### University of Nebraska - Lincoln

## DigitalCommons@University of Nebraska - Lincoln

Proceedings of the Eighteenth Vertebrate Pest Conference (1998)

**Vertebrate Pest Conference Proceedings** collection

1-1-1998

### **REVIEW OF BIRD REPELLENTS**

Larry Clark USDA APHIS Wildlife Services, larry.clark@aphis.usda.gov

Follow this and additional works at: https://digitalcommons.unl.edu/vpc18



Part of the Environmental Health and Protection Commons

Clark, Larry, "REVIEW OF BIRD REPELLENTS" (1998). Proceedings of the Eighteenth Vertebrate Pest Conference (1998). 6.

https://digitalcommons.unl.edu/vpc18/6

This Article is brought to you for free and open access by the Vertebrate Pest Conference Proceedings collection at DigitalCommons@University of Nebraska - Lincoln. It has been accepted for inclusion in Proceedings of the Eighteenth Vertebrate Pest Conference (1998) by an authorized administrator of DigitalCommons@University of Nebraska - Lincoln.

#### REVIEW OF BIRD REPELLENTS

LARRY CLARK, U.S. Department of Agriculture, Animal and Health Inspection Service, Wildlife Services, National Wildlife Research Center, 1716 Heath Parkway, Fort Collins, Colorado 80524.

ABSTRACT: Despite a general perception that there is an abundance of nonlethal control technologies, the fact remains that there are fewer registered products and active ingredients for repellents in the U.S. than there were 10 and 20 years ago. This review discusses the technical issues relating to the discovery, formulation, and delivery of chemical repellents, and suggests future avenues of research that would improve our ability to develop effective chemical repellents.

KEY WORDS: bird control, repellent, nonlethal control agents

Proc. 18th Vertebr. Pest Conf. (R.O. Baker & A.C. Crabb, Eds.) Published at Univ. of Calif., Davis, 1998.

#### INTRODUCTION

Previous reviews have given detailed consideration to the overall process by which repellents are developed, registered, and commercialized Mason and Clark (1992, 1997). In this review the regulatory and commercial status of nonlethal and lethal chemical control agents for birds is summarized. In addition, some of the emerging areas of research affecting the development of effective formulations are reviewed.

In 1988, the Federal Fungicide, Insecticide and Rodenticide Act (FIFRA) was revised by the U.S. Environmental Protection Agency (Fagerstone 1998, this volume). The revision of FIFRA called for more data to evaluate the environmental impact of chemical control agents, and its implementation has profoundly affected the availability of control agents and products. Prior to the

revision, the number of active ingredients remained stable from 1978 to 1988. After the amendment, the number of registered lethal control agents decreased 40%, and the number of registered nonlethal control agents decreased by 30% (Table 1). The relative availability of nonlethal active ingredients has decreased by 6% relative to lethal agents over that same period. Similarly, the number of products for lethal bird control has decreased by 66% over the past 20 years. Nonlethal products for bird control have decreased by 41% over the same period. Despite a general perception that there is an abundance of nonlethal control technologies, the fact remains that there are fewer such products and active ingredients than there were 20, and even 10 years ago (Figure 1, Table 2, cf. Schafer 1979; Eschen and Schafer 1986).

Table 1. Summary of EPA registered bird control agents.

|                    | 1978 |    | 1988 |    | 1998 |    |
|--------------------|------|----|------|----|------|----|
|                    | No.  | %  | No.  | %  | No.  | %  |
| Product Labels     |      |    |      | -  |      |    |
| Lethal             | 35   | 52 | 32   | 49 | 12   | 40 |
| Nonlethal          | 32   | 48 | 33   | 51 | 18   | 60 |
| Active Ingredients |      |    |      |    |      |    |
| Lethal             | 5    | 33 | 5    | 33 | 3    | 38 |
| Nonlethal          | 10   | 67 | 10   | 67 | 5    | 62 |

# SUMMARY OF ACTIVE INGREDIENTS AND THEIR MODE OF ACTION

#### Lethal Control Agents

The objective of lethal control agents is to eliminate local populations of birds. Fenthion was originally developed as an organophosphate insecticide and acaricide, but because of its potent irreversible inhibition of acetylcholinesterase it found some utility as a lethal control agent for birds as a dermally delivered (roost)

poison (Pope and Ward 1972). Compound DRC-1339 is an avian specific toxicant affecting the renal function of birds (DeCino et al. 1966; Westberg 1974). 1,4-aminopyradine is a toxicant that produces effects similar to central nervous system stimulants (Schafer et al. 1973). Birds ingesting this material die violently, albeit quickly. The repellent effect occurs via observational avoidance learning by nearby conspecifics (Besser 1976).

| EPA#                | Active Agent                                 | CAS                  | Product   | Company                          |
|---------------------|--|----------------------|---|----------------------------------|
| 66330-19            | Lindane, captan                              | 58-89-9; 133-06-2    | Isotox Seed Treater   | Tomen Agro Inc.                  |
| 58035-13            | methyl anthranilate                          | 134-20-3             | ReJeX-iT AG-145   | R.J. Advantage, Inc.             |
| 58035-9             | methyl anthranilate                          | 134-20-3             | ReJeX-iT AG-36  | R.J. Advantage, Inc.             |
| 58035-8             | methyl anthranilate                          | 134-20-3             | ReJeX-iT MA   | R.J. Advantage, Inc.             |
| 58035-7             | methyl anthranilate                          | 134-20-3             | ReJeX-iT TP-40  | R.J. Advantage, Inc.             |
| 58035-6             | methyl anthranilate                          | 134-20-3             | ReJeX-iT AP-50  | R.J. Advantage, Inc.             |
| 66550-1             | methyl anthranilate                          | 134-20-3             | Bird Shield Bird Repellent Concentrate                            | Dolphin Trust                    |
| 58630-2             | Naphthalene                                  | 1146-65-2            | Dr. Ts Rabbit, Squirrel, Bat and Bird Repellent                   | Dr. T's Nature Products, Inc.    |
| 876-437             | Polybutene                                   | 9003-29-6; 9003-28-5 | Roost No More Repels Nuisance Birds                               | Velsicol Chemical Corp.          |
| 1621-17             | Polybutene                                   | 9003-29-6; 9003-28-5 | Tanglefoot Bird Repellent   | Tanglefoot Co.                   |
| 1621-16             | Polybutene                                   | 9003-29-6; 9003-28-5 | Tanglefoot Bird Repellent   | Tanglefoot Co.                   |
| 8254-4              | Polybutene                                   | 9003-29-6; 9003-28-5 | 4 The Birds" Transparent Bird Repellent                           | Bird Control International Corp. |
| 8254-3              | Polybutene                                   | 9003-29-6; 9003-28-5 | 4 The Birds" Transparent Bird Repellent                           | Bird Control International Corp. |
| 8254-1              | Polybutene                                   | 9003-29-6; 9003-28-5 | 4 The Birds" Transparent Bird Repellent                           | Bird Control International Corp. |
| 9731-1              | Polybutene                                   | 9003-29-6; 9003-28-5 | Preferred Brand" Bird and Squirrel Repellent                      | Inter-State Oil Co., Inc.        |
| 55943-1             | Polybutene                                   | 9003-29-6; 9003-28-5 | Hot Foot Bird Repellent   | Hot Foot America                 |
| 876-436             | Polybutene, Aliphatic petroleum hydrocarbons | 9003-29-6; 9003-28-5 | Roost No More Bired Repellent                                     | Velsicol Chemical Corp.          |
| 876-435             | Polyisobutylene                              | 9003-29-6; 9003-28-5 | Roost No More Bird Repellent Liquid                               | Velsicol Chemical Corp.          |
| 34704-665           | Thiram                                       | 137-26-8             | Thiram 42% Dyed Flowable seed Protectant                          | Platte Chemical Co., Inc.        |
| 34704-664           | Thiram                                       | 137-26-8             | Thiram 42% Dyed Flowable seed Protectant                          | Platte Chemical Co., Inc.        |
| 45735-2             | Thymol, denatonium saccaride                 | 89-83-8, 90823-38-4  | RO-PEL Animal, rodent and Bird Repellent                          | Burlington Scientific Corp.      |
| 757 <del>9-</del> 2 | Fenthion                                     | 55-38-9              | Rid-a-Perch 1100 Solution   | Rid-a-Bird Inc.                  |
| 11649-12            | 4-AMINOPYRADINE                              | 504-24-5             | Avitrol FC Corn Chops   | Avitrol Corp.                    |
| 11649-10            | 4-AMINOPYRADINE                              | 504-24-5             | Avitrol Concentrate   | Avitrol Corp.                    |
| 11649-8             | 4-AMINOPYRADINE                              | 504-24-5             | Avitrol Double Strength Whole Corn                                | Avitrol Corp.                    |
| 11649-7             | 4-AMINOPYRADINE                              | 504-24-5             | Avitrol whole Corn  | Avitrol Corp.                    |
| 11649-6             | 4-AMINOPYRADINE                              | 504-24-5             | Avitrol Corn Chops  | Avitrol Corp.                    |
| 11649-5             | 4-AMINOPYRADINE                              | 504-24-5             | Avirtol Double Strength Corn Chops                                | Avitrol Corp.                    |
| 11649-4             | 4-AMINOPYRADINE                              | 504-24-5             | Avitrol Mixed Grains  | Avitrol Corp.                    |
| 56228-30            | 3-CHLORO-P-TOLUIDINE HYDROCHLORIDE           | 7745-89-3            | Compound DRC-1339 Concentrate-Staging Areas                       | USDA-APHIS                       |
| 56228-29            | 3-CHLORO-P-TOLUIDINE HYDROCHLORIDE           | 7745-89-3            | Compound DRC-1339 98% Concentrate-Livestock & Fodder Depredations | USDA-APHIS                       |
| 56228-28            | 3-CHLORO-P-TOLUIDINE HYDROCHLORIDE           | 7745-89-3            | Compound DRC-1339 98% Concentrate-Pigeons                         | USDA-APHIS                       |
| 56228-10            | 3-CHLORO-P-TOLUIDINE HYDROCHLORIDE           | 7745-89-3            | Compound DRC-1339 Starling posion 75% Concentrate                 | USDA-APHIS                       |

331

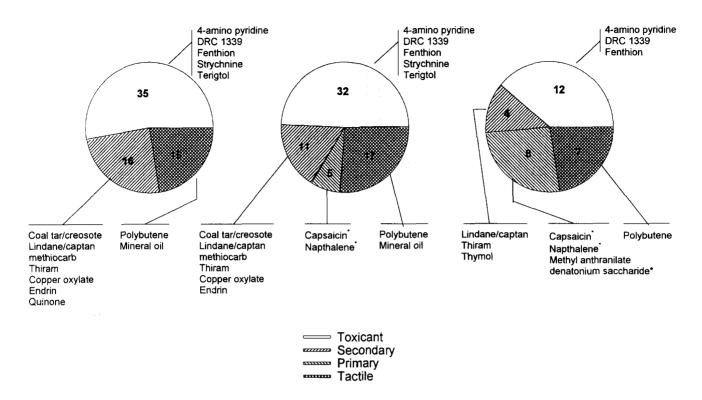


Figure 1. The breakdown of the proportion of U.S. Environmental Protection Agency registered labels by repellent category for the past three decades. The numerical insets within each pie chart reflect the actual number of registered products available at the end of each decade. The registered active ingredients for category of repellent is indicated. Ingredients designated with an asterisk do not have independent peer reviewed evidence as being effective bird repellents.

#### Tactile Repellents

A variety of registered labels contain compounds that are sticky or oily, and birds avoid these materials based upon their textural and tactile properties. These compounds consist of aliphatic petroleum hydrocarbons, polybutenes, and polyisobutenes, and are applied to surfaces from which birds are to be repelled.

#### Secondary Repellents

The currently registered secondary bird repellents are derivatives of agricultural products registered for other uses. Methiocarb is a carbamate insecticide whose use was adapted for bird repellency. Cabamates are reversible acetylcholinesterase inhibitors (Hayes 1963; Casarett and Doull 1975; Deichmann and Gerarde 1969). Although Methiocarb was once commonly available for a variety of uses (Dolbeer et al. 1994), there are no currently available commercial products containing this active ingredient. Lindane was initially used as an insecticide; its utility as a bird repellent stems from its stimulatory effect on the central nervous system (Fitzwater 1956; Crosier et al. 1970). Captan and thiram were initially used as fungicides; their utility as bird repellents stems from their action as central nervous system depressants (Fitzwater 1956). Birds apparently detect the physiologic effects of all of these compounds and learn to avoid associated sensory cues (e.g., taste, visual dyes and targets, paired with the toxicants) (Rogers 1974). One product contains the fungicide thymol and a bittering agent, denatonium saccharide. Birds are ordinarily unresponsive to bitter flavors (Mason and Clark 1998). The utility of the bittering agents is their use as conditional stimuli to the toxic effects of unconditional stimuli such as fungicides or insecticides (i.e., thymol). Schafer (1981) provides a review of additional compounds previously registered as secondary bird repellents.

#### Primary Bird Repellents

Primary bird repellents act as irritants or unpalatable flavor cues that produce a congenital avoidance response by birds (Clark 1998a). There currently is only a single effective registered primary bird repellent, methyl anthranilate. Two other compounds, naphthalene and capsaicin, are registered as bird repellents and can function as primary mammalian repellents. However, there is no evidence to indicate that they, by themselves, are effective against birds (Mason et al. 1991; Clark 1997; Dolbeer et al. 1988). Indeed, over 30 years of basic research has shown that birds lack peripheral

receptors for the detection of capsaicin, the active principal in capsicum (reviewed in Clark 1998a).

## PRINCIPLES IMPORTANT FOR DEVELOPING EFFECTIVE REPELLENTS

Repellents are tools used by humans to manipulate animal behavior. Thus, the tool can be thought of as a communication device that sends a signal from which the animal extracts a message. Critical to the design of any tool is a careful consideration of form and function, such that when used, its action is efficient in producing the desired effect. For chemical repellents five major factors to consider in the development process can be categorized:

- Mode of Action
- Identification of the Active Ingredient
- Delivery System
- Formulation
- Behavioral and Ecological Context of Application

#### Mode of Action

Chemical repellents operate along one of three principles: they cause pain, illness, or they scare an animal. Thus, the first myth to dispel about repellents is that they are benign pest management strategies. Repellents are aversive signals that have consequences that an animal presumably is motivated to avoid. Perhaps when considered against lethal control strategies, chemical repellents can be viewed as a less extreme management action, but repellents are by no means benign.

Primary chemical repellents are agents that are avoided upon first exposure because they are olfactorally offensive, distasteful, or cause irritation/pain. example, predator odors are sometimes avoided by prey, presumably because there is a congenital fear response to being eaten (Sullivan et al. 1988a, b). The avoidance response is directly related to double-bonded sulfur compounds contained in predator urines (Nolte et al. The presence of sulfurs in the urine is a consequence of protein metabolism and is in direct proportion to the amount of flesh contained in the diet of the predator. Another example of an odor-mediated primary repellent is alarm pheromones. These are chemical signals produced by conspecifics that alert individuals to take evasive action, or in some cases, aggressive defensive action. More often than not these chemical signals are thought to occur primarily in invertebrates (Bell and Carde 1984) and fish (Garcia et al. 1992), but there is evidence for alarm odors in all vertebrate classes (Kavalier et al. 1992; Jones and Roper

The notion that some chemicals are avoided because they are heuristically unpleasant is untenable. For this to be true, the animal would have to be evaluating the odor on the basis of an aesthetic sense that we have no reason to believe exists. It is more parsimonious to search for a biological basis for the congenital avoidance of odors. Such a less colorful mechanistic approach has utility. Once the underlying basis for avoidance is identified, then the prospect of discovering additional repellents operating along similar principles is improved.

Gustatory-mediated primary chemical repellents are principally bitter or sour compounds. A popular

hypothesis is that avoidance of such taste principles is an evolved sensitivity to toxicants and, thereby, is a congenital mechanism to regulate intake of potentially poisonous plant metabolites. While this hypothesis is appealing, the single test of the hypothesis shows that there is no relationship between the palatability threshold for bitter (i.e., alkaloids) and the toxicity of the compounds (Glendening 1994). All of this is not to say that some compounds perceived as bitter or sour cannot be congenitally avoided. However, at the present time there is no *a priori* way of predicting the identity of those compounds. Nonetheless, compounds that are perceived as sour or bitter are potent conditioned stimuli (Riley and Tuck 1985).

Nociceptively mediated primary chemical repellents are compounds that produce irritation and painful sensations (Clark 1998a). For birds, examples of nociceptive repellents are methyl anthranilate, cinnamamide, coniferyl benzoates, and acetophenones (Clark 1997). Chemical irritants form the largest pool of potential primary repellents. Animals have chemoreceptive fibers in their somatosensory and trigeminal systems that respond chemical to neurotransmitters. These transmitters are released when there is tissue damage, stimulating the appropriate nerve fibers and ultimately leading to the perception of irritation or pain. Exogenous chemicals useful as repellents may cause minor tissue damage, thus setting forth the natural defensive mechanism for pain perception in an animal. Alternatively, the exogenous chemical may be a functional analog of the neurotransmitters, thus directly affecting the receptor mechanisms of the nociceptive systems, but without actually causing actual tissue damage. In the latter case, the animal is "fooled" into perceiving tissue damage when, in fact, there is none. While animals may experience physiological sensory adaptation to irritants if they are applied continuously, animals do not adapt or habituate to nociceptive primary repellents when they are applied in an ecological context.

Secondary repellents are agents that cause illness, or an otherwise unpleasant experience, and promote learned avoidance of associated sensory cues. For birds, examples of secondary repellents are anthraquinone and Methiocarb. The persistence of the learned avoidance response is a function of the magnitude of the unpleasant experience and the salience of the associated cue (Pelchat et al 1983). By salience, the author means the appropriateness of the cue relative to the context for which it is presented. Thus, taste cues have high relevance to an animal rendered ill in the context of feeding. Visual and odor cues can be relevant if they are directly paired with food. Sound would have lower salience in the acquisition and retention of avoidance in a feeding context, as would smells not directly paired with the food.

Primary repellents can function as the unconditional stimulus (the aversive experience) and can be used to condition animals to avoid associated sensory cues. However, because primary repellents have a direct and immediate adverse consequence, animals tend to limit their exposure to the agent. Thus, the magnitude of the unpleasant experience is generally less than would be achieved by the poisoning effect of a typical ingested

secondary repellent. Hence, the acquisition and persistence of the avoidance response to the associated sensory cues is generally diminished relative to situations when secondary repellents are used (Clark 1996; Pelchat et al. 1983).

It should be clear from the above discussion that a critical feature in the design of a successful repellent is to obtain an understanding of the mode of action appropriate to the application, and be aware of the mechanism (i.e., the target receptor systems) by which the repellent will be mediated.

As indicated above, a next step in the development of a repellent is to identify the appropriate mediating sensory systems of the target species. Repellents designed to be applied to food to prevent consumption by the target species should be directed to affect sensory systems in the mouth. If the same repellent formulation is applied to a substrate in the hope of preventing the target species from standing on a treated surface, there is little reason to expect any degree of success. Yet, this category error occurs with some frequency. For example, the avian repellent, methyl anthranilate, is incorporated into the commercially available formulated product ReJeX-iT AG-36 intended for application to turf. The grass is potentially a food resource for grazing geese, and when the active ingredient is present, the repellent works reasonably well (i.e., geese reduce their feeding attempts on treated turf) (Cummings et al. 1991). However, the treatment will not prevent the geese from standing on the turf. The chemical's ability to penetrate the foot and access receptors sensitive to MA is nonexistent in this application scenario. Thus, if the reason geese are on a patch of turf is to feed, then there is a reasonable expectation of success for the repellent. If the geese are on a patch of turf for other reasons (e.g., loafing), then there is little chance that a topical treatment of the turf will repel the geese.

#### **Delivery Systems**

Careful consideration must be given to the mediating sensory system because this will influence the type of delivery strategy that will be employed. For example, contact irritants or texturally unpleasant materials should be designed to target the skin. Animals can learn to avoid treated substrates because the unpleasant sensation is closely coupled to position and movement. However, an agent that can be absorbed through the skin and result in illness will probably not be effective as a repellent because their is no clear localizable sensory cue to associate with the illness. The best repellents are those that unambiguously provide a clearly localizable sensory signal with a consequence. Tactile repellents work because the unpleasant sensation is perceived at the point of contact with the repellent. Tactile toxicants that are absorbed without an obvious peripheral sensation at the point of contact, then subsequently produce illness, lack such clear associations. Thus, the consequence (i.e., illness) cannot be clearly associated with any source (i.e., perch). It is conceivable that an area repellency can be formed, but such responses require a great deal of training and the learned avoidance extinguishes rapidly. Thus, such techniques are of limited use to pest managers.

Repellents that are ingested target oral receptors if they are primary repellents, or gastro-intestinal receptors if they are secondary repellents. In the latter case, tastes, visual cues, or smells associated with food are associated cues that animals can readily learn to avoid. The more clearly the associated cue is paired with the process of ingestion, the stronger will be the learned avoidance. Thus, the taste, smell, or appearance of a food object produces a strong learned avoidance. Smells and appearance of objects in proximity to ingested food containing the repellent will require more training for learned avoidance to occur, if at all. Thus, the key to success is not only the ability to locate and associate the conditional cue, but that cue must also be likely to co-occur with food.

Finally, an aerosol delivery might target multiple sensory systems, skin, eye, nose and oral receptors. Such a delivery of repellents will almost always contain irritants. Because the source will invariably be broad, the likely response is to promote undirected escape behavior by the target animal. Thus, of all the strategies, aerosols are the most likely to succeed as areas repellents. The disadvantage of aerosols is that they are of short duration because of rapid atmospheric dispersal. However, beside their direct effect on behavior via irritation, such repellents might be used as reinforcing stimuli to other nonchemical hazing devices, pyrotechnics, and sound where habituation is a problem over long periods of time.

From these examples, one can see how targeting a particular sensory system may relate to the design of the formulation and delivery system, and to the ecological context under which the repellent is applied.

#### Identification of the Active Ingredient

At the beginning of this paper, the author reviewed how many registered repellents were derived from existing pesticides owing to their general physiological effects (see also Schafer 1981). Such derivative repellents are falling from regulatory favor because of there broad toxicological effects on vertebrates (Hushon 1997; Mason and Clark 1997).

Other sources of repellents include screening natural products (Greig-Smith et al. 1983; Crocker and Perry 1990; Reichardt 1997) and food and flavor ingredients (Mason and Clark 1992). However, there is no guarantee that such compounds are intrinsically safer from an environmental or toxicological perspective (Secoy and Smith 1983). But there is a general perception that the likelihood of finding environmentally safe repellents from such compounds is higher (Liss 1997).

A predictive model for identification of primary bird repellents would be of great utility in minimizing research and development costs for new repellents. Considerations of primary and toxicity effects, formulation considerations, registration hurdles and production and market considerations all can eliminate candidate repellents from the development process. Reliance on serendipitous discovery of repellents only reduces the likelihood that nonlethal control methods will be successfully developed. The pharmacophore approach to rational repellent design so successfully used for product identification in the pharmaceutical and food industries

can also be used in developing repellents. The fundamental premise behind molecular structure-activity models is to numerically characterize chemicals and relate the descriptor variables to a relevant biological response. Availability of software packages to characterize the semiempirical quantum mechanical, topological, physicochemical attributes of molecules has greatly facilitated this approach (Lipkowitz and Boyd 1991). The QSAR approach to simple aromatic compounds has been successfully employed to develop a robust statistical model predicting primary bird repellents (Clark and Shah 1991, 1994; Clark et al. 1991; Shah et al. 1991; Clark and Aronov 1998). However, more work is needed to extend the predictive power of the model to other classes of compounds (e.g., terpenoids, alkaloids).

Current methods for identification of active ingredients rely on behavioral testing. When large numbers of compounds are screened, this can be an expensive animal intensive effort. Recent advances in cell culture technology allow for the rapid screening of large numbers of compounds (Banker and Goslin 1991). In particular, trigeminal cultures for several species of mammals and birds have now been developed. These cultures will allow the bioactivity level to be evaluated for large numbers of candidate primary repellents (Bryant, Clark and Mason, unpublished).

#### Formulation Considerations

Once the active ingredient is settled upon, incorporating it into a formulation appropriate for a specific delivery mode is critical. Chemical repellents are rarely delivered in raw or reagent form. In the simplest case they are diluted by water and applied according to label instructions. However, uniformity of application, adhesion to the treated substrate and uniform coverage can be enhanced by using agricultural adjuvants. adjuvants may be classified as: 1) spreaders, stickers, buffers, foliar nutrients; 2) penetrants, crop oil concentrates, extenders; and 3) drift control agents, deposition agents, or retention agents (Harvey 1992). Spreader/ stickers control the deposition of the active agent on the treated substrate and control the life of the active agent. Wetting agents and spreaders decrease the surface adhesion of the applied materials, thereby allowing increased uniform coverage. Sticker/extending agents control the life of the active agent by encapsulating the agent and slowing down environmental degradation (e.g., biodeterioation and weathering losses). However, one must always bear in mind compatibility constraints with the carriers and active ingredients. Chemical interactions may occur that effectively render the active agent unavailable to the receptor systems of the target species. Some of these interactions may be predictable, and with consultation with a formulation chemist or manufacturer of the adjuvants, such problems may be avoided prior to field trials or operations. However, most likely trial and error matching adjuvants and repellent formulations will be necessary, having run these trials in small pilot studies.

There may be circumstances where mixtures of active agents may be desirable. The relationship between a chemical's concentration and its repellent effect has

been described for a wide range of compounds (Clark 1997). These concentration-response studies are useful for their simplicity and straightforward interpretation in setting standards for formulation development. However, to attain practical validity, the interaction of agents in mixture must also be studied. This entails studies of interaction of multiple active agents with each other, and with interactions of agents with the other ingredients in formulations.

Formulations composed of multiple active agents may exert an additive effect. That is to say, the repellency observed is simply the average of the expected concentration-specific response of the component ingredients. Thus, studies based on single agent concentration response profiles theoretically are useful in making predictions about the activity level of the mixture. Unfortunately, this is rarely the case. In other sensory systems (i.e., olfaction and gustation), an animal's responsiveness to a mixture is often predicted based upon its reaction to the most stimulatory component in the mixture. It is as if the animal screens out the sensory information of the mixture and attends to a single sensory input of the strongest stimulus. However, there also are numerous examples where animals perceive mixtures not on the basis of their individual components, but as an unique quality (i.e., an integration of the components) where the concentration-response to the mixture is not predictable based upon a knowledge of the component's Under these concentration-response relationships. circumstances the perceived intensity of the mixture may be less than the sum of its parts (antagonism of components), or greater than the sum of its parts (synergism). Trying to identify principles that allow investigators to predict precisely what type of interaction among agents may occur is an area of considerable interest in chemosensory biology. Recent studies from the author's laboratory have begun to address these issues for primary repellents (Clark 1997, 1998b; Clark and Mason 1998), but this remains a largely unexplored area of research from an applied wildlife management perspective.

The stability of active agents in formulation can be affected by several other factors such as carriers, stabilizers, solvents, binders, biocides and antioxidants, just to name a few. Microbial degradation of early formulations of MA were serious considerations in the developmental process (Clark et al. 1993; Aronov and Clark 1996). Even today, the success of MA containing products is directly related to the life expectancy of the active ingredient, and this varies according to the environmental conditions regulating weathering and microbial attack (Clark et al. 1998; Mason and Clark 1995, 1996; Dorr et al. 1998). Such considerations are critical in evaluating the effectiveness of repellent formulations. When a formulation fails to meet performance expectations, the first consideration should be an evaluation for the presence of the active agent. Regrettably the early literature on product performance in the field is rampant with studies that concluded inappropriately that the active agent was not a good repellent, rather than the possibility that the application strategy and formulation were not appropriate for the

environmental and ecological circumstance under study. In effect, many studies "threw the baby out with the bath water."

#### Behavioral and Ecological Context of Application

The myriads of social and environmental factors affecting the efficacy of repellents is beyond the scope of this review. Nonetheless, they are critical to the final successful use of repellents (Clark 1998a).

In summary, the development of a successful repellent formulation is seen more than simply discovering a single "new" compound. A basic understanding of the mediating sensory system of the repellent is needed to best develop a formulation and delivery system. Moreover, given the technical, commercial, and regulatory constraints, reliance on a single candidate repellent at the outset is a strategy unlikely to lead to a viable product. Thus, methods to generate families of candidate repellents and rapidly validate the bioactivity of the repellents are needed. These processes are critical for the development of new wildlife management tools because the number of nonlethal methods and products has actually decreased over the past 10 years.

#### LITERATURE CITED

- ARONOV, E. V., and L. CLARK. 1996. Degradation studies of the non-lethal bird repellent, methyl anthranilate. Pestic. Sci. 47:335-62.
- BANKER, G., and K. GOSLIN. 1991. Culturing nerve cells. MIT Press Cambridge, MA.
- BELL, W. J., and R. T. CARDE. 1984. Chemical ecology of insects. Sinauer Associates, Sunderland, MA.
- BESSER, J. F. 1976. 4-aminopyridine for protecting crops from birds—a current review. Proc. Vertebr. Pest Conf. 7:11.
- CASARETT, L. J., and J. DOULL. 1975. Toxicology—The basic science of poisons. Macmillan, NY.
- CLARK, L. 1998a. Physiological, ecological, and evolutionary bases for the avoidance of chemical irritants by birds. Pages 1-37 in Current ornithology, V. Nolan and E. Ketterson, eds., Vol. 14. Plenum, NY.
- CLARK, L. 1998b. Bird repellents: interaction of chemical agents in mixture. Physiol. Behav., in press.
- CLARK, L. 1997. A review of the bird repellent effects of 117 carbocyclic compounds. Pages 343-352 in Repellents in Wildlife, J. R. Mason, ed., National Wildlife Research Center, Fort Collins, CO.
- CLARK, L. 1997. Bird repellents: interaction of agents in mixture. *In* Chemical Signals in Vertebrates, R. B. Johnson and H. Muller-Schwarze, eds., Vol. 8. Plenum, NY, in press.
- CLARK, L. 1996. Trigeminal repellents do not promote conditioned odor avoidance in European starlings. Wilson Bull. 108:36-52.
- CLARK, L., and E. V. ARONOV. 1998. Structure-activity studies of bird repellents: carbocyclic and heterocyclic compounds. Pestic. Sci., in press.

- CLARK, L., J. L. CUMMINGS, J. E. DAVIS, and P. A. POCHOP. 1998. Evaluation of a macro encapsulated repellent to reduce risk of white phosphorous ingestion by waterfowl foraging in a contaminated marsh. Inter'l Biodeter. Biodegrad, in press.
- CLARK, L., J. L. CUMMINGS, S. BIRD, and E. ARONOV. 1993. Acute toxicity of the bird repellent, methyl anthranilate, to fry of Salmo salar, Oncorhynchus mykiss, Ictalurus punctatus and Lepomis macrochirus. Pestic. Sci. 39:313-17.
- CLARK, L., and J. R. MASON. 1998. Interaction of bird repellents in mixture: suppression, independence and enhancement. Int'l Pest Manage., in press.
- CLARK, L., J. R. MASON, and P. S. SHAH. 1991. Chemical repellency in birds: relationship between chemical structure and avoidance response. J. Exp. Zool. 260:310-322.
- CLARK, L., and P. SHAH. 1994. Tests and refinements of a general structure-activity model for avian repellents. J. Chem. Ecol. 20:321-39.
- CLARK, L., and P. SHAH. 1991. Nonlethal bird repellents: in search of a general model relating repellency and chemical structure. J. Wildl. Manage 55:538-45.
- CROCKER, D. R., and S. M. PERRY. 1990. Plant chemistry and bird repellents. Ibis 132:300-308.
- CROSIER, W. F., A. NASH, and D. C. CROSIER. 1970. Dry nonphytotoxic bird and insect repellent. Proc. Assoc. Off. Seed Anal. 60:206.
- CUMMINGS, J. L., J. R. MASON, D. L. OTIS, and J. F. HEISTERBERG. 1991. Evaluation of dimethyl and methyl anthranilates as a Canada goose repellent on grass. Wildl. Soc. Bull. 19:184-90.
- DECINO, T. J., D. J. CUNNINGHAM, and E. W. SCHAFER, JR. 1966. Toxicity of DRC-1339 to starlings. J. Wildl. Manage. 30:249.
- DEICHMANN, W. B., and H. W. GERARDE. 1969. Toxicology of Drugs and Chemicals. Academic Press, NY.
- DOLBEER, R. A., M. A. LINK, and P. P. WORONECKI. 1988. Naphthalene shows no repellency for starlings. Wildl: Soc. Bull. 16:62-64.
- DOLBEER, M. L. AVERY, and M. E. TOBIN. 1994. Assessment of field hazards to birds from methiocarb applications to fruit crops. Pestic. Sci. 40:147-161.
- DORR, B. S., L. CLARK, J. F. GLAHN, and I. MEZINE. 1998. Evaluation of ReJeX-iT TP-40 bird repellent for reducing Great Blue Heron predation on catfish. J. World Aquacul., in press.
- DOTY, R. L., and D. MULLER-SCHWARZE. 1992. Chemical Signals in Vertebrates. Plenum, NY.
- ESCHEN, M. L., and E. W. JR. SCHAFER. 1986. Registered bird damage chemical controls—1985. Denver Wildlife Research Center Bird Damage Report 356:1-16.
- FITZWATER, W. D. 1956. Control of Animal Pests. II. Am. Nurseryman 104:14.
- GARCIA, C., É. ROLANALVAREZ, and L. SANCHEZ. 1992. Alarm reaction and alert state in gambusia affinis (pisces, poeciliidae) in response to

- chemical stimuli from injured conspecifics. J. Ethol. 10:41-46.
- GLENDENNING, J. I. 1994. Is the bitter rejection response always adaptive? Physiol. Behav. 56:1217-28
- GREIG-SMITH, P. W., M. F. WILSON, C. A. BLUNDEN, and G. M. WILSON. 1983. Bud eating by bullfinches (*Pyrruhula pyrrhula*) in relation to chemical constituents of two pear cultivars. Ann. Appl. Biol. 103:335-43.
- HARVEY, L. E. 1994. Spatial patterns of inter-island plant and bird species movements in the Galapagos-Islands. J. Royal Soc. NZ 24:45-63.
- HAYES, W. J. 1963. Clinical Handbook on Economic Poisons. Public Health Service, U.S. Department of Health, Education and Welfare, 476, Washington, DC.
- HUSHON, J. M. 1997. Review of regulatoryimposed marketing constraints to repellent development. Pages 423-428 in Repellents in wildlife management, J. R. Mason, ed., National Wildlife Research Center, Fort Collins, CO.
- KAVALIERS, M., D. INNES, and K. -P. OSSENKOPP. 1992. Predator-odor analgesia in deer mice: neuromodulatory mechanisms and sex differences. Pages 529-535 in Chemical Signals in Vertebrates, R. L. Doty and D. Muller-Schwarze, eds., Vol. 6. Plenum, NY.
- LIPKOWITZ, K. B., and D. B. BOYD. 1991. Reviews in computational chemistry. VCH Publishers, Inc., NY.
- LISS, C. A. 1997. The public is attracted by the use of repellents. Pages 429-433 in Repellents in Wildlife Management, J. R. Mason, ed., National Wildlife Research Center, Fort Collins, CO.
- MASON, J. R., and L. CLARK. 1998. The chemical senses in birds. Pages 39-56 in Sturkie's Avian Physiology, G. A. Whittow, ed., Academic Press, NY.
- MASON, J. R., and L. CLARK. 1997. Avian repellents: options, modes of action, and economic considerations. Pages 371-392 in Repellents in Wildlife Management, J. R. Mason, ed., National Wildlife Research Center, Fort Collins, CO.
- MASON, J. R., and L. CLARK. 1996. Grazing repellency of methyl anthranilate to snow geese is enhanced by a visual cue. Crop Prot. 15:97-100.
- MASON, J. R., and L. CLARK. 1995. Evaluation of methyl anthranilate and activated charcoal as snow goose grazing deterrents. Crop Prot. 14:467-469.
- MASON, J. R., and L. CLARK. 1992. Nonlethal repellents: the development of costeffective, practical solutions to agricultural and industrial problems. Proc. Vert. Pest Conf. 15:115-29.
- MASON, J. R., N. J. BEAN, P. S. SHAH, and L. CLARK. 1991. Taxon-specific differences in

- responsiveness to capsaicin and several analogs: correlates between chemical structure and behavioral aversiveness. J. Chem. Ecol. 17:2539-51.
- NOLTE, D. L., J. R. MASON, G. EPPLE, E. ARONOV, and D. L. CAMPBELL. 1994. Why are predator urines aversive to prey? J. Chem. Ecol. 20:1505-16.
- PELCHAT, M. L., H. J. GRILL, P. ROZIN, and J. JACOBS. 1983. Quality of acquired responses to tastes by *Rattus norvegicus* depends on type of associated discomfort. J. Comp. Psychol. 97:140-153.
- POPE, G. G., and P. WARD. 1972. Effects of small applications of an organophosphorous poison, fenthion, on the waver-bird, *Quelea quelea*. Pestic. Sci. 3:197.
- REICHERT, P. B. 1997. The chemistry of plant/animal interactions. Pages 91-100 in Repellents in Wildlife Management, J. R. Mason, ed., National Wildlife Research Center, Fort Collins, CO.
- RILEY, A. L., and D. L. TUCK. 1985. Conditioned taste aversions: a behavioral index of toxicity. Ann. N.Y. Acad. Sci. 443:272-92.
- ROGERS, J. G. JR. 1974. Responses of caged red-winged blackbirds to two types of repellents. J. Wildl. Manage. 38:418.
- SCHAFER, E. W. JR. 1981. Bird control chemicals-nature, modes of action and toxicity. Pages 129-39 in CRC Handbook of Pest Management in Agriculture, Vol. III, A. A. Hanson, ed., CRC Press, Boca Raton, FL.
- SCHAFER, R. B. BRUNTON, and D. J. CUNNINGHAM. 1973. A summary of the acute toxicity of 4-aminopyridine to birds and mammals. Toxicol. Appl. Pharmacol. 26:532.
- SECOY, D. M. and A. E. SMITH. 1983. Use of plants in control of agricultural and domestic pests. Econ. Botany 37:28-57.
- SHAH, P. S., L. CLARK, and J. R. MASON. 1991. Prediction of avian repellency from chemical structure: the aversiveness of vanillin, vanillyl alcohol, and veratryl alcohol. Pestic. Biochem. Physiol. 40:169-175.
- SULLIVAN, T. P., DR. R. CRUMP, and D. S. SULLIVAN. 1988. Use of predator odors as repellents to reduce feeding damage by herbivores. III. Montane and meadow voles (*Microtus montanus* and *M. pennsylvanicus*). J. Chem. Ecol. 14:363-77.
- SULLIVAN, T. P., D. S. SULLIVAN, D. R. CRUMP, H. WEISER, and E. A. DIXON. 1988. Predatory odors and their potential role in managing pest rodents and rabbits. Proc. Vertebr. Pest Conf. 13:145-50.
- WESTBERG, G. L. 1974. Comparative Studies of the Metabolism of 3-Chloro-p-toluidine and 2-Chlor-4-acetotouluidine in rats and chicks and methology for the determination of 3-Chloro-p-toluidine and metabolites in animal tissues. University of California, Davis, CA.