Proceedings of the Eighth International Conference on Urban Pests
Gabi Müller, Reiner Pospischil and William H Robinson (editors) 2014
Printed by OOK-Press Kft., H-8200 Veszprém, Papái ut 37/a, Hungary

PIRIMIPHOS-METHYL 300CS, THE REINVENTION OF AN EFFECTIVE MOSQUITO ADULTICIDE

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Abstract Control of the Anopheline vectors is the most effective approach to malaria control. Reductions in mortality and morbidity from malaria have been achieved through the use of pyrethroid treated bed nets, pyrethroid resistant mosquitoes threaten the effectiveness of this valuable intervention. Insecticide resistance management (IRM) dictates that the target insect should not be continually exposed to the same class of insecticide to break the selection pressure for a resistance mechanism. Currently this cannot be achieved with the use of World Health Organisation's Pesticide Evaluation Scheme (WHOPES) approved Long Lasting Insecticide Treated bed Nets (LN). One approach to break the cycle of continual pyrethroid exposure is to employ indoor residual wall spraying (IRS) with a non-pyrethorid insecticide. IRS has been shown to be an effective method of controlling the Anopheline vectors of malaria. Pirimiphos-methyl is a WHOPES approved organophosphate insecticide which has been used as an emulsifiable concentrate formulation for IRS, and has been shown to control pyrethroid resistant mosquitoes. On some wall surfaces season long mosquito control may not be delivered. Supported by the Integrated Vector Control Consortium Syngenta developed a microencapsulated formulation of pirimiphos-methyl which provides control of *Anopheles* mosquitoes on typical wall surfaces. This paper discusses the biological behaviour of the microencapsulated formulation of the organophosphate insecticide, pirimiphos-methyl, developed specifically for use in mosquito vector control.
Key words Insecticide resistance management, bed nets, malaria

INTRODUCTION

It has been estimated that between 2001 and 2012 3.3 million deaths due to malaria were averted WHO (2013). The significant increase in vector control interventions has played a major role in this success, particularly the increased use of long lasting insecticide treated bed nets (LNs). However, during this period, the only LNs approved by WHOPES employed pyrethroid insecticides. Together with the continued use of pyrethroid insecticides for IRS, it is not surprising that pyrethroid resistance has developed in the Anopheline vectors of malaria, and is rapidly spreading throughout Africa (Ranson et al., 2011). As insecticide resistance continues to develop and spread, there is a real danger that these valuable vector control tools will be lost.

One approach to break the cycle of continual pyrethroid exposure is to employ IRS with a non-pyrethorid insecticide. IRS has been shown to be an effective method of controlling the Anopheline vectors of malaria (Mabaso et al., 2004) and to have an epidemiological impact on malaria (Pluess et al., 2010). One such non-pyrethroid, WHOPES approved, insecticide is the organophosphate pirimiphos-methyl, marketed by Syngenta under the trade name Actellic©.

Field studies have shown pirimiphos-methyl EC to have excellent residual insecticidal activity against Anopheline mosquitoes. Fuseini et al. (2011) found that pirimiphos-methyl EC effectively controlled *Anopheles gambiae* (Giles), identified as being resistant to pyrethroids, carbamates, dieldrin and DDT, when applied to concrete rendered walls at the end of the 15 week study period, in a trial in Ghana. Other studies, however, have found the pirimiphos-methyl EC formulation to be less robust in

some circumstances. Okumu et al. (2012) found that when sprayed on mud walls or palm ceilings, the insecticidal activity of these surfaces rapidly decayed over two months.

Particulate insecticide formulations are known provide greater residual activity than EC formulations against mosquitoes when applied in IRS (Hadaway et al., 1970). Much research has gone into the development of particulate formulations specifically for the residual control of insects of public health importance, as exemplified by the development of a microencapsulated formulation of lambda-cyhalothrin, described by Wege et al. (1999). Given that pirimiphos-methyl has WHOPES approval, and shows promising insecticidal activity against pyrethroid resistant *Anopheles* species, a project was undertaken, in partnership with the IVCC, to develop a particulate formulation based on capsule suspension technology, the results of which are reported in this paper.

MATERIALS AND METHODS

Experimental substrates were treated using a track-sprayer fitted with a TeeJet 8003 nozzle to apply the formulations, diluted in de-ionised water, with an application volume of 40 ml/m^2. Treated substrates were stored at 26°C under low light conditions until used.

Bioassays were undertaken with three day old non-blood fed adult female mosquitoes, either *Aedes aegypti* (L.), *Anopheles stephensi* (Liston) or *An. aconitus* (Dönitz) Mosquitoes were exposed to the treated surface for one hour using a 9 cm Petri dish exposure chamber, they were then removed from the treated surface and placed in a recovery cup with access to a 10% sucrose solution. Assessment of mortality was made 24 hours post exposure. Given the non-excito-repellent nature of pirimiphos-methyl, a one hour exposure period was considered representative of likely field exposure.

RESULTS AND DISCUSSION

Laboratory Bioassays

Microencapsulation produces a particulate formulation that facilitates tarsal pickup, and hence bioavailability, of the insecticide by the mosquitoes from treated surfaces. The study presented in Table 1 demonstrated that pirimiphos-methyl 300CS remained bioavailable on porous, unglazed ceramic tile for at least 24 weeks, and controlled both *Ae. aegypti* and *An. stephensi* adult females exposed to the treated surfaces. The study presented in Table 2 supports these findings, highlighting the benefit of a particulate formulation on highly porous cement and mud, compared with an EC formulation.

Microencapsulation also physically separates the insecticide from the external environment, offering a degree of protection from aggressive surfaces, such as cement and mud, as highlighted by the study presented in Table 3. The residual insecticidal activity of pirimiphos-methyl 300CS was degraded to a much less extent on cement, than a bendiocarb wettable powder formulation, remaining effective on both surfaces for a minimum of 24 weeks. The study presented in Table 4 supports these findings, demonstrating the robust activity of pirimiphos-methyl 300CS on highly porous mud blocks, originating from Cote d'Ivoire, providing at least four months residual mosquito control.

Table 1. Mortality of female *An. stephensi* and *Ae. agypti* exposed to pirimiphos-methyl CS 1 g/m^2 residual deposits on unglazed ceramic tile. WAT = weeks after treatment.

	24 h % mortality at WAT				
Formulation	**1**	**7**	**12**	**20**	**24**
An. stephensi P-methyl 300CS	100	100	100	100	97
Ae. aegypti P-methyl 300CS	100	100	90	100	100
An. stephensi Control	3	3	0	7	7
Ae. aegypti Control	3	0	7	3	0

Table 2. Mortality of female mosquitoes exposed to residual insecticides. Trial stopped at 24 weeks.

Species	Surface	Weeks of >80% mortality 24 h post exposure	
		Pirimiphos-methyl 500 EC	Pirimiphos-methyl 300CS
Ae. aegypti	Cement	8	24*
Ae. aegypti	Mud	12	24*
An. aconitus	Cement	12	24*
An. aconitus	Mud	8	24*

Field Data

These laboratory results are confirmed by field trials. Chanda et al. (2013) report a study that treated cement and mud walls in houses in Zambia with pirimiphos-methyl 300CS at a rate of 1g/m^2. WHO cone bioassays were undertaken at intervals with laboratory reared *An. gambiae*. Complete mortality of exposed mosquitoes was recorded on both cement and mud walls five months after application, with eight months of greater than 90% control recorded on cement. The authors concluded that pirimiphos-methyl 300CS could be recommended for intra-domiciliary spraying for malaria control, as part of an IRM strategy. In a study undertaken by Rowland et al. (2013), it was found that in experimental huts with cement lined walls, pirimiphos-methyl 300CS at 1g/m^2 provided greater than 80% control of free flying pyrethroid resistant *An. gambiae* for nine months. The authors also concluded that pirimiphos-methyl 300CS applied at 1g/m^2 showed great promise for providing prolonged control of pyrethroid resistant *An. gambiae*.

Table 3. Mortality of adult female *Ae. aegypti* exposed to residual insecticide formulations applied to cement or unglazed ceramic tile (UGT).

Formulation	g ai/m^2	Surface	24 hour % mortality at WAT						
			1	2	4	8	12	16	24
P-methyl 300CS	1	UGT	100	100	100	100	100	97	93
P-methyl 300CS	1	Cement	100	100	93	90	90	87	83
Bendiocarb 80WP	0.4	UGT	100	100	83	17	17	20	13
Bendiocarb 80WP	0.4	Cement	20	7	0	0	0	17	13
Control		UGT	0	0	3	0	0	0	0
Control		Cement	3	0	3	0	0	0	0

Table 4. Mortality of adult female *Ae. aegypti* exposed to residual insecticide formulations applied to mud blocks originating in Cote d'Ivoire.

Formulation	g ai/m^2	24 hour % mortality at WAT					
		1	2	4	8	12	16
Pirimiphos-methyl 300CS	1	100.0	90.0	93.3	100.0	100.0	96.7
Labmda-cyhalothrin 10CS	0.025	100.0	100.0	100.0	93.3	93.3	53.3
Control		0.0	0.0	0.0	3.3	6.7	6.7

Taken together, these findings demonstrate that the rational reformulation of an established insecticide can rejuvenate its utility for IRS. Sufficient residual insecticidal activity has been demonstrated by pirimiphos-methyl 300CS to warrant its inclusion in IRS programmes, and highlights its utility in IRM programmes, particularly where pyrethroid resistance is present in the target mosquito population.

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