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Can we replace toxicants, achieve biosecurity, and generate market position with semiochemicals?

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Biosecurity covers both long-term management of existing pests and the urgent government responses to alien invasive species which have yet to become fully established. Mating disruption, mass trapping and lure and kill systems all have potential to be used in pest management and against new incursions of certain types of organisms, predominantly moths, and beetles. Straight chained lepidopteran sex pheromones have emerged as a source of potential market advantage in pest management, with trapping systems and residue-free multiple species disruption systems being increasingly adopted to reduce insecticide use and meet private standards. Semiochemicals can also offer new surveillance tools in pre-border biosecurity, greatly improving the chances for successful eradication of alien invasive species. However, a rising frequency of incursions of alien invasive species and consequent rise in official eradication programs due to globalization points strongly to the need for further investment in the areas of discovery and development of surveillance and eradication technologies, from a sound knowledge of chemical ecology.

Keywords: pheromone, semiochemical, biosecurity, surveillance, TRAP, invasive, eradication

INTRODUCTION

WHAT IS BIOSECURITY, AND HOW CAN CHEMICAL ECOLOGY CONTRIBUTE?

Biosecurity is the discipline of responding to organism threats to natural and productive ecosystems at the national level. It includes pre-border responses, including official control or eradication programs of alien invasive species which have yet to fully establish, (Tobin et al., 2014) or post-border pest management, where a number of tactics such as biological control, selective insecticides or other tools are employed to achieve suppression below the economic threshold (Blommers, 1994). The potential for chemical ecology to contribute to pest management has been widely canvassed elsewhere, (Gut et al., 2004; Witzgall et al., 2010) and this short article will focus more on the emerging role for chemical ecology against organisms undergoing rapid range expansion, although comparisons and contrasts with pest management require some commentary.

There are a number of terms and concepts involved in pre-border biosecurity that differ from pest management. For example, the concept of eradication is defined by the International Plant Protection Convention (IPPC, 1998) as an emergency measure to prevent establishment or spread of a pest following its recent entry (re-establish a pest free area), or a measure to eliminate an established pest (establish a pest free area). So far, more than 100 countries are recognized as having undertaken official arthropod eradication programs (Kean et al., 2015). In an eradication, the drivers include risk analysis to identify those organisms that warrant intervention, followed by an urgent need for delimitation. This is where chemical ecology can contribute significantly, since we know from a recent analysis that the presence of a lure can increase the probability of successful eradication by more than 20-fold for a diverse range of insect taxa (Diptera (259 cases), Coleoptera (133 cases), Lepidoptera (133 cases), Hymenoptera (61 cases), and Hemiptera (31 cases) (Tobin et al., 2014). Next, there is consideration of the efficiency of the eradication tools, which may also include lures ideally with known use for the same or a related species in pest management, but in another jurisdiction. Finally, there is the issue of availability of a suitable formulation or system of use for rapid deployment, with known operational parameters to support it. Some insects, such as those using vibration or other modalities apparently do not rely on the use of semiochemicals involving long range mate location, and are less likely to be amenable to the general approaches discussed below.

PRE-BORDER BIOSECURITY—INVASIVE SPECIES SURVEILLANCE, CONTAINMENT AND ERADICATION

Pre-border biosecurity can be conceived as being formed of five themes: risk assessment, pathway analysis, diagnostics, surveillance and response/eradication (www.b3nz.org). The understanding and application of knowledge of semiochemicals can be seen in host range prediction for risk assessment, in the development and combination of attractants for improved surveillance, as well as eradication tools. In practice, tools for surveillance and eradication are likely to come from work done for pest management in another jurisdiction, and more than 3500 semiochemicals are reported on the Pherobase website by taxonomic grouping (El-Sayed, 2015). Therefore, is it possible to note that the most widely developed and tested semiochemicals are found targetting certain families of Lepidoptera, followed by Coleoptera (**Figure 1**), since this knowledge can have strategic value in countries where particular organisms are not yet present (Suckling et al., 2014a). A notably important pest group responding to attractants is the Dacinae (Tephritidae), which is the basis for a very strong track record of success in eradications of this group (Suckling et al., 2014b). In specific cases, chemical ecology has contributed to the development of lures for surveillance and male annihilation, but also in other ways, such as improving competitiveness in sterile insects by exposure to odorants prior to release (Shelly et al., 2004).

If risk assessment from host range, climate suitability, and impact assessment warrants a response at the national level, then surveillance may be considered, provided that suitable biology or symptoms exist enabling detection and delimitation. The question of whether to undertake an attempt at eradication is difficult, yet in a study of hundreds of arthropod eradication programs, the rate of increase of official eradication programs is evidently rising rapidly, tracking globalization (Tobin et al., 2014). According to the Global Eradication Database, there have been at least 287 eradication programs against 27 species of Diptera (not including mosquitoes), with 138 programs against 28 species of Coleoptera, 144 programs against 28 species of Lepidoptera, 74 programs against 18 species of Hymenoptera, and 45 programs against 27 species of Hemiptera (Kean et al., 2015).

BIOSECURITY TOOLKIT FOR SURVEILLANCE AND ERADICATION

The toolkit of potential control or management tactics available for responding to insect incursions in agricultural landscapes may be larger than that available in urban situations, where pesticides and even pheromones may be less than favorably received, as was seen in California with the light brown apple moth (Suckling and Brockerhoff, 2010; Suckling et al., 2014c). In part, this may be

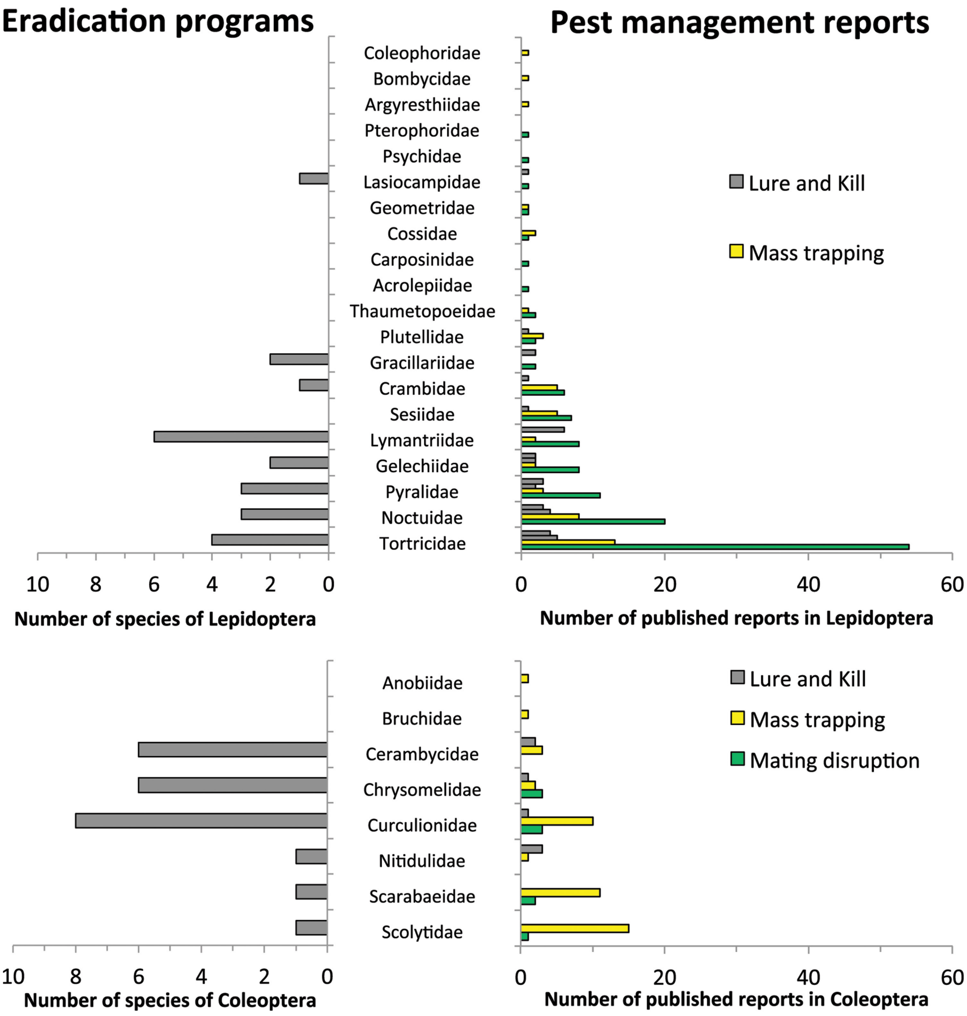

FIGURE 1 | Reported tactical tests of pheromones for pest management by family in Left: Lepidoptera, and Right: Coleoptera (data from www.pherobase.com), with an indication of the number of species in each family with eradication programs attempted (data from www.b3.net.nz/gerda/index.php).

due to the greater familiarity of rural people with the pragmatic aspects of pest management (and consequences of its failure on food supply). However, in urban and other sensitive ecosystems such as national parks, there appears likely to be a preference seen for tactics involving lower environmental and personal impact, such as sterile insect release (Gamble et al., 2010). To an extent this may depend on the extent to which people feel directly threatened by the pest also.

For some pest groups (Tephritidae in particular), (Suckling et al., 2014b) there are acknowledged protocols which are widely used for suppression. For most other organisms, there is a more limited history of responses using benign materials such as pheromones or other semiochemicals, although there are examples including the use of mating disruption (Kean et al., 2015); **Table 1**. Future surveillance tools could include multiple species traps, (Vargas et al., 2012; Brockerhoff et al., 2013) or generic floral or other lures to widen the target group (El-Sayed et al., 2008) but innovation is needed in socially-acceptable eradication tactics also. Examples include attempts to develop novel control tactics based on cross species communication disruption between fruit flies (Suckling et al., 2007), release of sterile male Mediterranean fruit flies treated with moth sex pheromone for mating disruption, (Suckling et al., 2011) and trail pheromone disruption of ants (Suckling et al., 2012a; Westermann et al., 2014).

FEATURES, BENEFITS AND LIMITATIONS OF SEMIOCHEMICALS

For insects, most signaling molecules are highly selective (El-Sayed, 2015) and of very low hazard. Their development is knowledge intensive, as it requires specific new information for application which can take time to generate (Gregg et al., 2010). Compounds are active at extremely low concentrations from lures, or as high as the ppb range for control systems like mating disruption (Suckling et al., 1999).

The avoidance of broadcast use of broad-spectrum or persistent insecticides is frequently used as the justification for research into alternatives such as biopesticides or semiochemicals, as well as pest management involving natural enemies, where chemical ecology may play a role (Gut et al., 2004) For some species, suppression to the economic threshold can be achieved using mating disruption (Walker et al., 2011; Suckling et al., 2012b), and the examplar for large scale adoption of pheromones has been codling moth (Thomson et al., 2009). Where this is possible, a reduction in the application of insecticides from substitution with sex pheromones for control by mating disruption (especially in the later part of the season) can lead to reduced residues at harvest (Suckling and Shaw, 1995). An example of the modern development and uptake of integrated pest management (IPM) against a pest complex by overcoming the disadvantages of selectivity by combining pheromone components is the case of spray-free (and consequently residue-free) high value market access for New Zealand apples, based on "4-Play"™ which is a single mating disruption dispenser controlling four pest species (Lo et al., 2013). The high brand value of the New Zealand apples includes novel fruit varieties, and is supported by a sex pheromone-based system that enables high value exports to pest-free areas (Suckling et al., 2012c; Walker et al., 2013).

Table 1 | Operational eradication programs of Lepidoptera that have used mating disruption (usually with other tactics) (accessed from Kean et al., 2015; global eradication and response database. http://b3.net.nz/gerda/index.php).

Start	Genus	Species subspecies	Authority	Location	State	Country	Mating disruption method	Outcome
1977	*Lymantria*	*dispar dispar*	(L.)	Waukesha Co.	WI	US	Aerial	Likely eradication
1988	*Lymantria*	*dispar dispar*	(L.)	Giles County	VA	US		
1990	*Lymantria*	*dispar dispar*	(L.)	Sequatchie Co.	TN	US	Aerial[1]	Confirmed eradication
1991	*Lymantria*	*dispar dispar*	(L.)	Rockbridge, Botetou Co.	VA	US	Aerial[1]	Confirmed eradication
1992	*Lymantria*	*dispar dispar*	(L.)	Carroll, Floyd Co.	VA	US	Aerial	Confirmed eradication
1992	*Lymantria*	*dispar dispar*	(L.)	Roanoke, Bedford Co.	VA	US	Aerial[1]	Confirmed eradication
1998	*Cydia*	*pomonella*	L.	Dwelling up	WA	AU	Ground	Confirmed eradication
2001	*Pectinophora*	*gossypiella*	(Saunders)	Arizona-CA	AZ, CA	US	Aerial	Large areas of freedom
2006	*Lymantria*	*dispar asiatica*	Vnukovskij	Oak Hill	TX	US	Aerial	Confirmed eradication
2007	*Epiphyas*	*postvittana*	Walker	State wide	CA	US	Ground	Failure to eradicate
2008	*Epiphyas*	*postvittana*	Walker	Santa Barbara	CA	US	Ground	Local extinction
2010	*Epiphyas*	*postvittana*	Walker	Yolo Co.	CA	US	Ground	Local extinction

[1] *Single tactic treatment with mating disruption.*

However, major research gaps include very patchy discovery and development across other insect groups, where chemical communication systems are not always amenable to being harnessed. This can be illustrated by sorting meta data obtained courtesy of the Pherobase website compiled by El-Sayed, (El-Sayed, 2015) into three control applications, by family for moths (20) and beetles (8) and matched here with eradication programs from the Global Eradication Database (**Figure 1**). All of the families listed contain invasive pest species. Interestingly, a comparison of the target of eradication attempts against both beetles and moths shows a general concentration of scientific effort in the same families where work has been done on pheromone-based control for IPM (**Figure 1**).Therefore, it is suggested that analysis of pheromone-based tactics to family level, which have been tested for pest management of some pest species, enables general prediction of the feasibility of pheromone-based tools in related species, should they become invasive in new areas (which has obviously occurred). Furthermore, because the availability of attractive lures can increase the probability of eradication, (Tobin et al., 2014) the species listed by El-Sayed probably represent the more eradicable target group of possible pests, other things being equal. Furthermore, incursion prediction is difficult, but generic solutions for Biosecurity responses could be envisaged with "plug and play" odourants supported by usage for pest management in the market to maintain the availability of a generic formulation. Ready adaptation could follow when the need arises for a new tool to deal with an incursion. An example of such a versatile matrix is the Specialised Pheromone And Lure Application Technology, or SPLAT™ (Brockerhoff et al., 2012; Mafra-Neto et al., 2013).

INTEGRATED PEST MANAGEMENT

If a native or exotic pest organism is established and has ecological or economic impact, investigations are often made of mitigation options to minimize insecticide use through IPM. IPM has strong market drivers in some sectors such as horticulture, where it has broad appeal in the western world because of the desire to avoid insecticide residues on food. This has led to the emergence of private standards with lower than legally required maximum residue limits for pesticides. Lowering or avoiding residues, which can bring an improved market value to produce, can come from monitoring and decision support (Suckling et al., 2012c) or insecticide replacement through the use of mating disruption (Suckling et al., 2014b).

REGULATORY ISSUES AND OTHER CHALLENGES

Bringing a new pheromone to market is difficult in many regulatory regimes (Weatherston and Stewart, 2002; Rodriguez and Niemeyer, 2005) although recommendations from the Organisation for Economic Cooperation and Development are supportive of less regulation of such low risk materials as moth pheromones. Requirements in some locations can involve study of efficacy vs. the economic threshold requiring multiple seasons and issues like time and the cost of new solution development are easily underestimated. Despite this, many semiochemicals have been registered over time (Jones, 1998; Witzgall et al., 2010) and innovation from information technology is also underway, such as "Smart Traps" which can provide information in a more timely fashion (Guarnieri et al., 2011; Chinellato et al., 2013).

Progress has certainly been made with rapid registration of straight chained lepidopteran sex pheromones by the US Environmental Protection Agency (Boyd-Wilson et al., 2012; Thomson and Jenkins, 2014). Under the Federal Insecticide, Fungicide, and Rodenticide Act, (Leahy et al., 2014) pheromones (and identical or substantially similar compounds) labeled for use only in pheromone traps for monitoring and pheromone traps in which those chemicals are the sole active ingredients are not subject to regulation For control using mating disruption in USA, a pheromone regulatory relief program gave exemptions from the requirement of a tolerance and set forth certain policies raising the acreage limits to 250 acres for experimental use permit requirements for the testing of many pheromones (Leahy et al., 2014). Under the Hazardous Substances and New Organisms Act (1996), New Zealand has a Group Standard approach to managing items of similar risk, so that paints and cosmetics, or moth pheromones for example, can be labeled and handled appropriately to the level of risk (Boyd-Wilson et al., 2012). In Europe, other concerns including consumer protection that require efficacy tests with accepted protocols have inhibited product development and it is suggested that the greatest gains could come from harmonization (Speiser et al., 2011). Even the more relaxed regulatory regimes can still face challenges in enabling timely access to new pheromones or semiochemicals during an urgent official response program to a new invader.

In contrast, most semiochemicals beyond straight chained lepidopteran sex pheromones face tremendous challenges and look set to move much more slowly through regulatory hurdles (Boyd-Wilson et al., 2012). These wider challenges include research gaps such as patchy discovery and development (including synthesis), biological and natural product limitations including the relative roles of different sensory modalities and attractants of motile stages in different taxa, regulatory issues including the need for Material Safety Data Sheets and toxicological information for new structures with no established market, and potentially market failure, before potential users can even access the products. Where killing agents are combined with odourants in lure and kill systems there are the additional regulatory challenges, although alternatives to broadcast of insecticides are desirable.

Case studies like the vine mealybug pheromone registration for mating disruption in USA are rare (http://suterra.com/agpests/vine-mealybug/), and the high cost of a full toxicological data package partly explains this. In Australia, it took close to 10 years to develop and register a lure and kill product using natural volatile plant compounds against *Helicoverpa armigera*, called Magnet™ (Gregg et al., 2010), and some active host plant odorants were not included because of regulatory concerns. Regulatory regimes appear to lack expertise on volatile organic compounds already being released in nature to appropriately evaluate their risk from usually insignificant synthetic sources, and risk stifling innovation. Development costs are high and hard to recoup commercially from niche products in small markets, but successful products can clearly make inroads on reducing broadcast insecticide use and gain market share as a result of improved sustainability and avoidance of residues.

CONCLUSIONS

Good opportunities for the application of chemical ecology occur in monitoring or surveillance traps and flow through into IPM and Integrated Pest Eradication (Suckling and Brockerhoff, 2010; Suckling et al., 2014a). Not surprisingly and as highlighted here, the same types of pests are targeted for research to underline human intervention globally, because they have or are likely to have economic impact, increase the need for pesticides or otherwise create unwanted risks.

The benefits of semiochemicals are clear but their availability in a form that can be readily used remains limited, with a few exceptions. Many areas are under-developed for practical application due to a lack of follow-through, and published work does not always lead to any adoption. Greater availability of pheromones and other semiochemicals could increase the benefits of more targeted pest management including pesticide reduction or avoidance, and provide new solutions for organisms which have yet to reach their full geographic range. This is a good area for significant further investment but the easy work has been done. The challenge for the research community is to increase the rate of innovation and to develop semiochemicals to solve large and costly pest problems with global scale, rather than merely niches at the wealthy end of the market as generally occurs at present. It has been possible to reduce the regulatory burden for moth pheromones in several jurisdictions but the international challenges presented by invasive species demand a bigger international effort on a wider range of pests.

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GLOSSARY

Attractants: Lures can help by greatly enabling organism delimitation and thereby yield an improvement of >20 fold in probability of eradication (Tobin et al., 2014).

Biosecurity: This term encompasses pre-border biosecurity, with risk assessment, pathway risk analysis, diagnostics, surveillance and eradication (www.b3nz.org), and post-border pest management.

Diagnosis: This is needed to identify the organism, a major theme in Biosecurity. Pheromones for the correct species must be used (El-Sayed et al., 2005).

Integrated Pest Eradication: This term relates to the combined use of a range of tools to effect extirpation (Suckling et al., 2014a).

Integrated Pest Management: IPM relates to the use of multiple suppression methods where eradication is not possible (Blommers, 1994).

Monitoring: The use of pheromone traps in IPM can provide decision support to reduce unnecessary insecticide treatment or improve timing (Rodriguez and Niemeyer, 2005).

Smart Trap: Traps which report catch and transmit the information can be achieved with a range of designs and electronic functionality including web-enabled cameras (Guarnieri et al., 2011; Chinellato et al., 2013).