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Allometric Models for Interspecies Extrapolation of Wildlife Toxicity Data

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Toxicity data are not available for all contaminants or wildlife species that may be considered in an ecological risk assessment. Consequently, extrapolation of toxic responses observed in avian and mammalian test species to the wildlife endpoint species of interest is necessary. Allometric scaling is one commonly employed extrapolation approach. It is based on the observation that many biological properties vary directly with body weight or a power of body weight (Davidson et al. 1986), such that: $A = a(BW)^b$, where A= biological attribute, a = intercept, BW = body weight, b = allometric scaling factor. Allometric scaling factors that have been applied in toxicology include: $BW^{0.66}$ (equivalent to body surface area [Pinkel 1958]), $BW^{0.75}$ (equivalent to metabolic rate [Travis and White 1988]), and BW^1 (simple body weight scaling [Travis and White 1988]). EPA (1992) recommends the application of a 0.75 scaling factor for extrapolation of carcinogenicity data from test animals to humans. For wildlife risk assessment, Sample et al. (1996) applied scaling factors of 1 and 0.75 to avian and mammalian toxicity data, respectively. If a toxicity value for a given test species (A_t), an allometric scaling factor (b), and the body weights of the test species and a selected wildlife species (e.g., BW_t and BW_w, respectively) are known, then the unknown toxicity value for a particular wildlife species (A_w) may be estimated (Sample et al. 1996):

$$A_w = A_t \left(\frac{BW_t}{BW_w} \right)^{1-b}$$

Despite widespread use, the basis for the application of a given scaling factor is weak. The mammalian data are based primarily on Frierich et al. (1966). These data have been re-analyzed by multiple authors resulting in scaling factors of 0.66 to 0.75 (Travis and White 1988; Goddard and Krewski 1992; Travis and Morris 1992; Watanabe et al. 1992). Mineau et al. (1996) have conducted the only study on extrapolation factors in avian species, and reported variable scaling factors for 37 pesticides (primarily organophosphate and carbamate insecticides) with a mean of approximately 1.2. Previous research concerning allometric scaling of acute toxicity data has focused on anti-cancer drugs (e.g., Frierich et al. 1966) or pesticides (e.g., Mineau et al. 1996). Information concerning allometric relationships for chemicals likely to be encountered in ecological risk assessments at hazardous wastes sites (e.g., metals and other inorganics, chlorinated and non-chlorinated solvents, phthalates, etc.) are lacking. In addition, no studies have compared the allometric responses of birds and mammals for the same chemicals to determine if they differ. Therefore, the purpose of this study was to investigate the allometric relationships for acute avian and mammalian toxicity data across a wide variety of chemicals, to determine the applicability of existing allometric

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scaling factors, and to determine if allometric relationships differ between birds and mammals.

MATERIALS AND METHODS

Acute avian and mammalian toxicity values were obtained from published and unpublished studies from the Denver Wildlife Research Center, and from the NIOSH Registry of Toxic Effects of Chemical Substances (RTECS) database. Original sources cited in RTECS were obtained to verify toxicity values. Criteria for selection of data for analyses generally followed those described by Mineau et al. (1996). Data were restricted to oral exposure; other exposure routes (dermal, subcutaneous, inhalation, etc.) were excluded. Body weights of test species were obtained from each study, or from Silva and Downing (1995), Dunning (1993) or EPA (1988). Analyses were based on median values if: body weights or toxicity values were reported by sex, or LD_{50} was reported as a range. Median LD_{50} and body weights were used if multiple observations per species per chemical were obtained. LD_{50} values reported as open-ended ranges were rejected. Simple linear regression models of ln-LD_{50} (mg/animal) of each analyte on ln-body weight (kg) were developed for birds and mammals (as data permitted) where the number of species was ≥ 3. Analyses were performed using SAS PROC REG (SAS 1988). Student's t-tests were performed to determine if the slope or scaling factor (b) differed significantly from 0, 0.66, 0.75, and 1. For those chemicals for which adequate data were available, avian and mammalian regression models were compared using the F-test procedure for comparing regression lines outlined in Draper and Smith (1966). All differences were considered significant if $p \leq 10.05$.

RESULTS AND DISCUSSION

A total of 2853 acute avian and mammalian toxicity values were obtained, representing 194 and 167 chemicals, 72 and 81 species, 23 and 24 families, and nine and eight orders for birds and mammals, respectively. One hundred and thirty eight and 94 chemicals (for birds and mammals, respectively) had toxicity values for ≥ 3 species. The median number of animal species tested per chemical was six for birds and five for mammals. Mean (± SE) chemical-specific scaling factors were 1.19 ± 0.052 (range - 1.16 to 3.09) for birds and 0.94 ± 0.029 (range -0.15 to 1.69) for mammals. For most chemicals, body weight accounted for much variability in acute toxicity. Mean (± SE) r^2 values were 0.76± 0.02 for birds and 0.89± 0.02 for mammals. Allometric scaling factors, grouped by chemical categories, are presented in Table 1. Student's t-test results indicate that many chemical-specific scaling factors (b) did not differ significantly fromconventional scaling factors (e.g., 0.66, 0.75, and 1; Tables 1 and 2), with most not differing from 1. For example, chemical-specific scaling factors did not differ significantly from 1 for 57.9% of chemicals for birds and 70.2% for mammals. In contrast, 37.6% of chemicals for birds and 56.4% for mammals differed from 0.75 and 28.9% of chemicals for birds and 41.5% for mammals differed from 0.66. Among chemicals for which adequate data were available to compare models for both birds and mammals, approximately 2/3 showed no significant difference between the classes (Table 1).

Our mean avian scaling factor, which includes alkaloids, inorganics, organochlorines, and drugs, is similar to that reported by Mineau et al. (1996) for organophosphates, carbamates, and several miscellaneous pesticides. This suggests that a scaling factor of 1.2 may be appropriate for avian inter-species extrapolations for many chemicals. We found no papers with scaling information specific to mammalian wildlife, however our results suggest that

Table 1. Allometric scaling factors based on acute avian and mammal oral toxicity data for selected chemicals.

Chemical Name	CAS #	Test Species Class[1]	N	Allometric Scaling Factor (± SE)	r^2	Test Results	
						Scaling Factor[2]	Test Class[3]
ALKALOIDS							
Nicotine sulfate	65-30-5	A	11	1.555 ± 0.248	0.81	F	NA
Strychnine alkaloid	57-24-9	A	8	1.015 ± 0.206	0.80	H	NS
Strychnine alkaloid	57-24-9	M	16	1.181 ± 0.104	0.90	F	NS
Strychnine sulfate	60-41-3	A	3	1.066 ± 0.076	0.99	D	NS
Strychnine sulfate	60-41-3	M	4	0.888 ± 0.062	0.99	F	NS
CARBAMATES							
ACD 7029	14285-43-9	A	8	1.005 ± 0.422	0.49	I	NA
Aldicarb	116-06-3	A	7	1.358 ± 0.232	0.87	H	NS
Aldicarb	116-06-3	M	4	1.244 ± 0.120	0.98	A	NS
Bufencarb	8065-36-9	A	6	1.283 ± 0.575	0.55	A	NA
Carbanolate	671-04-5	A	11	1.165 ± 0.170	0.84	F	NA
Carbaryl	63-25-2	A	6	1.466 ± 0.403	0.77	A	NS
Carbaryl	63-25-2	M	8	1.041 ± 0.054	0.98	F	NS
Carbofuran	1563-66-2	A	14	1.151 ± 0.200	0.73	I	$p \leq 0.05$
Carbofuran	1563-66-2	M	3	0.879 ± 0.515	0.74	F	$p \leq 0.05$
Ethiofencarb	29973-13-5	M	4	1.686 ± 0.473	0.86	I	NS
Landrin	2686-99-9	A	12	1.030 ± 0.243	0.64	F	NS
Landrin	2686-99-9	M	4	0.971 ± 0.111	0.97	A	NS
Matacil	2032-59-9	A	4	0.624 ± 0.305	0.68	E	NA
Methiocarb	2032-65-7	A	32	1.373 ± 0.084	0.90	B	NA
Methomyl	16752-77-5	A	8	0.912 ± 0.107	0.92	H	NA
Mexacarbate	315-18-4	A	15	0.776 ± 0.148	0.68	F	$p \leq 0.05$
Mexacarbate	315-18-4	M	4	1.051 ± 0.077	0.99	H	$p \leq 0.05$
Mobam	1079-33-0	A	6	1.596 ± 0.884	0.45	A	NA
Propoxur	114-26-1	A	19	1.337 ± 0.082	0.94	F	NA
RH 908	51594-86-0	A	3	0.495 ± 0.245	0.80	F	NA
Thiram	137-26-8	M	4	0.776 ± 0.205	0.88	F	NA
Zineb	12122-67-7	A	5	1.657 ± 0.481	0.80	F	NS
Zineb	12122-67-7	M	4	0.740 ± 0.093	0.97	C	NS
DRUGS							
Allobarbital	52-43-7	A	6	0.990 ± 0.164	0.90	I	NA
Allylbarbital	77-26-9	A	7	1.003 ± 0.225	0.80	C	NA
Amethocaine	94-24-6	A	3	0.857 ± 0.409	0.81	I	NA
Butacaine sulfate	149-15-5	A	3	-0.120 ± 0.649	0.03	F	NA
Butobarbital	77-28-1	A	4	0.978 ± 0.142	0.96	C	NA
Chloral hydrate	302-17-0	M	5	0.967 ± 0.109	0.96	I	NA

Table 1. (Cont.)

Chemical Name	CAS #	Test Species Class[1]	N	Allometric Scaling Factor (± SE)	r^2	Test Results	
						Scaling Factor[2]	Test Class[3]
Indecainide		M	3	0.754 ± 0.057	0.99	A	NA
Librium	438-41-5	A	4	1.797 ± 0.307	0.94	B	NS
Librium	438-41-5	M	4	0.988 ± 0.091	0.98	A	NS
Phencyclidine HCl	956-90-1	A	14	1.133 ± 0.228	0.67	I	NA
Profundol	115-44-6	A	6	0.902 ± 0.089	0.96	H	NA
Scoline chloride	71-27-2	A	3	0.286 ± 0.352	0.40	I	NA
Sodium pentabarbital	57-33-0	A	11	0.979 ± 0.128	0.87	F	NS
Sodium pentabarbital	57-33-0	M	5	0.853 ± 0.085	0.97	F	NS
Sodium pentothal	71-73-8	A	4	1.226 ± 0.107	0.98	C	NA
Sodium probarbital	143-82-8	A	5	2.155 ± 0.456	0.88	A	NA
Sodium secanol	309-43-3	A	9	1.125 ± 0.066	0.98	B	NA
Tribromethanol	1329-86-8	A	3	1.462 ± 0.049	1.00	F	NA
Valium	439-14-5	M	4	0.820 ± 0.098	0.97	H	NA
INORGANICS							
Arsenic trioxide	1327-53-3	M	6	0.874 ± 0.130	0.92	A	NA
Arsenic acid	7778-39-4	M	3	0.491 ± 0.217	0.84	I	NA
Barium chloride	10361-37-2	M	5	0.746 ± 0.101	0.95	E	NA
Borax	1303-96-4	M	4	1.047 ± 0.131	0.97	H	NA
Cadmium	7440-43-9	M	3	0.440 ± 0.358	0.60	H	NA
Cadmium sulfate	10124-36-4	M	3	0.969 ± 0.232	0.95	I	NA
Cadmium chloride	10108-64-2	M	4	0.893 ± 0.038	1.00	F	NA
Ceresan L	8003-37-0	A	4	1.009 ± 0.129	0.97	C	NA
Ceresan-M	517-16-8	A	4	0.714 ± 0.148	0.92	I	NA
Hexamethyldistannane	661-69-8	M	4	1.282 ± 0.232	0.94	F	NA
Lithium carbonate	554-13-2	M	3	0.976 ± 0.056	1.00	F	NA
Magnesium arsenate	10103-50-1	M	3	0.023 ± 0.202	0.01	I	NA
Mercuric chloride	7487-94-7	M	5	0.983 ± 0.087	0.98	F	NA
Methyl-mercuric chloride	115-09-3	M	3	0.642 ± 0.120	0.97	A	NA
Potassium cyanide	151-50-8	M	5	0.785 ± 0.074	0.97	C	NA
Sodium arsenite	7784-46-5	A	3	2.080 ± 0.059	1.00	I	NA
Sodium cyanide	143-33-9	A	6	1.003 ± 0.227	0.83	F	NS
Sodium cyanide	143-33-9	M	4	0.796 ± 0.073	0.98	F	NS
Sodium fluoride	7681-49-4	M	7	1.018 ± 0.071	0.98	I	NA
Sodium metavanadate	13718-26-8	M	3	1.201 ± 0.033	1.00	A	NA
Sodium selenite	10102-18-8	M	7	1.013 ± 0.059	0.98	H	NA
Thallium sulfate	10031-59-1	A	3	1.326 ± 0.161	0.99	F	$p \leq 0.05$
Thallium sulfate	10031-59-1	M	6	0.808 ± 0.066	0.97	I	$p \leq 0.05$
Zinc chloride	7646-85-7	M	3	0.851 ± 0.139	0.97	E	NA

Table 1. (Cont.)

Chemical Name	CAS #	Test Species Class[1]	N	Allometric Scaling Factor (± SE)	r^2	Test Results	
						Scaling Factor[2]	Test Class[3]
Zinc phosphide	1314-84-7	A	3	-0.439 ± 0.500	0.44	F	$p \leq 0.05$
Zinc phosphide	1314-84-7	M	15	0.956 ± 0.136	0.79	H	$p \leq 0.05$
Zinc sulfate	7733-02-0	M	3	-0.154 ± 0.653	0.05	I	NA
Zinc sulfate hept	7446-20-0	M	3	0.970 ± 0.016	1.00	H	NA
ORGANOCHLORINES							
Aldrin	309-00-2	A	13	1.338 ± 0.253	0.72	I	NS
Aldrin	309-00-2	M	8	0.858 ± 0.120	0.90	E	NS
BHC	608-73-1	A	3	-1.157 ± 0.482	0.85	I	NA
BHC	608-73-1	M	4	0.855 ± 0.181	0.92	A	NA
Chlordane	57-74-9	A	3	2.492 ± 1.534	0.73	A	NS
Chlordane	57-74-9	M	7	0.829 ± 0.127	0.90	A	NS
Chlordecone	143-50-0	M	3	1.119 ± 0.340	0.92	F	NA
Dieldrin	60-57-1	A	15	1.201 ± 0.216	0.70	F	NS
Dieldrin	60-57-1	M	14	1.055 ± 0.081	0.93	A	NS
Endosulfan	115-29-7	M	6	0.563 ± 0.190	0.69	C	NA
Endrin	72-20-8	A	8	1.250 ± 0.234	0.83	I	$p \leq 0.05$
Endrin	72-20-8	M	9	0.967 ± 0.120	0.90	H	$p \leq 0.05$
Heptachlor	76-44-8	M	6	1.086 ± 0.160	0.92	F	NA
Lindane	58-89-9	A	5	1.813 ± 0.367	0.89	F	NS
Lindane	58-89-9	M	7	0.615 ± 0.144	0.78	F	NS
Methoxychlor	72-43-5	M	3	1.224 ± 0.248	0.96	I	NA
Pentachlorophenol	87-86-5	M	5	0.817 ± 0.146	0.91	F	NA
p,p,-DDT	50-29-3	M	9	1.268 ± 0.052	0.99	F	NA
Telodrin	297-78-9	A	7	1.402 ± 0.218	0.89	C	$p \leq 0.05$
Telodrin	297-78-9	M	9	0.744 ± 0.065	0.95	F	$p \leq 0.05$
Toxaphene	8001-35-2	A	7	0.928 ± 0.372	0.55	I	NS
Toxaphene	8001-35-2	M	11	1.003 ± 0.074	0.95	D	NS
TCDD	1746-01-6	M	7	0.537 ± 0.438	0.23	G	NA
ORGANOPHOSPHATES							
Acephate	30560-19-1	A	4	1.277 ± 0.246	0.93	A	NS
Acephate	30560-19-1	M	4	1.666 ± 0.351	0.92	H	NS
Allied GC-6506	3254-63-5	A	4	1.158 ± 0.079	0.99	I	NA
Azinphos methyl	86-50-0	A	5	1.854 ± 0.122	0.99	F	NS
Azinphos methyl	86-50-0	M	6	1.112 ± 0.152	0.93	C	NS
Bay 75546	7682-90-8	A	8	1.361 ± 0.153	0.93	A	NA
Bay 79845	32575-80-7	A	7	0.801 ± 0.444	0.39	A	NA
Bay 93820	24353-61-5	A	4	2.443 ± 0.936	0.77	F	NA
Bayer HOL-0574	35335-60-5	A	9	0.699 ± 0.240	0.55	F	NA

Table 1. (Cont.)

Chemical Name	CAS #	Test Species Class[1]	N	Allometric Scaling Factor (± SE)	r^2	Test Results	
						Scaling Factor[2]	Test Class[3]
Baythion	14816-18-3	A	6	1.663 ± 0.401	0.81	I	NA
Chlorofenvinphos	470-90-6	A	10	1.146 ± 0.320	0.62	I	NS
Chlorofenvinphos	470-90-6	M	6	0.901 ± 0.169	0.88	F	NS
Chlorpyrifos	2921-88-2	A	10	1.270 ± 0.144	0.91	F	$p \leq 0.05$
Chlorpyrifos	2921-88-2	M	5	1.452 ± 0.103	0.99	F	$p \leq 0.05$
Coumaphos	56-72-4	A	10	1.482 ± 0.312	0.74	I	NA
DDVP	62-73-7	A	8	0.859 ± 0.100	0.92	F	$p \leq 0.05$
DDVP	62-73-7	M	3	1.142 ± 0.033	1.00	F	$p \leq 0.05$
Demeton	8065-48-3	A	11	1.260 ± 0.187	0.84	F	NA
Diazinon	333-41-5	A	8	0.701 ± 0.405	0.33	A	$p \leq 0.05$
Diazinon	333-41-5	M	3	0.964 ± 0.006	1.00	H	$p \leq 0.05$
Dichlofenthion	97-17-6	A	6	1.298 ± 0.874	0.36	H	NA
Dicrotophos	141-66-2	A	12	1.159 ± 0.126	0.89	I	NA
Disulfoton	298-04-4	A	4	0.852 ± 0.961	0.28	E	NS
Disulfoton	298-04-4	M	3	0.554 ± 0.030	1.00	H	NS
Dowco 160	35944-82-2	A	4	3.088 ± 0.980	0.83	C	NA
EPN	2104-64-5	A	10	1.253 ± 0.200	0.83	A	NA
Ethoprop	13194-48-4	A	6	1.506 ± 0.095	0.98	A	NA
Ethyl parathion	56-38-2	A	15	1.210 ± 0.207	0.73	C	NS
Ethyl parathion	56-38-2	M	8	1.007 ± 0.190	0.82	A	NS
Fenitrothion	122-14-5	A	8	1.139 ± 0.431	0.54	C	NS
Fenitrothion	122-14-5	M	5	0.869 ± 0.314	0.72	F	NS
Fenophosphon	327-98-0	A	7	1.126 ± 0.643	0.38	F	NS
Fenophosphon	327-98-0	M	7	1.150 ± 0.169	0.90	A	NS
Fensulfothion	115-90-2	A	11	1.314 ± 0.135	0.91	C	NA
Fenthion	55-38-9	A	20	1.204 ± 0.140	0.80	C	NA
Fonofos	944-22-9	A	6	1.062 ± 0.327	0.72	F	NA
Gophacide	4104-14-7	A	6	1.241 ± 0.533	0.58	F	NS
Gophacide	4104-14-7	M	16	0.976 ± 0.106	0.86	I	NS
Malathion	121-75-5	A	3	1.053 ± 0.531	0.80	C	NS
Malathion	121-75-5	M	3	0.851 ± 0.327	0.87	I	NS
Methidathion	950-37-8	A	4	-0.316 ± 0.609	0.12	E	NA
Methyl demeton	8022-00-2	A	6	0.888 ± 0.234	0.78	H	NA
Methyl demeton R	301-12-2	A	6	0.889 ± 0.235	0.78	F	NA
Methyl parathion	298-00-0	A	4	1.007 ± 0.062	0.99	I	NS
Methyl parathion	298-00-0	M	10	0.743 ± 0.222	0.58	C	NS
Monocrotophos	919-44-8	A	13	0.994 ± 0.128	0.85	I	$p \leq 0.05$
Monocrotophos	919-44-8	M	3	1.121 ± 0.077	1.00	I	$p \leq 0.05$

Table 1. (Cont.)

Chemical Name	CAS #	Test Species Class[1]	N	Allometric Scaling Factor (± SE)	r^2	Test Results	
						Scaling Factor[2]	Test Class[3]
Nemaphos	297-97-2	A	6	0.822 ± 0.239	0.75	F	NA
Phorate	298-02-2	A	6	1.167 ± 0.456	0.62	F	NA
Phosdrin	7786-34-7	A	9	0.872 ± 0.238	0.66	I	NA
Phosphamidon	297-99-4	A	9	1.079 ± 0.159	0.87	I	$p \leq 0.05$
Phosphamidon	297-99-4	M	3	0.798 ± 0.133	0.97	H	$p \leq 0.05$
Phospholan	947-02-4	A	7	1.217 ± 0.406	0.64	A	NA
Temefos	3383-96-8	A	8	1.158 ± 0.165	0.89	F	NA
Trichlorfon	52-68-6	A	7	1.105 ± 0.177	0.89	I	NA
PHTHLALATE ESTERS							
Bis(2-ethylhexyl) phthalate	117-81-7	M	4	1.531 ± 0.290	0.93	F	NA
Diethyl phthalate	84-66-2	M	4	0.716 ± 0.236	0.83	F	NA
Di-n-butylphthalate	84-74-2	M	3	1.345 ± 0.005	1.00	I	NA
SOLVENTS							
1,1-Dichloroethylene	75-35-4	M	3	1.539 ± 0.229	0.98	C	NA
1,1,1-Trichloroethane	71-55-6	M	5	0.648 ± 0.200	0.78	H	NA
1,1,2,2-Tetrachloroethylene	127-18-4	M	5	1.050 ± 0.098	0.97	I	NA
1,2-Dichloroethane	107-06-2	M	5	0.835 ± 0.318	0.70	A	NA
Acetone	67-64-1	M	4	1.128 ± 0.053	1.00	F	NA
Benzene	71-43-2	M	3	0.818 ± 0.078	0.99	F	NA
Carbon tetrachloride	56-23-5	M	6	0.703 ± 0.132	0.88	A	NA
Chloroform	67-66-3	M	5	1.192 ± 0.043	1.00	H	NA
Ethyl acetate	141-78-6	M	3	1.047 ± 0.032	1.00	A	NA
Methanol	67-56-1	M	6	0.775 ± 0.176	0.83	I	NA
Methylene chloride	75-09-2	M	4	0.813 ± 0.202	0.89	F	NA
Trichloroethene	79-01-6	M	5	1.111 ± 0.048	0.99	E	NA
MISCELLANEOUS CHEMICALS							
2-Chloro-4-acetotoluidide	7149-79-3	A	5	2.169 ± 0.271	0.96	I	NA
2-Methoxyaniline	90-04-0	A	3	1.008 ± 0.532	0.78	F	NA
2-Nitroaniline	88-74-4	A	3	1.000 ± 0.000	1.00	I	NA
2-Pyridylamine	504-29-0	A	4	1.460 ± 0.691	0.69	F	NA
2-Pyridylmethanol	586-98-1	A	3	2.856 ± 0.771	0.93	C	NA
2-Toluidine	95-53-4	A	3	0.416 ± 0.552	0.36	A	NA
2,4-D	94-75-7	A	4	0.889 ± 0.055	0.99	A	NS
2,4-D	94-75-7	M	9	0.801 ± 0.105	0.89	A	NS
2,5-Diaminoanisole sulfate	66671-82-7	A	4	0.696 ± 0.276	0.76	F	NA
3-Chloroaniline	108-42-9	A	3	1.681 ± 0.679	0.86	H	NA
3-Chloropyridine	626-60-8	A	4	1.303 ± 0.275	0.92	A	NA
3-Cyanoaniline	2237-30-1	A	4	1.212 ± 0.332	0.87	F	NA

Table 1. (Cont.)

Chemical Name	CAS #	Test Species Class[1]	N	Allometric Scaling Factor (± SE)	r^2	Test Results	
						Scaling Factor[2]	Test Class[3]
3-Ethylaniline	587-02-0	A	3	0.756 ± 0.929	0.40	A	NA
3-Methoxyaniline	536-90-3	A	3	0.767 ± 0.130	0.97	F	NA
3-Methyl-6-chlorophenol	615-74-7	A	4	1.106 ± 0.166	0.96	A	NA
3-Methylpyridine	108-99-6	A	3	1.000 ± 0.000	1.00	F	NA
3-Methylthiobenzenamine	1783-81-9	A	3	1.233 ± 0.130	0.99	A	NA
3-Pyridyl methyl ketone	350-03-8	A	3	2.949 ± 1.923	0.70	F	NA
3-Toluidine	108-44-1	A	3	1.453 ± 0.539	0.88	H	NA
4-Acetylaminopyridine	5221-42-1	A	5	0.414 ± 0.471	0.20	A	NA
4-Acetylaniline	99-92-3	A	5	0.945 ± 0.267	0.81	I	NA
4-Amino-2-chlorotoluene	95-74-9	A	11	0.957 ± 0.591	0.23	A	NA
4-Amino-3-methylpyridine	1990-90-5	A	5	1.913 ± 0.415	0.88	A	NA
4-Aminobenzonitrile	873-74-5	A	4	1.267 ± 1.533	0.25	A	NA
4-Aminothiophenol	1193-02-8	A	4	0.878 ± 0.191	0.91	F	NA
4-Ethylaniline	589-16-2	A	4	2.089 ± 1.016	0.68	A	NA
4-Nitroaniline	100-01-6	A	3	2.827 ± 1.216	0.84	I	NA
4-Picoline 1-oxide	1003-67-4	A	3	0.630 ± 0.375	0.74	A	NA
Alpha-chloralose	15879-93-3	A	13	1.062 ± 0.127	0.86	F	$p \leq 0.05$
Alpha-chloralose	15879-93-3	M	3	1.100 ± 0.016	1.00	A	$p \leq 0.05$
Avitrol	504-24-5	A	37	0.984 ± 0.096	0.75	F	$p \leq 0.05$
Avitrol	504-24-5	M	4	0.895 ± 0.058	0.99	A	$p \leq 0.05$
Bay-COE 3664 (9CI)	39457-24-4	A	9	1.347 ± 0.146	0.92	A	NA
Bay-COE 3675	39457-25-5	A	9	1.691 ± 0.140	0.95	F	NA
Bayer 74747		M	4	0.979 ± 0.242	0.89	F	NA
Bayer 75752		M	4	1.065 ± 0.123	0.97	H	NA
Compound 1080	62-74-8	A	12	1.009 ± 0.118	0.88	C	NS
Compound 1080	62-74-8	M	61	0.752 ± 0.077	0.62	H	NS
Dowco 210	2864-61-1	A	5	1.115 ± 0.173	0.93	I	NA
EL 919	73618-59-4	A	4	1.463 ± 0.636	0.73	I	NA
Metomidate	5377-20-8	A	12	1.090 ± 0.156	0.83	I	NA
Metomidate HCl	35944-74-2	A	7	1.155 ± 0.060	0.99	F	NA
Nifluridide	61444-62-0	A	6	1.272 ± 0.604	0.53	I	NA
p-Chloraniline	106-47-8	A	4	2.310 ± 1.015	0.72	E	NA
Phenylamine	62-53-3	A	3	1.229 ± 0.137	0.99	F	NA
Phillips 2133	35944-73-1	A	7	1.274 ± 0.204	0.89	I	NA
Phillips 2605	12712-28-6	A	6	1.382 ± 0.311	0.83	C	NA
Picolinic acid	98-98-6	A	4	2.147 ± 0.508	0.90	A	NA
p-Thioanisidine	104-96-1	A	3	1.451 ± 0.662	0.83	F	NA
p-Toluidine	106-49-0	A	4	0.525 ± 1.116	0.10	I	NA

Table 1. (Cont.)

Chemical Name	CAS #	Test Species Class[1]	N	Allometric Scaling Factor (± SE)	r^2	Test Results	
						Scaling Factor[2]	Test Class[3]
RS 150	29025-67-0	A	5	2.440 ± 0.451	0.91	I	NA
Ryanicide	15662-33-6	A	6	1.054 ± 0.445	0.58	C	$p \leq 0.05$
Ryanicide	15662-33-6	M	5	0.834 ± 0.219	0.83	H	$p \leq 0.05$
SKF 10812A	37841-33-1	A	3	0.733 ± 0.083	0.99	E	NA
Starlicide	7745-89-3	A	31	0.905 ± 0.235	0.34	A	NA
T,4-Diaminobenzene	106-50-3	A	4	-0.355 ± 0.515	0.19	C	NA
Tebuthiuron	34014-18-1	M	3	0.852 ± 0.066	A	A	NA
TEPA	545-55-1	A	7	0.745 ± 0.217	C	C	NA

[1] A = avian; M = mammalian.

[2] Results of t-tests to determine if scaling factors (b) differed significantly ($p \leq 0.05$) from 0, 0.66, 0.75, and 1. A: b not different from any value; B: b different from all values but >0 and <1; C: b significantly>1; D: b not different from 0 and $b \neq 0.66$, 0.75, or 1; E: b not different from 0.66 or 0.75 and $b \neq 0$ or 1; F: b not different from 0.66, 0.75, or 1 and $b \neq 0$; G: b not different from 0.75 and $b \neq 0$, 0.66, or 1; H: b not different from 0.75 or 1 and $b \neq 0$ or 0.66; I: b not different from 1 and $b \neq 0$, 0.66, or 0.75.

[3] Results of f-test comparing avian and mammalian regression models. NA = insufficient data to compare class; NS = classes not statisically different ($p>0.05$); $p \leq 20.05$ = classes statistically different.

Table 2. Summary of t-test results to determine if scaling factors (b) differed significantly ($p<0.05$) from 0, 0.66, 0.75, and 1.

Result (H_0: b=0, 0.66, 0.75, or 1)	Percent of Chemicals	
	Birds	Mammals
b significantly different from 0 but not from 0.66, 0.75, and 1.	27.5%	31.9%
b significantly different from 0, 0.66, and 0.75 but not from 1.	21.7%	23.4%
b not significantly different from 0, 0.66, 0.75, or 1.	30%	7.4%
b significantly>l.	11%	7.4%
b significantly different from 0 or 0.66 but not 0.75 or 1.	8.7%	14.9%
b significantly different from 0 and 1 but not 0.66 or 0.75.	1.4%	9.6%
b significantly different from 0.66, 0.75, and 1 but not 0.	0.7%	1.1%
b significantly different from 0, 0.66, and 1 but not 0.75.		1.1%
b significantly different from all values but >0 and <l		3.2%

scaling factors of 0.66 or 0.75, while suitable for anti-cancer drugs, are not broadly applicable to all chemicals classes. Our results indicate that on average, a scaling factor of 0.94 is most appropriate for mammals.

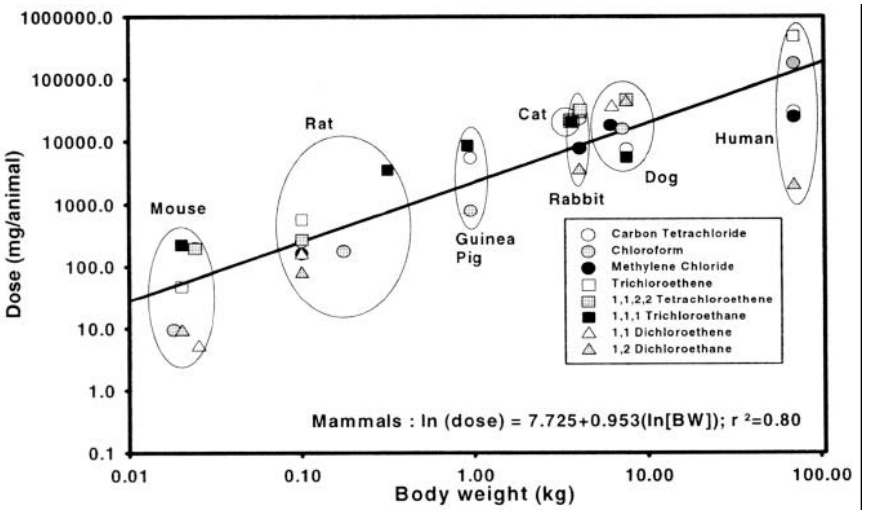

Figure 1. Scatterplot of mammalian acute toxicity data for chlorinated organics. Regression model fit to all data.

Despite preliminary results which indicate that birds and mammals have similar scaling factors for a majority of the chemicals evaluated, extrapolations between birds and mammals should be approached with extreme caution. For example, although scaling factors did not differ between classes for the majority of chemicals, we found no clear pattern for differences based on chemical categories. Our results, therefore, do not support extrapolations between classes. Similarly, Luttik and Aldenberg (1997) developed safety factors for birds and mammals based on the number of LD_{50} values available for particular chemicals and concluded that there is a real difference between birds and mammals precluding extrapolations between these two classes.

To achieve the maximal reduction in uncertainty associated with inter-species extrapolation of toxicity data, use of a chemical-specific scaling factor is recommended. Scaling factors however, are not available for all chemicals. Despite many chemical-specific scaling factors being not statistically different from 1 (Table 2), we believe that due to the variability of observed chemical-specific scaling factors, that the mean (±SE) scaling factor provides a better representation of the scaling factor for an unknown chemical and will result in toxicity estimates with lower associated uncertainties than would a default scaling factor based simply on statistical significance (e.g., a scaling factor of 1). Therefore, in the absence of a chemical-specific scaling factor, scaling factors of 1.2 and 0.94 should be used for birds and mammals, respectively. As an alternative to chemical-specific scaling or relying on mean scaling factors over many diverse chemicals, scaling based on groups of like chemicals could be employed (e.g. Fig.1). To address the limitations associated with application of a single scaling factor for all chemicals or relying on the limited number of chemicals with chemical-specific scaling factors, future work will focus on developing and evaluating scaling factors based on broader groupings (e.g., chemical classes, mode of action, and taxonomic groupings).

Finally, it should be noted that the scaling factors presented here are most appropriate for acute toxicity data. Their applicability to chronic toxicity data is unknown. The modes of action for acute and chronic effects differ for many chemicals. As a consequence, it is likely that scaling factors based on chronic toxicity data will also differ from those based on acute toxicity data. Because ecological risk assessments rely primarily on chronic toxicity data, allometric scaling factors for chronic data need to be developed to reduce the uncertainty associated with applying acute scaling factors to chronic data.

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