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Opportunities and barriers to the adoption of potential new grain protectants and fumigants

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The scientific literature shows that many and diverse synthetic chemicals and chemicals derived from natural sources have been investigated as potential treatments for controlling insect pests of stored grain. Why is it then that so few chemicals investigated have been adopted for use in grain storage? Also, of those chemicals that are adopted, why are some used widely but others not? This paper reviews the opportunities and barriers to the adoption of potential new grain protectants and fumigants internationally. The factors influencing their adoption or likely adoption fall under four broad categories: biological, technical, legal and commercial. Mode of action and the susceptibility of different species and resistant strains within species are important biological factors. Technical factors include the availability of appropriate application technology and industry requirements or constraints. Important legal constraints include registration, trade requirements and occupational health and safety. Owners of candidate chemicals must also consider the commercial viability of registering these compounds for stored grain. To a great extent, these biological, technical, legal and commercial factors explain why so few chemicals investigated are adopted, and why adoption is not always widespread.

Introduction

During the 20th century the management of arthropod pests of agricultural crops underwent a revolution with the increasing adoption of chemical control options. Despite ongoing problems with resistance to pesticides, agriculture still relies heavily on chemical control and will do so for the foreseeable future. Similarly, stored grain protection has become reliant on chemical control, principally in the form of grain protectant insecticides and the fumigants methyl bromide and phosphine, and has been dogged by the threat of resistance development in a range of pest species. The importance of chemical control in stored grain protection is reflected by the numerous published studies on the potential of a wide range of chemicals, both synthetic and naturally derived, to control stored grain pests. Despite this extensive and ongoing research few chemicals have been adopted for use in grain storage, and adoption has not always been widespread. This paper attempts to identify opportunities and barriers to the adoption of potential grain protectants and fumigants internationally. The key factors influencing the adoption or likely adoption of protectants and fumigants are discussed under four broad categories: biological, technical, legal and commercial.

Research and adoption

Chemical control of insect pests of stored grain has long been a subject of laboratory and

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field research as demonstrated by the number of papers published in a range of scientific journals. Many such studies have been published in the Journal of Stored Products Research since its inception in 1965. From 1990 to 2005 alone, over 150 papers were published on what might broadly be considered chemical control, i.e. synthetic insecticides and fumigants, diatomaceous earths and botanicals. All have the potential to leave residues in stored grain unlike controlled atmospheres such as high carbon dioxide or nitrogen treaments. Most were on synthetic insecticides, followed by botanicals, fumigants and diatomaceous earths (Figure 1.). Despite this level of research interest over many decades, relatively few chemicals have been adopted for grain storage. Some candidates never proceed beyond the laboratory but even those that reach field trials may not be adopted. Table 1, for example, shows 13 candidate protectants which reached the stage of large scale field evaluation in Australia, of which only five are registered currently, five have never been registered, and three were registered for a limited time. In the case of fumigants, phosphine and methyl bromide have been adopted most widely. Despite the extensive research on botanicals few appear suitable for commercial level grain storage. Notable examples of recently registered grain treatments are the protectant spinosad, the fumigant sulfuryl fluoride and an ethyl formate plus carbon dioxide fumigant formulation.

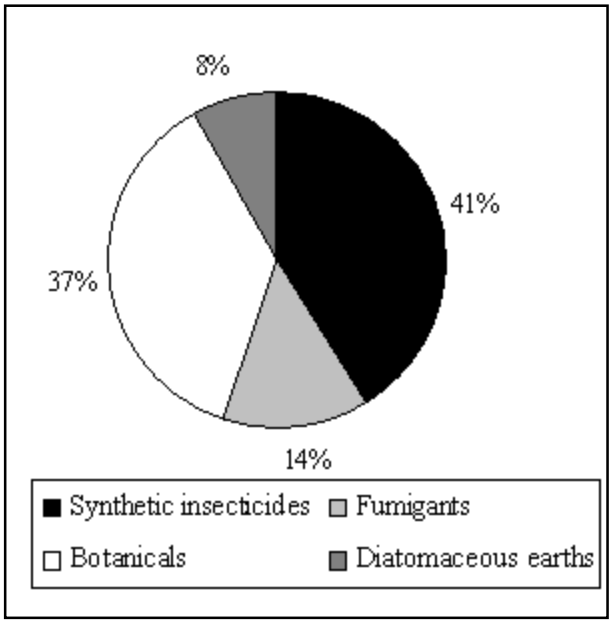

Figure 1. Breakdown of papers published in the Journal of Stored Products Research from 1990 to 2005 on chemical control.

Table 1. Examples of potential grain protectants evaluated (alone or in combination) in silo scale trials in Australia.

Chemical	Type	Registration status	Reference
Bifenthrin	Pyrethroid	Never registered	Daglish et al., 2003
Bioresmethrin	Pyrethroid	Previously registered	Ardley and Desmarchelier, 1978
Carbaryl	Carbamate	Previously registered	Desmarchelier et al., 1987
Chlorpyrifos-methyl	Organophosphorus compound	Registered	Bengston et al., 1980
Deltamethrin	Pyrethroid	Registered	Bengston et al., 1983
Diflubenzuron	Chitin synthesis inhibitor	Never registered	Daglish and Wallbank, 2005
Fenitrothion	Organophosphorus compound	Registered	Ardley and Desmarchelier, 1978
Fenvalerate	Pyrethroid	Never registered	Bengston et al., 1983
Methacrifos	Organophosphorus compound	Never registered	Bengston et al., 1980
Methoprene/s-methoprene	Juvenile hormone analogue	Registered	Daglish et al., 1995
Permethrin	Pyrethroid	Never registered	Bengston et al., 1983
Phenothrin/(1R)-phenothrin	Pyrethroid	Previously registered	Desmarchelier et al., 1987
Pirimiphos-methyl	Organophosphorus compound	Registered	Bengston et al., 1980

Key factors affecting adoption

Biological

Mode of action and the susceptibility of different species and resistant strains within species are important biological factors. Stored grain can be infested by a wide range of potential pest species with a number of species of particular concern, e.g. the lesser grain borer (*Rhyzopertha dominica* (F)), the rust red flour beetle (*Tribolium castaneum* (Hersbst)), the rice weevil (*Sitophilus oryzae* (L.), the saw tooth grain beetle (*Oryzaephilus surinamensis* (L.) and the flat grain beetle (*Cryptolestes ferrugineus* (Stephens)). Grain protectants and fumigants are rarely equally effective against all species of interest, as the following examples illustrate.

Juvenile hormone analogues, such as methoprene which has been used extensively as a grain protectant in Australia since the early 1990s, have low potency against *Sitophilus* species. McGregor and Kramer (1975), for example, found that *S. oryzae* was the least affected by methoprene of four species tested. Spinosad is a bacterial derived insecticide with a unique mode of action which has been investigated as a new grain protectant. Among beetles, spinosad is more effective against *R. dominica* than *S. oryzae*, *T. castaneum* and *O. surinamensis*; and among psocids, spinosad is more effective against *Liposcelis entomophila* (Enderlien) than *L. bostrychophila* Badonnel, *L. decolor* (Pearman) and *L. paeta* Pearman (Fang et al., 2002; Nayak et al., 2005). In addition, spinosad is effective against *R. dominica* resistant to either methoprene or pyrethroids (Nayak et al., 2005; Naya and Daglish, 2006).

Phosphine efficacy has long been known to vary among species and developmental stages within species, with eggs and pupae of *Sitophilus* species being identified as particularly tolerant (Hole et al., 1976), and recent research has demonstrated the impact of resistance on efficacy against *R. dominica* than *S. oryzae* (Daglish et al., 2002; Collins et al., 2005). Efficacy of the potential fumigant carbonyl sulfide was found to vary among adults of stored grain beetles, and among the developmental stages in the one species that was investigated in more detail (Zettler et al., 1997). Weller and Morton (2001) found that *S. oryzae* eggs were more tolerant than adults to carbonyl sulfide.

For grain protectants there is the opportunity to use combinations to overcome the weaknesses and exploit the strengths of individual protectants. Chlorpyrifos-methyl plus methoprene, for example, proved to be effective against a range of pests (Daglish et al., 1995). Within limits, there is the opportunity to increase fumigant concentrations or exposure periods to control different species, development stages or resistant strains (e.g. Daglish et al., 2002; Collins et al., 2005).

Technical

Technical factors include the availability of appropriate application technology and industry requirements or constraints. Technical factors tend not to be a problem for grain protectants which can be sprayed onto small or large quantities of grain quite simply. Problems are more likely to be found with fumigants, mainly in relation to gas-tightness of fumigation structures or enclosures, and sorption of the fumigant by the commodity. Despite several decades of phosphine use in Australia, approximately 20 % of the Australian harvest is not fumigated with phosphine, probably reflecting the storage capacity that is unsuitable for phosphine fumigation. Sorption is the major limiting factor for ethyl formate as a potential fast-acting fumigant with almost complete sorption possible within 24 h (Damcevski and Annis, 2006). Split applications and forced application of a combination of ethyl formate and carbon dioxide have been investigated, in part to minimise this problem (Ren and Mahon, 2006; Haritos et al., 2006). A challenge to adoption of DEs can be industry constraints. In Australia, for example, the major bulk handling companies will not accept grain that has been admixed with DEs, because of concerns about potential abrasion of equipment and changes to the grain's angle of

repose in storage, and therefore handling characteristics and worker safety.

Legal

Important legal constraints include registration, trade requirements and occupational health and safety. Maximum Residue Limits (MRLs) are established internationally by the Codex Alimentarius Commission through the Codex Committee on Pesticides Residues (CCPR). In addition, it is Codex policy to delete MRLs for existing compounds that come under periodic review if specific data requirements are not met. Many other countries establish their own MRLs. In Australia, for example, this is done through the Australian Pesticides and Veterinary Medicines Authority. The cost of generating data to support registration, particularly data relating to risks to human health (consumers and workers) is costly and may be a major obstacle to the adoption of many potential protectants and fumigants and this applies to botanicals as well. Natural pyrethrins, for example, are extracted from pyrethrum flowers but still require registration and MRLs. Recognition of appropriate MRLs by grain purchasers and strict adherence to these MRLs by grain sellers is critical to the successful trading of grain in many domestic and international markets. While many markets will accept or even require protectant treated grain, some countries or regions do not accept protectant treated grain at all. Indian law forbids the use of residual chemicals on grain thereby limiting chemical control to fumigation, and a similar policy applies in the state of Western Australia.

Commercial

Owners of candidate chemicals must also consider the commercial viability of registering these compounds for stored grain. Companies will be aiming to maximise their return on investment (i.e. research, development and registration) while they have data protection. There is also the cost of defending longstanding registrations that have come under periodic review. In many cases, stored grain protection is likely to be a small market compared to other markets (e.g., crop protection, and veterinary or urban uses), so that efforts to register and commercialise new compounds may focus on areas other than grain protection. Table 1 shows that many potential grain protectants have been evaluated in Australia to the level of field trials, but not all have been registered, and not all of those that were registered remain registered. Commercial decisions were the main reasons behind failure to register, or re-register, the protectants in these cases.

Case studies

The following case studies examine opportunities and barriers to the adoption of several grain protectants and fumigants: the fumigant phosphine which has been used widely for many years, the protectant methoprene which has been used less widely and for a much shorter period, the recently registered protectant spinosad, and ethyl formate, a formulation of which has been registered recently for grain fumigation.

Phosphine

Phosphine is the most widely used chemical grain treatment around the world and has been so for many years. There are several reasons for this level of adoption. Initially, phosphine was developed as an aluminium phosphide formulation which reacted with moisture to release phosphine gas. This made the application of phosphine a relatively simple process, and this remains the most commonly used formulation. Later, cylinderised formulations of phosphine plus carbon dioxide (ECO$_2$FUME®) or pure phosphine for on-site blending with carbon dioxide (VAPORPH$_3$OS®) became available requiring more specialised application methods. Phosphine is effective against a wide range of species provided sufficient gas is retained long

enough (e.g. Hole et al., 1976). Even phosphine resistance appears to be manageable to some extent. In Australia, for example, when phosphine resistance was investigated in detail, it became evident that resistant populations could be controlled at realistic concentrations and exposure periods (e.g., Daglish et al., 2002; Collins et al., 2005). The Australian registration label for cylinderised phosphine formulations has been revised in light of this research.

Methoprene

Research on methoprene for control of stored grain insects goes back many years (e.g. McGregor and Kramer, 1975), but this compound has only been used since the 1980s and has not been adopted widely. Two versions of methoprene have been available as grain protectants: methoprene comprising a racemic mixture of two enantiomers (R and S in a ratio of 1:1), and s-methoprene comprising the active S enantiomer only. Amongst grain protectants, methoprene has several advantages and disadvantages. Being a juvenile hormone analogue it has a different mode of action from the other major chemical groups from which grain protectants have been drawn (principally organophosphorus compounds and pyrethroids). It is also viewed as much safer to humans than other synthetic grain protectants. Methoprene impairs immature development but causes little mortality of the parental adults. It is active against a range of beetle pests excluding *Sitophilus* species, but combining methoprene with an organophosphorus protectant such as chlorpyrifos-methyl can overcome this weakness (e.g. Daglish et al., 1995). In Australia, methoprene was first used in the 1990s principally as an alternative to pyrethroids for control of *R. dominica*, and its use has grown steadily with time. In contrast, there has only been limited use of methoprene as a grain protectant in the USA, where the racemic mixture was registered from the 1980s for a time, and s-methoprene has been registered since 2002 (Arthur, 2004). Resistance is a major challenge to the sustainability of methoprene as a grain protectant, because methoprene resistance has already been detected in *R. dominica* (Collins, 1998). A resistance strategy in which methoprene was rotated with another protectant which controls *R. dominica* such as a pyrethroid or spinosad (see below) should be employed to minimise selection pressure on methoprene.

Spinosad

Spinosad is the newest grain protectant and one with completely new chemistry to earlier protectants. It is already registered in the USA but has not yet been commercialised there, and registration is being sought in other countries including Australia. Spinosad is very effective against *R. dominica* and *C. ferrugineus* (Fang et al., 2002; Huang et al., 2004). *Rhyzopertha dominica* has proven to be capable of developing resistance to pyrethroids and methoprene (Collins et al., 1993; Lorini and Galley, 1999; Collins, 1998), and so a significant advantage of spinosad is that it is effective against strains of *R. dominica* that are resistant to pyrethroids or methoprene (Nayak et al., 2005). Spinosad residues and efficacy against *R. dominica* are relatively stable even at high temperature and humidity (Daglish and Nayak, 2006). Spinosad will need to be applied in combination with other protectants to obtain broad spectrum control. In laboratory tests on resistant straians, for example, spinosad 1 mg/kg plus chlorpyrifos-methyl 10 mg/kg controlled four out of five species, the exception being a strain of *O. surinamensis* resistant to organophosphorus compounds (unpublished data). This combination also has the potential to control the principal psocid pests of stored grain for at least 3 months (Nayak and Daglish, in press). The key threat to the long-term sustainability of spinosad would appear to be resistance development in *R. dominica*, although there is no evidence yet of the potential for spinosad resistance in this species. The best strategy, therefore, to maintain spinosad for the long-term would be to use spinosad in rotation with other *R. dominica* protectants such as

pyrethroids and methoprene. Such a strategy would reduce the selection pressure on spinosad, as well as pyrethroids and methoprene against which *R. dominica* is capable of developing resistance.

Ethyl formate

Recent research on the potential of ethyl formate as a grain fumigant has resulted in the registration in Australia of a cylinderised formulation containing ethyl formate and carbon dioxide (Vapormate®) for specific uses excluding farm silos. Ethyl formate is fast acting against grain insects (Haritos et al., 2006; Ren and Mahon, 2006), and occurs naturally in grain (Vu and Ren, 2004). Ethyl formate is rapidly sorbed in grain (Damcevski and Annis, 2006), which means that application methods must be developed to ensure that insect infestations receive lethal exposures. The forced application of ethyl formate plus carbon dioxide was developed to minimise this problem, and has proven to be effective in field trials (Haritos et al., 2006), although this method requires specialised equipment and training. Ren and Mahon (2006) found two split applications to be effective in field trials, but the method of application used has practical shortcomings. In Australia, efforts are being made to reduce the climbing hazard that silos pose to farmers, but these trials involved pouring liquid ethyl formate into several 1.2 m PVC tubes inserted 1 m into the grain surface to facilitate distribution of the fumigant. The cylinderised ethyl formate plus carbon dioxide formulation has immediate potential as a grain fumigant, but methods for application of liquid ethyl formate need to be improved.

Conclusions

Insects remain the major threat to the safe storage of grain for human and animal consumption, and grain protectants and fumigants have provided an opportunity to minimise this threat. The challenge is to retain the treatments that are effective against stored grain insects, particularly in the face of resistance development, and to identify new chemicals as potential alternatives. In this paper I have provided examples of factors (biological, technical, legal and commercial) affecting the adoption of existing treatments or likely adoption of potential new treatments. To a great extent, these biological, technical, legal and commercial factors explain why so few chemicals investigated are adopted, and why adoption is not always widespread.

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