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Ordering birds and mammals by their sensitivity to chemical compounds: a principal component analysis of acute toxicity data.

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ABSTRACT

In this study the variation in sensitivity of birds and mammals for pesticides is analyzed. It is part of a project aimed at the development of Quantitative Species-Sensitivity Relationships (QSSRs). A statistical technique (principal component analysis) is used to detect sensitivity patterns in sets of acute toxicity data of birds and mammals. As in previous studies, patterns in compound toxicity are less complex than patterns in species sensitivity. Ranking of compounds by their over all species averaged toxicity explains around 65% of the variation in the data set. Sensitivity differences within the birds and mammals are limited. For risk assessment purposes this indicates that testing of more than one bird or mammal will have little influence on the outcome of the final assessment, due to other sources of uncertainty in the assessment procedures.

SAMENVATTING

Dit rapport maakt deel uit van een project om Quantitative Species-Sensitivity Relationships (QSSRs) te ontwikkelen. QSSRs kunnen de gevoeligheid van soorten voor chemische stoffen voorspellen. Daarvoor wordt de variatie in de gevoeligheid van soorten voor chemische stoffen bestudeerd. Voor deze studie zijn acute toxiciteitsgegevens van stoffen (pesticiden) voor vogels en zoogdieren gebruikt. Een statistische patroonherkenningstechniek, Principale Componenten Analyse, is gebruikt om patronen in de gegevens te vinden. De volgende conclusies kunnen worden getrokken. Net als in voorgaande studies kunnen de patronen in de toxiciteit van stoffen eenvoudig worden beschreven. Een ordening van stoffen van lage naar hoge toxiciteit verklaart ongeveer 65% van de totale variatie in de dataset. Voor de vogels waren fensulfothion en fenitrothion respectievelijk de meest en de minst toxische verbinding. Voor de zoogdieren waren dat respectievelijk isobenzan en carbaryl.
Patronen in de gevoeligheid van soorten zijn complexer. Meerdere componenten zijn nodig om meer dan 60% van de totale variatie te verklaren. De patronen laten zien dat soorten uit dezelfde taxonomische groep, klasse of orde, meer op elkaar te lijken, dan soorten uit verschillende groepen van hetzelfde taxonomische niveau. In het algemeen zijn vogels gevoeliger dan zoogdieren. Dit is het duidelijkst voor pesticiden die acetylcholine-esterase remmen (organofosfaten en carbamaten). Het verschil tussen vogels en zoogdieren is het kleinst voor neurotoxische stoffen. Om vogels en zoogdieren veilig te stellen voor pesticiden in het milieu, op basis van acute toxiciteitsgegevens, kan in principe volstaan worden met toetsresultaten van vogels. Als de stof neurotoxisch is, is het raadzaam tevens gebruik te maken van gegevens van zoogdieren. Een meest gevoelige soort bestaat niet. De Californische kwartel *(Cappipepla californica)* en de roodsnavel-quelea *(Quelea quelea)* zijn over het algemeen de meest gevoelige vogelsoorten en daarom geschikte toetsorganismen. Voor de zoogdieren blijven de uitspraken speculatief, omdat slechts enkele soorten vertegenwoordigd waren in de dataset. De hond *(Canis domesticus)* en de cavia *(Cavia dercella)* lijken gevoeligheidspatronen te hebben die als typisch voor zoogdieren beschouwd kunnen worden. De spreiding in soortgevoeligheid per stof was zowel bij de vogels als bij de zoogdieren klein. De Sensitivitey Ratio $_{95.5}$ zijn kleiner dan 100. De gevoeligheid van een andere soort vogel of zoogdier ligt naar verwachting binnen een factor 10. Voor risico-beoordelingsdoeleinden is het testen van meer dan 1 soort vogel of zoogdier niet nodig. Door andere bronnen van onzekerheid in de beoordelingsprocedures zal een nauwkeuriger bepaalde gevoeligheid van een soort, slechts een zeer kleine invloed op de uiteindelijke beoordeling hebben.

1 INTRODUCTION

This report describes research carried out as part of a project studying the variation in the sensitivity of species to toxicants. The object of this research is to develop Quantitative Species Sensitivity Relationships (QSSRs) which predict the sensitivity of a species to a chemical compound. The development of QSSRs may explain differences between species and this information may be used for generalization and prediction. More systematic knowledge concerning species differences may help to predict the sensitivity of untested species-compound combinations. In general no or only few toxicity data are available for species that have particular interest of environmental and nature policy makers. Estimation of the sensitivity of these 'species of concern' to compounds of interest may improve the development and evaluation of environmental management. The development of QSSRs may also help to determine the choice of appropriate species for toxicity tests and strategic choices of input data for the derivation of safe environmental concentrations. Earlier results of this project are published in Hoekstra *et al.*, 1992; Vaal *et al.*, 1993; Hoekstra *et al.*, 1994; Vaal *et al.*, in prep; Vaal *et al.*, 1994; Van der Wal *et al.*, 1995; Vaal and Hoekstra, 1994 and Karman *et al.*, in prep.

This report is based on data collected at the RIVM on toxicity of compounds (pesticides) to birds and mammals. The aim of this study is to ascertain whether certain groups of chemicals are especially toxic to specific species or groups of species. The approach chosen is similar to that in Vaal *et al.*, 1994 and Van der Wal *et al.*, 1995 where, for aquatic organisms, patterns in acute and chronic toxicity were studied respectively. A pattern recognition technique called Principal Component Analysis (PCA) is applied to the data. The results are presented primarily in graphical form.

2 METHODS

2.1 Selection of data

The data set of LD_{50}s (Lethal Dose killing 50% of the animals tested, expressed as μMOL/kg bodyweight) analyzed here was originally collected to study assessment factors for use with small samples (Luttik, in press). The original data set contained records on more species and compounds than are presented here. The data is put together as a matrix with species on the rows and compounds in the columns. Because the selected statistical method requires a matrix with few missing data, some species and compounds could not be used. In constructing the data sets species and compounds were discarded when they had less than 40% of data available. If multiple data per species-compound combination were available, the geometric mean was taken. Two LD_{50}-data sets were constructed: one for bird species and one for mammalian species.

In Tables 1 and 2 information on the species and the compounds used in this report is listed. Table 1 gives complete Latin names for the species, abbreviations used in other Tables and Figures, and information on taxonomy. The species of the order Passeriformes will be referred to as a group as passerines, similarly galliforms will be used to denote species that belong to the order Galliformes.
Table 2 lists data on the compounds such as name, abbreviation, CAS registry number, molecular weight, octanol-water partitioning coefficient and the data set in which the compound is used. The molecular weights have been used to convert the data from mg/kg bodyweight to μMOL/kg bodyweight.

2.2 Principal Component Analysis

Principal component analysis (PCA) is a multivariate statistical technique used to detect patterns in (large) data matrices. A data matrix consists of rows of objects and columns of variables. A short description of PCA is given in Vaal *et al.* (1994), while more detailed information can be found in Kowalski (1983). For the calculation of the PCAs the SIMCA program was used (Umetri, 1994). This package was selected because of its robustness when used with data sets containing missing data.
Depending on how the data in the matrix is arranged the focus of the analysis shifts. With species as objects and compounds as variables the search is for *patterns in species sensitivity*. The other way around, with compounds as objects and species as variables, PCA detects *patterns in the toxicity of compounds*.

2.3 Data transformation

Data were ^{10}log transformed. Subsequently they were multiplied with -1 to ease the interpretation of the PCA. In this way species and compounds behave so that when interpreting the graphs, a species with a similar position as a compound in the corresponding graph is sensitive for that compound. When instead of analysing species sensitivity

the focus is on compound toxicity, it is better to speak of specific toxicity of the compound for that particular species.

When analysing the matrix for *patterns in the toxicity of compounds*, data was centered and scaled. Scaling is used to ensure that all species are equally important in the resulting model. There are no objective reasons to favour some species over other species.
When analysing the matrix for *patterns in species sensitivity*, no scaling of data was used, only centering on the mean. In this way compounds with a large range in toxicity towards species are more important in determining the resulting model than compounds with a narrow range.

3 RESULTS

3.1 Birds

3.1.1 Data, descriptive statistics

For the birds the data set consists of 14 species and 25 compounds. The species include 6 passerines, 6 galliforms, a duck and a dove. All of the compounds classify as organic compounds with a specific mode of action (Class IV) according to Verhaar *et al.* (1992). Table 3 presents the matrix with the log LD_{50} per species-compound combination expressed as μMOL/kg bodyweight. The matrix contains data for 76% of the species-compound combinations. Species sensitivity, averaged over all compounds, ranges from 1.01 to 2.17 (row marked Averages). Toxicity of compounds, averaged for all species, ranges from 0.41 to 2.52 (column marked Averages). The extreme observations in the matrix are for fensulfothion and red-billed quelea (*Quelea quelea*): -0.11 and fenitrothion and mallard (*Anas platyrhynchos*): 3.79.

3.1.2 Variance and source of variation

The results of a two-way ANOVA are presented in Table 4. It shows that the major part of the variance is associated with the species ($MS=3.91$, $p<0.001$). Variance associated with the compounds is a bit less ($MS=2.28$, $p<0.001$). To improve the understanding of the relative magnitude and consistency in the variation between species and compounds the variance components were estimated for the following model:
$^{10}\log LD_{50}$ = overall mean + species contribution + compound contribution + 'remainder'.
The remainder absorbs both random variation and interactions between species and compounds; each will increase the remainder component. The method used for variance components estimation was equating the adjusted mean squares to their expectation (Graybill, 1961). The square roots of the estimated variance components are:

between species:	$\sigma_{species}$	= 0.57
between compounds:	$\sigma_{compounds}$	= 0.31
remainder:	$\sigma_{remainder}$	= 0.73

Species are a larger source of variation in this data set than the compounds are, but both are smaller than the remainder. Much of the variation that is attributed to the remainder may be due to interactions between species and compounds. This would lead to the conclusion that no single bird species from the data set consistently is the most sensitive species or the least sensitive species.

3.1.3 Patterns in bird species sensitivity

The components generated by the model are presented in Table 5. Five components make a significant contribution to the model and together they explain 62.1% of the variation. The first component is the most important explaining 27.4% of the variation with the

second component adding another 23.8% and the third less then 10%. For interpretation of the results, only the first two components will be presented as two-dimensional graphs (Figures 1 and 2). Together the first two components explain 51.2% of the variation.

When viewing Figures 1 and 2, which respectively show compound loadings and species scores of the PCA model, the following has to be considered. A central position in the plots - near the origin - usually indicates that an object (species) or a variable (compound) is not important in the model. The species and compounds in the off-center parts of the plots are most important for the interpretation. The galliforms are generally sensitive to the drins-group of compounds on the right and less sensitive for the compounds on the left like EPN, methiocarb, parathion, carbofuran, strychnine and propoxur. The passerines as a group are more sensitive to carbamates and the OP-pesticides; both groups are on the left side in the graphs. Within the group of OP-pesticides a distinction must be made. For most of the OP-pesticides the passerines are more sensitive than the galliforms. These compounds include EPN, parathion, fensulfothion and fenthion. For dimethoate and fenitrothion patterns are less clear. A similar complex pattern, but with inverted high and low sensitivities is found for mexacarbate. In the case of dimethoate, fenitrothion and mexacarbate no clear distinction between passerines and galliforms can be made regarding their sensitivity to these compounds. The mallard is very sensitive to carbamates like methiocarb and carbofuran and the neurotoxic strychnine. The sensitivity pattern of the dove resembles that of the passerines.

3.1.4 Patterns in the toxicity of compounds for birds

Analysing the birds data set in its transposed form with compounds as objects and species as variables, using centered, scaled data, two components were calculated. Neither of these two components is significant according to the rules implemented in SIMCA. As a rule of thumb principal components with a normalized Eigenvalue of 2 or more are significant for data sets consisting of over 20 objects and over 20 variables (Umetri, 1994). Judging significance by examining the normalized Eigenvalues (Table 6), it is likely that the first component is significant. This first component accounts for 62.1% of the variation.

Figures 3 and 4 show that in this analysis the first component can be regarded as a weighted average of all species sensitivities resulting in an overall toxicity for the compounds. All species are weighted about equally to calculate the average, with weights ranging from 0.20 to 0.35. Note that the origin in Figure 3 is situated on the left edge of the graph. In Figure 4 the compounds scores are ranking the compounds with the most toxic to the far right (fensulfothion, endrin and carbofuran) and the least toxic to the far left (fenitrothion and trimethacarb).

3.2 Mammals

3.2.1 Data, descriptive statistics

The mammalian data set consists of 10 species and 10 compounds. All compounds classify as Class IV, which means they have a specific mode of action (Verhaar *et al.*, 1992). Three species are artiodactyls (even-hoofed), four are rodents, one is a lagomorph (hare-like) and two are carnivores. In Table 7 the matrix with the log LD_{50} per species-compound combination expressed as μMOL/kg bodyweight is presented. The matrix has data for 73% of the species-compound combinations. Species sensitivity, averaged over all compounds, ranges from 2.21 to 3.03 (row marked Averages). Toxicity of compounds, averaged for all species, ranges from 1.08 to 3.36 (column marked Averages). Extreme observations in this matrix are: dog (*Canis domesticus*) and isobenzan: 0.59 and pig (*Sus scrofa*) and carbaryl: 3.93.

3.2.2 Variance and sources of variation

The results of a two-way ANOVA are presented in Table 8. The major part of the variance in the data set is associated with the species ($MS=4.49$, $p<0.001$). The variance associated with the compounds is less ($MS=2.59$, $p=0.014$). Variance components were computed in the same manner as for the birds data set (Graybill, 1961). The squared roots from the estimated variance components are:

between species:	$\sigma_{species}$	$= 0.70$
between compounds:	$\sigma_{compounds}$	$= 0.47$
remainder:	$\sigma_{remainder}$	$= 1.02$

As was the case with the birds data set most of the matrix variance can be related to interactions between species and compounds: a single most or least sensitive species is not likely to exist.

3.2.3 Patterns in mammalian species sensitivity

In Table 9 the results of the principal components analyses of the mammalian data set are given. Two components were calculated, but neither of these is statistically significant according to rules incorporated in the software. However since the Eigenvalues of both components do suggest importance (cf. paragraph 3.1.3.2.), the results will be discussed. The first component explains one third of the variation present in the matrix, the second component adds nearly 9%, giving a total percentage of variance explained for both axes of 42%. Figures 5 and 6 graphically depict the model. Pyriminil is the compound for which rat is the most sensitive species. This combination of species and compound is of great influence on the PCA model. Dog is most sensitive for isobenzan. Both pig and dog are unsensitive to pyriminil. Cow and sheep are most sensitive for dimethoate, while the model suggests high sensitivity for this compound for pig as well. For diquat cow is the most sensitive species. In this case the model suggests high sensitivity for diquat for both sheep and pig. Especially sensitive to DNOC is the guinea pig.

3.2.4 Patterns in the toxicity of compounds for mammals

The results of this analysis are summarized in Table 10. Two components have been calculated. Only the first component, explaining some 69% of the variance, is significant. The second component explains 10% of the variance. It has a small Eigenvalue and is of minor importance compared to the first component.

Figure 7 plots the loadings on the first and second principal component for the species. The first thing to notice is that both sheep and cow are positioned away from all the other species. In Figure 8 the scores of the compounds are shown. The most sensitive species for both dimethoate and diquat is cow, which is in accordance with Table 7 and the analysis of species sensitivity. For sheep this position is likely to be the result of being the second most sensitive species for dimethoate. Neither of these two species has data available for isobenzan and carbaryl, so there is no ground on which to explain their position based on these compounds. On the other hand this analysis predicts high toxicity of carbaryl for cow and sheep, whereas the toxicity of isobenzan is expected to be relatively low. The first axis separates the animals like cow and sheep that ruminate from the others who do not. The second component is in large part due to the combination of rat and pyriminil which behaves differently from the other species-compound combinations.

4 DISCUSSION

4.1 Birds

In the birds data set species form a larger source of variation than compounds. This is likely to be, at least in part, a result of the limited range of compounds compared with matrices of LC_{50}s and NOECs for aquatic species (Vaal *et al.*, 1994; Van der Wal *et al.*, 1995). The major difference is that all compounds have a specific mode of action (Class IV, Verhaar *et al.*, 1992). The absence of other modes of action, e.g. narcotic and reactive compounds, limits the variation between compounds. Typically compounds with a specific mode of action are more toxic than compounds with a narcotic mode of action and also have a broader distribution of species sensitivities (Vaal *et al.*, in prep.). The fact that the species are representatives of a taxonomically homogeneous group, is a further reason for less variation compared with previous data sets.

The results of the PCA-modelling can be used to estimate values for the empty cells in the matrices. The chosen method is to use the principal component model that gives the largest reduction in variance. Since the best description of the data is with the compound toxicity model, the first component of this analysis is used. Using the principal component analysis for this estimation is a crude form of QSSR. From the resulting matrix the mean log LD_{50} per compound can be calculated and also the Sensitivity Ratio ($SR_{95:5}$). For birds the $SR_{95:5}$s are given in Table 11. The $SR_{95:5}$ is a measure for the differences in sensitivity when testing the same compound with different species (Hoekstra *et al.*, 1994). Large $SR_{95:5}$s mean that a compound is highly variable in this aspect. The highest $SR_{95:5}$ calculated for the birds is 112 for fenitrothion. For comparison with the present values the highest $SR_{95:5}$ in the aquatic LC_{50}-study was 4349 for malathion and in the aquatic NOEC-study the highest was 7678 for chromium(VI). In the following text the $SR_{95:5}$s values will be discussed further.

The PCA-analysis does not present a clear picture of species sensitivity (Figures 1 and 2). The mallard (*Anas platyrhynchos*) and the passerines are most sensitive for EPN, parathion, fenthion and fensulfothion from the group of OP-pesticides and also for the neurotoxic compound strychnine and the carbamates except mexacarbate. For mexacarbate the mallard is the most sensitive species. The passerines and galliforms are similar in their sensitivity for mexacarbate. Passerines and galliforms are equally sensitive for many OP-pesticides like fenitrothion, chlorfenvinphos, temephos, dimethoate. For aldrin, dieldrin and endrin the galliforms are the most sensitive group followed by the passerines and the mallard is the least sensitive species.
Table 11 lists the mean log LD_{50}s and the $SR_{95:5}$s, calculated as described above. The log LD_{50}-values differ by 2 units between the most toxic compound fensulfothion and the least toxic compound fenitrothion. The $SR_{95:5}$s are low compared to previous studies; most are smaller than 20. For parathion in this study a $SR_{95:5}$ of 56 is calculated, in the LC_{50}-study a value of 3428 is calculated and in Vaal *et al.* (in prep.) a value of 5308 is given. For

dieldrin the respective values are 31, 433 and 951. Most of these differences in value between this and other data sets are attributable to larger taxonomic differences between the species in the other data sets. These differences are likely to be on a higher taxonomic level than that of the species. The number of species in the LC_{50}-study is not really larger than in the present study. At class level however there are ten groups instead of only one. The compound with the greatest difference in sensitivity between species is fenitrothion (112), other compounds with a relatively high sensitivity ratio are: methiocarb (81), parathion and EPN (50).
For fenitrothion the compound with the highest $SR_{95:5}$ (112) the California quail (*Callipepla californica*) is the most sensitive species and the red-billed quelea (*Quelea quelea*) is second. The quelea is also among the most sensitive species for most other compounds. Based on the principal component analysis and considering the Sensitivity Ratios the California quail and the red-billed quelea would be good choices for routine testing. Other species with different sensitivity patterns that would add to our knowledge of the patterns in species sensitivity are the mallard and the chicken (*Gallus gallus*).
For the compounds the first principal component is a measure of general compound toxicity based on observations on bird species (Figures 3 and 4). For the purpose of predicting the toxicity of a compound for a bird , no clues can be derived from its toxicological mode of action. No relation is present between the sensitivity ratio and either the mean log LD_{50} or the mode of action. Of the three groups of toxicological action represented by more than one compound -organophosphates, carbamates and neurotoxicants- no group shows a systematically higher or lower toxicity. Of each group a compound is among the three most toxic compounds as well as the three least toxic compounds (Table 11). When we combine the conclusions from the species sensitivity analysis and the compound toxicity analysis California quail would be the best choice for either drins-like compounds or OP-pesticides, while quelea should be favoured when testing carbamates or OP-pesticides.

4.2 Mammals

Sensitivity of mammalian species as analyzed using PCA yields a picture as presented in Figures 5 and 6. Cow (*Bos taurus*) is the most sensitive for diquat and is expected to be sensitive to dimethoate. Sheep (*Ovis aries*) and pig (*Sus scrofa*) are most sensitive for dimethoate and are expected to be sensitive to diquat. The rodents, especially rat (*Rattus norvegicus*), are sensitive for pyriminil and DNOC. Pig is one of the least sensitive for these two compounds and for DNOC sheep is also insensitive. For both pyriminil and DNOC cow is expected to be similar in sensitivity to pig and sheep. The patterns in species sensitivity for diquat and dimethoate on the one hand and pyriminil and DNOC on the other seem mirror images of each other. Dog (*Canis domesticus*) is the most sensitive species for isobenzan. Least sensitive for this compound are the rodents.
Mammalian species are very sensitive to isobenzan, it is on average the most toxic compound in Table 12, which lists mean log LD_{50}s and $SR_{95:5}$s. The least toxic compound is carbaryl. It is observed that the three most toxic compounds, isobenzan, dieldrin and

toxaphene, are all neurotoxicants, indicating that mammals are very sensitive for compounds with this mode of action. Noteworthy is the small $SR_{95:5}$ of dieldrin: 3. It is the lowest SR for a compound calculated with the mammalian data. This suggests dieldrin will be equally toxic to other mammals. Comparison with $SR_{95:5}$s for dieldrin calculated from other data sets shows this value to be low. In the birds data set (this report), the aquatic LC_{50} data (Vaal *et al.* , 1994) and the sensitivity ratio data (Vaal *et al.*, in prep.) dieldrin showed intermediate sensitivity ratios within each data set, with values of 31, 433 and 951 respectively. For PCP the following $SR_{95:5}$s were calculated: 8 (this study), 468 (Vaal *et al.*, 1994), 107 (Van der Wal *et al.*, 1995) and 143 (Vaal *et al.*, in prep.). The presence of several classes results in considerably larger values for the sensitivity ratio calculated from previous data sets, as opposed to small values and only one class in the present study. Compounds with a large $SR_{95:5}$, considering the small number of species involved, are isobenzan (82) and pyriminil (86). These compounds are important in defining the model.

When the analysis is focused on compound toxicity, most species receive a considerable loading on the first component (Figure 7 and 8). They are sensitive for isobenzan and not sensitive for carbaryl and dimethoate. A low weight is given to sheep and cow on the first component of this PCA. Both species show untypical behaviour in the compounds for which they are sensitive. Isobenzan is the most toxic compound for all species involved. It is positioned to the far right in Figure 8 and so are most of the species in Figure 7. As can be seen in both Figure 8 and in Table 12 the three most toxic compounds for mammals are neurotoxicants. Among these three the relatively low hydrophobicity of isobenzan accentuates the high toxicity of this compound. The two least toxic compounds are dimethoate and carbaryl, both AcetylCholine-esterase inhibitors. The range between the most toxic and the least toxic compound spans nearly two orders of magnitude. A difference in the sensitivity of mammals for neurotoxicants (sensitive) and their sensitivity for AChE-inhibitors of both the organophosphates and carbamate types (insensitive) appears to exist. When taking the influence of hydrophobicity (as measured by the log *Kow*) into account, the low toxicity of carbaryl is even more exceptional. For dimethoate with low hydrophobicity low toxicity is less deviating from the expectations. In previous studies a comparison of relative toxicity between compounds was made based on the difference between observed toxicity and estimated baseline toxicity as predicted by log *Kow*. Here this comparison cannot be made, since data for estimating baseline toxicity is lacking.

When choosing mammalian species for use as testorganisms the results suggest that cow, sheep and pig are not typical in their sensitivity for toxic compounds. Similarly the pattern for the rat seems aberrant with a high sensitivity for pyriminil. As mammalian test organisms the dog and the guinea pig (*Cavia dorcella*) could be good candidates. Both species are important in defining the model and appear to have a pattern of sensitivity that does not deviate strongly from that of other mammals.

Generalizing the results to an advice for using a particular species for testing a particular compound is not possible at present. The following reasons preclude this generalization: small amount of available data; no clear patterns; small among-species-differences.

4.3 Comparison of sensitivity patterns of birds and mammals

Comparing the values of the $SR_{95:5}$ from this study with those of previous studies (Vaal *et al.*, 1994, Van der Wal *et al.*, 1995, Vaal *et al.*, in prep.) poses problems. The limitation of species to only one taxonomic group makes the values incomparable. Further the number of compounds present in more than one of the data sets is very small. A pattern of large sensitivity ratios combining with high toxicity as observed with the NOEC and LC_{50} data sets for class 4 compounds is not present. Also absent is a relation between toxicological mode of action of class 4 compounds and the sensitivity ratios as observed with aquatic species in Vaal *et al.* (in prep.).

It is clear that no single species can be regarded as 'the most sensitive species'. Mammals and birds as a group have no single group member that is consistently the most sensitive. The species that is the most sensitive, changes with the compound. When planning a test, the results presented here can be used to select a species expected to be sensitive for the test-compound. For birds the California quail (*Callipepla californica*) and the red-billed quelea (*Quelea quelea*) are the most appropriate choices. For the mammals a similar conclusion cannot be made because of insufficient data. Certainty on the appropriateness of the suggested selection of species does not exist. Testing of more than one species from within a class is not necessary since the within-class-differences are small compared to experimental variation. There is even less need for testing several species from within the same order, as at this lower hierarchical taxonomic level the expected among-species-difference is smaller yet.

When comparing values of the $SR_{95:5}$ between the birds and the mammals there is evidence that within each class the magnitude of the differences in sensitivity is similar. Between the classes there is a clear difference in sensitivity as judged by average LD_{50}s. This is also concluded from a principal component analysis of a combined data set of birds and mammals (not presented here). As a group the mammals are less sensitive than the birds. This finding is as expected. From a comparison of Tables 11 and 12, it can be learned that the mammals are particularly sensitive for neurotoxic compounds and that for such compounds the sensitivity of mammals is only slightly lower than that of birds. Therefore it would be prudent that risk assessment procedures involving neurotoxic compounds use data on both groups, birds and mammals. For compounds other than neurotoxicants the assumption that mammals will be sufficiently protected if and when the birds are, seems valid.

On the point of risk assessment indications have been found that other bird species can be more sensitive for some compounds or groups of compounds than those in the present set. An example of this has been found with an earlier version of the birds data set which included the American sparrowhawk (*Falco sparverius*). This species is similar in its sensitivity pattern to the passerines for most compounds, but more sensitive for OP-

insecticides. Traas *et al.* (submitted) report similar findings regarding higher sensitivity for OP-insecticides for raptorial birds, like the American sparrowhawk.

When species behave differently regarding their sensitivity to toxic compounds in a PCA model, testing of several species makes sense. However within the birds as a group the most and the least sensitive species differ by less than a factor 100 (or 2 units on log scale) for the same compound. For the mammals this range usually is even smaller with a factor of 10 (or 1 unit on log scale) or less. This can be seen in Tables 11 and 12 where the majority of sensitivity ratios lies below a hundred. This value means that test results of other group members are likely to be within a factor 10 of the first.
For the purpose of risk assessment the above may be a good reason to test no more than one species out of each class. This goes even stronger for orders. Especially when considering that besides experimental variation other sources of uncertainty in assessing environmental risks, like e.g. exposure in the field, secondary poisoning and multi-stress effects, also play their roles. Knowing the sensitivity of a related group of species with more precision, will have little influence on the final outcome of risk assessment procedures.

5 CONCLUSIONS

From the principal component analyses of patterns in species sensitivity and patterns in the toxicity of compounds for the birds and mammals data sets presented in this report the following conclusions can be drawn.

As in previous pattern analyses the first component is a weighted average of species sensitivities, resulting in a ordering of compounds according to their general toxicity. The first component commonly explains around 65 percent of the total variance. Species sensitivity gives patterns in two or more dimensions. Patterns in species sensitivity show that there is a tendency of species belonging to the same taxonomic group - either class or order - to be more alike than species that belong to different groups of the same taxonomic level. What mechanism lies behind this similarity, e.g. similar ecological characteristics or physiological traits, is a topic for further research and discussion. With patterns in species sensitivity the first components of the analyses presented in this study explained around 30 percent of total variance.

It is clear that no single species can be regarded as 'the most sensitive species'. With the compound the most sensitive species changes. Birds tend to be more sensitive for pesticides than mammals. This difference in sensitivity is clearest for pesticides with a acetylcholine-esterase inhibiting mode of action, like the organophosphates and the carbamates. The difference between birds and mammals is smallest for neurotoxicants like the drinses and e.g. lindane. When aiming to safeguard both birds and mammals against the adverse effects of pesticides in the environment, on base of acute toxicity data, it could be sufficient to use test results for bird species only. If the compound in question is neurotoxic, it is advisable to use test results from mammals as well.

Within a group of species, a class or an order, not all species are equally sensitive. If sensitivity to toxic compounds is a desirable criterion for the selection of test organisms appropriate choices are California quail (*Callipepla californica*) and red-billed quelea (*Quelea quelea*). California quail is most sensitive for compounds like the drinses and is sensitive for organophosphate pesticides. Quelea is sensitive for carbamate-type pesticides and organophosphate pesticides.
For mammalian species the results need to be more tentative, because only a few species were represented in the data set. From the species in the data set it appears that the dog (*Canis domesticus*) and the guinea pig (*Cavia dorcella*) have patterns of sensitivity that can be regarded as typical for a mammal.

The range of variation in sensitivity for a single compound is small within a group of taxonomically related species like the birds or the mammals. The majority of calculated Sensitivity $Ratio_{95:5}$s is less than 100. This signifies that the sensitivity of other class members is likely to within a factor 10. For risk assessment procedures it indicates that

testing of more than one species from a class is therefore unnecessary. Knowing the sensitivity of a related group of species with more precision, will have little influence on the final outcome of risk assessment procedures.

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TABLE 1 Species and taxonomic groups used in the analyses.

Common name	Species name	Class	Order	Abbreviation
Mallard	*Anas platyrhynchos*	Aves	Anseriformes	Mallard
Rock Dove	*Columba livia*	Aves	Columbiformes	Dove
Rock Partridge	*Alectoris graeca*	Aves	Galliformes	Partridge
California Quail	*Callipepla californica*	Aves	Galliformes	C Quail
Bobwhite	*Colinus virginianus*	Aves	Galliformes	Bobwhite
Japanese Quail	*Coturnix coturnix*	Aves	Galliformes	J Quail
Chicken	*Gallus gallus*	Aves	Galliformes	Chicken
Common Pheasant	*Phasianus colchicus*	Aves	Galliformes	Pheasant
House Finch	*Carpodacus mexicanus*	Aves	Passeriformes	Finch
Red-winged Blackbird	*Agelaius phoeniceus*	Aves	Passeriformes	Blackbird
Common Grackle	*Quiscalus quiscula*	Aves	Passeriformes	Grackle
House Sparrow	*Passer domesticus*	Aves	Passeriformes	Sparrow
Red-billed Quelea	*Quelea quelea*	Aves	Passeriformes	Quelea
Starling	*Sturnus vulgaris*	Aves	Passeriformes	Starling
Sheep	*Ovis aries*	Mammalia	Artiodactyla	Sheep
Cow	*Bos taurus*	Mammalia	Artiodactyla	Cow
Pig	*Sus scrofa*	Mammalia	Artiodactyla	Pig
Dog	*Canis domesticus*	Mammalia	Carnivora	Dog
Cat	*Felis domesticus*	Mammalia	Carnivora	Cat
Rabbit	*Oryctolagus cuniculus*	Mammalia	Lagomorpha	Rabbit
Hamster	*Cricetus cricetus*	Mammalia	Rodentia	Hamster
Mouse	*Mus domesticus*	Mammalia	Rodentia	Mouse
Rat	*Rattus norvegicus*	Mammalia	Rodentia	Rat.
Guinea Pig	*Cavia dorcella*	Mammalia	Rodentia	Guinea pig

TABLE 2 Compounds and chemical classes used in the analyses.

Compound name	CAS-nr	Molecular Weight	Toxicological Mechanism	log *Kow* *	Abbreviation	Data set [1]
Aldicarb	116063	190.3	AChE-inh. carbamate	1.13	Aldicarb	b
Carbaryl	63252	201.2	AChE-inh. carbamate	2.36	Carbaryl	m
Carbofuran	1563662	221.3	AChE-inh. carbamate	2.32	Carbofuran	b
Methiocarb	2032657	225.3	AChE-inh. carbamate	2.92	Methiocarb	b
Methomyl	16752775	162.2	AChE-inh. carbamate	0.60	Methomyl	b
Mexacarbate	315184	222.3	AChE-inh. carbamate	1.39 °	Mexacarbate	b
Propoxur	114261	209.3	AChE-inh. carbamate	1.52	Propoxur	b
Trimethacarb	12407862	193.3	AChE-inh. carbamate	2.66	Trimethacarb	b
Chlorfenvinphos	470906	359.5	AChE-inh. organophosphate	3.82	Chlorfenvinphos	b
Chlorpyrifos	2921882	350.6	AChE-inh. organophosphate	5.27	Chlorpyrifos	b
Dicrotophos	141662	237.2	AChE-inh. organophosphate	0.00	Dicrotophos	b
Dimethoate	60515	229.3	AChE-inh. organophosphate	0.78	Dimethoate	b, m
EPN	2104645	323.3	AChE-inh. organophosphate	4.57 °	EPN	b
Fenitrothion	122145	277.2	AChE-inh. organophosphate	3.30	Fenitrothion	b
Fensulfothion	115902	308.4	AChE-inh. organophosphate	2.23	Fensulfothion	b
Fenthion	55389	278.3	AChE-inh. organophosphate	4.09	Fenthion	b
Mevinphos	7786347	224.2	AChE-inh. organophosphate	1.20	Mevinphos	b
Monocrotophos	6923224	223.2	AChE-inh. organophosphate	-0.20	Monocrotophos	b
Parathion	56382	291.3	AChE-inh. organophosphate	3.83	Parathion	b
Phosphamidon	13171216	299.7	AChE-inh. organophosphate	1.74 °	Phosphamidon	b
Temephos	3383968	466.5	AChE-inh. organophosphate	5.96	Temephos	b
Aldrin	309002	364.9	neurotoxic (cyclodiene)	6.50	Aldrin	b
Dieldrin	60571	380.9	neurotoxic (cyclodiene)	5.20	Dieldrin	b, m
Endrin	72208	380.9	neurotoxic (cyclodiene)	5.20	Endrin	b
Isobenzan	297789	411.8	neurotoxic (cyclodiene)	3.70 °	Isobenzan	m
Toxaphene	8001352	413.8	neurotoxic (cyclodiene)	4.33 °	Toxaphene	b, m
Strychnine	57249	334.3	neurotoxic (strychnine)	1.93	Strychnine	b
Diquat	85007	344.1	Pesticide	-0.36	Diquat	m
Paraquat	1910425	257.1	Pesticide	4.19	Paraquat	m
Pyriminil	53558251	272.3	Pesticide	1.76 °	Pyriminil	m
Dinitro-o-cresol	534521	198.1	Uncoupler of oxidation	2.13	DNOC	m
Pentachlorophenol	87865	266.3	Uncoupler of oxidation	2.14	PCP	m

* : log Kow, experimental value from Thor database (Leo and Weininger, 1989)

° : log Kow, ClogP calculated value from Thor database

[1] : b = birds, m = mammals

TABLE 3 Matrix of Birds data set, mean log LD_{50} (μmol/kg bodyweight) per species-compound combination, overall mean, standard deviation and percentage of matrix fill per species and per compound.

LD50 as log(µmol/kg bodyweight) Species	Mallard	Dove	Partridge	C Quail	Bobwhite	J Quail	Chicken	Pheasant	Finch	Blackbird	Grackle	Sparrow	Quelea	Starling	Average	St.dev.	n = 14	% avail. data
Compound																		
Aldicarb	1,29	1,22	-	1,26	1,46	1,35	1,67	2,18	-	0,98	0,60	0,95	-	1,35	1,30	0,41	11	78,6%
Carbofuran	0,32	0,78	-	-	1,51	0,95	1,92	1,27	0,53	0,65	0,97	0,89	0,34	1,40	0,96	0,49	12	85,7%
Methiocarb	0,89	1,93	-	2,03	1,98	1,60	2,90	2,91	1,07	1,53	1,65	1,90	1,32	1,94	1,82	0,60	13	92,9%
Methomyl	1,98	1,79	-	-	-	2,16	2,24	1,97	-	1,79	2,04	2,10	-	2,16	2,03	0,16	9	64,3%
Mexacarbate	1,13	1,43	1,37	-	-	1,09	-	1,31	-	1,71	1,53	1,94	-	2,09	1,51	0,34	9	64,3%
Propoxur	1,78	2,01	2,06	2,09	2,09	2,22	3,20	1,88	1,40	1,26	1,80	1,82	1,54	1,86	1,93	0,46	14	100,0%
Trimethacarb	2,06	2,94	2,49	-	-	2,56	-	2,43	-	1,96	-	2,38	-	-	2,40	0,32	7	50,0%
Chlorfenvinphos	2,38	1,61	-	-	-	2,33	2,21	2,36	1,82	1,50	1,69	1,57	1,56	1,38	1,86	0,39	11	78,6%
Chlorpyrifos	2,32	1,67	2,24	2,29	2,14	1,65	2,02	1,54	-	1,58	1,39	1,62	1,66	1,74	1,83	0,32	13	92,9%
Dicrotophos	1,25	1,06	1,61	0,90	-	1,38	-	1,13	1,08	0,73	0,88	1,18	0,77	1,34	1,11	0,26	12	85,7%
Dimethoate	2,31	-	-	-	1,64	2,65	2,33	1,88	-	1,67	-	-	-	2,14	2,09	0,38	7	50,0%
EPN	1,16	1,19	1,65	2,05	2,41	1,35	-	2,46	-	0,99	1,12	1,23	-	1,37	1,54	0,53	11	78,6%
Fenitrothion	3,79	-	-	-	2,00	2,54	3,26	2,20	3,06	1,88	-	3,06	1,84	1,60	2,52	0,73	10	71,4%
Fensulfothion	0,39	0,26	-	0,66	1,04	0,76	0,87	0,64	-	-0,06	0,13	0,02	-0,11	0,26	0,41	0,38	12	85,7%
Fenthion	1,12	1,01	1,97	1,73	1,20	1,69	2,05	1,81	1,62	0,90	1,31	1,38	0,82	1,54	1,44	0,39	14	100,0%
Mevinphos	1,32	-	-	-	1,27	2,02	1,53	0,79	-	0,90	1,27	0,90	0,80	1,38	1,22	0,39	10	71,4%
Monocrotophos	1,33	1,19	1,46	0,53	0,59	1,25	-	1,10	1,80	0,65	1,28	0,82	0,66	1,24	1,07	0,39	13	92,9%
Parathion	0,78	0,80	1,92	1,76	1,43	1,23	-	1,77	0,91	0,91	1,29	0,86	0,97	2,43	1,31	0,52	13	92,9%
Phosphamidon	1,10	1,15	1,60	-	-	1,24	1,48	1,15	-	0,90	1,27	1,02	-	1,27	1,22	0,21	10	71,4%
Temephos	2,43	2,03	2,74	1,61	-	2,23	2,96	1,85	2,08	2,02	-	1,85	-	2,27	2,19	0,40	11	78,6%
Aldrin	3,15	2,18	-	-	1,26	2,06	1,84	1,66	-	1,81	1,31	1,49	-	1,42	1,82	0,56	10	71,4%
Dieldrin	3,00	2,18	1,80	1,36	-	2,21	1,90	2,32	-	1,67	2,04	1,82	-	2,79	2,10	0,48	11	78,6%
Endrin	1,18	1,00	-	0,49	-	1,04	-	0,67	-	0,79	0,54	0,74	-	0,86	0,81	0,23	9	64,3%
Toxaphene	2,05	2,73	-	1,76	2,32	2,33	2,53	1,99	-	-	-	-	-	-	2,24	0,33	7	50,0%
Strychnine	0,94	1,80	1,68	2,53	-	1,83	-	1,63	-	-	-	1,18	-	-	1,66	0,51	7	50,0%
Average	1,66	1,54	1,89	1,54	1,62	1,75	2,17	1,72	1,54	1,25	1,27	1,42	1,01	1,63	1,58	0,41	266	
St.dev.	0,87	0,66	0,40	0,65	0,52	0,56	0,65	0,59	0,72	0,54	0,50	0,65	0,58	0,56	0,60	0,66		
n = 25	25	22	13	15	15	25	17	25	10	23	19	23	12	22	266		350	
% avail. data	100,0%	88,0%	52,0%	60,0%	60,0%	100,0%	68,0%	100,0%	40,0%	92,0%	76,0%	92,0%	48,0%	88,0%				76,0%

TABLE 4 Analysis of variance for Birds data set, species and compounds as sources of variation

Source of Variation	SS	df	MS	F	P-value	F crit
Compounds	54.68	24	2.28	4.24	<0.001	1.55
Species	50.79	13	3.91	7.26	<0.001	1.75
Error	167.80	312	0.54			
Total	273.27	349				

TABLE 5 Analysis of patterns in species sensitivity for Birds data set, description of principal components, unscaled centered data.

Component	SS expl. [1]	Total SS expl.	Variance expl.	Total Variance expl.	Normalized Eigen value	Residual matrix variance	Significant [2]
1	38.6%	38.6%	27.4%	27.4%	5.40	0.13	Yes
2	27.2%	65.8%	23.8%	51.2%	3.81	0.09	Yes
3	9.2%	75.0%	4.5%	55.7%	1.29	0.08	Yes
4	7.4%	82.4%	3.9%	59.6%	1.03	0.08	Yes
5	5.7%	88.1%	2.5%	62.1%	0.79	0.07	Yes

[1] : SS expl. = percentage Sum of Squares explained.

[2] : Significance of the principal components at the 5% confidence level is based on SIMCA cross validation rules (Umetri, 1992)

TABLE 6 Analysis of patterns in compound toxicity for Birds data set, description of principal components, scaled centered data.

Component	SS expl. [1]	Total SS expl.	Variance expl.	Total Variance expl.	Normalized Eigen value	Residual matrix variance	Significant [2]
1	67.7%	67.7%	62.1%	62.1%	9.48	0.38	No
2	12.0%	79.7%	9.4%	71.6%	1.68	0.28	No

[1] : SS expl. = percentage Sum of Squares explained.

[2] : Significance of the principal components at the 5% confidence level is based on SIMCA cross validation rules (Umetri, 1992)

TABLE 7 Matrix of Mammals data set, mean log LD_{50} (μmol/kg bodyweight) per species-compound combination, overall mean, standard deviation and percentage of matrix fill per species and per compound.

LD50 as log(µmol/kg bodyweight)	Species																
Compound	Sheep	Cow	Pig	Dog	Cat	Rabbit	Hamster	Mouse	Rat	Guinea pig	Average	St.dev.	n = 10	% avail. data			
Carbaryl	-	-	3,93	3,35	2,94	3,55	-	3,22	3,39	3,14	3,36	0,32	7	70,0%			
Dimethoate	2,54	2,48	-	3,16	2,64	3,27	2,90	2,74	3,04	3,31	2,90	0,31	9	90,0%			
Dieldrin	2,20	-	2,20	2,33	-	2,09	-	2,20	2,18	1,96	2,17	0,11	7	70,0%			
Isobenzan	-	-	-	0,59	1,08	0,99	1,41	1,39	1,29	0,78	1,08	0,31	7	70,0%			
Toxaphene	2,38	2,08	-	1,87	1,99	2,14	2,68	2,25	2,41	2,71	2,28	0,29	9	90,0%			
Diquat	-	1,97	-	2,66	-	2,65	-	2,63	2,99	2,46	2,56	0,34	6	60,0%			
Paraquat	2,38	2,31	-	2,13	2,20	2,69	-	2,78	2,69	2,07	2,41	0,28	8	80,0%			
Pyriminil	-	-	3,26	3,26	2,36	3,04	-	2,52	1,41	2,31	2,60	0,66	7	70,0%			
DNOC	3,00	-	2,70	-	2,40	2,08	-	2,38	2,28	2,06	2,42	0,34	7	70,0%			
PCP	-	-	-	2,57	-	2,74	2,81	2,65	2,67	2,57	2,67	0,09	6	60,0%			
Average	2,50	2,21	3,03	2,44	2,23	2,52	2,45	2,48	2,44	2,34	2,45	0,31	73				
St.dev.	0,31	0,23	0,74	0,86	0,59	0,73	0,70	0,48	0,68	0,71	0,60	0,64					
n = 10	5	4	4	9	7	10	4	10	10	10	73		100				
% avail. data	50,0%	40,0%	40,0%	90,0%	70,0%	100,0%	40,0%	100,0%	100,0%	100,0%				73,0%			

TABLE 8 Analysis of variance for Mammals data set, species and compounds as sources of variation

Source of Variation	SS	df	MS	F	P-value	F crit
Compounds	23.35	9	2.59	2.52	0.014	2.00
Species	40.40	9	4.49	4.35	<0.001	2.00
Error	83.55	81	1.03			
Total	147.31	99				

TABLE 9 Analysis of patterns in species sensitivity for Mammals data set, description of principal components, unscaled centered data.

Component	SS expl. [1]	Total SS expl.	Variance expl.	Total Variance expl.	Normalized Eigen value	Residual matrix variance	Significant [2]
1	52.5%	52.5%	33.5%	33.5%	5.25	0.08	No
2	21.0%	73.4%	8.8%	42.3%	2.10	0.07	No

[1] : SS expl. = percentage Sum of Squares explained.

[2] : Significance of the principal components at the 5% confidence level is based on SIMCA cross validation rules (Umetri, 1992)

TABLE 10 Analysis of patterns in compound toxicity for Mammals data set, description of principal components, scaled centered data.

Component	SS expl. [1]	Total SS expl.	Variance expl.	Total Variance expl.	Normalized Eigen value	Residual matrix variance	Significant [2]
1	77.6%	77.6%	68.7%	68.7%	7.76	0.31	Yes
2	12.6%	90.3%	10.2%	78.9%	1.26	0.21	No

[1] : SS expl. = percentage Sum of Squares explained.

[2] : Significance of the principal components at the 5% confidence level is based on SIMCA cross validation rules (Umetri, 1992)

TABLE 11 Ordering of compounds by their toxicity to species and their Sensitivity Ratio's, Birds data set, centered data.

Compound	log LD_{50} [1]	$SR_{95:5}$ [2]
Fensulfothion	0.44	19
Endrin	0.89	13
Carbofuran	1.00	35
Monocrotophos	1.12	22
Dicrotophos	1.17	10
Phosphamidon	1.18	6
Mevinphos	1.25	14
Aldicarb	1.27	22
Parathion	1.36	56
Fenthion	1.44	20 [3]
Mexacarbate	1.52	15
EPN	1.53	50
Strychnine	1.58	27
Aldrin	1.78	44
Chlorpyrifos	1.83	10
Methiocarb	1.84	81
Chlorfenvinphos	1.87	14
Propoxur	1.93	32 [3]
Methomyl	1.98	5
Dimethoate	2.00	12
Dieldrin	2.04	31
Temephos	2.11	20 [3]
Toxaphene	2.11	11
Trimethacarb	2.33	13
Fenitrothion	2.49	112

[1] Mean LD_{50} (µmol kg/bodyweight), missing species-compounds combinations estimated by first component of Compounds PC model

[2] Sensitivity ratio 95% percentile:5% percentile of the distribution of LD_{50}s over all species (Hoekstra *et al.*, 1994). $SR_{95:5}$ calculated assuming log-normal distribution of data. $SR_{95:5}$ based on same data as mean log LD_{50}

[3] Distribution of data significantly different from log-normal distribution (α=0.05).

TABLE 12 Ordering of compounds by their toxicity to species and their Sensitivity Ratio's, Mammals data set, centered data.

Compound	log LD_{50} [1]	$SR_{95:5}$ [2]
Isobenzan	1.34	82
Dieldrin	2.14	3
Toxaphene	2.30	12
DNOC	2.37	10
Paraquat	2.48	14
Pyriminil	2.54	86
Diquat	2.60	14
PCP	2.63	8 [3]
Dimethoate	2.99	23
Carbaryl	3.16	41

[1] Mean LD_{50} (µmol kg/bodyweight), missing species-compounds combinations estimated by first component of Compounds PC model

[2] Sensitivity ratio 95% percentile:5% percentile of the distribution of LD_{50}s over all species (Hoekstra *et al.*, 1994). $SR_{95:5}$ calculated assuming log-normal distribution of data. $SR_{95:5}$ based on same data as mean log LD_{50}

[3] Distribution of data significantly different from log-normal distribution (α=0.05).

FIGURE 1 Loadings of compounds that determine patterns in species sensitivity, Birds data set, centered data.

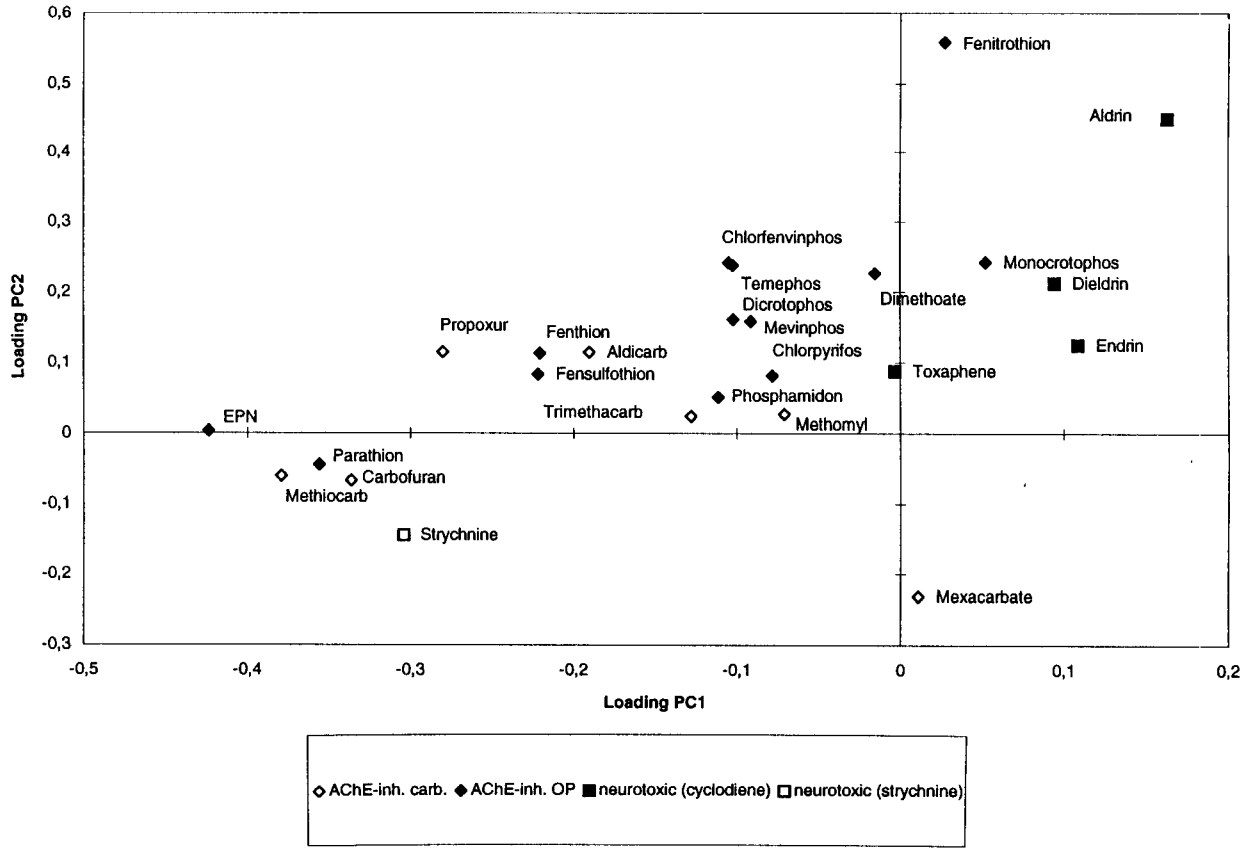


FIGURE 2 Patterns in species sensitivity, plot of scores of species, Birds data set, centered data.

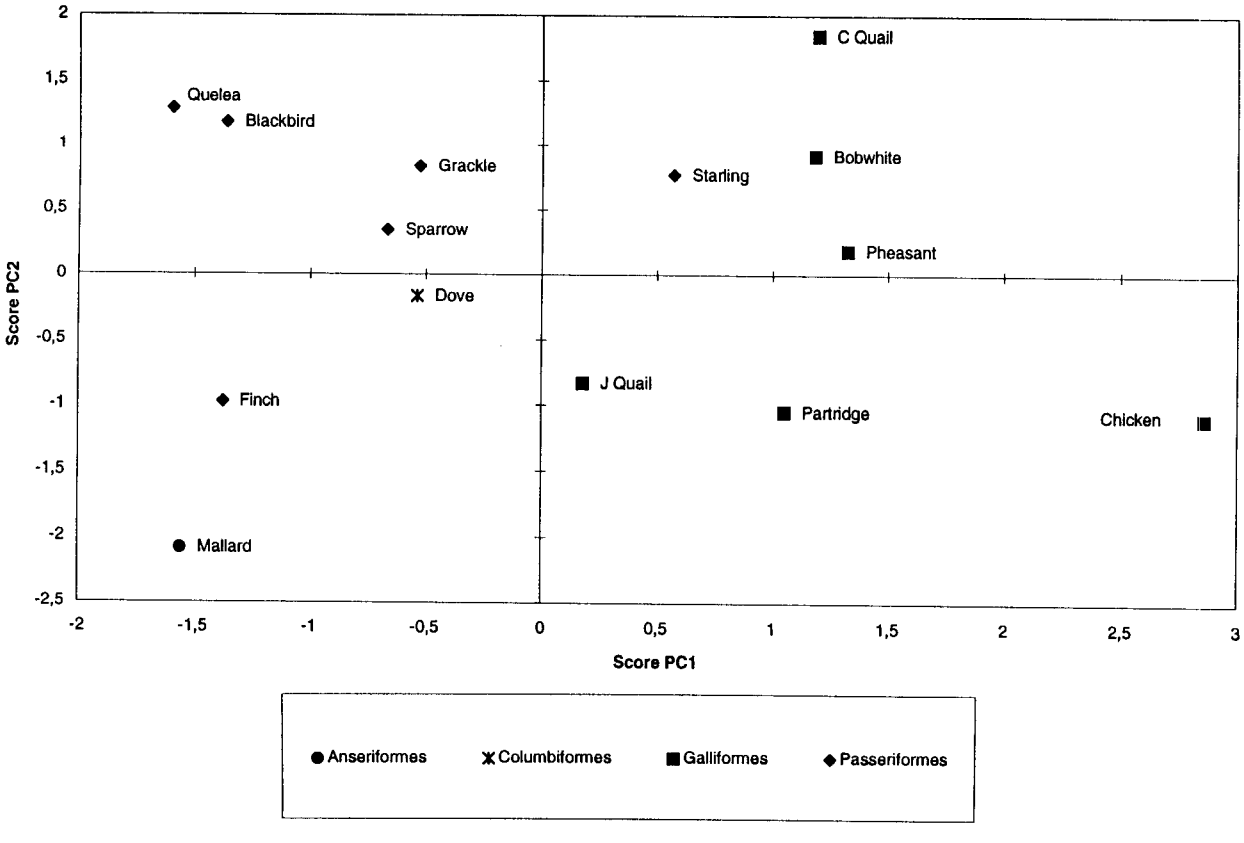


FIGURE 3 Loadings of species that determine patterns in compound toxicity, Birds data set, scaled and centered data.

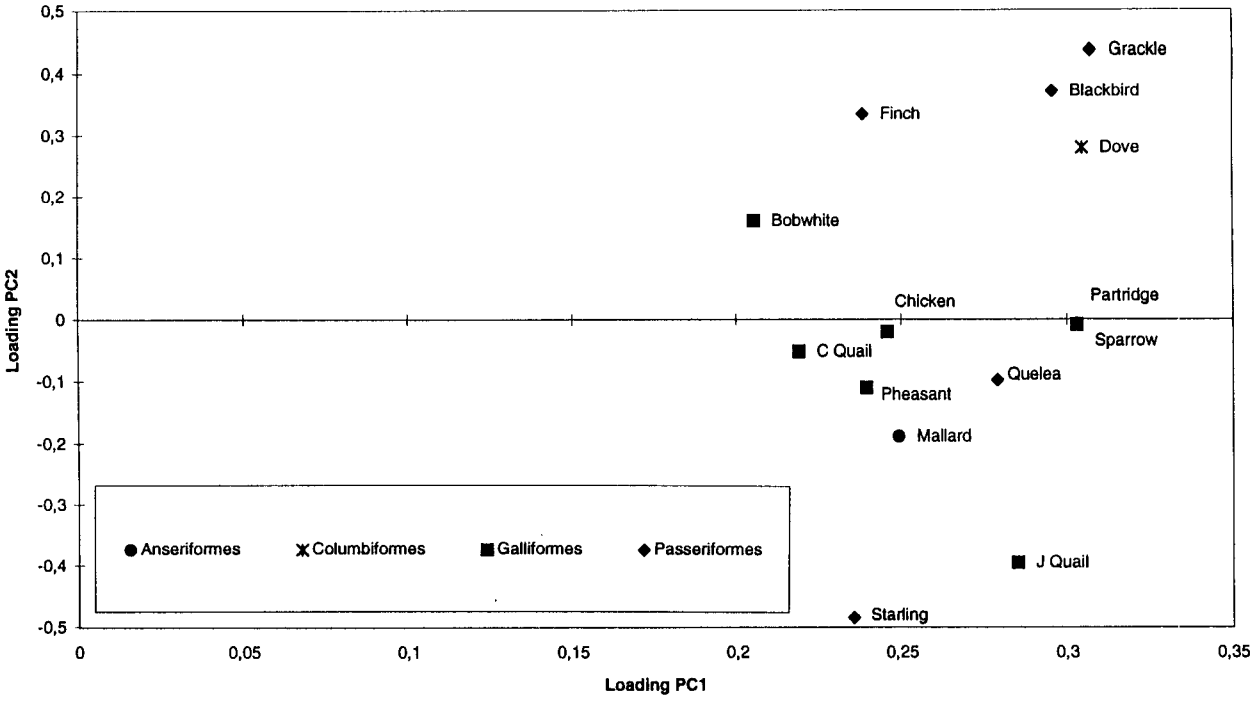


FIGURE 4 Patterns in compounds toxicity, plot of scores of compounds, Birds data set, scaled and centered data.

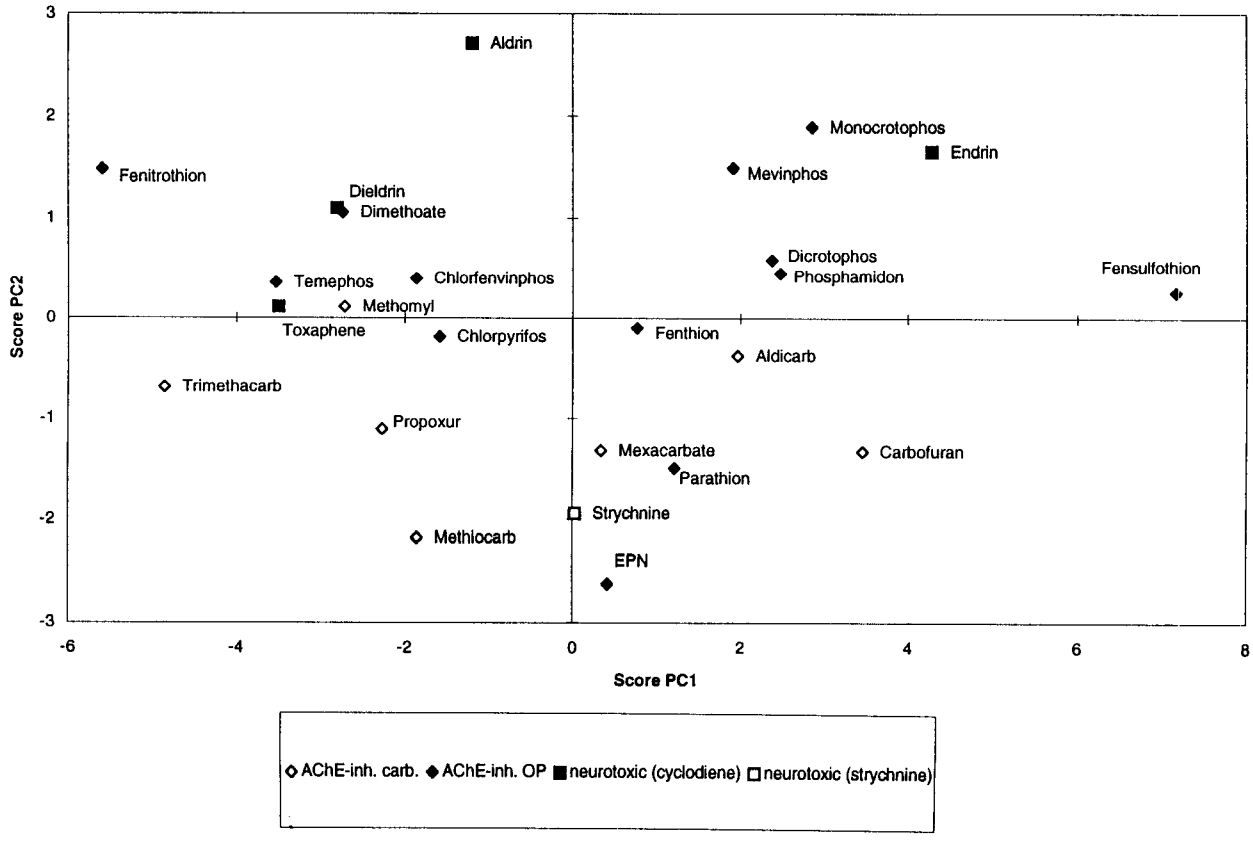


FIGURE 5 Loadings of compounds that determine patterns in species sensitivity, Mammals data set, centered data.

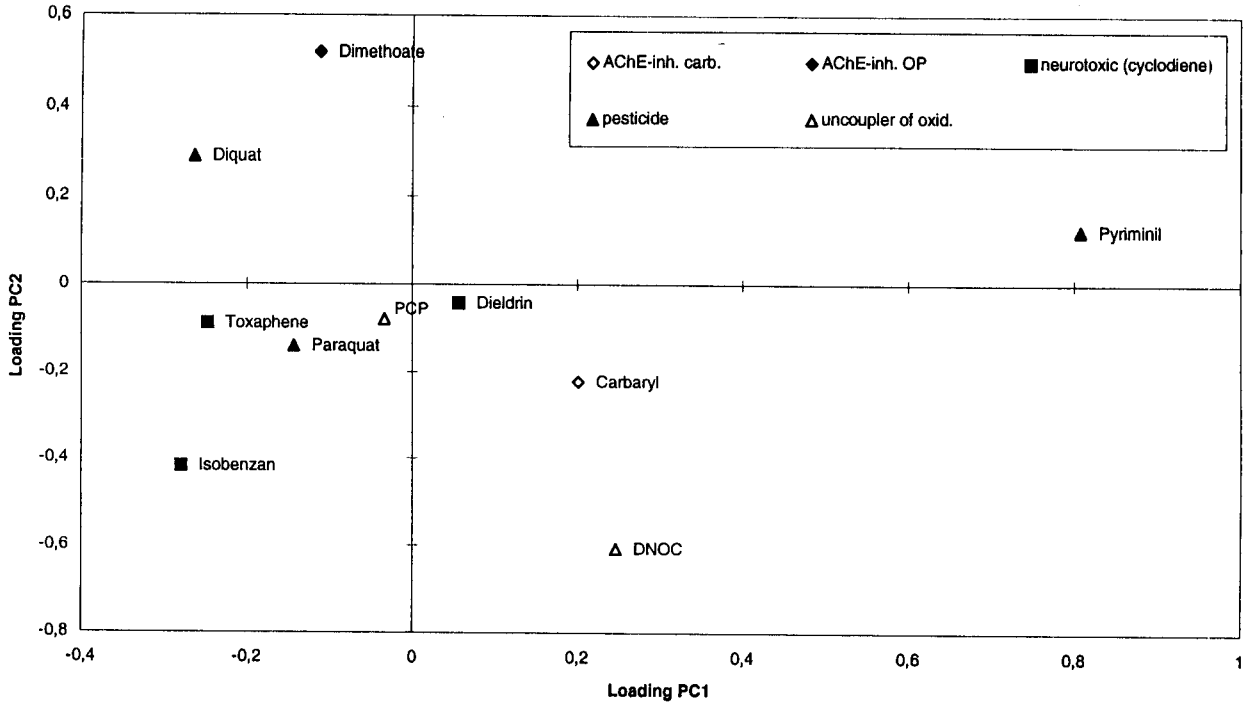


FIGURE 6 Patterns in species sensitivity, plot of scores of species, Mammals data set,

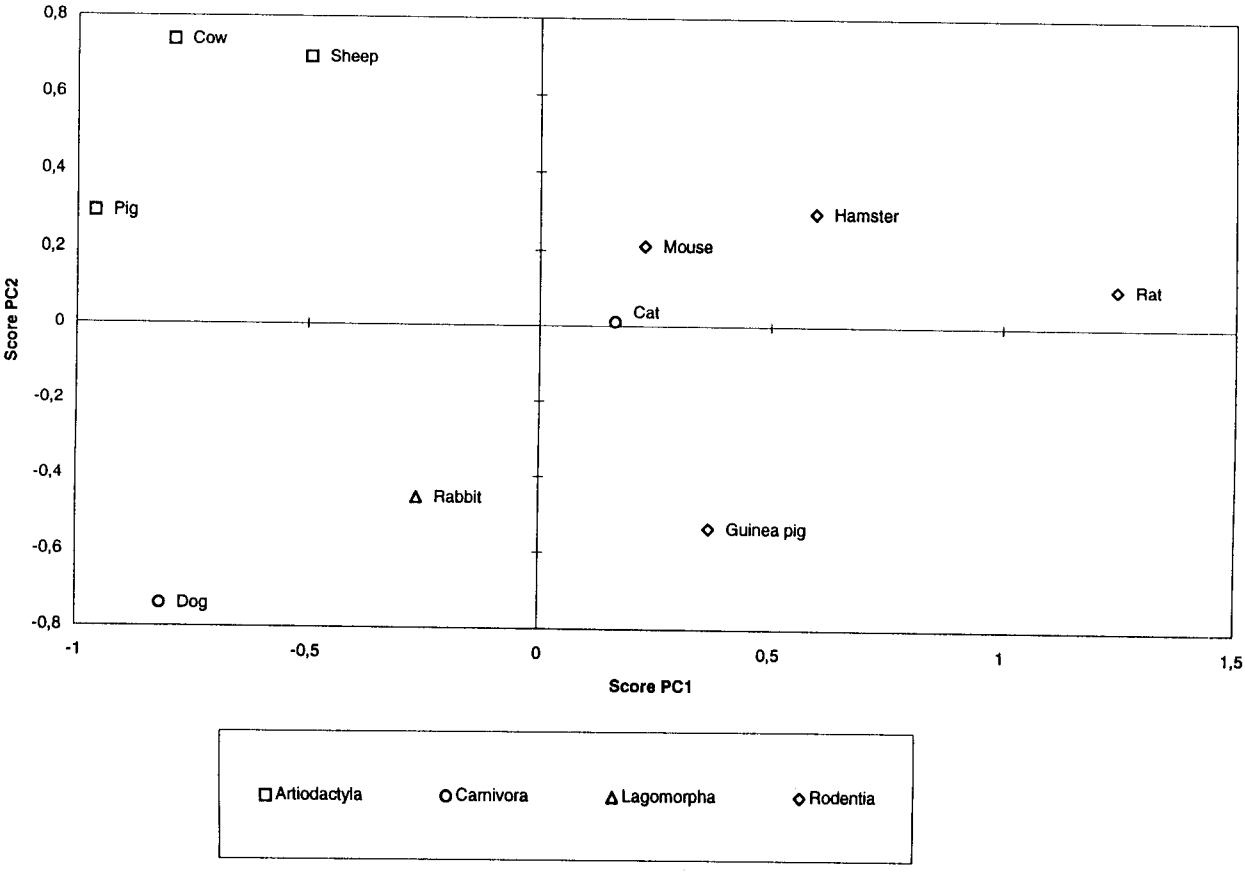


FIGURE 7 Loadings of species that determine patterns in compound toxicity, Mammals data set, scaled and centered data.

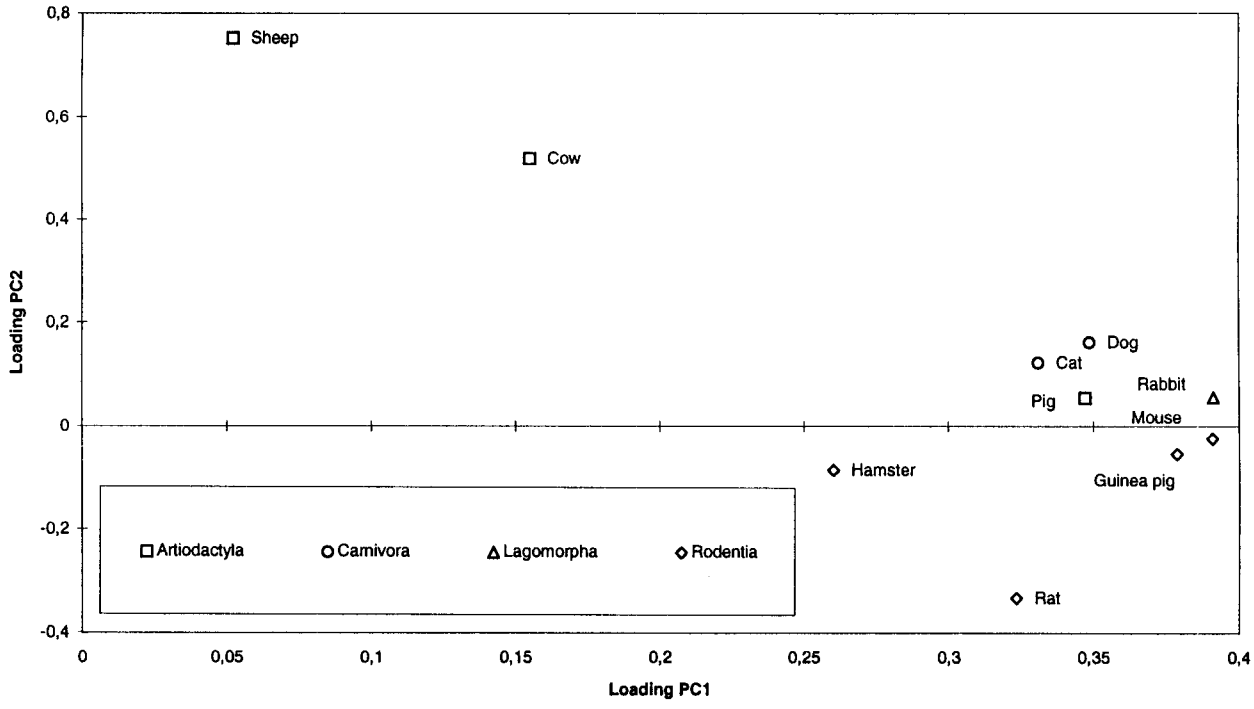
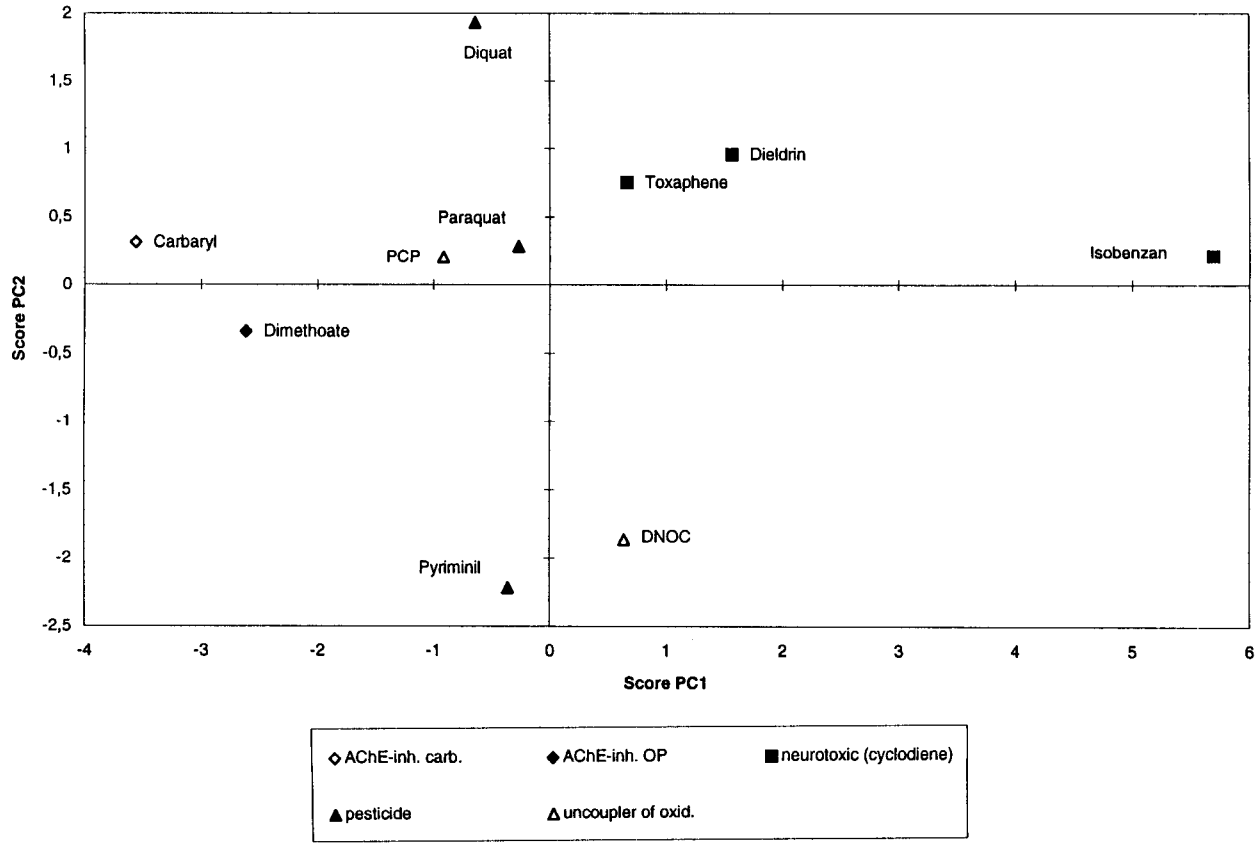


FIGURE 8 Patterns in compounds toxicity, plot of scores of compounds, Mammals data set, scaled and centered data.



APPENDICES

APPENDICES FROM BIRD DATASET

APPENDIX 1 Analysis of patterns in species sensitivity for Birds data set, fractions of Variance explained, unscaled centered data.

Variable	% Variance expl.					
	PC 1	PC 2	PC 3	PC 4	PC 5	Total
Aldicarb	33.27	5.21	-8.67	35.94	17.01	82.76
Carbofuran	91.18	1.74	-0.18	0.56	0.40	93.71
Methiocarb	74.05	-0.89	-0.25	16.74	6.91	96.55
Methomyl	29.36	-7.31	4.97	11.89	-17.32	21.60
Mexacarbate	-14.16	51.06	-5.72	-16.29	-5.74	9.14
Propoxur	66.34	7.10	2.91	0.51	0.83	77.68
Trimethacarb	4.83	-22.76	3.38	-40.35	-96.91	-151.81
Chlorfenvinphos	5.25	47.26	-5.90	-0.84	19.65	65.42
Chlorpyrifos	2.80	0.91	-9.70	9.34	36.64	39.99
Dicrotophos	11.55	55.10	4.74	0.01	2.62	74.03
Dimethoate	-19.48	55.93	8.31	3.96	-28.74	19.99
EPN	69.90	-3.76	8.60	6.66	12.59	93.99
Fenitrothion	-12.15	85.40	11.94	-2.88	6.85	89.17
Fensulfothion	59.99	3.64	-3.13	-0.43	26.49	86.57
Fenthion	53.96	8.93	7.93	-2.98	-3.07	64.77
Mevinphos	0.86	14.67	3.03	61.94	-0.69	79.81
Monocrotophos	-6.49	53.36	23.96	-3.65	4.53	71.70
Parathion	58.01	-3.00	36.73	-0.86	-1.25	89.62
Phosphamidon	47.81	1.58	0.18	24.28	-6.52	67.33
Temephos	3.22	51.35	-5.14	0.17	-5.00	44.60
Aldrin	5.34	80.49	-2.28	-0.05	0.02	83.52
Dieldrin	-3.37	21.46	30.95	28.00	-3.73	73.31
Endrin	13.28	42.37	-0.91	-11.22	-17.73	25.79
Toxaphene	-19.97	-11.06	20.88	-46.69	49.28	-7.56
Strychnine	40.33	5.48	-17.93	-2.14	-66.05	-40.32

APPENDIX 2 Analysis of patterns in species sensitivity for Birds data set, loadings of compounds as variables, unscaled centered data.

Variable	Loading				
	PC 1	PC 2	PC 3	PC 4	PC 5
Aldicarb	-0.19	0.11	0.02	-0.39	0.25
Carbofuran	-0.34	-0.07	0.05	0.10	-0.09
Methiocarb	-0.38	-0.06	-0.13	-0.43	-0.26
Methomyl	-0.07	0.03	0.08	0.11	-0.03
Mexacarbate	0.01	-0.23	0.10	0.03	-0.21
Propoxur	-0.28	0.12	-0.15	0.12	-0.14
Trimethacarb	-0.13	0.02	-0.24	0.10	-0.20
Chlorfenvinphos	-0.10	0.24	-0.05	-0.16	0.33
Chlorpyrifos	-0.08	0.08	-0.04	0.21	0.34
Dicrotophos	-0.10	0.16	0.11	0.07	-0.11
Dimethoate	-0.02	0.23	0.19	0.18	-0.15
EPN	-0.42	0.00	-0.24	-0.21	0.28
Fenitrothion	0.03	0.56	-0.35	-0.03	-0.34
Fensulfothion	-0.22	0.08	-0.06	0.13	0.31
Fenthion	-0.22	0.11	0.19	0.03	-0.06
Mevinphos	-0.09	0.16	0.19	0.45	0.10
Monocrotophos	0.05	0.24	0.29	0.00	-0.18
Parathion	-0.36	-0.04	0.46	-0.03	-0.02
Phosphamidon	-0.11	0.05	0.07	0.14	0.00
Temephos	-0.10	0.24	0.06	0.15	-0.13
Aldrin	0.16	0.45	-0.02	-0.13	0.14
Dieldrin	0.09	0.21	0.40	-0.36	-0.06
Endrin	0.11	0.13	0.07	-0.01	0.03
Toxaphene	0.00	0.09	-0.31	0.08	-0.33
Strychnine	-0.30	-0.15	-0.02	0.22	0.10

APPENDIX 3 Analysis of patterns in species sensitivity for Birds data set, scores of species as objects, unscaled centered data.

Object Name	Initial	PC 1			PC 2			PC 3			PC 4			PC 5		
	S^2O [1]	S^2O [1]	Score	Olev [2]	S^2O [1]	Score	Olev [2]	S^2O [1]	Score	Olev [2]	S^2O [1]	Score	Olev [2]	S^2O [1]	Score	Olev [2]
Ana.pla	0.33	0.26	-1.56	0.32	0.05	-2.09	0.41	0.06	-0.03	0.38	0.07	0.17	0.37	0.04	-0.62	0.37
Col.liv	0.08	0.07	-0.54	0.11	0.08	-0.17	0.09	0.07	0.68	0.13	0.08	0.06	0.13	0.06	0.57	0.14
Ale.gra	0.15	0.11	1.05	0.21	0.09	-1.05	0.23	0.09	-0.37	0.23	0.06	-0.96	0.25	0.08	0.01	0.25
Cal.cal	0.23	0.17	1.20	0.24	0.07	1.85	0.34	0.09	0.00	0.32	0.08	-0.58	0.32	0.04	-0.71	0.33
Col.vir	0.20	0.13	1.18	0.24	0.09	0.92	0.23	0.08	0.61	0.24	0.08	-0.38	0.23	0.03	-0.72	0.25
Cot.cot	0.09	0.10	0.18	0.04	0.07	-0.83	0.13	0.08	-0.32	0.13	0.07	-0.58	0.15	0.08	-0.22	0.15
Gal.gal	0.39	0.11	2.86	0.58	0.05	-1.10	0.48	0.04	0.50	0.46	0.05	-0.15	0.44	0.03	0.51	0.43
Pha.col	0.19	0.12	1.33	0.27	0.14	0.18	0.21	0.16	-0.07	0.20	0.03	1.46	0.28	0.02	-0.28	0.27
Car.mex	0.22	0.13	-1.37	0.28	0.08	-0.98	0.26	0.06	-0.63	0.26	0.08	-0.01	0.25	0.10	0.17	0.25
Age.pho	0.16	0.10	-1.37	0.28	0.03	1.17	0.28	0.03	0.19	0.27	0.04	0.12	0.26	0.04	-0.17	0.25
Qui.qui	0.08	0.08	-0.53	0.11	0.06	0.83	0.15	0.06	-0.42	0.16	0.07	-0.32	0.16	0.06	0.44	0.16
Pas.dom	0.09	0.08	-0.67	0.14	0.08	0.34	0.12	0.07	0.61	0.14	0.09	0.08	0.14	0.05	0.81	0.17
Que.que	0.23	0.11	-1.60	0.33	0.02	1.28	0.32	0.03	0.10	0.30	0.04	0.11	0.29	0.04	-0.16	0.28
Stu.vul	0.18	0.19	0.57	0.12	0.18	0.77	0.15	0.03	-1.71	0.29	0.03	0.14	0.28	0.03	0.30	0.27

[1] : Residual object variance (Initial value after centering)

[2] : Object leverage

APPENDIX 4 Analysis of patterns in compound toxicity for Birds data set, fractions of Variance explained, scaled centered data.

Variable	% Variance expl.		
	PC 1	PC 2	Total
Mallard	57.55	29.59	87.14
Dove	81.77	1.52	83.30
Partridge	56.99	-2.20	54.79
C Quail	41.50	38.45	79.95
Bobwhite	39.22	34.21	73.43
J Quail	76.66	6.10	82.76
Chicken	62.43	15.73	78.15
Pheasant	52.81	13.85	66.66
Finch	47.11	47.15	94.26
Blackbird	85.52	-0.17	85.35
Grackle	73.00	-1.60	71.40
Sparrow	86.81	-0.64	86.16
Quelea	90.33	-1.06	89.26
Starling	48.59	2.81	51.40

APPENDIX 5 Analysis of patterns in compound toxicity for Birds data set, loadings of species as variables, scaled centered data.

Variable	Loading	
	PC 1	PC 2
Mallard	0.25	-0.19
Dove	0.30	0.28
Partridge	0.30	-0.01
C Quail	0.22	-0.05
Bobwhite	0.21	0.16
J Quail	0.29	-0.39
Chicken	0.25	-0.02
Pheasant	0.24	-0.11
Finch	0.24	0.34
Blackbird	0.30	0.37
Grackle	0.31	0.44
Sparrow	0.30	-0.01
Quelea	0.28	-0.10
Starling	0.24	-0.48

APPENDIX 6 Analysis of patterns in compounds toxicity for Birds data set, scores of compounds as objects, scaled centered data.

Object Name	Initial	PC 1			PC 2		
	S^2O [1]	S^2O [1]	Score	Olev [2]	S^2O [1]	Score	Olev [2]
Aldicarb	0.50	0.25	1.96	0.13	0.27	-0.38	0.12
Carbofuran	1.06	0.19	3.46	0.23	0.06	-1.33	0.22
Methiocarb	0.80	0.62	-1.85	0.12	0.22	-2.18	0.17
Methomyl	0.74	0.19	-2.72	0.18	0.22	0.11	0.16
Mexacarbate	0.72	0.83	0.34	0.02	0.90	-1.32	0.08
Propoxur	0.60	0.25	-2.27	0.15	0.16	-1.11	0.15
Trimethacarb	2.13	0.18	-4.86	0.32	0.19	-0.69	0.30
Chlorfenvinphos	0.49	0.25	-1.86	0.12	0.28	0.40	0.11
Chlorpyrifos	0.45	0.30	-1.58	0.10	0.34	-0.19	0.10
Dicrotophos	0.53	0.06	2.47	0.16	0.06	0.45	0.15
Dimethoate	0.70	0.25	-2.74	0.18	0.17	1.06	0.18
EPN	0.62	0.70	0.42	0.03	0.24	-2.63	0.16
Fenitrothion	2.73	0.62	-5.60	0.37	0.48	1.49	0.35
Fensulfothion	3.90	0.12	7.17	0.47	0.13	0.26	0.43
Fenthion	0.18	0.16	0.77	0.05	0.18	-0.10	0.05
Mevinphos	0.59	0.37	1.91	0.13	0.26	1.50	0.15
Monocrotophos	1.03	0.47	2.85	0.19	0.21	1.89	0.21
Parathion	0.59	0.54	1.22	0.08	0.42	-1.50	0.12
Phosphamidon	0.56	0.12	2.37	0.16	0.12	0.59	0.15
Temephos	1.17	0.28	-3.53	0.23	0.31	0.36	0.21
Aldrin	0.64	0.62	-1.19	0.08	0.14	2.71	0.18
Dieldrin	1.24	0.72	-2.81	0.19	0.74	1.10	0.18
Endrin	1.64	0.26	4.28	0.28	0.08	1.65	0.28
Toxaphene	1.04	0.28	-3.50	0.23	0.35	0.11	0.21
Strychnine	0.54	0.66	0.03	0.00	0.41	-1.94	0.12

[1] : Residual object variance (Initial value after scaling and centering)

[2] : Object leverage

APPENDICES FROM MAMMALS DATASET

APPENDIX 7 Analysis of patterns in species sensitivity for Mammals data set, fractions of Variance explained, unscaled centered data.

Variable	% Variance expl.		
	PC 1	PC 2	Total
Carbaryl	10.99	-7.59	3.40
Dimethoate	-6.63	84.24	77.61
Dieldrin	-0.15	-19.33	-19.47
Isobenzan	31.73	36.45	68.18
Toxaphene	28.83	-8.40	20.42
Diquat	28.89	17.02	45.91
Paraquat	0.28	-8.84	-8.56
Pyriminil	94.45	-0.38	94.07
DNOC	16.15	70.08	86.23
PCP	-14.00	-7.04	-21.04

APPENDIX 8 Analysis of patterns in species sensitivity for Mammals data set, loadings of compounds as variables, unscaled centered data.

Variable	Loading	
	PC 1	PC 2
Carbaryl	0.20	-0.22
Dimethoate	-0.11	0.52
Dieldrin	0.06	-0.04
Isobenzan	-0.28	-0.42
Toxaphene	-0.25	-0.09
Diquat	-0.26	0.29
Paraquat	-0.14	-0.14
Pyriminil	0.81	0.12
DNOC	0.25	-0.61
PCP	-0.03	-0.08

APPENDIX 9 Analysis of patterns in species sensitivity for Mammals data set, scores of species as objects, unscaled, centered data.

Object Name	Initial	PC 1			PC 2		
	S^2O [1]	S^2O [1]	Score	Olev [2]	S^2O [1]	Score	Olev [2]
Rat	0.20	0.03	1.25	0.58	0.04	0.10	0.47
Mouse	0.03	0.03	0.23	0.10	0.03	0.21	0.12
Rabbit	0.07	0.07	-0.26	0.12	0.06	-0.46	0.20
Guinea pig	0.10	0.10	0.37	0.17	0.08	-0.54	0.25
Dog	0.13	0.06	-0.82	0.38	0.01	-0.74	0.42
Cat	0.07	0.08	0.16	0.08	0.11	0.01	0.06
Sheep	0.11	0.11	-0.50	0.23	0.02	0.69	0.32
Pig	0.24	0.07	-0.96	0.45	0.09	0.29	0.38
Cow	0.16	0.11	-0.79	0.37	0.03	0.74	0.41
Hamster	0.08	0.05	0.60	0.28	0.05	0.30	0.25

[1] : Residual object variance (Initial value after centering)

[2] : Object leverage

APPENDIX 10 Analysis of patterns in compound toxicity for Mammals data set, fractions of Variance explained, scaled centered data.

Variable	% Variance expl.		
	PC 1	PC 2	Total
Rat	59.58	22.10	81.67
Mouse	92.87	-0.88	91.99
Rabbit	93.04	-0.22	92.83
Guinea pig	86.42	-1.23	85.19
Dog	80.79	2.50	83.30
Cat	92.98	2.55	95.53
Sheep	-30.88	117.58	86.70
Pig	80.17	-16.35	63.82
Cow	-14.44	46.76	32.32
Hamster	83.43	-9.55	73.88

APPENDIX 11 Analysis of patterns in compound toxicity for Mammals data set, loadings of species as variables, scaled centered data.

Variable	Loading	
	PC 1	PC 2
Rat	0.32	-0.33
Mouse	0.39	-0.02
Rabbit	0.39	0.06
Guinea pig	0.38	-0.05
Dog	0.35	0.16
Cat	0.33	0.12
Sheep	0.05	0.75
Pig	0.35	0.05
Cow	0.16	0.52
Hamster	0.26	-0.08

APPENDIX 12 Analysis of patterns in compounds toxicity for Mammals data set, scores of compounds as objects, scaled centered data.

Object Name	Initial		PC 1			PC 2	
	S^2O [1]	S^2O [1]	Score	Olev [2]	S^2O [1]	Score	Olev [2]
Carbaryl	1.85	0.04	-3.56	0.47	0.03	0.31	0.43
Dimethoate	0.87	0.16	-2.62	0.35	0.18	-0.34	0.31
Dieldrin	0.52	0.27	1.57	0.21	0.19	0.96	0.22
Isobenzan	4.40	0.02	5.69	0.76	0.01	0.22	0.68
Toxaphene	0.24	0.24	0.67	0.09	0.20	0.75	0.12
Diquat	0.37	0.43	-0.64	0.08	0.06	1.93	0.24
Paraquat	0.17	0.21	-0.27	0.04	0.26	0.28	0.05
Pyriminil	0.61	0.78	-0.36	0.05	0.36	-2.22	0.27
DNOC	0.57	0.68	0.64	0.08	0.24	-1.86	0.23
PCP	0.13	0.03	-0.91	0.12	0.03	0.20	0.11

[1] : Residual object variance (Initial value after scaling and centering)

[2] : Object leverage