ENTOMOLOGY

Evaluation of the mosquitocidal activity of *Photorhabdus* and *Xenorhabdus* extracts against the larvae of *Aedes aegypti* (Diptera: Culicidae)

Supawan Pansri,[1] Chanakan Subkrasae,[1] Jiranun Ardpairin,[1] Abdulhakam Dumidae,[1] Wipanee Meesil,[1] Wandee Wattanachaiyingcharoen,[2,3] Sarunporn Tandhavanant,[4] Helge B Bode,[5] Aunchalee Thanwisai,[1,3,6] Apichat Vitta[1,3,6]

[1]Department of Microbiology and Parasitology, Faculty of Medical Science, Naresuan University, Phitsanulok, Thailand; [2]Department of Biology, Faculty of Science, Naresuan University, Phitsanulok, Thailand; [3]Center of Excellence for Biodiversity, Faculty of Sciences, Naresuan University, Phitsanulok, Thailand; [4]Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; [5]Department of Natural Products in Organismic Interactions, Max Planck Institute for Terrestrial Microbiology, Marburg, Germany; [6]Center of Excellence in Medical Biotechnology, Faculty of Medical Science, Naresuan University, Phitsanulok, Thailand

Correspondence: Apichat Vitta, Department of Microbiology and Parasitology, Faculty of Medical Science, Naresuan University, Phitsanulok 65000, Thailand.
Tel.: +66 55 964653. Fax: +66 55 964770.
E-mail: apichatv@nu.ac.th,

Key words: *Aedes aegypti*, biological control, entomopathogenic nematode, *Photorhabdus*, *Xenorhabdus*.

Contributions: SP, designed the study, performed experiments, prepared figures, and was involved in writing draft manuscripts; CS, AD, JA, WM, performed experiments and was involved in writing draft manuscripts; WW, provided materials and was involved in writing draft manuscripts; ST, analyzed data, prepared figures of survival curves, and was involved in writing draft manuscripts; HBB, provided materials and analyzed data of HPLC-MS, and was involved in writing draft manuscripts; AT, performed experiments, provided materials, and was involved in writing draft manuscripts; AV, designed the study, performed experiments, analyzed data, managed projects, and was involved in writing drafts and reviewing manuscripts. All authors read and approved the final manuscript.

Conflict of interest: the authors declare no conflict of interest. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Ethics approval and consent to participate: not applicable.

Availability of data and materials: data and materials are available from the corresponding author upon request.

Funding: this study was funded by the Royal Golden Jubilee (RGJ) Ph.D. Program through the National Research Council of Thailand (NRCT) (Grant No. N41A640215). Also, this work was partially supported by Naresuan University (NU) and the National Science, Research and Innovation Fund (NSRF) (Grant No. R2567B034).

Acknowledgments: the authors would like to thank Miss Chamaiporn Fukruksa, Miss Thatcha Yimthin, Mr. Manawat Suwannaroj, Miss Temsiri Yooyangket, and Dr. Paramaporn Muangpat for helping them keep and collect the symbiotic bacteria.

Received: 17 January 2025.
Accepted: 5 April 2025.

Publisher's note: all claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article or claim that may be made by its manufacturer is not guaranteed or endorsed by the publisher.

Journal of Entomological and Acarological Research 2025; 57:13641
doi:10.4081/jear.2025.13641

Abstract

Aedes aegypti is the main vector for dengue viruses. Alternative control of this mosquito was proposed because of its resistance to chemical insecticides. The symbiotic bacteria *Photorhabdus* associated with Heterorhabditid nematodes and *Xenorhabdus* associated with Steinernematid nematodes may be alternative resources for controlling this mosquito vector. Therefore, the present study evaluated extracts from *Photorhabdus* and *Xenorhabdus* bacteria against *A. aegypti* larvae. The larvicidal bioassay was performed according to the World Health Organization guidelines for laboratory and field testing of mosquito larvicides. Survival curves were analyzed to compare the mortality of the *A. aegypti* larvae between the ethyl acetate extracts and the control group. In addition, high-performance liquid chromatography-mass spectrometry analysis was performed to elucidate the natural compounds produced by these bacteria. Among 4 *Photorhabdus* isolates, the *Photorhabdus luminescens* subsp. *hainanensis* (bWT8.5_TH) extracts resulted in the greatest mortality (69%), whereas among 8 *Xenorhabdus* isolates, the *Xenorhabdus stockiae* (bWT8.5_TH) extracts resulted in the greatest larvicidal activity against A. aegypti, with 99% mortality after exposure to the 1% extracts for 96 hours. In contrast, at concentrations of 0.1, 0.01, and 0.001% of the extracts, no or less mortality of *A. aegypti* larvae was detected after exposure to the extracts for 24, 48, 72, and 96 hours. A natural compound, xenoamicine, is a common natural compound produced by *Xenorhabdus* bacteria. Therefore, extracts of

Xenorhabdus and *Photorhabdus* bacteria may be used as biocontrol compounds for killing *A. aegypti* larvae.

Introduction

Aedes aegypti, a culicine mosquito in the order Diptera, is the main vector for several viruses, such as Japanese encephalitis, West Nile, Chikungunya, and dengue viruses (Martinet *et al*., 2019). *Aedes* spp. have also been reported as vectors for the Zika virus, which is considered a major public health threat worldwide (Benelli & Mehlhorn, 2016; Gebre *et al*., 2016). In addition, *Aedes* spp. are vectors of filarial worms, which are the cause of elephantiasis in humans (Gleave *et al*., 2016). Importantly, *A. aegypti* is recognized as the main vector for dengue virus, which causes hemorrhagic fever in humans (Bhatt *et al*., 2013). In the last two decades, the number of dengue cases has increased from 505,430 cases in 2000 to over 2.4 million in 2010 and 5.2 million in 2019 (World Health Organization, 2022). In Thailand, from January 1 to September 28, 2020, 59,842 dengue cases with 38 deaths were reported from all regions of the country (Department of Disease Control, Ministry of Public Health, 2022).

Efforts to control *Aedes* mosquitoes must be implemented while the development of vaccines and effective drugs for the treatment of their associated diseases are still in progress. In general, chemical control for *Aedes,* applying organophosphates and organochlorines, is commonly used because these are highly efficient and rapidly effective on both adult and larval mosquitoes. However, the repeated use of these chemicals has led to the emergence of chemical-resistant mosquitoes (Elia-Amira *et al*., 2018). Moreover, accumulated insecticidal chemicals are toxic to animal and human health (Hassaan & El Nemr, 2020). The biological control of *Aedes* may be an alternative method to overcome these problems. Several organisms have been reported to have the potential to control *Aedes* mosquitoes. Copepods, turtles, tilapia, and entomopathogens are effectively used to control *A. aegypti* larvae (Marten *et al*., 2022; Maurya *et al*., 2022). In addition, the entomopathogenic bacteria *Photorhabdus* and *Xenorhabdus* are promising biocontrol agents for *Aedes* mosquitoes (da Silva *et al*., 2020).

Photorhabdus and *Xenorhabdus* are gram-negative bacilli belonging to the Enterobacteriaceae family and are symbiotically associated with entomopathogenic nematodes in the genera *Heterorhabditis* and *Steinernema*, respectively (Sajnaga & Kazimierczak, 2020). The nematode-bacterium complex produced by their secondary metabolites causes the death of insect larvae within 24 to 48 hours (Goodrich-Blair & Clarke, 2007; Askary & Abd-Elgawad, 2021). *Photorhabdus* and *Xenorhabdus* bacteria have been reported as biocontrol agents for controlling several insect pests (Cimen *et al*., 2022; Tomar *et al*., 2022). These symbiotic bacteria also showed molluscicidal activity against mollusks (Ardpairin *et al*., 2024; Dumidae *et al*., 2024). These bacteria produce several secondary metabolites with a broad range of bioactivities, including insecticidal (Bode, 2009; Shi *et al*., 2022; Mollah, 2024) and apoptotic activity (Mollah, Yeasmin, *et al*., 2020) to kill insects. In an earlier study on the use of these bacteria, *Photorhabdus* and *Xenorhabdus* were reported to be orally pathogenic agents to *Aedes* spp. (da Silva *et al*., 2013). During the present decade, more than 30 isolates of *Xenorhabdus* and *Photorhabdus,* with approximately 10 species, have shown potential larvicidal activity against *Aedes* spp. following oral treatment (Fukruksa *et al*., 2017; Vitta *et al*., 2018; Yooyangket *et al*., 2018; Suwannaroj *et al*., 2020; Thanwisai *et al*., 2021; Thanwisai *et al*., 2022; Subkrasae *et al*., 2022). However, a study on the use of extracts from *Xenorhabdus* and *Photorhabdus* has been experimentally evaluated for the control of *Aedes* mosquitoes (Subkrasae *et al*., 2022). In addition, the ethyl acetate extract of *Xenorhabdus ehlersii* KSY was shown to be immunosuppressive to *Spodoptera exigua*, an agricultural pest (Kim *et al*., 2018). Therefore, we hypothesized that ethyl acetate extracts of *Photorhabdus* and *Xenorhabdus* might have good potential to kill *Aedes* larvae. With this connection, the objective of the present study was to evaluate the ability of the ethyl acetate extracts of different *Photorhabdus* and *Xenorhabdus* Thai isolates to kill *A. aegypti* larvae. Moreover, natural compounds produced by these symbiotic bacteria were identified by high-performance liquid chromatography-mass spectrometry (HPLC-MS) analysis.

Materials and Methods

Bacterial strains

Four *Photorhabdus* and eight *Xenorhabdus* isolates were randomly selected for evaluation of their potential to control *A. aegypti* larvae (Table 1). The bacteria recovered from culture stocks at -40°C were cultured on nutrient bromothymol blue agar (NBTA) in the dark at room temperature (RT) for 4 days.

Table 1. Bacterial isolates used for testing their mosquitocidal activity against *Aedes aegypti*.

Bacteria	Isolate code	GenBank Accession Number (*recA* gene)	References
Photorhabdus luminescens subsp. *akhurstii*	bCM17.3_TH	KY436924	Fukruksa *et al.* (2017)
Photorhabdus luminescens subsp. *akhurstii*	bNN121.4_TH	MG209233	Yooyangket *et al.* (2018)
Photorhabdus luminescens subsp. *hainanensis*	bWT8.5_TH	MK478134	Suwannaroj *et al.* (2020)
Photorhabdus asymbiotica subsp. *australis*	bWT11.2_TH	MK478133	Suwannaroj *et al.* (2020)
Xenorhabdus ehlersii	bMH9.2_TH	KY404034	Fukruksa *et al.* (2017)
Xenorhabdus japonica	bNN165.4_TH	MG209251	Yooyangket *et al.* (2018)
Xenorhabdus stockiae	bCTK4.4_TH	MK478088	Suwannaroj *et al.* (2020)
Xenorhabdus stockiae	bNSM40.5_TH	KY809288	Yimthin *et al.* (2021)
Xenorhabdus stockiae	bWB4.2_TH	MK478098	Suwannaroj *et al.* (2020)
Xenorhabdus stockiae	bWB5.4_TH	MK478100	Suwannaroj *et al.* (2020)
Xenorhabdus stockiae	bWB9.1_TH	MK478104	Suwannaroj *et al.* (2020)
Xenorhabdus stockiae	bWT12.5_TH	MK478108	Suwannaroj *et al.* (2020)

Extraction of organic compounds

The crude organic compounds from whole-cell cultures of selected bacteria were extracted using ethyl acetate. A single colony of each isolate on the NBTA was transferred into a 15-mL centrifuge tube containing 5 mL of Luria-Bertani (LB) broth. The tube was incubated at RT with shaking at 180 rpm for 24 hours. Subsequently, 5 mL of each bacterial culture was transferred into a 2000-mL Erlenmeyer flask containing 500 mL of LB broth. The flask was then placed in an incubator at 180 rpm with shaking at 28°C for 72 hours. Then, 1000 mL of ethyl acetate was added to the bacteria-culture flask and mixed well by shaking. To allow the crude organic compounds from bacteria to dissolve in the ethyl acetate, the flask was placed at RT for 24 hours or up to one week. The top layer, containing the bacterial organic compounds dissolved in ethyl acetate, was transferred to the evaporating flask. All the crude organic extracts were concentrated via a rotary vacuum evaporator (Buchi, Flawil, Switzerland). Extraction from each bacterial isolate was performed 3 times to maximize the amount of crude organic compounds. The condensed extracts of all the bacterial isolates were weighed and stored at -20°C until use.

Mosquito strains

Eggs of *A. aegypti* (laboratory strain) on filter paper were purchased from the Taxonomy and Reference Museum of the Department of Medical Sciences at the National Institute of Health of Thailand, Ministry of Public Health, Nonthaburi Province, Thailand. The eggs were placed in distilled water to allow the first instar larvae to hatch, which were fed minced pet food. Late third- and early fourth-instar larvae were used in the bioassays.

Biological assay

The mosquitocidal activity of the bacterial extracts against the larvae of *A. aegypti* was performed according to guidelines for laboratory and field testing of mosquito larvicides (World Health Organization, 2005). The crude organic compounds were thawed at RT for 1 hour. To prepare a 1% stock solution (10 mg/mL) in dimethyl sulfoxide (DMSO), 0.2 g of each crude organic compound from each bacterial isolate was dissolved in 20 mL of DMSO. A 10-fold dilution of the 1% stock solution with DMSO was subsequently performed to obtain dilutions of 0.1, 0.01, and 0.001%. For the biological assay, a 7-oz plastic container (plastic cup) was used. A total of 25 third- or early fourth-instar larvae of *A. aegypti* were carefully pipetted into a plastic cup containing 100 mL of dechlorinated water (5 cm depth). A total of four cups (100 larvae/time/concentration) were used for each bacterial extract. Subsequently, 1 mL of each extract (1, 0.1, 0.01, or 0.001%) was added to each cup. Cups containing dechlorinated water and 2% DMSO were used as a control. The assay was performed at RT (25-28°C) with a photoperiod of 12:12 hours (L:D). The dead larvae in each tested cup were observed and counted at 24, 48, 72, and 96 hours after exposure to the extracts. The larvae were considered dead when they remained immobilized after activation by light or a toothpick. The experiment was performed 3 times on different days. The average mortality of *A. aegypti* larvae after exposure to the bacterial extracts was calculated from 12 replicates.

Analysis of bacterial extracts

The secondary metabolites produced by the symbiotic bacteria were determined by HPLC-MS. The symbiotic bacteria were cultured in LB broth for 72 hours. Subsequently, the bacterial cultures were dissolved in a 1/10 culture volume of methanol. HPLC-MS analysis was performed *via* a a Dionex Ultimate 3000 system (Thermo Fisher Scientific, Massachusetts, USA) coupled with a Bruker AmaZon X mass spectrometer (Bruker Corporation, Massachusetts, USA) and an Acquity UPLC BEH C18 1.7 µm RP column (Waters Corporation, Milford, Massachusetts, USA) with an acetonitrile (0.1% formic acid) in H_2O (0.1% formic acid) gradient ranging from 5 to 95% over 16 minutes at a flow rate of 0.4 mL/min at 40°C. The Bruker Compass Data Analysis version 4.3 program was used to analyze the chromatograms.

Data analysis

The cumulative mortality of the larvae of *A. aegypti* was calculated. Survival analysis for comparing mortality among the control and tested bacterial isolates was statistically analyzed *via* a stata version 13 (StataCorp LP, College Station, Texas, USA) (Kaplan-Meier estimate, $p<0.05$).

Results

Larvicidal activity of bacterial extracts against Aedes aegypti

A. aegypti larvae began to die at 24 hours after exposure to the highest dose of the *Photorhabdus* and *Xenorhabdus* extracts. Among the *Photorhabdus* extracts at 24 hours after exposure, the highest mortality (60%) of *A. aegypti* larvae was observed after exposure to the 1% extract of *P. luminescens* subsp. *hainanensis* (bWT8.5_TH). At 96 hours, the mortality of *A. aegypti* gradually increased to 69% after exposure to the 1% extract of this bacterial isolate (bWT8.5_TH). In contrast, at concentrations of 0.1, 0.01, and 0.001%, no or less mortality of *A. aegypti* larvae was detected after exposure for 24, 48, 72, and 96 hours. In the control groups (2% DMSO and dechlorinated water), the mortality of the larvae was similar to that of the low-concentration extract (Table 2 and Figure 1). At 96 hours after exposure, the highest mortality of *A. aegypti* larvae was observed after treatment with *P. luminescens* subsp. *hainanensis* (bWT8.5_TH) extracts, whereas the lowest mortality was found after contact with *P. luminescens* subsp. *akhurstii* extracts (bCM17.3_TH).

Among the *Xenorhabdus* extracts at 24 hours after exposure, the highest mortality (49%) of *A. aegypti* larvae was observed after exposure to the 1% extract of *Xenorhabdus stockiae* (bWT9.1_TH), and the mortality rate gradually increased to 85% at 96 hours after exposure. Similar to the findings with *X. stockiae* (bWT9.1_TH) extracts, the mortality rate was the highest (99%) in this study after larvae were exposed to *X. stockiae* (bNSM40.5_TH) extracts. In contrast, at extract concentrations of 0.1, 0.01, and 0.001%, no or less mortality of *A. aegypti* larvae was detected after exposure for 24, 48, 72, and 96 hours (Table 3 and Figure 2).

High-performance liquid chromatography-mass spectrometry analysis

Two symbiotic bacteria in this study were selected for the detection of their natural compounds. The extracts from *X. stockiae* (bWT12.5_TH) contained xenocoumacine II (Xcn2), xenocoumacine I (Xcn1), GameXPeptide (GXPs) C, and xenoamicine. Another isolate, *X. ehlersii* bMH9.2_TH, produced tetrapeptide, xenoamicine, and protoporphyrin IX (*Supplementary Table 1*). These natural metabolites have been identified as common compounds produced by *Photorhabdus* and *Xenorhabdus* bacteria.

Table 2. Mortality rates of *Aedes aegypti* larvae after exposure to crude extracts from *Photorhabdus*.

Symbiotic bacteria	Isolate code	Extract concentration (%)	Mortality rate (%) ± standard deviation *Aedes aegypti*			
			24 hours	48 hours	72 hours	96 hours
Photorhabdus luminescens subsp. *akhurstii*	bCM17.3_TH	1	22±7.29	34±6.15	35±5.38	35±4.81
		0.1	0±0.00	1±0.48	1±0.40	4±0.59
		0.01	0±0.00	1±0.28	1±0.28	4±1.32
		0.001	1±0.89	2±0.68	4±0.75	7±0.99
Photorhabdus luminescens subsp. *akhurstii*	bNN121.4_TH	1	13±2.23	26±2.42	34±2.24	43±2.11
		0.1	0±0.29	0±0.20	0±0.17	1±0.20
		0.01	0±0.00	0±0.00	0±0.00	0±0.00
		0.001	0±0.00	0±0.00	0±0.00	0±0.00
Photorhabdus luminescens subsp. *hainanensis*	bWT8.5_TH	1	60±8.80	67±9.23	68±8.42	69±7.67
		0.1	0±0.00	0±0.00	0±0.00	0±0.00
		0.01	0±0.00	0±0.00	0±0.00	0±0.00
		0.001	0±0.00	0±0.00	0±0.00	0±0.00
Photorhabdus asymbiotica subsp. *australis*	bWT11.2_TH	1	29±6.40	44±5.31	47±4.90	48±4.51
		0.1	0±0.00	0±0.00	0±0.17	0±0.14
		0.01	0±0.00	0±0.00	0±0.00	0±0.00
		0.001	0±0.00	0±0.00	0±0.00	0±0.00
2% dimethyl sulfoxide: control			0±0.00	0±0.00	0±0.00	0±0.14
Dechlorinated water: control			0±0.00	0±0.00	0±0.00	0±0.00

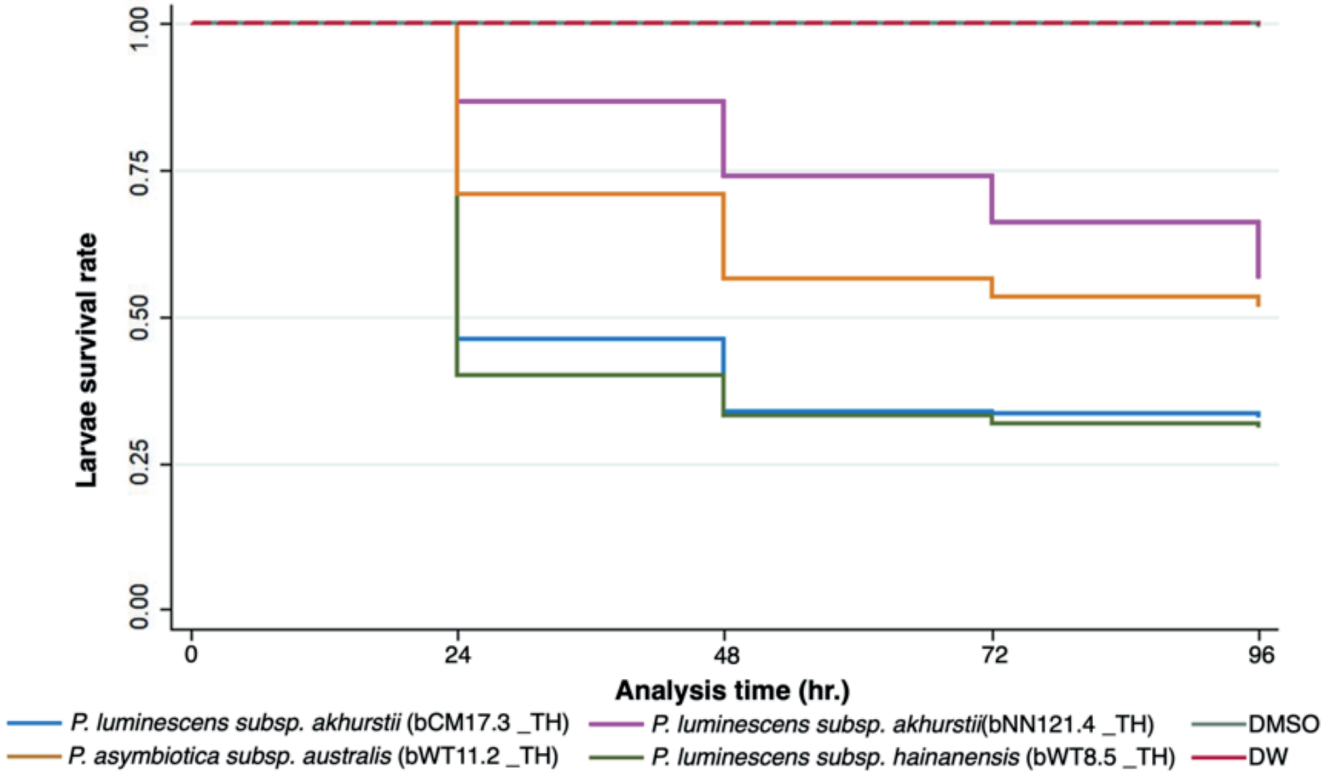

Figure 1. Survival curves of *Aedes aegypti* larvae after exposure to 1% crude extracts of four *Photorhabdus* isolates, 2% dimethyl sulfoxide (DMSO), and dechlorinated water (DW) at 24, 48, 72, and 96 hours.

Table 3. Mortality rates of *Aedes aegypti* larvae after exposure to a crude extract of *Xenorhabdus*.

Symbiotic bacteria	Isolate code	Extract concentration (%)	Mortality rate (%) ± standard deviation *Aedes aegypti*			
			24 hours	48 hours	72 hours	96 hours
Xenorhabdus ehlersii	bMH9.2_TH	1	2 ±0.51	5±1.01	8±1.05	10±1.02
		0.1	1±0.58	1±0.41	1±0.33	1±0.29
		0.01	0±0.00	0±0.00	0±0.00	0±0.00
		0.001	0±0.00	0±0.00	0±0.00	0±0.00
Xenorhabdus japonica	bNN165.4_TH	1	27±4.96	35±4.32	37±3.95	41±3.55
		0.1	0±0.00	0±0.00	0±0.00	0±0.00
		0.01	0±0.00	0±0.00	0±0.17	0±0.14
		0.001	0±0.00	0±0.00	0±0.00	0±0.00
Xenorhabdus stockiae	bCTK4.4_TH	1	2±0.79	6±1.00	14±1.49	22±1.78
		0.1	0±0.00	0±0.00	0±0.00	0±0.00
		0.01	0±0.00	0±0.00	0±0.00	0±0.00
		0.001	0±0.00	0±0.00	0±0.00	0±0.00
Xenorhabdus stockiae	bNSM40.5_TH	1	22±5.85	74±6.11	91±5.85	99±5.78
		0.1	0±0.29	2±0.66	3±0.59	5±0.87
		0.01	0±0.00	0±0.00	1±0.46	2±0.42
		0.001	0±0.00	2±1.00	4±1.04	5±0.95
Xenorhabdus stockiae	bWB4.2_TH	1	27±7.18	55±5.70	71±5.00	85±4.67
		0.1	1±0.39	2±0.41	2±0.40	2±0.36
		0.01	1±0.58	3±0.97	3±0.81	4±0.76
		0.001	0±0.00	1±0.61	3±0.69	4±0.66
Xenorhabdus stockiae	bWB5.4_TH	1	1±0.65	4±0.78	6±0.74	7±0.71
		0.1	1±0.39	1±0.34	1±0.28	3±0.76
		0.01	0±0.00	0±0.20	2±0.51	3±0.54
		0.001	0±0.29	1±0.34	3±0.48	3±0.43
Xenorhabdus stockiae	bWB9.1_TH	1	49±7.74	65±7.36	79±6.71	85±6.29
		0.1	1±0.62	1±0.45	1±0.37	3±0.54
		0.01	0±0.00	1±0.48	3±0.54	4±0.56
		0.001	1±0.62	1±0.45	2±0.42	2±0.37
Xenorhabdus stockiae	bWT12.5_TH	1	14±3.92	45±4.53	57±4.15	80±3.89
		0.1	0±0.29	0±0.20	1±0.23	3±0.68
		0.01	0±0.00	0±0.00	0±0.00	0±0.14
		0.001	2±1.44	3±1.09	4±0.92	9±1.89
2% dimethyl sulfoxide: negative control			0±0.00	0±0.00	0±0.00	0±0.14
Dechlorinated water: negative control			0±0.00	0±0.00	0±0.00	0±0.00

Discussion and Conclusions

A. aegypti is the major insect vector of dengue virus, which is the cause of dengue hemorrhagic fever and is a global public health concern. Biological control of *A. aegypti* is an alternative disease control measure. Our report revealed that *Photorhabdus* and *Xenorhabdus* extracts were highly effective against *A. aegypti* larvae. In earlier research, the oral toxicity of *Photorhabdus* and *Xenorhabdus* was elucidated, with variable effectiveness against *A. aegypti* larvae. Da Silva *et al*. (2013) reported that *P. luminescens* was effective at killing *A. aegypti,* with 73% and 83% mortality in fed and unfed larvae, respectively. A lower mortality rate was observed in *A. aegypti* treated with *X. nematophila* in both fed (52%) and unfed (42%) larvae.

In addition, the culture fluid of *X. nematophila* was more effective against *A. aegypti* larvae, with a mortality rate of up to 50% after exposure for 8 days (da Silva *et al.*, 2017). Fukruksa *et al.* (2017) demonstrated *X. ehlersii* bMH9.2_TH with 100% efficiency and *X. stockiae* bLPA18.4_TH with above 60% efficiency for killing *A. aegypti* larvae under both fed and unfed conditions. In contrast, the ethyl acetate extracts of *X. ehlersii* bMH9.2_TH in the present study showed low effectiveness against *A. aegypti* larvae. This might be due to bacteria that produce various natural compounds with variable bioactivities. Vitta *et al.* (2018) reported that the mortality rate of *A. aegypti* was as high as 87-99% at 96 hours after exposure to *X. stockiae* (bNBP22.2_TH). Yooyangket *et al.* (2018) reported that the highest larval mortality of *A. aegypti* was 99% after exposure to *X. stockiae* (bNN112.3_TH) at 96 hours. Additionally, Suwannaroj *et al.* (2020) reported that *Xenorhabdus* WB5.4_TH and *Xenorhabdus* WB12.5_TH, which are closely related to *X. stockiae*, resulted in high mortality of *A. aegypti* (99.99% and 70%, respectively) at 96 hours after exposure. In addition, the larvicidal activity of the *X. stockiae* strain KUT6 was observed against *A. aegypti* within 24 to 72 hours after treatment (Jissin & Vani, 2020). Like in previous reports, *X. griffiniae* whole cells showed potential larvicidal activity against *A. aegypti* (91% mortality at 72 and 96 hours after exposure) (Thanwisai *et al.*, 2021). Recently, Subkrasae *et al.* (2022) reported that ethyl acetate extracts from *X. indica* (bSNK8.5_TH) caused 50% mortality in *A. aegypti* larvae after 96 hours of exposure. Similarly, whole cells of *Photorhabdus* (bPP7.1_TH) presented moderate mortality (48.89%) because they killed *A. aegypti* larvae after 96 hours of exposure (Thanwisai *et al.*, 2022). Most recently, cell-free supernatants from *X. cabanillasii* resulted in 100% mortality of *A. aegypti,* and fabclavine was proven to be an effective compound

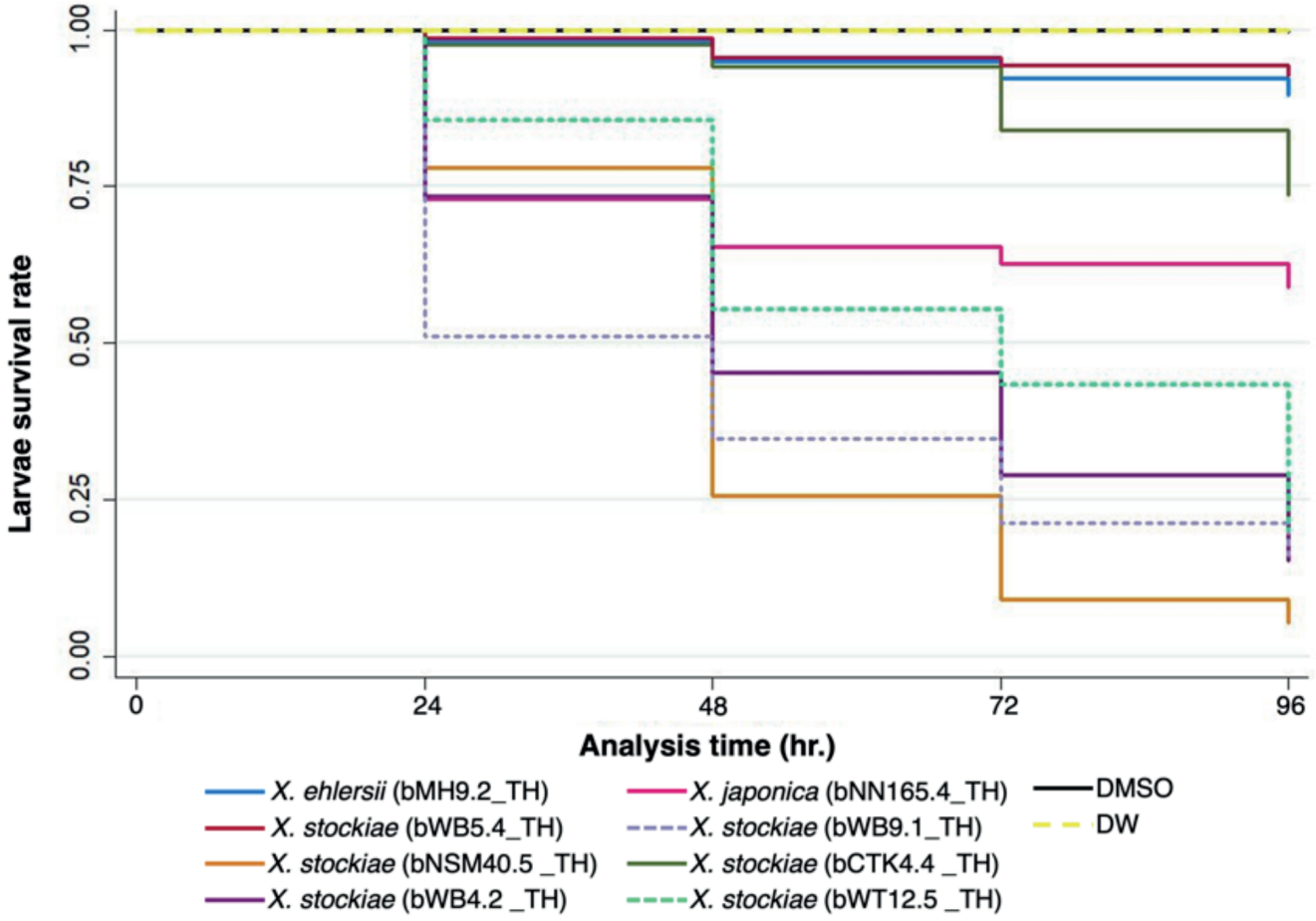

Figure 2. Survival curves of *Aedes aegypti* larvae after exposure to 1% crude extracts of eight *Xenorhabdus* isolates, 2% dimethyl sulfoxide (DMSO), and dechlorinated water (DW) at 24, 48, 72, and 96 hours.

against the larvae of this *A. aegypti* (Ulug *et al.*, 2024). Therefore, several forms of *Photorhabdus* and *Xenorhabdus* spp., including live whole cells, cell-free supernatants, and ethyl acetate extracts, have shown potential for killing *A. aegypti* larvae with variable mortality. Further studies on the sustainable effectiveness of these symbiotic bacteria against *A. aegypti* are needed. The identification and isolation of effective natural compounds may overcome this issue.

In the present study, xenoamicine, Xcn1, Xcn2, GXPs C, and protoporphyrin IX were identified in *Xenorhabdus* spp. In general, *Photorhabdus* and *Xenorhabdus* help their symbiotic nematodes by producing secondary metabolite compounds that kill the insect host and protect the host cadaver from other competing microorganisms (Reimer *et al.*, 2013; Fuchs *et al.*, 2014; Stock, 2019; Zhang *et al.*, 2019). This natural compound induces immunosuppression, allowing bacteria and nematodes to survive within host insect cadavers (Hasan *et al.*, 2019). These bacteria are effective biocontrol agents because they can produce compounds with antibiotic and antifungal properties that inhibit the growth of pathogens and produce insecticidal toxins that are harmful to a wide range of insect pests (da Silva *et al.*, 2020). A previous study by Ji and Kim (2004) revealed that compounds produced by *X. nematophila* can significantly inhibit the formation of hemocyte nodules, one of the immune response processes to insect-invading pathogens, similar to the findings of Mollah, Dekebo *et al.* (2020), who demonstrated that butanol extracts from *X. hominickii* culture broth effectively inhibited phospholipase A_2 (PLA_2) activity in *S. exigua* hemocytes, which is a primary cellular defense mechanism against insect pathogens. This mechanism is involved in inhibiting PLA_2, which is required for eicosanoid production and the activation of insect immune responses (da Silva *et al.*, 2020; Mollah & Kim, 2020). The inhibition of PLA_2 leads to a weakened immune system and septicemia in insects (Singh *et al.*, 2023). Ji *et al.* (2004) reported that the first PLA_2-inhibiting compound produced by *X. nematophila* was benzylideneacetone, which exhibited antibacterial activity against plant pathogenic bacteria. In addition, proline-tyrosine (PY), acetylated phenylalanine-glycine-valine, cis-PY, indole, oxindole, and p-hydroxyphenyl propionic acid have been identified as PLA_2 inhibitors produced by *X. nematophila* and *P. temperata* subsp. *temperata* (Shrestha *et al.*, 2010; Seo *et al.*, 2012; Mollah, *et al.*, 2020).

Another important compound produced by symbiotic bacteria is GXPs, which are synthesized by the NRPS enzyme GXP synthetase (GxpS) in *P. luminescens* TTO1. These GXPs are closely linked to the environment of the insect host. GXPs, consisting of GXP-A to GXP-D (Jin *et al.*, 2023) and GXP-E to GXP-H (Nollmann *et al.*, 2015), are produced only when the bacteria are inside the insect larvae because insect larvae can produce precursors for GXP production, such as p-aminophenylalanine (PAPA) and its monomethylated derivative. However, homologs of the GxpS gene have been found in several *Xenorhabdus* strains, which do not produce PAPA derivatives.

Analysis of various strains of symbiotic bacteria revealed that while most strains are capable of producing GXPs, only some, including a few *Xenorhabdus* strains, produce PAPA-derived peptides (Nollmann *et al.*, 2015). In the present study, the identification of GXP produced by *X. stockiae* revealed that this species can produce these peptides. However, further research is needed to fully understand the presence and production of GXP in *X. stockiae*. A previous study revealed that GXP significantly increased the toxicity of *B. thuringiensis* to *S. exigua* larvae, effectively suppressing the insect immune response (Hrithik *et al*., 2022). In particular, synthetic GXP-A was found to significantly inhibit the cytoplasmic expansion of hemocytes in *S. exigua*. Although GXP-A did not affect phenoloxidase activation, an insect humoral immune response that regulates the coagulation and melanization of hemolymph in response to pathogens, it was able to significantly reduce nodule formation in a dose-dependent manner, with an IC50 value of 25.8 ng per larva (Shi *et al*., 2022), suggesting that this reduction in nodule formation was related to the suppression of the host immune response.

In addition to their immunosuppressive properties, symbiotic bacteria also produce other compounds, such as xenocoumacins, which are benzopyran rings in the amino acid chain, including Xcn1 and Xcn2. They are produced in the insect hemocoel and are active against both gram-positive and gram-negative bacteria and some fungi (Han *et al.*, 2024). These compounds are synthesized by nonribosomal peptide synthetases (NRPSs) and polyketide synthases (Park *et al.*, 2009; Qin *et al*., 2021). Xcn1 has more potent antifungal activity, however, the accumulation of Xcn1 is toxic to cells. To prevent self-toxicity, bacteria have evolved a mechanism to convert the stronger antibiotic Xcn1 into the weaker Xcn2. This regulatory mechanism helps bacteria avoid self-toxicity and optimizes antibiotic production for competitive advantage within the insect host (Park *et al.*, 2009; Dong *et al.*, 2020). Therefore, xenocoumacins are involved in antibiotic activity (Park *et al.*, 2009). Our findings suggest that xenocoumacins may be effective against *Aedes* larvae. Moreover, a recent study revealed that fabclavines identified from various *Photorhabdus* and *Xenorhabdus* species (Tobias *et al*., 2017) exhibit strong ovicidal and larvicidal effects against *A. aegypti* (Ulug *et al*., 2024) and *A. albopictus* (Touray *et al*., 2024). *Xenorhabdus cabanillasi* is the most effective and causes high egg-hatching inhibition and larval mortality (Ulug *et al*., 2024). Fabclavines can also disrupt cell membranes, similar to xenorhabdus lipoprotein toxin, which causes cell apoptosis and membrane perforation in the anterior midgut of larvae (Kim *et al*., 2017; Ulug *et al*., 2024). Fabclavines also act as antibiotics (Fuchs *et al*., 2014).

Overall, the effects of secondary metabolites produced by *Photorhabdus* and *Xenorhabdus* bacteria on mosquito larvae include immune response dysfunction, disruption of crucial gut structures, and direct toxicity (Eom *et al.*, 2014; Kim *et al.*, 2017; Ulug *et al.*, 2024). In addition, this study identified GXP, xenoamicin, and protoporphyrin IX from *Xenorhabdus* bacteria. These natural compounds may be involved in the decrease in the gut microbiota of *A. aegypti* larvae, the imbalance of the immune response in *A. aegypti*, and direct toxicity to the intestinal tract, which subsequently leads to the death of *A. aegypti* larvae. Further research is needed to understand the function and role of these compounds in mosquito larvae.

In summary, *X. stockiae* extract has potential insecticidal and larvicidal effects on *A. aegypti*. Xenocoumacine is commonly found in *Xenorhabdus* bacteria and may be an effective compound against *A. aegypti*. *Xenorhabdus* bacteria are bioresources for identifying alternative insecticides.

References

ARDPAIRIN J., SUBKRASAE C., DUMIDAE A., PANSRI S., HOMKAEW C., MEESIL W., KUMCHANTUEK T., PHOUNGPETCHARA I., DILLMAN AR., PAVESI C., BODE HB., TANDHAVANANT S., THANWISAI A., VITTA A., 2024 - Symbiotic bacteria associated with entomopathogenic nematodes showed molluscicidal activity against Biomphalaria glabrata, an intermediate host of Schistosoma mansoni. - Parasit. Vectors 17: 529.

ASKARY T.H., ABD-ELGAWAD M.M.M., 2021 - Opportunities and challenges of entomopathogenic nematodes as biocontrol agents in their tripartite interactions. - Egypt. J. Biol Pest. Control 31: 42.

BHATT S., GETHING P.W., BRADY O.J., MESSINA J.P., FARLOW A.W., MOYES C.L., DRAKE J.M., BROWNSTEIN J.S., HOEN A.G., SANKOH O., MYERS M.F., GEORGE D.B., JAENISCH T., WINT G.R., SIMMONS C.P., SCOTT T.W., FARRAR J.J., HAY S.I., 2013 - The global distribution and burden of dengue. - Nature 496: 504-507.

BENELLI G., MEHLHORN H., 2016 - Declining malaria, rising of dengue and Zika virus: insights for mosquito vector control. - Parasitol. Res. 115: 1747-1754.

BODE H.B., 2009 - Entomopathogenic bacteria as a source of secondary metabolites. - Curr. Opin. Chem. Biol. 13: 224-230.

CIMEN H., TOURAY M., GULSEN S.H., HAZIR S., 2022 - Natural products from Photorhabdus and Xenorhabdus: mechanisms and impacts. - Appl. Microbiol. Biotechnol. 106: 4387-4399.

DA SILVA O.S., PRADO G.R., DA SILVA J.L., SILVA C.E., DA COSTA M., HEERMANN R., 2013 - Oral toxicity of Photorhabdus luminescens and Xenorhabdus nematophila (Enterobacteriaceae) against Aedes aegypti (Diptera: Culicidae). - Parasitol. Res. 112: 2891-2896.

DA SILVA L.R., SCHWALM F.U., SILVA C.E., DA COSTA M., HEERMANN R., DA SILVA O.S., 2017 - Larvicidal and growth-inhibitory activity of entomopathogenic bacteria culture fluids against Aedes aegypti (Diptera: Culicidae). - J. Econ. Entomol. 110: 378-385.

DA SILVA W.J., PILZ-JÚNIOR H.L., HEERMANN R., DA SILVA O.S., 2020 - The great potential of entomopathogenic bacteria Xenorhabdus and Photorhabdus for mosquito control: a review. - Parasit. Vectors 13: 376.

DEPARTMENT OF DISEASE CONTROL, MINISTRY OF PUBLIC HEALTH, THAILAND, 2022 - Weekly Disease Forecast No. 281_Dengue. Available from: https://ddc.moph.go.th/en/details.php?topic=high.

DONG Y., LI X., DUAN J., QIN Y., YANG X., REN J., LI G., 2020 - Improving the yield of xenocoumacin 1 enabled by in situ product removal. - ACS Omega 5: 20391-20398.

DUMIDAE A., HOMKEAW C., SUBKRASAE C., ARDPAIRIN J., PANSRI S., POLSEELA R., PHOUNGPETCHARA I., KUMCHANTUEK T., TANDHAVANANT S., THANWISAI A., VITTA A., 2024 - Molluscicidal property of symbiotic bacteria associated with entomopathogenic nematodes against Indoplanorbis exustus and Radix rubiginosa, the intermediate hosts of trematode parasites. - Parasite Epidemiol. Control. 27: e00375.

ELIA-AMIRA N.M.R., CHEN C.D., LAU K.W., LEE H.L., LOW V.L., NORMA-RASHID Y., SOFIAN-AZIRUN M., 2018 - Organophosphate and organochlorine resistance in larval stage of Aedes albopictus (Diptera: Culicidae) in Sabah, Malaysia. - J. Econ. Entomol. 111: 2488-2492.

EOM S., PARK Y., KIM Y., 2014 - Sequential immunosuppressive activities of bacterial secondary metabolites from the entomopathogenic bacterium Xenorhabdus nematophila. - J. Microbiol. 52: 161-168.

FUCHS S.W., GRUNDMANN F., KURZ M., KAISER M., BODE H.B., 2014 - Fabclavines: bioactive peptide–polyketide-polyamino hybrids from Xenorhabdus. - Chembiochem. 15: 512-516.

FUKRUKSA C., YIMTHIN T., SUWANNAROJ M., MUANGPAT P., TANDHAVANANT S., THANWISAI A., VITTA A., 2017 - Isolation and identification of Xenorhabdus and Photorhabdus bacteria associated with entomopathogenic nematodes and their larvicidal activity against Aedes aegypti. - Parasit. Vectors 10: 440.

GEBRE Y., FORBES N., GEBRE T., 2016 - Zika virus infection, transmission, associated neurological disorders and birth abnormalities: a review of progress in research, priorities and knowledge gaps. - Asian Pac. J. Trop. Biomed. 6: 815-824.

GLEAVE K., COOK D., TAYLOR M.J., REIMER L.J., 2016 - Filarial infection influences mosquito behavior and fecundity. - Sci. Rep. 6: 36319.

GOODRICH-BLAIR H., CLARKE D.J., 2007 - Mutualism and pathogenesis in Xenorhabdus and Photorhabdus: two roads to the same destination. - Mol. Microbiol. 64: 260-268.

HAN Y., ZHANG S., WANG Y., GAO J., HAN J., YAN Z., WANG Y., 2024 - Enhancing the yield of Xenocoumacin 1 in Xenorhabdus nematophila YL001 by optimizing the fermentation process. - Sci. Rep. 14: 13506.

HASAN M.A., AHMED S., MOLLAH M.M.I., LEE D., KIM Y., 2019 - Variation in pathogenicity of different strains of Xenorhabdus nematophila; differential immunosuppressive activities and secondary metabolite production. - J. Invertebr. Pathol. 166: 107221.

HASSAAN M.A., EL NEMR A., 2020 - Pesticides pollution: classifications, human health impact, extraction and treatment techniques. - Egypt. J. Aquat. Res. 46: 207-220.

HRITHIK M.T.H., PARK Y., PARK H., KIM Y., 2022 - Integrated biological control using a mixture of two entomopathogenic bacteria, Bacillus thuringiensis and Xenorhabdus hominickii, against Spodoptera exigua and other congeners. - Insects 13: 860.

JI D., KIM Y., 2004 - An entomopathogenic bacterium, Xenorhabdus nematophila, inhibits the expression of an antibacterial peptide, cecropin, of the beet armyworm, Spodoptera exigua. - J. Insect Physiol. 50: 489-496.

JI D., YI Y., KANG G.H., CHOI Y.H., KIM P., BAEK N.I., KIM Y., 2004 - Identification of an antibacterial compound, benzylideneacetone, from Xenorhabdus nematophila against major plant-pathogenic bacteria. - FEMS Microbiol. Lett. 239: 241-248.

JIN G., HRITHIK M.T.H., LEE D.H., KIM I.H., JUNG J.S., BODE H.B., KIM Y., 2023 - Manipulation of GameXPeptide synthetase gene expression by a promoter exchange alters the virulence of an entomopathogenic bacterium, Photorhabdus temperata temperata, by modulating insect immune responses. - Front. Microbiol. 14: 1271764.

JISSIN M., VANI C., 2020 - Biogenic larvicidal formulation of metabolites from Steinernema saimkayi symbiont Xenorhabdus stockiae KUT6 against dengue vector Aedes aegypti. - Trop. Biomed. 37: 791-802.

KIM H., KEUM S., HASAN A., KIM H., JUNG Y., LEE D., KIM Y., 2018 - Identification of anentomopathogenic bacterium, Xenorhabdus ehlersii KSY, from Steinernema longicaudum GNUS101 and its immunosuppressive activity against insect host by inhibiting eicosanoid biosynthesis. - J. Invertebr. Pathol. 159: 6-17.

KIM I.H., ENSIGN J., KIM D.Y., JUNG H.Y., KIM N.R., CHOI B.H., GOODMAN W.G., 2017 - Specificity and putative mode of action of a mosquito larvicidal toxin from the bacterium Xenorhabdus innexi. - J. Invertebr. Pathol. 149: 21-28.

MARTEN G.G., CABALLERO X., LARIOS A., BENDAÑA H., 2022 - Proof of concept for eliminating Aedes aegypti production by means of integrated control including turtles, copepods, tilapia, larvicides, and community participation in Monte Verde, Honduras. - Acta Trop. 227: 106269.

MARTINET J.P., FERTÉ H., FAILLOUX A.B., SCHAFFNER F., DEPAQUIT J., 2019 - Mosquitoes of north-western Europe as potential vectors of arboviruses: a review. - Viruses 11: 1059.

MAURYA R.P., KORANGA R., SAMAL I., CHAUDHARY D., PASCHAPUR A.U., SREEDHAR M., MANIMALA N.R., 2022 - Biological control: a global perspective. - Int. J. Trop. Insect Sci. 42: 3203-3220.

MOLLAH M.M.I., 2024 - Ligands of HMG-like dorsal switch protein 1 of Spodoptera exigua leads to mortality in diamondback moth, Plutella xylostella. - Heliyon 10: e27090.

MOLLAH M.M.I., DEKEBO A., KIM Y., 2020b - Immunosuppressive activities of novel PLA2 inhibitors from Xenorhabdus hominickii, an entomopathogenic bacterium. - Insects 11: 505.

MOLLAH M.M.I., KIM Y., 2020 - Virulent secondary metabolites of entomopathogenic bacteria genera, Xenorhabdus and Photorhabdus, inhibit phospholipase A 2 to suppress host insect immunity. - BMC Microbiol. 20: 359.

MOLLAH M.M.I., ROY M.C., CHOI D.Y., HASAN M.A., BAKI M.A.A., YEOM H.S., KIM Y. 2020. - Variations of indole metabolites and NRPS-PKS loci in two different virulent strains of Xenorhabdus hominickii. - Front. Microbiol. 11: 583594.

MOLLAH M.M.I., YEASMIN F., KIM Y., 2020a - Benzylideneacetone and other phenylethylamide bacterial metabolites induce apoptosis to kill insects. -J. Asia Pacific Entomol. 23: 449-457.

NOLLMANN F.I., DAUTH C., MULLEY G., KEGLER C., KAISER M., WATERFIELD N.R., BODE H.B., 2015 - Insect-specific production of new GameXPeptides in Photorhabdus luminescens TTO1, widespread natural products in entomopathogenic bacteria. - Chembiochem 16: 205-208.

PARK D., CIEZKI K., VAN DER HOEVEN R., SINGH S., REIMER D., BODE H.B., FORST S., 2009 - Genetic analysis of xenocoumacin antibiotic production in the mutualistic bacterium Xenorhabdus nematophila. - Mol. Microbiol. 73: 938-949.

QIN Y., JIA F., LI X., LI B., REN J., YANG X., LI G., 2021 - Improving the yield of xenocoumacin 1 by PBAD promoter replacement in Xenorhabdus nematophila CB6. - Agriculture 11: 1251.

REIMER D., COWLES K.N., PROSCHAK A., NOLLMANN F.I., DOWLING A.J., KAISER M., BODE H.B., 2013 - Rhabdopeptides as insect-specific virulence factors from entomopathogenic bacteria. - Chembiochem 14: 1991-1997.

SAJNAGA E., KAZIMIERCZAK W., 2020 - Evolution and taxonomy of nematode-associated entomopathogenic bacteria of the genera Xenorhabdus and Photorhabdus: an overview. - Symbiosis 80: 1-13.

SEO S., LEE S., HONG Y., KIM Y., 2012 - Phospholipase A2 inhibitors synthesized by two entomopathogenic bacteria, Xenorhabdus nematophila and Photorhabdus temperata subsp. temperata. - Appl. Environ. Microbiol. 78: 3816-3823.

SHI Y.M., HIRSCHMANN M., SHI Y.N., AHMED S., ABEBEW D., TOBIAS N.J., GRÜN P., CRAMES J.J., PÖSCHEL L., KUTTENLOCHNER W., RICHTER C., HERRMANN J.,

MÜLLER R., THANWISAI A., PIDOT S.J., STINEAR T.P., GROLL M., KIM Y., BODE H.B., 2022 - Global analysis of biosynthetic gene clusters reveals conserved and unique natural products in entomopathogenic nematode-symbiotic bacteria. - Nat. Chem. 14: 701-712.

SHRESTHA S., HONG Y.P., KIM Y., 2010 - Two chemical derivatives of bacterial metabolites suppress cellular immune responses and enhance pathogenicity of Bacillus thuringiensis against the diamondback moth, Plutella xylostella. - J. Asia Pac. Entomol. 13: 55-60.

SINGH G., GUPTA N., GHOSH C., RATHORE J.S., 2023 - New face in the row of bioactive compounds and toxin-antitoxin modules: Xenorhabdus nematophila. - J. Asia Pac. Entomol. 26: 102148.

STOCK S.P., 2019 - Partners in crime: symbiont-assisted resource acquisition in Steinernema entomopathogenic nematodes. - Curr. Opin. Insect Sci. 32: 22-27.

SUBKRASAE C., ARDPAIRIN J., DUMIDAE A., JANTHU P., MUANGPAT P., POLSEELA R., TANDHAVANANT S., THANWISAI A., VITTA A., 2022 - Larvicidal activity of Photorhabdus and Xenorhabdus bacteria isolated from insect parasitic nematodes against Aedes aegypti and Aedes albopictus. - Acta Trop. 235: 106668.

SUWANNAROJ M., YIMTHIN T., FUKRUKSA C., MUANGPAT P., YOOYANGKET T., TANDHAVANANT S., THANWISAI A., VITTA A., 2020 - Survey of entomopathogenic nematodes and associate bacteria in Thailand and their potential to control Aedes aegypti. - J. Appl. Entomol. 144: 212-223.

THANWISAI A., MUANGPAT P., DUMIDAE A., SUBKRASAE C., ARDPAIRIN J., TANDHAVANANT S., VITTA A., 2021 - Identification of entomopathogenic nematodes and their symbiotic bacteria in national parks of Thailand, and mosquitocidal activity of Xenorhabdus griffiniae against Aedes aegypti larvae. - Nematology 24: 193-203.

THANWISAI A., MUANGPAT P., MEESIL W., JANTHU P., DUMIDAE A., SUBKRASAE C., ARDPAIRIN J., TANDHAVANANT S., YOSHINO T.P., VITTA A., 2022 - Entomopathogenic nematodes and their symbiotic bacteria from the national parks of Thailand and larvicidal property of symbiotic bacteria against Aedes aegypti and Culex quinquefasciatus. - Biology 11: 1658.

TOBIAS N.J., WOLFF H., DJAHANSCHIRI B., GRUNDMANN F., KRONENWERTH M., SHI Y.M., BODE H.B., 2017 - Natural product diversity associated with the nematode symbionts Photorhabdus and Xenorhabdus. - Nat. Microbiol. 2: 1676-1685.

TOMAR P., THAKUR N., YADAV A.N., 2022 - Endosymbiotic microbes from entomopathogenic nematode (EPNs) and their applications as biocontrol agents for agro-environmental sustainability. - Egypt. J. Biol. Pest Control 32: 80.

TOURAY M., CIMEN H., BODE E., BODE H.B., HAZIR S., 2024 - Effects of Xenorhabdus and Photorhabdus bacterial metabolites on the ovipositional activity of Aedes albopictus. - J. Pest Sci. 97: 2203-2215.

ULUG D., TOURAY M., HAZAL GULSEN S., CIMEN H., HAZIR C., BODE H.B., HAZIR S., 2024 - A taste of a toxin paradise: Xenorhabdus and Photorhabdus bacterial secondary metabolites against Aedes aegypti larvae and eggs. - J. Invertebr. Pathol. 205: 108126.

VITTA A., THIMPOO P., MEESIL W., YIMTHIN T., FUKRUKSA C., POLSEELA R., MANGKIT B., TANDHAVANANT S., THANWISAI A., 2018 - Larvicidal activity of Xenorhabdus and Photorhabdus bacteria against Aedes aegypti and Aedes albopictus. - Asian Pac. J. Trop Biomed. 8: 31-36.

WORLD HEALTH ORGANIZATION, 2022 - Dengue and severe dengue. Available from: https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue.

WORLD HEALTH ORGANIZATION, □2005 -□ Guidelines for laboratory and field testing of mosquito larvicides. Available from: https://apps.who.int/iris/handle/10665/69101.

YIMTHIN T., FUKRUKSA C., MUANGPAT P., DUMIDAE A., WATTANACHAIYINGCHAROEN W., VITTA A., THANWISAI A., 2021 - A study on Xenorhabdus and Photorhabdus isolates from Northeastern Thailand: identification, antibacterial activity, and association with entomopathogenic nematode hosts. - PloS One 16: e0255943.

YOOYANGKET T., MUANGPAT P., POLSEELA R., TANDHAVANANT S., THANWISAI A., VITTA A., 2018 - Identification of entomopathogenic nematodes and symbiotic bacteria from Nam Nao National Park in Thailand and larvicidal activity of symbiotic bacteria against Aedes aegypti and Aedes albopictus. - PloS One 13: e0195681.

ZHANG S., LIU Q., HAN Y., HAN J., YAN Z., WANG Y., ZHANG X., 2019 - Nematophin, an antimicrobial dipeptide compound from Xenorhabdus nematophila YL001 as a potent biopesticide for Rhizoctonia solani control. - Front. Microbiol. 10:1765.

Online supplementary material:

Supplementary Table 1. High-performance liquid chromatography results.