NEW ALTERNATIVES FOR CHAGAS' DISEASE CONTROL

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Seventy-five years after being discovered Chagas' disease still represents one of the most important parasitic diseases affecting man in Latin America. In spite of the resources spent in research and control campaigns the high incidence of vectors in houses in most of the endemic areas continues and, as a consequence, a high level of transmission within the human population remains. In some areas, such as northeastern Brazil the picture is still worse, with the expansion of the geographic area occupied by those species of triatomines that are the most efficient vectors of this trypanosomiasis (Castro Filho & Silveira, 1979). What is the reason for this unchanging or worsening situation after so many years of study an effort to control this disease?

In the first place it is apparent that the greater part of the time invested in research during these 75 years has been directed along lines, such as immunology and chemotherapy, which are less fruitful in terms of producing short-term results. At present there is no vaccine and little prospect of an immunization process in the near future. Also there is no widely accepted curative drug available for large scale use. There are two or three drugs in use nowadays but their prescription is very limited because they are usually only suppressive or curative in acute cases, and besides this produce many undesirable side effects. In such a situation, if something is to be done now to avoid transmission and spread of the disease over unaffected areas, it is firstly the control of the vector, and secondly, special care with blood transfusion, second in importance in the transmission of Chagas' disease.

Reviewing our own experience on triatomine control research and related papers in the literature it is possible to enumerate a reasonable set of tentative vector control methods all of them possessing advantages and drawbacks. Insect growth regulators e.g. juvenile hormone mimics (Oliveira Filho et al., 1984) and precocenes (Oliveira Filho et al., 1980) are active only in part of the life cycle and are slow acting, often unstable compounds. Their principal effect is the sterilization of the adult bugs but this does not prevent transmission of Trypanosoma cruzi by the insects of the generation that received treatment. The lack of persistence associated with these compounds would also require the use of special slow-release matrices for their application. One advantage is that they are fairly safe to mammals. Another, the specificity of target, may become a disadvantage since there will be limited commercial interest in producing a compound with a small restricted market.

Biological control through the use of Microhymenoptera that parasitise eggs of triatomines such as Telenomus farai (Barret, 1975) already proved to be ineffective in field conditions. Insect pathogens like Metarrhizium would seem to suffer limitations in their use because of the special environmental conditions necessary for the survival of this fungus. Preliminary field testing of this pathogen has however been initiated in Brazil although economic feasibility data are lacking at present. The use of traps with attractants (pheromones, kairomones) or without attractants (hiding places for nymphs and adults) has also proved to be ineffective in terms of control, being of some utility only for monitoring low level infestations. Genetic control as used for same insect pests e.g. by the release of sterile males, is unacceptable for a vector of an incurable disease.

Housing construction or modification such as plastering of walls and substitution of palm thatch roofs by tiles are, to some extent, effective but if there is no simultaneous improvement of socio-economic conditions of the population, associated with health education, this measure will not have lasting results. People will soon begin to add new rooms, chicken houses, etc., built in the old way with the resulting cracks and crevices in the walls, readily infested with vectors from the old houses. By accumulating boxes, sacks and bric-a-brac inside their homes they will also again create enough hiding places to maintain large populations of vectors and the transmission of the disease will continue. Housing modification to be persistent and effective must be made by the population itself, through the improvement of living standards. Also health education must arise through increased public awareness as a result of community participation in vigilance schemes to avoid re-emergent infestations. At present, in the countries where Chagas' disease is endemic, the heavily infested areas are economically very poor and it seems that such a modification is a matter of generations.

With this picture in mind it is easy to see that the only practical weapon that health authorities can count on at the moment to diminish transmission in affected areas in the use of insecticides. They give a quick response in lowering bug populations and consequently transmission and the method is relatively cheap and feasible when compared with the others already mentioned. Of course all efforts must be directed to improve rural development, leading to better housing construction and maintenance and the

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willingness to receive health education all of which in the long run will be the definitive measures for the control of transmission of Chagas’ disease. In common with other methods, the use of insecticides has its disadvantages like toxicity to man and domestic animals and also the rapid loss of activity when applied to alkaline walls.

The majority of Government directed campaigns against vectors of Chagas’ disease in South and Central America have been based on the repeated spraying of infested houses with BHC or dieldrin. These organochlorines are gradually losing favour with public health authorities, principally because of their detrimental environment impact. In Brazil BHC wettable powder containing 30% gamma isomer has been used for more than 30 years in national or state campaigns. After being banned in more developed countries, the use of BHC for agricultural purposes was also prohibited in Brazil due mainly to its contamination of foodstuffs. Although its use for public health purposes is still accepted at the moment in view of the limited places of application (inside houses) reduced probability of killing non-target insects and little chance of producing ecological problems, the tendency to exclude BHC can be expected to extend to public health use.

In 1984 SUCAM, the Federal Institution responsible for Chagas’ disease campaigns in Brazil, had almost all the endemic area mapped and surveyed and the plan was to spray each infested house with insecticide in a wide range campaign that would also include noninfested houses in affected neighborhoods. This general application would be followed later by selective spraying of houses which remained infested or were reinfested. However, in spite of good organization the plan failed for lack of funds (the campaign was simply interrupted). This factor, the financial problem, is very common in developing countries when the Government is dealing with a non productive area. In fact with few exceptions, failure is the general rule with existing methods of vector control — they are neither applied correctly, nor frequently enough nor over a wide enough area to produce a lasting effectiveness.

The main problem with BHC is that activity does not persist for much time in the houses treated, making necessary frequent reapplications which are time and money consuming. Application is expensive not only from the direct cost of the insecticide, but principally because of expenditure with fuel and personnel. Furthermore in Venezuela strains of Rhodnius prolixus, the main vector in that region, resistant to dieldrin and cross-resistant to BHC have already been found, and there is concern that this phenomenon may become more widespread (Nelson & Colmenares, 1979). Another problem of practical order is that this insecticide is becoming increasingly scarce in the world market because of the widespread restrictions to its use. Thus there is presently a need for alternative insecticides.

Reliance on organochlorines is largely traditional — equipment and application technique already exist. Also there are few published papers on well done field assays with other insecticides, which could help health authorities in the choice of better alternatives. In some Latin American countries like Argentina and Venezuela, organophosphates (e.g. malathion and fenitrothion) and carbamates (e.g. propoxur) have seen limited use in Chagas’ campaigns, but their short persistence on mud walls makes them almost inefficient. There are, however some organophosphates with high intrinsic toxicity to triatomines whose persistence surpasses that of BHC, and which maintain houses free-bug for more than six months. Chlorpyrifos ethyl and chlorphoxin are good examples of this kind that are worthy of mention among the many products tested by our research group (Oliveira Filho, 1983, 1984). There is need now to establish the cost-efficiency ratio for those in new and larger field assays. Another group of insecticides which entered the market more recently, with high toxicity and good persistence for the mentioned vectors, comprises the synthetic pyrethroids. In general they are more expensive than insecticides of other chemical groups, but in the long run they may prove to be cost efficient because of the lower dosages employed and the higher persistence observed. At the moment, from this group can be selected deltamethrin, permethrin (Pinchin et al., 1980; Pinchin, Oliveira Filho & Gilbert, 1981) and cypermethrin (Pinto Dias, Benedito & Vasconcelos, 1984). Newer compounds are in the laboratory screening phase and the field results to follow will perhaps increase this list.

The analysis of vector control using insecticides always leads to consideration of recovery of bug populations some time after spraying. Are these insects descendents of post-spray survivors or do they result from immigration from untreated foci? Schofield (1982) affirms that the answer to this question is very important because if reinestation stems from survivors more frequent respraying or more residual compounds would be necessary, whereas if the problem is caused mainly by immigrant bugs, then a greater geographic coverage would be recommended. In our opinion a single solution exist — if the treatment is made with a sufficiently persistent insecticide both survival and immigration will be avoided. In the first case the survivors would be killed when coming out of their hiding places, or from the eggs, in search of blood and in the second the recolonization of the house would not occur during the period of activity of the insecticide. The main problem is to find insecticides with such persistence on porous, alkaline, mud walls and which are yet safe enough to be applied inside inhabited houses. As already pointed out there are some organophosphorus and synthetic pyrethroids that almost fit this requirement. But is there many way of protecting more degradable and safer insecticides from the rapid environmental and so of maintaining their activity for many months, thus creating new options for an efficient vector control?

Our research group have been pursuing the answer for this question during many years and a number of slow-release formulations have been developed. Unfortunately many of them had serious draw-
backs for use in large scale campaigns against Chagas' disease due to their appearance or to difficulties in application which was often time consuming or required special equipment. This paper will describe the results of laboratory and field experiments with a new slow-release formulation, demonstrating the possibility of using insecticides not normally considered persistent, in Chagas' disease campaigns, with little adaptation of the equipment already in use.

MATERIALS AND METHODS

Insecticides and ingredients of formulations – Malation was supplied either as a 50% emulsifiable concentrate (EC) or 50% wettable powder (WP) by Cyanamid Quimica do Brasil Ltda. Chlorpyrifos-ethyl came from Dow Quimica S/A as Dursban MC in methylene chloride containing 720g/L of active ingredient. BHC WP, containing 30% of gamma isomer, was obtained from SUCAM, the division of the Brazilian Ministry of Health responsible for public health campaigns. The latexes of polyvinyl acetate (PVA) were furnished either by Tintas Ypiranga Ltda, Rhodia S/A, Texsa S/A or Glastrit do Brasil Ltda. The latex of SBR (styrene, butadiene rubber) was supplied by Petroflex Indústria e Comércio Ltda. and the oxidized bitumen either by 3M do Brasil Ltda. or Texsa S/A. The alkyd resins (phthalic anhydride glycerol) came from the Instituto de Macromoléculas of this University. The tetramethrin-phenothrin (4:1 mixture of neopyrimin-sumithrin, 0.125 total pyrethroids in kerosene) was donated by Sumitomo Chemical Co. Ltd.

Laboratory tests – The formulations were prepared on the small scale by mixing malation 50% EC or WP or Dursban MC 720 g/L with the other components and adding, when necessary, carriers (surfur, asbestos or paraffin wax), emulsifiers and organic solvents. The final concentration that varied from 4.1 to 10.2% (but in general was 10%) active ingredient, was calculated on the basis of the dry weight of the formulation, after evaporation of the water or organic solvents used for the dilution of the components. The formulations were applied using manual sprayers or brushes onto one surface (12 x 12cm) of unbaked mud bricks in order to give the appropriate dose which varied from 3.3 to 10.6g of a.i./m², but in general was 4.0g.

For each test, 10 fifth instar nymphs of Panstrongylus megistus, from a laboratory colony maintained at 27 ± 2°C and 65 ± 15% R.H. were placed on the treated surface after the formulation had dried. To keep the insects on this surface they were put inside cones of transparent plastic with a hole in the upper part (WHO cones for bioassay with adult mosquitoes), fixed to the bricks using rubber bands. The nymphs stayed in contact with the treated surface during 21 days. Readings of the percent mortality (moribund + dead) were performed at 1, 2, 3, 7, 14 and 21 days of permanent contact, but only the results of the last reading are presented in the results. The same bricks were tested again at 42, 91, 182, 273, 365, 455 and 540 days of aging under the laboratory conditions already described, exposed to air and light.

Field tests – The trial was conducted in October 1983 in Ribeirãozinho, Barra do Riacho and Vila Brasil, in the municipality of Barreiras, Bahia state, Brazil (12°09'S, 44°05'W) and involved 80 houses heavily infested with Triatoma infestans. House wall construction was brick, adobe or mud packed onto a wood lattice. Tile roofing predominated.

The trial area was surveyed at 18, 16 and 3 months before treatment, however many of the houses were closed on one or other occasion. The group treated with BHC was only surveyed six months pre-treatment. The sampling techniques used called flushing-out and systematic timed-capture method (Pinchin et al., 1982) was as follows: two trained workers entered the house and while one searched beds, bedding, boxes of clothes and other similar possible bug hiding places, the other sprayed a 0.125% solution of tetramethrin and phenothrin (Pinchin, Oliveira Filho & Pereira, 1980) into the cracks in the walls suspected of harbouring bugs. After 2-5 minutes both workers, equipped with flash lights and long pincers, searched the walls for triatomines in the same prearranged sequence that the pyrethroid flushing-out spray was applied. The search was limited to 10 minutes per house, after which the bugs captured were classified by instar, counted and killed.

The houses previously numbered and mapped, were divided between the treatment groups as randomly as possible. Only houses which had been found colonized by nymphs during the pre-treatment readings were included in the trial. A few houses could not be treated because they were closed, had a newborn child or occupants in ill health that could not be removed. We have not met any case of entry denied.

For the insecticide spraying Hudson-X-Pert pumps fitted with Teejet 8002 nozzles were used. A little modification was necessary to permit application of the slow-release formulation, i.e., the filter inside the handle grip of the pump must be removed permanently to avoid polymerization of the matrix at this point. It was also helpful to maintain the nozzle in water, between the application of two houses for the same reason. Pump charges of BHC were prepared mixing 350g of the 30% WP in 10/L of water for a target dosage of 0.7g of gamma isomer/m², as recommended by SUCAM. For commercial malathion, 600ml of 50% EC were added to 10/L of water for a target dosage of 2g a.i./m². For the slow-release emulsifiable suspension (SRES), prepared just before application, 900ml of malathion 50% EC were mixed to 6.5/L of PVA latex with 56% solids plus emulsifiers and water to give 10/L of formulation containing 45g of a.i./L. The target dose was 4g a.i./m². The final formulation had 11% of a.i. in relation to the dry weight of the latex. The mean rate of application for the 3 groups was near 70ml/m².
Prior to application all foodstuffs, drinking water, kitchen utensils and domestic animals were removed from the houses and the heavy furniture moved out from the walls. The spraying reached all the inside wall surfaces, the underside of the roof, bed frames and the backs of furniture. During the treatment performed by the field staff of this research group, the sprayers were equipped with overalls, rubber gloves and visors. The approximate surface area sprayed (A) for each house was calculated from the formula: $A = 8 \times (L + W) + LW$ (Pinchin et al., 1978) for a house with sides of length L and width W. Thus, the average dose applied was calculated from the total liters of formulation used divided by the sum of the values of A obtained for the houses sprayed with that formulation.

The post-spray sampling was made at 1, 3, 6, 9, 12 and 14 months, in the same way as the pre-spray readings. Several houses were eliminated during the trial because they were abandoned, demolished or reconstructed. The percentage of infestation was calculated considering the number of houses in which a bug of any stage was captured, in relation to the number of houses actually inspected at that time. The average number of insects captured per man-hour was calculated taking into account only the houses infested at the reading.

RESULTS

Table I shows the results obtained until 540 days in the bioassay of 19 formulations designed for slow-release liberation of insecticides. It also shows the main components and characteristics of each formulation to make the comparison between them easier. Thus this table contains the polymer matrix employed, the percentage of solids and the pH of this matrix, the initial formulation (commercial) that was the source of the active ingredient (malathion), the compounds used as carriers and the percentage of a.i. in relation to the dry weight of the polymer, which means the final concentration of the formulation after being applied. This table also shows the dose applied to the surface of the bricks. For easy interpretation, only the results of the 21 days reading are shown.

TABLE I

Percent mortality of 5th instar nymphs of Panstrongylus megistus after 21 days of permanent contact with unbaked mud bricks treated with a malathion formulation designed for slow release. The bricks were tested on the days of application and again after 42, 91, 182, 273, 365, 455 and 540 days of aging under laboratory conditions. For each formulation, data are presented, which include the polymer used, its percentage of solids, and the pH of the polymer. Also given are initial formulation of the malathion used (50% emulsifiable concentrate or 50% wettable powder), other main component of the slow-release formulation (carrier) and the percentage of active ingredient calculated in relation to the dry weight of the final formulation. The doses applied over the bricks in grams of active ingredient/m² are also presented.

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As can be easily seen the formulations that gave better persistence are mostly based on PVA, (see numbers 1 to 12). Of these, the best results were obtained with formulations 1, 2, 4 and 6, all them giving more than one year of persistence. They have in common the same PVA with 56% of solids and pH 4.5. Formulations 1 and 2, still giving 100% kill after 540 days of aging, were tested under conditions different from those used for the other formulations based on PVA. The first, besides being formulated at 10% of a.i. was tested at 10.6g of a.i./m² nearly 2.5 times greater than the others, that were mostly 4g/m². The second was applied at 4.5g/m², close to the normal dosage tested, but the formulation was less concentrated in active ingredient, and thus contained a greater quantity of polymer per unit surface.
Formulation 9, which was based on a commercial paint, and 10 to 12, with high pH, presented weak persistence. Alkyd resins and elastomers like SBR were also not efficient in retaining activity of malathion. The group of oxidized bitumen based formulations also did not give meaningful results when using malathion as the a.i. but in a separate test, when using chlorpyrifos-ethyl at the same concentration but at a higher dosage (10g/m²) the formulation remained 100% active until the 91 days reading and was showing 80% mortality in the one year reading, the last made at the time of writing.

In order to save time, when the laboratory tests reached the 91 days assay it was decided to start field testing with one of the most simple and promising formulations at that reading. The formulation number 6 was chosen since it was giving 100% control and had no carriers like asbestos, sulfur or paraffin that would complicate preparation in field conditions. Prepared in the field this formulation (Slow-Release Emulsifiable Suspension – SRES) was a little bit more concentrated (11%) than in the laboratory. The target dose was 4g/m² but due to an overestimation of the spraying rate the real dose applied was actually 3g/m². Simultaneously an other group of houses was treated with the same insecticide but with the commercial formulation 50% EC with a target dose of 2g/m² as recommended by the manufacturer, the actual dose being 1.8g/m². Another group was treated with BHC 30% WP at 0.7g/m² to permit comparison with the SUCAM spraying technique.

Table II gives the results of the pre- and post-treatment readings. One month after treatment the activity measured by the percentage of houses bug-free was almost the same for the 3 groups, but from then on it is easy to see the increasing difference between the good performance of the SRES formulation compared with the other two groups. After 3 months the malathion 50% EC and BHC already showed a decline in activity as demonstrated by the percentage of houses bug-free and an increase in the number of insects captured per man-hour in the houses already infested. With 6 months these two groups were almost totally reinfested due to the low level of control. Instead of this the SRES group showed little variation around the level of control reached at 3 months, maintaining between 83 and 93% of the houses uninfested. This is also valid for the number of insects captured per house which average stayed around 3 until 13 months, increasing to 6 only 14 months after treatment.

![Table II](https://www.example.com/table_ii.png)

**DISCUSSION**

One of the main problems faced by the worker interested in the use of slow-release formulations of insecticides is the method of application, which is generally unconventional. Most of the formulations our research group has developed envisaging the control of Chagas' disease vectors are very efficient in killing triatomines for a prolonged period under laboratory conditions, but failed during the real application. This succeed because of various factors, like the need of special equipment for application or because they were not well accepted by the population due to the unpleasant smell, color or place of application. The inhabitants of endemic areas for malaria and Chagas' disease are accustomed to see the inner walls of their houses sprayed by men in uniforms, using pumps and almost anything different would hardly be accepted. Thus, for the experiments herein described the choice of matrices for laboratory screening was more pragmatic, having in mind their possible future application in campaigns.

For oxidized bitumen based insecticide paints developed in the past by this research group, the presence of a carrier, i.e., a compound that constantly migrates from the inner mass to the other surface of the paint, carrying with it the a.i. that otherwise would remain inside the matrix or migrate at a very small rate, was essential (Oliveira Filho et al., 1980). Having this fact in mind, some of the formulations during the screening laboratory phase were mixed with asbestos, sulfur or paraffin wax to see if this would help with other polymers as well. Looking at the results of the group of formulations based on PVA with 56% solids (1 to 6) and putting apart formulations 1 and 2 because they were either prepared or applied differently, we can see that the order of persistence is 4 > 6 > 5 > 3. This means that sulfur increased the efficacy of the formulation and asbestos decreased it; for example number 6, with no carrier, is more active.
than 5 or 3 which have carriers. The pH seemed also to play an important role. Low pH formulations preserved the insecticide for more time.

Increasing the dose also increased persistence as regard formulation number 1, which, when applied at 10.6g/m² is still killing 100% bugs after 540 days. The amount of latex in the formulation also seemed to be an important factor because, formulation 2 applied almost at the same dosage as the others, gave better results probably because it was less concentrated, thus having greater quantity of polymer in the surface of the brick. The commercial paint containing PVA was not effective probably because of the presence of other components used as pigments or fillers that may react with the insecticide. Alkyd resins (phthalic anhydride glycerol) as well as SBR and oxidized bitumen with or without rubber, gave poor results. With oxidized bitumen another organophosphorus (Dursban) gave better results showing that other active ingredients can be used in these formulations.

The PVA that turned out to be the best matrix has characteristics that will allow it to be easily accepted by the population because it can be applied with insecticides using conventional pumps and after drying (about 30 minutes) it becomes transparent giving origin to a thin plastic film that will impermeabilize the porous mud walls, even making them more resistant to abrasion. Furthermore the smell of the insecticide becomes weaker due to less evaporation as the a.i. is protected by the matrix, avoiding unnecessary loss soon after application. The a.i. is also protected from the extremely degradative surface of the walls, which explains its longer persistence.

The SRES dispersed readily in water and had good suspsibility. On the other hand the WP of BHC was hardly possible to disperse in water and sedimanted rapidly from suspension. Even agitating the pumps frequently some 10-20% of the formulation was lost and had to be discarded before refilling the pump. The EC formulation of malathion was the easiest to use.

Apart from some minor skin irritation caused by exposure to BHC, no signs of intoxication were observed in members of the spray team, houseowners or domestic animals. As regard similar formulations studied before in relation to toxicity to mammals (Pinchin, 1983) the SRES is also expected to show a lower toxicity because the greater part of the insecticide is not available for immediate action since it is completely involved by the matrix. The polymer will only allow small amounts of the a.i. to migrate to the surface where it will act.

Of course there are also some disadvantages in the use of this kind of slow-release formulation. If the sprayman leaves the pump without use for more than 10 minutes the latex will polymerize in the nozzle, causing blockage. It is not difficult to clean it but it is time consuming. To overcome this problem the nozzles were put in a recipient with water while refilling the pumps or when the sprayman was preparing the house for treatment. The major disadvantage is that the greater part of the liquid used to prepare the formulation, i.e., the latex, must be available not far from the place where the applications are occurring. This is a limitation because this technique will be useful only in places where it is possible to go with a vehicle. With BHC the sprayman just carries with him some packets of 350g which will be dulited with the water he finds in the houses to be sprayed. Another problem is the preparation of the formulation in the field. Our research group is at present developing a formulation that could be used just mixing water, which will ease application. It will probably be maintained as an emulsifiable suspension, as concentrated in a.i. as possible, in which the particles are maintained in suspension in the liquid phase. This overcomes the problem of particle aggregation, easy to occur in a formulation of this kind.

In conclusion the results here expressed demonstrate a new possible alternative for Chagas' disease vector control, which does not rely on another new insecticide. Better than this, it enables the use of insecticides very toxic to triatomines but safe to mammals that were discarded in the past due to their lack of persistence. These can perhaps now find their place in the campaigns, creating many options of choice for the health authorities. Further development is now necessary to ease transport and preparation of the final product to be applied. It is also necessary to evaluate, in a larger scale field trial, the cost/effectiveness of products applied in this slow-release matrix when compared with commercially available insecticides and principally with BHC in the way it is used at present.

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