



Permeation of methomyl in Lannate L™ through nitrile gloves

Xuesong Lu, Shane S. Que Hee *

Department of Environmental Health Sciences and the UCLA Center for Occupational and Environmental Health, UCLA School of Public Health, 10833 LeConte Avenue, Los Angeles, CA 90095-1772, USA

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Abstract

The influence of the inert components on the permeation of methomyl in Lannate L water miscible pesticide formulation through 0.64 mm thick unsupported lined nitrile at 30°C was assessed using an ASTM-type permeation cell with isopropanol liquid collection medium. Gas chromatography/mass spectrometric (GC/MS) analysis of 0.100 ml aliquots of the collection fluid taken every 10 min revealed that the breakthrough time for permeation of methomyl was > 200 min with a steady state permeation rate of $5.24 \pm 1.00 \mu\text{g cm}^{-2} \text{min}^{-1}$. Reconstituted formulation with concentrations of methomyl, methanol and isopropanol being those found by direct GC/MS of Lannate L showed that these components did not explain all the permeation kinetic data. © 1998 Elsevier Science B.V.

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1. Introduction

Wearing gloves is necessary when handling liquid formulations of non-volatile pesticides since skin absorption is the major route of exposure to workers, sprayers and garden users [1–3]. Solid pesticides do not permeate efficiently since minimal wetting and contact of the glove surface occur to facilitate barrier entry. Emulsifiable concentrate formulations of pesticides contain [4] liquid inert components such as solvents, surfactants, and other adjuvants to permit effective spraying in water carrier. These components may also promote permeation of dissolved pesticides. A chemical that does

* Corresponding author. Tel.: +1-310-206-7388; fax: +1-310-794-2106; e-mail: squehee@ucla.edu.

not permeate alone may do so when in a mixture of components that do, as for example, organic solvents [5,6].

Methomyl [(CH₃S)(CH₃)C=N–O–(C=O)–NH–CH₃ or *S*-methyl-*N*-(methylcarbamoyl)oxylthioacetimidate] is a carbamate pesticide introduced by Du Pont in 1966 that has a melting point of 78–79°C, decomposes above 180°C, has a vapor pressure of 6.65 mPa at 25°C, and has a water solubility of 58 g l⁻¹ at 25°C [7]. Methomyl is the active ingredient of the commercial pesticide formulations Du Pont 1179, Flytek, Kipsin, Lannate, Lanox, Memilene, Methavin, Methomex, and Nudrin, and is often coformulated with tetradifon, dicofol, and muscalure. It is used against many insects including spider mites on fruits and vegetables, and flies in animal/poultry houses and dairies. It is a major ovicide, larvicide, and acaricide. The World Health Organization Acceptable Daily Intake is 30 μg kg⁻¹ body weight [7]. The 1997 Threshold Limit Value-Time Weighted Average is 2.5 mg m⁻³ [8]. It is a ‘reversible’ cholinesterase inhibitor with atropine as antidote [7]. The human oral lethal dose is 12–15 mg/kg⁻¹ body weight [9]. Fatalities in Crete occurred in 1991–1993 after Lannate ingestion [10]. Lannate 25 is genotoxic [11,12]. Methomyl is positive in the Mutatox Test for genotoxicity but is much more potent on S₀ activation [13].

There are very few garment permeation studies on methomyl and none on gloves. One study showed the resistance of polyethylene Tyvek and Saranex-23 Tyvek (I.E. Du Pont de Nemours, Wilmington, DE) of unspecified thicknesses to Lannate where methomyl had a breakthrough time $t_b < 15$ min, with steady state permeation rates $P_s < 0.1$ μg cm⁻² min⁻¹ [14]. The present study investigated the permeation of Lannate L through protective gloves and the influence of its solvent inert components.

2. Materials and methods

2.1. Glove and formulation selection

The methomyl formulation was Lannate L (Du Pont), a water-miscible formulation nominally containing 24% methomyl and 76% inert ingredients. The material safety data sheet had methanol ingestion warnings. Thus, the formulation was examined to detect and quantify methomyl by dilution in isopropanol, volatile components by dilution in toluene, and by headspace analysis utilizing gas chromatography (GC)/mass spectrometry (MS). A Hewlett-Packard (Palo Alto, CA) 5890A GC was equipped with a 30 m × 0.32 mm ID DB-1701 chemically bonded fused-silica capillary column (J&W/Alltech, Deerfield, IL), connected to a Hewlett-Packard 5988A quadrupole MS operated in the positive ion electron impact mode at 70 eV over m/z range 1–500. Total ion current GC/MS allowed the detection and analysis of methanol, isopropanol, and methomyl in the formulation.

The next step was to choose the glove type. The Ansell Edmont catalog (Ansell-Edmont, Coschocton, OH) [15] was consulted for a material that resisted methanol and isopropanol, the latter being the collection fluid. The nominal P_s for isopropanol was < 0.9 μg cm⁻² min⁻¹ with $t_b > 360$ min for Sol-Vex nitrile, for unsupported neoprene, and for Neox-supported neoprene, all being equally protective. Thus, isopropanol

as a collection solvent is not expected to degrade or permeate through these materials. Other glove types like PVA-supported polyvinyl alcohol, polyvinyl chloride and natural rubber were much inferior, thus eliminating them from consideration. Methanol permeates [15] nitrile at a P_s of 90–900 $\mu\text{g cm}^{-2} \text{min}^{-1}$ (t_b , 11 min), unsupported neoprene at $P_s < 0.9 \mu\text{g cm}^{-2} \text{min}^{-1}$ (t_b , 60 min), and Neox-supported neoprene at $P_s < 0.9 \mu\text{g cm}^{-2} \text{min}^{-1}$ (t_b , 15 min). Unsupported neoprene therefore is the most protective glove, then Neox-supported neoprene, and finally nitrile for this formulation in terms of methanol, the major solvent of the inert ingredients and the one with the highest permeation rate.

If the hypothesis that the inert components determine the permeation rate of methomyl through the cosolvent effect is correct, the permeation of methomyl is related to the methanol content but will be modified by the presence of isopropanol and methomyl in the formulation. Since isopropanol and methomyl are less polar (higher $\log K_{ow}$) than methanol and assuming dissolved methomyl does not react with nitrile, the maximum permeation rate for methanol for Lannate L must be $< 900 \mu\text{g cm}^{-2} \text{min}^{-1}$ with $t_b > 11$ min, extending the protective period relative to the t_b of pure methanol. Though unsupported neoprene was predicted to be the most protective glove, neoprene would not provide as fast a confirmation of the hypothesis. Nitrile is also the most used industrial glove, and is inexpensive.

Since a liquid collection medium was to be utilized in an ASTM-type permeation cell system [16], the medium also had to facilitate GC/MS analysis. Isopropanol did not interfere with methomyl analysis, was resolved from methanol, allowed methomyl to be solubilized, and was only a minor component of the formulation.

2.2. Materials

The major materials included lined Sol-Vex gloves (Ansell-Edmont, catalog no. 37–165, 22 mil, 38 cm in length), I-PTC 600 ASTM type permeation cells (Pesce Lab Sales, Kennett Square, PA), a moving tray shaker water bath (Fisher Scientific, Fairlawn, NJ, model 125 No. 429), a torque wrench (Mechanics Products, Kent, WA), a micrometer screw gauge (L.S. Starrett, Athol, MA), vernier calipers (Mitutoyo, Tokyo, Japan), and Eppendorf micropipets (Brinkman Instruments, Westbury, NY). The chemicals were Lannate L formulation (Du Pont), methomyl of 97% nominal purity (Chem Service, West Chester, PA), and toluene, methanol, and isopropanol (Optima grades, Fisher Scientific). The reconstituted pesticide formulation was prepared by dissolving the appropriate methomyl mass in the methanol/isopropanol solution to fit the GC/MS composition of the pesticide.

2.3. GC/MS analyses

The injector, transfer line, and ion source temperatures were 260°C. The injection volume was 2 μl . The analysis conditions for permeation samples were: solvent delay 7 min at 40°C and temperature program 10°C min^{-1} to 170°C until all peaks eluted at a

helium carrier flow rate of $3.0 \pm 0.1 \text{ ml min}^{-1}$. Inert component analysis utilized the same program with no solvent delay as did headspace analysis (10 ml samples in gas-tight syringes). Isopropanol/methanol standardizations were in toluene, and methomyl, Lannate L, and Lannate L reconstitution solution standardizations were in isopropanol.

All standardizations were in the linear range of the analytes that allowed coefficients of variation (CV) of the slope of $\leq 10\%$. The linear ranges were: methomyl, 163–1210 pg using m/z 105; methanol, 314–1570 pg using m/z 32; and isopropanol, 312–1560 pg using m/z 45. Toluene and isopropanol were used as solvents as appropriate. Retention times were: methanol 1.763 min; isopropanol, 2.504 min, toluene 6.8 min, and methomyl 14.1 min. Identifications were by retention time and mass spectra obtained in the total ion current mode. Quantitations were at the above selected ion monitoring m/z conditions.

2.4. Permeation experiments

The full technique has been described elsewhere [16]. In summary, the glove was equilibrated at least 24 h at $(65 \pm 1)\%$ relative humidity in a desiccator containing saturated aqueous sodium dichromate at room temperature ($21.1 \pm 0.3^\circ\text{C}$). Circular glove material was cut of $3.80 \pm 0.09 \text{ cm}$ diameter (vernier calipers) from the palm. The thickness from four micrometer screw gauge measurements was $0.64 \pm 0.13 \text{ mm}$ for each specimen. The material was placed between the two Teflon gaskets, and the two glass chambers screwed into the stainless steel flanges to a torque of 16 in/lb (torque wrench). The exposed surface area was 4.34 cm^2 . The cell was then immersed by clamp in the moving tray water bath at $30.0 \pm 0.5^\circ\text{C}$ to test for leaks, and then 10 ml of isopropanol collection medium added, followed by 15 ml of challenge solution. The water bath was then set at $8.5 \pm 0.5 \text{ cm s}^{-1}$ horizontal velocity to ensure homogeneous mixing (dye test). Clean 1-ml Teflon-lined screw capped vials (Wheaton, Fisher Scientific) were precooled to -20°C . Aliquots of $100 \mu\text{l}$ were sampled every 10 min by Eppendorf from the collection side into the vials, the vial caps bound with Teflon tape, and stored at -20°C until GC/MS analysis. Each permeation study lasted 4 h. The challenge solution was Lannate L or the reconstituted methomyl/methanol/isopropanol mixture as found from GC/MS analysis. After the initial run, samples were taken every 10 min from 30 min before breakthrough to define the steady state section better. Volumes of the challenge and collection sides before and after experiments were sampled and analyzed. Vial headspace analysis was done. The total methomyl mass permeated at a given time was calculated from the mass injected from the standardization curve corrected for fraction sampled and for collection medium volume changes from prior samplings. After each experiment, the material was dried at room temperature, and the thickness remeasured.

Linear regression of the steady state section yielded the lag time t_1 (the theoretical time of zero permeated mass for the extrapolated steady state section), the mass transfer rate, and P_s (the mass transfer rate at steady state divided by contact area). The t_b for first detection in the collection medium was also noted. The diffusion coefficient D_p was calculated from $D_p = l^2/6 t_1$ [16].

3. Results

3.1. GC/MS studies

The Lannate L formulation contained in % (w/w): methanol, 61.5 ± 0.5 ; isopropanol, 7.3 ± 0.1 ; and methomyl, 23.6 ± 0.1 . Two other peaks at 10.3 min and 10.9 min were probably unreacted methyl isocyanate and methyl thiolacetohydroxamate from methomyl synthesis [17] since they were also present in the methomyl ‘pure’ standard. The pesticide formulation inert component solvents methanol and isopropanol constituted $68.8 \pm 0.7\%$ compared with the expected 76%, significantly different at $p \leq 0.05$ for $n = 3$ (2-tailed test). The methomyl content was not statistically different from the nominal of 24% at $p \leq 0.05$. The mass balance was $92.4 \pm 0.8\%$. The mass imbalance of $7.6 \pm 0.8\%$ was not accounted for by the presence of the two synthetic byproducts of methomyl synthesis. GC/MS analysis confirmed the purity of standard methomyl to be 97%.

3.2. Permeation studies

The permeation results for Lannate L and for the reconstituted formulation are shown in Table 1. There was only one steady state section for both permeation curves. No increased isopropanol was observed in the challenge side after permeation experiments, indicating no significant backpermeation of collection medium. The average material thickness after permeation was 0.66 ± 0.10 mm. No significant swelling or shrinkage occurred at $p \leq 0.05$.

Table 1

The permeation data for Lannate L and the reconstituted formulation for lined Sol-Vex gloves of thickness 0.64 ± 0.13 mm

Challenge	Glove	t_b	t_1 (S.D.)	P_s (S.D.)
<i>Lannate L</i>				
	1	190–200	190(11)	4.40(0.32)
	2	210–220	164(11)	5.76(0.22)
	3	230–240	209(14)	6.40(0.39)
	4	220–230	220(14)	18.9(1.1)
	5	230–240	194(22)	4.40(0.27)
	Average (S.D.)	190–240 ^a	195(21)	5.24(1.00) ^b
<i>Reconstituted</i>				
	1	110–120	114(7.4)	22.7(1.4)
	2	120–130	131(6.8)	16.6(1.1)
	Average (S.D.)	110–130 ^a	123(12)	19.7(4.3)

^aRange.

^bWithout glove 4 data.

t_b , breakthrough time in minutes; t_1 , lag time in minutes; SD, standard deviation in the same units as its arithmetic mean; P_s , steady state permeation rate in $\mu\text{g}/\text{cm}^2/\text{min}$ for methomyl.

The average methomyl t_b for Lannate L at the lower end of the linear dynamic range was 216 ± 17 min ($n = 5$) and the average t_1 was 195 ± 21 min. The t_b and t_1 did not differ statistically at $p \leq 0.05$. The CVs for both were $\leq 11\%$. The average P_s was $5.24 \pm 1.00 \mu\text{g cm}^{-2} \text{min}^{-1}$ ($n = 4$) with $\text{CV} = 19\%$ when one outlier was deleted by Q -Test. When the latter was included, the average was $7.97 \pm 6.17 \mu\text{g cm}^{-2} \text{min}^{-1}$, clearly non-Gaussian, even though the offending run had t_b and t_1 not significantly different at $p \leq 0.05$ from their respective populations.

For the reconstituted formulation (Table 1), the average t_b was 120 ± 10 min much shorter than for the Lannate L challenge. The average t_1 was also much shorter at 123 ± 12 min. Again, the mean t_b and t_1 values were not statistically different at $p \leq 0.05$. The average P_s was much higher at $19.7 \pm 4.3 \mu\text{g cm}^{-2} \text{min}^{-1}$, with $\text{CV} = 22\%$. The reconstituted formulation was thus about $(19.7/5.24) = 3.76$ times more permeative than Lannate L in terms of P_s . The ratios for average t_b , t_1 , and P_s for Lannate L to reconstituted formulation were 1.80, 1.59, and 0.266, respectively. There was no statistical difference between the t_b and t_1 ratios at $p \leq 0.05$.

The average D_p for methomyl in Lannate L was $(3.5 \pm 0.4) \times 10^{-4} \text{mm}^2 \text{min}^{-1}$ for permeation through this material in this ASTM type cell using the average data. The analogous value for the reconstituted formulation was $(5.6 \pm 0.6) \times 10^{-4} \text{mm}^2 \text{min}^{-1}$. The difference is statistically significant at $p \leq 0.025$ even though the two challenges have the same methomyl, methanol, and isopropanol challenge masses and the same glove material thickness.

4. Discussion

The data indicate the safe period to wear Sol-Vex nitrile gloves for protection against methomyl in Lannate L is about 200 min. Direct measurement of methomyl t_b is still necessary to be able to define the safety period and when to dispose of old gloves and wear new ones.

While methanol must be the major methomyl carrier of the two alcohols since isopropanol alone does not permeate nitrile, three different competing effects are operating. One effect is modulation of the overall polarity of the predominantly methanol solution by isopropanol and methomyl to produce a challenge solution of lower bulk polarity than pure methanol [18]. A second effect is differential partitioning of methomyl between the inert components and the glove material within the glove leading to chromatographic behavior and different t_b of the mixture components [18]. The calculated $\log K_{ow}$ for methomyl from its water solubility at 25°C of 57.9g/l [7] is 0.93 from the empirical equation [19] $\log K_{ow} = 4.5 - 0.75 \log S$ (S in mg/l). This is significantly more non-polar than methanol. The measured $\log K_{ow}$ for the lower alcohols are: ethanol, -0.32 ; isopropanol, -0.16 ; and n -butanol, 0.88 [19]. The $\log K_{ow}$ for methanol is lower than for ethanol and is probably about -0.48 . The partitioning/chromatographic effect is also present in the reconstituted formulation data. The first two effects do contribute since the methomyl t_b for the reconstituted formulation is longer than the t_b for pure methanol, but account at most for $(120 - 11)/(216 - 11) = 0.53$ or about half of the t_b increase for Lannate L relative to that for

pure methanol. In the steady state period, methanol facilitates the continuing methomyl permeation but this is modified by the other components. The third effect is the probable influence of an unknown adjuvant in the Lannate L formulation as part of the unaccounted mass balance. This is presently being investigated. Nevertheless, the qualitative prediction that methomyl would have a longer t_b than the methanol t_b of 11 min based on polarity considerations was borne out by direct observation. The actual length of the safety period and the time to dispose of gloves and wear new ones must still be found by direct measurement however.

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