

REPELLENCY AND TOXICITY OF 55 INSECT REPELLENTS
TO RED-WINGED BLACKBIRDS (Agelaius phoeniceus)

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ABSTRACT

A joint research program was initiated in 1979 to investigate the potential avian repellency and toxicity of 55 selected insect repellents originating from or related to naturally occurring chemicals. Seven of the chemicals or extracts tested exhibited avian repellency and two of these were considered to be moderately active, with R_{50} 's (analogous to LD_{50}) of 0.237 (trans-asarone) and 0.240% (safrole). None of the 55 chemicals or extracts exhibited acute oral toxicity at 100 mg/kg or less to the red-winged blackbird (Agelaius phoeniceus).

INTRODUCTION

The U.S. Departments of Agriculture and Interior maintain a number of research programs designed to identify and develop chemicals to alleviate insect and wildlife deprecations to many

agricultural crops. Although most of the chemicals tested in these programs are synthetic, an expanded effort has been made to identify and quantify the efficacy of chemicals of natural origin. In 1979, the authors and their respective laboratories (USDA's Agricultural Environmental Quality Institute and the USDI's Denver Wildlife Research Center) instituted an informal cooperative program for testing the response of wild birds to a number of naturally occurring chemicals or extracts that had demonstrated repellency to insects¹. The purpose of this effort was three-fold: (1) to test a number of natural plant products that are repellent to insects for biological effects on birds; (2) to determine if any gross relation exists between effects on insects and birds; and (3) to observe relations between compound structure and bird response.

METHODS AND MATERIALS

Expressed neem oil was obtained from Chemiloids Ltd., Vijayawada, India. Extracted neem oil was obtained by extracting crushed dried seed kernels of Azadirachta indica A. Juss. (obtained in India through the courtesy of the American Embassy, New Delhi) overnight with ether in Soxhlet extractors and evaporating the solvent from the resulting extract.

Tetrahydropyranyl (THP) ethers of the alcohols and phenols were prepared (in >90% yield) as follows: to a stirred solution of 0.5 mole of the alcohol or phenol and 4 drops of concentrated HCl in 75 ml of reagent grade ether was added dropwise a 20% excess of dihydropyran. After addition was complete, the solution was refluxed for 4.5 h, the solvent and excess dihydropyran were removed by evaporation at reduced pressure, and the residue was dissolved in ether. The solution was washed twice with cold 5% sodium bicarbonate solution and once with saturated sodium chloride solution, dried over sodium sulfate, and freed of solvent at reduced pressure. The resulting THP ethers were purified by distillation.

The compound 1,2,4-Trimethoxy-5-propylbenzene was prepared by hydrogenating trans-asarone in ethanol solution. All other compounds were purchased from Aldrich Chemical Company, Milwaukee, Wisconsin.

Chemical Abstract Service (CAS) registry numbers and the 9th Collective Index (9CI) names were obtained from various CAS sources, or were assigned by CAS at the authors' request.

Red-winged blackbirds (Agelaius phoeniceus) were wild-trapped in the South Platte River Valley of Colorado and were held under communal aviary conditions for 2 to 8 weeks before testing. Avian repellency (R_{50} which is analogous to LD_{50}) values were calculated from tests conducted under no-choice conditions for 18 consecutive hours, using groups of five individually caged red-wings. The procedures we used were those described by Starr et al.² as modified by Schafer and Brunton³. For acute oral avian LD_{50} tests, birds were dosed by gavage with known levels of candidate chemicals. Propylene glycol was used as the carrier and two individually caged redwings per dose level were used to estimate toxicity^{4,5}. Both data sets were evaluated statistically by the moving point interpolation method of W. R. Thompson⁶.

RESULTS

The chemicals which were subjected to redwing screening were divided into six basic structural categories, as indicated in Table 1.

Three of nine 9,10-anthracenediones had redwing R_{50} 's $\leq 1.000\%$ (Compounds 1,4,6) and exhibited no oral toxicity at 100 mg/kg. Although seven of the nine chemicals indicated some degree of avian repellent activity (food consumption $<100\%$ at the 1.000% treatment level), relations between the structure of a compound and its repellency were somewhat confusing. Based on R_{50} values, the 1- and 2-mono-substituted compounds (chloro- and amino-) showed inconsistent activity (i.e., compounds 1 and 4 were

TABLE 1
 Identification and Avian Repellency and Toxicity of 55 Chemicals
 Related to Natural Plant Products

Com- pound	CAS Registry Number	Chemical Name (9CI)	Red-winged blackbird		
			LD ₅₀ (mg/kg)	Percent food consumed*	
9,10 Anthracenediones					
1	00082440	1-Chloro-9,10-anthracenedione	>1000	0.422	22.4
2	00131099	2-Chloro-9,10-anthracenedione	> 316	>1.000	>52.0
3	00082451	1-Amino-9,10-anthracenedione	> 316	>1.000	<89.6
4	00117793	2-Amino-9,10-anthracenedione	> 316	0.340	<58.4
5	00082462	1,5-Dichloro-9,10-anthracenedione	> 316	>1.000	>52.0
6	00082439	1,8-Dichloro-9,10-anthracenedione	> 316	0.649	<58.4
7	00072480	1,2-Dihydroxy-9,10-anthracenedione	> 316	>1.000	<89.6
8	00081641	1,4-Dihydroxy-9,10-anthracenedione	> 316	>1.000	<80.8
9	00117102	1,8-Dihydroxy-9,10-anthracenedione	> 316	>1.000	<89.6
Benzenes (methoxy)					
10	00150765	4-Methoxypheno1	> 113	>1.000	>52.0
11	00642717	3,4,5-Trimethoxyphenol (antiarol)	>1000	>1.000	83.2
12	00102567	2,5-Dimethoxybenzenamine	> 100	>1.000	>52.0
13	00634366	1,2,3-Trimethoxybenzene (methylsyringol)	>1000	>1.000	100

15	00621238	1,3,5-Trimethoxybenzene	>1000	>1.000	100
16	04460860	2,4,5-Trimethoxybenzaldehyde (asaronaldehyde)	422	>1.000	79.2
17	00490642	2,4,5-Trimethoxybenzoic acid (asaronic acid)	>1000	>1.000	84.8
	(propyl)				
18	00099876	1-Methyl-4-(1-methylethyl)benzene (<i>p</i> -cymene)	> 316	>1.000	100
19	00104450	1-Methoxy-4-propylbenzene (dihydroanethole)	> 316	>1.000	100
20	05888528	1,2-Dimethoxy-4-propylbenzene	> 316	>1.000	78.4
		(4-propylveretrole)			
21	6906656	1,2,4-Trimethoxy-5-propylbenzene	> 100	>1.000	96.0
	(propenoic acid)				
22	00090506	3-(3,4,5-Trimethoxyphenyl)-2-propenoic acid	422	>1.000	100
23	25173722	3-(3,4,5-Trimethoxyphenyl)propanoic acid	422	>1.000	100
24	33130040	3-(2,3,4-Trimethoxyphenyl)propanoic acid	1000	>1.000	100
	(propenyl)				
25	00104461	1-Methoxy-4-(1-propenyl)benzene (anethole)	316	>1.000	64.8
26	00093163	1,2-Dimethoxy-4-(1-propenyl)benzene (isohomogenol)	> 316	>1.000	86.4
27	02883989	(<i>E</i>)-1,2,4-Trimethoxy-5-(1-propenyl)benzene	> 100	0.237	9.60
28	05273869	(<i>Z</i>)-1,2,4-Trimethoxy-5-(1-propenyl)benzene (<i>cis</i> -asarone)	750	>1.000	94.4
29	00097541	2-Methoxy-4-(1-propenyl)phenol (isoeugenol)	> 316	>1.000	98.4

(continued)

TABLE 1 (continued)

Com- pound	CAS Registry Number	Chemical Name (9CI)	Red-winged blackbird		
			LD ₅₀ (mg/kg)	R ₅₀ (%)	Percent food consumed*
30	00120581	5-(1-Propenyl)-1,3-benzodioxole (isosafrrole)	> 316	0.750	43.2
31	00140670	1-Methoxy-4-(2-propenyl)benzene (estragole)	> 316	>1.000	100
32	00093152	1,2-Dimethoxy-4-(2-propenyl)benzene (methyl Eugenol)	> 316	>1.000	62.4
33	00097530	2-Methoxy-4-(2-propenyl)benzene (eugenol)	> 316	>1.000	100
34	00094597	5-(2-Propenyl)-1,3-benzodioxole (safrole)	> 316	0.240	48.0
35	00523808	4,7-Dimethoxy-5-(2-propenyl)-1,3-benzodioxole (Apiole)	> 316	>1.000	
Bicyclo[2.2.1]heptanes					
36	04695629	(1R)-1,3,3-Trimethylbicyclo[2.2.1]heptan- 2-one (D-fenchone)	> 316	>1.000	85.6
37	07787204	(1S)-1,3,3-Trimethylbicyclo[2.2.1]heptan- 2-one (L-fenchone)	> 316	>1.000	86.4
38	13851111	1,3,3-Trimethylbicyclo[2.2.1]heptan-2-ol acetate (fenchyl acetate)	> 316	>1.000	92.8
39	05655618	(1S-endo)-1,7,7-Trimethylbicyclo[2.2.1]- heptan-2-ol acetate (L-bornyl acetate)	316	>1.000	88.0

1,4-Naphthalenediones					
40	00130154	1,4-Naphthalenedione	133	0.562	25.6
41	02348825	2-Methoxy-1,4-Naphthalenedione	316	>1.000	100
42	00058275	2-Methyl-1,4-Naphthalenedione	> 316	>1.000	96.8
43	00117806	2,3-Dichloro-1,4-Naphthalenedione	> 316	>1.000	<89.6
Tetrahydro-2H-pyrans					
44	31535065	3-Chloro-2-ethyltetrahydro-2H-pyran	>1000	>1.000	68.0
45	04203503	Tetrahydro-2-phenoxy-2H-pyran	>1000	>1.000	94.2
46	20443883	Tetrahydro-2-(4-methoxyphenoxy)-2H-pyran	> 562	>1.000	96.0
47	81603625	2-(2,3-Dimethoxyphenoxy)tetrahydro-2H-pyran	> 316	>1.000	80.0
48	81603636	3-(2'-Tetrahydropyranyloxy)pentane	> 562	>1.000	82.4
49	79802601	3-(2'-Tetrahydropyranyloxy)pentene	> 316	>1.000	91.2
50	51378519	3-(2'-Tetrahydropyranyloxy)pentyne	> 562	>1.000	69.6
Others					
51	00089827	(R)-5-Methyl-2-(1-methylethylidene)cyclohexanone ([+]-pulegone)	> 316	>1.000	51.2
52	00079776	(E)-4-(2,6,6-Trimethyl-1-cyclohexen-1-yl)-3-buten-1-one(B)	> 562	>1.000	90.4
53	05490471	2H,8H-Benzo [1,2-b':5,4-b'] bipyran-2-one (lonchocarpic acid)	> 100	>1.000	89.6
54	08002651	Neem oil (expressed)	>1000	>1.000	81.6
55	08002651	Neem oil (extracted)	1000	>1.000	68.8

* Average percent of food treated at 1.00% consumed by birds in test period.

effective but 2 and 3 were not). None of the dihydroxy compounds (7-9) showed R_{50} activity. The 1,8-dichloro derivative (Compound 6) showed weak food reduction, but the 1,5-dichloro derivative (Compound 5) did not.

Of the 25 benzene derivatives tested, 8 contained primarily methoxy substituents and no alkane/alkene substituents (Compounds 10-17). Most of the other 17 benzene derivatives contained methoxy substituents, and either one or more propyl (Compounds 18-21), propenoic acid (Compounds 22-24), or propenyl (Compounds 25-35) group. None of the eight methoxy-substituted benzenes showed any R_{50} activity, although four compounds did cause a slight reduction in food consumption at the 1.000% treatment level (Compounds 11,14,16,17). Three of the four compounds that caused a reduction in feeding included at least one substituent that was not methoxy. Two of the 4-propyl-substituted benzenes caused some reduction in food consumption, although none showed any measurable R_{50} activity. None of the propanoic acid derivatives caused any reduction in food consumption or showed any R_{50} activity.

We tested 11 propenylbenzenes, 2 of which (Compounds 27,34) indicated some potential bird repellency based on R_{50} values (<0.316%). One other compound (30) in this series showed R_{50} activity and 9 of the 11 compounds reduced food consumption at the 1.000% level. Of the 11 compounds tested in this series, trans-asarone (Compound 27) showed the greatest potential. Little difference between 1-propenyl and 2-propenyl derivatives was noted; however the presence of the benzodioxole substituent at the 3- and 4-position relative to the propenyl group appeared to enhance repellency (Compounds 34, 26). We also tested four bicyclo[2.2.1]heptanes (Compounds 36-39), none of which showed any R_{50} activity, even though all four caused consistent but small reductions in food consumption.

Four 1,4-naphthalenediones (Compounds 40-43) were tested; one (Compound 40) showed R_{50} activity at less than 1.000% and three

of the four caused some reduction in food consumption; however, the repellency of the parent compound (1,4-naphthalenedione) was greater than that of the compounds containing substituents. Seven tetrahydropyrans (Compounds 44-50) were also tested, none showed any R_{50} activity, although all seven reduced food consumption to various degrees. The final group of five compounds or extracts that we tested (Compounds 51-55) showed minimal or no avian repellency.

DISCUSSION

Of the substituted benzenes, trans-asarone (Compound 27) was the most effective bird repellent found, and it appears that the trans-propenyl configuration may be essential for repellency since the compounds with a cis-configuration (Compound 28) and hydrogenated asarone (Compound 21) were inactive. Replacement of the propenyl group with aldehydic (Compound 16) or carboxylic acid (Compound 17) groups resulted in much less activity as did complete removal of the propenyl group (Compound 14). Some repellency was noted in the 1,4-naphthalenediones and the 9,10-anthracenediones, although no relation between structure of the compound and repellency could be established due to the small number of chemicals tested in each group.

Although the avian repellency of the compounds tested was not strong enough to warrant further testing or development, it is our opinion that more promising compounds could probably be found by investigating substituted trimethoxypropenylbenzenes, 9,10-anthracenediones, and 1,4-naphthalenediones more thoroughly. One very encouraging aspect of all the compounds we tested which are present in nature or related to natural products is that they are not very toxic to birds; none of the 55 chemicals had acute oral LD_{50} 's less than 100 mg/kg.

The limited number of compounds that were observed to have avian repellency in our screening program would seem to preclude

the use of insect data as a potential data source for recommending chemicals for potential avian repellent use. In fact, however, using insects to select chemicals for avian testing appears to be at least as effective as random screening. Our present ratio of compounds showing avian repellency to those randomly tested is about 5%, and with selectively procured chemicals is about 10% (unpublished data).

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