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IRAC: Mode of action classification and insecticide resistance management

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ABSTRACT

Insecticide resistance is a long standing and expanding problem for pest arthropod control. Effective insecticide resistance management (IRM) is essential if the utility of current and future insecticides is to be preserved. Established in 1984, the Insecticide Resistance Action Committee (IRAC) is an international association of crop protection companies. IRAC serves as the Specialist Technical Group within CropLife International focused on ensuring the long term efficacy of insect, mite and tick control products through effective resistance management for sustainable agriculture and improved public health. A key function of IRAC is the continued development of the Mode of Action (MoA) classification scheme, which provides up-to-date information on the modes of action of new and established insecticides and acaricides and which serves as the basis for developing appropriate IRM strategies for crop protection and vector control. The IRAC MoA classification scheme covers more than 25 different modes of action and at least 55 different chemical classes. Diversity is the spice of resistance management by chemical means and thus it provides an approach to IRM providing a straightforward means to identify potential rotation/alternation options.

1. Introduction

Insecticide resistance (see [1–3] for definitions) has been a major factor influencing insect control and pest management for more than half a century. The first paper documenting insecticide resistance was published 100 years ago and involved lime sulfur and the San Jose scale [4]. Thereafter, a few sporadic cases of insecticide resistance were reported through the mid-1940s (Fig. 1, [5]). The introduction of the synthetic organic insecticides (i.e. DDT, cyclodienes and organophosphorus insecticides) in the 1940s lead to great improvements in insecticidal efficacy and spectrum, with the consequent large scale, expanded use of these new tools for pest insect control. Not surprisingly, there was also a rapid rise in the number of cases of resistance due to extensive, repeated use of these products. Since the late 1940s, the number of cases of insecticide resistance, and the number of species and compounds involved has been continually increasing (Figs. 1 and 2). The 1960s and 1970s saw the appearance of resistance to herbicides and fungicides (Fig. 2). However, the cases of insecticide resistance continue to far exceed the number of cases of herbicide and fungicide resistance (Fig. 2).

In light of its importance, approaches to studying insecticide resistance and insecticide resistance management (IRM) have been widely discussed (e.g. [6–14]). The crop protection industry has long recognized the importance of, and need for effective, proactive resistance management [15–22]. The time, effort, and increasingly very large costs involved in the discovery and development of new insecticides [23] dictate that the chances for the development of resistance be minimized as much as possible to ensure that the very substantial investment made to bring any new insecticide product or trait to the market is not wasted. Likewise, it is equally important to ensure minimize the chances of resistance developing for existing products, since in many instances alternative compounds that possess the same attributes or low cost may not be available. Thus, resistance management is of utmost importance and continues to be a critical concern for all stakeholders involved in modern applied pest control.

Abbreviations: AChE, acetylcholiesterase; APRD, Arthropod Pest Resistance Database; Bt, *Bacillus thuringienis*; CC, chloride channel; CSI, chitin synthesis inhibitor; EcR, ecdysone receptor; GGCC, GABA gated chloride channel; GMO, genetically modified organism; IRAC, Insecticide Resistance Action Committee; IPM, Integrated Pest Management; IRM, Insecticide Resistance Management; JH-R, juvenile hormone receptor; MET, mitochondrial electron transport; MoA, mode of action; nAChR, nicotinic acetylcholine receptor; NTX, nereistoxin analogs; OA-R, octopamine receptor; Ox-Ph, oxidative phosphorylation; RNAi, RNA interference; Ry-R, ryanodine receptor; VGSC, voltage gated sodium channel; WG, working group; UN, unknown or uncertain mode of action.

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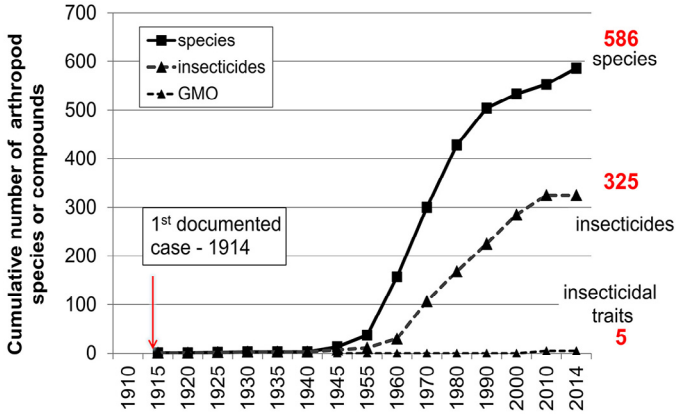

Fig. 1. Cumulative increase in (a) the number of species resistant to one or more insecticides, (b) number of insecticides for which one or more species has shown resistance, and (c) number of GMO traits for which resistance has been reported.Data adapted from: [2,3,47–50] and David Mota-Sanchez, Michigan State University, personal communication, 2014.

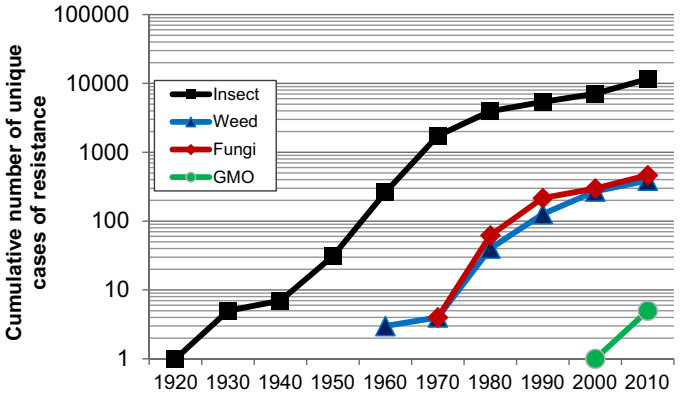

Fig. 2. Cumulative increase in the number of individual cases of resistance for insecticides, herbicides and fungicides. Herbicides and fungicide data adapted from [51,52]. Insecticide data kindly provided by Drs. David Mota-Sanchez, and Mark Whalon, Michigan State University.

2. Insecticide Resistance Action Committee (IRAC)

One response to the need for improved resistance management by the crop protection industry was first the formation of the Pyrethroid Efficacy Group and later on the Insecticide Resistance Action Committee (IRAC) [15,16,18,19,21,22] in 1984. IRAC, part of CropLife International, is a technical working group that focuses on providing a coordinated effort by the crop protection industry to prevent or delay the development of resistance in insect, mite and tick pests [22]. The mission of IRAC is twofold: (a) facilitate communication and education on insecticide and trait resistance, and (b) promote the development and facilitate the implementation of insecticide resistance management strategies to maintain efficacy and support sustainable agriculture and improved public health [1,22].

2.1. IRAC mode of action (MoA) classification

One of the key tools from IRAC is the MoA Classification Scheme. The MoA Classification Scheme provides state and government agencies, consultants, advisors, growers, universities and extension staff with guidelines for the selection of insecticides and acaricides when used in an alternation or rotation-based resistance management program (see below). Included in the MoA Classification is background information on resistance management and how the MoA Classification can be used for IRM. The MoA classification scheme is available in different formats such as posters (different language versions), a mini booklet and a smartphone App which are regularly updated (Fig 3).

The MoA Classification scheme is based on the best available evidence for the target-sites or MoA of currently available insecticides and acaricides (currently excludes nematicides). Details of the listing have been reviewed and approved by internationally recognized academic and industrial experts in insecticide toxicology, resistance and MoA. Currently the MoA Classification encompasses more than 25 different MoAs. A condensed listing of the MoA groups with representative examples of the chemistries currently covered by the MoA Classification is presented in Table 1; a more comprehensive listing is available on the IRAC website (http://www.irac-online.org/). In addition to data from the IRAC MoA classification scheme (main group and primary site of action, chemical subgroup/exemplifying active), Table 1 also provides additional information on the total number of compounds in each group/subgroup, the year the first compound in the group was introduced, and the 2013 end-user market value [24] for that group or subgroup.

Fig. 3. Different formats of the MoA classification scheme available on the IRAC website include posters, a mini-booklet and a smartphone App (displayed with permission of IRAC).

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Table 1
Modes of action (based on IRAC MoA classification) for current insecticide groups.

IRAC group	Primary site of action/MoA[a]	Chemical subgroup/exemplifying active	1st year[b]	No. of products[c]	Market[d] value
Nerve and Muscle Targets					
1	AChE inhibitor	1A carbamates	1950	30	$667
		1B organophosphates	1944	90	$1794
2	GGCC antagonist	2A cyclodienes	1950	7	$7
		2B fiproles	1990	3	$801
3	VGSC modulator	3A pyrethroids and pyrethrins	1977	30	$2777
		3B DDT and analogs	1944	7	$<1
4	nAChR agonist	4A neonicotinoids	1990	8	$4650
		4B nicotine	1763	1	–
		4C sulfoximines	2013	1	$8
		4D butenolides	2014	1	–
5	nAChR allosteric	Spinosyns	1997	2	$401
6	CC activators	Avermectins and milbemycins	1978	4	$1261
9	Modulators of chordotonal organs	9B pymetrozine	1994	1	$72
		9C flonicamid	2005	1	$112
14	nAChR blocker	Nereistoxin analogs	1965	4	$124
19	OA-R agonist	Formamidines	1971	1	$8
22	VGSC blocker	22A oxadiazines	1997	1	$235
		22B semicarbazones	2007	1	$99
28	Ry-R allosteric	Diamides	2008	5	$1411
Growth and Development Targets					
7A	JH-R agonist	7A juvenoids	1973	3	$6
		7B fenoxycarb	1985	1	$12
		7C pyriproxyfen	1995	1	$56
10	MGI	10A clofentezine	1983	3	$63
		10B oxazoles	1998	1	$44
15	CSI	Benzoylureas	1975	14	$441
16	CSI	Buprofezin	1984	1	$162
17	CSI	Cyromazine	1985	1	$14
18	EcR agonist	Diacylhydrazines	1993	6	$177
23	Acetyl CoA carboxylase	Tetronic/tetramic acids	2002	3	$456
	Respiration targets				
12	ATP synthase	12A diafenthiuron	1991	1	$44
		12B organotin miticides	1968	3	$39
		12C propargite	1964	1	$47
		12D tetradifon	1954	1	$1
13	Ox-Ph uncouplers	Chlorfenapyr	1892	3	$81
20A	MET III inhibitors	20A hydramethylnon	1977	1	$<2–3
		20B acequinocyl	1999	1	$43
		20C fluacrypyrim	2002	1	$22
21	MET I Inhibitors	21A MET I inhibitors	1990	6	$274
		21B rotenone	1848	1	$<2–3
24	MET IV inhibitors	24A phosphine	–	4	$101
		24B cyanide	1877	1	–
25	MET II inhibitors	β-ketonitrile derivatives	2007	2	$50
	Midgut targets				
11	Midgut membr.	11A *Bacillus thuringienis*	1970	14	$234
		11B *Bacillus sphaericus*	1982?	1	–
Miscellaneous					
8	Miscellaneous non-specific (multi-site) inhibitors	8A alkyl halides	1932	–	$327
		8B chloropicrin	1908	1	$285
		8C sulfuryl fluoride	2004	1	$44
		8D borates	–	1	–
		8E tartar emetic	–	1	–
Unknown or Uncertain MoA					
UN	–	UN azadirachtin	1995?	1	$~5–7[5]
	–	UN benzoximate	1971	1	$1
	–	UN bifenazate	1999	1	$42
	–	UN bromopropylate	1967	1	$<1
	–	UN chinomethionat	1960	1	$~8–9
	–	UN cryolite	–	1	$8
	–	UN dicofol	1950	1	$2
	–	UN pyridalyl	2004	1	$118
	–	UN pyrifluquinazon	2010	1	$29

[a] Abbreviations: AChE, acetylcholiesterase; GGCC, GABA gated chloride channel; CC, chloride channel; VGSC, voltage gated sodium channel; nAChR, nicotinic acetylcholine receptor; OA-R, octopamine receptor; Ry-R, ryanodine receptor; JH-R, juvenile hormone receptor; EcR, ecdysone receptor; CSI, chitin synthesis inhibitor; MET, mitochondrial electron transport; Ox-Ph, oxidative phosphorylation; UN, unknown or uncertain mode of action.

[b] First year (or approximate) of appearance of compounds in this class.

[c] Approximate number of products in each class (current and historic). Based, in part, on data from Alan Wood Compendium of Pesticide Common Names [40] ISO Common Names (http://www.alanwood.net/pesticides/index.html) and Cropnosis [53].

[d] 2013 sales (end user, millions USD) for the different IRAC Groups or subgroups of insecticides – data from Agranova ([24]).

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The compound list for the MoA Classification Scheme is based, in part, on compounds appearing in the Pesticide Manual [25]. For new entries, a classification is provided for compounds registered in at least one country, or will soon be. The IRAC MoA Working Group (WG) is responsible for providing a classification for each compound. Companies interested in a classification for a new chemistry submit a request to the MoA WG for a classification and can suggest a potential grouping based on their research. Depending on the nature of the compound, a company requesting classification is typically asked to provide data to the MoA WG for review regarding the biochemistry and mode of action. As outlined in the IRAC MoA Classification document, companies may elect to provide internal data/information to support a classification request; however the preference is for data published in peer-reviewed journals.

2.2. Mode of action grouping and subgrouping

The MoA Classification scheme is principally based on the target site, and secondarily on novelty of the chemistry, differential action on the same target site and/or susceptibility to metabolic resistance mechanisms. A compound acting through a target site that is different from all others will be placed in a separate group (e.g. pyrethroids [Group 3] and neonicotinoids [Group 4]). Likewise, compounds acting at different sites in the same target (e.g. sodium channel modulators; pyrethroids [Group 3] and sodium channel blockers; indoxacarb and metaflumizone [Group 22]) [26,27] are also placed in different groups. Following a similar logic, compounds sharing a common target site, but representing very different types of chemistry (e.g. acetylcholinesterase inhibitors; carbamates [Group 1A] and organophosphates [Group 1B]) are placed in different subgroups because they can have distinctly different metabolic profiles minimizing the chances for metabolic cross-resistance. Similar examples exist for a number of other Groups (Table 2).

As outlined in the IRAC MoA Classification, rotation of compounds in the same Group, but in different subgroups (e.g. carbamates 1A and organophosphates 1B) is not recommended unless there are no other chemistries available that are in totally different groups (i.e. different modes of action). This recommendation is due to the increased chance of selecting for a common target site-based resistance mechanism thereby limiting the utility of both chemical classes of insecticides. Currently there are 25 specific MoAs listed in the MoA Classification along with some multi-site chemistries and a number that are either unknown or currently have insufficient data to formally classify them at this time (Table 2).

2.3. IRAC MoA classification and resistance management

Integrated pest management (IPM) in crop protection encompasses a range of approaches including biological control, cultural control, autocidal techniques, crop rotation, semiochemicals, host plant resistance, chemical control, and genetically modified (GMO) plants [28,29]. Among the tools on the horizon is sprayable RNAi [30,31], which provides a new approach to pest control with the potential of combining ease of spray application with a molecular targeting approach used in transgenic plants allowing for new modes of action and selectivity. As such sprayable RNAi is a conceptual bridge linking conventional chemical control, GMO crops and the older sprayable Bts. All of the above approaches seek to reduce pest pressure below economic damage thresholds on a crop. However, in spite of the many newer approaches available, for many specific cases of “crop, pest, locations”, the use of chemical insecticides remains a primary tool. As such, preservation of the long term efficacy for current and new insecticides is essential since the availability of new, replacement insecticides may be very challenging given the time, increasing expense and increasingly stringent regulatory requirements [23]. One outcome associated with the increasing costs and rising regulatory requirements, has been a dramatic consolidation that has occurred in the agrochemical industry resulting in far fewer companies involved in pesticide discovery than a few years ago [23]. With fewer companies involved in insecticide discovery, the number of new insecticides with new modes of action may be limited in the future. As such, resistance management has become a critical consideration in seeking to preserve the future efficacy of existing and new insecticides. In some regions such as Europe it is even mandatory to provide documents covering resistance risk assessment for (re)registration purposes of pesticides [32].

IRM seeks to delay or prevent the evolution of resistance to insecticides. IRM can also aid in regaining susceptibility of a pest insect/mite population that has already developed some degree of resistance to a particular chemistry. The primary means to accomplish these goals is to reduce the selection pressure directed toward any particular insecticide in a given crop or use. A number of approaches have been investigated on how best to use the available insecticide tools including alterations/rotations/sequences, mixtures, and mosaics [33].

Among these insecticide-based approaches, alteration/rotation/sequences of insecticides are one of the more direct/simplest to execute having the fewest assumptions regarding the implementation [33,34]. A rotation approach often uses a “window” or block strategy [1,22] that is frequently defined by the length of a pest

Table 2
Modes of action for future chemistries currently in various stages of development.

Primary site of action/MoA[a]	Chemical class/exemplifying active	Example compound[b]	1st year[c]	Reference
GGCC allosteric	Isoxazolines	Fluralaner	2010	[54]
GGCC allosteric	Isoxazolines	Afoxolaner	2014	[55]
GGCC allosteric	Metadiamides	Broflanilide	2013	[40]
nAChR agonist	Cycloxaprid	Cycloxaprid	2011	[56]
nAChR	Mesoionics	Triflumezopyrim	2013	[57]
Ry-R allosteric	Diamides	Cyclaniliprole	2013	[40]
Ry-R allosteric	Diamides	Tetraniliprole	2014	[40]
UN	Pyropenes	Afidopyropen	2012	[58]
UN	Flometoquin	Flometoquin	2011	[40]
UN	Fluhexafon	Fluhexafon	2014	[40]

[a] Abbreviations: GGCC, GABA gated chloride channel; nAChR, nicotinic acetylcholine receptor; Ry-R, ryanodine receptor; UN, unknown.
[b] Example compound – example or representative member of this class of chemistry.
[c] First year (or approximate) of appearance of compounds in this class in the Alan Wood database (http://www.alanwood.net/pesticides/index.html) or in the literature.

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generation or crop growth stages [35–37]. Such an approach has been effective in a number of instances as exemplified by experiences in Australia [35], Hawaii [36] and others [37], and involves rotating compounds with different MoAs according to a series of defined windows or blocks during the crop growing season to minimize selection for cross-resistance [1,37]. Always in such programs, local experts should be consulted for the best options for a particular pest–crop scenario.

The IRAC MoA Classification Scheme provides a means to select insecticide options for these types of rotation schemes by providing up-to-date information on the MoA of existing and newly registered insecticides. Compounds are assigned to MoA Groups that can then serve as simple means for selecting what compounds to put into an IRM program or rotation scheme. Depending on local conditions, typically one or more applications of a given insecticide may be acceptable within a window. However, it is critical that the next window or generation is not treated with a compound that is from the same MoA Group as the prior window/generation. The IRAC MoA Groups provide a ready means to identify compounds that have a different MoA relative to the insecticide just applied. In an increasing number of countries, the IRAC Group number is now on the product label (in some even mandatory) simplifying the process of determining if the next compound being considered for use has the same or different mode of action.

2.4. Methods for resistance detection

Key to addressing insecticide resistance issues is the ability to reliably detect the presence of insecticide-resistant strains of pest insects. Some of the first standardized tests for insecticide resistance were developed by the World Health Organization in the 1950s for mosquito vectors of disease [6]. During the past 30 years, IRAC, through the Methods WG, has also developed and validated 30 standardized methods for resistance detection targeting a wide range of pest species, and primarily focused on crop insect and mite pests. The IRAC bioassay methods are characterized by being simple to perform, reliable, reproducible, and consistent in identifying susceptible versus resistant phenotypes [1]. In addition the Methods WG maintains a searchable reference database of nearly 160 other resistance bioassay methods that have been documented in scientific literature [1].

2.5. Documentation and communication

For IRM to be effective, ready access to information along with education is needed; this role is central to IRAC's activities. The IRAC Communication & Education WG makes a variety of resources available to academia, industry, research groups, conferences, and growers regarding resistance management. A variety of material including monographs such as the vector manual, pamphlets, booklets, posters, references, and links are available covering for example IRM, test methods, and pest insect biology available on the IRAC website. Furthermore IRAC publishes resistance alerts on new resistance issues such as the recent *Myzus persicae* neonicotinoid target-site resistance alert (see [38]).

Another critical need in understanding and managing insecticide resistance is documentation of which pests and/or insecticides have had resistance developed. The Arthropod Pesticide Resistance Database (APRD) (http://www.pesticideresistance.com/search.php), available to the public, provides extensive listings of cases of insecticide resistance searchable by pest, year, and active ingredient [2]. The database documents insecticide resistance incidences from as early as 1914 through the present day. IRAC has had a long collaboration with Michigan State University to support, maintain and expand the APRD [2].

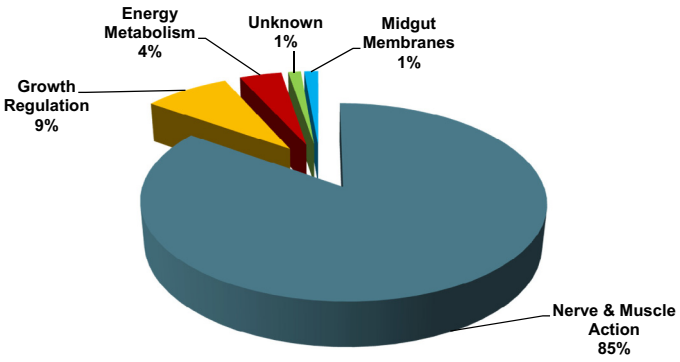

Fig. 4. Distribution of total insecticide sales (percent of total value) by broad mode of action. Total value = $17016 million; excludes fumigants. Based on 2013 End-user sales data from Agranova [24], July 2014.

3. Perspective

Among the more than 25 MoAs currently in the IRAC classification, 85% of the value of these MoAs is derived from insecticides that act on the insect nerve–muscle system (Fig. 3; for review see [39]). In contrast, insecticides altering growth and development account for only 9% of the total insecticides sales, while those disrupting energy production (respiration targets) account for only 4% (Fig 4). Because small perturbations in the nervous system are quickly amplified, the insect nervous system has been and remains a prime target for new insecticides. Within the nerve–muscle acting insecticides, the neonicotinoids predominate with 27% of the market, nearly as much as the current organophosphates, carbamates and pyrethroids combined (31%) (Fig. 5). Although a relatively new class of chemistry, the diamides acting on ryanodine receptors now account for about 8% of total global end-user insecticide sales, a number that has been steadily increasing, and that is certain to continue to increase with the potential addition of other new diamides to the marketplace (Table 2). An interesting comparison is the number of compounds in each IRAC MoA Group or Subgroup (Table 2; includes current and historic compounds). There are in total 288 insecticidal compounds, excluding fumigants [40], and the number of organophosphate insecticides that became products (90; 31%) far exceeds any other Group or Subgroup, and yet today accounts for just 11% of the end-user sales. A similar situation exists

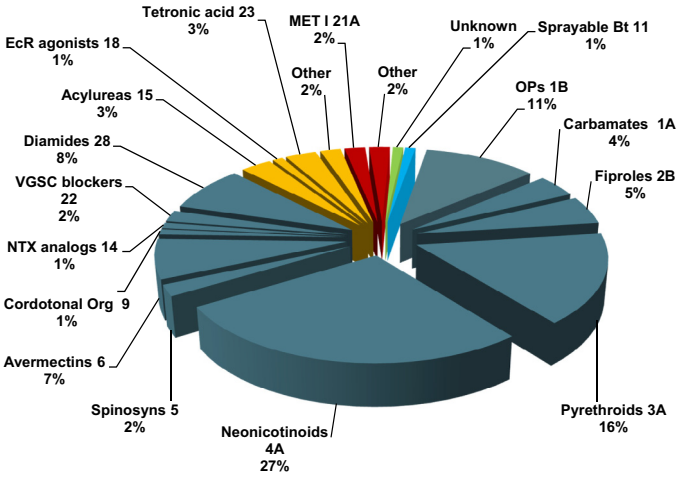

Fig. 5. Distribution of total insecticide sales (percent of total value) by IRAC MoA Group or Subgroup. Total value = $17,016 million; excludes fumigants. Based on 2013 End-user sales data from Agranova [24], July 2014.

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Table 3
Top 12 resistant insect species.[a]

Species	Common name	Order	No. of compounds	No. of cases[b]
Tetranychus urticae	Two-spotted spider mite	Acari	93	414
Plutella xylostella	Diamondback moth	Lepidoptera	91	576
Myzus persicae	Green peach aphid	Hemiptera	75	402
Musca domestica	House fly	Diptera	58	303
Bemisia tabaci	Sweet potato whitefly	Hemiptera	54	555
Leptinotarsa decemlineata	Colorado potato beetle	Coleoptera	54	279
Aphis gossypii	Cotton aphid	Hemiptera	48	231
Panonychus ulmi	European red mite	Acari	48	197
Helicoverpa armigera	Cotton bollworm	Lepidoptera	47	692
Boophilus[c] *microplus*	Southern cattle tick	Ixodida	44	167
Blattella germanica	German cockroach	Blattodea	43	219
Spodoptera litura	Mediterranean climbing cutworm	Lepidoptera	38	457

[a] Based on the number of different compounds for which resistance has been reported. Data from the APRD [50], July 2014.
[b] Number of unique instances of resistance reported for each species in the APRD [50]; July 2014.
[c] *Rhipicephalus*.

for the carbamates, and to a lesser extent, the pyrethroids (Table 1). In contrast, there are relatively few neonicotinoids in the marketplace (Table 2), and yet at present they account for a very sizable portion of the global insecticide sales (Fig. 5, Table 1).

In addition to existing (but still relatively new) MoAs, several new classes of insecticides targeting new or as yet undetermined target sites/MoAs are in varying stages of development (Table 2). At present, none of these potential new insecticides are registered crop protection products and thus too early to be considered for inclusion in the IRAC MoA Classification. However, these new, potential insecticides highlight the fact that the agrochemical industry is continuing to explore and develop new tools for pest arthropod control, therein providing new opportunities for developing or continuing IRM programs.

At the same time, due to the continuing expansion of insecticide resistance, regulatory and/or other considerations, many of the existing insect and mite control tools may not be as suitable or even available for use in future IPM and IRM programs. Also, the number of options available is pest–crop–region dependent. As such, many of the insecticide options in the 25 MoA Groups may, or may not be available or viable, with the result that in some crop systems the number of options may be very limited. Thus, any new insecticide options, especially those bringing forward new MoAs, should be treated as limited, finite resources that need to be used with care. If these new MoAs become over-used or mis-used with the resultant rapid development of resistance and consequent loss of efficacy and utility, all of agriculture will be the loser.

Such scenarios have been played out many times. For example when spinosad was introduced into Hawaii for control of the diamondback moth (*Plutella xylostella*) in 2000, the lack of suitable alternatives and the continuous weekly applications quickly (~2 years) led to resistance and a loss of efficacy and utility [41,42]. In a more recent example, resistance to chlorantraniliprole appeared to diamondback moth within 3 years of introduction in China due to its almost exclusive use for control in many regions [43]. Other historic examples of rapid resistance development include control of house flies with DDT [44], Colorado potato beetle control with a wide number of insecticides including the pyrethroids [5], and the control of horn flies with pyrethroids in cattle ear tags [45]. Some of the above insect pests and others including the diamondback moth, two-spotted spider mite, green peach aphid, cotton aphid, sweet potato whitely, etc. (Table 3) have a history of developing resistance to insecticides with some species having developed resistance to more than 90 different insecticides (Table 3). Nearly all of the pests in Table 3 have 200 or more instances of resistance.

As also demonstrated by the experience with spinosad resistance in diamondback moth in Hawaii, attempting to reverse resistance once it has developed is difficult. Even if initially successful, resistance reversal can be temporary [42,46] if the resistance selection has proceeded to the point where the frequency of the resistant alleles becomes high. As also exemplified by the diamondback moth, many of the pests in Table 3 have a short generation time, high fecundity, are highly mobile and attack crops where there may be few other control options or where little crop damage can be tolerated. As such, IPM and IRM programs involving these species deserve special consideration and planning when bringing a new insecticide tool into use due to their long history of resistance development.

4. Conclusions

Agrochemical industry responsibly addresses the importance of IRM as demonstrated by the activities and expanded agrochemical company membership of IRAC during the past 30 years. As noted above, the increasingly expensive and complex process of discovering new insect control products dictates that it is vital that the current and new insecticide tools be used in a rational manner in order to safeguard their long term efficacy and utility. Thus through its communication and education programs IRAC has been and continues to stress the importance of IRM inside and outside of the agrochemical industry, as well as the agricultural community. The IRAC-developed MoA Classification Scheme and the associated MoA labeling and IRM recommendations now common on the container labels for insecticides in many countries is just one demonstration of the agrochemical industry's IRM commitment. IRM is of paramount importance for growers, crop protection specialists, university and industry alike. As noted in past IRAC publications (e.g. [22]), and numerous presentations [1], IRM is not optional; it is essential to ensure that valuable, often scarce, insect control tools are not mis-used or over-used, and continue to be available to address the expanding global need for the production of food and fiber as well as for improved public health.

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