

US EPA ARCHIVE DOCUMENT

DATA EVALUATION RECORD

1. CHEMICAL: Avermectin B₁
2. FORMULATION: Technical Avermectin B₁ (91.43% purity)
3. CITATION: Fink, Robert and Joann Beavers. 1981. Acute oral LD₅₀ of L-676, 836-00V50 to mallard duck. Final report by Wildlife International LTD. Submitted to Merck Sharp & Dohme, Rahway N.J. Accession No. 246358 in 618-EUP-10.
4. REVIEWED BY: Mary L. Gessner
Fishery Biologist
HED/EEB
5. DATE REVIEWED: 12/21/81
6. TEST TYPE: Avian single-dose oral LD₅₀
Test species: Mallard duck (Anas platyrhynchos)
7. REPORTED RESULTS: The acute oral LD₅₀ of L-676, 863-00V50 in Mallard ducks is 85 mg/kg, 95% C.I. - 67-120 mg/kg
8. REVIEWER'S CONCLUSIONS: This study is scientifically sound, but is not adequate to fulfill the guideline requirement pertaining to avian single-dose oral LD₅₀ testing. Regurgitation of test material, by all test birds, nullified the measurability of the doses received.

Materials/Methods

Test Procedure

Five month-old mallard ducks, from the Wildlife International production flock, were utilized in this test. Birds were acclimated to test conditions for two weeks. Any group of birds exhibiting abnormal behavioral patterns were not used in the test. At the end of the acclimation period, the birds were randomly assigned to treatment pens. Five males and five females were utilized per treatment level. Feed was withheld from the control and test birds for 15 hours prior to oral administration of the experimental material. The experimental material was dispersed in distilled water and intubated directly into the crop with a stainless steel catheter. Each bird was weighed and dosed on the basis of milligrams of material per kilogram of body weight. The control birds received a corresponding volume of distilled water only. Body weight was recorded individually at initiation, and by pen at day 3,7, and 14. Food consumption was measured, but is presented as an estimate due to wastage by the birds. Birds were housed in indoor pens, measuring 72x90x33 cm. Temperature was maintained between 65 and 75°F, and relative humidity ranged between 30 and 80%. The photoperiod was maintained at 14 hours of light per day. Symptoms of toxicity and mortality were recorded daily throughout the study. Food and water were available ad libitum throughout the study.

Statistical Analysis

Mortality was analyzed statistically by probit analysis.

Discussion/Results

There were no mortalities in the negative control group during the course of the study. All birds were normal in both appearances and behavior throughout the test period. The birds regurgitated immediately after dosing at all treatment levels. At the 10.0 mg/kg dosage level, slight lethargy and loss of coordination was noted immediately after dosing, and continued through Day 1. At the 17.8 mg/kg dosage level, some lethargy was observed immediately after dosing, with lethargy, loss of coordination, prostrate posture and lower limb rigidity evident during Day 1. All birds at both dosage levels appeared normal by Day 2. At the 31.6 mg/kg level, lethargy, prostrate posture, and lower limb rigidity were observed after dosing and during Day 1. One drake continued to exhibit lethargy during Day 2, but all birds appeared normal by Day 3. Prostrate posture and lower limb rigidity were observed following dosing and during Day 1 at the 56.2 mg/kg level. Lethargy was still

apparent on Day 2, with one hen also exhibiting lower limb weakness. All surviving birds appeared normal by Day 3. Symptoms of toxicity observed prior to death at the 100 mg/kg level included depression, loss of coordination, prostrate posture, loss of righting reflex, and lower limb rigidity. Surviving birds at this dosage level continued to exhibit lethargy through Day 4. All surviving birds at all dosage levels appeared normal from Day 5 until termination of the study. There was a dose related reduction in body weight of surviving birds for the first 3 days of the study at the 56.2 and 100 mg/kg dosage levels. A compensatory body weight gain had occurred at both levels by the end of the study.

One mortality occurred at the 56.2 mg/kg level, and 7 mortalities occurred at the 100 mg/kg level.

Reviewer's Evaluation

A. Test Procedure

Test procedure generally followed EPA-recommended protocol. Several deviations occurred, as follows. Birds were not weighed prior to the holding period, to determine any weight loss during the acclimation period. Water was used as the diluent, which is not recommended with compounds that are not water-soluble. No indication was given that gross necropsies were performed. All birds regurgitated immediately after dosing.

B. Statistical Analysis

Data analysis was verified by the Stephan's program, with the following results:

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CONC.          NUMBER      NUMBER      PERCENT      BINOMIAL
                EXPOSED      DEAD        DEAD        PROB. (PERCENT)
100             10             7           70          17.1875
56.2            10             1           10          1.074219
31.6            10             0            0           0.09765625
17.8            10             0            0           0.09765625
10              10             0            0           0.09765625
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THE BINOMIAL TEST SHOWS THAT 56.2 AND +INFINITY CAN BE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC₅₀ FOR THIS SET OF DATA IS 83.53436

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
1	0.509802	83.53436	66.97781	130.4825

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
13	0.480495	1	0.9997307

SLOPE = 7.307879
95 PERCENT CONFIDENCE LIMITS = 2.24222 AND 12.37354

LC50 = 84.63026
95 PERCENT CONFIDENCE LIMITS = 66.56575 AND 119.405

LC10 = 56.72058
95 PERCENT CONFIDENCE LIMITS = 24.07946 AND 70.72705

C. Discussion/Results

At all dosage levels, the birds regurgitated immediately after dosing. This renders the study useless since loss of the test material nullifies the measurability of the dose. The number of toxic symptoms exhibited at all test levels and mortalities at the higher levels indicate that the test material is certainly toxic to mallard ducks. Disappearance of toxic symptoms after several days at all dose levels suggests that the toxic action of this chemical is reversible in waterfowl. In this case, accurate determination of the acute oral toxicity of the compound is of extreme importance. Since bobwhite quail are less likely to regurgitate than other species, they are the recommended test species.

D. Conclusions

1. Category: Supplemental
2. Rationale: Regurgitation of test material by ducks nullified the measurability of the doses received.
3. Repairability: None