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Letter to the Editor

Larvicidal activity of prenyl xanthones from *Garcinia mangostana* against dengue vector

Sir,

Aedes aegypti is the vector of arbo viruses responsible for major diseases like dengue, chikungunya and zika. Dengue fever is endemic in the Southeast Asia and India, Bangladesh and Pakistan (Akram and Ahmed, 2005) and continues to increase with more severe forms of the disease such as dengue haemorrhagic fever and dengue shock syndrome or with unusual symptoms such as central nervous system involvement Pancharoen et al., 2002). In recent years, mosquito control programmes had a setback because of the ever-increasing insecticide resistance. Besides synthetic insecticidal resistance, the increased cost of insecticides and public concern over environmental contamination have demanded to search for alternative vector control strategies which are expected to reduce the hazards to human and other organisms in the environment (Liu et al., 2005). Larvicidal, as a natural product have been demonstrated their efficacy as an insecticidal and could be used as alternative to synthetic pesticides due to their specificity towards target organisms and biodegradability (Dinesh et al., 2014).

Mangosteen (*Garcinia mangostana* L.) is a tropical plant which belongs to the family of Guttiferae and is named as "the queen of fruits" mainly found in India, Myanmar, Srilanka, and Thailand. In Ayurvedic medicine, the pericarp of this fruit has wide use against diarrhea, cholera and dysentery (Chopra et al., 1956). In Southeast Asia it used for centuries in the treatment of skin infections and wounds, antiplasmodial, anticancer and also fruit was reported to contain rich in prenylated and oxygenated xanthones (Mahabusarakam et al., 2006).

G. mangostana were purchased from Ooty in Nilgiris District, Tamil Nadu, India. The pericarp was removed, cleaned and shade-dried. 50 g of pulverized pericarp was macerated in methanol with intermittent shaking. Methanol extract was collected and dried with rotator evaporator. The dried chloroform residue obtained from methanolic extract was sequentially partitioned with hexane, diethyl ether, ethyl acetate and finally methanol. The methanol partitioned fraction was again sequentially partitioned with diethyl ether, ethyl acetate, and methanol. The obtained diethyl ether residue was purified with following combination of solvent (hexane: ethyl acetate: methanol 3:2:1) to give a compound **(1)** pale yellow crystal (mp: 142-145°C; yield: 216 mg). The obtained methanol fraction residue was sequentially partitioned with hexane, ethyl acetate, chloroform and methanol. Methanol residue was dried and purified with hexane/ethyl acetate/methanol (3:1:1) to give a compound **(2)** bright yellow amorphous powder (mp: 179°-181°C; yield: 1250 mg). Both compounds showed positive test for phenolic group (alc. $FeCl_3$ test) and flavonoid (Shinoda test). The structures of the compounds were elucidated based on the spectral data obtained from UV-Vis, FT-IR, ^{13}C NMR, ^{1}H NMR and ESI-MS (data not shown). The spectral data of the isolated compounds were closely resembled (Ee et al., 2006) to the respective prenyl xanthone derivatives, compound **(1)** is dulxanthone and compound **(2)** is alpha-mangostin (Figure 1).

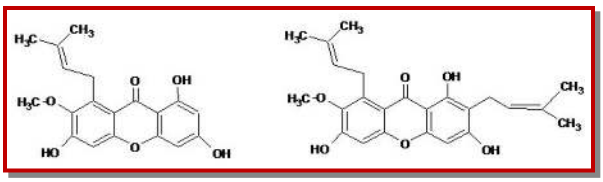

Figure 1: Chemical structure of dulxanthone (left) and alpha-mangostin (right)

Eggs, larvae, and adults of *A. aegypti* were obtained from the stock culture maintained at Entomology Research Institute, Loyola College, Chennai, which were free of exposure to pathogens, insecticides, or repellents. Laboratory rearing (Kamakshi et al., 2015) was done at a temperature of 27 ± 2°C, 75-85% relative humidity, and a photoperiod of 11 ± 0.5 hours. Larvicidal activity was evaluated by the methods (WHO, 2005) with slight modifications. Ten numbers of late third instar larvae of *A. aegypti* was introduced into the test containers. The sample taken in four concentrations were 10, 7.5, 5.0 and 2.5 ppm. Normal control and solvent control (acetone in water) were maintained separately. Mortality rate was registered after 48-hours exposure period. The moribund and dead larvae were collected, and larval mortality was calculated for each concentration. The bioassays were performed at a room temperature of 27 ± 1°C with three replicates for each concentration. Percent mortality was calculated using the following formula.

Table I

Larvicidal activity of prenyl xanthones from *G. mangostana* against *A. aegypti*

Treatment	LC_{50} (ppm)	95% Fiducial limit		LC_{90} (ppm)	95% Fiducial limit		Slope ± SE	Intercept ± SE	χ^2
		Lower limit	Upper limit		Lower limit	Upper limit			
α- Mangostin	23.3	14	34.1	59.9	23.7	87.5	3.1 ± 1.3	0.6 ± 1.2	0.7*
Dulxanthone	8.81	7.75	10.62	19.09	14.53	32.17	3.8 ± 0.6	1.3 ± 0.5	4.1*

$p \leq 0.05$, level of significance of chi-square (χ^2) values

$$\% \text{ Mortality} = \frac{\text{Number of dead larvae}}{\text{Number of larvae introduced}} \times 100$$

The result of prenyl xanthones of larvicidal activity was depicted in Table I. Both compounds showed moderate larvicidal effects; however the highest larval mortality was found in dulxanthone with LC_{50} and LC_{90} values of 8.8 and 19.1 ppm than alpha mangostin which showed LC_{50} and LC_{90} values of 23.3 and 59.9 ppm, respectively. The LC_{50} and LC_{90} were determined by EPA probit analysis software.

The prenylated xanthones act as like sterol carrier protein inhibitors (SCPIs) and it is novel class of insecticides that target the SCP-2, which is partially responsible for intracellular cholesterol transport in insects (Larson et al., 2008) and the mode of action that suppresses cholesterol uptake from the dietary source. Cholesterol trafficking is essential for insects because they are unable to synthesize cholesterol *de novo,* and as a result, insects rely on dietary sources or symbiotic microbes to acquire cholesterol for proper development and viability (Kim and Lan, 2010). α-Mangostin is identified as a mosquito SCPI *via* high throughput screening. The mechanism of SCPIs is the reduction and inhibition of cholesterol uptake, as a result, disruption in cell proliferation and ecdysone biosynthesis for growth and survival (Larson et al., 2010). This is the first report on the larvicidal assay of dulxanthone against the mosquito vector *A. aegypti*.

The bioactive compound thus could be used for maximizing the effectiveness and specificity in future insecticidal design with specific or multiple target sites, while ensuring the economic and ecological sustainability. The results from this study clearly showed that dulxanthone and other xanthones may have strong potential as a new botanical larvicidal alternative to synthetic to control disease causing vector mosquitoes.

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