Review

Received: 17 February 2010 Revised: 26 May 2010 Accepted: 27 May 2010

(wileyonlinelibrary.com) DOI 10.1002/ps.2001

Is *Apis mellifera* more sensitive to insecticides than other insects?

Melissa C Hardstone and Jeffrey G Scott*

Abstract

BACKGROUND: Honey bees (*Apis mellifera* L.) are among the most important pollinators in natural and agricultural settings. They commonly encounter insecticides, and the effects of insecticides on honey bees have been frequently noted. It has been suggested that honey bees may be (as a species) uniquely sensitive to insecticides, although no comparative toxicology study has been undertaken to examine this claim. An extensive literature review was conducted, using data in which adult insects were topically treated with insecticides. The goal of this review was to summarize insecticide toxicity data between *A. mellifera* and other insects to determine the relative sensitivity of honey bees to insecticides.

RESULTS: It was found that, in general, honey bees were no more sensitive than other insect species across the 62 insecticides examined. In addition, honey bees were not more sensitive to any of the six classes of insecticides (carbamates, nicotinoids, organochlorines, organophosphates, pyrethroids and miscellaneous) examined.

CONCLUSIONS: While honey bees can be sensitive to individual insecticides, they are not a highly sensitive species to insecticides overall, or even to specific classes of insecticides. However, all pesticides should be used in a way that minimizes honey bee exposure, so as to minimize possible declines in the number of bees and/or honey contamination.

Supporting information may be found in the online version of this article.

Keywords: comparative toxicology; pyrethroid; neonicotinoid; organophosphate; carbamate

1 INTRODUCTION

Honey bees (*Apis mellifera* L.) are invaluable to the operation of commercial agriculture, to the propagation of plants through pollination and to human society by producing various products.[1] Overall, the direct and indirect benefits provided by bees to agriculture are estimated at \$10–33 billion annually in the United States.[2–5] The economic value of honey bees as pollinators ranges from \$80 million[6] to \$14 560 million[5] in the United States, and lies at £190 million[7] in the United Kingdom. Honey bee declines can have a direct impact on the food market and on the price of commodity foods.

Honey bee exposure to insecticides has primarily been measured by worker mortality in the field, as well as by detection of residues from the bee body[8] or in pollen loads.[9,10] In spite of evidence that foraging bees are exposed to pesticide residues and may be exposed during field applications of pesticides,[11,12] interpretation of insecticide residue levels on bees and in pollen has created some debate regarding whether exposure is the direct cause of honey bee deaths.[8,13] Bee poisoning observations have been recorded since the late nineteenth century.[14] The economic impact of honey bee kills resulted in the legislation of the Bee Indemnity Act of 1970 (Pub. L. 91–524) which mandates/requires the USDA to pay beekeepers for losses that have ‘occurred as a result of the use of economic poisons which had been registered and approved for use by the Federal Government’.[6]

While honey bees are unquestionably exposed to various pesticides, statements about honey bees serving as environmental indicators[8,15] owing to their ‘extreme susceptibility’,[15–20] or honey bees being particularly sensitive to insecticides because they have lower total numbers of cytochrome P450s[21] than other insects, are often made with no citations given.

To date, no comprehensive review of the susceptibility of *A. mellifera* to insecticides compared with other insect species has been reported. Therefore, the goal of this paper was to summarize toxicity data of insecticides in a comparative manner between *A. mellifera* and other insects to determine the relative sensitivity of honey bees to insecticides. Toxicity data obtained from the literature were reviewed, the relative sensitivities of honey bees to 62 insecticides from six classes were compared and implications of these findings were examined.

2 MATERIALS AND METHODS

The guidelines used to assess how sensitive honey bees are to insecticides were as follows:

1. Only literature in which adult topical assays using analytical- or technical-grade material (minimum purity = 60% AI) was included.

---

* Correspondence to: Jeffrey G Scott, Department of Entomology, Comstock Hall, Cornell University, Ithaca, NY 14853-0901, USA. E-mail: JGS5@CORNELL.EDU

Department of Entomology, Comstock Hall, Cornell University, Ithaca, NY, USA

2. If data were obtained from multiple field-collected populations, only the lowest LD_{50} (most likely to reflect the value of a susceptible strain) was included.
3. If data were obtained from a study on resistance mechanisms or resistance level determinations of field populations, only the susceptible strain LD_{50} value was included.

In cases where LD_{50} values were reported on a per insect basis, the µg g^{-1} equivalents were calculated using published body weights of the specific species or insect type (details and references in the supporting information). In the present approach, an extensive search of the literature for toxicity data on honey bees was conducted, following the above guidelines. The literature was then searched for toxicity data on other insects using insecticides for which honey bee data were available. The insecticides that were included in this review were those that contained LD_{50} values from three or more insect species. LD_{50} values from all insect species were converted to µg g^{-1} measurements based on the average weight of that insect species. For each insecticide, the average honey bee LD_{50} was ranked in relation to the LD_{50} values of the other insect species (if one species had multiple LD_{50} values, the average for that species was used) in order to obtain the sensitivity percentile ranking of *A. mellifera*.

3 RESULTS

3.1 Overall observations

The relative sensitivity of *Apis mellifera* to insecticides ($n = 62$) for which there were available data is shown in Figs 1, 2 and 3 (Tables S1 to S6 in the supporting information). Overall, across the six classes of insecticides there was no evidence that *A. mellifera* is highly sensitive to insecticides relative to other insects. There were 25, 10 and 27 cases where the honey bee was in the bottom 50%, the middle or the top 50% of the sensitive species respectively. There were five cases where *A. mellifera* was the most sensitive species, and nine cases where it was the least sensitive species.

3.2 Carbamates

In the case of carbamates, *A. mellifera* was about equally sensitive overall compared with the other species tested (Fig. 1). There were three (aminocarb, methomyl and propoxur), two (aldicarb and carbaryl) and three (bendiocarb, carbofuran and maxacarbate) cases where the honey bee was in the bottom 50%, the middle or the top 50% of the sensitive species respectively. *Apis mellifera* was the most sensitive species to bendiocarb, with a mean LD_{50} of 2.64 (range 1.00–4.28) µg g^{-1} compared with an average LD_{50} of 24.3 (range 8.09–52.2) µg g^{-1} derived from the other three species (Table 1 and Table S1). Of the other insects examined, the housefly (*Musca domestica* L.) and cat flea (*Ctenocephalides felis* Bouché) tended to be the least sensitive species. No particular species was consistently most sensitive (Table 1).

3.3 Neonicotinoids

Apis mellifera was among the most sensitive species for three of the five neonicotinoids, compared with the other species tested (Table S2). Honey bees were not the most sensitive species to any of the neonicotinoids. The sensitivity rankings of the honey bee to dinotefuran, imidacloprid and nicotine were all in the top 50%. For these three neonicotinoid insecticides, the LD_{50} ranges associated with the other species examined often overlapped with honey bee LD_{50} means and ranges, but the averages were larger, indicating that, overall, the other species were not as sensitive (Table 1). The honey bee ranked in the middle for species sensitivity to nitenpyram and thiamethoxam (Fig. 1). For both of these insecticides, the average LD_{50} range of the honey bee overlapped with the average LD_{50} range of the other insect species (Table 1). Other *Apis* species such as *A. indica* Fabricius and *A. florae* Fabricius rank as more sensitive than *A. mellifera* to imidacloprid and equally sensitive to thiamethoxam (Table 1). The individual species of the other insects tested showed no pattern of being more or less sensitive to neonicotinoids (Table 1).

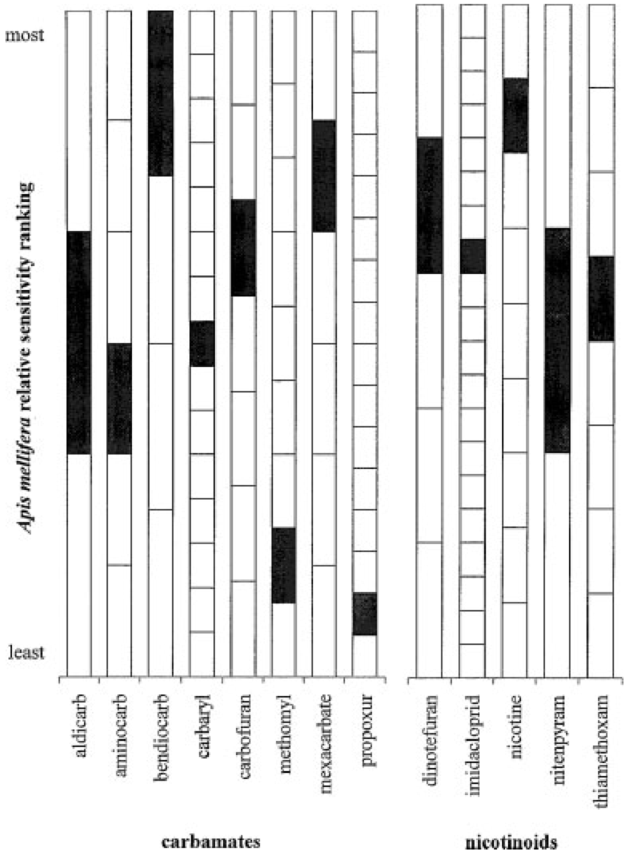

Figure 1. The relative sensitivity ranking of *Apis mellifera* compared with other insect species to carbamate and neonicotinoid insecticides. Bars are divided into the total number of insect species LD_{50} values available for that insecticide. Shaded boxes indicate the position of *A. mellifera* compared with the other insect species.

3.4 Organochlorines

Apis mellifera tended to be of average or less sensitivity overall to organochlorines when compared with the other species tested (Fig. 2). There were four insecticides, chlordane, DDT, endosulfan and methoxychlor, where the honey bee ranked in the bottom 50% of sensitive species. In fact, the honey bee was the least sensitive species to endosulfan (out of three species) and methoxychlor (out of four species). For endosulfan, the average LD_{50} for the honey bee was 120 µg g^{-1}, while the average LD_{50} for the other insects was 1.83 µg g^{-1} (Table 2). The average LD_{50} for the honey bee to methoxychlor was 236 µg g^{-1}, whereas the average LD_{50} for the other insects was 11.4 µg g^{-1} (Table 2). *Aphis mellifera* ranked in the middle for sensitivity to three organochlorines: aldrin, dieldrin and lindane. Of the other insects examined for susceptibility to

Table 1. LD_{50} values of *Apis mellifera* and other species to carbamate and neonicotinoid insecticides

	Apis mellifera LD_{50} (µg g^{-1})			Other species LD_{50} (µg g^{-1})		
Insecticide	Mean	Range	n^a	Mean	Range	Species[b,c,d]
Carbamates						
Aldicarb	2.36	1.52–2.85	3	3.61	1.71–5.50	L.dec, **M.dom**
Aminocarb	4.40	0.850–11.2	3	21.4	1.10–85.0	A.ery, M.rot, O.fas, **B.ter, M.dom**
Bendiocarb	2.64	1.00–4.28	2	24.3	8.09–52.2	**B.ger, B.asa, C.fel**
Carbaryl	7.87	0.53–18.4	15	132	0.35–900	*L.hes, A.qua*, A.ste, C.qui, D.vir, A.aeg, V.pen, A.ery, **H.arm, M.rot, O.fas, B.ter, C.fel, M.dom**
Carbofuran	1.55	1.49–1.60	2	3.18	0.920–5.36	*A.ste, A.aeg*, **O.fas, L.dec, M.dom, D.vir**
Methomyl	14.0	12.9–15.1	2	27.81	0.900–162	*V.pen, B.dor, S.fru, M.bee, M.dom*, N.per, T.nig, **M.cro**
Mexacarbate	1.77	0.477–3.08	6	17.7	0.986–66.3	A.ery, M.rot, **B.ter, O.fas, M.dom**
Propoxur	11.4	7.21–13.5	3	36.7	0.320–478	*L.hes, B.ori, A.ste, I.ver, P.bru, P.aus, P.ame, B.asa, P.ful, A.aeg*, B.vag, B.ger, D.vir, **M.dom, C.fel**
Neonicotinoids						
Dinotefuran	0.220	n/a	1	5.42	0.180–13.8	*A.gam*, **L.dec, A.aeg, C.qui**
Imidacloprid	0.403	0.128–0.750	12	8.23	0.001–133	*T.aur, A.pis, A.ind, A.flo*, N.per, A.qua, L.dec, N.mel, T.irr, **H.con, A.erv, A.aeg, C.vir, C.qui, M.rot, C.fel, M.per, B.ger, M.dom**
Nicotine	173	30.0–315	2	777	150–3200	O.fas, A.tri, **L.dec, M.dom, B.ger, P.ame, P.jap, T.mol**
Nitenpyram	1.10	0.810–1.38	2	0.970	0.230–1.70	*L.dec*, **C.fel**
Thiamethoxam	0.202	0.067–0.299	3	0.431	0.001–1.34	*T.aur*, A.ind, A.flo, **L.dec, N.per, C.vir, T.irr**

[a] Number of LD_{50} determinations.

[b] A.aeg, *Aedes aegypti*; A.bip, *Adalia bipunctata*; A.erv, *Aphidius ervi*; A.ery, *Andrena erythronii*; A.flo, *Apis florae*; A.gam, *Anopheles gambiae*; A.ind, *Apis indica*; A.ips, *Agrotis ipsilon*; A.pis, *Acyrthosiphon pisum*; A.qua, *Anopheles quadrimaculatus*; A.ste, *Anopheles stephensi*; A.sus, *Anastepha suspense*; A.tri, *Anasa tristis*; A.vit, *Acalymma vittata*; B.agr, *Bombus agrorum*; B.asa, *Blatella asahinai*; B.dor, *Bactrocera dorsalis*; B.ger, *Blattella germanica*; B.luc, *Bombus lucorum*; B.ori, *Blatta orientalis*; B.ter, *Bombus terricola*; Bo.ter, *Bombus terrestris*; B.vag, *Blattella vaga*; Bom, *Bombus* spp.; C.asp, *Crioceris asparagi*; C.bal, *Collops balteatus*; C.cat, *Ceratonia catalpa*; C.eur, *Coriscus eurinus*; Co.eur, *Colias eurytheme*; C.fel, *Ctencephalides felis*; C.mac, *Coleomegilla maculate lengi*; C.nen, *Conotrachelus nenuphar*; C.pen, *Chauliognathus pennsylvanicus*; C.qui, *Culex quinquefasciatus*; C.r/o/c, *Crysopa rufilabris/oculata/carnea*; C.san, *Cercopis sanguinolenta*; C.tra, *Coccinella transversoguttata*; C.tri, *Coccinella trifasciata*; C.vir, *Crotalus viridis*; D.und, *Diabrotica undecimpunctata howardi*; D.vir, *Diabrotica virgifera*; E.pen, *Epicauta pennsylvanica*; Ene/Ish, *Enellagma/Ishnura* spp.; F.san, *Formica sanguine*; G.mel, *Galleria mellonella*; G.pun, *Geocrois punctipes*; H.arm, *Heliothis armigera*; H.con, *Hippodamia convergens*; H.gla, *Hippodamia glacialis*; H.par, Hippodamia parenthesis; H.tre, *Hippodamia tredecimpunctata tibialis*; Hep, Heptageniidae; Hyd, *Hydrophilus* spp.; I.ver, *Ichnura vericalis*; L.dec, *Leptinotarsa decemlineata*; L.hes, *Lygus hesperus*; L.lin, *Lygus lineolaris*; L.mig, *Locusta migratoria*; M.bee, *Melipora beecheii*; M.cro, *Microplitis croceipes*; M.dif, *Melanoplus differentialis*; M.dom, *Musca domestica*; M.fem, *Melanoplus femur-rubrum*; M.per, *Myzus persicae*; M.pis, *Macrosiphum pisi*; M.rot, *Megachile rotundata*; N.ame, *Nabis americoferus*; N.fas, *Nemobius fasciatus*; N.mel, *Nomia melanderi*; N.per, *Nannotrigona perilampoides*; N.que, *Neolygus quercalbae*; O.fas, *Oncopeltus fasciatus*; O.mel, *Oulema melanopus*; P.ame, *Periplaneta americana*; P.aus, *Periplaneta australasiae*; P.bru, *Periplaneta brunnea*; P.fas, *Phymata fasicata*; P.ful, *Periplaneta fuliginosa*; P.jap, *Popilla japonica*; P.ope, *Phthorimaea operculella*; S.fru, *Spodoptera frugiperda*; T.aur, *Toxoptera aurantii*; T.cas, *Tribolium castaneum*; T.irr, *Trigona irridipenis*; T.mol, *Tenebrio molitor*; T.nig, *Trigona nigra*; T.tet, *Tetraopes tetrophthalmus*; V.pen, *Vespula pensylvanica*

[c] LD_{50} values listed in increasing order. LD_{50} of other species $<$ LD_{50} of *A. mellifera* (*italic font*); LD_{50} of other species $=$ LD_{50} of *A. mellifera* (plain font); LD_{50} of other species $>$ LD_{50} of *A. mellifera* (**bold font**).

[d] References are provided in the supporting information.

organochlorines, the housefly (*M. domestica*) tended to be the most sensitive species and the grasshopper (*Melanoplus differentialis* Thomas) was similar in sensitivity to the honey bee, while the milkweed bug (*Oncopeltus fasciatus* Dallas) tended to be the least sensitive (Table 2).

3.5 Organophosphates

Honey bee sensitivity to organophosphates was variable, but tended to rank in the middle for sensitivity relative to other species (Fig. 2). Out of the 27 organophosphate insecticides, there were 11, four and 12 cases where the honey bee was in the bottom 50%, the middle or the top 50% of the sensitive species respectively. *Apis mellifera* was the least sensitive species to bromophos (four species), mipafox (four species), naled (three species) and sulprofos (four species). Honey bees were the most sensitive species to two organophosphates, azinphos-methyl (four species) and phorate (four species).

There are multiple types of organophosphate insecticides,[22] but they can generally be classified as those that require bioactivation (e.g. phosphorothionates) and those that do not (e.g. phosphates).

Table 2. LD_{50} values of *Apis mellifera* and other species to organochlorine and organophosphate insecticides

	Apis mellifera LD_{50} ($\mu g\ g^{-1}$)			Other species LD_{50} ($\mu g\ g^{-1}$)		
Insecticide	Mean	Range	*n*[a]	Mean	Range	Species[b,c,d]
Organochlorines						
Aldrin	3.26	1.49–4.50	4	232	1.38–1140	*M.dom, M.dif*, P.ame, **O.fas, D.vir**
Chlordane	40.1	14.0–88.0	5	273	6.04–1660	*M.dom*, M.dif, B.ger, V.pen, A.qua, **O.fas, D.vir**
DDT	73.0	7.00–164	11	687	0.090–9380	*N.mel, L.hes, B.ger, A.aeg, A.ste, P.ame, A.qua, M.rot, M.dom, P.ope*, V.pen, G.mel, **C.fel, O.fas, M.dif**
Dieldrin	1.59	1.33–2.20	6	4.25	1.04–15.0	*M.dom*, M.dif, P.ame, A.ste, **A.aeg, A.qua, O.fas**
Endosulfan	120	70.0–218	5	1.83	0.510–3.14	*L.dec, H.arm*
Lindane	2.50	0.350–5.62	8	8.55	0.963–32.5	M.dom, A.ste, M.dif, A.aeg, **A.qua, P.ame, O.fas**
Methoxychlor	236	n/a	1	11.4	6.20–18.9	*M.dom, V.pen, A.qua*
Organophosphates						
Azinphos-methyl	1.99	0.550–4.28	7	9.33	8.79–10.2	**M.dom, L.dec, M.cro**
Bromophos	39.6	n/a	1	6.91	2.32–10.3	*M.dom, A.aeg, A.ste*
Chlorpyrifos	0.847	0.590–1.14	5	9.00	0.280–66.7	*P.ame, L.dec, B.vag*, Ene/Ish, **B.asa, S.cal, M.dom, B.ori, P.aus, Hep, P.bru, B.ger, Bo.ter, P.ful, C.nen, M.cro, D.vir, H.con, Hyd, C.san, L.lin**
Demeton	17.3	11.1–26.0	4	52.1	0.300–147	*N.mel, M.rot*, C.r/o/c, M.dom, H.con, **G.pun, C.bal, N.ame**
Demeton-S-methyl	4.98	2.60–9.37	5	9.55	0.285–16.7	*M.per*, **B.agr, B.luc, Bo.ter, M.dom**
DFP	30.0	n/a	1	59.0	5.00–160	*M.pis, M.dom*, **B.ger**
Diazinon	2.10	1.37–3.72	5	8.19	0.300–27.0	*A.erv, A.qua, A.aeg*, M.dom, **A.pis, M.rot, H.arm, V.pen, M.bee,N.mel, B.asa, B.ger, C.qui, H.con, D.vir, N.per, T.nig, C.fel**
Dichlorvos	2.73	0.290–5.01	4	13.5	2.08–25.0	M.dom, **T.cas**
Dicrotophos	1.72	0.410–3.05	5	41.2	0.010–124	*M.rot, N.mel*, **M.cro**
Dimethoate	1.62	1.00–2.47	11	23.2	0.260–78.0	*L.hes, M.per*, M.dom, **B.agr, B.luc, Bo.ter, B.ger, O.fas**
Disulfoton	42.7	14.6–61.2	7	217	8.00–607	*B.agr, B.luc, L.dec*, **D.vir**
Fenitrothion	1.66	0.180–3.83	7	7.03	1.10–29.6	A.aeg, M.rot, A.ste, A.ery, **M.dom, B.ter, L.hes, B.dor, B.ger, P.ame**
Fenthion	3.14	3.08–3.19	2	4.15	1.30–11.3	*I.ver, B.dor, M.dom*, **C.fel**
Formothion	1.79	n/a	1	2.27	1.12–3.41	*B.dor*, **M.dom**
Malathion	4.19	1.10–7.26	6	22.5	0.130–111	*L.hes, M.pis, A.sus, A.sol*, I.ver, V.pen, A.ste, A.qua, A.aeg, **B.dor, M.cro, T.cas, M.dom, H.arm, C.fel, O.fas, B.ger**
Methyl parathion	1.76	0.610–3.24	8	1.86	0.490–5.28	*D.vir, M.pis*, C.bal, C.r/o/c, H.con, M.dom, H.arm, B.ger, G.pun, **N.ame, M.cro**
Mevinophos	1.82	0.250–3.60	5	2.16	0.025–4.85	*N.mel*, M.dom, **M.rot**
Mipafox	57.3	n/a	1	16.0	7.89–20.0	*M.dom, B.ger, M.pis*
Naled	2.93	1.00–4.85	2	1.46	1.08–1.84	M.dom, B.dor
Paraoxon	0.600	n/a	1	1.21	0.030–4.50	*C.asp, A.vit, Bom, O.fas, L.mig, M.pis, N.fas, M.dom*, **B.ger, H.con, P.ame, C.pen, D.und, F.san, C.eur, N.que, Co.eur, M.fem, P.fas, T.tet, E.pen**
Parathion	1.36	0.100–3.50	7	6.62	0.020–47.0	*N.mel*, M.rot, M.fem, M.dom, L.mig, P.ame, B.ger, **D.vir, O.fas**
Phorate	2.45	0.910–3.20	4	6.27	4.27–8.26	**M.dom, B.agr, B.luc**
Phosphamidon	4.89	0.020–14.5	3	22.8	0.010–106	M.rot, N.mel, C.r/o/c, H.con, **G.pun, N.ame, C.bal**
Sulprofos	72.0	n/a	1	34.1	13.4–54.7	*H.arm, M.cro*
Temephos	14.8	14.0–15.5	2	288	0.110–478	*L.hes*, **A.aeg, D.vir, L.lin**
TEPP	0.410	0.010–1.20	3	0.814	0.037–1.59	N.mel, **M.rot**
Trichlorfon	24.0	5.81–36.7	4	472	0.430–3290	*L.hes*, B.dor, G.pun, N.ame, M.dom, **H.con, A.ery, V.pen, C.r/o/c, M.rot, C.bal, B.ter**

[a,b,c,d] As per Table 1.

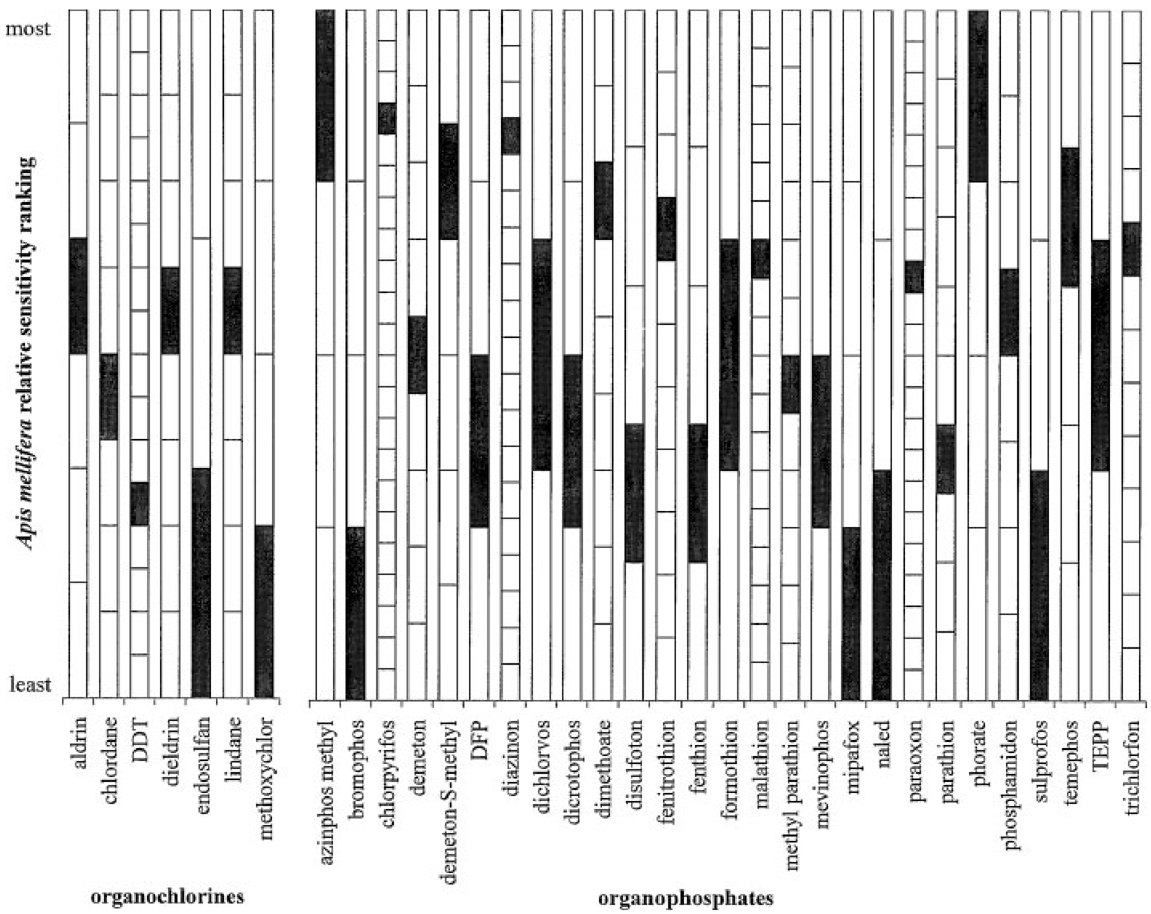

Figure 2. The relative sensitivity ranking of *Apis mellifera* compared with other insect species to organochlorine and organophosphate insecticides. Bars are divided into the total number of insect species LD_{50} values available for that insecticide. Shaded boxes indicate the position of *Aphis mellifera* compared with the other insect species.

For those organophosphates for which activation is not required, honey bees were not uniquely sensitive overall, as there were five, two and five cases where the honey bee was in the bottom 50%, the middle or the top 50% of the sensitive species respectively. *Apis mellifera* was the least sensitive species to two of these organophosphates (mipafox and naled). Examination of the other insects tested showed no pattern of an individual species being consistently more or less sensitive to organophosphates (Table 2).

For organophosphates that require activation, honey bees were not uniquely sensitive overall, as there were seven, two and six cases where the honey bee was in the bottom 50%, the middle or the top 50% of the sensitive species respectively. *Apis mellifera* was the least sensitive species to two of these organophosphates (bromophos-methyl and sulprofos), and was the most sensitive species to two of these organophosphates (azinphos-methyl and phorate). Examination of the other insects tested showed no pattern of an individual species being consistently more or less sensitive to these organophosphates (Table 2).

3.6 Pyrethroids

Apis mellifera was about equally sensitive to a variety of pyrethroids compared with the other species tested (Fig. 3). The honey bee was in the bottom 50% for five pyrethroids, in the middle for two pyrethroids and in the top 50% sensitivity ranking for three pyrethroids. *Apis mellifera* was the most sensitive species to pyrethrins (seven species) and the least sensitive species to allethrin (seven species) and cyhalothrin (nine species) (Table 3). For the pyrethroids for which data concerning Colorado potato beetle (*Leptinotarsa decemlineata* Say) and cat flea (*C. felis*) are available, the sensitivity ranking of these species tends to be less than that of the honey bee (Table 3).

3.7 Miscellaneous insecticides

In the case of miscellaneous insecticides (those not fitting into one of the classes previously referenced), *A. mellifera* was about equally sensitive overall compared with the other species tested (Fig. 3). There were two, zero and three cases where honey bee sensitivity ranked in the bottom 50%, the middle or the top 50% of the sensitive species respectively. The honey bee was the most sensitive species to spinosad (eight species) and the least sensitive to rotenone (five species) (Table 3). Analysis of the other insects tested showed that the mosquito species *Aedes aegypti* L., *Anopheles quadrimaculatus* Say and *Culex quinquefasciatus* L. were all generally less sensitive than the honey bee to the miscellaneous insecticide compounds (Table 3).

4 DISCUSSION

A limitation to this type of analysis is that for every insecticide there is not a large number of species that have reported LD_{50} values. Thus, for insecticides with a smaller number of

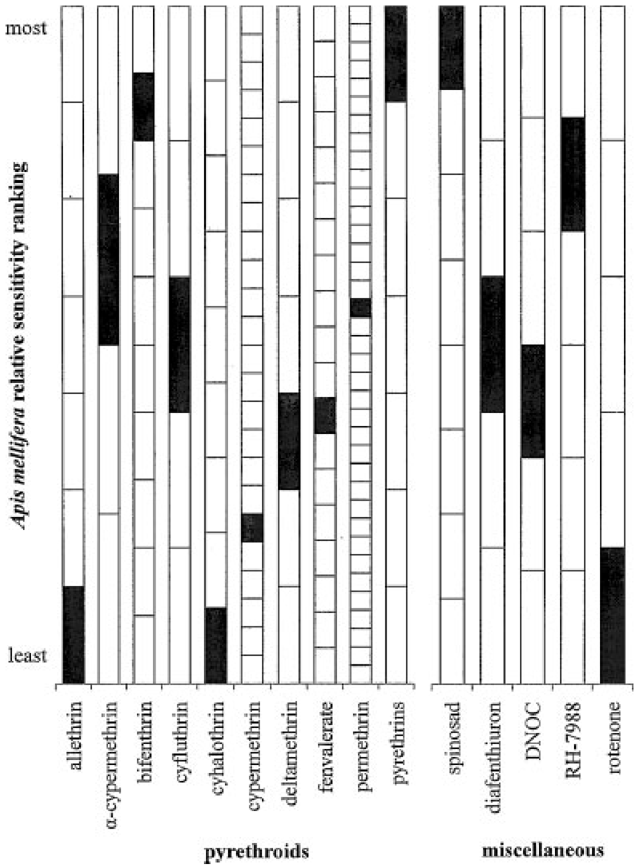

Figure 3. The relative sensitivity ranking of *Apis mellifera* compared with other insect species to pyrethroid and miscellaneous insecticides. Bars are divided into the total number of insect species LD_{50} values available for that insecticide. Shaded boxes indicate the position of *A. mellifera* compared with the other insect species.

species in which comparisons are possible, there is a chance (owing to a random sampling error) that the honey bee could appear uniquely sensitive or insensitive. This may be the case for the present analysis, because the honey bee was found to be the most or least sensitive species in 14 cases, and in nine of these (bendiocarb, endosulfan, methoxychlor, azinphos-methyl, bromophos, mipafox, naled, phorate and suprofos) there were less than five species compared. For this reason, when conclusions were drawn, greater weight was allotted to the relative ranking of *A. mellifera* (Figs 1 to 3) rather than considering the number of times it was the most/least sensitive species or using a direct comparison of the averaged LD_{50} values (Tables 1 to 3).

Many previous reports on honey bee sensitivity have not incorporated the comparative aspect addressed in this review, because often the susceptibility of *A. mellifera* to an insecticide has been described using a hazard indicator rather than with raw data. The hazard scale was used by Johansen,[12] in which insecticides were categorized into general 'poisoning hazard classes'. The classes were further defined by Atkins *et al.*,[23] and the following definitions were adopted by the United States Environmental Protection Agency.[24] Group 1 pesticides are highly toxic (LD_{50} 0.001–1.99 µg bee^{-1}), causing severe bee losses if applied when bees are present at treatment time, Group 2 (LD_{50} 2.0–10.99 µg bee^{-1}) compounds are moderately toxic and can be used in a location where bees are present if application is conducted properly. Pesticides in group 3 are relatively non-toxic ($LD_{50} > 11.0$ µg bee^{-1}) such that they can be used around bees with minimal harm.[23,25]

To gain a greater understanding of the relative sensitivity of honey bees, it would be desirable to evaluate other life stages and/or bioassay endpoints other than mortality. Unfortunately, insufficient information is available to evaluate the relative susceptibility of larval honey bees to other insect species. For social insects, insecticides that have sublethal effects on behavior could present problems to the colony, although comparative data for these effects are sparse and do not permit an analysis of honey bee sensitivity relative to other species. Atkins and Kellum[26] put forth the interesting hypothesis that pesticides that are fast acting and kill the foraging bees quickly provide a means by which the brood and the rest of the colony will not be exposed to the toxic effects of exposure. However, foragers with insecticide residues on their cuticle and in their pollen load do return to the hive. In addition, pollen may contain naturally occurring toxic allelochemicals. Thus, the idea that honey bees are uniquely sensitive to insecticides as a way to prevent toxins from reaching hive members does not appear to be likely.

Inglesfield[27] noted that the low toxicity of pyrethroids to wild bee populations in the field was not comparable with the higher levels of toxicity observed to the same chemicals in laboratory analyses. These types of finding can create uncertainty in the assessment of bee sensitivity to insecticides, highlighting the importance of comparing equivalent toxicity data within a species to multiple insecticides.

Based on the available literature using adult topical bioassay data, it was found that, in general, honey bees were no more sensitive to insecticides than other insect species. While it is true that honey bees can be particularly sensitive to individual insecticides, it is not the case that they are among the most sensitive species to all insecticides. This suggests that, even though honey bees have a lower number of cytochrome P450 genes,[21] this does not reflect a greater sensitivity to insecticides. The toxicities associated with other bee species (*Apis* and *Bombus*) were also compared. Although the data are extremely limited (only two neonicotinoid insecticides, imidacloprid and thiamethoxam), *A. indica* and *A. florae* are generally as sensitive to insecticides as *A. mellifera* (Table 1). Conversely, bumble bees (*Bombus agrorum* Fabricius, *B. terricola* Kirby, *B. terrestris* L., *B. lucorum* L. and *Bombus* spp.) tended to be less sensitive than the honey bee to various compounds across the insecticide classes (Tables 1 to 3). The economic and agricultural impact of honey bees (and other wild bees) is enormous. While they do not appear to be uniquely sensitive to insecticides as a species, all pesticides are toxic and should be used in a way that minimizes honey bee exposure, so as to minimize declines in the number of foragers and/or honey contamination.

ACKNOWLEDGEMENTS

The authors thank the Cornell University library staff for technical assistance. This work was supported by the Sarkaria Institute of Insect Physiology and Toxicology.

SUPPORTING INFORMATION

Supporting information may be found in the online version of this article.

Table 3. LD$_{50}$ values of *Apis mellifera* and other species to pyrethroid and other insecticides

	Apis mellifera LD$_{50}$ (μg g^{-1})			Other species LD$_{50}$ (μg g^{-1})		
Insecticide	Mean	Range	*n*[a]	Mean	Range	Species[b,c,d]
Pyrethroids						
Allethrin	47.0	34.0–60.0	2	13.7	1.60–46.0	*A.qua, A.ste, I.ver, A.aeg, B.ger*, O.fas
α-Cypermethrin	0.400	0.300–0.500	2	1.15	0.280–2.40	B.ger, **B.ter, L.dec**
Bifenthrin	0.100	n/a	1	1.35	0.077–6.50	*A.aeg*, Ene/Ish, **A.gam, C.qui, Hep, D.vir, B.ger, Hyd, H.con**
Cyfluthrin	0.677	n/a	1	1.10	0.290–2.69	*B.ger, M.dom*, **B.dor, B.ter**
Cyhalothrin	0.270	n/a	1	0.045	0.011–0.079	*P.ame, P.bru, P.aus, P.ful, B.ori, B.asa, B.ger, B.vag*
Cypermethrin	1.18	0.200–3.70	4	1.13	0.003–6.10	A.bip, C.mac, M.dom, O.fas, H.tre, H.par, D.lon, O.mel, Ene/Ish, B.asa, C.tri, H.zea, H.gla, C.tra, Hep, B.ger, S.fru, H.con, B.dor, A.ips, **Hyd, L.dec, C.fel**
Deltamethrin	0.440	0.370–0.510	2	0.600	0.018–2.38	*A.gam, M.dom, C.qui, B.ger*, **C.fel, L.dec**
Fenvalerate	2.45	0.800–4.08	4	23.6	0.022–376	*A.bip, D.lon, H.tre, C.mac, O.mel*, C.tra, P.ope, B.asa, L.dec, H.con, H.par, B.ger, C.tri, H.arm, **H.gla, S.fru, B.dor, M.cro**
Permethrin	1.18	0.173–2.02	5	15.8	0.100–318	*A.bip, A.qua, C.mac, A.aeg, A.ery, O.mel, D.lon, C.tri, H.par*, M.dom, M.rot, Hep, P.ope, H.tre, Ene/Ish, A.gam, H.gla, C.tra, B.ter, H.zea, N.per, M.bee, C.qui, S.fru, **A.ips, T.nig,H.arm, Bo.ter, B.ger, Hyd, P.ame, H.con, C.fel, L.dec, M.cro, B.dor**
Pyrethrins	1.28	0.460–2.10	2	25.9	7.00–50.0	**A.tri, O.fas, P.ame, T.mol, P.jap, M.dom**
Other						
Spinosad	0.402	0.025–0.780	3	3.20	0.580–13.4	M.rot, N.mel, **A.aeg, A.qua, M.dom, C.qui, B.dor**
Diafenthiuron	15.0	n/a	1	27.03	11.12–48.0	*A.ind, A.qua*, **C.qui, A.aeg**
DNOC	31.7	n/a	1	25.0	10.0–35.0	*L.mig, P.ame, A.aeg*, **A.qua, C.qui**
RH-7988	26.2	n/a	1	81.3	0.520–203	*A.pis*, **A.erv, N.mel, H.con, M.rot**
Rotenone	360	120–600	2	22.1	2.00–42.5	*C.cat, T.mol*, P.jap, O.fas

[a,b,c,d] As per Table 1.

REFERENCES

1 Allen-Wardell G, Bernhardt P, Bitner R, Burquez A, Buchmann S, Cane J, *et al*, The potential consequences of pollinator declines on the conservation of biodiversity and stability of food crop yields. *Conserv Biol* **12**:8–17 (1998).

2 Losey JE and Vaughan M, The economic value of ecological services provided by insects. *BioScience* **56**:311–323 (2006).

3 Pimentel D, Acquay H, Biltonen M, Rice P, Silva M, Nelson J, *et al*, Environmental and economic costs of pesticide use. *BioScience* **42**:750–760 (1992).

4 Southwick EE and Southwick L, Estimating the economic value of honey bees (Hymenoptera: Apidae) as agricultural pollinators in the United States. *J Econ Entomol* **85**:621–633 (1992).

5 Morse RA and Calderone NW, The value of honey bees as pollinators of U.S. crops in 2000. *Bee Culture* **128**:1–15 (2000).

6 Pimentel D, Andow D, Dyson-Hudson R, Gallahan D, Jacobson S, Irish M, *et al*, Environmental and social costs of pesticides: a preliminary assessment. *Oikos* **34**:126–140 (1980).

7 *The Health of Livestock and Honeybees in England*. Department for Environment, Food and Rural Affairs, National Audit Office, Great Britain (2009).

8 Greig-Smith PW, Thompson HM, Hardy AR, Bew MH, Findlay E and Stevenson JH, Incidents of poisoning of honeybees (*Apis mellifera*) by agricultural pesticides in Great Britain 1981–1991. *Crop Prot* **13**:567–581 (1994).

9 Chauzat M-P, Faucon J-P, Martel A-C, Lachaize J, Cougoule N and Aubert M, A survey of pesticide residues in pollen loads collected by honey bees in France. *J Econ Entomol* **99**:253–262 (2006).

10 Mullin CA, Frazier M, Frazier JL, Ashcraft S, Simonds R, van Engelsdorp D *et al*, High levels of miticides and agrochemicals in North American apiaries: implications for honey bee health. *PLoS ONE* **5**:e9754 (2010).

11 Koch H and Weißer P, Exposure of honey bees during pesticide application under field conditions. *Apidologie* **28**:439–447 (1997).

12 Johansen CA, Digest on bee poisoning, its effects and prevention. *Bee World* **47**:9–25 (1966).

13 Rortais A, Arnold G, Halm M-P and Touffet-Briens F, Modes of honeybees exposure to systemic insecticides: estimated amounts of contaminated pollen and nectar consumed by different categories of bees. *Apidologie* **36**:71–83 (2005).

14 Shaw FR, Bee poisoning: a review of the more important literature. *J Econ Entomol* **34**:16–21 (1941).

15 Hashimoto JH, Ruvolo-Takasusuki MCC and de Toledo VdAA, Evaluation of the use of the inhibition esterases activity on *Apis mellifera* as bioindicators of insecticide thiamethoxam pesticide residues. *Sociobiology* **42**:693–699 (2003).

16 Porrini C, Sabatini AG, Girotti S, Ghini S, Medrzycki P, Grillenzoni F, *et al*, Honey bees and bee products as monitors of the environmental contamination. *Apiacta* **38**:63–70 (2003).

17 Metcalf RL, Insecticides in pest management, in *Introduction to Insect Pest Management*, ed. by Metcalf RL and Luckmann WH. John Wiley & Sons, Inc., New York, NY, pp. 245–314 (1975).

18 Torchio PF, Relative toxicity of insecticides to the honey bee, alkali bee, and alfalfa leafcutting bee (Hymenoptera: Apidae, Halictidae, Megachilidae). *J Kansas Entomol Soc* **46**:446–453 (1973).

19 Johnson RM, Pollock HS and Berenbaum MR, Synergistic interactions between in-hive miticides in *Apis mellifera*. *J Econ Entomol* **102**:474–479 (2009).

20 Atkins EL, Injury to honey bees by poisoning, in *The Hive and the Honey Bee*, ed. by Graham JM. Rev. Dadant and Sons, Hamilton, IL, p. 1324 (1992).

21 Claudianos C, Ranson H, Johnson RM, Biswas S, Schuler MA, Berenbaum MR, *et al*, A deficit of detoxification enzymes: pesticide sensitivity and environmental response in the honeybee. *Insect Mol Biol* **15**:615–636 (2006).

22 Matsumura F, *Toxicology of Insecticides*. Plenum, New York, NY (1985).

23 Atkins EL, Kellum D and Atkins KW, Reducing pesticide hazards to honey bees: mortality prediction techniqes and integrated

management strategies. Div. Agric. Sci., Univ. Calif. Leaflet No. 2883 (1981).

24 Environmental hazards, in *EPA Label Review Manual*. EPA, Washington, DC, Ch. 8, pp. 1–16 (2008).

25 Anderson LD and Atkins EL, Pesticide usage in relation to beekeeping. *Annu Rev Entomol* **13**:213–238 (1968).

26 Atkins EL and Kellum D, Comparative morphogenic and toxicity studies on the effect of pesticides on honeybee brood. *J Apicult Res* **25**:242–255 (1986).

27 Inglesfield C, Pyrethroids and terrestrial non-target organisms. *Pestic Sci* **27**:387–428 (1989).

28 Drees H and Godesberg B, Der gegenwärtige Stand unserer Kenntnisse über die Bienengiftigkeit und Bienengefährlichkeit unserer Pflanzenschutzmittel (in German). *Gesunde Pflanzen* **22**:21–23 (1970).

29 Atkins EL, Greywood EA and Macdonald RL, Toxicity of pesticides and other agricultural chemicals to honey bees: laboratory studies. *University of California, Agricultural Extension* **M-16**:1–38 (1975).

30 Johnston RL and Sandvol LE, Susceptibility of Idaho populations of Colorado potato beetle to four classes of insecticides. *Am Potato J* **63**:81–85 (1986).

31 Helson BV, Barber KN and Kingsbury PD, Laboratory toxicology of six forestry insecticides to four species of bee (Hymenoptera: Apoidea). *Arch Environ Contam Toxicol* **27**:107–114 (1994).

32 Abdelwahab AM, Khalil FM and Hussein MH, Toxicity of insecticides to honey bees in laboratory and field. *Bull Entomol Soc Egypt, Econ Ser* **7**:83–89 (1973).

33 Jao LT and Gordon HT, Toxicity of certain pyrethroids and carbamates to the CS strain of *Oncopeltus fasciatus*. *J Econ Entomol* **62**:612–615 (1969).

34 Bull DL, Wadleigh RW and Patterson RS, Pharmacodynamics of malathion and carbaryl in susceptible and multiresistant German cockroaches (Dictyoptera: Blattellidae). *J Econ Entomol* **82**:1512–1519 (1989).

35 Wadleigh RW, Koehler PG and Patterson RS, Comparative susceptibility of North American *Blattella* (Orthoptera: Blattellidae) species to insecticides. *J Econ Entomol* **82**:1130–1133 (1989).

36 Moss JI and Scott JG, Tetrodotoxin protects German cockroaches (Dictyoptera: Blattellidae) from type I pyrethroid and carbamate insecticide poisoning. *J Econ Entomol* **89**:51–55 (1996).

37 Scott JG, Cochran DG and Siegfried BD, Insecticide toxicity, synergism, and resistance in the German cockroach (Dictyoptera: Blattellidae). *J Econ Entomol* **83**:1698–1703 (1990).

38 Siegfried BD, Scott JG, Roush RT and Zeichner BC, Biochemistry and genetics of chlorpyrifos resistance in the German cockroach, *Blattella germanica* (L.). *Pestic Biochem Physiol* **38**:110–121 (1990).

39 Lee C-Y, Yap H-H and Chong N-L, Insecticide toxicity on the adult German cockroach, *Blattella germanica* (L.) (Dictyoptera: Blattellidae). *Malaysian J Sci* **17A**:1–9 (1996).

40 Scharf ME, Hemingway J, Reid BL, Small GJ and Bennett GW, Toxicological and biochemical characterization of insecticide resistance in a field-collected strain of *Blattella germanica* (Dictyoptera: Blattellidae). *J Econ Entomol* **89**:322–331 (1996).

41 Moyses EW and Gfeller FJ, Topical application as a method for comparing the effectiveness of insecticides against cat flea (Siphonaptera: Pulicidae). *J Med Entomol* **38**:193–196 (2001).

42 Pridgeon JW, Pereira RM, Becnel JJ, Allan SA, Clark GG and Linthicum KJ, Susceptibility of *Aedes aegypti, Culex quinquefasciatus* Say, and *Anopheles quadrimaculatus* Say to 19 pesticides with different modes of action. *J Med Entomol* **45**:82–87 (2008).

43 Hadaway AB and Barlow F, The toxicity of carbamates to adult *Anopheles stephensi*. *Bull Wld Hlth Org* **28**:63–67 (1963).

44 Barlow F and Hadaway AB, Chemical structure and physical properties of candidate insecticides in relation to residual toxicity to adult mosquitos. *Pestic Sci* **1**:117–119 (1970).

45 Batista GC, Amaral E and Passarela Neto A, Toxicidade de alguns inseticidas e acaricida para operárias híbridas de *Apis mellifera ligustica* L. e *Apis mellifera adansonii* L. (Hymenoptera: Apidae). *An Soc Entomol Brasil* **4**:73–77 (1975).

46 Barker RJ, Cholinesterase reactivators tested as antidotes for use on poisoned honey bees. *J Econ Entomol* **63**:1831–1834 (1970).

47 Georghiou GP and Metcalf RL, Carbamate insectides: comparative insect toxicity of Sevin, Zectran, and other new materials. *J Econ Entomol* **55**:125–127 (1962).

48 Stevenson JH, Toxicity of insecticides to bees. Rothamsted Experimental Station Report, pp. 166–167 (1964).

49 Georghiou GP and Atkins EL, Temperature coefficient of toxicity of certain *N*-methylcarbamates agains honeybees, and the effect of the synergist piperonyl butoxide. *J Apicult Res* **3**:31–35 (1964).

50 Stevenson JH, The acute toxicity of unformulated pesticides to worker honey bees (*Apis mellifera* L). *Plant Path* **27**:38–40 (1978).

51 Danka RG, Rinderer TE, Hellmich RL and Collins AM, Comparative toxicities of four topically applied insecticides to Africanized and European honey bees (Hymenoptera: Apidae). *J Econ Entomol* **79**:18–21 (1986).

52 Ball HJ, Topical toxicity of insecticides to *Diabrotica virgifera* adults. *J Econ Entomol* **62**:1172–1174 (1969).

53 Meinke LJ, Siegfried BD, Wright RJ and Chandler LD, Adult susceptibility of Nebraska western corn rootworm (Coleoptera: Chrysomelidae) populations to selected insecticides. *J Econ Entomol* **91**:594–600 (1998).

54 Leonova IN and Slynko NM, Comparative study of insecticide susceptibility and activities of detoxification enzymes in larvae and adults of cotton bollworm, *Heliothis armigera*. *Arch Insect Biochem Physiol* **32**:157–172 (1996).

55 Leigh TF and Jackson CE, Topical toxicity of several chlorinated hydrocarbon, organophosphorus, and carbamate insecticides to *Lygus hesperus*. *J Econ Entomol* **61**:328–330 (1968).

56 Johansen CA and Davis HG, Toxicity of nine insecticides to the western yellowjacket. *J Econ Entomol* **65**:40–42 (1972).

57 Erdoğan C and Gürkan MO, Investigations on the susceptibilities of different Colorado potato beetle (*Leptinotarsa decemlineata*) (Say) (Coleoptera: Chrysomelidae) populations against some insecticides (in Turkish). *Türk Entomol Derg* **21**:299–309 (1997).

58 Hsu J-C, Feng H-T and Wu W-J, Resistance and synergistic effects of insecticides in *Bactrocera dorsalis* (Diptera: Tephritidae) in Taiwan. *J Econ Entomol* **97**:1682–1688 (2004).

59 Valdovinos-Nunez GR, Quezada-Euan JJG, Ancona-Xiu P, Moo-Valle H, Carmona A and Sanchez ER, Comparative toxicity of pesticides to stingless bees (Hymenoptera: Apidae: Meliponini). *J Econ Entomol* **102**:1737–1742 (2009).

60 Powell JE, King EG and Jany CS, Toxicity of insecticides to adult *Micoplitis croceipes* (Hymenoptera: Braconidae). *J Econ Entomol* **79**:1343–1346 (1986).

61 Shono T and Scott JG, Spinosad resistance in the housefly, *Musca domestica*, is due to a recessive factor on autosome 1. *Pestic Biochem Physiol* **75**:1–7 (2003).

62 Brewer MJ and Trumble JT, Field monitoring for insecticide resistance in beet armyworm (Lepidoptera: Noctuidae). *J Econ Entomol* **82**:1520–1526 (1989).

63 Hadaway AB, Barlow F, Grose JEH, Turner CR and Flower LS, Evaluation of compounds for insecticidal activity on adult mosquitoes; 1. Responses of adult mosquitoes to some new insecticides. *Bull Wld Hlth Org* **42**:353–368 (1970).

64 Valles SM, Koehler PG and Brenner RJ, Comparative insecticide susceptibility and detoxification enzyme activities among pestiferous Blattodea. *Comp Biochem Physiol, Part C* **124**:227–232 (1999).

65 Siegfried BD and Scott JG, Mechanisms responsible for propoxur resistance in the German cockroach, *Blattella germanica* (L.). *Pestic Sci* **33**:133–146 (1991).

66 Collins WJ, A comparative study of insecticide resistance assays with the German cockroach. *Pestic Sci* **6**:83–95 (1975).

67 Estenik JF and Federle PF, The susceptiblity of an adult damselfly, *Ischnura verticalis*, to selected insecticides. *Ohio Talaromyces* **75**:81–82 (1974).

68 Leigh TF, Jackson CE, Wynholds PF and Cota JA, Toxicity of selected insecticides applied topically to *Lygus hesperus*. *J Econ Entomol* **70**:42–44 (1977).

69 Chadwick PR, The activity of some pyrethroids against *Periplaneta americana* and *Blattella germanica*. *Pestic Sci* **10**:32–38 (1979).

70 Metcalf RL, Methods of topical application and injection, in *Methods of Testing Chemicals on Insects*, ed. by Shepard HH. Burgess Publishing Co., Minneapolis, MN, pp. 92–113 (1958).

71 Stark JD, Jepson PC and Mayer DF, Limitations to use of topical toxicity data for predictions of pesticide side effects in the field. *J Econ Entomol* **88**:1081–1088 (1995).

72 Thompson HM, Assessing the exposure and toxicity of pesticides to bumblebees (*Bombus* sp.). *Apidologie* **32**:305–321 (2001).

73 Yuval B, Kaspi R, Shloush S and Warburg MS, Nutritional reserves regulate male participation in Mediterranean fruit fly leks. *Ecol Entomol* **23**:211–215 (1998).

74 Hinkle NC, Koehler PG, Kern WH and Patterson RS, Hematophagous strategies of the cat flea (Siphonaptera: Pulicidae). *Fla Entomol* **74**:377–385 (1991).

75 Kang J and Krupke CH, Influence of weight of male and female Western corn rootworm (Coleoptera: Chrysomelidae) on mating behaviors. *Ann Entomol Soc Am* **102**:326–332 (2009).

76 Gelman DB, Bell RA, Liska LJ and Hu JS, Artificial diets for rearing Colorado potato beetle, *Leptinotarsa decemlineata*. *J Insect Sci* **1**:7–18 (2001).

77 Chyb S and Simpson SJ, Dietary selection in adult *Locusta migratoria*. *Entomol Exp Appl* **56**:47–60 (1990).

78 Glynn Tillman P and Cate JR, Effect of host size on adult size and sex ratio of *Bracon mellitor* (Hymenoptera: Braconidae). *Environ Entomol* **22**:1161–1165 (1993).

79 Givens RP, Dimorphic foraging strategies of a Salticid spider (*Phidippus audax*). *Ecology* **59**:309–321 (1978).

80 Chapman JW and Goulson D, Environmental versus genetic influences on fluctuating asymmetry in the house fly, *Musca domestica*. *Biol J Linn Soc* **70**:403–413 (2000).

81 Klowden MJ, Held GA and Bulla LA, Toxicity of *Bacillus thuringiensis* subsp. *israelensis* to adult *Aedes aegypti* mosquitoes. *Appl Environ Microbiol* **46**:312–315 (1983).

82 Makee H and Saour G, Factors influencing mating success, mating frequency, and fecundity in *Phthorimaea operculella* (Lepidoptera: Gelechiidae). *Environ Entomol* **30**:31–36 (2001).

83 Binns TJ, The comparative toxicity of malathion, with and without the addition of triphenyl phosphate, to adults and larvae of a susceptible and two resistant strains of *Tribolium castaneum* (Herbst) (Coleoptera: Tenebrionidae). *J Stored Prod Res* **22**:97–101 (1986).

84 Corbel V, Duchon S, Zaim M and Hougard J-M, Dinotefuran: a potential neonicotinoid insecticide against resistant mosquitoes. *J Med Entomol* **41**:712–717 (2004).

85 Iwasa T, Motoyama N, Ambrose JT and Roe M, Mechanism for the differential toxicity of neonicotinoid insecticides in the honey bee, *Apis mellifera*. *Crop Prot* **23**:371–378 (2004).

86 Mota-Sanchez D, Hollingworth RM, Grafius EJ and Moyer DD, Resistance and cross-resistance to neonicotinoid insecticides and spinosad in the Colorado potato beetle, *Leptinotarsa decemlineata* (Say) (Coleoptera: Chrysomelidae). *Pest Manag Sci* **62**:30–37 (2006).

87 Kumar S, Regupathy CM and Regupathy A, Risk assessment of neonicotinoids applied to coffee ecosystem. *Internat Pest Cont* **47**:82–87 (2005).

88 Nauen R, Ebbinghaus-Kintscher U and Schmuck R, Toxicity and nicotinic acetylcholine receptor interaction of imidacloprid and its metabolites in *Apis mellifera* (Hymenoptera: Apidae). *Pest Manag Sci* **57**:577–586 (2001).

89 Schmuch R and Keppler J, Clothianidin – ecotoxicological profile and risk assessment. *Pflanzen Nach Bayer* **56**:26–58 (2003).

90 Suchail S, Guez D and Belzunces LP, Characteristics of imidacloprid toxicity in two *Apis mellifera* subspecies. *Environ Toxicol Chem* **19**:1901–1905 (2000).

91 Wen Z and Scott JG, Cross-resistance to imidacloprid in strains of German cockroach (*Blattella germanica*) and house fly (*Musca domestica*). *Pestic Sci* **49**:367–371 (1997).

92 Ghadamyari M, Talebi K, Mizuno H and Kono Y, Oxydemeton-methyl resistance, mechanisms, and associated fitness cost in green peach aphids (Hemiptera: Aphididae). *J Econ Entomol* **101**:1432–1438 (2008).

93 Menusan H, Comparative toxicity of insecticides administered in various ways to several species of insects. *J Econ Entomol* **41**:302–313 (1948).

94 Beard RL, Species-specificity of toxicants as related to route of administration. *J Econ Entomol* **42**:292–300 (1949).

95 Soloway SB, Naturally occurring insecticides. *Environ Health Perspect* **14**:109–117 (1976).

96 Schmuch R, Schöning R, Stork A and Schramel O, Risk posed to honeybees (*Apis mellifera* L., Hymenoptera) by an imidacloprid seed dressing of sunflowers. *Pest Manag Sci* **57**:225–238 (2001).

97 Senn R, Hofer D, Angst M, Wyss P, Brandl F, Maienfisch P, *et al*, CGA 293′343: a novel broad-spectrum insecticide supporting sustainable agriculture worldwide. *Proc Brighton Crop Prot Conf – Pests Dis*, BCPC, Alton, Hants, UK, pp. 27–36 (1998).

98 Beran F and Neururer J, Zur Kenntnis der Wirkung von Pflanzenschutzmitteln auf die Honigbiene (*Apis mellifera* L.) (in German). *Pflanzen Berichte* **15**:97–147 (1955).

99 Ripeanu M and Nica D, Bee poisoning by chlorine derivatives (in Romanian). *Apicultura* **32**:18–21 (1959).

100 Giannotti O, Metcalf RL and March RB, The mode of action of aldrin and dieldrin in *Periplaneta americana* (L.). *Ann Entomol Soc Am* **49**:588–592 (1956).

101 Ludvik GF, Topical application of insecticide solutions to *Anopheles quadrimaculatus*. *J Econ Entomol* **46**:364–365 (1953).

102 Shono T, Zhang L and Scott JG, Indoxacarb resistance in the house fly, *Musca domestica*. *Pestic Biochem Physiol* **80**:106–112 (2004).

103 Graves JB and Mackensen O, Topical application and insecticide resistance studies on the honey bee. *J Econ Entomol* **58**:990–993 (1965).

104 Tahori AS, Sobel Z and Soller M, Variability in insecticide tolerance of eighteen honey-bee colonies. *Entomol Exp Appl* **12**:85–98 (1969).

105 Scott JG and Matsumura F, Evidence for two types of toxic actions of pyrethroids on susceptible and DDT-resistant German cockroaches. *Pestic Biochem Physiol* **19**:141–150 (1983).

106 Scott JG, Ramaswamy SB, Matsumura F and Tanaka K, Effect of method of application on resistance to pyrethroid insecticides in *Blattella germanica* (Orthoptera: Blattellidae). *J Econ Entomol* **79**:571–575 (1986).

107 Scott JG and Matsumura F, Characteristics of a DDT-induced case of cross-resistance to permethrin in *Blattella germanica*. *Pestic Biochem Physiol* **16**:21–27 (1981).

108 Metcalf RL, *Organic Insecticides: Their Chemistry and Mode of Action*. Interscience Publishers, Inc., New York, NY (1955).

109 Torchio PF, Relative toxicity of insecticides to the honey bee, alkai bee, and alfalfa leafcutting bee (Hymenoptera: Apidae, Halictidae, Megachilidae). *J Kansas Entomol Soc* **46**:446–453 (1973).

110 Keeratikasikorn M and Hooper GHS, The comparative toxicity of some insecticides to the potato moth *Phthorimaea operculella* (Zeller) (Lepidoptera: Gelechiidae) and two of its parasites *Orgilus lepidus* Muesebeck and *Copidosoma desantisi* Annecke and Mynhardt. *J Aust Entomol Soc* **20**:309–311 (1981).

111 Hadaway AB, Barlow F, Grose JEH, Turner CR and Flower LS, Evaluation of compounds for insecticidal activity on adult mosquitos; 1. Responses of adult mosquitos to some new insecticides. *Bull Wld Hlth Org* **42**:353–368 (1970).

112 Smolarz S, Estimation of the contact toxicity of azofos, lindan, malathion, terpentol A and B, and acarizidol E20 towards the honey bee (in Polish). *Pszcel Zeszyty Nauk* **9**:77–91 (1965).

113 Beran F, Selektivität einiger Phosphorinsektizide mit besonderer Berücksichtigung ihrer Bienentoxizität (in German). *Pflanzen Berichte* **32**:37–57 (1965).

114 Powell JE, King EG and Jany CS, Toxicity of insecticides to adult *Micoplitis croceipes* (Hymenoptera: Braconidae). *J Econ Entomol* **79**:1343–1346 (1986).

115 Kupetz WH, Nieder G and Wegner H, Ergebnisse von Untersuchungen zur Bienengefährlichkeit und Bienentoxizität von Pflanzenschutzmitteln und deren Wirkstoffen (in German). *Pflanzen Berichte* **45**:165–188 (1976).

116 Kenaga EE, Whitney WK, Hardy JL and Doty AE, Laboratory tests with Dursban insecticide. *J Econ Entomol* **58**:1043–1050 (1965).

117 Kaakeh W, Reid BL and Bennett GW, Toxicity of fipronil to German and American cockroaches. *Entomol Exp Appl* **84**:229–237 (1997).

118 Dong K and Scott JG, Synergism of chlorpyrifos against the German cockroach, *Blattella germanica*. *Med Vet Entomol* **6**:241–243 (1992).

119 Marletto F, Patetta A and Manino A, Laboratory assessment of pesticide toxicity to bumblebees. *Bull Insectol* **56**:155–158 (2003).

120 Siegfried BD, Comparative toxicity of pyrethroid insecticides to terrestrial and aquatic insects. *Environ Toxicol Chem* **12**:1683–1689 (1993).

121 Stanković S, Zabel A, Kostic M, Manojlovic B and Rajkovic S, Colorado potato beetle [*Leptinotarsa decemlineata* (Say)] resistance to organophosphates and carbamates in Serbia. *J Pestic Sci* **77**:11–15 (2004).

122 Lingren PD and Ridgway RL, Toxicity of five insecticides to several insect predators. *J Econ Entomol* **60**:1639–1641 (1967).

123 Stevenson JH and Racey PA, Toxicity of insecticides to bumblebees. Rothamsted Experimental Station Report, pp. 176–177 (1966).

124 Hamilton JT and Attia FI, *Myzus persicae* (Sulzer): strains resistant to demeton-S-methyl and dimethoate in Australia. *J Aust Entomol Soc* **17**:63–64 (1978).
125 Sawicki RM, Devonshire AL, Rice AD, Moores GD, Petzing SM and Cameron A, The detection and distribution of organophosphorus and carbamate insecticide-resistant *Myzus persicae* (Sulz.) in Britain in 1976. *Pestic Sci* **9**:189–201 (1978).
126 Krueger HR and Casida JE, Toxicity of fifteen organophosphorus insecticides to several insect species and to rats. *J Econ Entomol* **50**:356–358 (1957).
127 Zettler JL and Arthur FH, Dose–response tests on red flour beetle and confused flour beetle (Coleoptera: Tenebrionidae) collected from flour mills in the United States. *J Econ Entomol* **90**:1157–1162 (1997).
128 Meister RT, *Crop Protection Handbook*. Meister Publishing Company, Willoughby, OH (2009).
129 Gough HJ, McIndoe EC and Lewis GB, The use of dimethoate as a reference compound in laboratory acute toxicity tests on honey bees (*Apis mellifera* L.) 1981–1992. *J Apicult Res* **33**:119–125 (1994).
130 Murray A, Acute and residual toxicity of a new pyrethroid insecticide, WL85871, to honey-bees. *Bull Environ Contam Toxicol* **34**:560–564 (1985).
131 Tornier I, Kling A and Schur A, Honey bee testing in southern Europe: from the laboratory to the relevant crop in the field. *Bull Insectol* **56**:185–187 (2003).
132 Winteringham FPW, Mechanisms of selective insecticidal action. *Ann Rev Entomol* **14**:409–442 (1969).
133 Hsu J-C and Feng H-T, Insecticide susceptibility of Oriental fruit fly (*Bactrocera dorsalis* (Hendel)) (Diptera: Tephritidae) in Taiwan. *Chinese J Entomol* **20**:109–118 (2000).
134 Khoo BK and Sutherland DJ, The susceptibility status of *Aedes sollicitans* adults to topically applied malathion. *Mosquito News* **43**:441–444 (1983).
135 Nigg HN, Mallory LL, Fraser S, Simpson SE, Robertson JL, Attaway JA, *et al*, Test protocols and toxicity of organophosphate insecticides to Caribbean fruit fly (Diptera: Tephritidae). *J Econ Entomol* **87**:589–595 (1994).
136 Purcell MF, Stark JD and Messing RH, Insecticide effect on three Tephritid fruit flies and associated Braconid parasitoids in Hawaii. *J Econ Entomol* **87**:1455–1462 (1994).
137 Metcalf RL and March RB, Properties of actylcholine esterases from the bee, the fly and the mouse and their relation to insecticide action. *J Econ Entomol* **43**:670–676 (1950).
138 Stringer A, The insecticidal activity of some organophosphorus compounds against the migratory locust (*Locusta migratoria migratorioides* Reiche & Fairm.). *Ann Appl Biol* **44**:506–510 (1956).
139 Metcalf RL and March RB, Studies on the mode of action of parathion and its derivatives and their toxicity to insects. *J Econ Entomol* **42**:721–728 (1949).
140 Ahmad Z and Johansen C, Selective toxicity of carbophenothion and trichlorfon to the honey bee and the alfalfa leafcutting bee. *Environ Entomol* **2**:27–30 (1973).
141 Hadaway AB, Barlow F, Grose JEH, Turner CR and Flower LS, Evaluation of compounds for insecticidal activity on adult mosquitos; 5. Toxicity to adult mosquitos and residual properties of some pyrethroids. *Bull Wld Hlth Org* **42**:387–398 (1970).
142 Torun G and Gürkan MO, Investigations on the effect of temperature on toxicity of some synthetic pyrethroids on *Leptinotarsa decemlineata* (Say) (Coleoptera, Chrysomelidae) (in Turkish). *Turk Entomol Derg* **20**:295–307 (1996).
143 Johnson RM, Wen Z, Schuler MA and Berenbaum MR, Mediation of pyrethroid insecticide toxicity to honey bees (Hymenoptera: Apidae) by cytochrome P450 monooxygenases. *J Econ Entomol* **99**:1046–1050 (2006).
144 Smart LE and Stevenson JH, Laboratory estimation of toxicity of pyrethroid insecticides to honeybees: relevance to hazard in the field. *Bee World* **63**:150–152 (1982).
145 Coats SA, Coats JR and Ellis CR, Selective toxicity of three synthetic pyrethroids to eight Coccinellids, a Eulophid parasitoid, and two pest Chrysomelids. *Environ Entomol* **8**:720–722 (1979).
146 Usmani KA and Knowles CO, Toxicity of pyrethroids and effect of synergists to larval and adult *Helicoverpa zea, Spodoptera frugiperda*, and *Agrotis ipsilon* (Lepidoptera: Noctuidae). *J Econ Entomol* **94**:868–873 (2001).
147 Delabie J, Bos C, Fonta C and Masson C, Toxic and repellent effects of cypermethrin on the honeybee: laboratory, glasshouse and field experiments. *Pestic Sci* **16**:409–415 (1985).
148 Valles SM, Dong K and Brenner RJ, Mechanisms responsible for cypermethrin resistance in a strain of German cockroach, *Blattella germanica*. *Pestic Biochem Physiol* **66**:195–205 (2000).
149 Perić I, Miloševski N and Kljajić P, Insecticide susceptibility of the Colorado potato beetle in the vicinity of Belgrade, Yugoslavia. *Acta Horticult* **462**:983–990 (1997).
150 Pap L, Kelemen M, Tóth A, Székely I and Bertók B, The synthetic pyrethroid isomers II. Biological activity. *J Environ Sci Health, Part B* **31**:527–543 (1996).
151 Abd-El-Salam M, Merzouk MA, Mohanna N and Kahmis A, Studies on synthetic pyrethroids. 10 – Toxicity of deltamethrin, fensvalerate, fenpropathrin, flucythrinate and its 1-(2-phenoxybenzoyl)-2-propyl esters to honey bees, *Apis mellifera*. *Alex J Agric Res* **33**:283–296 (1988).
152 Cao XM, Song FL, Zhao TY, Dong YD, Sun CX and Lu BL, Survey of deltamethrin resistance in house flies (*Musca domestica*) from urban garbage dumps in northern China. *Environ Entomol* **35**:1–9 (2006).
153 Scott JG, α-Tocopherol antagonizes the toxicity of the pyrethroid insecticide permethrin in susceptible and *kdr*-resistant insects. *J Pestic Sci* **23**:399–401 (1998).
154 Liu N and Scott JG, Inheritance of CYP6D1-mediated pyrethroid resistance in house fly (Diptera: Muscidae). *J Econ Entomol* **90**:1478–1481 (1997).
155 Shono T, Kasai S, Kamiya E, Kono Y and Scott JG, Genetics and mechanisms of permethrin resistance in the YPER strain of house fly. *Pestic Biochem Physiol* **73**:27–36 (2002).
156 Kasai S and Scott JG, Overexpression of cytochrome P450 CYP6D1 is associated with monooxygenase-mediated pyrethroid resistance in house flies from Georgia. *Pestic Biochem Physiol* **68**:34–41 (2000).
157 Stevenson JH, Laboratory studies on the acute contact and oral toxicities of insecticides to honeybees. *Ann Appl Biol* **61**:467–472 (1968).
158 Mayes MA, Thompson GD, Husband B and Miles MM, Spinosad toxicity to pollinators and associated risk. *Rev Environ Contam Toxicol* **179**:37–71 (2003).
159 Hsu J-C and Feng H-T, Development of resistance to spinosad in Oriental fruit fly (Diptera: Tephritidae) in laboratory selection and cross-resistance. *J Econ Entomol* **99**:931–936 (2006).
160 Scott JG, Toxicity of spinosad to susceptible and resistant strains of house flies, *Musca domestica*. *Pestic Sci* **54**:131–133 (1998).
161 Stanley J, Chandrasekaran S, Preetha G and Kuttalam S, Toxicity of diafenthiuron to honey bees in laboratory, semi-field and field conditions. *Pest Manag Sci* **66**:505–510 (2010).