Conclusions

When extracted with the most efficient solvent, dichloromethane:methanol (80:20), brodifacoum was found to be very stable. Brodifacoum degraded in soil, with approximately 50% remaining after 10 weeks. Because the primary thrust of this study was to evaluate extraction/quantification schemes, an insufficient number of samples was taken at intervals to adequately define the degradative kinetics.

The recommended method for extraction of ¹⁴C-brodifacoum and ¹⁴C-degradation products from soil is as follows: 2 x 18 hour "cold" extraction (25°C) with dichloromethane:methanol (80:20).

On silica gel TLC plates, the most efficient solvent system tested for separating brodifacoum from its degradative products was found to be chloroform:methanol:ethylacetate (60:30:10:), while dioxan:80°-100°C petroleum spirits (30:70) gave the best separation efficiencies for the cis and trans isomers.

4.1.5 Recommendations

This study was very well done, and contains considerably more detail than was reported in this review. It seems more than adequate to support future studies which may use these procedures (such as hydrolysis, photolysis, aerobic soil metabolism, etc.)

4.2 Newby, S.E. and B.G. White. BRODIFACOUM: Adsorption and Desorption in Soils Measured Under Laboratory Conditions. Report Series TMJ 1764 B. 17 July 1979 ICI Plant Protection Division. (confidential)

4.2.1 Introduction

This study evaluates the adsorption/desorption of brodifacoum in three soil types (coarse sand, sandy clay loam, and calcareous sandy loam), using pesticide ¹⁴C-labeled on the coumarin ring as in the previous study.

Brodifacoum is a non-ionic, highly lipolytic substance, and would be expected to bind strongly to soil organic matter. Both the cis and trans isomers have been found to exhibit similar rodenticidal activity.

4.2.2 Methods and Materials

Three soil types were used in this study. Each was air dried, sieved to pass a 1 mm mesh. A 2gm aliquot was then equilibrated with 20ml 0.01M CaCl₂ solution to make a slurry.

Methods of analysis for soil characteristics are described in detail in the text.

Soil Characteristic	Sandy Clay Loam	Calcareous Sandy Loam	Coarse Sand
pH.....	7.1	7.6	6.6
% Organic Matter	6.3	11.4	1.2
Particle Size Analysis (%)			
Coarse Sand.....	38.0	7.7	67.5
Fine Sand.....	22.0	41.7	22.5
Silt.....	17.0	31.6	2.9
Clay.....	23.0	19.0	7.1
Cation Exchange Capacity (MEQ/100gm)...	16.5	30.0	4.5
Moisture Holding Capacity (1/3 bar)....	29.6	43.7	5.4
Available Nutrients (ppm)			
Phosphorus.....	>101.	28	38
Potassium.....	336.	90	<37
Magnesium.....	138.	108	10

Particle sizes:

- Coarse Sand = 0.2 - 2.0 mm
- Fine Sand = 0.02 - 0.2 mm
- Silt = 0.002 - 0.02 mm
- Clay = <0.002 mm

Positions 5,6,7,8,9, and 10 of the coumarin ring were ^{14}C -radio-labeled. Both cis and trans isomers of brodifacoum were prepared in dichloromethane, and labeled SM82 and SM83, respectively. Both had specific activity of 14.75 mCi/mM, and were, respectively, 97.6% and 95.6% pure.

For purposes of this experiment, a 64:36 cis:trans isomer ratio was utilized, representing the usual occurrence of isomers in routinely produced brodifacoum. Brodifacoum was stored in dichloromethane until needed. Then, the solvent was exchanged with acetone.

To equilibrated soil slurries, radio-brodifacoum was added, at rates of 0.9, 1.8, 2.7, 3.6 and 4.5 ppm. Slurries were kept in constant agitation with a vortex shaker. Subsequently, samples were transferred to an end-over-end shaker(4 RPM), which was kept at constant temperature (21-22°C), in the dark for 16 to 20 hours.

At the end of this period, slurries were centrifuged at 2000 RPM for 15 minutes and aliquots of clear supernatant withdrawn for analysis by LSC (see previous review for details of equipment used). An identical volume of 0.01M CaCl_2 solution was then added to maintain the initial volume.

The end-over-end mixing was then continued for another 16-20 hour period (etc.) until all samples had been obtained.

Aliquots were taken at the following times (hrs): 48, 72, 96, 120, and 192.

Extraction, chromatography, combustion and LSC counting were virtually identical to that used in the previously reviewed study.

4.2.3 Results and Discussion

Brodifacoum was found to bond strongly to each of the soils tested. In Coarse Sand, the computed K_d ranged from 301 - 635; in Sandy Clay Loam, from 811 - 1379; and in Calcareous Sandy Loam 842- 1280.

Degradates were found to have bonded less strongly to the soil than had the parent compound, so that K_d figures should be considered as minimums.

Very little degradation of brodifacoum was observed during this experiment, confirming its aquatic stability.

4.2.4 Conclusions

Brodifacoum is highly immobile in three different soil types and does not appear to hydrolyse readily. Adsorption seem to correlate roughly with %OM in the soil, as with other lipophylic, non-ionic chemicals.

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4.2.5 Recommendations

This study was very well done, and contains considerably more detail than was reported in this review.

4.3 Stevens, J.E.B. and I.R. Hill. BRODIFACOUM: Leaching on Soil Thick-Layer Chromatograms. Report Series RJ 0072 B. 8 October 1979. ICI Plant Protection Division. (confidential)

4.3.1 Introduction

This experiment was designed to evaluate the mobility of a 40:60 cis:trans mixture of brodifacoum using descending thick-layer soil chromatography. Four soil types were selected to give a range of conditions. Application rate was similar to that of actual field use (0.6kg/Ha), and at an exaggerated rate (6 kg/Ha) to mimic the possible effects of a localized spill from a bait box caused by rainfall or abrasion. It was found that <2% of the applied ¹⁴C-brodifacoum leached more than 2 cm in any of the soils tested.

4.3.2 Methods and Materials

Four soil types were used in this study. Each was air dried, sieved to pass a 7 mm mesh, and stored in polythene until needed. Methods of analysis for soil characteristics are described in detail in the text.

Soil Characteristic	Coarse Sandy Loam	Calcareous Clay Loam	Coarse Sand	Fen Peat
pH.....	7.1			
% Organic Matter	6.8	7.6	6.6	4.3
Particle Size Analysis (%)		11.2	1.4	71.2
Coarse Sand.....	38.2	7.7	66.4	ND
Fine Sand.....	25.4	41.7	26.1	ND
Silt.....	13.0	19.0	5.0	ND
Clay.....	23.4	31.6	2.5	ND
Cation Exch.Capac.(MEQ/100gm).....	16.5	30.0	4.5	112.1
Moisture Holding Cap.(1/3 bar).....	29.6	43.7	5.4	116.9
Available Nutrients (ppm)				
Phosphorus.....	>101.	24	38.	35.
Potassium.....	336.	84	0	130.
Magnesium.....	138.	85	10	37.

Positions 5,6,7,8,9, and 10 of the coumarin ring were ¹⁴C-radio-labeled. Stock solutions of each radio-isomer were purified by TLC by elution with chloroform:methanol:ethyl acetate (60:30:10). Final purity was >= 98%. Prior to soil application, a 40:60 cis:trans mixture was prepared. For comparison, a parallel experiment was conducted with ¹⁴C-Atrazine, which was determined to be 93.4% radiopure, with a specific activity of 2.3mCi/mM.

Preparation of the soil thick layers involved finely grinding an aliquot of each soil type, and placing the wet slurry on a 5cm wide by 30 cm long aluminum plate. A cloth wick was attached to the upper end of the plate. A 1 cm wide band of soil was then removed from the upper end of the plate approximately 2-3cm from the wick, and replaced with a known amount of pesticide-treated soil. The actual chromatography was then carried out using a 0.01M CaCl₂ solution. All leachate running off of the plate was collected for analysis.

Once all of the CaCl₂ had been used up, the plate, while still wet, was sectioned and sampled for analysis. Radioactivity was located using a Radio-chromatograph Scanner (model RTLS-1A), which had been modified to accept soil thick-layer chromatograms. Each radioactive section was scraped from the plate, air dried, weighed, and then quantified using the LSC techniques described earlier in this review.

4.3.3 Results and Discussion

On three of the four soils treated (exception was the coarse sand) no ¹⁴C-brodifacoum was detected in the leachate at either application rate. In the coarse sand, about 0.002 ug of brodifacoum equivalent/ml was detected, in the 6 kg/ha application.

Less than 2% of the applied ¹⁴C-brodifacoum was found to have leached more than 2cm, in all experiments.

Under the same conditions, atrazine (which is considered to be moderately mobile in most soils) was found to have leached as follows: 10 cm in the coarse sand, 7 cm in the calcareous clay loam, 4 cm in the coarse silty loam and <1 cm in the fen peat. Between 75 and 87% of the atrazine was found to have leached more than 2 cm in the three mineral sols. In the fen peat, at least 25% of the applied atrazine had leached more than 2 cm.

4.3.4 Conclusion

Brodifacoum has a very low mobility in several different soils even at exaggerated application rates.

4.3.5 Recommendation

This study was well done, and clearly elucidates the mobility characteristics of brodifacoum.

4.4 Gowman, M.A. and D. Riley. Determination of the Physical and Chemical Properties of Soils. (Method in use at Jealott's Hill Research Station.) Report Series TMJ 1190A. 19 January 1976. ICI Plant Protection Division. (confidential)

4.4.1 Introduction

This section deals with the perfection of the following techniques for measuring soil properties:

- a. Particle Size Distribution
- b. Soil Water Retention Properties
- c. Organic Matter Content
- d. Cation Exchange Capacity
- e. Soil pH
- f. Available Phosphorus
- g. Available Potassium

4.1.2 Discussion

This paper does not contain information related to data requirements. It does, however, provide background information on the methods used in the various soil studies submitted. As such, this paper is informative.

4.1.3 Conclusion

The methods used by ICI are reasonable, acceptable and, in virtually all cases, similar to those used routinely by regulatory laboratories in this country.

5.0 Overall Recommendations

5.1.1 These studies clearly elucidate the behavior of brodifacoum in a variety of soil types. The studies were well done, and adequately support the proposed amendment to add outdoor (use against commensal rodents) via enclosed bait stations. We concur with this proposed amendment.

5.1.2 Due to the relatively slow degradation of this product, other field uses, such as by dispersion, would require a more detailed evaluation of the data.



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