CAF2020 Paper No. P-8-7-68

Ryan R, Dominiak BC (2021) Ethyl formate: review of a rapid-acting fumigant. Pp. 269-275. In: Jayas DS, Jian F (eds) Proceedings of the 11th International Conference on Controlled Atmosphere and Fumigation in Stored Products (CAF2020), CAF Permanent Committee Secretariat, Winnipeg, Canada.

Ethyl formate: review of a rapid-acting fumigant

Robert Ryan[1*], Bernard C Dominiak[2]

[1]Principal Consultant, VAPORFAZE, Sans Souci NSW 2219, Australia.
[2]NSW Dept. Primary Industries, Orange, New South Wales 2800, Australia.
*Corresponding author's email: robert.ryan.consultant@gmail.com

Abstract

Ethyl formate (EF) is a historical flammable liquid fumigant to disinfest dry fruits, with uses extended to horticulture and cereal grains. Enhanced efficacy is achieved when EF is applied in a non-flammable vaporized carbon dioxide (CO_2) mixture. Ethyl formate is an effective bulk grain fumigant (complete control at 70 g/m^3 in 24 h) with sorption issues being accommodated by rapid dispensing ensuring uniform distribution. Recent review found 78 insect species controlled by EF, albeit at different rates or exposure times. Ethyl formate is registered by the Australian Pesticides and Veterinary Medicines Authority (APVMA) to control 41 species of these pests. Current APVMA Permit allows for in-transit EF fumigation. Registration of EF has not kept pace with recent research. The brown marmorated stink bug (EF probit 9 efficacy reported as 10.5 g/m^3, 10°C , 4 h), khapra beetle, tomato potato psyllid, and tramp ants are candidates for EF fumigation.

The EF usually requires relatively high dose (70 g/m^3); however, its predominant attribute, like methyl bromide (MBr), is short exposure times (i.e., hours not days). Ethyl formate can be used at lower temperatures than other fumigants. The volatile and flammable EF is a proven fumigant and a candidate for replacing ozone depleting MBr. Unlike other MBr alternatives, EF kills insects rapidly and has advantages for worker and environment safety. Ethyl formate (Threshold Limit Value, TLV = 100 ppm) is an effective and less toxic fumigant for horticulture and stored product pests, including during transit on road and sea. Recent research identified EF as a candidate alternative fumigant for MBr (TLV=5 ppm) in the elimination of exotic quarantine pests. An effective low dose of EF allows for non-flammable on-site EF mixing to be competitive with the existing MBr quarantine fumigation. In addition, other benefits include environmental release (unlike MBr, EF is not an ozone depletor and has limited life in the atmosphere).

Keywords: Quarantine fumigation, Non-flammable fumigants, On-site mixing fumigant, Methyl bromide, Alternative fumigants, Food grade fumigant

Introduction

Ethyl formate (EF) is a historical liquid fumigant (1929) to disinfest dry fruits and its use has been extended to horticulture and cereal grains. Ethyl formate also has a history of safe use as a food additive. Interest in EF as a fumigant declined following the introduction of carbon disulphide and

subsequently of methyl bromide (MBr) and phosphine (PH_3) in the 1950's (Ren and Mahon, 2006). However, in 2002, carbon disulphide was deregistered for use as a fumigant in Australia (Ren and Mahon, 2006). Methyl bromide is the fumigant with the widest range of applications (Bell, 2000) but was due to be phased out for stored commodities after 2005 (Ren and Mahon, 2006). There are restrictions on the use of MBr as mandated by the Montreal Protocol on substances that deplete the ozone layer (TEAP, 2000). The use patterns of fumigants continue to change because there are continuing pressures on fumigants due to registration requirements, atmospheric emissions controls, fears on safety or human health, the incidence of resistance. These changes are occurring as the world expects increasingly high standards of pest control in international trade (Bell, 2000). The registrations of EF have not kept pace with recent research due to the existing preference for other fumigants.

Ethyl formate background

Ethyl formate is also known as ethyl methanoate, formic acid ethyl ester, ethyl formic ester, and formic ether (Merck Index, 1989; Ryan and De Lima, 2012). Ethyl formate is present naturally in soil, water, vegetation, and in a range of plant and animal products. These products include food grains, fruits, vegetables, beer, wine and spirits, tuna, meat, mussels, milk, cheese and bread (Desmarchelier et al., 1999; Ren and Mahon, 2006; Ryan and De Lima, 2012). Ethyl formate is a central nervous system depressant (Ryan and De Lima, 2012). Ethyl formate can irritate eyes, skin, mucous membranes and the respiratory system, particularly above 100 ppm (Ryan and De Lima, 2012; Safe Work Australia, 2019). The gas is weakly pungent at 100 ppm and annoyingly pungent at 1,000 ppm (Safe Work Australia, 2019). Agarwal et al. (2015) found that EF had a pleasant aromatic odour. Ethyl formate has the characteristic smell of rum and is partly responsible for the flavour of raspberries (Ryan and De Lima, 2014). Commercially, EF is used in the manufacture of artificial rum, as a flavour for lemonade and essences, as a fungicide, larvicide and as an organic solvent (Merck Index, 1989; Safe Work Australia, 2019). In industry, EF is used as a solvent for cellulose nitrate, cellulose acetate, oils and greases (Ryan and De Lima, 2012).

The oral LD_{50} for rats and rabbits is >1,800 mg/kg and TLV 100 ppm (Safe Work Australia, 2019). Ethyl formate is not classified as a carcinogen (Safe Work Australia, 2019) and holds "generally regarded as safe" (GRAS) status with the US Food and Drug Administration (FDA) for its use as a food additive (Ducom, 2006; Haritos et al., 2006). EF has the advantage of a very short fumigation period, low toxicity to mammals and the environment, and a rapid breakdown with minimum or no residues (Coetzee et al., 2019; Haritos et al., 2006). Some pests are controlled after one hour of fumigation and one hour of venting (Bikoba et al., 2019).

Ethyl formate uses

The low toxicity EF can require relatively high dose (70 g/m^3); however, its predominant attribute, like MBr, is short exposure times (i.e., hours not days). Mixing with an inert gas is required to achieve a non-flammable mixture. Unlike PH_3, EF kills insects rapidly and its residues break down to naturally occurring products such as formic acid and ethanol (Desmarchelier et al., 1999; Ren and Mahon, 2006). In Australia, there are no Maximum Residue Level required for EF when used for baled hay, as a fumigant for cereals, pulses and canola and associated storage structures and machinery, as a fumigant for cocoa, and as a post-harvest fumigant of fruit and vegetables (Reuss et al., 2001; Ren and Mahon, 2006). Ethyl formate is rapidly sorbed and degraded by most

commodities where they have high moisture or are warm (Ren and Mahon, 2006). Itis effective on many horticulture insect pests. Additionally, EF is efficacious on stored product insects and has synergist effects when applying non-flammable EF/CO_2 vapour on stored grain insects (Haritos et al., 2006). Ethyl formate was an effective bulk grain fumigant with sorption issues being mitigated by rapid dispensing (Dojchinov et al., 2010). Ethyl formate can be removed from rice products through unforced ventilation (Reuss et al., 2001).

Ethyl formate is registered in Indonesia, Israel, Malaysia, New Zealand, Philippines and South Korea (Wolmarans et al., 2017; Simpson et al., 2007). There are three EF products registrations with the Australian Pesticides and Veterinary Medicines Authority (APVMA), one as a 98% liquid product and two with EF/CO_2 liquefied gas mixtures (Ryan and De Lima, 2014). Ethyl formate is registered by APVMA to control 41 pest species. Additionally, the APVMA has issued permits (Permit 87993) for the use of EF for the movement of foodstuffs and general goods to the environmentally sensitive Barrow Island in Western Australia. The application rate must be sufficient to ensure that the concentration × time (Ct) is greater than 270 g.h/m^3. Permit 86953 allows in-transit fumigation with EF at 90 g/m^3 for 6 h.

To minimize flammability, an EF/CO_2 in a 1:5 non-flammable mixture in high pressure industrial gas cylinders was patented (Ryan and Bishop, 2003; Haritos et al., 2003; Damcevski et al., 2003). Addition of carbon dioxide to the EF significantly enhanced efficacy of the fumigant (Haritos et al., 2006). Also, CO_2 accelerates the penetration of insecticides into insects' spiracles (Ryan and De Lima, 2014). Since about 2000, EF was effective in controlling a range of insects in citrus, grapes, strawberries, bananas, sweet corn, stored cereals, pulses, dates and fodder crops (Ryan and De Lima, 2014).

Treatment periods are frequently 1-2 h (Simpson et al., 2007; Agarwal et al., 2015). Ethyl formate is efficacious at low fumigation temperatures (e.g., 9.2°C); these temperatures are not recommended for fumigation with MBr or some other fumigants (Tarri et al., 2007). Cold (5°C) Navel oranges did not need to be warmed prior to treatment with EF and CO_2 to treat bean thrips (Bikoba et al., 2019) hence prolonging fruit shelf life and minimizing handling costs and time. Chhagan et al. (2013) also treated apricots at 5°C without adverse effect on fruit. De Lima (2011) tested EF successfully in temperatures ranging from 10°C to 20°C.

On farm fumigation

The Australian Commonwealth Scientific and Industrial Research Organization (CSIRO) were early adopters of EF fumigation with Allen and Desmarchelier (2000) initiating the treatment of grain sampling equipment at grain export terminals. Another significant input was CSIRO Entomology (2013) report on the GRDC project (#CSE009) which detailed EF/CO2 as a fast insecticide fumigant for small grain storages (50-200 t). The data generated in this project was used to extend the APVMA pesticide registration approval. This report concluded EF could be used as a PH_3 resistance management tool. The availability of effective alternative treatments is a method of supporting PH_3 use in the industry. Ethyl formate is completely effective against PH_3 resistant insects. Ethyl formate acts rapidly to kill insects. Application takes less than 15 min and fumigation takes as little as 3 h. Ethyl formate sorption is minimized by rapid dispensing, one gas exchange of EF in 12 min. Venting of the gas at the end of fumigation takes less than 2 h. Grain can then be safely out loaded without a withholding period. This means growers who want to sell

grain quickly but find it is infested can treat and outload in less than a day. The grain can be immediately out loaded for sale and use for human and animal purposes after venting of excess fumigant. Silo requirements include an aeration fan and some level of sealing. This CSIRO project developed an application technology that is specifically designed for small scale silos (50-200 t) thereby directly benefiting growers who choose to store on-farm. Mixed age cultures of three stored grain insects were chosen for the major efficacy studies based on the frequency these insects are found in storages, the economic damage they cause to stored grains and their known tolerance of insecticidal treatments. These included a highly PH_3 resistant field strain of the lesser grain borer, and laboratory strains of the flour beetle and the rice weevil.

A Draeger X-AM 7000 multi gas detector (www.draeger.com) measures EF and CO_2 fumigation levels, and the Miran® SapphIRe (Thermo Environmental Instruments; www.thermofisher.com /Miran) programmable infra-red gas analyzer measures EF at occupational exposure levels (100 ppm) and below.

The major outcome of project CSE00009 has been the successful delivery of a new grain fumigant for the Australian grains industry and in particular, farm-scale storers of grain.

Treatment of exotic quarantine pests

Brown marmorated stink bug (BMSB), *Halyomorpha halys* (Stål), is highly polyphagous and is found on at least 211 plants across 88 plant taxa. Currently, there are three approved treatment options for BMSB detections at the Australian border in international cargo (DAWE, 2020). Heat treatments require that consignments be treated at 56°C or higher at the coldest surface of the goods, for a minimum of 30 min or 60°C or higher at the coldest surface of the goods, for a minimum of 10 min.

Alternatively, MBr is an option with a dose of 24 g/m³ or above, at 10°C or above, for a minimum of 12 h (but less than 24 h), with all start time concentration readings above 24 g/m³ and a minimum end point reading of 12 g/m³. Another fumigant option in Australia is sulfuryl fluoride. The treatment dose is 24 g/m³ or above, at 10°C or above, for a minimum of 12 h (but less than 24 h), with all start time concentration readings above 24 g/m³ and a minimum end point reading of 12 g/m³. The treatment has failed if the concentration of fumigant falls below the minimum end point reading at any point during the treatment (DAWE, 2020).

Ethyl formate is a potential BMSB quarantine fumigant. Kawagoe et al. (2017) presented data requiring low EF doses (median 10 g/m^3, 4 h) to eliminate BMSB. The Lethal Exposure, LE_{99} (Ct) varied from 20.52 (10.26 mg/L) for 2 h exposure to 29.29 (2.44 mg/L) for 12 h exposure. Probit Curve data gave the LE_{99} (Ct) of 33.02 (16.5 mg/L) for 2 h exposure, 41.9 (10.5 mg/L) for 4 h and 58.77 (4.9 mg/L) for 12 h exposure. Also, these results were achieved at 10°C (below the recommended temperature limit for many fumigants). The majority of current MBr fumigation for BMSB are carried out in low density packed containers (e.g., motor cars and associated non-food shipments) which avoids issues of sorption and uniform distribution related to densely packed grain storage. In the consumables required to eliminate BMSB at the USDA, median 10 g/m^3, 4 h exposure, fumigation would be cost competitive with the current MBr treatment.

Ethyl formate can be used in-transit shipping containers and offers savings in labour cost, elimination of the time for a container to remain stationary in a fumigation facility and a significant decrease in time spent between dispatch and receival (Coetzee et al., 2019). There were nil detections of EF in the immediate surroundings, up to 15 m downwind or inside and outside of the truck cabin (Coetzee et al., 2019). Similarly, EF (90 g/m^3) and nitrogen fumigation of 20 ft shipping containers were monitored during an overnight voyage (Coetzee et al., 2020).

Conclusions

Recent review (Ryan and Dominiak, 2020) found 78 insect species that could be controlled by EF, albeit at different rates or exposure times. These insects include five weevils, six aphids, six thrips, seven moths, 18 scale and mealy bugs, and ten beetles. Of these, EF is registered to control 41 of these pests. There is an opportunity to add more pests to the registered uses based on available science. Also, there is opportunity to evaluate more pests from the more established EF control groups such as thrips, moths and beetles to assist interstate trade.

Unlike some alternatives, EF kills insects rapidly (Ren and Mahon, 2006). Ethyl formate has advantages for worker and environment safety (Ren and Mahon, 2006; Coetzee et al., 2019). EF is much safer for human use compared to MBr (Ryan and De Lima, 2014; Park et al., 2020). Ethyl formate is an effective and less toxic fumigant for horticulture and stored product pests, including during transit on road and sea. Research identified EF as a candidate alternative fumigant for MBr in the elimination of exotic quarantine pests. The effective low dose of EF allows for non-flammable on-site EF mixing to be competitive with the existing MBr quarantine fumigation. In addition, other benefits include environmental release (unlike MBr, EF is not an ozone depletor and has limited life in the atmosphere), occupational (TLV's: EF = 100 ppm and MBr = 5 ppm) and the reduced aeration time should reduce facilities costs. Ethyl formate has less onerous requirements for PPE and no recapture technology is required. Ethyl formate is an attractive alternative fumigant compared with many industry standards.

References

Agarwal M, Ren Y, Newman J, Learmonth S (2015) Ethyl formate: a potential disinfestation treatment for eucalyptus weevil (*Gonipterus platensis*) (Coleoptera: Curculionidae) in apples. J Econ Entomol **108**: 2566-2571.

Allen SE, Desmarchelier JM (2000) Ethyl formate as a fast fumigant for disinfestation of sampling equipment at grain export terminals. Pp. 82-88. In: Proc Aus Postharv Tech Conf, Adelaide, Australia.

Australian Pesticides and Veterinary Medicines Authority (APVMA) www.apvma.gov.au

Bell CH (2000) Fumigation in the 21st century. Crop Prot **19**: 563-569.

Bikoba VN, Pupin F, Biasi WV, Rutaganira FU, Mitcham EJ (2019) Use of ethyl formate fumigation to control adult bean thrips in Navel oranges. J Econ Entomol **112**: 591596.

Bond EJ, Monro HAU, Buckland CT (1967) The influence of oxygen on the toxicity of fumigants to *Sitophilus granarius*. Journal of Stored Products Research **3**: 289-294.

Cherfuka W, Kashi KP, Bond EJ (1976) The effect of phosphine electron transport on mitochondria. Pesticide Biochemistry and Physiology **6**: 65-84.

Chhagan A, Jamieson LE, Griffin MJ, Page-Weir NEM, Poulton J, Zulhendri F, Feng R, Connolly PG, Davis VA, Olsson S, Redpath SP, Kean AM, Woolf AB (2013) Postharvest management of New Zealand flower thrips (*Thrips obscuratus*) on apricots using ethyl formate or pyrethrum- based treatments. New Zealand Plant Prot **66**: 63-74.

Coetzee EM, Newman J, Coupland GT, Thomas M, van der Merwe J, Ren Y (2019) Commercial trials evaluating the novel use of ethyl formate for in-transit fumigation of shipping containers. J Environ Sci Health, Part B **54**: 717727.

Coetzee EM, Du X, Thomas ML, Ren Y, McKirdy SJ (2020) In-transit fumigation of shipping containers with ethyl formate + nitrogen on road and continued journey on sea. J Environ Sci Health, part B **55**: 820826.

CSIRO Entomology (2013) https://grdc.com.au/research/reports/report?id=77, GRDC Project CSE00009, Victoria Haritos (Principal Research Scientist) CSIRO Ecosystem Sciences, Canberra, Australia.

Damcevski KA, Dojchinov G, Haritos V (2003) Vapormate™, a formulation of ethyl formate with CO_2, for disinfestation of grain. In: Proc 3rd Aus Postharv Tech Conf Stored Grain in Australia, Canberra, Australia.

De Lima F (2011) Disinfestation of sweet corn for export using phosphine and controlled atmospheres. Project number VG01014. Horticulture Australia Ltd, Sydney. 32 p.

Department of Agriculture, Water and the Environment (2020) www.agriculture.gov.au/import/ Accessed 8 October 2020.

Desmarchelier JH, Johnston FM, Vu LT (1999) Ethyl formate, formic acid and ethanol in air, wheat, barley and sultanas: analysis of natural levels and fumigant residues. Pest Sci **55**: 815-824.

Dojchinov G, Damcevski KA, Woodman JD, Haritos VS (2010) Field evaluation of vaporized ethyl formate and carbon dioxide for fumigation of stored wheat. Pest Manage Sci **66**: 417-424.

Ducom PJF (2006) The return of the fumigants. Pp. 510-516. In: Lorini I, Bacaltchuk B, Beckel H, Deckers D, Sundfeld E, dos Santos JP, Biagi JD, Celaro JC, D'A Faroni LR, Bortolini LOF, Sartori MR, Elias MC, Guedes RNC, da Fonseca RG, Scussel VM (eds) Proc 9th Intern Working Conf Stored-Prod Prot, Campinas, São Paulo, Brazil.

Haritos VS, Damcevski KA, Dojchinov G (2006) Improved efficacy of ethyl formate against stored grain insects by combination with carbon dioxide in a "dynamic" application. Pest Manage Sci **62**: 325-333.

Kawagoe J, Abrams A, Walse S (2017) Ethyl formate fumigation for control of stinkbugs in vehicle consignments. Intern Res Conf Methyl Bromide Alternatives and Emissions Reductions (MBAO), San Diego, USA.

Lee DH, Short BD, Joseph SV, Bergh JC, Leskey TC (2013) Review of the biology, ecology, and management of *Halyomorpha halys* (Hemiptera: Pentatomidae) in China, Japan and the Republic of Korea. J Econ Entomol **42**: 627641.

Merck Index (1989) An Encyclopedia of Chemicals, Drugs and Biologicals. Merck and C., Rahway, N.J., USA, 600 p.

Park MG, Park CG, Yang JO, Kim GH, Ren Y, Lee BH, Cha DH (2020) Ethyl formate as a methyl bromide alternative for phytosanitary disinfestation of imported banana in Korea with logistical considerations. J Econ Entomol **113**: 1711-1717.

Ren Y, Mahon D (2006) Fumigation trials on the application of ethyl formate to wheat, split faba beans and sorghum in small metal bins. J Stored Prod Res **42**: 277-289.

Reuss R, Annis P, Khatri Y (2001) Fumigation of paddy rice and rice products with ethyl formate. Pp. 741-749. In: Donahaye EJ, Navarro S, Leesch JG (eds) Proc 6th Intern Conf Controlled Atm Fumi Stored Prod, Fresno, USA. www.ftic.co.il/2000FresnoPDF/76.pdf

Ryan RF, Bishop SR (2003) Vapormate Nonflammable ethyl formate/liquid carbon dioxide fumigant mixture. Pp.190-192. In: Wright EJ, Webb MC, Highley E (eds) Proc 3rd Aus Postharv Tech Conf Stored Grain in Australia, Canberra, Australia.

Ryan RF, De Lima CPF (2012) Overview of ethyl formate – 85 years as a fumigant. General Appl Entomol **41**: 49-54.

Ryan RF, De Lima CPF (2014) Ethyl formate fumigation an overview update. Pp. 969-978. In: Arthur FH, Kengkanpanich R, Chayaprasert W, Suthisut D (eds) Proc 11th Intern Working Conf Stored-Prod Prot, Chiang Mai, Thailand.

Ryan RF, Dominiak BC (2020) Review of ethyl formate use in Australia and possible future uses for emerging biosecurity risks. General Appl Entomol **48**: 81-90.

Safe Work Australia (2019). Ethyl formate. (109-94-4). 6 p. www.safeworkaustralia.gov.au

Simpson T, Bikoba V, Tipping C, Mitchum EJ (2007) Ethyl formate as a postharvest fumigant for selected pests of table grapes. J Econ Entomol **100**: 1084-1090.

Tarri CR, Reuss R, Clingeleffer PR, Annis P (2004) The use of ethyl formate for space fumigation of dried vine fruit. Pp. 193-205. In: Proc 7th Intern Conf Controlled Atm Fumi Stored Prod, Brisbane, Australia.

TEAP (2000) Technology and Economic Assessment Panel. Montreal Protocol on substances that deplete the ozone layer: UNEP technology and economic assessment panel. Report to the United Nations, TEAP, Cape Town, South Africa.

Wolmarans F, Bikoba V, Mitchum EJ (2017) A review of VAPORMATE™ (ethyl formate and CO_2): an effective post-harvest fumigant. Methyl Bromide Alternatives Outreach. San Diego, California 92108.