MICROENCAPSULATION OF RODENTICIDES[1]

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Microencapsulation materials and techniques have advanced significantly over the past two decades. Encapsulation techniques are now used in a wide range of products from drugs to perfumes and food fragrances. As an industry, microencapsulation had its beginning in the research laboratories of National Cash Register (NCR) in Dayton, Ohio, in the late 1930s. It came into commercial use in 1954 when carbonless copy paper was introduced on the market. The entire field has made enormous progress since that time. Microencapsulation and other associated controlled- release technology play an important role in time-release pesticides, giving them a delayed or longer action time.

Microencapsulation in the simplest of terms comprises minute particles of the active product sealed by one of a variety of methods within a thin-walled sac or shell (protective coating) that is composed of chemicals different from the active ingredient. Microcapsules generally measure from 5 to 500 microns in size. As a process, microencapsulation has become a highly technical and complex scientific field unto itself and far beyond the intended scope of this paper.

Over the past 20 years, several research papers have been published on the encapsulation or microencapsulation of rodenticides (Table 1), yet this means of improving rodenticide characteristics has not received broad or in-depth attention. Several factors are believed to have contributed to this.

Harlen Shuyler appears to have been one of the first researchers in rodent control to explore encapsulation of rodenticides. To quote Cornwell (1970), "As far as is known, the first study into the encapsulation of rodenticides was undertaken by Shuyler (U.S. Patent 2,957,804 [1960])." Shuyler's work involved an enteric coating of arsenic and strychnine. Field results were less than satisfactory, presumably due to incomplete coatings. No follow-up research was reported.

Sometime later, research with encapsulated rodenticides was conducted by Greaves et al. (1968), selecting norbormide and alphachloralose for their studies since these rodenticides were limited by their poor palatability or too rapid toxic action. Greaves and his colleagues found gelatin-encapsulated norbormide did not alter toxicity or the speed of action. In rat feeding studies encapsulated norbormide was consumed in significantly larger amounts than baits prepared with the technical compound.

Alphachloralose in an ethylcellulose encapsulation administered by gavage showed that the speed of action was related to dosage and that encapsulation delayed apparent symptoms of poisoning and reduced the toxicity. With mice, bait containing encapsulated alphachloralose was more readily consumed and resulted in consistently higher mortality even though the encapsulated material was lower in toxicity. Greaves concluded from his studies that microencapsulation warranted further studies in the field of rodenticides and rodenticide formulation.

Table 1. Microencapsulated rodenticides and repellents explored for use in vertebrate pest management with references.

Chemicals	References
Alpha-chlorohydrin	Ericsson et al. 1971
Alphachloralose	Greaves et al. 1968, Cornwell 1970
Arsenic	Shuyler, cited by Cornwell 1970; U.S. Patent 1960
Norbormide	Greaves et al. 1968, Cornwell 1970, Jackson 1974
Strychnine	Shuyler, cited by Cornwell 1970; Best et al. 1974; U.S. Patent 1960
Warfarin	Cornwell 1970, Abrams & Hinkes 1974
Zinc phosphide	Cornwell 1970, El-Sebae et al. 1978, Anonymous 1986

Peter Cornwell (1970) researched four rodenticides--warfarin, zinc phosphide, norbormide, and alphachloralose--in encapsulated forms, and this represents the most extensive encapsulation tests of rodenticides to appear in print. Cornwell studied about 150 different batches using varying phase ratios and coatings of ethyl cellulose, gelatin, gelatin/gum arabic, gelatin/carrageen, polyester wax, and polawax. These studies should be reviewed by those anticipating rodenticide encapsulation as they are the most comprehensive and revealing. The statement made by Cornwell (1970) best sums up this research: "Most have resulted in improved intake of active ingredient, but only rarely have they resulted in improved kill beyond the biological variation recognized to exist in groups of laboratory animals."

There is a wide range of proposed reasons why it may be desirable to microencapsulate rodenticide. These include the following:

1. Taste-masking to increase acceptance. (This could greatly improve the kill, permit higher bait

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concentrations to help overcome resistance problems, could do away with the need to prebait and reduce bait shyness.)
2. Odor-masking to increase acceptance.
3. Delay the release of the toxicant in the gastrointestinal tract (slow adverse symptoms).
4. Reduce the speed of detoxification by the rodent, permitting a lethal accumulation or dose to be timely achieved, whereby increasing mortality rates (i.e., enhance toxicity).
5. Modification of physical properties (e.g., converting liquid to solids).
6. Stabilizing rodenticides that are sensitive to environmental conditions to prolong shelf life (e.g., light sensitive or hygroscopic compounds).
7. Eliminate incompatibilities of bait-formulating ingredients.
8. Prevent vaporization of volatile compounds (e.g., zinc phosphide).
9. Reduce toxicity in handling rodenticides.
10. Increase the physical bulk to make it more difficult to overformulate the rodenticide.
11. Coatings may secondarily be used as a means of incorporating desirable flavors, dyes, biological tracers, and chemical stabilizers.
12. With a greater degree of efficacy, encapsulation may reduce the amount of pesticide needed in bait and/or used in the field, thus making the rodenticide environmentally more compatible.

Taste and/or odor-masking are the research objectives most often pursued in rodenticide microencapsulation with delaying of the release of the toxicant in the gastrointestinal tract being next in importance. The other reasons by themselves could rarely justify the additional cost involved for the encapsulation process. Achieving one goal, however, could at the same time encompass one or more of the others.

Some basic questions must be asked when embarking on microencapsulation of rodenticides.

1. How finely does the species masticate its food?
2. Where is the toxicant absorbed in the rodent's digestive tract?
3. Moisture levels and pH values through gastrointestinal tract.
4. How fast does the food move through the gastrointestinal tract?
5. Bacterial or fermentation action associated with food processing.

In many cases detailed information is wanting. The mastication of food by rodents has not been studied in depth, and the amount of encapsulation damage resulting in the feeding process is unknown for the various types of coatings and capsule sizes. Jackson (1974) reported that gelatin capsules of more than several hundred microns seemed to break in chewing by laboratory rats. Presumably mice would chew their food even finer. This information is of primary importance where taste or odor-masking is the primary objective.

The site or sites of toxicant or toxic breakdown products absorption is not fully known for some rodenticides or potential rodenticides and is essential if encapsulation is for controlling onset of symptoms or toxicosis. The pH of the rat stomach is reportedly low and that of the mouth and intestine on the basic side (pH>6.8) (Jackson 1974). However, this may differ for the various species of pest rodents (e.g., ground squirrels vs. house mice). The time for passage of food through the various components of the gastrointestinal tract is not thoroughly known, and these times presumably differ for different food items and water availability. The physical forces exerted in the upper portion of the digestive tract may be influential in food and capsule breakdown. The role of intestinal microflora in food digestion and nutrient uptake may need special consideration in relationship to pharmacokinetic studies. Along this same line, the significance of large caecums in some rodents to rodenticide pharmacological events is relatively unstudied.

Conditions for encapsulation release may be made dependent upon moisture, pH, physical force, or combinations of these. the mechanism for release (complete or partial) is generally associated with leaching, erosion, rupture, or other such actions, depending on the composition of the protective coating (Luzzi 1970). The element of time also plays a significant role.

The lack of this aforementioned biological data may be why so few past attempts at microencapsulation of rodenticides have been successful.

This becomes more complicated if the rodenticide proposed for encapsulation is to be used for several different rodent species, as the basic physical and physiological parameters may differ for each. It may become impossible to satisfy the collective criteria for more than one species of more distantly related species. Compromises may be possible but, if not, the ensuing encapsulated rodenticide may result in an enhanced specificity. Rodenticide specificity can be biologically desirable; on the contrary, a greater species specificity nearly always limits the marketing potential of the rodenticide, making it that much more difficult to achieve a favorable encapsulation cost/benefit ratio.

El-Sabae et al. (1978) compared three types of encapsulation (polyethylene glycol, nonsustained gelatin, and sustained gelatin) for zinc phosphide. The sustained gelatin encapsulation decreased the toxicity somewhat. Microencapsulation increased acceptance and palatability in white rats approaching two-fold when tested at a low level (0.033%) in baits.

Occidental Chemical Corporation of the United States spent considerable time and research effort on the development of a coated zinc phosphide rodenticide that reportedly improves rodent acceptance and overcomes shyness caused by odor/taste (Anon. 1985). Studies in our laboratories (Marsh and Howard, unpubl.), however, indicate only minor improvements in bait acceptance and palatability with the coated material when compared with baits prepared with technical grade zinc phosphide. The Occidental Chemical Corp. has discontinued for other reasons its sales of zinc phosphide and thus this new coated zinc phosphide was never marketed (Anon. 1985).

Researchers in Korea (Chyun 1973) worked with paraffin wax and stearic acid as coating for zinc phosphide to slow its environmental degradation in the field. These tests were not microencapsulation as such but more of a matrix-type coating over bait particles. The paraffin coatings were reported to increase bait acceptance but they did not significantly enhance mortality in Norway rats.

This is not unlike the paraffin-zinc phosphide coating used on cracked corn to make it more weather resistant when

used for Microtus spp. control in apple orchards of New York (Caslick 1970). The work of Chyun (1973) and Caslick (1970), although interesting and with some of the same objectives, does not fall within the same category as microencapsulation but rather a matrix composition and slurry bait coating. Along this same line, strychnine suspended in methyl cellulose has been explored for dingo control in Australia by Best et al. (1974) with inconclusive results.

Jackson (1974) discussed the potential value of encapsulated rodenticides and cellulose acetate phthalate (CAP) encapsulated norbormide. Bait consumption was enhanced and mortality increased when a relatively thick wall of CAP was produced. Thin-wall encapsulation was relatively ineffective in achieving the desired objectives. While promising, encapsulated norbormide never reached the marketing stage.

Ericsson et al. (1971) evaluated alpha-chlorohydrin, a toxicant-sterilant, in encapsulated form using several preparations of vinyl resin-based and cellulose-based encapsulation materials. The vinyl resin-based encapsulation proved more acceptable to Norway rats than cellulose-based wall material. Although encapsulated alpha-chlorohydrin was consumed in considerably greater amounts than uncoated material, mortality was greatly decreased, suggesting that the active ingredient was not being released in adequate quantities and probably passed through the rats.

The only rodenticide currently being sold is an encapsulated form of warfarin developed by the Wisconsin Alumni Research Foundation and marketed since 1974 under the registered trade mark TOX-HID®.

Technical warfarin is processed in Wurster Air Suspension Coating equipment to produce discrete particles consisting of 50% warfarin and 50% encapsulating material. The makeup of the coating material is not disclosed by the manufacturers. Rodenticide formulations containing encapsulated warfarin reportedly are 3 to 10 times more acceptable to rats in the laboratory than baits formulated of uncoated warfarin. Much of this research was reported on by Abrams and Hinkes (1974).

Encapsulated warfarin is being produced for commercial sale by Hopkins Agricultural Chemical Co. (Madison, Wisconsin) and distributed to the rodenticide and pest control industry by Crown Chemicals (Division of Hopkins), Rockford, Illinois, and Prentiss Drug and Chemical Co., New York. It is marketed as a 0.5% concentrate in corn starch to be formulated at a ratio of 1:19 in rodent bait to yield a 0.025% active warfarin finished bait. Several commercial ready-to-use rodent baits are formulated with encapsulated warfarin; however, there appears no major move in that direction. A good quality technical warfarin can be formulated into highly effective rodent baits without the need for encapsulation, hence relatively few bait formulators see the necessity to change. There is a lack of research data to prove that under field conditions encapsulated warfarin significantly enhances rodent control.

Encapsulation may not be all positive, and the following possible disadvantages must be considered:

1. It may lead to an overload of rodenticide in the target animal that could increase potential secondary hazards to predators and scavengers.
2. May make some rodenticides more palatable to target species.
3. May reduce natural emetic actions of rodenticides such as red squill and zinc phosphide, which serve as safeguards to some nontarget species.
4. May make some rodenticides more toxic (enhance susceptibility) to nontarget species.
5. Increase the toxicity of feces, which may be more hazardous to scavengers (greater environmental contamination).
6. Slow environmental breakdown leading to greater environmental contamination from residual bait.

Some of these were alluded to by Jackson (1974).

The results of rodenticide microencapsulation research, although somewhat promising, have seldom led to a useful product. Only encapsulated warfarin has been marketed; however, zinc phosphide and norbormide encapsulation received considerable research and showed some favorable promise. Unfortunately, neither progressed far enough to be highly effective.

The potential benefits from microencapsulation of rodenticides has been demonstrated and thus remain a method by which some can be improved. Microencapsulation will undoubtedly play a greater role in the future when there is a greater biological need and economic impetus to move in that direction.

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