

## Effects of Lambdacyhalothrin Incorporated into 1, 4-Dichlorobenzene on Sand Fly and Mosquito Vectors in Endemic Areas of Kenya

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### ABSTRACT

No new public health insecticides have been developed for mainstream vector control in disease endemic countries for 30 years. Marigat study site is an area that is endemic for both cutaneous and visceral leishmaniasis while Mwea is a malaria endemic area. Both sand flies and mosquito collections were carried out in the study households before interventions and after interventions using the CDC light traps. Effects of lambdacyhalothrin incorporated into 1, 4-dichlorobenzene on sand fly and mosquito vectors were evaluated in three phases: Immediately after treatment, 2-3 months and after 6 months post treatment. Vector collections were carried out before and after interventions, they were then counted identified and recorded. The sand flies and mosquito densities decreased significantly when exposed to PCB/ICON combination as opposed to ICON and PCB alone. The mean numbers of sand flies and mosquitoes collected from houses with in PCB/ICON combination was less as compared to PCB and ICON independently. From the results, there was a synergistic effect observed when lambda-cyhalothrin (ICON®) and 1, 4-dichlorobenzene (PCB®) are used in combination as compared to their individual treatments. This indicates that combinations are more effective in controlling vectors of malaria and leishmaniasis diseases.

**Keywords:** Lambdacyhalothrin, 1, 4-dichlorobenzene, leishmaniasis, and malaria, sand flies, mosquitoes;

### INTRODUCTION

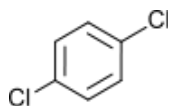
In recent years the use of environment friendly and easy biodegradable insecticides has received much attention for control of medically important arthropods. Vector borne diseases such as malaria and leishmaniasis still cause thousands of deaths and morbidity [1, 2]. The insecticide resistance in sand fly populations has been highlighted by Kishore et al. [3].

Lambdacyhalothrin (ICON®) is a synthetic pyrethroid insecticide that has been shown to be effective in killing mosquitoes and phlebotomine sand flies when used in low doses [4, 5, 6]. It has also been used for the control of intradomestic *Anopheles arabiensis* Patton in huts in South Africa [4]. It has no smell and has a long residual period of 6 months [4, 7] and unlike DDT it is not toxic to vertebrates [6, 5, 4, 8]. Unlike DDT no resistance has been reported for sand flies [9] and mosquitoes [8]. The

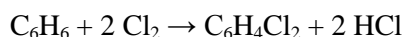
observed efficacy of lambdacyhalothrin in protecting people from bites of sand flies by studies carried out in Venezuela [10], its ready acceptance by users as was shown in Brazil [11], and its cost effectiveness make it a more useful insecticide for antimalarial and anti-leishmanial control.

1, 4-Dichlorobenzene (*para*-dichlorobenzene, *p*-DCB, PDB, 1, 4-dichlorobenzene) is an organic compound with the molecular formula C<sub>6</sub>H<sub>4</sub>Cl<sub>2</sub> and a structure shown below. This colourless solid has a strong sweet odour. It consists of two chlorine atoms substituted at opposing sites on a benzene ring. *p*-DCB is used as a pesticide and a deodorant, most famously in mothballs in which it is a replacement for the more traditional naphthalene ("National Pesticide Information Center - Mothballs Case Profile", 2009). *Para*-dichlorobenzene is also used as a precursor in the production of the polymer poly(*p*-phenylene sulfide) [12]

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PCB is produced by chlorination of benzene using ferric chloride as a catalyst.



The compound is purified by fractional crystallisation, taking advantage of its relatively high boiling point of 174°C and melting point of 53.5 °C. 1, 4-dichlorobenzene is poorly soluble in water (10.5mg/100ml at 20°C) and is not easily broken down by soil organisms. Like many hydrocarbons, paracide® is lipophilic and would accumulate in the fatty tissues. There is no direct evidence of carcinogenicity environmental protection agent (EPA). 1, 4-dichlorobenzene is registered by USA-EPA for water use at a concentration of 75µg per litre and also as a pesticide. There is no report of insecticidal resistance against 1, 4-dichlorobenzene in sand flies and mosquitoes in Kenya.

1,4-dichlorobenzene (Paracide®) when used as a deodorant and pesticide like lambdacyhalothrin lasts for six months. Incorporation of lambdacyhalothrin into 1, 4-dichlorobenzene under slow release basis will help not only to keep sand flies and mosquitoes away but also other household pests as well as freshening the houses. The use of the lambdacyhalothrin fortified with 1, 4-dichlorobenzene, which are cheap will help repel the two vectors especially in the areas they are sympatric. This kind of control method was evaluated to densities and hence feeding rates of the mosquitoes and sand flies in the laboratory and field.

The study determined the feeding success of mosquitoes and sand flies and compares the efficacy of lambdacyhalothrin fortified with 1, 4-dichlorobenzene in the control of endophilicphlebotomine sand flies and *Anopheles* mosquitoes.

### MATERIALS AND METHODS

This study was carried out in two study sites, Marigat and Mwea. Baringo lies 250 km North West of Nairobi and covers an area of approximately 10,000 km<sup>2</sup> and is located north of the Equator in Kenya's Rift Valley Province. The area is semi-arid with subtropical climate. Rainy seasons are from March to September with peaks in May and August. Annual rainfall is below 300 mm while temperatures range from 17-42°C. Natural vegetation in Marigat is

mainly composed of *Acacia* species either scattered or as forest in few cases, short bushes or patchy grassland. The ground is mostly bare soil or rocky with gullies in some areas. The Kenya government recently introduced *Prosopisjuliflora* to control desertification in the area which has changed the vegetation cover in the regions formerly devoid of vegetation. Rodent burrows are numerous in both vegetation covered and bare grounds. Termite mounds are common features in the area. There is a Perkerra irrigation scheme around Marigat that allows growth of various crops such as maize and vegetables. Animal husbandry is also practiced in the area whereby cattle, sheep and goats are kept.

Mwea a malaria endemic area that is not known to be endemic for leishmaniasis was used to test the efficacy of the repellent on malaria vectors, particularly *An.gambie* and *An. funestus*. Mwea is found in central Province, Kenya. Mwea Division is situated on the Eastern side of Mount.

Kenya at an altitude ranging between 1100 to 1350 metres above sea level. It is the centre of Mwea Rice Irrigation Scheme, a settlement scheme that produces 75% - 90% of the rice that is consumed in Kenya (NIB report). It covers an area of about 12,000 hectares. The division can be generally grouped into 2 distinct ecological settings, the low-lying irrigated rice paddies to the south and the elevated upland area to the north. Mwea Division has 3,270 families living in 60 villages [14].

In each of the study sites, 30 households separated between 100 metres each were selected. In the 30 experimental houses, treated disinfectant blocks were placed in all rooms where the inhabitants sleep and the kitchen was avoided because of smoke. Sand flies and mosquito collections were carried out in the study households before and after interventions. This was done using the CDC light traps Muirhead-Thomson [15].

Collections were carried out in houses for a minimum of 4 nights per month per area. CDC light traps were set in the houses at 1800hrs in the evening and cleared before 0800 hours the following day during the known high transmission season of malaria and leishmaniasis [4]. The caught vectors were knocked down using ice. Collections were carried out for a period of 2 years in all the study sites. All the mosquitoes and sand flies collected were preserved separately in collection cups. They were counted

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and the numbers were recorded awaiting identification.

### Data Management

Data were entered in a computer using MS excel and thereafter imported into STATA 9.2, (STACORP, TX USA) for analysis. Before the main analysis Fisher's exact tests were used to compare results for pre-interventions and post intervention. The average number of flies per trap (house) for each treatment was used as the units of analysis. Baseline data were compared with the intervention data using a paired *t* test. Data per treatment of sand flies and mosquitoes that fed/probed and on mortalities were compared student *t* test.

## RESULTS

### Effects of PCB/ICON Exposure on Mosquitoes in Mwea Study Site

There were a decreased number of mosquitoes after immediate exposure to ICON, PCB and PCB/ICON combination. The mean differences of mosquitoes trapped before and after immediate exposure to ICON, PCB and PCB/ICON combination were significantly different [( $P=0.0117$ ,  $67.8 \pm 24.893$ ,  $t=2.7237$ ), ( $P=0.0266$ ,  $52.8 \pm 23.74$ ,  $t=2.2235$ ), ( $P=0.0138$ ,  $64.9 \pm 24.74$ ,  $t=2.6229$ )] respectively.

Equally there was a significant reduction of mosquito densities after long term exposure (up to 6 months) to ICON ( $P=0.0232$ ,  $76.3 \pm 33.075$ ,  $t=2.3069$ ), PCB ( $P=0.0194$ ,  $66.2 \pm 27.4$ ,  $t=2.4158$ ) and PCB/ICON combination ( $P=0.0178$ ,  $68 \pm 27.5$ ,  $t=2.4685$ ) as shown in figure 1.

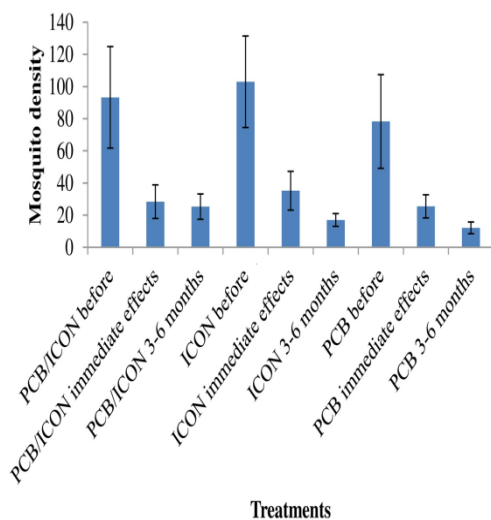


Figure1

### Effects of PCB/ICON Exposure on Sand flies in Mwea Study Site

There was a notable significant difference in sand fly density after immediate exposure with ICON alone ( $P=0.0032$ ,  $t=1.812461$ ) (Figure 2), but there was no significant difference in sand fly densities after immediate exposure with PCB and PCB/ICON combination ( $P>0.05$ ).

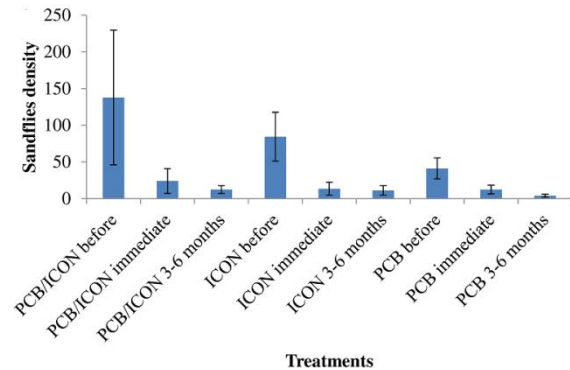


Figure2

There was significant decrease in sand fly densities before and after six months of treatment of the household with ICON ( $P=0.029007$ ,  $t=1.812461$ ,  $SEM \pm 25.9868$ ), PCB ( $P=0.024838$ ,  $t=1.812461$ ,  $SEM \pm 11.46322$ ) but the densities of sand fly were not comparable before and after treatment with the combination of PCB and ICON ( $P=0.113121$ ,  $t=1.833113$ ,  $SEM \pm 66.29991$ ). The decrease of sand fly populations following exposure to ICON, PCB and ICON/PCB is a good indication that all the trial insecticides can be used in their control.

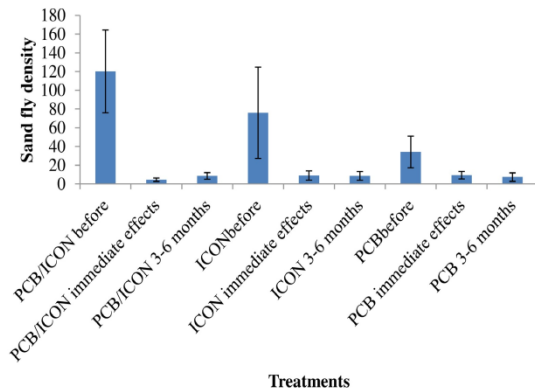
### Effects of PCB/ICON Combination Exposure to Sand flies in Baringo Site

There was no significant decrease in sand flies densities before and after immediate exposure with ICON ( $67 \pm 8.53$ ,  $t=1.3805$ ,  $P=0.1004$ ) and PCB ( $24.8 \pm 16.2$ ,  $t=1.5309$ ,  $P=0.0801$ ) as well as exposure after 6 months; ICON ( $67.4 \pm 48.0389$ ,  $t=1.4030$ ,  $P=0.0971$ ) and PCB ( $26.8 \pm 16.13$ ,  $t=1.6614$ ,  $P=0.0655$ ). However there was a significant decrease in sand fly population after treatment with PCB/ICON combination ( $115.6 \pm 42.98$ ,  $t=2.6894$ ,  $P=0.0124$ ) as shown in figure 3. Conversely there was a significant decrease in sandflies densities before and after treatment with PCB/ICON combination after exposure for 6 months ( $111.6 \pm 41.434$ ,  $t=2.6934$ ,  $P=0.0123$ ) (Figure 3).

In marigat site, baringo County, there was a significant difference in mosquito densities following immediate exposure to the ICON

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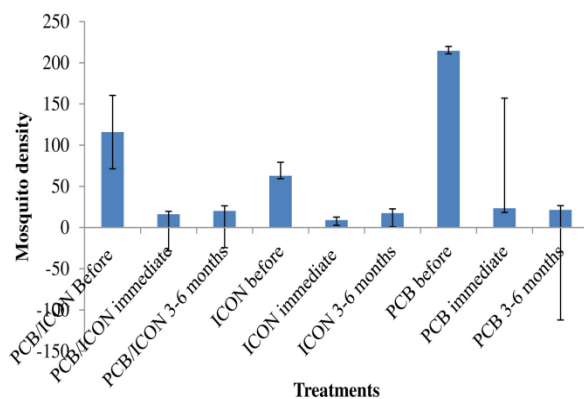
( $53.9 \pm 16987$ ,  $p=0.0057$ ) and PCB/ICON ( $99.7 \pm 42.057$ ,  $P=0.0209$ ) combination in their effectiveness in killing mosquitoes within 0-3 months (immediate effect), however there was no notable significant difference on exposure of mosquitoes to PCB alone ( $191.1 \pm 131.17$ ,  $P=0.0911$ ).



**Figure3**

### Efficacy of Insecticide Treatments on Mosquitoes over Time in Baringo County

The mosquito densities decreased significantly when exposed to ICON and PCB/ICON combination as opposed to PCB alone for 3-6 months period (figure 4). The differences in mosquito densities seen in collection from the houses which had ICON and the combination of ICON/PCB recorded a reduction as opposed to PCB alone shows that PCB alone cannot be effective alone when used for more than 3 months. Overall significance in reduction of mosquito densities after treatment with ICON ( $45.4 \pm 18.043$ ,  $P= 0.0165$ ) and PCB/ICON ( $95.7 \pm 43.147$ ,  $P= 0.0269$ ) was observed, however there was no significant difference when mosquitoes were exposed to PCB ( $193.3 \pm 131.94$ ,  $P= 0.0885$ ).



**Figure4**

## DISCUSSION

Survival of arthropod vectors is one of the most important components of transmission of a vector-borne pathogen [16]. Increased survival allows the vector to produce more offspring, to increase the chances of them becoming infected, to disperse over greater distances, to survive long enough to become infectious, and then to deliver more infective bites during the remainder of its lifetime.

PCB can be absorbed *via* ingestion, inhalation or dermal exposure. In mice, the oral route was found to be more rapid than inhalation in a study conducted with several human volunteers who were exposed to PDCB through inhalation [17]. As a result, small changes in survival rate cause large changes in the rate of pathogen transmission [18, 19, 20, 21]. In this study sandflies were exposed to ICON and PCB and their combination of the two for three months (immediate exposure) and compared to long time exposure (6 months). In mwea exposure of sand flies to ICON significantly reduced their densities unlike exposure to PCB and ICON/PCB combination. This study therefore suggests that ICON was effective on sandflies in Mwea site after exposure for a short period. However the Mwea study gave contrary findings with that of Baringo site, where ICON/PCB combination significantly reduced the sand fly densities as compared to ICON and PCB alone. It has been shown that temperature affects the activity of lambda-cyhalothrin. The efficacy of ICON and PCB can be attributed to geographical location due to Mwea and Baringo are two areas that have opposite climatic conditions from each other. This begs the need for further studies on how climatic conditions affect the efficacy of the two insecticides. Furthermore exposure of sandflies to ICON and PCB for 6 months, there was a significant decrease in the densities. In comparison with the three months exposure this study suggests that efficacy of ICON and PCB is dependent on the longevity of time exposure. There was a significant decrease in mosquito densities after exposure to ICON and ICON/PCB combination for three months, however no significant decrease in their densities when exposed to PCB. This observation was also seen in exposure for 6 months. It is therefore suggested that PCB alone cannot effectively kill mosquitoes but can synergize with ICON to be effective.



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In Mwea there was a significant decrease in mosquito densities after exposure to ICON, PCB and their combination both immediate and long term exposure. This indicates in Mwea site, PCB and ICON were able to kill mosquito individually as same as when they are combined, thus they didn't synergize each other. This is a peculiar finding that needs further investigations on geographical location, climatic differences and probably the genetic material of the mosquitoes in the two sites.

In the absence of pyrethroidspardichloro benzene which is cheaper, can be used to control mosquitoes and sandflies in malaria and leishmaniasis endemic regions in Kenya. In Marigat the weather conditions were very harsh with very high temperatures in dry season and impassable roads in wet season. This was forcing us to walk long distances to set traps and also collect traps.

### CONCLUSION

Lambdacyhalothrin and paradichlorobenzene alone or in combination can be used safely for effective control of indoor-feeding sand fly and mosquito vectors of human disease.

In the absence of pyrethroidspardichloro benzene which is cheaper, can be used to control mosquitoes and sandflies in malaria and leishmaniasis endemic regions in Kenya

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