Appendix H: Dermal Toxicity Estimation

In the March 2000 SAP for the implementation of probabilistic risk assessments, one question posed to the panel concerned dermal toxicity estimation. The SAP was concerned about the potential approach of applying the ratio of oral-to-dermal toxicity from mammals to birds. A limited set of data exists for evaluating the relationship between dermal toxicity and oral toxicity in birds (Table H-1). Definitive oral and dermal LD_{50}'s are available for 42 individual studies. These studies were conducted across a variety of species and several classes of chemicals.

Regression analysis was used to predict the dermal LD_{50} based on the oral LD_{50}. In addition, pesticide chemical properties were included into the regression model in an attempt to improve the model fit, similar to the approach taken by Mineau (2002). Prior to regression analysis, the dermal LD_{50} data and the oral LD_{50} data to were transformed to the log-base10 scale to better meet assumptions of normality and homogeneous variance.

In the log transformed scale, the correlation coefficient between the dermal and oral LD_{50} values was 0.55 (Figure H-1). The correlation coefficients between dermal LD_{50} and the evaluated chemical properties were much lower: -0.11, -0.03, and -0.03 for molecular weight (MW), density, and molecular volume (MV), respectively.

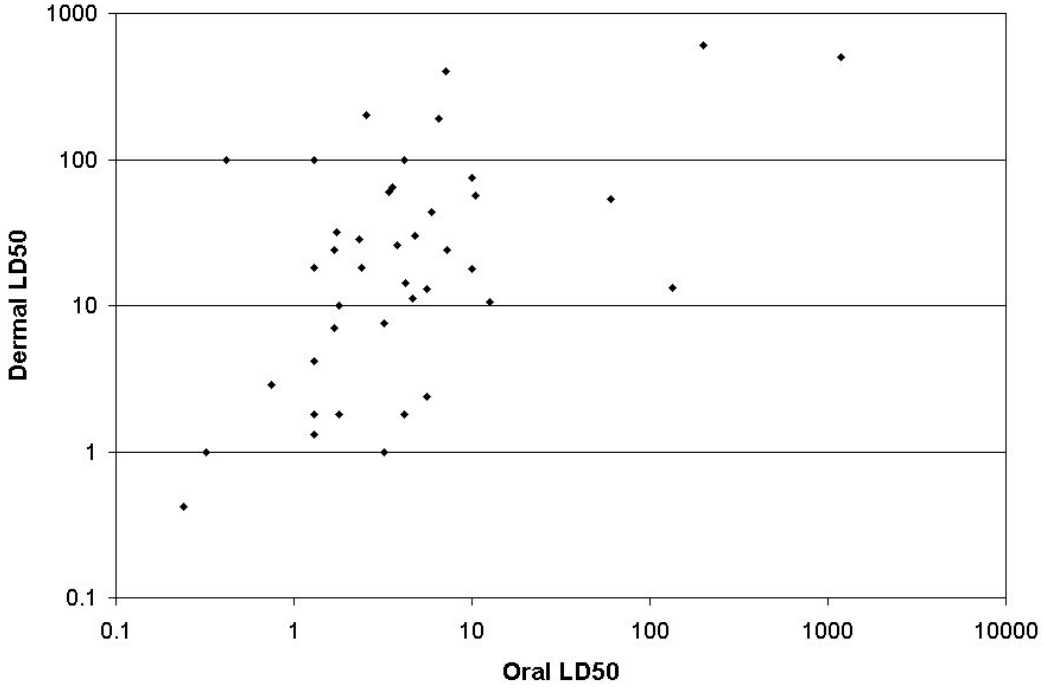

Figure H-1. Plot of dermal LD_{50} values vs. oral LD_{50} values in log-base 10 scale. The correlation coefficient was 0.55.

A summary of the evaluated regression models is provided in Table H-2. This analysis indicates that the addition of these chemical properties into the regression model do not significantly improve its predictive ability. The adjusted R-square (a modified R-square with a correction for the number of parameters included in the model) ranged between 0.2575 and 0.2857, indicating little difference in the predictive ability among the fitted models. The best fitting model to predict dermal LD_{50} was one based solely on oral LD_{50}:

$$\log DermalLD_{50} = 0.84 + 0.62 * \log OralLD_{50}$$
$$\text{standard errors: } (0.14)\ (0.15)$$

The p-value for the slope was 0.0002 and the R-square was 0.30. The chemical properties that were included did not provide significant improvement in the predictive ability of the model.

Table H-1: Raw Data from Regression Analysis of Avian Dermal LD_{50} and Oral LD_{50}

Compound	Class	Species	Oral LD50 (mg/kg)	Dermal LD50 (mg/kg)	Footnote[a]	Molecular Weight	Density	Molar Volume (mol/cm3)
Aldicarb	Carbamate	Mallard	3.4	60.0	1	190.26	1.195	159.21
Carbofuran	Carbamate	House sparrow	1.3	100.0	2	221.26	1.18	187.51
Carbofuran	Carbamate	Quelea	0.42	100.0	2	221.26	1.18	187.51
Coumaphos	OP	House sparrow	10	75.0	2	362.80	1.47	246.80
Coumaphos	OP	Quelea	3.2	7.5	2	362.80	1.47	246.80
Demeton	OP	Mallard	7.19	24	1	258.34	1.18	218.93
Demeton	OP	House sparrow	5.6	13.0	2	258.34	1.18	218.93
Demeton	OP	Quelea	1.3	1.8	2	258.34	1.18	218.93
Dicrotophos	OP	Mallard	4.24	14.2	1	237.19	1.216	195.06
Dicrotophos	OP	House sparrow	4.2	1.8	2	237.19	1.216	195.06
Dicrotophos	OP	Quelea	1.3	1.3	2	237.19	1.216	195.06
Disulfoton	OP	Mallard	6.54	192.0	1	274.39	1.144	239.85
Disulfoton	OP	Starling	133	13.3	3	274.39	1.144	239.85
Disulfoton	OP	Red-winged Blackbird	3.2	1.00	3, 4	274.39	1.144	239.85
Endrin	OChl	Mallard	5.64	>140.0[b]	1	380.93	1.7	224.08
EPN	OP	Mallard	7.09	400.0	1	323.31	1.3	248.70
Ethoprop	OP	Mallard	12.6	10.6	1	242.3	1.094	221.48
Fenamiphos	OP	Mallard	1.68	23.8	1	303.36	1.15	263.79
Fenitrothion	OP	Mallard	1190	504.0	1	277.23	1.33	208.44
Fensulfothion	OP	Mallard	0.749	2.86	1	308.35	1.202	256.53
Fensulfothion	OP	House sparrow	0.32	1.00	2	308.35	1.202	256.53
Fensulfothion	OP	Quelea	0.24	0.42	2	308.35	1.202	256.53

Compound	Class	Species	Oral LD50 (mg/kg)	Dermal LD50 (mg/kg)	Footnote[a]	Molecular Weight	Density	Molar Volume (mol/cm3)
Fenthion	OP	Mallard	5.94	44.0	1	278.32	1.25	222.66
Fenthion	OP	House sparrow	5.6	2.40	2	278.32	1.25	222.66
Fenthion	OP	Quelea	1.3	1.80	2	278.32	1.25	222.66
Methamidophos	OP	Starling	10.0	17.8	3	141.13	1.343	105.09
Methamidophos	OP	Red-winged Blackbird	1.73	31.6	3	141.13	1.343	105.09
Methiocarb	Carbamate	House sparrow	18	>100.0[b]	2	225.31	0.6	375.52
Methiocarb	Carbamate	Quelea	4.2	100.0	2	225.31	0.6	375.52
Methyl parathion	OP	Mallard	60.5	53.6	1	263.21	1.358	193.82
Mevinphos	OP	Mallard	4.63	11.1	1	224.15	1.25	179.32
Monocrotophos	OP	Mallard	4.76	30.0	1	223.17	1.3	171.67
Monocrotophos	OP	House sparrow	1.3	18.0	2	223.17	1.3	171.67
Monocrotophos	OP	Quelea	1.3	4.2	2	223.17	1.3	171.67
Paraquat Dichloride	Bipyridinium	Mallard	199	600.0	1	257.20	1.25	205.76
Parathion	OP	Mallard	2.34	28.3	1	291.26	1.267	229.88
Parathion	OP	House sparrow	1.3	1.8	2	291.26	1.267	229.88
Parathion	OP	Quelea	1.8	1.8	2	291.26	1.267	229.88
Phorate	OP	Mallard	2.55	203.0	1	260.38	1.167	223.12
Phosfolan	OP	House sparrow	2.4	18.0	2	255.28	1.3	196.37
Phosfolan	OP	Quelea	1.8	10.0	2	255.28	1.3	196.37
Phosphamidon	OP	Mallard	3.81	26.0	1	299.69	1.2132	247.02
TEPP	OP	Mallard	3.56	64.0	1	290.20	1.2	241.83
Thionazin	OP	Mallard	1.68	7.07	1	248.26	1.207	205.68

Footnotes:

1 Hudson, R.H., M.A. Haegele, and R.K. Tucker. 1979. Acute oral and percutaneous toxicity of pesticides to mallards:

Correlations with mammalian toxicity data. Toxicology and Applied Pharmacology 47:451-460.

2 Schafer, E.W., R.B Brunton, N.F. Lockyer, and J.W. DeGrazio. 1973. Comparative toxicity of seventeen pesticides to the quelea, house sparrow, and redwing blackbird. Toxicol. Appl. Pharmacol. 26:154-157.

3 Schafer, E.W. 1984. MRID 00146286

4 Schaefer, E.W. 1972. The acute oral toxicity of 369 pesticidal, pharmaceutical, and other chemicals to wild birds. Toxicol. Appl. Pharmacol. 21:315-330.

[b] Data value was censored (50% mortality not obtained at highest dose) and was not used in the statistical analysis.

Table H-2. Summary of fitted regression models to predict dermal LD_{50} from oral LD_{50} and the chemical properties molecular weight (MW), density, and molecular volume (MV).

Model	Included Dependent Variables	Adjusted R-square	Variables with p-value <0.25
1	Logoral, MW, density, MV	0.2575	Logoral
2	Logoral, MW, density	0.2678	Logoral
3	Logoral, MW, MV	0.2741	Logoral
4	Logoral, density, MV	0.2634	Logoral
5	Logoral, MW	0.2812	Logoral
6	Logoral, density	0.2762	Logoral
7	Logoral, MV	0.2677	Logoral
8	Logoral	0.2857	Logoral

Literature Cited

Mineau, Pierre. 2002 Estimating the probability of bird mortality from pesticide sprays on the basis of the field study record. Environmental Toxicology and Chemistry 21:1497-1506.