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# *Aedes aegypti* mosquito control studies on derivatives of Dapsone

**T.Gobi[1], N. Elangovan[1], T. Chinnamani[2], R. Sivakami[2] and T. Kolochi[1]***

[1]PG and Research Department of Chemistry, Arignar Anna Government Arts College Musiri-621 211, Tamilnadu, India.

[2]PG and Research Department of Zoology, Arignar Anna Government Arts College Musiri-621 211, Tamilnadu, India.

*Corresponding Author: *kolochi2004@yahoo.com*

## Abstract

Derivatives of dapsone(**I)** 4,4'-sulfonylbis(N-(4-chlorobenzylidene)aniline), **(II)** 4,4'-sulfonylbis(N-(4-methoxybenzylidene) aniline), **(III)** 4,4'-(((sulfonylbis(4,1-phenylene))bis(azanylylidene))bis(methanylylidene))diphenol, **(IV)** 3,3'-(((sulfonylbis(4,1-phenylene))bis(azanylylidene))bis(methanylylidene))diphenol, **(V)** 2,2'-(((sulfonylbis(4,1-phenylene)) bis(azanylylidene)) bis (methanylylidene))diphenol and **(VI)** 4,4'-sulfonylbis(N-(furan-2-ylmethylene)aniline were prepared and characterized by physical and analytical data, FTIR , $^{1}$H NMR, $^{13}$C NMR spectra and were screened against larvae of *Aedes aegypti.*

**Keywords:** dapsone, *Aedes aegypti*, larvicidal activity, *Aedes albopictus*, *Aedes polynesiensis*, *Aedes scutellaris*. 4-chlorobenzaldehyde, 4- methoxybenzaldehyde , 4-Hydroxybenzaldehyde 3-Hydroxybenzaldehyde, 2-Hydroxybenzaldehyde and Furan-2-carbaldehyde.

## Introduction

Anti-Dengue Day is observed every year on 15 June to create public awareness about dengue, mobilize resources for its prevention and control and, to demonstrate the Asian region's commitment in tackling dengue fever[1,2]. The first record of a case of probable dengue fever is in a Chinese medical encyclopedia from the Jin Dynasty (265–420 AD) which referred to a "water and food poison" associated with mosquitos. *Aedes aegypti*, spread out of Africa in the 15$^{th}$ to 19$^{th}$ centuries due in part to increased universalization secondary to the slave trade. There have been descriptions of epidemics in the 17$^{th}$ century, but the most plausible early reports of dengue epidemics are from 1779when an epidemic swept across Asia, Africa and North America. From that time until 1940, epidemics were infrequent. In 1906, transmission by the *Aedes aegypti* was confirmed, and in 1907 dengue fever was the second fever that was shown to be caused by a virus.

Dengue virus is generally transmitted by *Aedes aegypti*. It live between the latitudes of 35° North and 35° South below an elevation of 1,000 meters. It mainly bites during the early morning and in the evening and spread dengue virus. Other Aedes mosquitoes that transmit the fever include *Aedes albopictus, Aedes polynesiensis* and *Aedes scutellaris*. Human beings are the primary host of the dengue virus. The dengueviral infection can be acquired via a single bite of mosquitoes. A female *Aedes aegypti* that takes a blood meal from a person infected with dengue fever, during the initial 10-days incubation period, becomes itself infected with the virus in the cells lining its gut. About 10 days later, the virus spreads to other tissues including the *Aedes aegypti* salivary glands and is subsequently released into its saliva. The virus seems to have no detrimental effect on *Aedes aegypti*, which remains infected for its life time. *Aedes aegypti* is

particularly involved, as it prefers to lay its eggs in artificial water containers, to live in close proximity to humans, and to feed on many people rather than other vertebrates. Female *Aedes aegypti* lay eggs on the inner walls of artificial containers. When the small containers fill with water *Aedes aegypti* mosquito larvae hatch from the eggs. After developing four larval stages the larva metamorphoses into pupae. Then pupae is molted into mosquito.

The marked spread of dengue virus during and after the Second World War has been attributed to ecologic disruption. The same trends also led to the spread of different serotypes of fever to new areas, and to the emergence of dengue hemorrhagic fever. This severe form of the fever was first reported in the Philippines in 1953. It had become a major cause of child mortality and had emerged in the Pacific and the united states of Americas. Dengue hemorrhagic fever and dengue shock syndrome were first noted in Central and South America in 1981, as dengue virus-2 was contracted by many people who had previously been infected with dengue virus-1 several years earlier. When *Aedes aegypti* carrying dengue virus bites a person, the virus enters the skin together with the *Aedes aegypti* saliva. It binds to and enters white blood cells, and reproduces inside the cells while they move throughout the body of human being.

In recent years[3-5], derivatives of nucleic acid base were found to have potential non-toxic and non-antibiotic resistance of antibacterial, antifungal, mosquito larvicidal[6-17], antiparasitic and anticancer properties. They have been prepared by starting from nucleic acid bases like cytosine or adenine and aldehydes or ketones.

In the present study we have prepared **(I)** 4,4'-sulfonylbis(N-(4-chlorobenzylidene)aniline), **(II)** 4,4'-sulfonylbis(N-(4-methoxybenzylidene)aniline), **(III)** 4,4'-(((sulfonylbis(4,1-phenylene))bis(azanylylidene)) bis(methanylylidene))diphenol, **(IV)** 3,3'-(((sulfonylbis(4,1-phenylene))bis(azanylylidene)) bis(methanylylidene))diphenol, **(V)** 2,2'-(((sulfonylbis(4,1-phenylene))bis(azanylylidene)) bis(methanylylidene))diphenol and **(VI)** 4,4'-sulfonylbis(N-(furan-2-ylmethylene)aniline Schiff bases[18-23]and have been subjected to in vitro larvicidal activities[6-17] against larvae of *Aedes aegypti*.

## Materials and Methods

### Materials

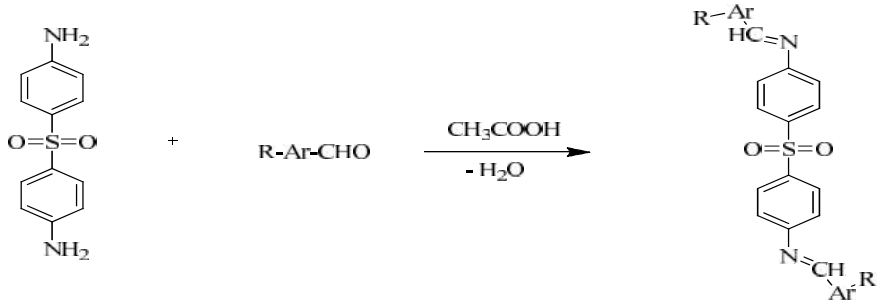
All the reagents used were of AR grade. Commercially available rectified spirit was dried over anhydrous quicklime for 24 hours, filtered and distilled before use (BP 78 $^{o}$C). Dimethylsulphoxide (sigma) and N,Ndimethylformamide (sigma) were used as such. dapsone, 4-chlorobenzaldehyde, 4- methoxy benzaldehyde , 4-Hydroxybenzaldehyde 3-Hydroxy benzaldehyde, 2-Hydroxybenzaldehyde and Furan-2-carbaldehyde were purchased from Alfa Aesar.

### Instruments

Melting points were determined using Elico melting point apparatus. Elemental analysis were performed using Elementar Vario EL III. IR spectra of the compounds were recorded with KBr pellets with carry 630 FTIR Spectrometer in the 4000-400 cm-1range. The 1HNMR and 13CNMRspectra were recorded on a Bruker 400 MHz FT- PMR Spectrometer.

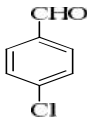
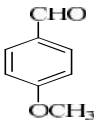
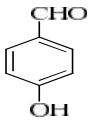
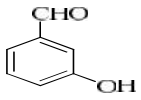
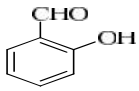
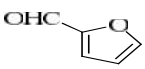
### General preparation of derivatives dapsone

All the azomethine compounds of derivatives of dapsone were prepared as reported in the literature[5,18-23]by the following scheme – 1.




Scheme 1

**Where, R-Ar-CHO =**

**Preparation of (I) 4,4'-sulfonylbis(N-(4-chlorobenzylidene)aniline)**[3-5]

Equimolar quantities of 0.01 mole of dapsone (2.48 g 0.01mol) and 4-chlorobenzaldehyde (2.81 g 0.02mol) were dissolved in 20 ml of DMSO and 3 drop of glacial acetic acid was added and refluxed for 3 hours. After completion of the reaction (monitored by TLC), some solvent was distilled out, the reaction mixture was poured on ice cold water and the solid 4,4'-sulfonylbis(N-(4-chlorobenzylidene)aniline) came out which was filtered and then recrystallized by DMSO and then dried over vacuum desiccator.

**Preparation of (II) 4,4'-sulfonylbis(N-(4-methoxybenzylidene)aniline)**

25ml of ethanolic solution of dapsone (2.48 g 0.01mol) was added to 25ml of ethanolic solution of 4-methoxybenzaldehyde (2.72 g 0.02 mol).Then three drops of acetic acid was added to the reaction mixture. The reaction mixture was heated and refluxed for about 5 hours at 90°C. The resulting solution was further concentrated by water bath. The product 4,4'-sulfonylbis (N-(4-methoxybenzylidene) aniline) obtained was precipitated, cooled and collected after filtration. The precipitate was purified by washing with distilled water and then with ethanol. The 4,4'-sulfonylbis(N-(4-methoxybenzylidene)aniline) was again recrystallized in ethanol and then dried over vacuum desiccator.

**Preparation of (III) 4,4'-(((sulfonylbis(4,1-phenylene))bis(azanylylidene))bis(methanylylidene) )diphenol**

4,4'-(((sulfonylbis(4,1-phenylene))bis(azanylylidene)) bis(methanylylidene))diphenol was prepared from equimolar quantity of dapsone (2.48 g 0.01mol) and 4-hydroxybenzaldehyde (2.44 g 0.02mol) in 30 ml of methanol were heated at 70°C on water bath for 4-hrs in presence of few drops of glacial acetic acid. The crude products were obtained after removal of methanol under reduced pressure. The products were recrystallized from methanol and then dried over vacuum desiccator.

**Preparation of (IV)3,3'-(((sulfonylbis(4,1-phenylene))bis(azanylylidene))bis(methanylylidene) )diphenol**

2.48 grams of dapsone (0.01mol) was mixed with 2.44 g of 3-hydroxybenzaldehyde (0.02mol) and was grained well in acidic acid medium at room temperature. The mixture was transferred into hundred milliliter Round Bottom flask and was refluxed for six hours in oil bath. The solid product 3,3'-(((sulfonylbis(4,1-phenylene))bis(azanylylidene)) bis (methanylylidene))diphenol was filtered and washed with ethanol and recrystallized in DMSO and then dried over vacuum desiccator.

**Preparation of (V) 2, 2'-(((sulfonylbis(4,1-phenylene))bis(azanylylidene))bis(methanylylidene) )diphenol**

The 2,2'-(((sulfonylbis(4,1-phenylene))bis (azanyl ylidene))bis(methanylylidene))diphenol was prepared by stirring a methanolic solution of dapsone (2.48 g 0.01mol) with 2-hydroxybenzaldehyde (2.44 g 0.02mol) in 1:2 stoichiometric ratio at room temperature over 24hours. The precipitate obtained were filtered and washed with methanol and recrystallized from methanol and then dried over vacuum desiccator.

### Preparation of (VI) 4,4'-sulfonylbis(N-(furan-2-ylmethylene)aniline)

Dapsone (2.48 g 0.01mol) was dissolved in 5ml of hot glacial acetic acid, 192 g (0.02 mol) of furfural was dissolved in 5ml of glacial acetic acid and were mixed. The reaction mixture was refluxed with stirring for 5 hours. The mixture was allowed to cool, and poured onto ice. The crude solid 4,4'-sulfonylbis(N-(furan-2-ylmethylene)aniline) was filtered off and washed with distilled water, then re-crystallized from acetic acid and then dried over vacuum desiccator.

### *Aedes aegypti* rearing

The *Aedes aegypti* larvae of *Aedes aegypti* and *Aedes albopictus* were collected from National centre for disease control, Government of India ministry of healthand family welfare, Southern India branch, field station, Mettupalayam, Coimbatore district, Tamilnadu, India. The larvae were kept in theplastic buckets half filled with tap water and fed with dog biscuit once a day initially and twice during the later stages of development. Water in rearing container was refreshed every day by removing a little quantity of water from the rearing buckets and replacing with fresh water. This was aimed at preventing scum from forming on the water surface.

### Larvicidal bioassay

The larvicidal activity[6-17] of six novel derivatives of dapsone were assessed by using the standard method as prescribed by WHO. From the stock solution, five different test concentrations (150, 200, 250and 300 ppm was prepared and tested against the freshly moulted (0 – 6 hrs) 4$^{th}$instar larvae of *Aedes aegypti* and *Aedes albopictus* DMSO (emulsifier) in water was treated as control. 10 larvae of these *Aedes aegypti* and *Aedes albopictus* species was introduced in 250-ml plastic cups containing 100 ml of aqueous medium (99 ml of dechlorinated water + 1ml of emulsifier) and the required amount of six novel derivatives of dapsone was added. The larval mortality was observed and recorded after 24 hrs of post treatment. For each experiment, five replicates were maintained at a time. The percentage of mortality was calculated by using Abbott's formula[24] (Abbott, 1925). The $LC_{50}$, $LC_{90}$, 95% confidence limit of Lower Confidence Limit (LCL) and Upper Confidence Limit (UCL), chi-square values and the degrees of freedom was calculated by using Probit analysis with Statistical Package for Social Sciences (SPSS) 16.0 Version in MS-Excel, 2007.

## Results and Discussion

The physical and analytical data of

**(I)** 4,4'-sulfonylbis(N-(4-chlorobenzylidene)aniline),
**(II)** 4,4'-sulfonylbis(N-(4-methoxybenzylidene) aniline),
**(III)** 4,4'-(((sulfonylbis(4,1-phenylene))bis (azanylylidene))bis(methanylylidene))diphenol,
**(IV)** 3,3'-(((sulfonylbis(4,1-phenylene)) bis(azanylylidene))bis(methanylylidene))diphenol,
**(V)** 2,2'-(((sulfonylbis(4,1-phenylene)) bis(azanylylidene))bis(methanylylidene))diphenol and
**(VI)** 4,4'-sulfonylbis(N-(furan-2-ylmethylene) aniline are given in table 1.

### [I] 4,4'-sulfonylbis(N-(4-chlorobenzylidene)aniline)

**FTIR (cm$^{-1}$):** 1652 cm$^{-1}$ ($-N=\overset{|}{C}H$), 1548 & 1148 cm$^{-1}$ ($S=O$), 804 cm$^{-1}$ ($Ar-Cl$) & 516 cm$^{-1}$ ($Ar-S$)

**$^{1}$HNMR δ (ppm):** 8.39 (s, 2H), 7.79 (d, 4H), 7.77 (d, 4H), 7.52 (d, 4H) & 7.50 (d, 4H)

**$^{13}$CNMR δ (ppm):** 160.0 (s), 157.0 (s), 139.9 (s), 136.6 (s), 134.5 (s), 130.6 (s), 129.6 (s), 128.9 (s) & 123.3 (s)

### [II] 4,4'-sulfonylbis(N-(4-methoxybenzylidene) aniline)

**FTIR (cm$^{-1}$):** 1668 cm$^{-1}$ ($-N=\overset{|}{C}H$), 1300 & 1148 cm$^{-1}$ ($S=O$), 1204 cm$^{-1}$ ($Ar-OCH_3$), 1020 cm$^{-1}$ ($ArO-CH_3$) & 636 cm$^{-1}$ ($Ar-S$)

**$^{1}$HNMR δ (ppm):** 8.39 (s, 2H), 7.97 (d, 4H), 7.84 (d, 4H), 7.50 (d, 4H), 7.06 (d, 4H) & 3.83 (s, 6H)

**$^{13}$CNMR δ (ppm):** 162.9 (s), 160.0 (s), 157.0 (s), 139.9 (s), 130.2 (s), 129.6 (s), 128.7 (s), 123.9 (s), 114.4 (s) & 55.8 (s)

### [III] 4,4'-(((sulfonylbis(4,1-phenylene)) bis(azanylylidene))bis(methanylylidene))diphenol

**FTIR (cm$^{-1}$):** 3442 & 715 cm$^{-1}$ ($ArO-H$), 1669 cm$^{-1}$ ($-N=\overset{|}{C}H$), 1336 & 1156 cm$^{-1}$ ($S=O$), 1282 cm$^{-1}$ ($Ar-OH$) & 598 cm$^{-1}$ ($Ar-S$)

**$^{1}$HNMR δ (ppm):** 8.39 (s, 2H), 7.79 (d, 4H), 7.78 (d, 4H), 7.50 (d, 4H), 6.85 (d, 4H) & 5.35 (s, 2H)

**$^{13}$CNMR δ (ppm):** 160.8 (s), 160.0 (s), 157.0 (s), 139.9 (s), 130.6 (s), 129.0 (s), 123.3 (s) & 116.0 (s)

**[IV] 3,3'-(((sulfonylbis(4,1-phenylene)) bis(azanylylidene))bis(methanylylidene))diphenol**

**FTIR (cm$^{-1}$):** 3226 & 706 cm$^{-1}$ (ArO−H), 1633 cm$^{-1}$ (−N=CH), 1318 & 1129 (S=O), 1201 cm$^{-1}$ (Ar−OH) & 607 cm$^{-1}$ (Ar−S)

**$^{1}$HNMR δ (ppm):** 8.39 (s, 2H), 7.97 (d, 4H), 7.50 (d, 4H), 7.46 (s, 2H), 7.39 (d, 2H), 7.25 (t, 2H), 7.02 (d, 2H) & 5.35 (s, 2H)

**$^{13}$CNMR δ (ppm):** 160.0 (s), 158.6 (s), 157.0 (s), 139.9 (s), 138.7 (s), 130.2 (s), 129.6 (s), 123.3 (s), 121.8 (s), 118.2 (s) & 114.9 (s)

**[V] 2,2'-(((sulfonylbis(4,1-phenylene)) bis(azanylylidene))bis(methanylylidene))diphenol**

**FTIR (cm$^{-1}$):** 3226 & 787 cm$^{-1}$ (ArO−H), 1633 cm$^{-1}$ (−N=CH), 1300 & 1120 cm$^{-1}$ (S=O), 1210 cm$^{-1}$ (Ar−OH) & 544 cm$^{-1}$ (Ar−S)

**$^{1}$HNMR δ (ppm):** 8.39 (s, 2H), 7.97 (d, 4H), 7.66 (d, 2H), 7.52 (t, 2H), 7.50 (d, 4H), 7.08 (t, 2H), 7.02 (d, 2H) & 5.35 (s, 2H)

**$^{13}$CNMR δ (ppm):** 161.1 (s), 160.0 (s), 157.0 (s), 139.9 (s), 132.4 (s), 132.1 (s), 129.6 (s), 123.3 (s), 121.4 (s), 120.5 (s) & 17.8 (s)

**[VI] 4,4'-sulfonylbis(N-(furan-2-ylmethylene) aniline)**

**FTIR (cm$^{-1}$):** 1636 cm$^{-1}$ (−N=CH), 1292 & 1084 cm$^{-1}$ (S=O), 1212 cm$^{-1}$ (−O−) & 660 cm$^{-1}$ (Ar−S)

**$^{1}$HNMR δ (ppm):** 7.97 (d, 4H), 7.75 (d, 2H), 7.50 (d, 4H), 7.50 (s, 2H), 6.93 (d, 2H) & 6.52 (t, 2H)

**$^{13}$CNMR δ (ppm):** 152.8 (s), 150.4 (s), 147.7 (s), 144.4 (s), 139.9 (s), 129.6 (s), 123.3 (s), 118.9 (s) & 112.6 (s)

**Table 1. The physical and analytical data of derivatives of dapsone**

| Derivatives of Cytosine | Molecular Weight | Nature of Appearance | % of yield | Elemental Analysis (in %) | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | C | H | O | N | S | Cl |
| [I] $C_{26}H_{18}Cl_2N_2O_2S$ | 493.4043 | Yellow Crystalline Solid | 65 | 63.29 | 3.68 | 6.49 | 5.68 | 6.50 | 14.37 |
| [II] $C_{28}H_{24}N_2O_4S$ | 484.5662 | Yellow Crystalline Solid | 72 | 69.40 | 4.99 | 13.21 | 5.78 | 6.62 | - |
| [III] $C_{28}H_{24}N_2O_4S$ | 484.5662 | Yellow Crystalline Solid | 68 | 69.40 | 4.99 | 13.21 | 5.78 | 6.62 | - |
| [IV] $C_{28}H_{24}N_2O_4S$ | 484.5662 | Yellow Crystalline Solid | 72 | 69.40 | 4.99 | 13.21 | 5.78 | 6.62 | - |
| [V] $C_{26}H_{20}N_2O_4S$ | 456.5130 | Lavender Crystalline Solid | 85 | 68.41 | 4.42 | 14.02 | 6.14 | 7.02 | - |
| [VI] $C_{22}H_{16}N_2O_4S$ | 404.4384 | Yellow Crystalline Solid | 81 | 65.33 | 3.99 | 16.92 | 15.82 | 7.93 | - |

**Table 2.**Larvicidalactivity of derivatives of dapsone are determined as recommended by WHO in 150,200, 250 and 300 ppm concentration in dimethyl sulfoxide(DMSO) solvent. The results of larvicidal activity of **(I)** 4,4'-sulfonylbis(N-(4-chlorobenzylidene)aniline), **(II)** 4,4'-sulfonylbis(N-(4-methoxybenzylidene)aniline), **(III)** 4,4'-(((sulfonylbis(4,1-phenylene))bis (azanylylidene)) bis(methanylylidene))diphenol,**(IV)** 3,3'-(((sulfonylbis (4,1-phenylene))bis(azanylylidene)) bis(methanyly lidene))diphenol, **(V)**2,2'-(((sulfonylbis (4,1-phenylene))bis(azanylylidene)) bis(methanylylidene)) diphenol and**(VI)** 4,4'-sulfonylbis(N-(furan-2-ylmethylene)aniline) are given in the Table 2.

The larvicidal activity of I-VI (Table2) clearly indicate that all the compounds control the growth of larvae. The nature of bonding and structure of azomethine organic compounds are elucidated as reported in the literature6 by the elemental analysis, melting point, FTIR, 1HNMR, 13CNMR, spectral analysis, chromatography and molar ratio methods. In accordance with the data obtained in the present investigation, it is found that the larvicidal activity of **(I)** 4,4'-sulfonylbis(N-(4-chlorobenzylidene)aniline), **(II)** 4,4'-sulfonylbis(N-(4-methoxybenzylidene) aniline), **(III)** 4,4'-(((sulfonylbis(4,1-phenylene))bis (azanylylidene))bis(methanylylidene))diphenol, **(IV)** 3,3'-(((sulfonylbis(4,1-phenylene))bis(azanylylidene)) bis(methanylylidene))diphenol, **(V)** 2,2'-(((sulfonylbis (4,1-phenylene))bis(azanylylidene)) bis (methanyly lidene))diphenol and**(VI)** 4,4'-sulfonylbis(N-(furan-2-ylmethylene)aniline)increases depend upon the functional groups present in the derivatives of adenine Schiff bases (III< II< IV< VI< I< V). Table 2.

**Table 2.Larvicidal activity of derivatives of dapsone against larvae of *Aedes aegypti***

| Compounds | Con. (ppm) | Larval mortality | 95% Confidence Limits (ppm) | | |
|---|---|---|---|---|---|
| | | | $LC_{50}$ (LCL-UCL) | $LC_{90}$ (LCL-UCL) | $\chi^2$ |
| I | 150 | 27.23±3.50 | 177.39 (159.91-193.45) | 331.85 (303.48-373.20) | 2.539 |
| | 200 | 41.21±3.24 | | | |
| | 250 | 67.30±3.30 | | | |
| | 300 | 88.20±2.20 | | | |
| II | 150 | 21.20±4.50 | 209.58 (192.10-227.86) | 379.01 (342.85-434.11) | 2.509 |
| | 200 | 33.40±3.50 | | | |
| | 250 | 56.30±4.30 | | | |
| | 300 | 79.40±1.20 | | | |
| III | 150 | 23.20±1.30 | 220.45 (200.61-242.69) | 417.14 (370.09-494.14) | 2.654 |
| | 200 | 32.10±2.20 | | | |
| | 250 | 51.50±3.40 | | | |
| | 300 | 74.30±2.44 | | | |
| IV | 150 | 21.20±3.20 | 177.39 (159.91-193.45) | 331.85 (303.48-373.20) | 2.539 |
| | 200 | 37.27±4.30 | | | |
| | 250 | 57.60±2.30 | | | |
| | 300 | 79.50±2.30 | | | |
| V | 150 | 24.50±2.30 | 165.97 (69.09-229.80) | 277.88 (218.40-563.40) | 7.266 |
| | 200 | 42.50±1.40 | | | |
| | 250 | 61.20±1.20 | | | |
| | 300 | 98.30±2.50 | | | |
| VI | 150 | 22.40±3.40 | 201.80 (57.89-365.84) | 353.44 (263.91-1690.46) | 7.836 |
| | 200 | 32.10±2.20 | | | |
| | 250 | 46.10±2.30 | | | |
| | 300 | 86.70±1.20 | | | |

Values are mean ± S.D of five replication; Number of larvae =10; $LC_{50}$=Lethal concentration 50 and $LC_{90}$=Lethal concentration 95; Values with different alphabet in column are statistically significant ($p<0.05$ level; DMRT).

## The role of juvenile hormone in mosquito development and reproduction

Derivatives of dapsone (I-VI) act as a Juvenile Hormone, growth regulator like methoprene analog against larvae of a Aedes aegypti when used as larvicides[6-17].Juvenile Hormone plays an antimetamorphic role during development, maintaining the status quo in preimaginal stages and preventing immature *Aedes aegypti* from precociously turning into adults. Juvenile Hormone are high while the larva is feeding and growing, but drop to permit metamorphosis. This hypothesis has not been tested in *Aedes aegypti*. The functions of Juvenile Hormone during preimaginal stages in *Aedes aegypti* have been mostly extrapolated from studies on other mosquitos or deduced from the phenotypic changes induced by topical application of Juvenile Hormone or its analogues.

Derivatives of dapsone and pyriproxyfen affect the development of *Aedes aegypti* at multiple stages. Derivatives of dapsone blocks the embryonic development of *Aedes aegypti* and inhibit egg hatching. Juvenile Hormone A also interfere with metamorphosis and prevent the emergence of adults. Derivatives of dapsone is particularly effective against 4th instar mosquito larvae. A majority of the Derivatives of dapsone-treated larvae died during the pupal stage. Larval exposure to Juvenile Hormone A affects metamorphic midgutre modelling. The metamorphic midgutre modelling includes two processes, formation of pupal/adult midguts through the division and differentiation of imaginal diploid cells, and programmed death of larval polytene midgut cells treating 4th instar *Aedes aegypti* larvae with derivatives of dapsone blocks degeneration of larval midgut epithelium. Derivatives of dapsone -treated larvae pupae, but the pupae developed from treated larvae contain two midgut epithelial layers, larval midgut and the pupal/adult midgut. This Derivatives of dapsone effect is presumably achieved through modulating the action of ecdysterone (20E), as the derivatives of dapsone treatment causes dysregulation of many genes involved in the stage-specific response to ecdysterone (20E), including ecdysone receptor.

Organisms are subject to “trade-offs” between the energetic demands of reproduction and the energy required to survive. JH is the central hormonal regulator of life-history trade-offs in many mosquitos, including *Aedes aegypti*. *Aedes aegypti* must not only allocate nutrients properly within each developmental stage but must also consider the effects of immediate resource allocations on future reproduction and overall fitness. Three major periods can be defined in the development of the ovaries during a gonotrophic cycle in *Aedes aegypti* mosquitoes: by apoptosis. By resorbing excess reproductive tissues, mosquitoes can alter previous reproductive decisions by redirecting resources away from reproduction in favour of competing physiological activities. Under this model, excessive allocations toward somatic physiology or reductions in incoming nutrition often result in reductions to reproductive output. The developmental fate of the remaining follicle is also sensitive to nutrition and Juvenile Hormone. Nutrients and transcripts related to VG accumulated in *Aedes aegypti* treated with the Juvenile Hormone analogue derivatives of dapsoneor fed 20% sucrose. These mosquitoes have increased fecundity and decreased follicle resorption after a blood meal. In addition to nutrition, mating triggers many changes in female mosquitoes that enhance reproductive success.

Many of the phenotypic, molecular and biochemical changes observed when manipulating nutrition and hormonal status Juvenile Hormone A- sterilizing effects have been described as mediated by suppressing the expression of ecdysone-regulated genes in female *Aedes aegypti* stressing the importance of the endocrine balance between Juvenile Hormone and ecdysterone (20E), during the gonotrophic cycle. It is concluded that the increase in the larval mortality of *Aedes aegypti* and *Aedes albopictus* depend upon the functional groups present in the Schiff bases (III< II< IV< VI< I< V). Table 2.

## Conclusion

The derivatives of dapsone**(I)** 4,4'-sulfonylbis(N-(4-chlorobenzylidene)aniline), **(II)** 4,4'-sulfonylbis(N-(4-methoxybenzylidene)aniline), **(III)** 4,4'-(((sulfonylbis (4,1-phenylene))bis(azanylylidene)) bis(methanyly lidene))diphenol, **(IV)** 3,3'-(((sulfonylbis(4,1-phenylene))bis(azanylylidene)) bis(methanylylidene)) diphenol, **(V)** 2,2'-(((sulfonylbis(4,1-phenylene))bis (azanylylidene)) bis(methanylylidene))diphenol and**(VI)** 4,4'-sulfonylbis (N-(furan-2-ylmethylene) aniline) were prepared and were screened against larvae of *Aedes aegypti*. It was concluded that the increase in the larval mortality of *Aedes aegypti* depend upon the functional groups present in the Schiff bases.

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