STUDIES IN MICROENCAPSULATION OF RODENTICIDES

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ABSTRACT: Warfarin, zinc phosphide, norbormide and alphachloralose have been microencapsulated by the technique of coacervation and fed to laboratory rats (R. norvegicus) and mice (M. musculus). Results are given of experiments in which the concentration of rodenticide, wall material and phase ratio have been varied separately and in combination. Experiments are also reported in which normal and encapsulated rodenticide have been fed together in the same test diet.

Microencapsulation can increase the intake of rodenticides, appreciably, whether or not alternative food is simultaneously available. Nevertheless, significantly higher kills from higher intakes of poison have not been achieved, indicating difficulties in optimising the characteristics of the capsule wall to achieve the desired release of ingested active ingredient.

INTRODUCTION

Microencapsulation can be defined as a chemical process by which minute amounts of solids or liquids are enclosed within a thin wall of suitable material to prevent their reaction with some component of the environment. The properties of the wall are so designed to keep the reactive materials apart until they are required to mix.

Microencapsulation, as an industrial process, has been developed for many applications by the National Cash Register Co. These include carbonless copying paper, drugs with designed release characteristics, as well as uses in the perfumery, adhesive and food industries (Gordon, 1965). The costs vary from 40 U.S. cents to $4 per kg. of encapsulated material (Watson, 1970) and many future applications have been proposed.

The use of this technique for the improvement of pest control chemicals has yet to be exploited. In 1948, Ripper et al postulated that if individual particles of a toxic compound could be coated with a substance digestible only by certain insects, specificity of action might be achieved. Subsequent tests on plants sprayed with particles of DDT, coated with degraded cellulose, showed that contact action against non-phytophagous insects had been eliminated, whereas plant-eating species succumbed.

Reviewing the possible uses of microencapsulation for improving crop sprays, Phillips (1968) lists the advantages: reducing the repellency of insecticides, protecting pesticides from degradation by weather and reducing the need for protective clothing. Studies have also been carried out into the encapsulation of bacteria (Raun & Jackson, 1966): by this means it would seem possible to extend the field activity of Bacillus thuringiensis without loss in efficacy against European corn borer (Ostrinia nubilalis).

Microencapsulation has been proposed as a technique for improving the efficiency of rodenticides: by preventing contact of the poison with the chemoreceptors of the rodent palate it may be possible to increase the intake of unpalatable poisons. At the same time, it would appear advantageous to design the properties of the coating material to cause the release of the internal phase (the rodenticide) at the right time and in the right quantity to increase kill.

As far as is known, the first study into the encapsulation of rodenticides was undertaken by Shuyler (U.S. Patent 2,957,804 of 1960). Arsenic and strychnine were prepared as enteric-coated "micro-pills", but field trials indicated that some were inadequately coated or partially lacking in enteric coat (personal communication). Subsequently, Greaves et al (1968) reported laboratory tests showing apparently improved kill from bait feeding tests with encapsulated norbormide and alphachloralose.

The purpose of this paper is to summarise some of the investigations into microencapsulation of rodenticides carried out at this laboratory. About 150 batches of encapsulated rodenticide have been prepared and a high proportion of these fed in baits to rats and mice. Studies have been made to improve the action of warfarin, zinc phosphide, norbormide and alphachloralose. Most have resulted in improved intake of active ingredient, but only rarely have they resulted in improved kill beyond the biological variation recognised to exist in groups of laboratory animals.

THE ENCAPSULATION PROCESS

Of the many methods of making microcapsules, the best known is coacervation, which was used exclusively in preparing test samples for the present work. In principle, the rodenticide to be encapsulated is dispersed and kept suspended in a liquid in which the active ingredient must be insoluble. A third material to provide the capsule wall (e.g. gelatin/gum arabic, or ethyl cellulose) is contained in the medium. By varying the temperature, pH, or addition of other material (e.g. carrageenan), the wall material is made insoluble (coacervation) and forms a continuous wall around the suspended particles. The ratio of internal to external phase (the phase ratio) can be modified within broad limits by varying the amounts of the various components in the system. Low phase ratios result in thicker walls being formed than high ratios. The size of encapsulated particles can be varied according to the uniformity of dispersion and the control exercised at the stage of coacervation. Particles encapsulated in gelatin are then usually hardened.

Spherical particles can be more easily and uniformly coated than elongate crystals. In the latter case, the wall is variable in thickness and the active particles are more likely to be encapsulated as aggregates rather than as discrete crystals.

THE RODENTICIDES STUDIED

Warfarin at the recommended concentrations for incorporation into baits (0.005 - 0.05%) is readily taken in the presence of alternative food by rats (R. norvegicus) and to a lesser extent by mice (M. musculus). Because of the increasing spread of resistance to warfarin in the U.K. by both species, leading to survival at the recommended levels, encapsulation was examined as a means of increasing the acceptance by rodents of high concentrations which would normally be rejected.

Zinc phosphide suffers from the defect of most acute poisons, that inadequate take of bait at the initial feed and the subsequent onset of symptoms of poisoning lead to discrimination against baits (bait shyness). As a result, prebaiting is recognised as a prerequisite for good rat control although this may not be necessary with zinc phosphide against mice.

The potential advantages of microencapsulation - taste masking and delaying the onset of symptoms - could therefore lead to an improvement in properties of zinc phosphide when used at the recommended concentration. It should be noted that this rodenticide has a density of 4.6 which causes problems in achieving good dispersion of particles during coacervation.

Norbormide (R)* offers selective action against Rattus spp. but also suffers from the defect of too rapid onset of poisoning symptoms. Detoxification of norbormide is fairly rapid, and sublethal doses lead to bait discrimination. Norbormide was encapsulated to increase bait intake and delay onset of symptoms but it is not easy to encapsulate this rodenticide in small discrete particles.

Alphachloralose, at a concentration of 4%, was introduced in the U.K. for mouse control in 1964. This compound interferes with thermo-regulation and is more effective at temperatures below 60°F, than above. The small body size of the mouse, with its high surface area to volume ratio, confers a considerable degree of specificity resulting in minimal hazard to domestic animals. Under favourable conditions, poisoning symptoms (ataxia) occur in mice in 5-10 minutes, and feeding usually ceases within 20 minutes, often leading to inadequate bait intake. Detoxification is also rapid leading to recovery in 6-8 hours. This rodenticide has a long thin crystal, least favourable to the production of uniform wall thickness during encapsulation.

DESIGN OF THE EXPERIMENTS

Albino mice (20-30g) and Wistar Albino rats (300-350g) were caged individually or in groups, with equal numbers of each sex. Rodenticides were formulated in 90% medium oatmeal and 10% sugar. In some tests, alternative food was provided at the same time as the poison, depending on the purpose of the experiment, the diets being alternated in position to avoid place preference. Availability of the test diet was in most cases limited to short periods, to reduce the influence of kill on bait intake.

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* The active ingredient of Raticate.

Comparisons were made in all tests with unencapsulated poison. Three variables were investigated, separately and in combination:

1. rodenticide concentration.
2. phase ratio (thickness of capsule wall).
3. composition of the capsule wall.

Examples are also given of experiments in which normal and encapsulated rodenticides were combined together in different proportions in test diets.

RESULTS

1. Varying the concentration of active ingredient.

a) Warfarin.

Examples of studies on rodenticide concentration, with and without microencapsulation, are given by two experiments with warfarin. The first, in which warfarin encapsulated in ethyl cellulose (at 6:1) was fed to rats at three concentrations (0.005%, 0.05% and 0.5%), with a choice of unencapsulated warfarin, and the second in which these same concentrations of both encapsulated and normal warfarin were fed with unpoisoned food as a choice.

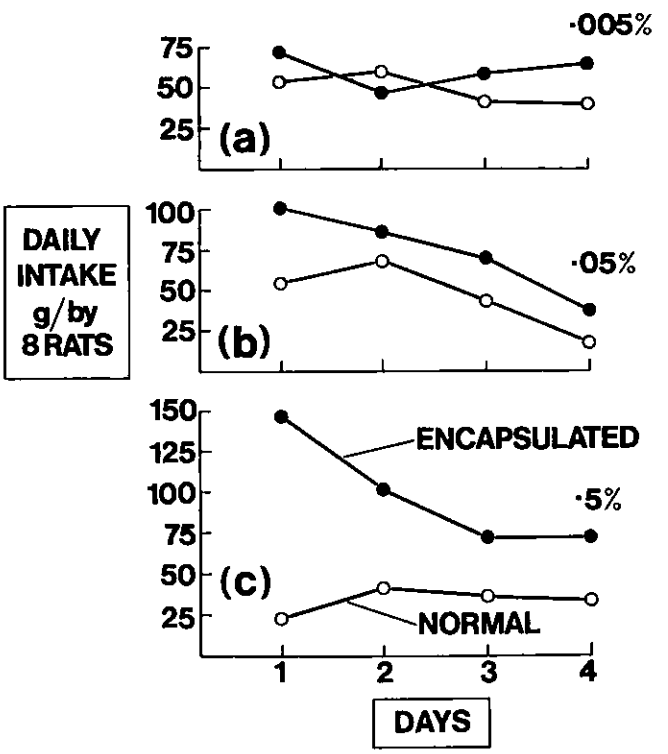


Fig. 1. Daily intake (g.) of diets containing normal and microencapsulated warfarin (ethyl cellulose 6:1) fed as a choice at three concentrations to rats (8 per treatment) for four days.

Low concentrations of warfarin (0.005%) are readily taken by rats and little improvement in acceptance from encapsulation is to be expected (Fig. 1a). With higher concentrations (0.05%), a small but consistently higher intake of encapsulated warfarin was obtained throughout the four-day feed (Fig. 1b). At the highest concentration (0.5%) which is markedly less palatable, encapsulation afforded a striking increase in bait intake (Fig. 1c).

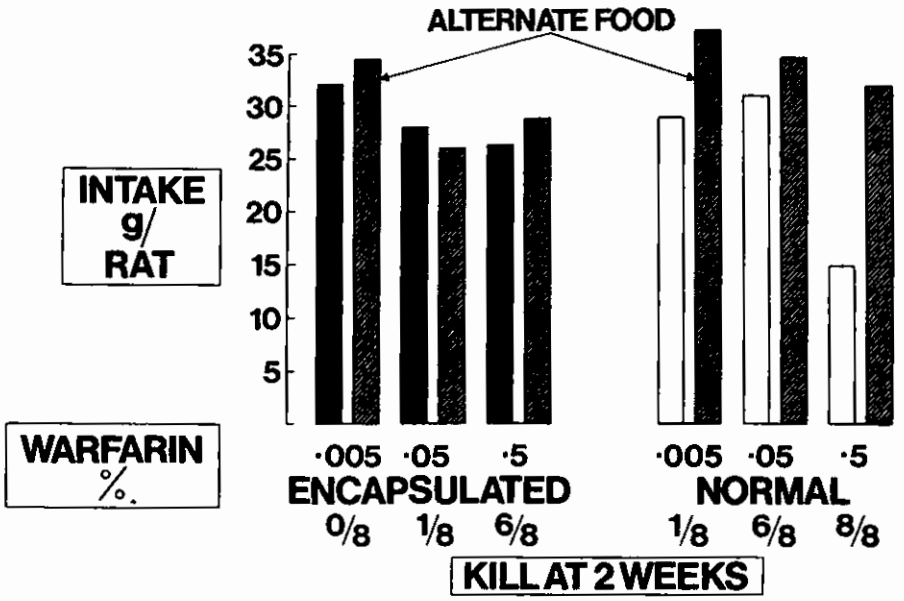


Fig. II. Intake (g/rat) of diets containing normal and microencapsulated warfarin (ethyl cellulose 6:1), fed at three concentrations to rats (8 per treatment) for four days with alternative food. Kill at two weeks.

When encapsulated warfarin was fed with unpoisoned food as the choice, only at the highest concentration (0.5%) did encapsulation markedly improve intake of the poison (Fig. II), but failed to increase mortality.

b) Zinc phosphide.

This acute rodenticide is far less acceptable to rats and mice than warfarin, even at concentrations well below the 4% normally used for rodent control. Taste masking could therefore provide a considerable advantage. When three concentrations (1%, 2% and 4%) of normal and encapsulated zinc phosphide (4:1 in ethyl cellulose) were fed to mice with alternative food, a similar 2-3 fold increase in intake was obtained by encapsulation, at all three concentrations and throughout the four-day feed (Fig. IIIa). Nevertheless, this higher intake of active ingredient failed to increase mortality above that obtained with unencapsulated zinc phosphide (Fig. IIIb).

2. Varying the phase ratio.

The experiments described in the previous section suggest that insufficient active ingredient was released through the wall coating to improve kill, or that it was not released sufficiently early in its passage through the gut to be adequately absorbed. An example of experiments to study the effects of different phase ratios of ethyl cellulose capsules, to improve release, is given by a test in which a very high concentration of alphachloralose (12%) was fed to batches of 16 mice for 24 hours at high temperature. The poison baits were then removed and alternative food provided.

In this test, a two-fold increase in intake of active ingredient was obtained with encapsulation at ratios of 20:1, 15:1 and 10:1 and a three-fold increase at 4:1 (Fig. IV). Measurements of symptom expression, scored on an arbitrary scale of five points ranging between normality and death, showed that a maximum was reached 1 hour after the beginning of feeding with normal alphachloralose and with encapsulation at 20:1. At 4 hours, maximum symptoms were obtained with 15 and 20:1, but by 24 and 48 hours, recovery was complete in almost all mice except a few showing symptoms, notably those fed at ratios 4:1 and 10:1. This indicates somewhat different release characteristics of alphachloralose with capsules of varying internal : external phase, but again, in no case was there a significant improvement in kill despite the higher intakes of active ingredient.

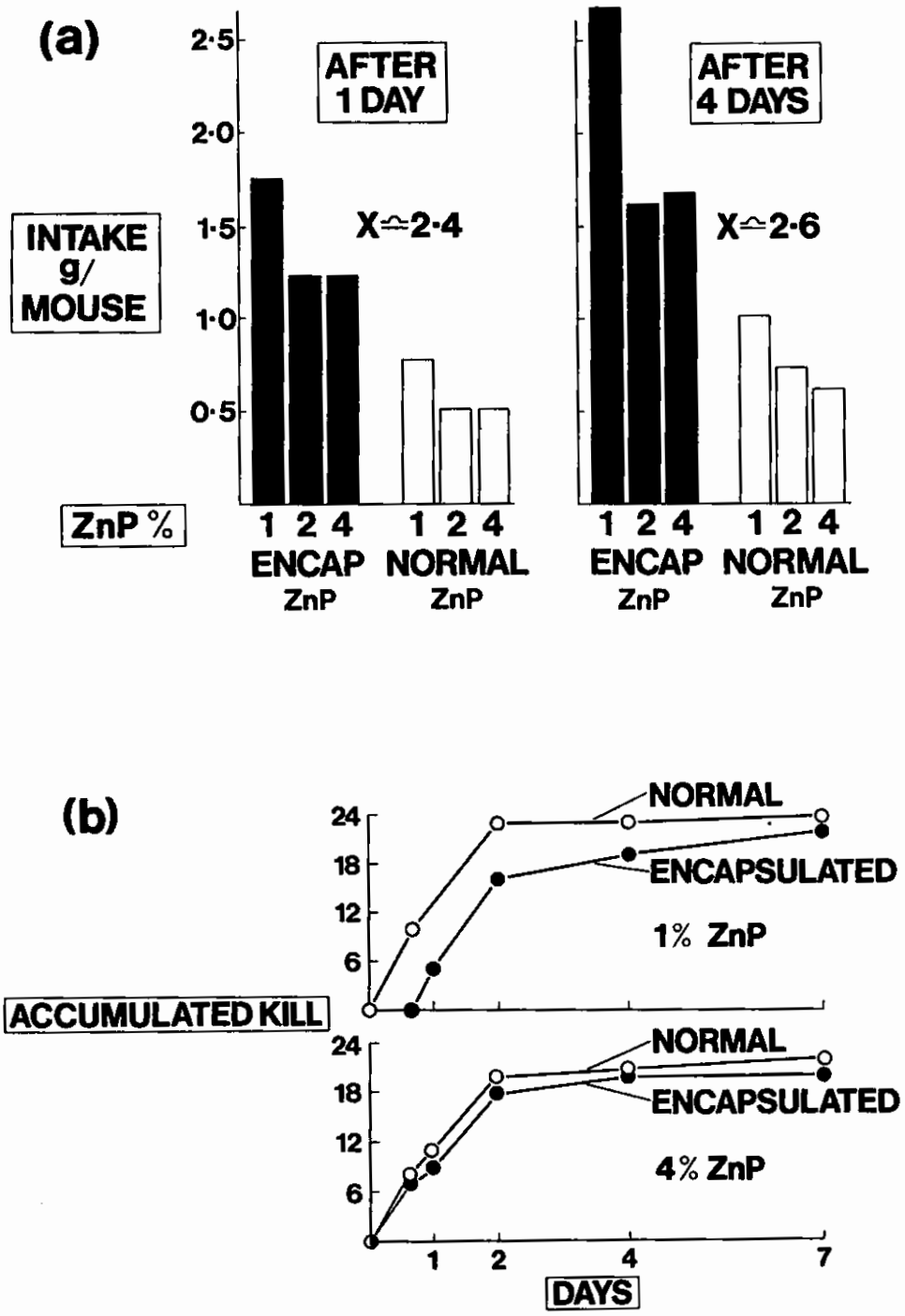


Fig. III. Diets containing normal and microencapsulated zinc phosphide (ethyl cellulose 4:1) fed at 1, 2 and 4% to mice (24 per treatment) for four days with alternative food.

a) Intake (g/mouse) after 1 and 4 days.

b) accumulated kill on diets containing 1 and 4%.

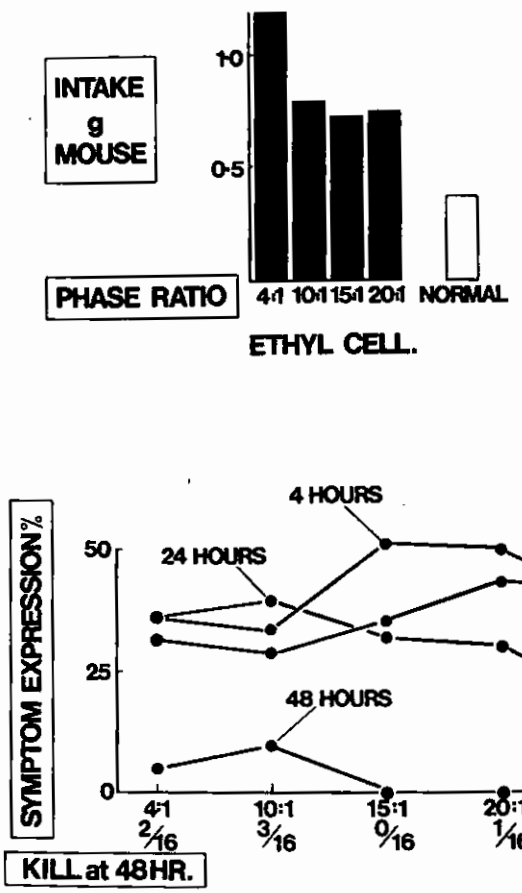


Fig. IV. Intake (g/mouse) of diets containing normal and microencapsulated alphachloralose, at various phase ratios, fed at 12% to mice (16 per treatment) at 72-75°F for 24 hours, followed by alternative food. Also symptom expression (%) and kill at 48 hours.

3. Varying the phase ratio and wall material.

Improvements in the palatability and kill which might be obtained from microencapsulation depend on optimising the release characteristics of the wall material. Gelatin and ethyl cellulose are both suitable for the encapsulation of rodenticides, but gelatin walls are modified by combination with gum arabic or carrageenan; ethyl cellulose is not modified by encapsulation as a hot or cold process but can be influenced by the use of various waxes, to improve uniformity of coating and to reduce wall permeability.

a) Gelatin and ethyl cellulose at low phase ratios.

Results for batches of 12 rats fed for 1 day on 0.25% and 0.5% norbormide, encapsulated in various systems, failed to give any striking improvement in kill over unencapsulated norbormide. Instead, a consistent loss in rodenticidal activity was obtained with all wall coatings at phase ratios of 4:1 and below (Fig. V). At these low ratios, ethyl cellulose coatings provided lower kills than gelatin systems.

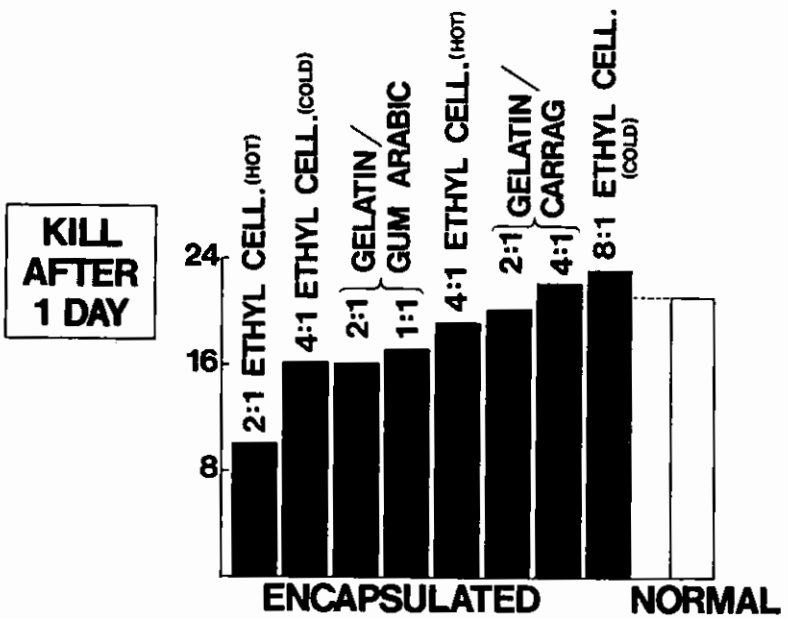


Fig. V. Mortality of rats fed diets containing 0.25% and 0.5% norbormide (normal and encapsulated in various systems) fed for one day without alternative food. (24 rats per treatment).

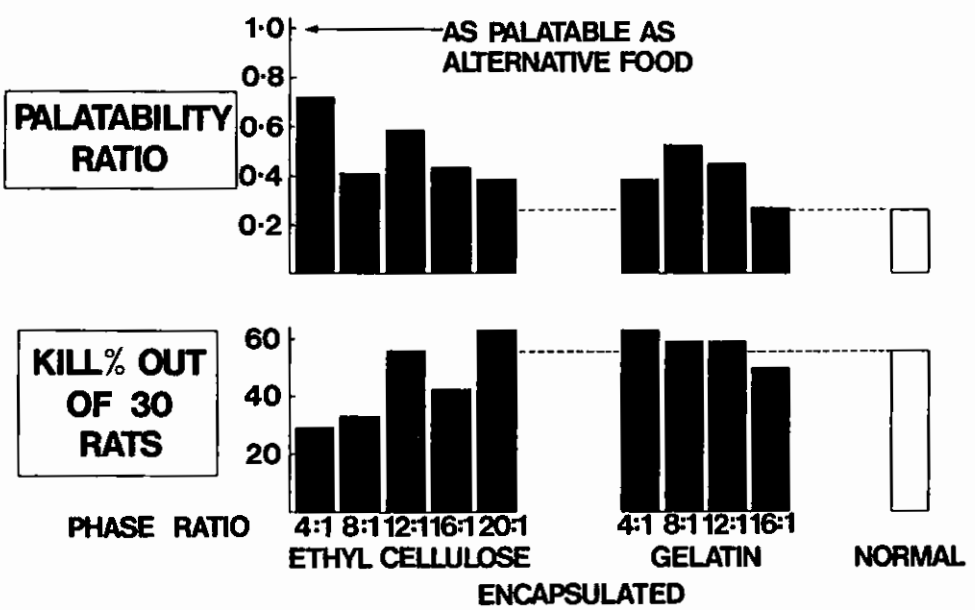


Fig. VI. Palatability ratio (poison : alternative food) of diets containing 0.5% norbormide (normal and microencapsulated in ethyl cellulose and gelatin at various phase ratios) fed to rats (30 per treatment) for 3 days with alternative food. Also kill (%) at 3 days.

b) Gelatin and ethyl cellulose at high phase ratios.

Examples of tests to evaluate walls of gelatin and ethyl cellulose at high ratios is again given for rats fed 0.5% encapsulated norbormide. In this case they were fed for 3 days with alternative food (Fig. VI). In 8 treatments out of 9, walls of both materials increased the ratio of intake of poison to the alternative food compared with unencapsulated poison. With ethyl cellulose as the wall material, lower kills were obtained with reducing phase ratios. With gelatin, however, mortality was not greatly modified by phase ratio and in no treatment was the kill different from norbormide *per se*.

c) Ethyl cellulose with wax spreaders.

To ensure more uniform encapsulation of the internal phase, waxes can be combined with ethyl cellulose during the encapsulation process. This also influences wall permeability. In addition, washing in a suitable solvent (methanol) was carried out, to ensure that no rodenticide contaminated the outside of the capsule wall.

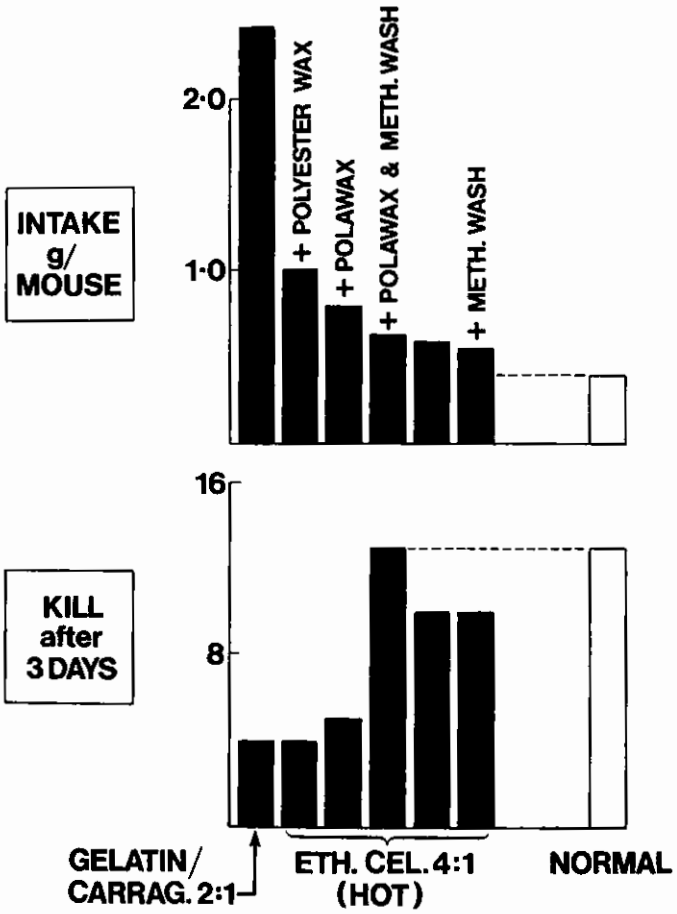


Fig. VII. Intake (g/mouse) of diets containing normal and microencapsulated alphachloralose (gelatin/carrageenan and ethyl cellulose by hot process) wax treated and methanol washed, fed to mice (16 per treatment) at 61-64°F. for 1 day, followed by alternative food. Also kill at 3 days.

The use of waxes improved the intake of encapsulated alphachloralose (Fig. VII) but apparently further reduced the amount of active ingredient released. The highest kill obtained with polawax, subsequently washed in methanol, but this was no greater than the kill obtained with normal alphachloralose.

4) Varying the phase ratio and concentration.

As early experiments tended to indicate that microencapsulation restricted the availability of "released" internal phase, especially at low phase ratios, tests were carried out to compare the effects of feeding low and high concentrations of encapsulated zinc phosphide and norbormide. Zinc phosphide was encapsulated in gelatin/carrageenan and norbormide encapsulated in gelatin. Both rodenticides were fed at a number of phase ratios.

a) Zinc phosphide.

In this experiment the test diets were fed to rats for 1 hour, and only then was alternative food made available. Restricting the test feed to a short period allows a more critical evaluation of palatability since symptoms of poisoning do not then interfere with "takes" in the various treatments.

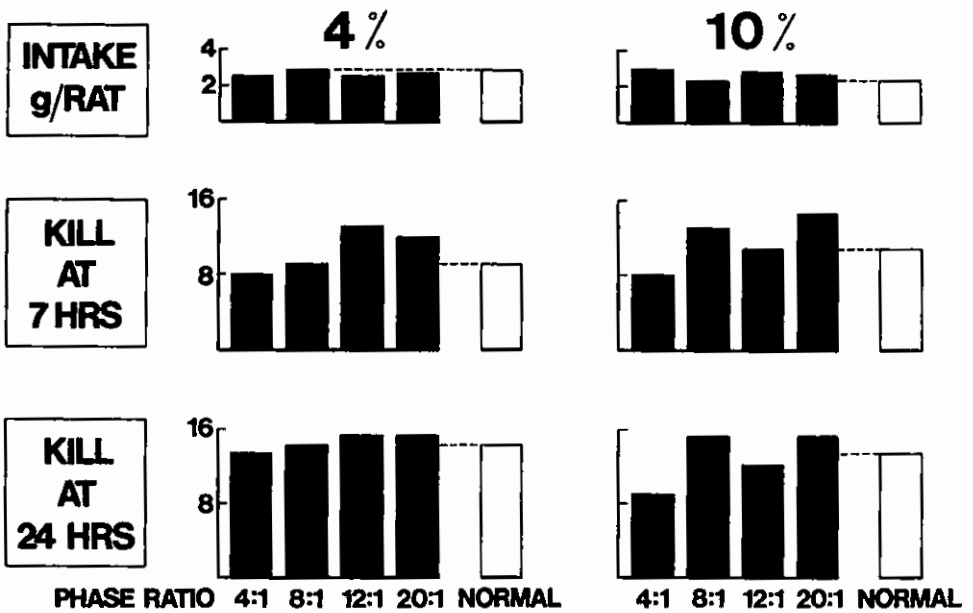


Fig. VIII. Intake (g/rat) of diets containing 4% and 10% zinc phosphide (normal and microencapsulated in gelatin/carrageenan, at various phase ratios) fed to rats (16 per treatment) for one hour. Also kill at 7 and 24 hours.

There were only minor differences in intake of the encapsulated zinc phosphide compared with the normal, but without any clear indication of improved intake at any phase ratio (Fig. VIII). The number of rats killed at the 4:1 ratio was somewhat lower than at higher ratios, and this occurred at both concentrations. At the higher ratios (8:1 to 20:1) there were small, but inconsistent improvements in kill compared with the unencapsulated poison, but which were no greater with the higher concentration of zinc phosphide (10%) than with the lower (4%).

b) Norbormide.

A further experiment to investigate the interaction of phase ratio and concentration was the study undertaken on norbormide to obtain confirmation of improved mortality reported by Greaves et al (1968). Gelatin capsules (4:1, 8:1 and 12:1) were fed at four concentrations (0.8%, 1.2%, 1.6% and 3.0%) to groups of 10 rats for three days with alternative food. A major difference, however, between this test and the work previously reported, was the much higher kill (70-90%) provided by the unencapsulated norbormide, upon which it was hoped to improve.

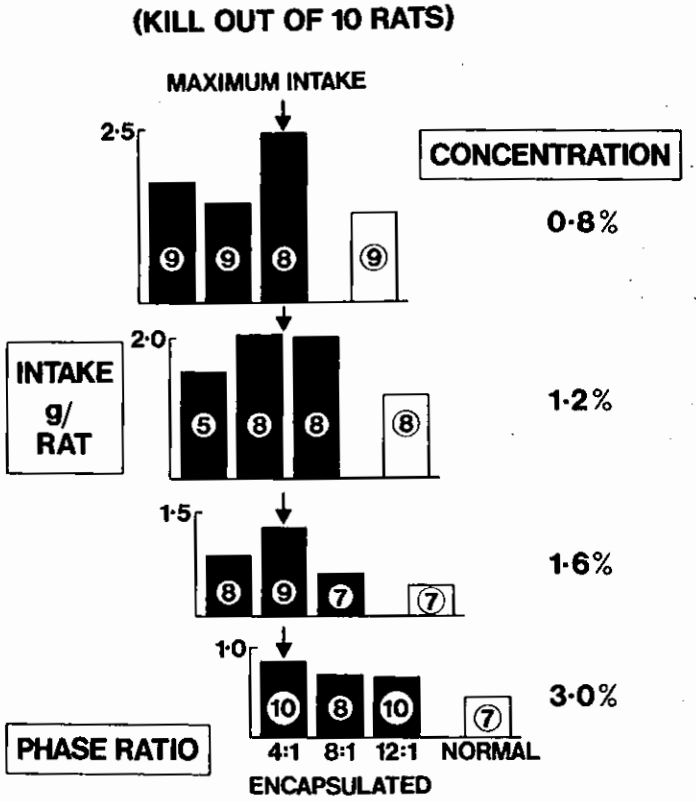


Fig. IX. Intake (g/rat) of diets containing 0.8, 1.2, 1.6 and 3.0% norbormide (normal and microencapsulated in gelatin at various phase ratios) fed to rats (10 per treatment) for 3 days with alternative food. Kill at 3 days shown in each histogram (see also Table I).

Higher intakes of active ingredient were obtained with all treatments involving encapsulated norbormide with evidence of a possible interaction between phase ratio and norbormide concentration (Fig. IX). Summing separately over concentrations and phase ratios the mortality obtained for each group of rats is shown in Table I. With the possible exception of diets containing 3% norbormide, encapsulation failed to increase kill beyond that obtained with unencapsulated norbormide.

Table I. Mortalities obtained by feeding diets containing 0.8, 1.2, 1.6 and 3.0% norbormide (normal and microencapsulated in gelatin at phase ratios of 4:1, 8:1 and 12:1) to rats (10 per treatment) for 3 days. (See also Fig. IX).

Summing over concentration.		Summing over phase ratio.		
			Encapsulated.	Normal.
Encapsulated 4:1	32/40	0.8%	26/30	9/10
8:1	34/40	1.2%	21/30	9/10
12:1	33/40	1.6%	24/30	7/10
		3.0%	28/30	7/10
Normal	31/40			

5) Combination of normal and encapsulated rodenticides in baits.

Experience in the laboratory and in the field use of alphachloralose, shows that a mouse eating this rodenticide exhibits obvious symptoms of poisoning in 15-30 minutes and becomes unconscious in 1-2 hours. If a sublethal amount is eaten, recovery occurs within 8 hours and is usually complete within 24 hours. Encapsulated alphachloralose has similar action but onset of symptoms is often delayed because of the capsule wall.

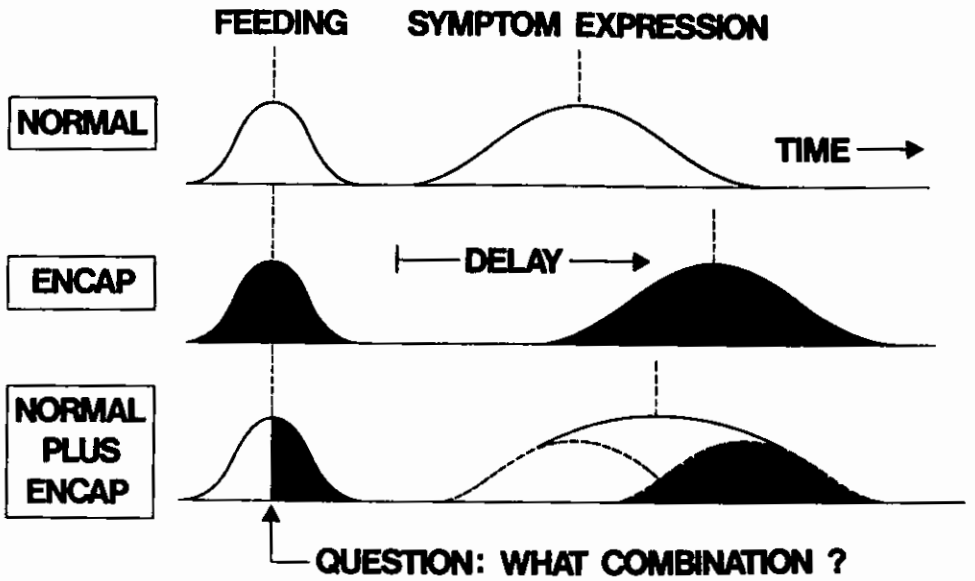


Fig. X. Possible advantage of combining normal and microencapsulated rodenticide in baits to obtain extended physiological action.

A "two-hit" system was therefore postulated (Fig. X) in which the level of alphachloralose in the blood might be raised to a high level by unencapsulated alphachloralose, and this high level maintained by continued release from encapsulated alphachloralose as a second component. This type of "sustained release" is already being exploited for improving the action of some pharmaceutical preparations.

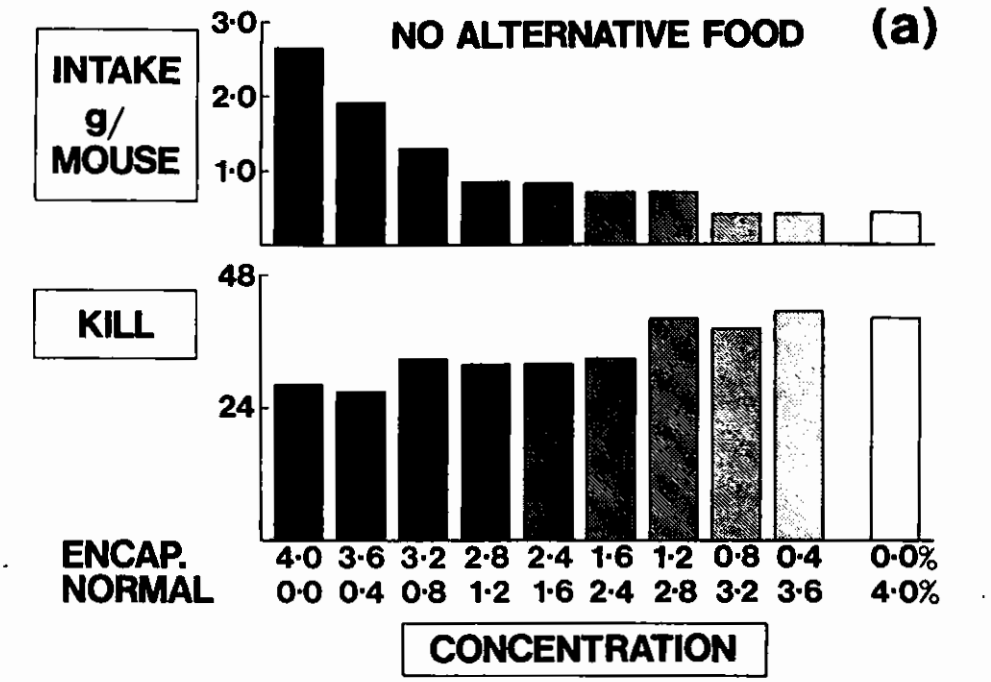
Experiments were thus carried out to examine the proportions of normal and encapsulated alphachloralose required in baits to provide increased kill. Two-component baits incorporating norbormide were also studied.

a) Alphachloralose.

In the first of two experiments, groups of 96 mice were fed a series of diets containing different proportions of normal and encapsulated alphachloralose totalling 4% active ingredient. At one end of the series the diet contained 4% normal alphachloralose and at the other, it contained 4% encapsulated. Encapsulation was carried out in ethyl cellulose at a phase ratio of 10:1 and the mice fed for 2 days at 50-59°F. Half the mice (48 per treatment) were fed with alternative food and the other half without.

The intake of rodenticide progressively increased with the amount of encapsulated alphachloralose, whether or not alternative food was available (Fig. XIa and XIb). Intake of the diet containing fully encapsulated poison was 3-5 times higher than that containing only normal alphachloralose.

Without alternative food (Fig. XIa), kill progressively decreased with increasing proportion of encapsulated poison. In the presence of alternative food, however, some combinations of normal and encapsulated poison (around 50% of each) resulted in kills in excess of the mortality (23%) obtained with the wholly unencapsulated diet (Fig. XIb). It should be noted that this "control" mortality was far lower than in the experiment which follows.



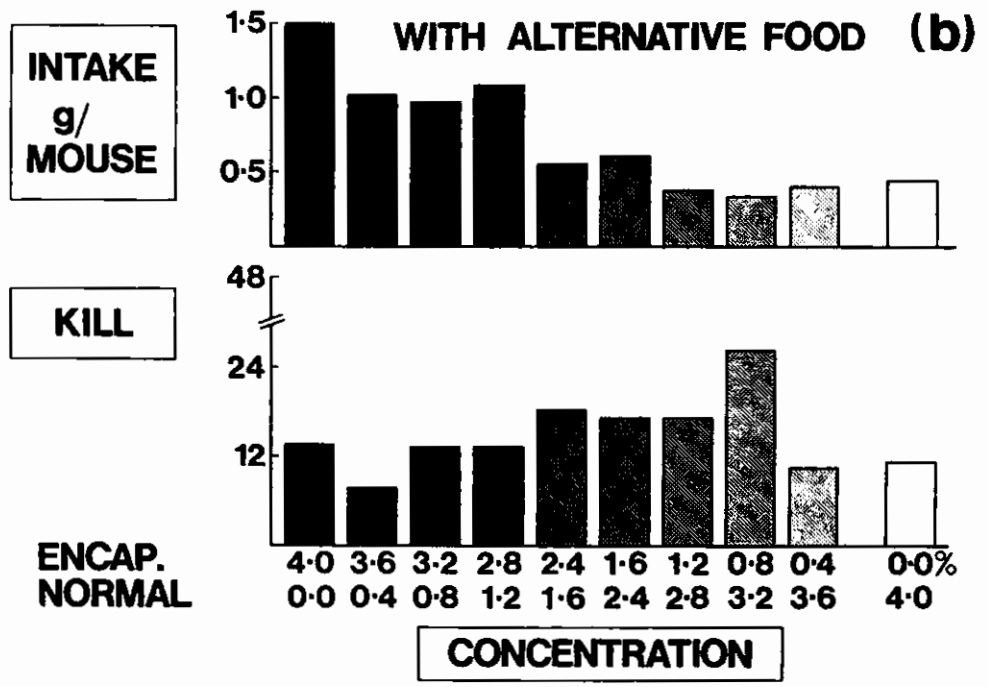


Fig. XI. Diets containing normal and microencapsulated alphachloralose (10:1 ethyl cellulose) fed in various proportions, at 4%, to mice (48 per treatment) for 2 days at 50-59°F .

a) intake (g/mouse) and kill with no alternative food.

b) same with alternative food.

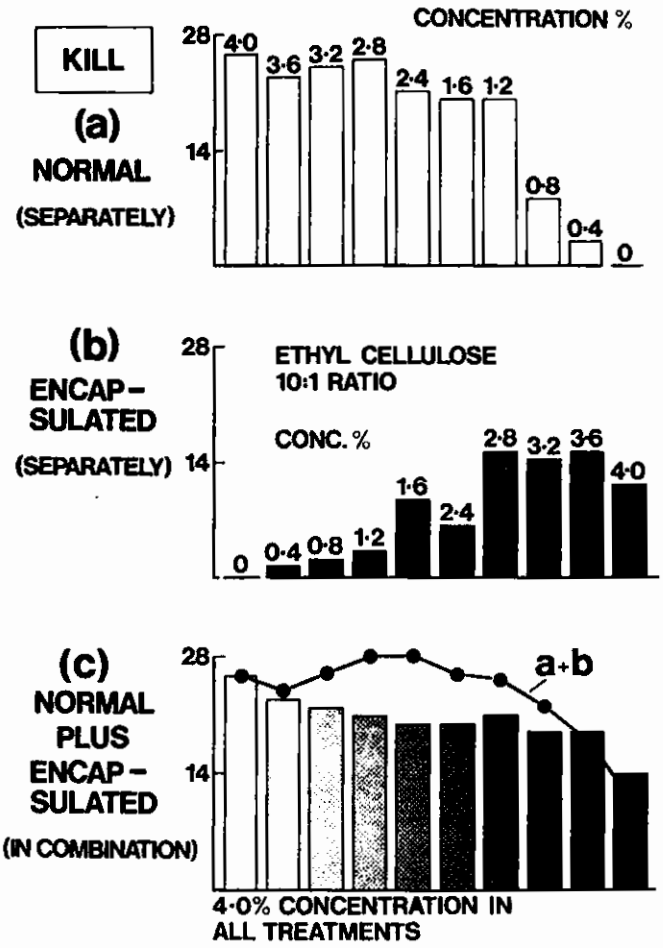


Fig. XII. Kill obtained with diets containing normal and microencapsulated alphachloralose (ethyl cellulose 10:1) fed at various concentrations to mice (28 per treatment), (a) normal alphachloralose separately, (b) encapsulated alphachloralose separately, (c) in combination at 4% active ingredient. The bottom graph also shows the total mortalities obtained by adding (a) plus (b).

A repeat of this experiment (Fig. XII) with identical combinations of encapsulated and unencapsulated alphachloralose failed however to substantiate this improvement. In this instance, the mice again had access to alternative food, but the temperature was somewhat lower (46-54°F) and mortality on the wholly unencapsulated diet was high (about 90%). As expected the kill of mice fed only normal alphachloralose, progressively decreased with reducing concentration (Fig. XIIa) and mortality on diets containing encapsulated alphachloralose alone progressively increased with concentration (Fig. XIIb). When normal and encapsulated alphachloralose was combined in different proportions, but always totalling 4%, no improvement in kill resulted (Fig. XIIc).

b) Norbormide.

In a final experiment, 0.25% norbormide (normal) with 0.75% norbormide (encapsulated) was fed in combination to rats. Intake and kill on the "combined" diet was again compared with normal and encapsulated norbormide fed separately (Fig. XIII). Two phase ratios of ethyl cellulose were investigated. In confirmation of the previous studies, the kill obtained with 1% norbormide not microencapsulated exceeded the mortality in all other treatments.

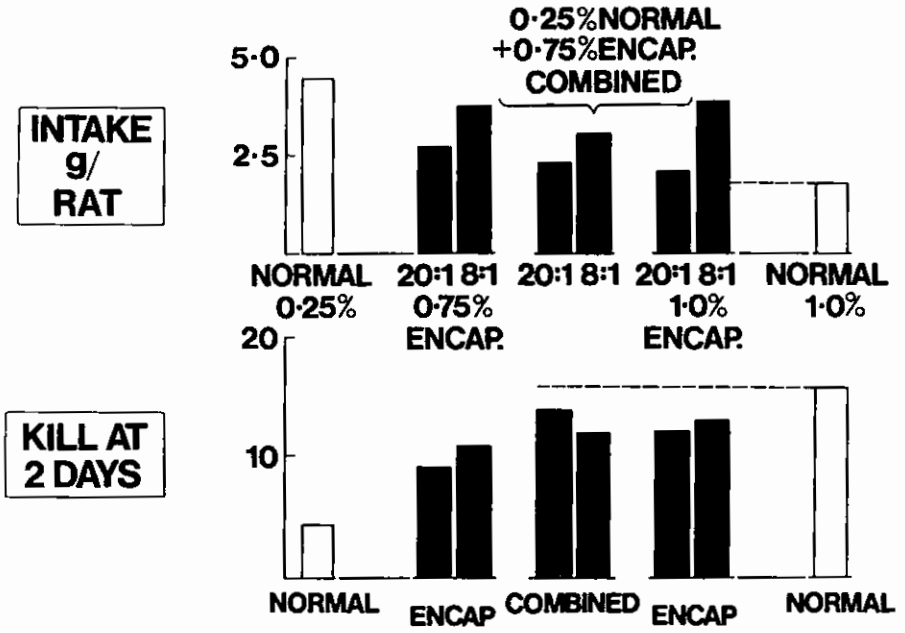


Fig. XIII. Intake (g/rat) and kill obtained with diets containing normal and microencapsulated norbormide (ethyl cellulose 8:1 and 20:1) fed at various concentrations, separately and in combination to rats (20 per treatment) for 2 days.

DISCUSSION

Careful use of warfarin against susceptible populations of wild Rattus norvegicus and Mus musculus can provide 100% control, but the efficiency of acute rodenticides varies between 50-90%, depending on the known extent of the rodent population, location of harbourages, availability of alternative food, skill in application, and the use of prebaiting. This generalisation serves to illustrate the need to be met by microencapsulation: that it should improve the efficacy of rodenticides above that already experienced in field use, to give mortalities of 90-100%. Most of the laboratory tests reported here were designed to explore this area of improvement.

The studies of Greaves et al (1968), which showed improved kill with norbormide (encapsulated in gelatin at 4:1) and alphachloralose (encapsulated in ethyl cellulose at 10:1), were not only conducted with very small numbers of animals, but in case was the kill obtained with the unencapsulated rodenticide above 50%. Thus, summing over the concentrations tested by these workers, encapsulation of norbormide increased kill from 24% to 52% and encapsulation of alphachloralose increased kill from 20% to 45%. Some of our tests have shown similar improvements, when mortality of the animals fed unencapsulated rodenticide is very low.

As a corollary, it is relevant to emphasise that in the limited tests of Greaves et al, kills of 80-100% obtained with normal alphachloralose, administered orally at high doses, were lowered when the poison was encapsulated.

From presently available information, it would appear, therefore, that with very low "takes" of rodenticide, caused by bait shyness or other environmental factors leading to reduced rodenticidal action, microencapsulation may provide a marginal improvement in the field. Where "takes" already result in 50-90% kill, encapsulation with the systems so far explored offers little advantage.

Microencapsulation can increase the intake of rodenticides considerably, low phase ratios giving higher intakes than high ratios and gelatin walls being more readily digested than walls of ethyl cellulose. In some instances the intake of active ingredient has been increased by up to 10 times, even in the presence of alternative food, but it is clear that a considerable proportion of the additional poison ingested is unavailable or physiologically inactive.

It is possible to postulate a number of reasons for failure to obtain improved kill:

1. Capsule wall not digested. The capsule wall is not digested sufficiently rapidly to allow absorption of active ingredient through the epithelial lining at the appropriate stage in the gut. Unhardened gelatin capsules are possibly less resistant to digestion than hardened walls.

2. Limited absorption. The high rate of action of both alphachloralose and norbormide is a clear indication that considerable absorption occurs in the stomach. There may be an upper limit to the rate at which these drugs will diffuse across the gastric mucosa and beyond this limit any increase in concentration of drug will not affect the rate of absorption by the blood. This being so, the encapsulation of rodenticides as liquids would not improve matters even if solvents compatible with encapsulation and palatability could be found.

3. Inhibited metabolic action. The amount of rodenticide released may inhibit metabolic action (interfering possibly with enzyme activity and movement of food through the gut) and thus prevent the absorption of the greater proportion of rodenticide remaining in the capsules. This could certainly apply to alphachloralose which induces hypothermia. Crystals of this rodenticide are not conducive to uniform coating, and release from partially coated crystals may be sufficient to cause mild symptoms preventing the release within the stomach of the bulk of encapsulated rodenticide.

4. Detoxification. With active ingredients released slowly through the capsule wall the rodent may be able to metabolise the rodenticide as it is released. This could apply to alphachloralose and norbormide.

FUTURE STUDIES

Any one, or a number of the above factors, alone or in combination, could preclude the advantage gained by getting a high concentration of rodenticide into the gut through improved palatability, or delayed onset of poisoning symptoms. Conditions in the gut which result in the "explosive release" of the internal phase from the capsules may help to improve rodenticidal action, but this may not be readily achieved. Improvements which have been made in the action of pharmaceutical preparations come from extending release, and therefore physiological action of drugs, taken acutely. With rodenticides, the requirement would appear to be the reverse: intake of the poison may be spread over minutes or hours and the objective of encapsulation would appear to be timed explosive release, to achieve a high "instantaneous" liberation of internal phase to bring about maximum physiological action.

The studies now being undertaken include the incorporation of enzymes in the encapsulated diets to assist in removal of the gelatin walls. These and other methods are first being investigated under the microscope in simulated gut fluids before the feeding studies are extended.

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