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ON

Insecticide Resistance in Insect Vector of Human Disease

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Insecticide Resistance in Insect Vector of Human Disease

ABSTRACT

Insecticides play an important role in controlling major vectors of diseases such as mosquitoes, sandflies, fleas, lice, triatomid bugs etc. Insecticide resistance is an increasing problem in many insect vector diseases. Over the years, due to inappropriate and over uses of insecticides, insect vectors grow resistance against insecticides which leads their control and management difficult. As a result, major insect vectors become resistant against the main groups of insecticide. *Ades spp.* is resistant to Deltamethrin, Fenitrothion and Organochlorine insecticides. *Anopheles spp.* exhibits resistance to Deltamethrin, Permethrin, DDT, Pyrethroids and carbamate but susceptible to Malathion.*Culex pipens* is resistant against DDT, Lambda-cyhalothrin, Deltamethrin, Cyfluthrin, Fanvelerate, Beta-cyfluthrin and Fenitothion. *Triatoma infestans* is resistant against Deltamethrin, but susceptible to Bendiocarb and Malathion. Bed bug is resistant to DDT and Pyrethroid insecticides. Sand flies show different resistance status at different regions. Head louse also shows some kinds of resistance against different essential oils and pyrethroids.

Key Words: Organochlorine, Deltamethrin, Malathion, Carbamate, Pyrethroids, DDT

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CHAPTER I

INTRODUCTION

Insecticides are considered to be a powerful weapon or silver bullets in the developing countries in order to increase the agriculture productivity. Insecticide resistance is a heritable, statistically defined as decrease in sensitivity to a chemical in a pest population relative to the response of susceptible populations that have never been exposed to pesticides and it is the natural ability of a biotype of an organism to survive exposure to a pesticide that would normally kill an individual of that species (Karunamoorthi *et al*.,2012).

Insecticide resistance is expected to directly and profoundly affect the reemergence of vector borne diseases and where resistance has not contributed to disease emergence, it is expected to threaten disease control (WHO,1992). Insect vector borne diseases are responsible for 17% of the global burden of parasitic and infectious diseases (WHO,2008). More than a billion people, mostly in developing countries, are now at the risk of contracting such diseases like malaria, filariasis, leishmaniasis, dengue, yellow fever, Japanese encephalitis, Plague, the relapsing fevers, and various rickettsial diseases (Pant,1987). In the 21st century, the emergence and resurgence of insect vector borne diseases constitute an important threat to human health, causing over a million death and considerable mortality worldwide. Therefore, at the moment, control of vector-borne diseases is becoming a great challenge (Karunamoorthi,2012).

The compounding factors such as inadequate resources and operational capability, insecticide resistance, and the use of adulterated or poor-quality insecticides, may combine to reduce the insecticides efficiency. The overuse and misuse of insecticides have led to the emergence of resistance, which limits the potentiality of vector control. The recurrent and inappropriate insecticide applications are the key sources for resistance which is a potential threat to the global public health. Therefore, it has to be addressed immediately to sustain the recent success of vector control, unless otherwise it would become uncertain (Karunamoorthi *et al*.,2012).

Keeping these considerations in view, the present study has aimed with the following **objective(s)**

- To review the resistance status of major insect vectors of human disease against the main groups of insecticides

CHAPTER II

MATERIALS & METHODS

This seminar paper is exclusively a review paper. All data and information are adopted as a secondary data. It has been prepared by reviewing the various articles published in different Books, Proceedings, Abstracts, Review papers, Journals, MS thesis, Ph.D. Dissertation etc. available in the library of Bangabandhu Sheikh Mujibur Rahman Agricultural University, Gazipur. For collecting recent information, I visited different websites through internet. The necessary thoughts, ideas, facts and findings has been collected through internet searching and incorporated with the body of the seminar. I prepared this paper in consultation with my learned major professor, and other concerned experts. After collecting necessary information, it has been compiled and arranged chronologically for better understanding and clarification.

CHAPTER III

REVIEW OF FINDINGS

3.1 Arthropod vectors transmit many new and reemerging diseases (William et al.,1998). A small group of arthropods become infamous as they parasitize higher vertebrates or act as carriers of pathogens and parasites.Vector-borne diseases were responsible for more deaths in humans than all other causes combined, until the early 20th century (Gubler,1998). Some common arthropods of human disease which act as insect vectors are listed (**Table 1**).

Table 1.Example of some major vectors of human disease

Insect vector or Pest	**Disease**
Anopheles spp.	Malaria , Filaria
Ades spp.	Dengue, Chikunguniya
Culex spp.	Filariasis, Japanese encephalitis, West Nile
Reduviids (Bed bugs,Triatominae)	Chagas disease
Lice	Epidemic fever, Trench fever
Ticks	Lyme disease, Rocky Mountain spotted fever, Q fever, Relapsing fever
Mites	Rickettsioses, Q fever
Fleas	Endemic typhus
Sandflies	Leishmaniasis, Sandfly fever, Vesicular stomatitis

(Source: Modified from William et al.,1998 & Kalluri *et al*.,2007)

3.2 Insecticide Resistance in Insect Vectors

3.2.1 Resistance in *Ades spp.* against Insecticides

Dengue fever become one of the major public health concern where millions of cases and thousands of deaths in every year in urban, suburban and rural tropical area (Guzman & Isturiz 2010). For the past 25 years, every three-five year outbreaks have occurred and their impacts have gradually strengthen over time, moving towards a hyperendemic situation. Therefore, the control of the two vectors, *Aedes aegypti* and *Aedes albopictus* is the most effective way for fighting the disease (Gomez-Dantes & Willoquet 2009).

A study was conducted in French Guiana to determine the resistance level of *Aedes Aegypti.* Five strains of *Ae. aegypti* were used which were Saint Laurent du Maroni (SLM), Kourou (KOU), Cayenne (CAY), SGO and PAEA. Four batches of 25 non-blood-fed females (2-5 days old) were exposed to exposure tube. Knocked-down and dead mosquitoes were recorded after 1 hour. After 24 h exposure mortality was recorded. 27-37% knocked-down of mosquitoes was caused by Deltamethrin, whereas fenitrothion caused a maximum of 1% (**Table 2**). All PAEA females were dead after the 24-h observation, regardless of the insecticide. F1 female mortality ranged from 14% (SLM) to 30% (SGO), in deltamethrin-treated tubes, (**Table 2**). All four populations were classified as resistant to deltamethrin, considering the WHO thresholds. Mortality was higher in fenitrothion-treated tubes than in deltamethrin treated tubes, ranging from 22-85%. Therefore, SGO, CAY and KOU populations also exhibited resistance to fenitrothion, whereas SLM displayed a tolerance with 85% mortality (Isabelle *et al.,2011*).

From table 2 it is evident that a strong resistance was established to Deltamethrin overall for all the four strains with a poor knockdown effect and low mortality. Therefore, Deltamethrin demonstrates poor efficacy against *Aedes Aegypti*, whereas Fenitrothion exhibits higher efficacy at 24 h post treatment.

Table 2. Percentages of 1 h knocked-down and 24 h corrected mortality for the five strains exposed to deltamethrin 0.06% and fenitrothion 0.5%

Insecticides	Doses	Strain	1hKDC[a] (%)	1hKDC[b] (%)	1hKDC[c] (%)	1hKDC[d] (%)
Deltamethrin	0.06	PAEA	0	100	1	100
		CAY	1	34	1	29
		KOU	0	31	3	23
		SGO	0	37	2	30
		SLM	1	27	5	14
Fenitrothion	0.5	PAEA	0	0	0	100
		CAY	0	0	5	41
		KOU	0	1	0	48
		SGO	0	0	0	22
		SLM	0	0	3	85

a: knocked-down in controls after 1 h; *b*: knocked-down in treated tubes after 1 h; *c*: mortality in controls after 24 h; *d*: corrected mortality in treated tubes after 24 h; CAY: Cayenne; KOU: Kourou; PAEA: susceptible reference strain; SGO: Saint Georges de l'Oyapock; SLM: Saint Laurent du Maroni.

(source: Isabelle *et al.*,2011*)*

Another study was conducted in Malaysia where two strains of *Ades sp*. namely Shah Alam and Pantai Dalam were used to observe resistance against Organochlorine pesticides. From the study, according to the criteria from Davidson and Zahar 1973, it was found that Shah Alam strain was considered having possibility to be resistant to the insecticide with 95% mortality rate and Pantai Dalam considered to be resistant with 79% mortality (**Figure 1**) (Farah *et al.*,2011).

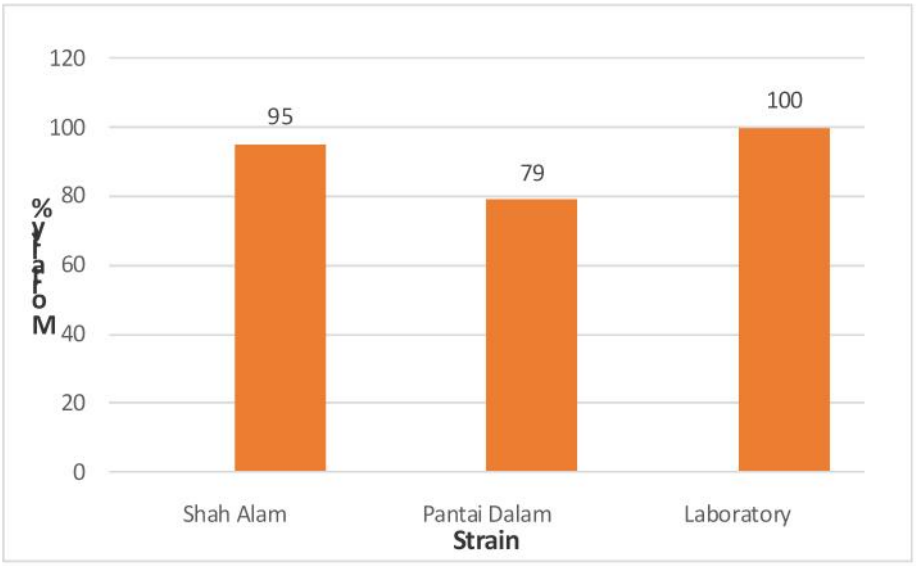

Figure 1: Mortality rate of Shah Alam and Pantai Dalam strain after 24 h

(Source: Modified from Farah *et al.*,2011)

3.2.2 Resistance in *Anopheles spp.* against Insecticide

A study was conducted in Nigeria to estimate resistance in *Anopheles gambiae*against insecticides (Oyewole *et al.*,2011). The study showed mortality percentage of *Anopheles gambiae* against different insecticides in Forest-savanna mosaic ecological zone (**Table 3**). Mortality % due to Deltamethrin, Permethrin and DDT is 78%, 69.2%, 84.6%, respectively. Applying the WHO criteria for determining resistance or susceptibility, 98-100% mortality indicates susceptibility; < 80% mortality suggests resistance while 80-97% mortality requires confirmation of resistance. Therefore, the study result demonstrates that *Anopheles gambiae* shows resistance to all the three insecticides in Forest-savanna mosaic ecological zone.

Table 3. Mortality percentage of *Anopheles gambiae* after 60 min exposure to insecticide in Forest-savanna mosaic ecological zone

Insecticide	Mortality %
Deltamethrin	78
Permethrin	69.2
DDT	84.6

(Source: Modified from Oyewole *et al.*,2011)

Another study was conducted to determine insecticide resistance in *Anopheles funestus* against DDT, Pyrethroids and carbamate insecticide (Djouaka *et al.*,2011). *Anopheles funestus* population was highly resistant to DDT with no mortality for females and only 14% mortality for males (**Figure 2**).Resistance was also observed against permethrin for females with a mortality of 66.7% while a moderate resistance for males with a mortality rate of 88.8%. Exposure to 0.05% deltamethrin, indicated that the *Anopheles funestus*is moderately resistant to this insecticide with 88.6% mortality for females and 96.7% for males. 0.1% bendiocarb, a carbamate insecticide, also revealed a resistance against the insecticide with a mortality rate of 65% and 78.1% respectively for females and males. A very moderate resistance was observed against 4% dieldrin with 93.3% mortality for females and 100% mortality for males although. A total susceptibility was observed against malathion which is an organophosphate, with 100% mortality for both females.

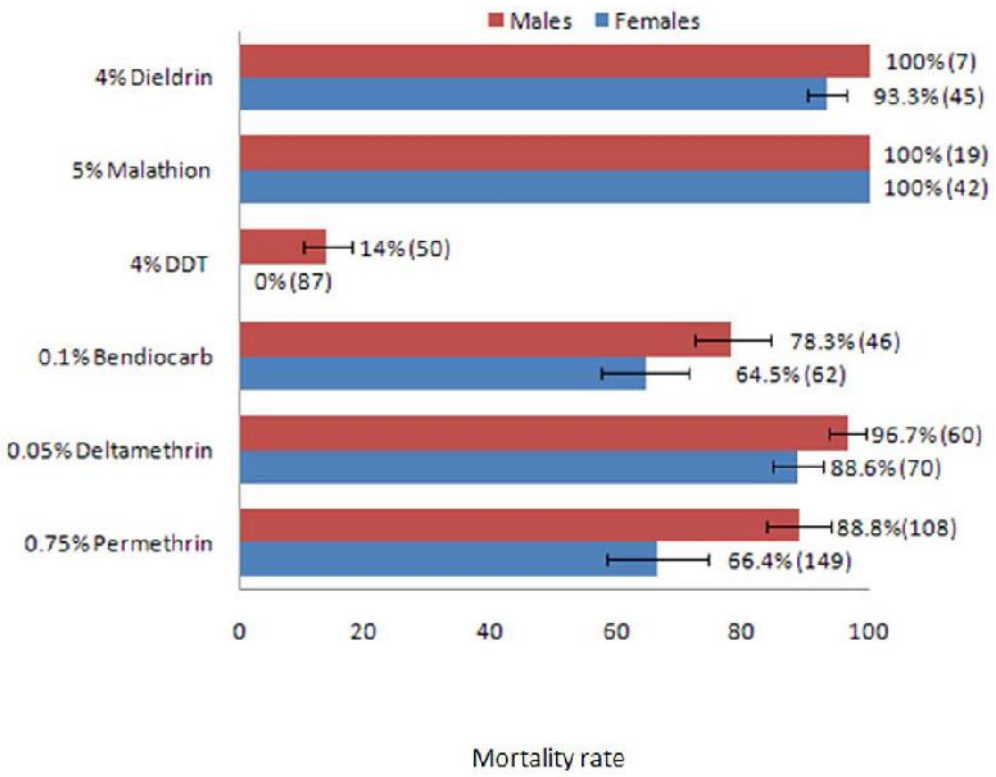

Figure 2:

Resistance status of *Anopheles funestus* against different insecticides

(Source: Djouaka *et al.,*2011)

3.2.3 Resistance in *Culex Spp.* against Insecticide

To demonstrate the resistance and susceptibility level of *Culex spp.,* a study was conducted in Tehran, Iran where different strains of *Culex pipens* were used (Salim *et al.*,2016).In this study laboratory strain and field populations and four Insecticides including DDT 4%, Lambda-cyhalothrin 0.05%, Deltamethrin 0.05%, Cyfluthrin 0.15% were used for evaluating susceptibility and resistance status of *Culexpipiens* **(Table 4**).

Table 4. Mortality rate and Resistance status of *Culex pipiens* (Lab and field population) exposed to different insecticides at 1hour exposure and 24 hours recovery period

Insecticides	MR±EB*		Resistance status**	
	Lab strain	Field Population	Lab strain	Field Population
Lambdacyhalothrin 0.05%	100	20±2	S	R
Deltamethrin 0.05%	98±1	18±3	S	R
Cyfluthrin 0.15%	100	66±3	S	R
DDT 4%	55±3	0	R	R

*Mortality Rate±Error Bar **R Resistance, S Susceptible (Source: Salim *et al.,*2016)

From the Table 4, it is evident that lab strain showed susceptibility to Lambda-cyhalothrin 0.05%, Deltamethrin 0.05%, Cyfluthrin 0.15% except DDT 4%, whereas field population exhibited resistance to all the insecticides.

Another experiment was held in Riyadh city to examine insecticide resistance of *Culex pipiens*populations (Al-Sarar,2010). Laboratory strain (S-LAB) and strain AL-W, WN1 and WN2 of field populations were used to test resistance against insecticides including fanvelerate, deltamethrin, Beta-cyfluthrin, Lambda-cyhalothrin, bifenthrin, fenitrothion. In case of fenvelerate LC_{50} value for S-LAB, WN1 and WN2 were 0.0049 ppm, 0.015ppm and 0.019ppm, respectively, whereas deltamethrin LC_{50} value for S-LAB, WN1 and WN2 were 0.0007ppm, 0.131 and 0.113, respectively (**Figure 3**).

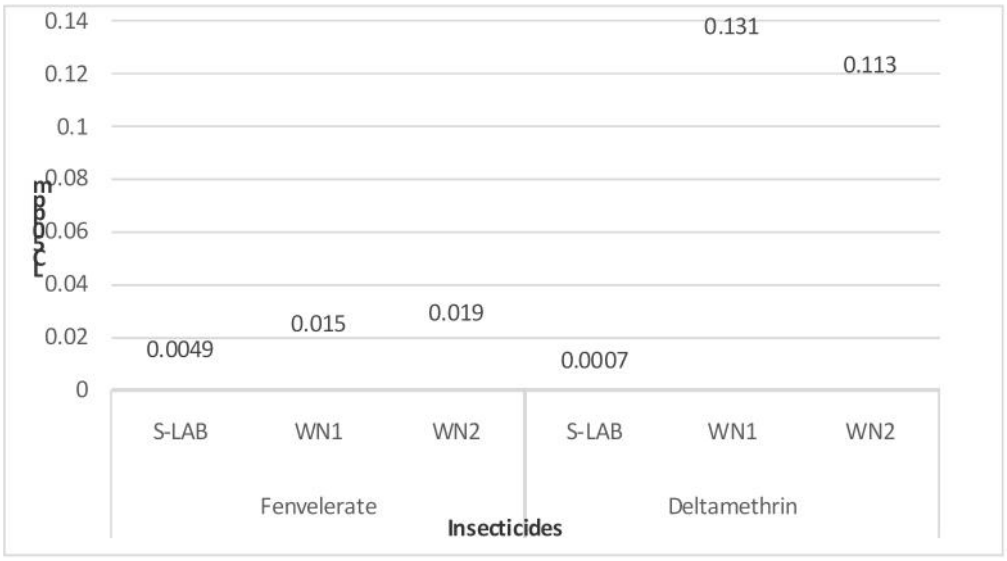

Figure 3. Toxicity of Fenvelerate and Deltamethrin to*Culex pipiens*

(Source: Modified from Al-Sarar,2010)

For pyrethroid insecticide, in case of Beta-cyfluthrin the LC_{50} value for S-LAB and AL-W strain were 0.0053ppm and 0.074ppm, respectively and in case of Lambda-cyhalothrin the LC_{50} value for S-LAB and AL-W strain were 0.0017ppm and 0.0065ppm, respectively (**Figure 4**).

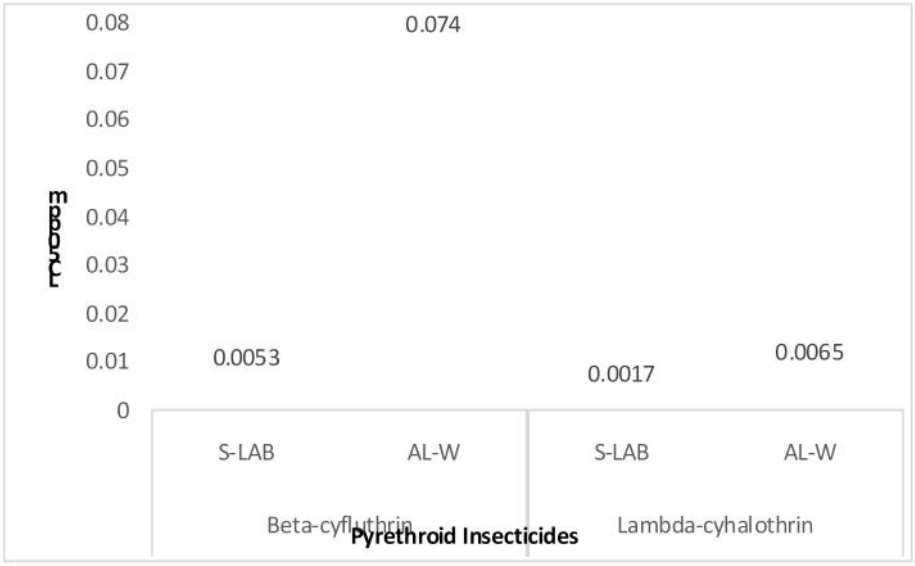

Figure 4. Toxicity of Beta-cyfluthrin and Lambda-cyhalothrin to*Culex pipiens*

(Source: Modified from Al-Sarar,2010)

The LC_{50} value for S-LAB and WN1 were 0.116 ppm and 0.198 ppm, respectively (**Figure 5**).

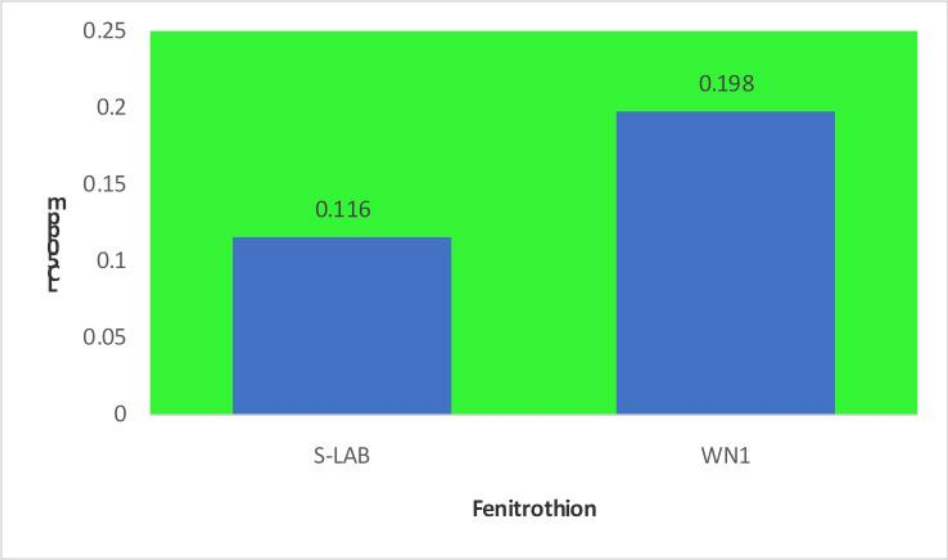

Figure 5. Toxicity of Fenitrothionto*Culex pipiens*

(Source: Modified from Al-Sarar,2010)

From this study, it is evident that WN1 and WN2 strains were highly resistant to Deltamethrin. For pyrethroid insecticides, AL-W strain showed moderate resistance to Beta-cyfluthrin and low resistance to Lambda-cyhalothrin and Fenitrothion.

3.2.4 Resistance in Chagas Disease Vector against Insecticides

Chagas disease is a chronic and incurable parasitic disease that causes disability and death. With more than 10 million human cases, Chagas disease is one of the most important parasitic diseases. It is caused by the protozoan *Trypanosoma cruzi* and is the major cause of cardiopathy in the world (Yacoub et al. 2008).The parasite is transmitted mainly by blood-sucking insects of the Triatominae family (Heteroptera, Reduviidae), which are responsible of more than 80% of human cases (Schofield 1994).There are 3 genera of triatomines particularly involved in the transmission of Chagas disease: *Triatoma*, especially *T. infestans, T.dimidiata* and *T. sordida*; *Rhodnius*, especially *R. prolixus* and *R. pallescens* and *Pastrongylus*, especially *P.megistus*

(Zerba,1989).As no treatment is available for the chronic forms of the disease and there is no immunological protection, chemical control of the vectors appears to be the best way to reduce the incidence of the disease (Metcalf,1975).

A study is conducted to assess the resistance status of various Bolivian field populations of *T. infestans* to deltamethrin, the pyrethroid insecticide, an organophosphate insecticide (malathion) and a carbamate (bendiocarb) insecticide (Frederic Lardeux *et al*.,2010).

Different strains of *T. infestans* were used to estimate resistance against Deltamethrin insecticide (**Table 5**) where all the strains except CIPEIN showed resistance.

Table 5. Resistance status of *Triatoma infestans* against Deltamethrin

Strain	LD_{50}(mg/kg)	Mortality %
CIPEIN (sensible reference strain)	0.24	100
Barrio	67.33	6
Icla	1.67	88
Machareti	8.09	17
Pajcha	5.08	48
Sotomayor	3.32	58
Tentami	78.44	0
Tiguipa	55.98	0
Anamo	34.47	3
Parani	0.91	92

(Source: Modified from Frederic *et al*.,2010)

The minimum dose for 100% mortality in *Triatoma infestans* was 11.15 mg/kg for CIPEIN strain. The percentage of mortality for all other strains was almost more than 97%, indicating the absence of resistance against Bendiocarb insecticide (**Table 6**).

Table 6.Resistance status of *Triatoma infestans* against Bendiocarb Insecticide

Strain	**LD_{50}(mg/kg)**	**Mortality %**
CIPEIN (sensible reference strain)	11.15	100
Los Sotos	17.67	100
Barrial	19.56	100
Berrety	15.18	98
Estacion Caiza	17.73	100
San Francisco	18.80	100
Tierras Nuevas	20.82	94
Villa Primavera	20.70	100
Yuchan	16.52	100

(Source: Modified from Frederic *et al*.,2010)

The minimum dose that caused 100% mortality in CIPEIN strain was 17.73 mg/kg and for the rest of the strains the mortality percentage were more than 97%, indicating the absence of resistance against Malathion insecticide (**Table 7**).

Table 7.Resistance status of *Triatoma infestans* against Malathion Insecticide

Strain	LD_{50} (mg/kg)	Mortality %
CIPEIN (sensible reference strain)	17.73	100
La Grampa	38.81	96
Laime	31.14	100
Yuchan	26.67	100

(Source: Modified from Frederic *et al*.,2010)

Bed bugs are sucking type insects which is also a vector of Chagas Disease.In spite of the initial effectiveness of DDT which used as a control agent, within 3 years of its introduction reports began to circulate that some bed bug populations had become DDT resistant (Johnson & Hill, 1948).

When some of the U.S. strains were tested for the resistance of bed bugs to DDT (Romero *et al*., 2007), an interesting pattern of mortality was observed,DDT gave good control of the WOR1 (laboratory) strain, but other strains showed resistance to DDT having mortality percentage of 30%,10% and 5% for DOV-1, CIN-1 and LEX-1, respectively (**Figure 6**).

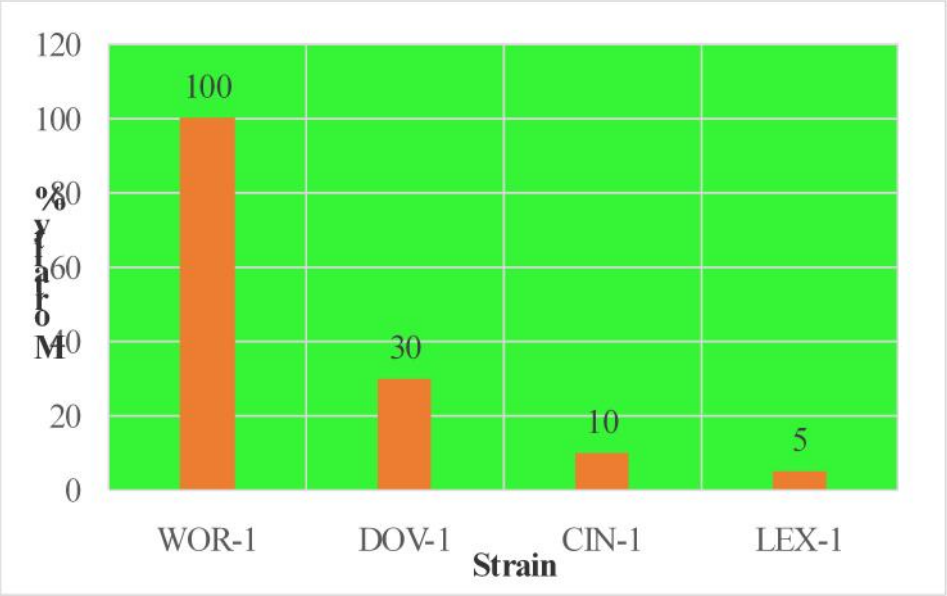

Figure 6. Mortality % of bed bug populations against DDT

(Source: Modified from Romero *et al*., 2007)

A study was done in USA to determine resistance of bed bug population against pyrethroid insecticides (Adelman *et al*., 2011). Two strains were used namely Harlan and Richmond, where Harlon is laboratory strain acting as control and Richmond is field strain. Against Deltamethrin, the LD_{50} value for Harlan and Richmond were 0.03 mg/kg and 155 mg/kg, respectively, where against beta-cyfluthrin the LD_{50} value for Harlan and Richmond were 0.04 mg/kg and 4.43 mg/kg, respectively (**Figure 7**). In both cases Field population of Richmond strain showed resistance to pyrethroid insecticides compare to laboratory Harlan strain.

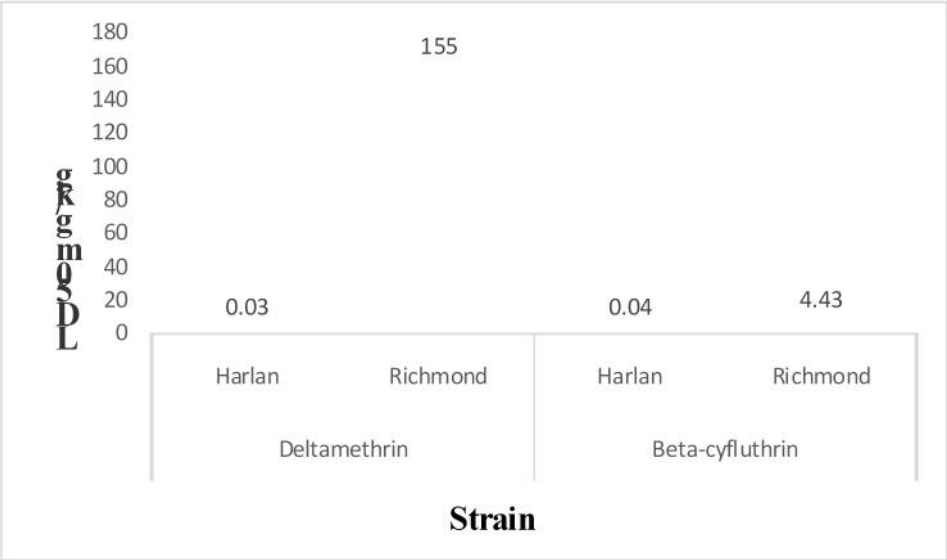

Figure 7. Mortality % of bed bug populations against Pyrethroid Insecticides

(Source: Modified from Adelman *et al*., 2011)

3.2.5 Resistance in Sand fly against Insecticides

Leishmaniasis is a vector borne disease caused by a parasite of genus Leishmania and considered a major public health problem, 88th in the world causing morbidity and mortality. The disease also causes serious economic loss and impedes socioeconomic development in many countries (WHO,2006). Among the species of sand flies *Phlebotomus papatasi* is one of the most medically important sand fly species in the Old World, serving as a vector of Leishmania parasites (Fawaz et al.,2016). This sand fly is established throughout much of North Africa, the Middle East, and India (Lewis 1982). Its habit of feeding on humans in and around human dwellings ensures that it will continue to play a leading role in the transmission of cutaneous leishmaniasis and sand fly fever (Fawaz et al.,2016).

To evaluate insecticide resistance in sand flies, an experiment was held in Sudan (Hassan *et al*.,2012). The sand flies used in this experiment were collected from three different regions namely Surogia, Rahad game reserve and the west nile region.*Phlebotomus papatasi* from the Rahad Game Reserve and White Nile area, with a mortality level of 100% 24 hours post-exposure, were fully susceptible to permethrin, DDT, malathion and propoxur. The Population of *P. papatasi* from Surogia village, with mortality rates of 100% 24hour post exposure, was fully susceptible to permethrin and DDT (**Table 8**).

Table 8. Mortality % of Sand fly population after 24h exposure

Sand fly Population	Insecticide tested	Mortality %
Surogia	Permethrin (0.75%)	100
	DDT (4%)	100
	Malathion (5%)	19
	Propoxur (0.1%)	09
Rahad Game Reserve Region	Permethrin (0.75%)	100
	DDT (4%)	100
	Malathion (5%)	100
	Propoxur (0.1%)	100
West Nile Region	Permethrin (0.75%)	100
	DDT (4%)	100
	Malathion (5%)	100
	Propoxur (0.1%)	100

(Source: Modified from Hassan *et al*.,2012)

The CDC bottle bioassay was also used to evaluate the insecticide resistance in the reared resistant strain of sand fly in Egypt (Fawaz et al.,2016). A dose of 150 mg permethrin for 2-h exposure was found to be the diagnostic dose-time in CDC bottle assay. A susceptible colony of *P. papatasi* reared in NAMRU-3's Vector Biology Research Program insectary since 1994 was used as a control and F3 resistance strain of sand fly was used, using the CDC bottle assay. A graph representing the percentage of mortality owing to the exposure for each dose of permethrin was constructed **(Figure 8**). The mortality of the F3 resistant strain was 50%, using the diagnostic dose-time in the CDC bottle assay. This finding confirms the resistance of the F3 of field-collected sand flies to permethrin.

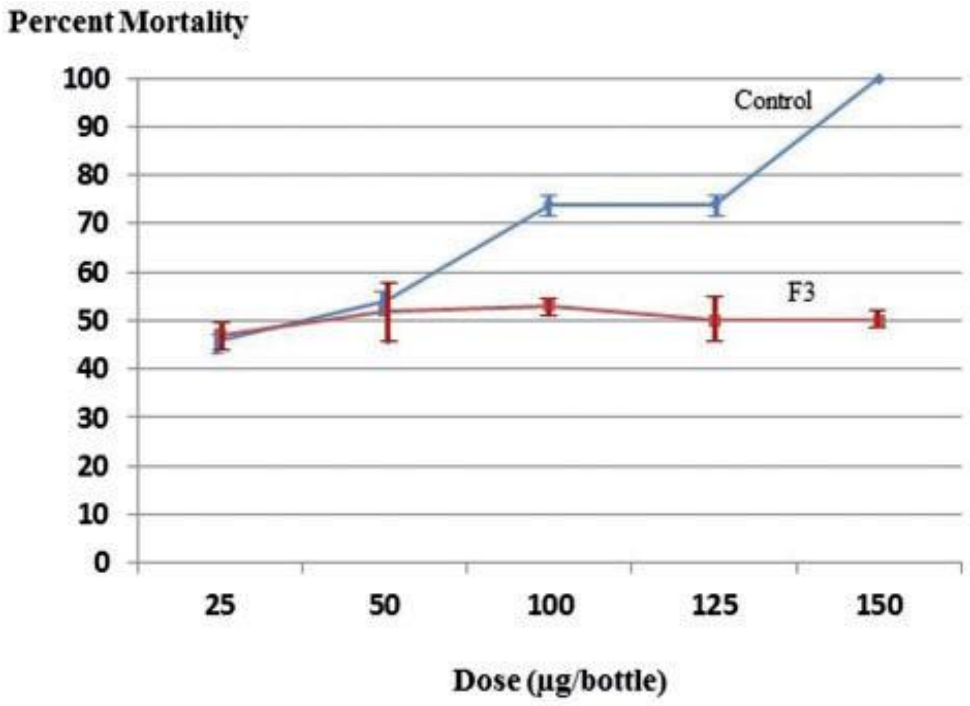

Figure 8. Mortality in susceptible and resistant colonies of *P. papatasi* after 2 h of exposure to different permethrin doses using the CDC bottle bioassay

(Source: Fawaz et al.,2016)

3.2.6 Resistance in human louse against insecticides

The human louse, *Pediculus humanus*is a blood-sucking ectoparasite that occurs worldwide and causes infestations with serious medical, economic and social consequences (Durden & Musser, 1994). Head louse infestations are more common, epidemiologically and mostly affect children, regardless of economic status or geographic region (Clark *et al.*, 2013). Control of human lice generally involves a combination of manual removal techniques and the use of diverse chemicals often called as pediculicides. However, many of the most widely used Insecticides have become ineffective as a result of the spread of resistant strains (Durand *et al.*,2012).

An experiment was held to assess insecticidal activity of plant essential oils against *Pediculus humanus* (Yang *et al,2004).* The LT_{50} value of Eucalyptus, Majoram, Pennyroyal, Rosemary, Phenothrin and Pyrethrum were 12.6, 19.6, 14.7, 22.4, 300 and 300 minutes, respectively (**Figure 9**).

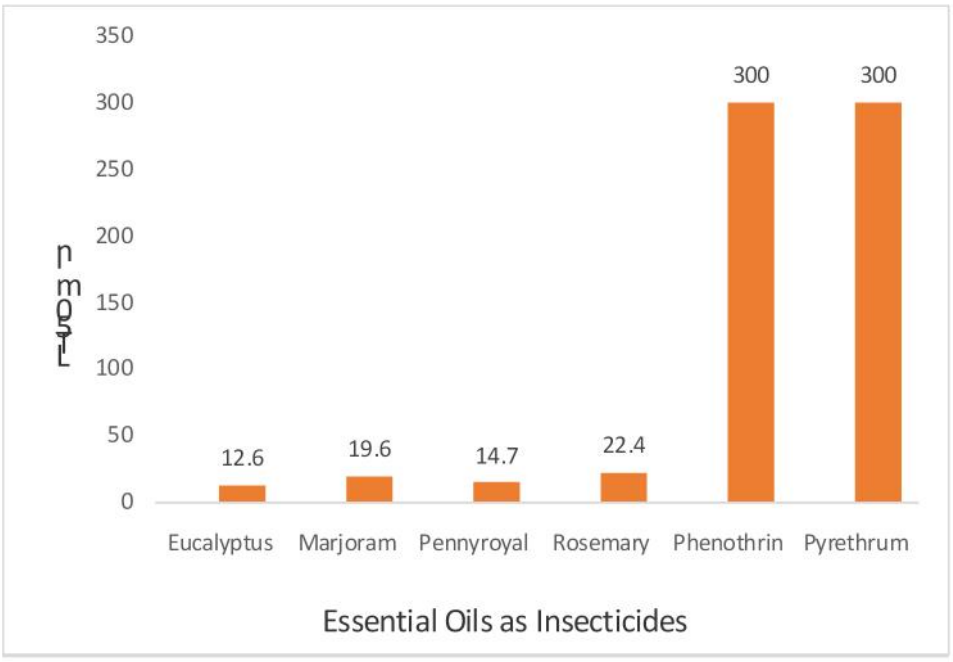

Figure 9. Relative toxicity of essential oils against *Pediculus humanus*

(Source: Modified from Yang *et al*,2004)

CHAPTER III

CONCLUSIONS

Most of the insect vectors of human disease grow resistance against different insecticides. *Aedes aegypti* showed strong resistance against Deltamethrin and Fenitrothion. In case of Organochlorine pesticides *Aedes spp*. also showed resistance. *Anopheles gambiae* showed resistance to Deltamethrin, Permethrin and DDT. *Anopheles funestus is* resistant to DDT, Pyrethroids and carbamate but susceptible to Malathion. *Culex pipens* showed resistance against DDT, Lambda-cyhalothrin, Deltamethrin, Cyfluthrin, Fanvelerate, Beta-cyfluthrin and moderate resistant to Fenitothion. *Triatoma infestans* is resistant against Deltamethrin and susceptible to Bendiocarb, Malathion. Bed bug is resistant to DDT and Pyrethroid insecticides. *Phlebotomus papatasi* fromSudan regionis fully susceptible to Permethrin, DDT and Malathion, but *Phlebotomus papatasi* from Egypt region is resistant against Permethrin. *Pediculus humanus* is resistant against Phenothrin and Pyrethrum insecticide.

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