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Microparticle Dispensers for the Controlled Release of Insect Pheromones

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The potential utility of micrometer-sized particles as controlled-release devices for the volatilization of insect pheromones for mating disruption applications is evaluated in this study for two pheromone/model compound systems (codlemone/1-dodecanol and disparlure/1,2-epoxyoctadecane). To expedite the measurement of release rates from these particle devices, two techniques based on thermogravimetric analysis (TGA) have been exploited: isothermal TGA (I-TGA) at elevated temperatures (40−80 °C) with N_2 convection and volatilization temperature (VT) by dynamic TGA. A correlation between these two methods has been established. Samples that exhibit a higher VT provide a lower release rate from a particle substrate. Using these techniques, it has been demonstrated that chemical interactions between adsorbed liquids and particle surfaces may play a small role in defining release characteristics under conditions of low surface area, whereas parameters associated with total surface area and micropore structure appear to be much more significant in retarding evaporation for uncoated particles containing an adsorbed liquid. Additional regulation of release rates was achieved by coating the particle systems with water-soluble or water-dispersible polymers. By careful selection of particle porosity and coating composition, it is envisioned that the evaporation rate of pheromones can be tailored to specific insect control applications.

KEYWORDS: Pheromones; controlled release; gypsy moth; codling moth; microparticles; codlemone; disparlure; thermogravimetric analysis; TGA

INTRODUCTION

The utility of pheromones in the process of insect mating disruption has been well established over the past several decades (*1*−*7*). A key element in a successful mating disruption program is to create a large number of point sources emitting pheromones, thereby creating many false trails that camouflage the location of a calling insect, usually the female. Furthermore, an effective controlled-release strategy is essential in maintaining the evaporation rate of the point source emitters at an appropriate level for insect response throughout the mating season. Lepidopteran pests (moths) are especially susceptible to the tactic of mating disruption, and field application of this method has proved to be very successful against a variety of forest and orchard pests including the gypsy moth (*8*−*11*) and codling moth (*5*, *7*, *12*) (*Lymantria dispar* and *Cydia pomonella*, respectively).

A broad spectrum of controlled-release devices for pheromones have been proposed: hollow fibers, plastic laminates, impregnated ropes, "twist-ties", wax formulations, and gel-like dispenser matrices (*1*−*3*, *13*). Although effective in many cases, these devices suffer from several inherent limitations:

(1) Depending on the device and formulation, release rates may vary with time. So-called "zero-order" release kinetics, where the evaporation rate is independent of time, are most desirable.

(2) For most pheromone dispensers, the airborne concentration of active ingredient falls off very rapidly with distance from the device, and they are effective only for relatively localized attraction and trapping of insects, assuming that a finite number of devices are applied. As a result, "multipoint source" pheromone emission is not typically achieved.

(3) Certain devices can be relatively expensive or time-consuming to fabricate and may not be amenable to mass production.

(4) Implementation in the field can be very manpower intensive if individual devices must be fastened to trees by hand, and reaching the upper tree canopy, where many pheromones are most effective, can be difficult.

(5) The polymeric device "packaging" is usually not biodegradable and can accumulate in the environment.

Alternative approaches have involved the use of microcapsules and plastic beads filled or saturated with pheromone that can be broadly distributed by spraying to provide an almost infinite number of point sources (*1*, *2*, *11*, *14*), but the other limitations cited above remain (cost, biodegradability, etc.).

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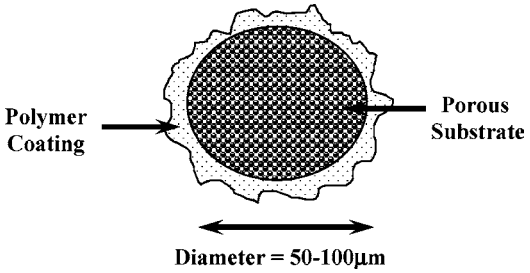

Figure 1. Polymer-coated porous substrate.

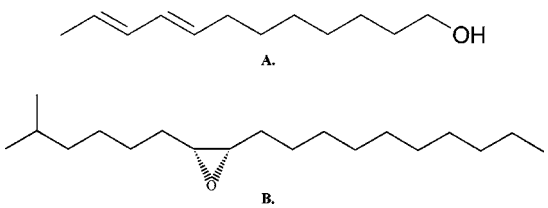

Figure 2. Structures of the codling moth (**A**) and gypsy moth (**B**) pheromones.

The primary objective of this study was to fabricate and characterize micrometer-sized biodegradable or environmentally benign particles suitable as vehicles for the widespread application of insect pheromones. A prototype particle design is provided in **Figure 1** wherein a pheromone can be immobilized on a porous substrate coated with a polymer film membrane.

It is envisioned that the pheromone-containing particles could be applied to areas requiring insect control by distribution from airplanes (*14*) or through conventional ground-based spraying equipment. Ultimately, it could become possible to control insect populations on a broader geographical level using microparticles, compared to devices such as "twist-ties", while maintaining the environmental and efficacy advantages of pheromones compared to conventional, nonspecific pesticide application.

In this study, attention was focused on the sex pheromones codlemone [(*E*,*E*)-8,10-dodecandien-1-ol] and (+)-disparlure [(*Z*)-7,8-epoxy-2-methyloctadecane], which are well-known to be effective in codling moth and gypsy moth control, respectively (*11*, *12*). The chemical structures of these compounds are provided in **Figure 2**. The specific objectives of the present work are as follows: (1) the development of new analytical methods to accelerate the quantification of evaporation rates from micrometer-sized controlled-release particles; (2) evaluation of the effect of chemical composition and surface morphology on the ability of particulate substrates to adsorb pheromones while moderating their evaporation to air; (3) the development of a process to coat pheromone-containing particles with a release rate controlling polymer membrane; and (4) extrapolation of the results of this project to pheromone applications under realistic field conditions.

MATERIALS AND METHODS

Materials. Samples of the pheromones codlemone [$C_{12}H_{22}O$, formula weight (FW) = 182.34] and (+)-disparlure ($C_{19}H_{38}O$, FW = 282.51) were obtained from Bedoukian Research Inc. and Aldrich Chemical Co., respectively. Model compounds, 1-dodecanol [$C_{12}H_{26}O$, FW = 186.34, boiling point (bp) = 260 °C] and 1,2-expoxyoctadecane ($C_{18}H_{36}O$, FW = 268.49, bp = 137 °C at 0. 5 mmHg), obtained from Aldrich, were selected as model compounds for codlemone (bp = 273 °C) and disparlure (bp = 146 °C at 0.25 mmHg), respectively, on the basis of their similar chemical structures and volatilities. Model compounds were employed to reduce cost. Boiling point data for 1,2-epoxyoctadecane (epoxyoctadecane) and disparlure were reported by the manufacturer, whereas results for 1-dodecanol (dodecanol) and codlemone were determined using a thermogravimetric analysis (TGA) method in our laboratory (TA Instruments TA-2950) using hermetic pans with pinhole tops. It should be noted that we did not characterize the release rate or particle adsorptive capacity of racemic disparlure, which has been used in control of the gypsy moth (*11*), although significant differences from the (+)-isomer were not expected, especially for particle substrates that are not optically active.

Table 1. Properties of Microparticle Substrates

material	surface chemistry	surface area (m^2/g)	particle size[a] (μm)
MCC	polar	<1	50
CMC	ionic, polar	0.6	<250[b]
HPC	hydrophobic	0.7	<800[b]
SF-14	polar	1.1	40–70
C18	hydrophobic	101	10
Super-Q	slightly polar	639	150

[a] Particle size distributions were not measured. [b] Converted from mesh size.

Particulate substrates representing a range of polarity (or hydrophobicity) and porosity were selected for this study. Samples were typically dried in a vacuum oven near 100 °C, but the actual moisture content of each particle type was not measured. Three different cellulosic materials were evaluated to assess the impact of chemical modification: underivatized, microcrystalline cellulose (MCC) obtained from FMC (product code PH-101); hydrophobically modified hydroxypropyl cellulose (HPC), obtained from Hercules; and ionic sodium carboxymethyl cellulose (CMC) purchased from Aldrich (M_w = 250 000; DS = 1.2). Micrometer-sized hollow glass spheres were obtained from the PQ Corp. (SF-14). Super-Q, a cross-linked divinylbenze/ethylvinylbenzene polymer resin used as a gas chromatography column packing, was purchased from Alltech Associates, Inc. A C18 high-performance liquid chromatography (HPLC) packing, based on derivatization of porous silica with octadecylsilane, was obtained from DC Scientific. Additional properties for each substrate are detailed in **Table 1**. Although micrometer-sized particles are considered to be most appropriate for actual pheromone applications, several of the substrates studied were of larger size.

Porous carbon particles were also evaluated to determine the impact of surface morphology, as determined by a N_2 adsorption−desorption isotherm method (see below), on the evaporation properties of pheromones. Two carbon black products were obtained from Cabot Corp. (Vulcan XC72R, surface area = 191 m^2/g; Black Pearl 2000, 1466 m^2/g). Graphite powder was purchased from Fisher Scientific (27 m^2/g), and C-100 carbon powder (126 m^2/g) was provided by the Chevron Chemical Co. A high surface area carbon powder, denoted APPO (2201 m^2/g), was synthesized in Professor I. Cabasso's laboratory at SUNY-ESF.

Several water-soluble polymer coatings were evaluated as a means to introduce an evaporation-retarding barrier around the pheromone-containing particle substrates. Examples include HPC (Hercules; designated "low molecular weight"), CMC (Aldrich Chemical; M_w = 250 000; DS = 1.2), and poly(sodium 4-styrenesulfonate) (PSS; Aldrich Chemical, M_w = 1 000 000).

Release Rate Measurement. The release rates of pheromones and model compounds from particle substrates were measured by two methods: (1) a gravimetric "oven method" based on weight loss with time in a forced-air oven held at elevated temperatures (40−80 °C) and (2) an instrumental method based on TGA run under isothermal conditions (I-TGA; 40−80 °C) over time. In both cases, weight loss was monitored as a function of time at a constant temperature and was assumed to result from pheromone and residual moisture evaporation. The loss of pheromone degradation products or substrate degradation (if any) could not be directly determined by these methods. Preliminary experiments demonstrated that moisture loss generally occurred within the first few hours in an forced-air oven experiment and within the first few minutes of an I-TGA run. As a result, pheromone release rates were calculated in the steady state weight loss regime that followed the initial period of moisture evolution. The ambient moisture content

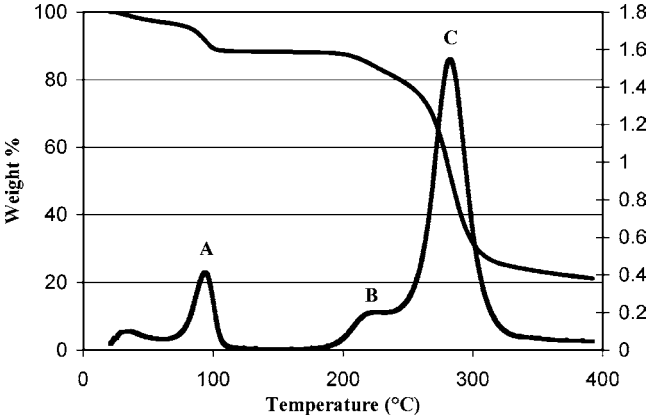

Figure 3. Dynamic TGA of dodecanol adsorbed on MCC coated with a water-soluble polymer: (**A**) dodecanol evaporation; (**B**) coating degradation; (**C**) cellulose pyrolysis. The upper curve is the actual weight loss thermogram, and the lower curve is the first derivative with respect to temperature of the thermogram.

of the particulate substrates examined in this study ranged from 2 to 10% water by weight of substrate.

Release rate measurements using the so-called oven method were accomplished by placing a known amount of controlled-release particles in an aluminum or plastic sample pan held at a specific temperature in a forced-air oven. Sample mass (total weight of the particles and pan − initial weight of pan) was recorded once or twice daily for periods up to 300 h, and a release rate was calculated according to the following expression in milligrams per hour: [sample mass (mg) at time = t − initial mass at $t = 0$ (mg)]/total t (h). The oven air circulation rate was determined to be ∼180 L/min using a laminar flow anemometer, and this was held constant for all experiments. The air flow rate was purposely selected to be significantly higher than typically experienced in the field to expedite the screening process of new particle substrates and coatings. For the model compound dodecanol, a linear relationship between air flow rate and evaporation rate over the range of 25−180 L/min was observed, suggesting that it should ultimately be possible to extrapolate oven method results to lower air flow rates more typical of actual applications.

As a less time-consuming alternative to the oven method, evaporation rates were also determined using a TA Instruments model TA-2950 TGA instrument. In this procedure, evaporative weight loss for a 20-mg sample (substrate plus pheromone or model compound) was measured as a function of time over 4−8 h at temperatures of 40, 50, and 60 °C. A nitrogen flow rate of 66 mL/min (0.066 L/min) through the heating furnace was typically employed. Weight loss results from this procedure were extrapolated to lower temperatures by using a regression analysis based on an Arrhenius-type plot of ln(release rate) versus 1/T (K) constructed from 40, 50, and 60 °C data.

In addition to monitoring the evaporation rate of pheromones from particulate controlled-release devices, an alternative approach was employed to very rapidly characterize the ability of specific substrates and coatings to bind volatile compounds. In this case, a dynamic TGA procedure was developed in which the temperature was ramped from ambient to 400 °C at, nominally, 10 °C/min. The temperature at which the pheromone compound was observed to evaporate from the substrate was designated the volatilization temperature (VT). More specifically, a so-called "high-resolution" procedure was employed wherein the temperature ramp decreases from its initial value (10 °C/min) when a significant weight loss is observed. This creates a sharper volatilization temperature compared to a constant heating rate experiment. High-resolution data are typically recorded at an instrument resolution setting of 4 (1 = low resolution, similar to a normal constant temperature ramp; 6 = highest resolution). VT is defined as the temperature associated with the peak of the derivative weight loss curve (see **Figure 3**).

Microparticle Procedures. Pheromones and model compounds were adsorbed onto particle substrates by manually mixing appropriate amounts in a vial with a glass stir rod at 40 °C to ensure that the volatile components were in the liquid state. Equilibration at 40 °C continued overnight in a sealed vial.

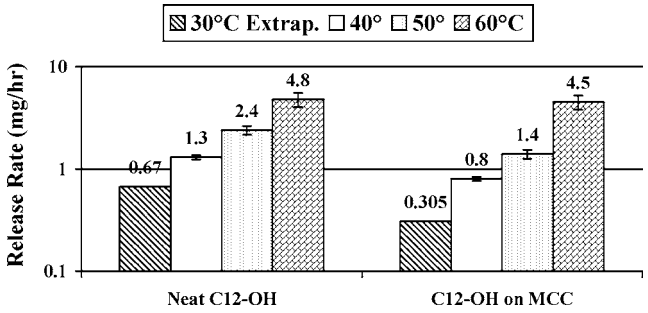

Figure 4. Comparison of evaporation rate of 1-dodecanol (C12–OH) neat versus dodecanol adsorbed on MCC (300 mg of dodecanol in each case). Results at 30 °C are extrapolated from higher temperatures using an Arrhenius plot of ln(release rate) versus 1/T. Error bars reflect one standard deviation from the mean for a series of three to four runs/sample.

Polymer-coated particles were prepared by dispersing pheromone-containing particle substrates into aqueous solutions of the polymers described above. Typically, 500 mg of particles was dispersed in 20−25 mL of a 5−10 wt % solution of polymer followed by a period of equilibration (1 h). The "wet" particles were then collected by vacuum filtration on Whatman no. 1 filter paper followed by drying overnight at room temperature. In some cases, the wet particles were dispersed in isopropyl alcohol to coagulate the polymer coating before drying to prevent particle agglomeration. After drying, the particles were pulverized to a fine powder that could pass through a 20-mesh screen (<800-μm particle size). A second procedure employed centrifugation to collect the particles instead of filtration. In all cases, the amount of pheromone and polymer adsorbed onto the pheromone-containing particle substrates was determined using a pyrolysis TGA method [see **Figure 3** (*15*)]. The amount of coating typically contained on the particles was 5−10 wt %.

Particle surface area and pore size measurements were made using a N_2 adsorption−desorption isotherm method using a NOVA-1200 gas sorption analyzer (Quantachrome Corp.). Calculations of total surface area, micropore surface area, total pore volume, micropore volume, and average pore diameter are based on the so-called Brunauer−Emmett−Teller (BET) equation (*16*) and the t method (*17*). Micropores are defined as pores with a diameter of <2 nm, whereas mesopores exhibit a size range of 2−50 nm. Macropores are >50 nm in diameter.

RESULTS AND DISCUSSION

Release Rate of Model Compounds from Particles: Effect of Temperature and Loading. Initial experimentation was focused on dodecanol as a model compound for codlemone. As shown in **Figure 4**, the evaporation rate of neat dodecanol in a forced-air oven experiment is significantly higher than that of a comparable amount of dodecanol adsorbed on MCC, especially at lower temperatures. A linear relationship between release rate and temperature in the range of 40−60 °C was observed for neat dodecanol when displayed as an Arrhenius plot [ln(release rate) vs 1/T (K); plot not shown]. In general, release rate was observed to approximately double for every increase of 10 °C in temperature. A more complex relationship is evident for dodecanol adsorbed on MCC where a larger increase in release rate with temperature is observed, perhaps due to surface area effects.

The influence of dodecanol loading (in weight percent) on its evaporation rate at 40 °C from a MCC substrate in a forced-air oven is shown in **Figure 5**. For the 10% dodecanol sample, a "leveling off" in release rate is evident as the dodecanol nears depletion from the substrate at long evaporation times. At 20 and 40% loadings, a linear relationship is observed between particle mass and time, indicating a constant release rate, which

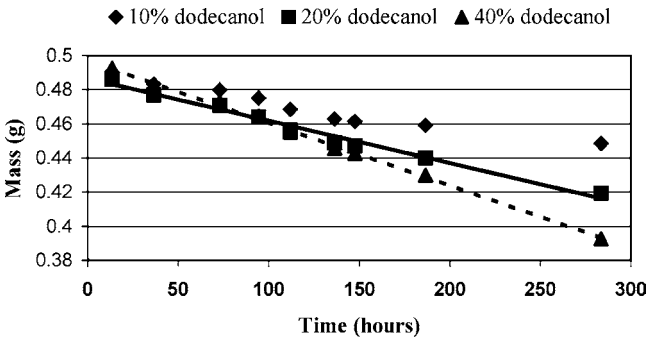

Figure 5. Impact of dodecanol loading on evaporation rate from MCC at 40 °C (oven method).

Table 2. Effect of Initial Dodecanol Loading on Evaporation Rate from MCC at 40 °C in a Forced-Air Oven

sample	initial mass[a] (g)	mass lost (g)	rate[b] (mg/h)
10% on MCC	0.500	0.043	0.17 ± 0.02
20% on MCC	0.500	0.062	0.25 ± 0.02
40% on MCC	0.500	0.099	0.39 ± 0.02

[a] Dodecanol plus MCC. [b] Plus or minus one standard deviation for three to four runs/sample; total experiment duration ~275 h.

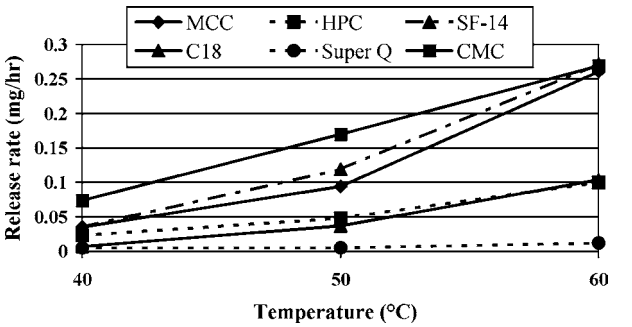

Figure 6. Effect of particle substrate on release rate at 10% dodecanol loading.

is very desirable for controlled-release devices. For these samples, however, only 50−70% of the available dodecanol was evaporated during the 300-h release experiment. How release kinetics might change near depletion was not investigated. It is also interesting that release rate does not increase linearly with increased dodecanol loading, as shown in **Table 2**. A 4-fold increase in dodecanol loading on MCC resulted in only a 2-fold increase in evaporation rate, suggesting a complex relationship may exist between surface chemistry and morphology (chemical affinity, surface area, porosity, etc.) and observed release characteristics. Each of these parameters was then evaluated in greater detail for particulate substrates of different composition, size, and surface area.

Effect of Particle Substrate on Release Rate. A preliminary hypothesis of this study was that the target pheromones, each containing a hydrophobic moiety plus a potentially hydrogen-bonding functionality (−OH or epoxy groups), would bind more or less strongly to substrates differing in composition depending on the polarity or hydrophobicity of the substrate. It was envisioned that this difference in affinity could form the basis of designing new controlled-release devices with "tailored" evaporation properties. The impact of particle substrate composition and morphology on release rate at three temperatures is shown in **Figure 6** for a data set recorded using the I-TGA method. From a comparison of the three cellulosic substrates, it may be concluded that the hydrophobically modified material

Table 3. Release Rate of Model Compounds and Pheromones from Substrates Using I-TGA (Milligrams per Hour; 20 mg Initial Sample Size)[a]

	60 °C		80 °C	
substrate	dodecanol	codlemone	epoxyoctadecane	disparlure
MCC	0.26	0.17	0.10	0.07
HPC	0.10	0.06	0.08	0.09
SF-14	0.27		0.12	
C18	0.1	0.05	0.04	0.02
Super-Q	0.012		0.003	

[a] Typical repeatability is ±10% as estimated by replicates available for some of the samples above.

(HPC) retards release compared to untreated MCC cellulose, whereas dodecanol adsorbs less strongly to ionic CMC. As shown in **Table 1**, the relative surface area of the cellulose particles is low compared to other substrates, so it is likely that the differences observed for the cellulose particles are due primarily to a chemical affinity of the hydrophobes. It is also interesting to note that over the temperature range of 40−60 °C, the release rate of dodecanol from MCC increases by >7-fold compared to ~4-fold for HPC. This may reflect a specific binding interaction between dodecanol and HPC, which does exist with underivatized cellulose.

Compared to MCC, the release rate of dodecanol from the C18 HPLC packing and Super-Q is significantly reduced. In the case of C18, it is possible that an affinity between the hydrophobic components of the particle and dodecanol could enhance adsorption, but the higher surface area of C18 could also play a major role. The surface area effect may be even more pronounced for the Super-Q, where a very low release rate and temperature dependence of release rate is observed. Activated carbon particles, where surface area and porosity can be systematically varied, will be discussed below as "model" systems for the porous particles described in this study.

To determine if the evaporation rate results observed for dodecanol on various substrates are generalizable to the pheromone codlemone, as well as the 1,2-epoxyoctadecane/disparlure system, additional I-TGA experiments were performed as shown in **Table 3**.

It is evident from **Table 3** that the effect of various substrates on the evaporation rate of dodecanol is also exhibited for codlemone and epoxyoctadecane. For these compounds, evaporation is retarded to the greatest degree by C18 and Super-Q and little effect is seen for SF-14 compared to MCC. In the case of disparlure, however, a slight increase in release rate is observed for the HPC substrate compared to MCC, which does not exist for the other three compounds. It is possible that the location of the epoxy ring on the disparlure molecule (internal 7,8 vs 1,2 for the model compound) sterically inhibits its ability to interact through weak hydrophobic association with the hydrophobic moieties of HPC, suggesting that epoxyoctadecane may not be a good model compound for this pheromone.

Release Rate Measurements by Dynamic TGA: Relationship of Volatilization Temperature to Controlled Release. To further probe the relationship between particle substrate and dodecanol affinity, we utilized dynamic TGA to determine an apparent VT for dodecanol adsorbed on a particulate substrate. VT is defined as the temperature associated with the "peak" in the differential curve of the thermogram associated with the evaporation of the pheromone or model compound of interest (point **A**, **Figure 3**). An assumption made in the application of this method is that a higher VT demonstrates that a compound

Table 4. Dynamic TGA Results for 10% Dodecanol Adsorbed on Particle Substrates

substrate	surface area (m^2/g)	volatilization temp (VT; °C)	release rate from I-TGA (mg/h at 60 °C; $\times 10^3$)
neat dodecanol		89	
CMC	<1	89	269
MCC	<1	92	261
SF-14	1	97	272
HPC	<1	104	100
C18	101	105	104
graphite	26	108	176
C100	126	112	157
XC72R	191	129	49
Super-Q	639	138	12
Black Pearl	1464	371	
APPO	2201	550	

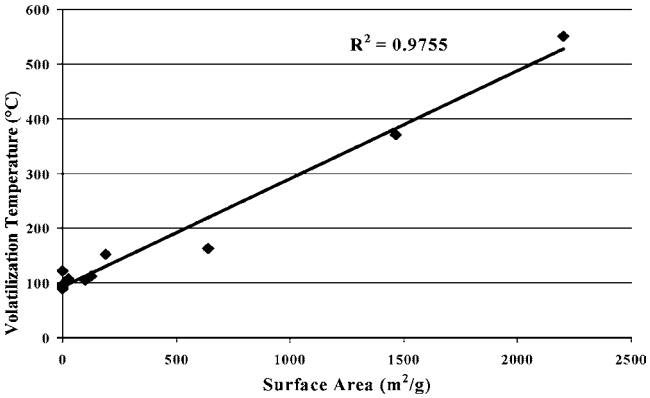

Figure 7. Relationship of particle surface area to apparent volatilization temperature (data from **Table 4**).

either is less volatile or is bound more strongly to a substrate compared to a system exhibiting a lower VT. Because the observed VT can depend on the sample mass employed in the dynamic TGA experiment, similar starting masses were employed (~10 mg). VT values for a series of particle substrates, including porous carbon particles containing adsorbed dodecanol, are provided in **Table 4** for a 10−12-mg starting sample size.

These results demonstrate that a higher VT for a dodecanol/substrate pair will result in a lower release rate (I-TGA) at a temperature below the VT. For the data shown in **Table 4**, a linear regression analysis of ln(I-TGA release rate at 60 °C) versus $1/T$ (K) provides an R^2 value of 0.92, suggesting that a strong relationship exists between release rate and VT (actual plot not shown). Because the VT experiment can usually be conducted in <1 h, dynamic TGA appears to be a potentially useful tool for characterizing the controlled release of pheromones and model compounds from particulate substrates. It is expected that this correlation will strictly apply only to those systems where the volatile compound is not soluble in the controlled-release matrix because solubility and matrix parameters (degree of swelling, for example) might change with temperature in a discontinuous fashion.

Table 4 also illustrates that particle surface area is a critical parameter in defining the VT and release rate of dodecanol from particle devices. **Figure 7** reveals a strong relationship between the total surface area (m^2/g) of the particles and dodecanol VT as determined by dynamic TGA for the samples described in **Table 4**. For these porous materials, total surface area reflects the length dimension of the tortuous pore structure of the internal domains of the particle substrate, which can effectively trap

Table 5. Relationship of Volatilization Temperature (VT) to Particle Surface Morphology

surface and pore parameter	linear regression[a] (R^2)
total surface area (m^2/g)	0.97
micropore surface area (m^2/g)	0.98
total pore vol (mL/g)	0.41
micropore vol (mL/g)	0.99
av pore diameter[b] (Å)	0.57

[a] R^2 for linear regression plot of surface or pore size parameter vs VT. [b] VT increases with decreasing pore diameter.

dodecanol, preventing it from reaching the particle surface where its volatilization rate is enhanced by flowing N_2 in the TGA furnace. The relationship of other pore morphology parameters, as determined by the N_2 adsorption/desorption experiment, to VT is highlighted in **Table 5**. These data demonstrate that total surface area, micropore surface area, and micropore volume are the most significant factors in determining VT and, presumably, evaporation rate as well.

In **Figure 7**, it is interesting to note that the VTs observed for the highest surface area carbon particles are greater than the equilibrium boiling point of neat dodecanol in open systems. This observation may reflect the well-known "capillary condensation" effect associated with adsorption of vapors onto porous solid materials (*18*, *19*). Due to the narrow radii of the pore structures, which create a very high surface energy meniscus, the pressure required to condense a vapor in a capillary is lower than the pressure required to condense the same vapor under equilibrium conditions on a flat surface. Conversely, because of the high surface tension of the meniscus, a higher vapor pressure is needed to volatilize a condensed liquid from small pores (that is to say, a higher temperature is required) than is typical of equilibrium conditions in the bulk (*19*). This surface tension effect on boiling point can be very significant. In the case of a small water vapor bubble (radius = 10^{-8} m) in liquid water at 1 atm pressure, vapor pressure reaches its equilibrium value at 272 °C compared to 100 °C for a flat liquid/vapor interface (*18*).

It is clear from the results in this section that the release of dodecanol from micrometer-sized particles is significantly influenced by parameters associated with the porous morphology of the substrates, especially the so-called micropores. This effect appears to be more pronounced than that seen when the chemical composition of the particles themselves was changed for the systems evaluated in this study. A significant influence of pore size on evaporation characteristics has also been reported for pheromones adsorbed into the channel pore structures of inorganic zeolites with smaller pores providing a higher degree of retention for *n*-decanol (*20*).

Effect of Polymer Coatings on Release Rate from Particles. Using I-TGA, the effect of coating on the release rate of dodecanol-containing MCC particles can be readily demonstrated as shown in **Figure 8**. For samples coated with 6% HPC (wt percent of total particle mass), a release rate reduction of 16−28% was observed over the range of temperatures studied, whereas at an 8% HPC coating level, release rate reductions were near 40%. Although these levels of additional controlled-release response were experimentally significant, higher levels of release rate reduction were desired. The PSS coating offered no reduction in release rate, perhaps suggesting that this polar, ionic, polymer did not adhere very well to a MCC substrate containing adsorbed dodecanol.

We also evaluated a commercially available enteric coating used for drug tablets and capsules that proved to be more

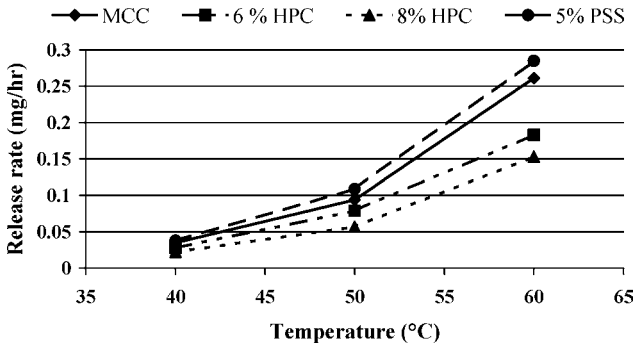

Figure 8. Effect of HPC coating on the release rate of MCC particles containing 10% dodecanol (initial mass ~20 mg) measured using I-TGA.

Table 6. Effect of Aquacoat on the *Relative* Release Rate of Model Pheromones (10 wt % Adsorbed on MCC; Oven Method at 40 °C; 0.2 g of Starting Particle Mass)

compound	no coating release rate (VT, °C)	plus coating release rate (VT, °C)	% release rate reduction
dodecanol	1 (92)	0.15 (165)	85
epoxyoctadecane	1 (162)	0.42 (173)	60

effective in retarding release rate. Aquacoat CPD, produced by the Pharmaceutical Division of FMC Corp., is an aqueous "pseudo-latex" dispersion of cellulose acetate phthalate (CAP) described by FMC as a "hydrophobic" polymer. This dispersion contains 30% CAP by weight. Typical coating levels of Aquacoat on cellulosic particle substrates were determined by TGA to be 22 wt % of the particle mass. The relative evaporation rates for model compounds adsorbed on MCC coated with Aquacoat are shown in **Table 6**.

These results suggest that the Aquacoat system offers a greater degree of evaporation control compared to HPC and PSS in the forced-air oven evaporation test. In addition to lowering the relative release rate at 40 °C, Aquacoat increases the apparent VT of the model compounds tested on MCC particles in the dynamic, high-resolution experiment.

Mechanism of Pheromone Release from Porous Particles. Models have been proposed that describe the release rate of drugs included in polymers and porous polymer matrices (*21*, *22*). For reservoir devices, where an active ingredient (drug or pheromone) exists as a neat liquid or solution surrounded by a porous membrane, release rate to an eluting fluid is determined according to eq 1, which is independent of time (*22*):

$$J = \epsilon D_L K_{L/S} \Delta C / \tau l_p \quad (1)$$

In eq 1 J = transport flux across the porous membrane, ϵ = porosity, D_L = diffusion coefficient of the active ingredient in the liquid that fills the pores, ΔC = concentration difference across the membrane, τ = tortuosity, $K_{L/S}$ = partition coefficient of the diffusant between the liquid in the pores and the liquid used as a suspending medium in the reservoir core formulation, and l_p = thickness of the porous membrane. Although this model directionally predicts the influence of tortuosity observed in the present study, that increasing τ retards the release rate, this kinetic expression is not an appropriate model for the particles fabricated in this study for a number of reasons: (1) the active ingredient is not soluble in the porous matrix material, so diffusion must proceed through pores directly connected to the external environment, and (2) release from the device occurs as evaporation directly to air compared to partitioning to a liquid medium surrounding the device, typical for most biomedical controlled-release devices. In our study, vapor pressure and air flow past the devices are important parameters analogous to concentration gradient and partition coefficient in eq 1.

A more realistic model for evaporation of a liquid from an uncoated porous microparticle can be derived from an expression developed for controlled release from hollow fibers, open at one end. In this model, evaporation to the external environment is envisioned as a three-step process: (1) volatilization at the liquid/vapor interface to the capillary region below the open end, (2) diffusion through the capillary column of vapor-air to the hollow fiber end, and (3) convection away from the capillary end into the external atmosphere. Stage 2 is considered to be rate limiting. Equation 2 defines evaporation rate based on the hollow fiber model (*23*, *24*).

$$\text{evaporation rate} = -McD\pi r^2 \ln(1 - P_{vap}/P_{atm})/L \quad (2)$$

In eq 2 M = molecular weight of liquid charge, c = molar density of vapor-air column, D = diffusion coefficient, r = inner radius of the hollow fiber capillary, P_{vap} = vapor pressure of the liquid, P_{atm} = atmospheric pressure, and L = distance from the liquid meniscus to the top of the capillary. It should be also noted that depending on the curvature of the meniscus between the fiber and the liquid, convex or concave, P_{vap} can be higher or lower than its true equilibrium value according to the "capillary condensation" principles discussed above.

For the relatively high surface area and high micropore volume samples evaluated in this study, the pores or capillaries that comprise these particle substrates are very long (meter length scale) compared to their cross-sectional radius (nm) based on the N_2 adsorption/desorption isotherm results. As a result, it is expected that the πr^2 term of eq 2 will be very small compared to L, so the latter will have a more significant impact on evaporation rate. Furthermore, if the pore size distribution becomes narrower, where the fluid/vapor meniscus is curved to a greater extent, P_{vap} will be lower (assuming that the fluid/fiber meniscus is concave on the vapor side, which is typical for many fluid/fiber systems, so P_{vap}/P_{atm} becomes smaller), and evaporation rate will be further reduced.

On the basis of these considerations, the retardation in evaporation rate that we observe with increasing particle and micropore surface area can be modeled using the hollow fiber concept of controlled release where the pheromone or model compound does not dissolve in or swell the particle matrix. In some controlled-release devices, however, the active ingredient is soluble in the polymer matrix and a so-called polymer/solvent interaction parameter, enthalpic in origin, has an influence on diffusion and release. In a capillary system, where the diffusant is not soluble in the capillary walls, this enthalphic parameter is less important, although surface interactions could play a minor effect. For polymer-coated particles, the transport properties of hydrophobic compounds across the membrane (either hydrophobic or hydrophilic) would provide an additional level of complexity to the hollow fiber evaporation rate expression, and many of the factors contained in eq 1 would become important. An analysis of the evaporation kinetics of pheromones from coated porous particles articles is beyond the scope of this study.

Application of Particulate Controlled-Release Devices in the Field. A major focus of the present study was to develop new methods to rapidly evaluate the controlled-release properties of micrometer-sized pheromone dispensers. Although this objective facilitated the development of new particle substrates and coatings, release rate data typical of field applications was

Table 7. Controlled-Release Properties of Commercial and Microparticle Devices

controlled-release device	release rate (mg/day/ha)	no. of dispensers or mass of particles (g/ha)	max control period (days/ha) at 20 °C[a]
Isomate-C+	784	1000 dispensers	162
10% dodecanol on MCC	784	18	24
10% dodecanol on MCC/ 10% HPC[b]	784	266	34
10% on C-100	784	284	36
10% on C18	784	1765	225
10% on XC72R	784	1815	232

[a] Approximate mean daily temperature for Isomate-C+ or I-TGA data extrapolation values for particles. [b] 10 wt % coating of HPC on MCC.

not generated directly. However, in an effort to relate the present results to field trails of pheromone efficacy for codlemone, I-TGA data for dodecanol on various substrates were extrapolated to appropriate temperatures followed by a comparison to actual field data on codling moth control provided by Pacific Biocontrol (PBC, Vancouver, WA) on their website (www.pacificbiocontrol.com) and in technical bulletins. I-TGA data were selected because the flow rate of N_2 past the sample was very modest (0.66 L/min) relative to the oven method data reported herein. It should be emphasized that dodecanol represents an excellent model compound for codlemone because of its similar chemical structure and the fact that female codling moths actually emit this molecule along with codlemone as part of a mixture of attractant compounds (*12*).

More specifically, the product Isomate-C+, marketed by PBC, is applied to orchards for codling moth control as a polymer twist tie at a recommended treatment level of 1000 dispensers per hectare (ha) before the first moth flight in early spring (late April, for example, in Yakima, WA). PBC data illustrate that a new Isomate-C+ dispenser contains 137 mg of codlemone and provides a release rate of ~0.784 mg/day for >160 days in the field at a mean weekly temperature ranging from 60 to 80 °F (15−27 °C). At this release rate, 1000 dispensers/ha would provide a total release rate of 784 mg/day/ha, assuming average temperatures near 20 °C.

I-TGA release rate results on microparticle devices containing 10% dodecanol were extrapolated to 20 °C using the Arrhenius relationship from results recorded at elevated temperatures (40−60 °C). Assuming that the minimum effective release dosage required is 784 mg/day/ha, the mass of particles needed to yield this rate was determined, and the maximum period of sustained evaporation was calculated on the basis of the initial loading of dodecanol on the particles (10 wt %). These results are summarized in **Table 7**.

Table 7 demonstrates that MCC and coated MCC particles can achieve the required daily release rate needed for codling moth control, but their capacity is insufficient to sustain this rate throughout the growing season and, as a result, reapplication would be needed several times. For C18 and XC72R, release rates are relatively low and a larger amount of particles is required to generate an appropriate level of daily release. These substrates, however, can provide both the required release rate and capacity for the entire growing season when applied at a higher treatment rate compared to MCC particles. Unfortunately, the C18 material is prohibitively expensive. At 20 °C, dodecanol evaporation from C-100 is faster than that from C18 and, as a result, it is depleted more quickly. The results highlighted in **Table 7** clearly suggest that it should be possible to "tailor" the release properties of porous particles to match both the release rate and dispenser longevity required for codling moth mating disruption applications. This objective could be accomplished either by mixing particle types (C-100 and XC72R) or by polymer coating a fast-releasing substrate. Optimization studies are in progress.

In the case of gypsy moths, a shorter period of sustained pheromone release is required for effective control by mating disruption compared to codling moths (6 weeks vs entire growing season of 160 days) (*10*, *11*). As a result, the higher potential release rates of the MCC-based particles compared to the more porous activated carbon systems might provide a better option in gypsy moth control. Optimizing the release characteristics of disparlure on particle substrates was not attempted in this study, however.

Conclusions. (a) I-TGA and VT appear to be useful tools for rapidly characterizing the controlled-release properties of pheromone-containing particles with and without polymeric coatings.

(b) For uncoated particles, the most significant parameters that define the release rate and VT of pheromones from particulate substrates are the surface area and micropore volume of the particle. Chemical composition effects are relatively modest in comparison, although they may be important when cellulosic substrates are compared (HPC vs MCC, for example).

(c) The coating of pheromone-containing particles with a polymer membrane can provide an additional degree of volatility control. An aqueous dispersion of cellulose acetate pthalate (CAP) performed especially well as a coating for particle controlled-release devices.

(d) Extrapolation of I-TGA data for dodecanol on various porous substrates to typical "average" field temperatures suggests that the required release rate and device longevity for effective codling moth control should be achievable at a particle treatment rate of ~1−2 kg/ha.

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