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Determination of insecticidal effect (LCD_{50} and LCD_{90}) of organic fatty acids mixture (C8910+silicone) against malaria vectors

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Malaria vectors have acquired widespread resistance to several insecticides; thus, there is a critical need for the development of alternative insecticides for use in vector control programs. The mosquito toxicity of a novel insecticide/repellent consisting of medium-chain carbon fatty acids (C8910) was examined. Determination of LCD_{50} and LCD_{90} was made against six colony-reared *Anopheles* species using probit analysis on mortality data generated by Centers for Disease Control and Prevention bottle bioassays. Eight different concentrations of C8910+silicone oil provided an LCD_{50} ranging from 55.4 (44.2 to 65.9) in *Anopheles minimus* to 132.6 (92.8 to 301.3) in *Anopheles dirus*. Similarly, LCD_{90} varied from 138.5 (107.9 to 207.9) to 1228.8 (449.8 to 21400), respectively. Further development of C8910 and similar compounds could provide vector control specialists novel, environmentally-safe insecticides for controlling insect disease vectors.

Key words: LCD_{50}, LCD_{90}, bottle bioassay, C8910, silicone, malaria, *Anopheles*.

INTRODUCTION

There is an increasing need for alternative insecticides and repellents to control disease-transmitting arthropods. The lack of available, novel insecticide classes for vector control has left experts with a limited set of chemicals to manage insecticide resistance. The emergence of vector resistance to insecticides currently deployed in malaria control programs, for example, can severely impact the effectiveness of principle interventions such as indoor residual spraying (IRS) and long-lasting insecticide-treated bed nets (Ochomo et al., 2013). Since the introduction of synthetic pyrethroids more than 30 years ago, no new mosquito adulticide classes have been

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approved for vector control by the World Health Organization (WHO) (Nauen, 2007). Because of this, compounds unrelated to the four classes (that is, organochlorines, organophosphates, carbamates, and pyrethroids) need to be investigated.

Research using plant essential oils and animal by-products as alternative compounds for arthropod control and repellency is growing (Isman, 2006; Chansang and Mulla, 2008; Hieu et al., 2010; Mng'ong'o, 2011). Plant oils and fatty acids are common in nature and have been shown to provide insecticidal or repellency effects against a variety of arthropods (Dolan et al., 2007; Chansang, 2008; Mullens et al., 2009; Hieu et al., 2010; Cantrell et al., 2011; Ali et al., 2012). C8910, a mixture of medium-chain octanoic (CH3(CH2)6COOH), nonanoic (CH3(CH2)7COOH) and decanoic (CH3(CH2)8COOH) acids in equal parts, discovered and developed by Stratacor, Inc., (Richmond, CA), has shown promise as both an insecticide and repellent (at higher doses) when formulated appropriately with carriers such as silicone oil or kaolin clay (Reifenrath, 2001). The average molecular masses of the three fatty acids (C8 = 144.2; C9 = 158.2; C10 = 172.3 g/mol) are less than half of dichloro-diphenyltrichloroethane (DDT) (=354 g/mol); thus, provide more than twice the number of fatty acid molecules compared to the same weight of DDT for example. Octanoic and decanoic acids are derived from palm kernel oil or coconut oil and nonanoic acid is derived from tallow; all of these products are inexpensive commodity chemicals. These fatty acids have been approved by the United States Food and Drug Administration (US FDA) as food additives in the U.S. since 1965 and are categorized as "Generally Recognized as Safe" (Reifenrath, 2001). The combination of these acids has shown to have selective repellent and/or toxic effect against mosquitoes and a variety of flies (Mullens et al., 2009; Reifenrath, 2006). Whereas, spiders, bumble bees, honey bees, and wasps are relatively insensitive (Reifenrath, 2001).

C8910 has shown repellency against house flies, biting flies, ticks, ants, sand flies, and mosquitoes [*Aedes aegypti* (L.)] (Reifenrath, 2006); however, no formal studies have been conducted to determine effective concentrations and insecticidal effects of C8910 against malaria vectors. In order to begin to determine an effective concentration of C8910 comparable to WHO Pesticide Evaluation Scheme (WHOPES) approved insecticides, the Centers for Disease Control and Prevention (CDC) bottle bioassay procedure was used to determine the LCD_{50} and LCD_{90} of this novel insecticide/repellent against six colony-reared, susceptible (to all insecticide classes) *Anopheles* species (*Anopheles dirus* Peyton and Harrison, *Anopheles farauti* Laveran, *Anopheles freeborni* Aitken, *Anopheles gambiae* Giles, *Anopheles minimus* Theobald, and *Anopheles stephensi*) representing species known from different geographical regions (Southeast Asia, South Pacific, North America, Africa, Southeast Asia/India, and India/Middle East, respectively). The primary objectives of this study were to determine the insecticidal effects, if any, against male and female *Anopheles* species and to establish baseline effective concentration data that can be used to further develop C8910 for controlling malaria vectors.

MATERIALS AND METHODS

Bottle bioassays

Insecticide susceptibility tests were performed at CDC Atlanta, GA using the CDC bottle bioassay under normal room conditions (23° C; RH ~50%) following protocols established by Brogdon and Chan (2010). Bottle bioassays were used to evaluate a range of concentrations to determine an effective concentration of C8910. Dose-fixing concentrations ranging from 15 to 120 µg C8910/bottle (250 ml glass Wheaton bottle; inside surface area = 370 cm^2) were used to compile mortality data. An initial stock solution of 10 mg (= 10.7 µl) of 15% C8910 + 85% silicone oil (silicone oil is a benign carrier and used with acetone allowed the C8910 to adequately treat and dry on glass bottles) in 100 ml acetone (carrier and drying agent) was made and provided a concentration (= dose) of 15 µg C8910 + silicone/bottle. Additional concentrations of 30, 45, 60, 75, 90, 105, and 120 µg C8910 + silicone/bottle were sequentially made after bioassays using lower concentrations of C8910 indicated mortality was not achieved. Brogdon and Chan (2010) recommend that it is best to align the dose so that 100% of mosquitoes are dead by 1 h or less. For the purposes of this study, we used a relatively low concentration of C8910 (15% C8910/85% silicone oil) tested previously (Reifenrath, 2001, 2006; Mullen et al., 2009) and conducted mortality counts up to 2 h. In order to provide comparative results to other WHOPES-approved insecticides, mortality data for the 30 min time interval (Brogdon and Chan, 2010) were used for LCD_{50}/LCD_{90} determination. Dose-fixing followed the procedures recommended by Robertson et al. (2007). Specifically, it is recommended that for estimation of LCD_{50} and LCD_{90}, a minimum of 4 to 5 doses using at least 200 test insects per dose are required. All C8910 + silicone/acetone stock solutions were stored at room temperature in a dark cabinet.

1 ml of stock solution for each concentration was deposited in each bottle to coat the inside surface and was allowed to air dry for approximately 24 h. One ml of acetone was used to treat the inside of the control bottle. Four treated bottles and one control bottle were used for each assay and each assay was considered one replicate. A total of five replicates (= bioassay rounds) for each concentration were performed. Replicates were not all performed on the same day. When coating/treating the inside surface of the bottles, bottles were slowly turned and rolled with the cap on to evenly treat the inside surface of the bottle and cap, and were checked a few minutes later and rolled again to make sure no 'puddling' occurred on the bottom of the bottle (doing this allowed for more thorough drying). Bottles were placed on their sides with caps off and left to dry overnight. Drying the bottles overnight ensured that the C8910/acetone mixture was dry before introducing mosquitoes and may have resulted in loss of volatiles, thus providing a conservative protocol.

Two to five day old, colony-reared *Anopheles* species (susceptible to all insecticide classes) were introduced to bottles and observed for up to 2 h with mortality counts made at 15 min intervals.

Table 1. LCD_{50} and LCD_{90} (C8910+silicone oil /bottle) of *Anopheles* sp. tested after 30 min exposure.

Species	LCD_{50}	Upper / Lower	LCD_{90}	Upper / Lower	Slope±SEM
An. dirus	132.592	301.263 / 92.889	1228.8	214.00 / 449.80	1.325±0.088
An. farauti	118.170	192.867 / 100.074	243.855	1249.959 / 164.114	4.073±0.273
An. freeborni	119.867	162.566 / 98.495	628.577	1599.870 / 372.223	1.781±0.101
An. gambiae	91.762	110.020 / 79.852	242.266	424.510 / 178.755	3.040±0.130
An. minimus	55.444	65.916 / 45.167	138.475	216.910 / 107.891	3.224±0.110
An. stephensi	112.576	212.715 / 86.986	329.757	2472.405 / 186.821	2.746±0.131

The upper and lower 95% confidence limits are also shown (Statistical analysis by PoloPlus 2.0). *An* = *Anopheles.*

The six species tested herein have been in colony at their current location (CDC, Roybal Campus, Atlanta, GA) since 2010; overall age of colonies and susceptibility testing history was not determined. Mosquitoes were randomly aspirated out of rearing containers and gently aspirated into bottles, and no attempt was made to separate (or count) males from females. Because mosquitoes were two to five days old, a reasonable assumption can be made that approximately 50% of each sex was represented in each test bottle and on average for all bioassay rounds. Approximately 15 to 25 mosquitoes were introduced to each bottle and the timer was started once all five bottles had a mosquito population. For counting purposes during assays, a mosquito was considered dead if it was unable to stand (Brogdon and Chan, 2010). During some of these assays, a few mosquitoes at lower concentrations would recover to a certain degree only to eventually die. These individuals were counted as alive at said time interval if they appeared to revive. To ensure a mosquito counted as dead at earlier time intervals did not recover fully, assays were conducted up to two hours. There was no category for moribund individuals. The bottle was tapped a few times before a final determination of dead or alive was made.

Determination of LCD_{50} and LCD_{90}

Percent mortalities, obtained for each concentration at 30 min, were plotted in a log-probit graphic using Polo-plus 2.0 (LeOra Software Company®, Petaluma, California; 2005). Percent mortalities and LCD_{50}/LCD_{90} analyses were calculated by combining the total individuals and number of individuals (assuming each sex was represented equally) that responded (= died) during each assay (that is, total individuals and total that responded in each bottle were analyzed using the aggregate of the four treated bottles per assay). Control totals were entered into Polo-plus as the aggregate of the five replicates for all eight concentrations. Parameters for data files analyzed by Polo-plus were as follows: probit model, natural response, and concentrations converted to logarithms. The LCD_{50} and LCD_{90} were then obtained together with 95% confidence upper and lower limits.

RESULTS

LCD_{50} and LCD_{90} and percent mortality

The C8910 + silicone formulation evaluated herein did not provide significant mortality at the concentrations tested; however, percent mortalities do increase over time and at higher concentrations. Eight different concentrations of C8910 + silicone oil provided an LCD_{50} ranging from 55.4 (44.2 to 65.9) in *An. minimus* to 132.6 (92.8 to 301.3) in *An. dirus*. Similarly, LCD_{90} varied from 138.5 (107.9 to 207.9) to 1228.8 (449.8 to 21400), respectively (Table 1). C8910 worked best against *An. minimus* and *An. gambiae*; both showed lower values of $LCD_{50/90}$ accompanied by narrow 95% CI when compared to $LCD_{50/90}$ estimates for the other four vector species tested. *Anopheles dirus*, *An. farauti*, *An. stephensi* and *An. freeborni* showed higher values of $LCD_{50/90}$. Mortality percentages at 30 min after being exposed to the higher C8910 doses was close to 50% in *An. dirus*, *An. freeborni*, *An. gambiae*, and *An. stephensi*. PoloPlus

Table 2. Average percent mortality of *An. dirus* (up to 120 min) in bottles treated with C8910+silicone oil.

Concentration (µg/bottle)	15	30	45	60	75	90	105	120
15 min	3.8	5.8	10.4	7.6	22.0	26.0	22.0	34.8
30 min	17.0	13.6	24.2	31.6	43.2	44.6	38.6	54.0
45 min	31.0	22.2	33.0	48.0	57.2	60.4	51.6	70.3
60 min	37.2	31.6	44.8	56.8	67.8	74.0	65.0	79.3
75 min	46.6	42.8	58.6	64.0	76.8	80.2	73.4	85.9
90 min	49.6	48.0	66.8	70.8	85.0	86.2	81.4	88.5
105 min	60.0	56.4	73.4	74.4	86.8	90.0	88.6	91.2
120 min	63.4	63.8	76.0	79.6	89.8	92.8	90.4	92.8
Control (at 120 min)	1.0	1.7	1.9	0	0	0	1.0	0.0
N	5	5	5	5	5	5	5	5

N =Total number of assays (1 assay=4 treated bottles and 1 control bottle).

Table 3. Average percent mortality of *An. farauti* (up to 120 min) in bottles treated with C8910+silicone oil.

Concentration (µg/bottle)	15	30	45	60	75	90	105	120
15 min	1.0	0.8	3.2	3.4	11.6	16.6	19.8	45.2
30 min	1.8	3.0	8.4	11.8	22.2	27.4	32.6	68.2
45 min	4.6	8.2	13.0	17.8	20.4	44.4	44.6	81.1
60 min	7.0	12.8	18.6	23.0	36.0	52.2	57.0	86.1
75 min	9.8	15.6	22.4	31.4	44.4	64.0	70.4	88.5
90 min	11.6	20.0	25.6	36.4	51.4	72.4	80.0	92.0
105 min	16.0	24.4	31.0	43.8	60.6	80.0	88.4	93.4
120 min	19.6	31.0	35.4	51.8	67.2	86.4	92.4	96.9
Control (at 120 min)	1	2.7	2.8	2.2	0.9	0	3.4	4.2
N	5	5	5	5	5	5	5	5

N=Total number of assays (1 assay=4 treated bottles and 1 control bottle).

regression lines showing percent response at 30 min for each species are included in Figures 1 to 6. Tables 2 to 7 show percent mortalities for each concentration at each time interval up to 120 min.

DISCUSSION

We evaluated a relatively low concentration C8910 formulation here to mirror previous studies. Mortality percentages (Tables 2 to 7) show that the relatively low concentration of C8910 used for these bioassays took longer than 30 min to provide greater than 90% mortality (for most species this was not achieved until 105 min or longer); however, PoloPlus software was able to predict LCD_{90} for test subjects (Table 1), showing that higher concentrations of C8910 + silicone is required to achieve LCD_{90}. This study provides and initial attempt to determine the insecticidal effects of one C8910 formulation; higher concentrations should be evaluated to demonstrate stronger C8910 efficacy. The senior author of this work has noted that pure C8910 (33% of each carbon) will incapacitate colony-reared *An. gambiae* within 5 min and kill all mosquitoes in test bottles by 30 min at concentrations of 500 µg C8910/bottle (unpublished data). Further tests against wild *Anopheles* populations are required, as colony strains may have reduced vigor. Concentrations of C8910 required for sufficient control of wild populations may be higher than those observed or predicted by PoloPlus herein. While we tested here both male and female mosquitoes to determine if C8910 + silicone demonstrated any sex-linked susceptibility differences, it is recommended that future studies use females only or sexes are tested separately; however, we did not note any differences in overall mortality between male and females during testing. Aïzoun et al. (2014) conducted CDC bottle bioassays using both sexes and noted that even though male *An. gambiae* were smaller

Table 4. Average percent mortality of *An. freeborni* (up to 120 min) in bottles treated with C8910+silicone oil.

Concentration (µg/bottle)	15	30	45	60	75	90	105	120
15 min	0.9	7.4	9.6	16.4	21.1	23.8	40.6	34.8
30 min	5.6	15.2	23.5	29.5	35.1	33.1	56.4	52.9
45 min	9.2	23.0	32.2	39.2	41.2	40.5	68.6	74.5
60 min	13.7	29.6	37.7	43.5	49.9	51.5	74.9	75.8
75 min	16.2	38.4	42.2	47.3	57.1	57.4	80.3	81.3
90 min	19.9	42.3	48.0	53.8	63.1	64.7	81.7	84.8
105 min	25.0	47.0	52.3	57.4	68.7	68.6	83.5	85.7
120 min	27.5	49.5	53.9	60.2	71.5	71.6	85.4	89.0
Control (at 120 min)	0.87	5.8	6.1	0	2.8	1	1	4
N	5	5	5	5	5	5	5	5

N=Total number of assays (1 assay=4 treated bottles and 1 control bottle)

Table 5. Average percent mortality of *An. gambiae* (up to 120 min) in bottles treated with C8910+silicone oil.

Concentration (µg/bottle)	15	30	45	60	75	90	105	120
15 min	0.0	0.6	7.9	23.7	19.3	33.7	41.5	42.0
30 min	0.0	3.1	23.8	35.3	38.2	54.5	55.8	58.0
45 min	1.1	6.3	32.6	45.0	46.7	67.7	67.9	65.0
60 min	3.6	11.8	40.3	52.2	53.2	73.7	71.8	72.8
75 min	5.2	14.9	44.0	56.0	55.9	78.1	76.0	80.6
90 min	7.5	18.6	46.2	59.8	58.7	80.6	77.9	83.5
105 min	8.8	21.0	47.9	60.8	60.1	81.6	82.4	89.3
120 min	45.6	23.9	51.9	62.5	63.1	84.4	85.3	92.9
Control (at 120 min)	3.6	8.6	2.8	1	2.1	5.0	2.8	12.1
N	5	5	5	5	5	5	5	5

N=Total number of assays (1 assay=4 treated bottles and 1 control bottle).

Table 6. Average percent mortality of *An. minimus* (up to 120 min) in bottles treated with C8910+silicone oil.

Concentration (µg/bottle)	15	30	45	60	75	90	105	120
15 min	0.0	2.2	19.7	38.6	50.0	49.0	58.1	69.4
30 min	1.2	13.5	47.6	63.6	72.1	68.4	72.7	89.1
45 min	5.9	25.5	58.5	72.5	83.4	75.5	78.8	94.1
60 min	8.3	32.9	62.7	80.2	86.7	82.0	84.9	96.2
75 min	9.6	40.5	64.4	82.3	92.4	86.5	89.7	98.2
90 min	10.0	46.7	69.6	83.7	94.6	91.5	91.2	98.4
105 min	13.6	50.3	74.9	83.9	96.3	93.4	92.6	98.6
120 min	15.3	53.8	79.8	86.0	97.8	95.6	92.8	99.3
Control (at 120 min)	0.0	0.0	3.0	0	2.0	0.0	0.9	0.0
N	5	5	5	5	5	5	5	5

N=Total number of assays (1 assay=4 treated bottles and 1 control bottle).

smaller and more fragile in appearance, there was no difference in susceptibility to permethrin. C8910's effect is fairly rapid on both sexes (within minutes of initial exposure, especially at higher concentrations), and the first signs of effect include rapid wing beats with individuals making only brief flights or hovering close to the bottom of the bottle. Time to death (that is, individuals without any movement) may take several hours, especially when

Table 7. Average percent mortality of *An. stephensi* (up to 120 min) in bottles treated with C8910+silicone oil.

Concentration (µg/bottle)	15	30	45	60	75	90	105	120
15 min	0.4	0.7	0.9	13.8	18.1	16.8	31.7	29.2
30 min	0.9	3.6	7.9	29.3	49.7	37.0	56.8	53.6
45 min	1.5	7.5	18.6	52.8	59.8	52.1	74.8	66.8
60 min	3.4	13.4	25.2	61.7	74.2	65.9	84.4	78.2
75 min	10.3	21.4	34.3	68.4	82.4	74.0	87.5	84.5
90 min	14.3	26.9	44.7	75.1	86.7	79.8	90.8	88.7
105 min	16.7	32.0	48.8	80.1	89.3	83.3	94.4	91.4
120 min	17.9	40.1	52.4	83.0	90.7	87.3	94.6	94.2
Control (at 120 min)	2.0	0.8	2.7	0.8	0	0	2.8	0.8
N	5	5	5	5	5	5	5	5

N=Total number of assays (1 assay=4 treated bottles and 1 control bottle).

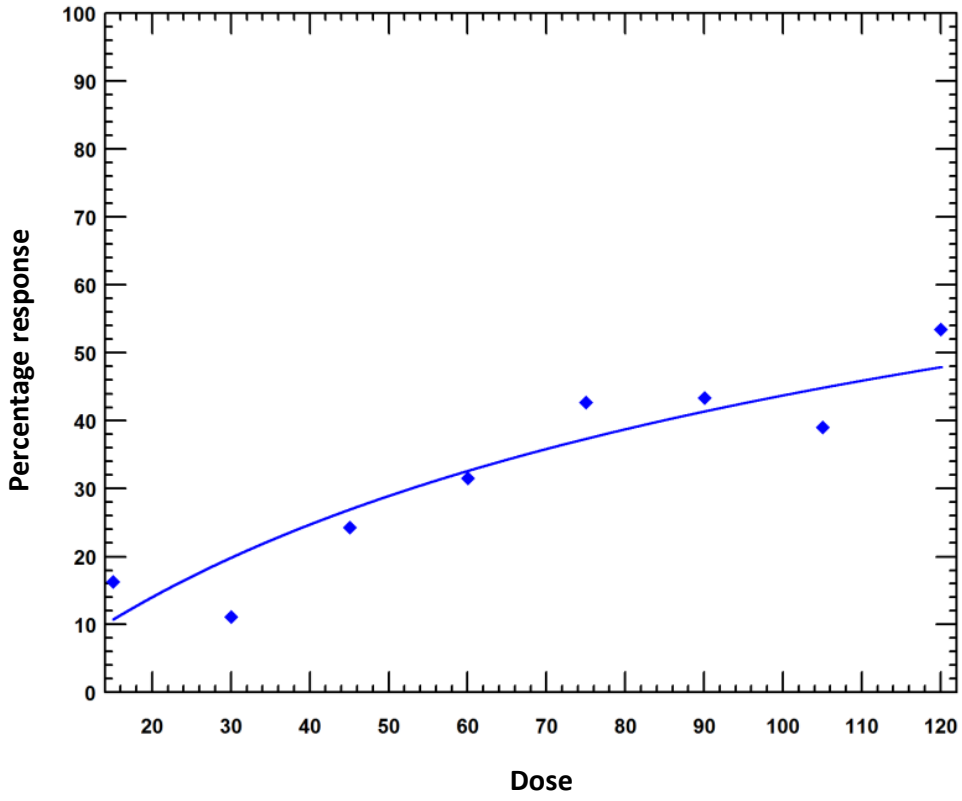

Figure 1. PoloPlus regression line showing percent response (= mortality) of *An. dirus* to C8910+silicone oil at 30 min.

exposed to the lower concentrations tested here. Several individuals were routinely observed attempting to fly after appearing 'dead' when the bottle was tapped/disturbed. Mosquitoes tested against the concentrations used during this study appeared to have an extended moribund period between knockdown and death but do eventually die as no individuals in treated bottles were alive 24 h post exposure. At higher concentrations of C8910, individuals were incapacitated at within 5 to 10 min following exposure.

C8910 in its basic form is an oily substance with a slight coconut odor, similar to sun tan lotion products.

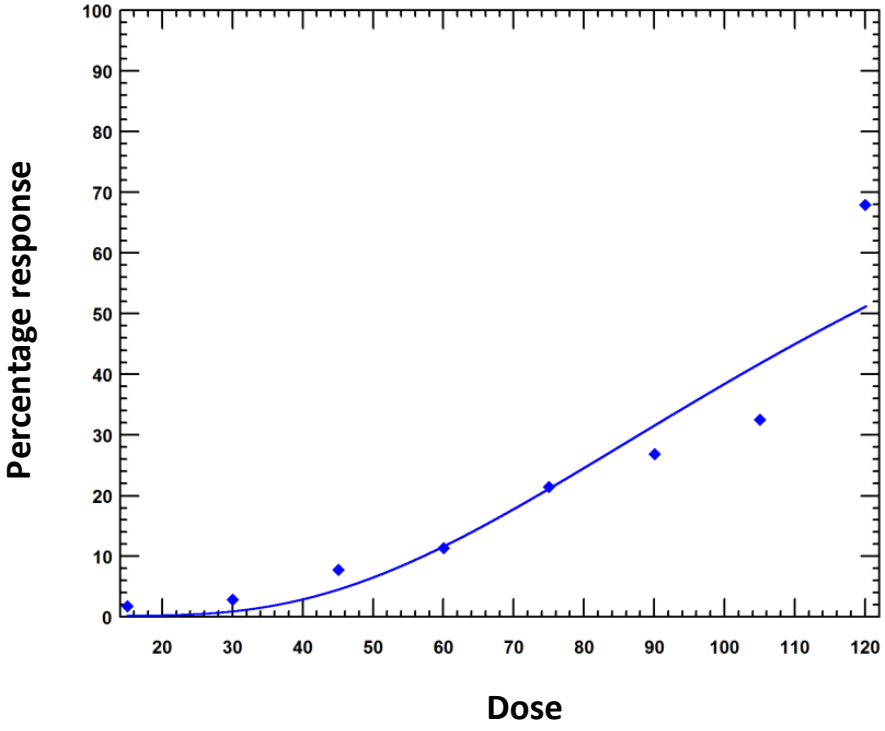

Figure 2. PoloPlus regression line showing percent response (=mortality) of *An. farauti* to C8910+silicone oil at 30 min

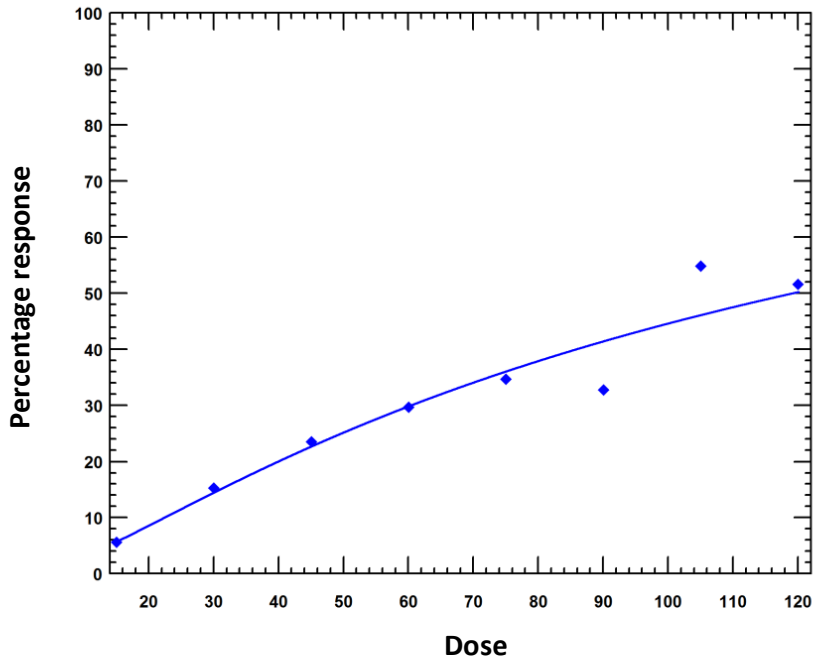

Figure 3. PoloPlus regression line showing percent response (=mortality) of *An. freeborni* to C8910+silicone oil at 30 min.

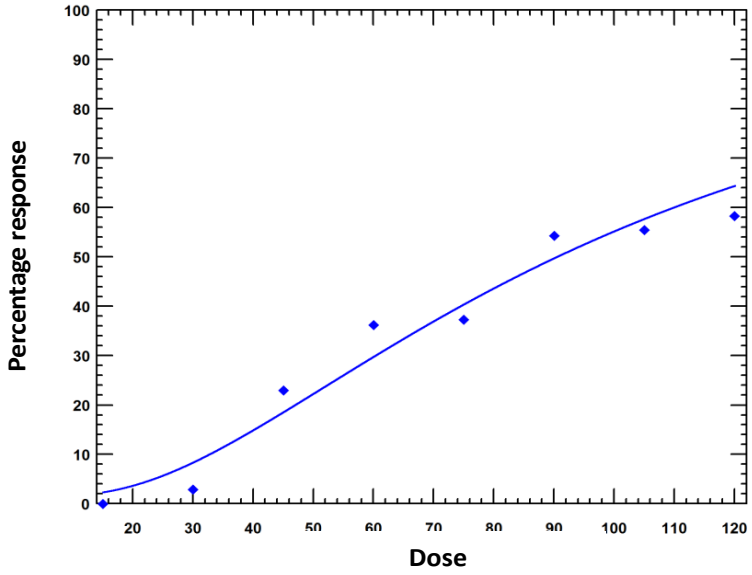

Figure 4. PoloPlus regression line showing percent response (=mortality) of *An. gambiae* to C8910+silicone oil at 30 min.

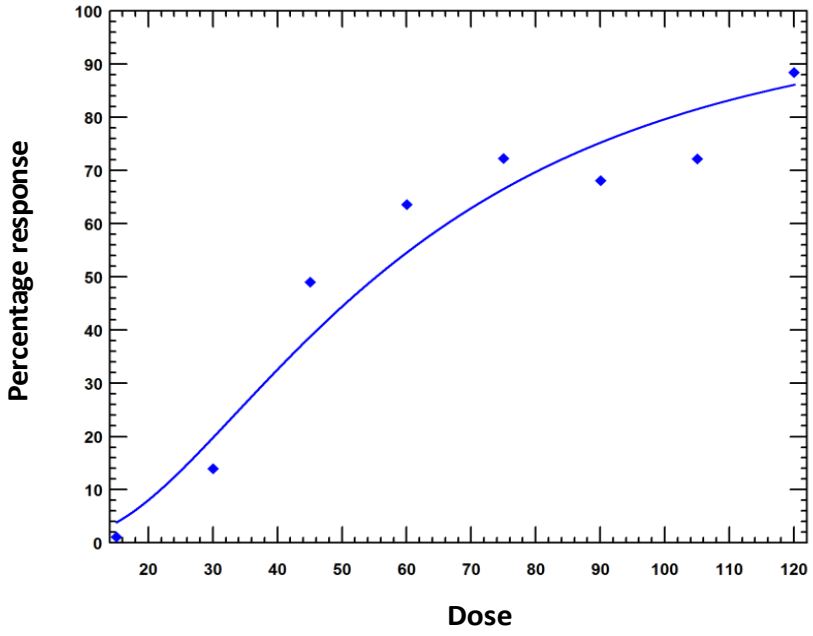

Figure 5. PoloPlus regression line showing percent response (=mortality) of *An. minimus* to C8910 at 30 min.

There is no apparent degradation of efficacy when C8910 is stored at room temperature for long periods of time (Dunford and Reifenrath, personal observations). However, further laboratory studies as well as field studies will be required to evaluate the residual efficacy of C8910. Because the fatty acids are semi-volatile organic compounds, it is thought that controlled release of the compounds would prolong their residual activity. Preliminary bioavailability evaluations using microencapsulated C8910 against *Ae. aegypti*, *Musca domestica* L.,

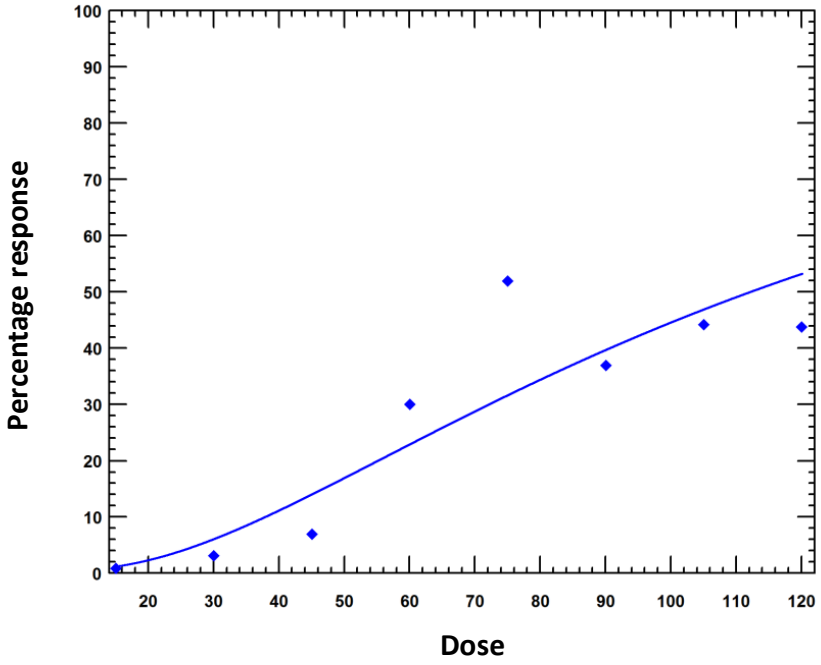

Figure 6. PoloPlus regression line showing percent response (=mortality) of *An. stephensi* to C8910+silicone oil at 30 min.

and *Blatella germanica* (L.) on treated filter paper showed significant mortality against *Ae. aegypti* at doses of 43.1 µg/cm^2 at 24 h, while house flies (431 µg/cm^2) and cockroaches were more resistant to the encapsulated C8910 (Reifenrath, unpublished data). Residual studies using controlled release C8910 formulations need to be further addressed.

The fatty acids comprising C8910 have been approved by the US FDA as food additives, suggesting they have low mammalian toxicity, an important quality for novel insecticides and probability they will pass current EPA (Environmental Protection Agency) regulatory statutes. Environmentally, the fatty acids are relatively benign, with low toxicity to bees and other beneficial insects (Reifenrath, 2001); however, this should be investigated further. When comparing our results with other WHOPES-approved insecticides against *Anopheles* species, concentrations of the C8910 formulation used herein required roughly 11 to 98 times (various pyrethroids) to 1.5 to 12 times (DDT) the diagnostic doses listed in Brogdon and Chan (2010) to achieve comparable mortality percentages; however, higher concentrations should be tested and may prove comparable to other insecticides. An alternative testing method, such as the WHO tube assay, should also be used to further determine if mosquitoes die after initial exposure and knockdown. Further development of C8910 formulations and associated production costs should be compared to traditional insecticides if products containing C8910 are used in the field for IRS (indoor residual spray) and/or treating bed nets.

C8910 is also being further developed for repellency attributes. It can be formulated for direct use on the skin, and topical formulations are being advanced for livestock use in the U.S. and for human use in South Africa. The minimum effective dose (MED) for C8910 to repel mosquitoes is estimated at a surface dose of 25 µg/cm^2, which is well above the LCD_{90} for all *Anopheles* species tested in Table 1. Since toxicity is dependent on contact, higher doses typically used for topical repellency (for example, 300 µg/cm^2) may exert mosquito toxicity only after the repellent dose decays below the MED. The repellency aspect of C8910 may not only provide a novel topical repellent, but it may also be a viable synergist to enhance other chemicals currently being used on treated bed nets. Synergistic interactions between insecticides and repellents have been shown to increase the residual life of impregnated materials and improve the control of pyrethroid-resistant mosquitoes (Pennetier et al., 2007). Pennetier et al. (2007) demonstrated a significant increase in residual efficacy by combining the repellents deet and KBR 3023 with pirimiphos methyl against *An. gambiae*. An earlier study also suggested a significantly higher efficacy was attributed to the combination of deet

with propoxur against pyrethroid-resistant *Ae. Aegypti* (Pennetier, 2005).

At present, the mode of action for C8910 has not been investigated, although preliminary studies suggest it is a respiratory inhibitor. The saturated fatty acids are seemingly simple organic compounds but have complex biological effects (Rioux and Legrand, 2007). Fatty acids have been shown to decrease respiratory activity and to uncouple oxidation from phosphorylation in isolated tissue preparations (Scholefield, 1963). Respiratory inhibition increased 2.5 fold for each carbon atom increase in chain length up to a maximum of 12 carbons (lauric acid). A further increase in carbon chain length results in a corresponding decrease in inhibitory activity. This inhibitory effect could be the result of surface tension effects on cell membranes as well as direct effects on enzyme systems. Insects that are sensitive to the toxic effect of low doses of C8910 tend to be repelled at higher doses, while other insects are insensitive to both repellent and toxic effects (Reifenrath, unpublished data). However, further research will be necessary to determine if the reactions are mechanistically related. C8910 shows promising characteristics for use in public health vector control. Future research directions involving C8910 should include the following: 1) description of the mode of action, 2) efficacy testing using stronger concentrations, 3) testing against resistant and other non-resistant mosquito species, to include wild populations, 4) determination of residual duration of controlled release C8910 and mortality results on building surfaces and fabrics, 5) potential use as a repellent against malaria vectors, 6) efficacy testing against other medically important arthropods such as filth flies, biting flies, fleas, kissing bugs, bed bugs, lice, and ticks, and 7) negative effects on non-target insects, birds, and mammals. Further development of C8910 and similar compounds may provide vector control specialists effective, environmentally-safe insecticides for controlling arthropod disease vectors, as well as a sustainable alternative to a growing insecticide resistance crisis.

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Conflict Interests

The authors declare that there is no conflict of interests

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