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International Journal of Zoology and Animal Biology
ISSN: 2639-216X

Effectiveness of Cimetrol SE 11.16 (Alfacypermethrin 4.65% + Pyriproxyfen 1.86% + Tetramethrin 4.65%) in *Aedes aegypti* and *Blatella germanica* control in Cuba

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Research Article

Volume 6 Issue 2

Received Date: March 22, 2023

Published Date: April 10, 2023

DOI: 10.23880/izab-16000460

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Abstract

In Cuba, insecticides to control *Aedes aegypti* mosquito and *Blatella germanica* cockroach has been frequently used with different formulations, such as emulsifiable concentrates, wettable powders, gels, microencapsulates and suspo-emulsions (SE): the latter is a type of formulation that combines the residuality of a suspension concentrate with the speed of effect of "oil in water" (EW) emulsions. The Cimetrol SE 11.16 formulation is composed of a mixture of two pyrethroid molecules with an insect growth regulator, providing the formulation with great residual power combined with eviction power, due to the mode of action of each one of them. In the following study, we evaluated the effectiveness of Cimetrol SE 11.16 in the control of *Ae. aegypti* through surface bioassays, and of *B. germanica* through residual treatment. The residual effect on tile, concrete and wood surfaces was evaluated for 10 weeks and fluctuated from the first weeks (but remained high > 80%). However, mortality on all surfaces remained above 80% until week 6. The highest mortalities occurred in plastic and metal during the 10 weeks (100%). To monitor the cockroach infestation rate, sticky traps (ERADIROACH) were used, which resulted in 95% reduction by the eighth week.

Keywords: *Aedes aegypti; Blatella germanica*; Cimetrol

Introduction

Aedes (S) aegypti (Linnaeus, 1762) is an effective vector of various arboviral diseases. Its greatest epidemiological importance is linked to its role as a transmitter of Yellow Fever, Dengue, Chikungunya and Zika [1,2]. The incidence of dengue has increased dramatically in the world. The majorities of cases are asymptomatic or mild and self-managed, so the actual number of dengue cases is not reported. Many cases are also misdiagnosed as other febrile illnesses [3].

The control of arboviral diseases depends exclusively on effective measures to combat the transmitting vector [4]. As a result of 1981epidemic in Cuba, the Program for *Aedes aegypti* Eradication and later the Program for *Ae. aegypti and Ae. albopictus* control were implemented which developed a whole series of measures focused on vector surveillance and control [5].

The application of insecticides with the aim of reducing mosquito populations always brings with it the generation of resistant individuals. In Cuba this is not an isolated phenomenon [6-8]. That is why other alternatives for vector control are investigated, in the short and medium term, such as obtaining new isolates of *Bacillus thuringensis* [9,10], the study of essential oils with insecticidal activity [11,12], the introduction of the sterile insect technique [13] in addition to interventions with other synthetic products such as growth inhibitors [14], However, chemical formulations continue being the most used and extended measure par excellence for this vector population control.

Of the known species of cockroaches, *B. germanica* is the species with the highest population development, the most distributed in the world and the one with the greatest contact with humans. This species proliferates rapidly because it has a short life cycle, in which the adult female is capable of producing between 4 and 8 oothecae with an average of 30 to 48 nymphs each. It is suggested that it is a cosmopolitan species, native to Asia and introduced to America from Europe [15].

Cockroaches are persistent household pests in urban areas worldwide of approximately 4 000 existing cockroaches' species. *B. germanica* (Linnaeus, 1767) "German cockroach" is the most abundant synanthropic species with a cosmopolitan distribution [15,16]. In addition to the inconvenience it causes, it affects the economy and is considered of great medical importance as it transmits innumerable pathogenic organisms such as viruses, fungi, helminths and bacteria; this species is also responsible for serious allergic diseases such as bronchial asthma and allergic rhinitis [17]. The presence of cockroaches in urban environments, such as day care centers, can cause serious problems in infants [17]. German cockroaches are heterogeneously distributed in the different environments they infect, and it is noted that chemical control has been used mainly for the control of this species [17].

The formulation of Cimetrol SE 11.16 is composed of (Alphacypermethrin 4.65% + pyriproxyfen 1.86% + tetramethrin 4.65%), this mixture of two pyrethroid molecules with an insect growth regulator, provides a great residual power combined with eviction power, due to the mode of action of each one of them. Alphacypermethrin and tetramethrin, like any pyrethroid, generate an alteration in the flow of sodium-potassium ions at the level of the neurons of the central nervous system of insects, initially producing nerve excitability, affecting both the peripheral and central nervous systems of insects, and later paralysis and death [16,17].

Pyriproxyfen is a growth regulator, belonging to the Pyridine chemical group, analogous to the action of the juvenile hormone that acts by competing and displacing it. In this way, a "false signal" is produced that determines the secretion of ecdysone, a molting-promoting hormone, accelerating the molting process thus generating an immature or juvenile stage that is not viable (cannot continue to develop). At the same time, the contact of pyriproxyfen with the females alters their reproductive capacity effecting their reproductive system, and together with this, their embryogenesis, that is, the eggs laid don not have the ability to develop an embryo inside, being non-viable eggs.

The objective of this study was to evaluate the efficacy of Cimetrol SE 11.16 formulated for *Ae. aegypti* and *B. germanica* control.

Materials and Methods

For the application of Cimetrol SE 11.16 formulation, a mixture was prepared at a rate of 5 ml/L of water, for a dose of 20-25 mg a.i./m2 to be distributed at a rate of 30-50 ml/m2. The application was made with the 1-gallon Guarany pre-compression sprayer. The equipment had 80-02 flat nozzles, which allows a mixing rate within the range recommended by the WHO of 760 ml/min ±15 ml. The spraying was carried out in vertical strips 75 cm wide, with an overlap of 5 cm, from top to bottom, keeping the tip of the sprinkler 45 cm from the surfaces to be treated to ensure the correct width of the strip following the WHO methodology [18].

After the treatment, two dwellings from the blocks treated intra- and extra-domiciliary and two control dwellings were used. Various surfaces were selected, such as, tile, wood, plastic, metal, etc. where the cones were placed.

The first bioassay was performed 24 hours after the surfaces were impregnated and weekly after the treatment. Batches of 20 females from 3 to 6 days after emergence were used from the population of *Ae. aegypti* Cárdenas, established in the insectarium of Varadero-based Mosquito Control Center as an exception, during the evaluation stage, for which all biological safety measures were adopted. Four replicates were evaluated for each type of surface. The exposed females remained in contact with the treated surfaces for one hour. After this time, they were extracted using a captor (glass exhauster) beginning with the controls and later the cones of the treated surfaces to avoid contaminating them. The mosquitoes were transferred to clean cups, which were covered with double mesh cloth placed on top and tied with an elastic band. The corresponding knockdown (KN =Knock Down) was recorded for each of the treated surfaces, including those used as control that were not exposed to the insecticide. A previously moistened piece of cotton was placed on the upper external part of each glass. Mortality was read 24 hours later. The test was repeated every 7 days for 10weeks, and it was discontinued when the mortality was less than 80%, according to the WHO criteria [19].

For each weekly bioassay, the change of place on each type of surface where the cones would be fixed was taken into account. It was not necessary to apply the Abbott, et al. [20] formula to correct the mortality of the bioassays, since it was less than 5% [19]. The temperature did not exceed 25ºC, and the relative humidity was > 50%.

To determine the cockroach infestation rates of the selected location before the application of the insecticide, sticky traps (ERADIROACH), carefully supplied by the manufacturer, of the formulated were used. Small ones were placed according to the infestation detected by visual inspection in the preferred sites of the species at a rate of 4 per 16 m^2. Traps were checked 48 hours after they were placed, and the number of specimens captured per unit and place of placement were counted. For the post-treatment surveys, the aforementioned methodology was followed. To carry out the treatment, 50 ml/5 liters of water, dose recommended by the manufacturer for high infestation in crawling insects (cockroaches, fleas, ants) were applied with the 1-gallon Guarany pre-compression sprayer.

The treatment was carried out in the dining room kitchen of a hotel, under the countertops, the shelves to store kitchen utensils, as well as the shelves where the different edible products are placed, and behind the refrigerator. After the treatment, weekly sampling was carried out using sticky traps during 8 weeks.

Results

After the intervention with Cimetrol SE 11.16, the residual effect on different surfaces treated post-treatment with *Ae. aegypti* was evaluated for 10 weeks. Figure 1A shows the high percentage of mortality obtained after that time. The residuality of tile followed by concrete and wood fluctuated from the first weeks (Figure 1A), but remained high (>80%) until week 6 for tile, concrete and wood until week 8. Mortality, on all surfaces remained above 80% until week 10. The highest mortality occurred on plastic and metal during the 10 weeks of the evaluation (Figure 1B). It is important to note that most of the water storage containers for human consumption are made of these materials.

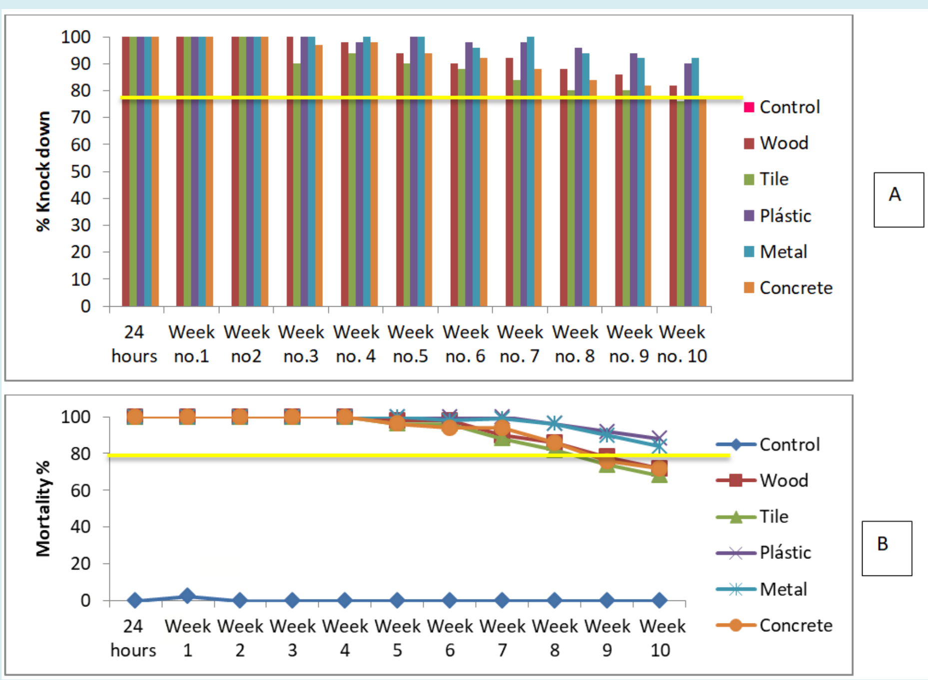

Figure 1: Knock down percentage (A) and mortality (B) obtained by exposing females from the Cárdenas population on surfaces impregnated in situ with Cimetrol SE 11.16 for 10 weeks post-treatment. The yellow line represents WHO criteria to discontinue the study (Knock down < 80%).

Table 1 shows the means of infestation and the percentages of reduction of *B. germanica* in the post-treatment surveys in the house where the treatment with Cimetrol SE 11.16 was carried out. In the data from the pre-treatment surveys, it is observed that the infestation rates were very high, so that with the first treatment carried out there was not a good reduction of these therefore, a second treatment had to be carried out, with which there was a reduction of infestation means and an increase in percent reduction compared to pretreatment.

Infestation Mean				
Weeks	**Adults**	**Nymphs**	**Total (average)**	**% of reduction**
pre-treatment	65	79	72	
Post- treatment				
1er treatment	34	40	37	48,6
2do treatment				
2	17	23	20	72,2
3	12	15	13,5	81,3
4	9	11	10	86
5	7	9	8	88,8
6	7	7	7	90
7	5	7	6	92
8	4	4	5	95

Table 1: Means of infestation and percentage of reduction of the population of *B. germanica* pre and post-treatment in the house treated with the insecticide Cimetrol SE 11.16 (Alfacypermethrin 4.65% + Pyriproxyfen 1.86% + Tetramethrin 4.65 %) at the dose of 50ml /5 liter of water.

Discussion

The applications of residual treatments have been generalized in America for the control of triatomines [21,22]. They are also used for the control of malaria and filaria worldwide [23,24], highlighting a growing interest in the implementation and generalization of this methodology for arbovirosis control [25].

Ae. aegypti adults normally rest indoors (endophilia), where they frequently and almost exclusively feed on human blood (anthropophilia) [26,27]. This explains why space fumigation outside the dwellings have little efficacy against this vector [28,29]. Indoor insecticide applications may have a more direct impact on resting adult mosquitoes [30]. This is particularly used during epidemics because it quickly kills adults that are presumably flying. It often happens that up to three applications are required to achieve maximum efficacy even if the durability is short [31].

Indoor application of residual insecticides can provide longer-term protection after a single application; however, the time spent can increase, since it is necessary to remove all the furniture and belongings of the dwellers from the house [31]. This reason makes the work more intense and less accepted by the community [32], which hinders its generalization for vector control specifically on *Ae. aegypti.* The effectiveness of a residual action intervention depends on several factors: a) the susceptibility of the vector mosquitoes to the sprayed insecticides, b) the type of formulation, the quality of the spray, the spray coverage, c) the nature of the surface and d) the cooperation of the inhabitants in not removing the spray from the surfaces through washing or painting [23,32-34] Regarding the formulation; Cimetrol SE 11.16, with few practical results published in the literature, is a potentiated suspension. Usually, this type of intervention is evaluated through cone tests [19] to determine the residuality in the different types of surface and thus the efficacy [34], although other methodologies could be followed [31].

According to some authors, these bioassays should ideally be carried out on impregnated surfaces in real human rooms, since bioassays under controlled conditions can show a longer residual effect [35]. In our study, using the cone methodology on treated surfaces in a house, a high percentage of mortality was obtained in mosquitoes exposed to metal and plastic surfaces for 10 weeks, followed by concrete, where mortality was above 90% from week 4 to 10. Dzib Florez, et al. [34] in tests carried out with *Ae. aegypti,* under controlled conditions with domestic sprays containing pyrethroids, durability lasted between 2 and 3 weeks. The wood and concrete surfaces evaluated with these sprays provided the longest residual time, results that partially coincide with ours.

In most studies, the mortality rates in the exposed groups are established as satisfactory when this indicator are greater than or equal to 80%, according to the criteria of Rodríguez, et al. [8]. In the case of the study carried out by Ibrahim, et al. [24], the knockdown and mortality rates at 24 hours were similar in the time intervals evaluated. In bioassays carried out by Corrêa, et al. [36], using deltamethrin on two types of surfaces, the mortality rates of *Anopheles (Nyssorhynchus) marajoara* remained above 80% for the 8 months of the experiment on painted wood and cement surfaces, mortality was higher for wood than for cement. In our study, the knockdown and mortality values at 24 hours remained similar until week 4. From week 6, mortality continued to be higher than 80% on most surfaces, except for metal and plastic, which remained on this indicator until the trial was discontinued at week 10. These results differ from studies by Ab Hamid, et al. [25] in the cement walls those that showed high mortality up to week 16.

The factors that may have influenced in our study, the low durability on some surfaces, may be from the smooth and poorly adherent texture of the tile to the porosity of the concrete. Some authors suggest that the rough and porous surface of the concrete walls are highly alkaline, tend to absorb the insecticide, degrade the active principle more quickly and reduce the residual effect [38-40], to which is incorporated the effect of temperatures and rainfall on the exterior walls of the houses. According to our previously exposed results, it is demonstrated that the Cimetrol SE 11.16 formulation is effective in controlling the *Ae. aegypti* mosquito.

Despite the fact that various intensive control activities against the German cockroach, both by government entities and by the affected population are being implemented, *B. germanica* is an important pest in public and medical health, and continues to infest buildings such as houses and restaurants at high and low population densities [41].

Many conventional insecticides are not effective in controlling massive infestations of *B. germanica,* due to its short life cycle of three to six months depending on the temperature. Therefore, it is very difficult to control this species in comparison with other species of cockroaches [17]. On the other hand, according to literature *B. germanica* shows resistance to insecticides such as Malathion and Propoxur [17]. In addition, this species shows a slight tolerance to Sumition and Tetramethorin [41]. Has found that field varieties of *B. germanica* show high to moderate resistance to cypermethrin. Our results show greater efficacy after 8 days of treatment. Previous studies have revealed that *B. germanica* massively infests kitchens in hospitals, apartments, hotels, private homes, and restaurants for breeding and feeding purposes, being able to visit other places to find its food [17,42]. These results were similar to ours, since higher densities of *B. germanica* were found in the kitchen.

Different methods have been used for the census of cockroaches such as visual counting and sticky traps. The visual count is carried out after 22:30, so the lights go out at 21:30 pm for one hour. Then the light is turned on and the cockroaches that are moving on the tables and feeding areas are observed and counted for 5 min. This method allows dividing cockroaches into three categories of infestation: high (>75), medium (25-75) and low (<25) density of cockroaches [41]. On the other hand, we propose to census cockroaches, by placing sticky traps in sufficient quantities close to their shelters to estimate the density and type of cockroach present.

Finally, our results indicate that the use of Cimetrol SE 11.16 formulation (Alfacypermethrin 4.65% + pyriproxyfen 1.86% + tetramethrin 4.65%) is recommended for the suppression of B*. germanica* population.

- **Acknowledgements**
  To Pelgar International for its Technical assistance and its logistical support.
- **Conflict of Interest Statement**
  The authors declare that they have no conflict of interest.
- **Contribution**
  All the authors contributed substantially to the concrescence of the manuscript.
- **Financing**
  No funding was available.

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