Original article:

LARVICIDAL ACTIVITY AND STRUCTURE ACTIVITY RELATIONSHIP OF CINNAMOYL AMIDES FROM ZANTHOXYLUM ARMATUM AND THEIR SYNTHETIC ANALOGUES AGAINST DIAMONDBACK MOTH, PLUTELLA XYLOSTELLA

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ABSTRACT

Cinnamoyl amides isolated from Zanthoxylum armatum (Rutaceae) and their synthetic analogues were tested for their insecticidal activity against the second instar larvae of diamondback moth, Plutella xylostella (L.) (Lepidoptera: Yponomeutidae) to determine the promising structures with insecticidal activity. Most of the test compounds showed promising activity against larvae of P. xylostella. However, the activities of different compounds varied depending on the presence of different substituents at various positions of both the aromatic rings A and B. Among the tested compounds, 8, N-(3-bromo-4-methoxyphenethyl)cinnamamide showed best larvicidal activity with an LC50 = 62.13 mg/L followed by 6, N-(3-bromophenethyl)cinnamamide (LC50=128.49 mg/L) and 2 N-(4-methoxyphenylethyl)cinnamamide (LC50 = 225.65 mg/L).

Keywords: Cinnamoyl amides, structure activity relationship, larvicidal activity, Plutella xylostella

INTRODUCTION

The diamondback moth, Plutella xylostella (L.) (Lepidoptera: Yponomeutidae) is most damaging insect pest of cruciferous crops throughout the world (Talekar, 1992) and greatest threat to crucifer production in many parts of the world, causing more than 90 % crop loss (Harcourt, 1962; Talekar and Shelton, 1993; Verkerk and Wright, 1996; Gu et al., 2010). Intensive use of chemical pesticides in its control has led to this pest developing resistance to a wide range of insecticides and caused serious damage to natural enemies (Harcourt, 1962; Ke et al., 1991). Several synthetic insecticides besides botanical and microbial control agents have been used for the control of this pest (Liu et al., 1982; Srinivasan and Kumar, 1982; Chaudhuri et al., 2001). Nearly two decades ago, the annual cost of controlling P. xylostella on a worldwide basis was estimated to be US $ 1 billion but in a recent study the
Overall management costs were estimated at US$ 4 billion (Zalucki et al., 2012).

Throughout the world, pesticides have dominated attempts to control *P. xylostella* for more than 40 years (Talekar and Shelton, 1993; Syed, 1992). The negative impacts of pesticides and increasing pesticide resistance have increased the interest in alternative control methods, with emphasis being placed on biological control, host plant resistance, cultural control, botanicals and other non-polluting methods (Cheng, 1988; Lim et al., 1996). Due to harmful effects of synthetic pesticides to health, environment and resistance development in pests, there is a need for the development of safer and effective alternative strategies to contain the pests.

*Zanthoxylum armatum* DC. (Rutaceae) is found abundantly throughout the Western Himalayas at altitudes of 1200-3000 m and is extensively used in the Indian system of medicine, as carminative, stomachic and anthelmintic. The extracts of this plant are known to possess insecticidal, anti-fungal and anti-microbial activities (Singh and Singh, 2011). Various pharmacological activities of this plant are attributed to the presence of amides as cinnamoyl amides isolated from various *Zanthoxylum* species and other plants have shown a wide spectrum of biological activities such as antiinflammatory, antiplasmodial, antiviral, antibacterial, antiplatelet aggregation, eukotriene biosynthesis in human polymorphonuclear leukocytes and anticancer activities (Wu et al., 1995; Ross et al., 2004).

Insecticidal activity of several amides has been reported against Lepidopteran insects (Ewete et al., 2000; Park et al., 2002; Dyer et al., 2003; Batista-Pereira et al., 2006). However, cinnamoyl amide conjugates of phe-nylethylamine derivatives isolated from *Z. armatum* or any other plant have not been investigated previously for their insecticidal activities. Keeping in view the great potential of cinnamoyl amides of plant origin, present study was conducted to screen a series of cinnamoyl amides isolated from *Z. armatum* and their synthetic analogues for their larvicidal activity against *P. xylostella* and determine structure activity relationship (SAR).

**MATERIALS AND METHODS**

**General**

Boric acid used for the synthesis of silica-supported boric acid (H$_3$BO$_3$-SiO$_2$) was purchased from Ranbaxy Chemicals Ltd. Silica gel (60–120 mesh) used for preparation of H$_3$BO$_3$-SiO$_2$ catalyst and column chromatography, was purchased from Sisco Research Laboratories Pvt. Ltd., India. The course of the reactions was monitored by TLC on pre-coated aluminium plates (silica gel 60 F$_{254}$) purchased from Merck, Germany. All other chemicals were purchased from Sigma-Aldrich, USA and were used without further purification. NMR spectra were recorded on Bruker Avance-300 and 600 spectrometers at room temperature using CDCl$_3$ or DMSO as solvents and TMS as internal standard.

**Extraction and isolation of compounds (10, 12 and 13) from Z. armatum**

Air dried powder of bark (1.0 Kg) of *Z. armatum* was extracted with methanol: H$_2$O (80: 20; v/v, 3 × 4L) in a percolator at room temperature for 12 h. Combined percolations were dried under reduced pressure to yield 238.2 g of crude extract. The extract thus obtained was suspended in water and sequentially fractionated with *n*-hexane, chloroform, ethyl acetate and *n*-butanol, and dried under vacuo to get corresponding fractions i.e. *n*-hexane (12.5 g), chloroform (34.3 g), ethyl acetate (12.1 g), *n*-butanol (92.4 g) and aqueous fraction (78.1 g). Chloroform fraction (25.0 g) was subjected to column chromatography over silica-gel (60-120 mesh) and eluted with 10, 20, 30, 50, 75 and 100 % ethyl acetate in *n*-hexane (5 x 200 mL each). Repeated column chromatography of fractions obtained in 50 % ethyl acetate/*n*-hexane led to the isolation of armatamide (12, 480 mg). Chromatographic purification of fractions eluted in 75 % ethyl acetate/*n*-

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hexane resulted in the isolation of zanthosin (10, 57 mg) and rubimamin (13, 23 mg).

**Synthesis of silica-supported boric acid (H$_3$BO$_3$-SiO$_2$)**

H$_3$BO$_3$-SiO$_2$ was synthesized by following our previously reported procedure (Kumar et al., 2011).

**General experimental procedure for the synthesis of cinnamoyl amides**

To a stirred mixture of phenethyamine derivative (1 mmol) and cinnamoyl chloride derivative (1.1 mmol) in toluene (4 mL) at room temperature, silica-supported boric acid (H$_3$BO$_3$-SiO$_2$, 1.5 mol %) was added. The reaction was kept at room temperature and progress of the reaction was monitored by TLC. After completion of the reaction, ethyl acetate (5 mL) was added and the catalyst was separated by filtration. The filtrate thus obtained was washed with brine (3×5 mL) and dried over anhydrous sodium sulphate. The product was purified by crystallization with ethanol. Isolated compounds were characterized by $^1$H and $^{13}$C NMR spectroscopy.

*N-(Phenylethyl)cinnamamide (1)*

$^1$H NMR (300 MHz, CD$_3$OD) $\delta$H 2.84-2.89 (m, 2H), 3.51-3.56 (m, 2H), 6.60 (d, 1H, J = 15.8 Hz), 7.20-7.23 (m, 1H), 7.26-7.29 (m, 4H), 7.36-7.41 (m, 3H), 7.51-7.56 (m, 3H); $^{13}$C NMR (75 MHz, CD$_3$OD) $\delta$C 35.5, 41.2, 120.8, 126.3, 127.8, 128.5, 128.8, 128.9, 129.7, 135.2, 139.5, 140.6, 167.6.

*N-(4-Methoxyphenylethyl)cinnamamide (2)*

$^1$H NMR (300 MHz, CD$_3$OD) $\delta$H 2.88-2.93 (m, 2H), 3.47-3.52 (m, 2H), 3.79 (s, 3H), 6.61 (d, 1H, J = 15.7 Hz), 6.84-6.92 (m, 2H), 7.14-7.21 (m, 3H), 7.37-7.41 (m, 2H), 7.50-7.51 (m, 3H); $^{13}$C NMR (75 MHz, CD$_3$OD) $\delta$C 33.7, 39.6, 55.2, 114.4, 120.9, 127.8, 128.6, 128.9, 129.7, 129.8, 135.3, 140.6, 159.3, 167.6.

*N-(2-Methoxyphenylethyl)cinnamamide (3)*

$^1$H NMR (300 MHz, CD$_3$OD) $\delta$H 2.86-2.90, 3.49-3.53 (m, 2H), 3.83 (s, 3H), 6.59 (d, 1H, J = 15.7 Hz), 6.87-6.95 (m, 3H), 7.14-7.20 (m, 2H), 7.36-7.38 (m, 3H), 7.53-7.56 (m, 2H); $^{13}$C NMR (75 MHz, CD$_3$OD) $\delta$C 30.3, 39.8, 54.7, 110.4, 120.5, 120.9, 127.4, 127.8, 127.9, 128.9, 129.7, 130.4, 135.3, 140.5, 158.1, 167.6.

*N-(3,4-Dimethoxyphenethyl)cinnamamide (4)*

$^{1}$H NMR (300 MHz, CD$_3$OD) $\delta$H 2.89-2.94 (m, 2H), 3.50-3.55 (m, 2H), 3.82 (s, 3H), 3.84 (s, 3H), 6.61 (d, 1H, J = 15.9 Hz), 6.78-6.94 (m, 3H), 7.37-7.39 (m, 3H), 7.50-7.56 (m, 3H); $^{13}$C NMR (75 MHz, CD$_3$OD) $\delta$C 33.1, 41.0, 55.5 (2 OCH$_3$), 112.4, 112.8, 121.2, 127.8, 128.3, 128.9, 129.8, 132.4, 135.2, 140.6, 148.8, 149.8, 167.6.

*N-(2-Bromophenethyl)cinnamamide (5)*

$^{1}$H NMR (300 MHz, CD$_3$OD) $\delta$H 3.01-3.06 (m, 2H), 3.54-3.59 (m, 2H), 6.60 (d, 1H, J = 15.6 Hz), 7.13-7.24 (m, 2H), 7.29-7.32 (m, 2H), 7.36-7.40 (m, 3H), 7.50-7.61 (m, 3H); $^{13}$C NMR (75 MHz, CD$_3$OD) $\delta$C 33.9, 39.5, 120.8, 124.2, 128.3, 128.9, 129.3, 129.8, 131.1, 132.9, 133.3, 135.2, 138.7, 140.7, 167.7.

*N-(3-Bromophenethyl)cinnamamide (6)*

$^{1}$H NMR (300 MHz, CD$_3$OD) $\delta$H 2.98-3.02 (m, 2H), 3.56-3.61 (m, 2H), 6.58 (d, 1H, J = 15.5 Hz), 7.17-7.26 (m, 3H), 7.36-7.45 (m, 3H), 7.52-7.58 (m, 4H); $^{13}$C NMR (75 MHz, CD$_3$OD) $\delta$C 34.0, 39.3, 121.3, 125.4, 127.1, 128.5, 128.9, 129.3, 130.9, 133.0, 133.8, 135.2, 137.9, 140.1, 167.5.

*N-(4-Bromophenethyl)cinnamamide (7)*

$^{1}$H NMR (300 MHz, CD$_3$OD) $\delta$H 2.96-3.01 (m, 2H), 3.55-3.59 (m, 2H), 6.63 (d, 1H, J = 15.9 Hz), 7.21-7.28 (m, 3H), 7.41-7.50 (m, 3H), 7.54-7.59 (m, 4H); $^{13}$C NMR (75 MHz, CD$_3$OD) $\delta$C 33.4, 39.0, 119.2, 126.2, 127.4, 128.2, 129.3, 130.0, 130.5, 134.6, 137.3, 139.2, 167.2.

*N-(3-Bromo-4'-methoxyphenethyl)cinnamamide (8)*

$^{1}$H NMR (300 MHz, CD$_3$OD) $\delta$H 2.84-2.89 (m, 2H), 3.46-3.52 (m, 2H), 3.90 (s, 3H), 6.63 (d, 1H, J = 15.7 Hz), 6.75 (d, 1H, J = 7.9 Hz), 7.13-7.19 (m, 2H), 7.28-7.36 (m, 3H), 7.46-7.53 (m, 3H); $^{13}$C NMR (75 MHz, CD$_3$OD) $\delta$C 33.8, 39.7, 55.6, 108.4, 113.4, 120.1, 127.9, 128.2, 128.9, 129.3, 129.7, 130.2, 132.0, 136.5, 141.3, 167.5.

*N-(2-Fluorophenethyl)cinnamamide (9)*

$^{1}$H NMR (300 MHz, CD$_3$OD) $\delta$H 3.05-
3.11 (m, 2H), 3.54-3.60 (m, 2H), 6.56 (d, 1H, J = 15.3 Hz), 7.01-7.07 (m, 1H), 7.18-7.29 (m, 3H), 7.35-7.46 (m, 3H), 7.56-7.64 (m, 3H); $^{13}$C NMR (75 MHz, CD$_3$OD) $\delta$C 34.7, 40.5, 121.8, 121.9, 124.4, 128.0, 128.4, 129.1, 129.7, 131.5, 131.7, 132.6, 132.7, 135.7, 138.3, 141.8, 143.2, 167.9.

Rubimamin (10) $^1$H NMR (300 MHz, CDCl$_3$) $\delta$H 2.83 (t, 2H, J = 6.9 Hz), 3.62-3.66 (m, 2H), 3.83-3.93 (m, 12H), 6.24 (d, 1H, J = 15.5 Hz), 6.74-6.84 (m, 4H), 6.99 (d, 1H, J = 1.8 Hz), 7.05 (dd, 1H, J = 1.8 Hz, 8.1 Hz), 7.56 (d, 1H, J = 15.5 Hz); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$C 35.6, 41.3, 56.3 (4 OCH$_3$), 110.1, 111.5, 111.8, 112.4, 118.9, 121.0, 122.3, 128.1, 131.8, 141.2, 148.1, 149.4, 149.5, 150.9, 166.6; HR-ESI-MS calcd. for C$_{21}$H$_{26}$NO$_5$ [M + H]$^+$ m/z 372.1811, found 372.1802.

N-(Phenylethyl)-3,4-methylenedioxy-cinnamamide (11) $^1$H NMR (300 MHz, CD$_3$OD) $\delta$H 2.83-2.88 (m, 2H), 3.49-3.54 (m, 2H), 5.97 (s, 2H), 6.40 (d, 1H, J = 15.6 Hz), 6.82 (d, 1H, J = 8.0 Hz), 7.01 (dd, 1H, J = 1.5 Hz, 8.0 Hz), 7.07 (d, 1H, J = 1.5 Hz), 7.19-7.29 (m, 5H), 7.44 (d, 1H, J = 15.6 Hz); $^{13}$C NMR (75 MHz, CD$_3$OD) $\delta$C 35.6, 41.2, 101.8, 106.0, 108.3, 118.7, 124.0, 126.3, 128.5, 128.8, 129.6, 139.5, 140.5, 148.8, 149.6, 167.8.

Armatamide (12) $^1$H NMR (300 MHz, DMSO-d$_6$) $\delta$H 2.70 (t, 2H, J = 6.9 Hz), 3.72 (s, 3H), 3.73-3.78 (m, 2H), 6.06 (s, 2H), 6.45 (d, 1H, J = 15.5 Hz), 6.88 (d, 2H, J = 7.0 Hz), 6.94 (d, 1H, J = 8.0 Hz), 7.05 (d, 1H, J = 8.0 Hz), 7.13-7.15 (m, 3H), 7.33 (d, 1H, J = 15.5 Hz); $^{13}$C NMR (75 MHz, DMSO-d$_6$) $\delta$C 33.7, 39.9, 54.3, 100.8, 105.6, 107.9, 113.1, 119.7, 122.5, 128.7, 128.9, 130.7, 137.7, 147.3, 147.8, 157.1, 164.4; HR-ESI-MS calcd. for C$_{19}$H$_{20}$NO$_4$ [M + H]$^+$ m/z 326.1392, found 326.1377.

Zanthosin (13) $^1$H NMR (300 MHz, CDCl$_3$) $\delta$H 2.84 (t, 2H, J = 6.9 Hz), 3.61-3.65 (m, 2H), 3.86 (s, 6H), 5.98 (s, 2H), 6.18 (d, 1H, J = 15.5 Hz), 6.74-6.88 (m, 4H), 6.95-7.00 (m, 2H), 7.53 (d, 1H, J = 15.5 Hz); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$C 35.6, 41.3, 56.2, 56.3, 101.8, 106.7, 108.8, 111.8, 112.4, 119.1, 121.0, 124.1, 129.6, 131.8, 141.1,148.1, 148.6, 149.4, 149.5, 166.4; HR-ESI-MS calcd. for C$_{29}$H$_{22}$NO$_4$ [M + H]$^+$ m/z 356.1498, found 356.1481.

N-(1-Hydroxy-1-phenylethyl)cinnamamide (14) $^1$H NMR (300 MHz, CD$_3$OD) $\delta$H 3.57-3.60 (m, 2H), 4.82-4.89 (m, 1H), 6.67 (d, 1H, J = 15.7 Hz), 7.28-7.57 (m, 11H); $^{13}$C NMR (75 MHz, CD$_3$OD) $\delta$C 46.4, 70.0, 120.7, 125.9, 126.1, 127.6, 128.3, 128.9, 135.2, 140.8, 142.9, 167.9.

Residual toxicity of cinnamoyl amides and their analogues against P. xylostella

Test insect

P. xylostella used for the experimental study was collected from cabbage (Brassica oleracea L.) field and reared on mustard, Brassica juncea (L.) seedlings in the laboratory for more than 50 generations at 26 ± 2 °C temperature, 60 ± 5 % relative humidity and photoperiod 16:8 L:D). Second/third instar larvae starred were used for the experiments.

Preliminary screening

Preliminary screening of cinnamoyl amides and their analogues at higher concentrations (10000 and 5000 ppm) were tested for their toxicity against second instar larvae of P. xylostella. Based on preliminary screening results, five concentrations were fixed and tested against target pest in the main experiment.

Residual toxicity of cinnamoyl amides and their analogues

Residual toxicity of ginger extracts and ginger oil against P. xylostella was tested following leaf dip bio-assay (Park et al., 2002; Kumar et al., 2016; Reddy et al., 2015) against second instar larvae of P. xylostella. Five concentrations (62.5 to 1000 mg/L) of test compounds were prepared either separately or by serial dilution from the solution of higher concentration. Commercial insecticide (chlorpyriphos at 25 to 400 mg/L) commonly used for the control of P. xylostella was used as a positive control. Observa-
tions on mortality were recorded at 72 and 96 h intervals.

**Data analysis**

Data from all bioassays were corrected for control mortality using Abbott formula (Abbot, 1925) and analyzed using SPSS 7.5 for calculating LC$_{50}$ values (concentration that causing 50 % mortality) by log-probit regression.

**RESULTS**

*Insecticidal activity against P. xylostella*

Initially, compounds 10, 12 and 13 isolated from *Z. armatum* were evaluated for their insecticidal activity against 2nd instar larvae of *P. xylostella*. Compound 12 (armatamide) showed promising activity with an LC$_{50} = 298.70$ mg L$^{-1}$ after 96 h, whereas compounds 10 and 13 did not show significant activity (Table 1). Further, in order to derive structure activity relationship various substituted analogues (1-9, 11 and 14) were synthesized by the reaction of corresponding acid halides and amines in the presence of silica-supported boric acid (H$_3$BO$_3$-SiO$_2$) as catalyst at room temperature (Figure 1) and tested for their activity. The structures of tested compounds (1-14) are given in Figure 2 and the results of activities of these compounds against *P. xylostella* in terms of lethal concentration to kill 50 % of the population relative to control (LC$_{50}$ values) and other regression parameters are summarized in Table 1.

Table 1: Toxicity of amides against larvae of *Plutella xylostella* after 96 h

| Compounds | LC$_{50}$ mg/L (95 % CL) | Slope ± SE | $\chi^2$ | P value |
|-----------|--------------------------|------------|---------|---------|
| 1         | 485.67 (310.03–1038.09)  | 1.10 ± 0.26| 0.75    | 0.86    |
| 2         | 225.65 (149.4–331.62)    | 1.34 ± 0.27| 0.64    | 0.99    |
| 3         | 591.85 (356.64–1686.43)  | 0.99 ± 0.26| 0.24    | 0.97    |
| 4         | 858.16 (418.98–12489.49) | 0.74 ± 0.26| 0.19    | 0.99    |
| 5         | 1582.35 (677.49–53035.29)| 0.66 ± 0.27| 0.40    | 0.94    |
| 6         | 128.49 (14.82–261.77)    | 0.66 ± 0.24| 0.27    | 0.96    |
| 7         | 412.94 (257.50–876.17)   | 1.02 ± 0.26| 0.51    | 0.91    |
| 8         | 62.13 (21.59–101.53)     | 1.31 ± 0.30| 1.15    | 0.76    |
| 9         | —                        | —          | —       | —       |
| 10        | —                        | —          | —       | —       |
| 11        | 623.89 (379.98–1722.70)  | 1.04 ± 0.26| 0.38    | 0.79    |
| 12        | 298.70 (171.95–588.77)   | 0.93 ± 0.25| 0.60    | 0.99    |
| 13        | —                        | —          | —       | —       |
| 14        | 467.90 (299.73–983.01)   | 1.09 ± 0.26| 0.49    | 0.99    |

| Chlorpyriphos | 88.32 (60.08–125.93) | 1.44 ± 0.27 | 0.41 | 0.94 |

LC$_{50}$: Concentrations causing 50 % toxicity; CL: Confidence limits; — LC$_{50}$ was not calculated for compounds showing < 50 % mortality

**Figure 1:** H$_3$BO$_3$-SiO$_2$ catalyzed synthesis of cinnamoyl amides of phenethylamine derivatives
Structure activity relationship (SAR)

It is evident that most of the test compounds showed promising activity against larvae of *P. xylostella*. However, the activities of different compounds varied depending on the presence of different substituents at various positions of both the aromatic rings A and B (Figure 3). As evident from Table 1, most of the test compounds exhibited toxicity against *P. xylostella* at 62.5 to 1000 mg L\(^{-1}\). Compound 8 showed 96.67% activity at 1000 mg L\(^{-1}\) followed by 2 (86.67%) and 3 (76.7%) (Figure 3). Probit analysis results showed that, among the tested compounds, 8, N-(3-bromo-4-methoxyphenethyl)cinnamamide was most active against larvae of *P. xylostella* with an LC\(_{50} = 62.13\) mg/L, followed by 6, N-(3-bromophenethyl)cinnamamide (LC\(_{50} = 128.49\) mg/L) and 2, N-(4-methoxyphenethyl)cinnamamide (LC\(_{50} = 225.65\) mg/L). The LC\(_{50}\) values for the other compounds 1, 3, 7, 11, 12 and 14 were 485.67, 591.85, 412.94, 623.89, 298.70 and 467.90 mg/L respectively.

The unsubstituted amide 1 showed significant activity with an LC\(_{50}\) value of 485.67 mg/L. The presence of oxygenated substituents at 3 and 4 positions of ring A (such as methylenedioxy and dimethoxy) reduced the activity as compared to unsubstituted amide 1 (Table 1, compounds 10-13). Compound 11 containing 3,4-methylenedioxy (ring A) was found to be 1.4 times less active (LC\(_{50} = 623.89\) mg/L) than 1. While the presence of 4'-OCH\(_3\) (ring B) led to increase in the activity by 2-fold (2, LC\(_{50} = 225.65\) mg/L), the presence of 3', 4'-OCH\(_3\) substitution on ring B led to reduction or complete loss in the activity (4, 10 and 13). Compound 12 having 3,4-methylenedioxy and 4'-OCH\(_3\) substituents showed LC\(_{50}\) value of 298.70 mg/L. Slight decrease in activity was observed for 2'-OCH\(_3\) (ring B) substituted derivative (3, LC\(_{50} = 591.85\) mg/L). In case of 3'-Br substituent on ring B (6, LC\(_{50} = 128.49\) mg/L), the activity was increased by...
4-fold, whereas in case of 4′-Br substituted cinnamoyl amide, a slight increase in the activity was observed (7, LC<sub>50</sub> = 412.94 mg/L). As 3′-Br and 4′-OCH<sub>3</sub> substitution showed increase in the activity individually, a compound having both these groups was synthesized (8) and was found to be most potent among all the tested compounds with an LC<sub>50</sub> of 67.31 mg/L. Halogen substituent at 2′ position (ring B) such as 2′-Br and 2′-F had negative influence on the activity as 5 (2′-Br) gave a very high LC<sub>50</sub> value of 1582.35 mg/L and 9 (2′-F) did not show significant activity. The presence of an –OH substituent on aliphatic chain of phenethylamine unit (14, LC<sub>50</sub> = 467.90 mg/L) did not show a significant effect on the activity as compared to unsubstituted amide 1.

The results from the present study showed that, the amide 8 was most active (LC<sub>50</sub> = 62.13 mg/L) against second instar larvae of P. xylostella and was comparable with the standard insecticide (chlorpyriphos) at 96 h after treatment followed by compound 6, (LC<sub>50</sub> = 128.49 mg/L) and compound 2 (LC<sub>50</sub> = 225.65 mg/L).

**DISCUSSION**

Cinnamoyl amides isolated from Z. armatum and their synthetic analogues were tested against the second instar larvae of P. xylostella for larvicidal activity. It is evident that most of the compounds showed larvicidal activity to larvae of P. xylostella and was comparable with the standard insecticide (chlorpyriphos) at 96 h after treatment followed by compound 6, (LC<sub>50</sub> = 128.49 mg/L) and compound 2 (LC<sub>50</sub> = 225.65 mg/L).

Most of the test compounds showed promising activity against larvae of P. xylostella. However, the activities of different compounds varied depending on the presence of different substituents at various positions of both the aromatic rings A and B. Among the tested compounds, 8, N-(3′-bromo-4-methoxyphenethyl)cinnamamide showed best larvicidal activity followed by 6, N-(3′-bromophenethyl)cinnamamide and 2 N-(4′-methoxyphenylethyl)cinnamamide.

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**Declaration of interest**

The authors declare that they have no conflict of interest.
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