Section: Fumigation, Modified Atmospheres and Hermetic Storage

Quo Vadis the fumigants?

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DOI: 10.5073/jka.2010.425.167

Abstract

Fumigation is the most widely used procedure to control stored product pests to prevent economic and quality losses by providing various application methods and penetration capability into the treated commodity. However, most of the available fumigants have limitations in use due to various reasons. Methyl bromide (MB), according to Montreal Protocol, is scheduled to be phased out worldwide by 2015. Sulphuryl fluoride (SF) is known to have limited efficiency on egg stages of insects. Reportedly, it also contributes to the greenhouse effects, which may jeopardize its future use. Currently, phosphine (PH_3) is the most widely used fumigant worldwide due to its low cost and ease of application, though resistance observed in major pest species threatens the continued use of PH_3. Recent studies in beetles reveal that phosphine resistance is governed through two genes on separate autosomal chromosomes. Research on new fumigants continue to be restricted due to concerns over the adverse effects of fumigant residues in food and the environment that led regulatory agencies to take actions by imposing strict limitations on fumigant registration. On the other hand the phase out of MB and resistance to PH_3 has stimulated significant interest on development of alternatives like modified atmospheres (MAs), thermal disinfestation and irradiation. In Turkey, MAs applications are preferred for the treatment of organic food products and are performed mostly in transportable PVC structures (Cocoons or Volcani Cubes). In museums high nitrogen or SF applications are the only procedures to eradicate structural pests. Under the given constraints of registration of new fumigants, it is anticipated that more attention will be devoted to develop novel alternative treatments that are economically feasible, sustainable, user friendly and environmentally benign.

Keywords: Fumigants, Modified atmospheres, Insect resistance, Stored products pests, Fumigant alternatives

1. Introduction

Fumigation plays an important role in the protection of stored products against insects, mites, and rodents. It is a practical approach targeting or benefiting from respiration, an obligatory and continuous process in energy production during the lifetime of insects. So far, a variety of fumigants have been used and in the meantime all of them have been faced with restrictions of varying degrees due to some adverse effects either to environment or to human health, or to some materials. The most recent example is the worldwide ban on the use of methyl bromide (MB) due to its detrimental effects on stratospheric ozone layer. According to the Montreal Protocol in 1987, with some exceptions, such as quarantine and pre-shipment use and critical use exemptions, MB has already been banned in developed countries in 2005. The ban on MB will be put into practice in developing countries in 2015 (UNEP, 2002). Besides the lost of such a valuable fumigant, the use of phosphine is also threatened by the development of high-level resistance in a number of pest species (Schlipalius et al., 2006; Aurelio et al., 2007; Lilford et al., 2009). Sulfuryl fluoride, apparently the most promising fumigant to replace MB, has already declared as a potent greenhouse gas (Andersen, 2009). In the future, with the increase of its use and depending on its concentration in the atmosphere, it may be subject to ban like MB was banned.

The future of the fumigants will thus be determined by their impacts on environment, human health, and pest resistance. Development of effective, available and cost-efficient alternatives will also affect the fate of the fumigants.

2. Current status of fumigants

During the course of combating with stored products pest, there have been at least a dozen of materials used as fumigants (Rajendran, 2001; Navarro, 2006). The questioning of the future of the fumigants has commenced with the strict ban on the use of MB.

2.1. Methyl bromide (MB)

The Montreal Protocol, an international treaty signed by 175 countries in 1987, is globally phasing out MB, which has average ozone depleting potential of 0.4. According to the protocol, MB production and use will be banned totally in a progressive manner till 2015. However, the ban on MB bears some exceptions, such as quarantine and pre-shipment (QPS) treatments, emergency uses and certain critical uses where no alternatives have yet been available (TEAP, 2000). MB is very important in pest control in durable and perishable commodities and particularly in quarantine treatments. One of the main advantages of MB as a commercially desired fumigant is its action speed. Moreover, it has a lot of additional features such as worldwide preference by quarantine authorities, broad registration for use, good penetration ability, and the rapid aeration of the commodity after exposure. However, it has also some disadvantages as a highly toxic, odourless gas that adversely affects of a number of durables in terms of loss of viability, quality changes, taint and residues (Navarro, 2006).

There is a possibility that MB exemptions regularly reviewed in international meetings might not continue in the future. This has led researchers to develop technologies that allow the recovery of MB to recycle or destroy instead of release it to the atmosphere. Such technologies have found some chance to be implemented currently in North America and Europe but still are complex, expensive and needs technical assistance (Navarro, 2006).

2.2. Phosphine (PH_3)

Currently, phosphine is the only available fumigant registered worldwide to control stored and structural pests. It is mainly used in solid preparation of aluminum or magnesium phosphide. To maintain rapid and continuous phosphine gas during the fumigation, on-site phosphine generators (e.g; Quickflo-R®) were developed. To ensure more uniform and continuous gas concentrations, advanced application technologies such as “Closed Loop System” in USA, SIROFLO®, SIROFUME® and SIROCIRC® in Australia and PHYTOEXPLO® in Europe have been developed for application in different storage conditions. Metal phosphide formulations with slow or altered rates of phosphine release have been developed in Australia (QuickPHlo-C) and in India. Degesch Phosphine Generator/Degesch Granules system is a device using Magtoxin® granules for the rapid production of phosphine gas. Degesch Speedbox, another phosphine fast-generating device uses magnesium phosphide plates to generate phoshine.

Cylinderized gas formulations of phosphine such as Phosfume, ECO_2FUME®, FRISIN®, and VAPORPH$_3$OS® are also commercially available to a lesser extent. Phosfume and ECO_2FUME® are the mixture of 2% phosphine and 98% carbon dioxide. While FRISIN® is a mixture of 1.7% phosphine in nitrogen (98.3%), VAPORPH$_3$OS® is mainly composed of phosphine gas (99.3%) and designed to be applied for on-site blending with carbon dioxide or dilution with the surrounding air. This blending or dilution is needed the use of specialized equipment for the generation of a 2% mixture of phosphine in carbon dioxide, making it essentially the same as ECO_2FUME®. The Horn Diluphos System® that is currently in use in Argentina, Australia, Chile, New Zealand, Uruguay, and U.S.A, dilutes pure cylindered phosphine directly with air.

2.3. Sulfuryl fluoride (SF)

Sulfuryl fluoride is an inorganic, nonflammable, odorless, colorless, and broad spectrum gas that is used to fumigate buildings, transport vehicles, wood (Cox, 1997), flour mills, food factories, dried fruits and tree nuts and cereal grains (Navarro, 2006). SF was first developed by Dow Chemical about six decades ago as a structural fumigant against termites. Today, it is produced in the USA under the trade names of Vikane (99.8% SF 0.2% inert materials) and Profume (Navarro, 2006) and in China under the trade name of Xunmiejin (Guogan et al., 1999). SF seems to be the most promising fumigant to replace MB in terms of similar exposure time of 24 h at normal conditions. Moreover, it has some advantages over MB such as faster diffusion rates than MB in the treated commodities (Navarro, 2006). However, the potential of SF acting as a greenhouse gas may restrain its use in the future as a fumigant.

Sulfuryl fluoride has a complex mode of action. After entering the body of an arthropod, through the stigmas in postembryonic stages or through the diffusion in egg stage, sulfuryl fluoride breaks down to fluoride and sulfate. Insecticidally active fluoride anion interferes with the metabolism of stored fats and carbohydrates by disrupting glycolysis and the citric acid cycle that the insect needs to maintain a sufficient energy for its survival. The fluoride ion is thought to bind to calcium (leading to spasms and seizures) as well as potassium and magnesium. Enzymes requiring a magnesium ion for their normal function are thus inhibited by SF. Among these enzymes are enolases (used to metabolize sugar) and ATPase, an enzyme that is important in cellular energy metabolism. The insect using protein and amino acids to produce energy cannot increase the metabolic rate sufficiently, and dies (Cox, 1997).

The egg stage is more tolerant to SF than any other stages. To overcome the failure in the control of egg stages of the pests during SF fumigation, Reichmuth and Klementz (2008) proposed the use of SF in combination with other fumigants such as hydrogen cyanide (HCN), CO_2, phosphine, or heat. They stated that in Germany, a combination of 2 g m^{-3} of HCN and about 30 g m^{-3} of SF within 40 hours has successfully been applied. According to the different research works in the literature, the same authors concluded that combining of SF also with heat would provide the complete control of egg stages of main stored products pests in the course of disinfestations. Sulfuryl fluoride can also be applied under low pressures yielding with much shortened exposure times (Zettler and Arthur, 2000).

There is a tremendous infestation by wood boring insects in historical palaces of Turkey. Disinfestations of museums in Turkey had been based on using MB at a concentration of 60 g m^{-3} (Ferizli and Emekci, 2008). The historical palaces were fumigated with SF in 2008 in Turkey due to the complete ban of MB in 2005. With the help of 12,000 m^3 h^{-1} capacity gas mixture circulating fans, a closed gas circulating system was used to maintain uniform gas concentrations throughout the palaces. Dosage was calculated using ProFume Fumiguide system.

2.4. Propylene oxide (PPO)

Beside its use in chemical industry as an intermediate to produce commercial and industrial products, including polyether polyols, propylene glycols, propylene glycol ethers; etc., Propylene oxide is commonly used in the sterilization of packaged food items against bacteria, mould and yeast contamination. It has also been registered in the USA since 1984 as a fumigant for the control of stored-product insects in processed spices, cocoa and processed nutmeats (except peanuts). In contrast to MB, PPO is not an ozone depletor and degrades into nontoxic, biodegradable propylene glycol in the soil and in the human stomach. Since PPO is flammable from 3 to 37% in air, it has to be use under low pressures or in CO_2-enriched atmospheres to avoid flammability (Isikber et al., 2006). A complete mortality for all life stages of *P. interpunctella* followed by 4-h laboratory fumigations with PPO at 30°C at 100 mm Hg were reported by Isikber et al. (2006). Thus, commercial scale application of PPO with low pressure can replace MB in quarantine and pre-shipment (QPS) conditions where low pressure treatments are technically and economically available and feasible (Isikber et al., 2006).

2.5. Carbonyl sulfide (COS)

A major sulfur compound naturally present in the atmosphere at 0.5 (± 0.05) ppb, Carbonyl sulfide, is a colorless gas (Wright, 2000) and is present in foodstuffs such as cheese and prepared vegetables of the cabbage family. Traces of COS are naturally found in grains and seeds in the range of 0.05-0.1 mg kg^{-1} (Wright, 2000; Navarro, 2006). The use of COS as a fumigant for the fumigation of durable commodities and structures was patented worldwide in 1992 by CSIRO, Australia. COS has also been trademarked in Australia as COSMIC®. BOC Limited has an agreement with CSIRO for its manufacture and worldwide distribution (Ducom, 2006).

COS at reasonable concentrations from 10 to 40 g m^{-3} was shown to be effective on a wide range of postharvest pests in all stages, including mites at exposure times between 1-5 days at temperatures above 5°C (Desmarchelier, 1994). Amongst the tested pests, *Sitophilus oryzae* (L.) was found to be the most tolerant species to COS and could be controlled at 20 g m^{-3} for 5 days of exposure. Researches on COS in Australia, Germany and the USA revealed that egg stage was highly tolerant to the fumigant, however, the effective exposure period was half that of phosphine at temperatures above 5ºC (Rajendran, 2001).

There has not been found any adverse effect on quality of bread, noodles or sponge cake (wheat) (Desmarchelier et al., 1998), on malting and brewing characteristics of barley or on oil content/color of canola (Ren et al., 2000). Seed germination in wheat, oats, barley and canola was not affected by COS fumigations (Wright, 2000). However, there are contradictory reports in the literature on negative effects of COS on germination of cereals except sorghum and barley, off odors in walnuts, in milled rice, and color change in soybeans (Navarro, 2006).

COS did not show any reaction with a variety of materials including hard and soft timbers, paper, iron, steel and galvanized sheet, PVC, polyethylene, and brick applied with high concentrations at high temperature and r.h. (Wright, 2000). However, avoiding of corrosion on copper, Ren and Plarre (2002) suggested that COS for direct use as a fumigant must be manufactured to eliminate contamination (to <0.05%, v/v), or the fumigant scrubbed of H_2S before application on site.

2.6. Ethyl formate (EF)

Ethyl formate is known as a solvent and is used as a flavoring agent in the food industry (Rajendran, 2001; Navarro, 2006). EF is a volatile compound that occurs naturally in a variety of products, including beef, cheese, rice (Desmarchelier 1999), grapes and wine and is generally recognized as a safe (GRAS) compound.

EF is a volatile, highly flammable liquid at normal ambient temperatures, boils at 55°C, and vaporises readily at normal grain temperatures. Ethyl formate was previously registered in the USA for control of several stored-product pests, including *Tribolium confusum* Jacqueline du Val and *Ephestia figulilella* Gregson. Registrations for the use of EF in the United States of America have expired. Currently in Australia, EF has been used for the fumigation of dried sultanas, in particular. Studies in Australia indicate that, unlike phosphine, ethyl formate is rapidly toxic to storage insects (Annis and Graver, 2000). Effective commodity dosage ranged from 300 to 400 g m^{-3} with 72 h exposure period (Rajendran, 2001). BOC Limited has recently developed and registered Vapormate®, a cylinderised formulation of 16.7% (w/w) ethyl formate in liquid carbon dioxide (for use in Australia). It is a new cereal grain, stored-product and fresh produce fumigant for application by pressurized cylinders. It is a rapid-acting fumigant, effective in a range of from 4 to 24 hours. It is a safe fumigant since the TLV is 100 ppm for EF and 5000 ppm for CO_2 (Ducom, 2006). The CO_2 acts as both a solvent and propellant for the mixture and dramatically reduces any flammability risk due to ethyl formate. In tests with a highly phosphine resistant field strain of *Ryzopertha dominica* (F.); laboratory strains of *Tribolium castaneum* (Herbst) and *S. oryzae*, a single dose of 450 g m^{-3} of Vapormate was found to be sufficient to obtain high level mortality (> 99%) of all stages of *T. castaneum* and *R. dominica* when the grain is held for 24 hours and moderate control (86%) of *S.oryzae* (Haritos et al., 2006b). Forced flow application of ethyl formate and CO_2 vapor through the grain by means of a pump at a flow rate of 6 L min^{-1}., not only provides more even distribution of the fumigant but also causes very high levels of mortality of *S. oryzae* and *T. castaneum* mixed stage cultures (Haritos et al., 2006a).

EF can be used with methyl isothiocyanate (MITC). MITC, originally a soil fumigant against nematodes and fungi, can significantly reduce the dosage of EF to below the flammable level, additionally MITC increases the toxicity of EF. A mixture of EF and MITC (95% EF plus 5% MITC) has recently patented under the name of GLO2 (Ren et al., 2008). GLO2 was shown effective against all life stages of the major grain insect pests. It is fast acting (less than 24 hrs) and requires a short withholding period, about 8 days, but much less with aeration (Ren, et al., 2008).

2.7. Hydrogen cyanide (HCN)

Hydrogen cyanide is currently registered in India and New Zealand (Navarro, 2006). HCN has previously been used to fumigate mills in various countries, including France, Germany, and Switzerland (Rambeau et al., 2001). It is a colorless liquid and smells of bitter almonds. It is lighter than air and has a boiling point of 26°C. HCN is flammable, but in fumigation conditions, concentrations are far under the explosion limits. HCN is very toxic and extremely quick-acting on most living organisms. Due to high degree of sorption at atmospheric pressure, it does not have the quick effective penetration that MB has. It is easily dissolved in water and thus will bind with moisture and can be difficult to ventilate. HCN may be used for the fumigation of many dry foodstuffs, grains, and seeds. Although HCN is strongly sorbed by many materials, this action is usually reversible when they are dry, and, given time, all the fumigant vapors are desorbed (Navarro, 2006). Rambeau et al. (2001) reported that all stages of major mill and food factory pests, including *T. confusum, T. castaneum*, *Plodia interpunctella* (Hübner)*,* and *Sitophilus granarius* (L.) could be controlled at a Ct product of 10 gh m^{-3}, though to ensure HCN penetration and kill insects at a depth of about 10 cm in flour heaps, the prevailing Ct product should be around 60 gh m^{-3}. In the presence of minor leaks, initial HCN concentration was proposed as 5 g m^{-3}.

2.8. Carbon disulfide (CS_2)

Carbon disulfide, an old fumigant, is used for on-farm fumigation of bulk grains in grain silos, bagged grain stored in sheds and bulk gains stored in sheds in Australia and to a limited extent in China (TEAP, 2000). High flammability, long exposure period, persistence in the treated commodity, adversely affected baking quality lack of residue limits set by Codex Alimentarius and high human toxicity were mentioned among the limitations of the fumigant (Rajendran, 2001; Navarro, 2006).

2.9. Methyl iodide (MI)

Methyl iodide, a patented pre-plant soil fumigant against soil inhabiting pests and structural fumigant against termites and wood rotting fungi is also known to be very effective as a space fumigant, being most toxic to eggs and least toxic to adults of *S. granarius*, *Sitophilus zeamais* Motschulsky, *T. confusum*, and *P. interpunctella* (Goto et al., 2004). Though MI is considered as a carcinogenic compound, The U.S. Environmental Protection Agency (EPA) registered MI as a soil fumigant on October 5th, 2007 (EPA, 2009).

2.10. Ethane Dinitrile (EDN)

Ethane dinitrile is also referred to as Cyanogen (C_2N_2). It is a broad range spectrum fumigant; effective against weed seeds, soil insects, nematodes, and fungi. It is an environmentally safe, colorless gas with an almond-like odor. It is a gas at ambient temperatures with a boiling point of –21.2°C. It is soluble in water. The threshold limit value (TLV) of 10 ppm (v/v) compares favorably with that of both methyl bromide (5 ppm) and phosphine (0.3 ppm). It is highly toxic to stored-product insects and is fast acting (except *Sitophilus* spp) (Ducom, 2006). It has a good penetration capability through the grain mass and it desorbs quickly. It also affects germination of treated seeds due to its phytotoxic properties. It is rather considered for space and flour/rice mill fumigations and disinfestations (Navarro, 2006). CSIRO's Division of Entomology, Australia currently holds patents for use of EDN as a fumigant in the major worldwide markets till 2014. BOC Limited has signed an exclusive global license agreement with CSIRO for EDN as a soil, timber fumigant and grain sterilant. EDN is marketed under the trade names of Sterigas 1000 Fumigant (Active Constituent 1000 g kg^{-1} Ethanedinitrile; Flammable) and Sterigas 200 Non-Flammable Fumigant (Active Constituent 200 g kg^{-1} Ethanedinitrile; EDN 20 wt% in liquid carbon dioxide) (Ryan et al., 2006).

2.11. Ozone

Ozone is a powerful oxidant that reduces or inhibits mold spore development and kills stored product insects. It can be used as an insect control agent in food commodities at levels less than 45 ppm (Rajendran 2001, Navarro, 2006). It can be generated on the treatment site without any residue on the treated product. A major disadvantage with ozone is its corrosive property towards most of the metals (Mason et al., 1999). Moreover, it quickly transforms or decays into two molecules of oxygen within less than an hour. Therefore, a special ozone air delivery and return system is needed for an effective ozonation treatment of a storage facility (Campabadal et al., 2007). Ozonation experiments carried out at a popcorn facility yielded 100% mortality for *S. zeamais* and *T. castaneum*, placed 0.6 m below the grain surface (Campabadal et al., 2007).

2.12. Volatile essential oils of botanical origin

There are many research articles in the literature confirming the fumigant toxicity of different volatile essential oils of botanical origin on stored-product insects (Shaaya et al., 1997; Stamopoulos et al., 2007; Isikber et al., 2008; Korunic et al., 2008). These researches were mostly carried out in empty fumigation chambers and thus may not reflect the actual fumigation situations where penetration of the plant extracts into deep layers fails, due to the strong absorption by the commodity. Moreover, aromatic scents of the essential oils permit them only to be applied in empty premises or to commodities such as seeds where the scent of the volatile essential oil would not present a restriction after the treatment. Another important constraint for the use of botanical extracts is that such alternatives of plant origin also need toxicological and safety data for registration for use as fumigants (Navarro, 2006). Physical properties of essential oils such as high boiling point, high molecular weight and very low vapour pressure prevent the use of essential oils for large-scale fumigations. Thus, essential oils are believed to have the potential for small-scale treatments and space fumigations (Rajendran and Sriranjini, 2008).

2.13. Modified atmospheres (MAs)

The use of MAs has dated back to ancient Egyptians in the form of hermetic storage of grain by which grain itself through respiration creates an atmosphere rich in carbon dioxide and low in oxygen (White and Leesch, 1996). Today, MAs have increasingly gained attention as pesticide-free organic food demands have increased. It aims to create an atmosphere lethal to pests in stored commodities rich in CO_2 or low in O_2 by using CO_2, N_2 or their mixtures at normal or altered atmospheric pressure within the storage facility. So far, MAs composed of either CO_2, N_2 or inert gases have classically been used in different parts of the world for the fumigation of a variety of commodities including grains, pulses, tree nuts, dried fruits, coffee and cocoa beans, spices, medicinal herbs, geophytic bulbs and historic artifacts (Adler et al., 2000)

Turkey is one of the leading countries in the world in exporting dried fruits and hazelnut. MB has a critical importance in the production of dried figs, in particular. Each year, Turkey exports some 40 thousand tonnes of dried figs. Dried figs are harvested between mid of August and late September. There are some 50 dried fig-processing plants in Turkey, most of them family sized plants that run 3 months during the fig-processing season. Processing of 40 thousand tonnes of dried figs in a three-month period in small sized plants needs fast fumigation procedures to eliminate *Carpophilus* spp and *Cadra cautella* (Walker), which are the main pests of dried figs infecting the crop in the orchards. Thus, due to time limitation, exposure time lasting more than a day is not tolerated. This makes MB unique for dried fig production in Turkey. Research carried out to find alternatives to MB in Turkey showed that MAs applications using high CO_2 in flexible PVC units (Volcani Cubes) were effective and could be used against the main pests of dried figs, however, the exposure time of 5 days was needed to attain a complete kill (Emekci et al., 2007). Thus, MAs applications currently in use in Turkey are mostly restricted to organic food products of various kinds.

Museum objects were disinfested by means of MAs applications due to the complete ban on the use of MB in Turkey in 2005. High nitrogen gas treatments of historical artifacts in PVC cubes of 30 m^3 volume led to a complete mortality of all life stages of Khapra beetle, lesser grain borer, confused and red flour beetles after 30 days of exposure at ambient temperatures. Nitrogen gas was obtained from a gas generator of 4 $Nm^3\ h^{-1}$ outlet flow capacity to maintain a low oxygen atmospheres around 1% O_2, a PLC Scada system was set up to restore nitrogen levels in different cubes when the oxygen level increased above 1% (Emekci and Ferizli, 2008).

MAs applied in combination with positive pressure or elevated temperature increase the performance of MAs. Significant reduction in exposure time to a few hours can be obtained with the use of high carbon dioxide under high pressures ranging between 10-37 bars. Generally, increase in pressure decrease the lethal exposure time. Eggs, especially in early stages of development were known to be less sensitive to high pressure carbon dioxide treatments than other stages (Adler et al., 2000; Navarro, 2006). The cost of high pressure chambers limits the use of this method only to the treatment of valuable commodities such as dried fruits, nuts, spices, herbs and cocoa beans (Adler et al., 2000; Navarro, 2006). Elevated temperatures also help MAs to decrease the lethal exposure time significantly (Donahaye et al., 1994).

2.1.4. Vacuum treatments

Low O_2 atmospheres can be mechanically obtained by vacuum. The primary mechanisms of action of vacuum treatment on insect survival are shown to be lack of oxygen and dehydration due to removal of water vapor (Navarro, 2006). The need for massive, rigid and expensive structures withstanding the low-pressures was the main barrier in using low pressures at the large-scale commercial level. With the development of flexible plastic units, GrainPro Cocoons®, sufficiently low pressures (25-50 mmHg absolute pressure) to kill the insects can be obtained using a commercial vacuum pump and maintained for indefinite periods of time (Finkelman et al., 2003). This technology, known as vacuum-hermetic fumigation (V-HF) is currently in use at commercial level for pest treatment of organic soybeans and flours in Israel (Navarro, 2006).

2.1.5. Resistance to phosphine and its management

Resistance, as in the case of phosphine, is the inevitable result of the continuous use of the fumigants in leaky conditions, improper applications and exposures. Although stored-products insects can develop resistance to the fumigants and modified atmospheres, resistance in field conditions is currently limited to phosphine. The number of pest populations showing resistance to phosphine has been increasing worldwide since it was first shown by a global FAO survey on pesticide susceptibility in 1972/1973 (Champ and Dyte, 1976).

Zuryn et al. (2008) proposed that phosphine targets the mitochondria in vivo and direct alteration of mitochondrial function may be related to phosphine resistance. They believed that multiple factors that influence metabolism, and specifically mitochondrial function, have a direct influence on both phosphine toxicity and resistance against its toxic effects. Mitochondrial membrane potential, rate of electron flow through the mitochondrial respiratory chain (Chaudhry, 1997), ATP levels, metabolic supply versus demand, and mitochondrial generated oxidative stress are all thought as metabolic factors that may contribute to phosphine sensitivity or resistance. There is a significant interrelation between respiration rate and phosphine resistance. The populations with lower carbon dioxide production showed a higher resistance ratio, suggesting that the lower respiration rate is the physiological basis of phosphine resistance by reducing the fumigant uptake in the resistant insects (Aurelio et al., 2007). The reduced uptake of the phosphine in resistant insects might be due either to the presence of a phosphine insensitive target site or to a membrane-based efflux system that excludes phosphine gas in resistant insects (Chaudhry, 1997).

In terms of phosphine resistance, there are three types of phenotypes: susceptible type, weakly (mildly) resistant type and highly resistant type. Phosphine resistance was found to be governed by multiple genes in both mildly and highly resistant phenotypes, at least one of which contributes a major factor to resistance in each type (Collins et al., 2002; Ebert et al., 2003; Athie and Mills, 2005; Lilford et al., 2009). Ebert et al. (2003) using molecular genetic techniques found that two major genes primarily control resistance in highly resistant strains of *R. dominica*. The first gene is responsible for ‘weak’ resistance, whereas, insects with a stronger level of resistance have the gene responsible for ‘weak’ resistance plus another gene. The second gene has little effect on its own but strongly enhances the effect of the first gene. Resistance is characterized by incompletely recessive alleles on these major genes. Thus heterozygous individuals show a limited expression of a lower level of resistance similar to susceptible insects. Schlipalius et al. (2002) showed that strongly resistant strain carrying resistance alleles has two loci on different chromosomes. Both Collins et al. (2002) and Schlipalius et al. (2002) conclude that one of the genes determining resistance in the strongly-resistant strain is also present in the weakly-resistant strain. Schlipalius et al. (2006) proposed that the gene (rph_1) shared between the weakly-resistant strain and the strongly-resistant strain was responsible for the initial emergence of phosphine resistance in Australia. Selection of the recessive allele for rph_1 under fumigation subsequently caused the selection of the recessive allele at an additional, secondary resistance gene (rph_2). Thus, strong level of resistance is depending on the presence of resistance alleles on both rph_1 and rph_2 (Collins, 1998). For *R. dominica* resistance for those homozygous with both copies of the sensitive gene has been determined to be well over 250X those with no copies of the resistance genes, whereas there is a resistance factor of 2.5X to 30X if the resistance genes are present in only one of the two locations, depending on which location (Lilford et al., 2009).

Collins (2006) predicts that in about 10 years weak resistance in *R. dominica* will reach a frequency of 100% all over Australia and strong resistance to phosphine will become a major problem in a few years time when weak resistance frequency reaches 80% throughout the country unless resistance is managed. Beside the increasing frequency of resistance, Collins (2006) also worries about its potential increase in strength. A strain of rice weevil imported under quarantine from southern China was revealed to be about 50% more resistant to phosphine than the most resistant strain of any species in Australia (Nayak et al., 2003). This situation may lead in the future that phosphine will be either ineffective, or almost useless because effective fumigations will require long fumigation periods and very high concentrations of gas (Collins, 2006). Moreover, Ebert et al. (2003) concluded that the resistance alleles would be completely persistent in the field, even without the selective pressure of phosphine fumigation. Thus, rotation of control chemicals would not, of itself, lead to a reduction in the frequency of phosphine resistance alleles in the field. Thus, to combat resistance, fumigations must be fully effective.

The most of the phosphine-resistant populations exhibits reduced developmental and population growth rates than the susceptible counterpart populations. This implies that phosphine resistance is associated with fitness cost, which can potentially compromise the fixation and dispersal of the resistant genotypes (Pimentel et al., 2007). However, some phosphine-resistant populations did not show a fitness cost. Therefore, resistance management strategies based on minimizing phosphine use aiming at eventual reestablishment of phosphine susceptibility and subsequent reintroduction of this fumigant will be useful only for insect populations exhibiting a fitness cost associated with phosphine resistance. Therefore, recognition of the prevailing phosphine-resistant genotypes in a region is important to direct the management tactics to be adopted (Sousa et al., 2009).

For the management of phosphine resistance, early detection of the resistance and its strength is very important. There are several test methods for checking resistance in the field or in the laboratory. Of these, the use of resistance testing kits to test the pests before the application of the fumigant, and varying the phosphine concentration and the exposure time respectively, so that resistant beetles are also treated successfully with phosphine dosage accordingly can be useful. Reducing the selection pressure by limiting the application number against the populations exhibiting fitness cost or by applying non-chemical alternatives such as cooling and hygiene is recommended. Resistant insects must be totally eradicated only using approved rates of phosphine that are researched and known to control resistant insects, and by using alternative fumigants or protectants where available (Collins, 2006).

3. Conclusions

Worldwide ban on MB is no doubt threatening the future of stored-products protection against insect and mites. Currently, phosphine is the fumigant of choice regarding its low cost, availability, versatility in application, ease of use, and global acceptance as a residue free treatment. However, major stored-product insects have already developed strong resistance against phosphine and unfortunately resistance is spreading throughout the world. Sulfuryl fluoride, the most promising alternative, has not yet been available worldwide. There are other alternative fumigants, each of which is suitable only for treating a particular commodity or for application in specific situations. Thus, proper use of fumigants, particularly phosphine, is very important for protecting stored products against pests and for extending the use of phosphine. The monitoring and rapid detection of resistance and its strength is also vital for the safe use of fumigants. In case of the resistance, necessary actions must be taken immediately according to the nature of the resistance, i.e. whether it is weak, strong or is associated with fitness cost or not.

Use of non-chemical IPM tools, such as pest exclusion, hygiene, MAs, natural enemies, physical factors are also very important and efficient in pest controlling without the use of the fumigants. It is shown that by the implementation of an IPM program based on insect monitoring to detect infestation loci to intervene timely, there was no need to make regular annual fumigation with MB in a flour mill in Italy (Savoldelli and Panzeri, 2008). Similarly, heat disinfestation treatments are successful for the control of insect pests in flour mills or in empty grain bins. MAs including high CO_2, N_2 applications, vacuum treatments (Navarro, 2008), or hermetic storage (Rodriguez et al., 2008) provide excellent alternatives that is economic, sustainable, available, safe and environmentally benign to the use of traditional chemical fumigants in different situations, including bulk storage of grain and pulses, protection of organic food, protection of historic artefacts', museums and libraries, and modified atmosphere packaging for the food industry.

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