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Synthesis of heterocyclic and study activities in agriculture as anti-dubas on date palm trees via cholinesterase inhibitors

Sabreen Mohsan Hassan [1], Shurooq A. Hassan [1], Abbas K. Abbas [1,*], Mohammed R. Najem [1] and Nasreen R. Jber [2]

[1] *Muthanna Agriculture Directorate, Ministry of Agriculture, Al-Muthanna, Iraq.*
[2] *Department of Chemistry, College of Science, Al-Nahrain University, Baghdad, Iraq.*

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Abstract

Thiazine derivatives, particularly chalcones, have garnered attention owing to their broad agricultural applications. This study aimed to synthesize chalcone derivatives and evaluate their insecticidal efficacy against Dubas bugs on date palm trees. In this study, we synthesized chalcone derivatives (A and B) via the condensation of p-substituted acetophenone and terephthalaldehyde in a basic medium. The compounds were characterized using 1H-NMR and FT-IR spectroscopy and evaluated for their insecticidal activity against Dubas bugs affecting date palm trees. Compound C, synthesized at a concentration of 7000 ppm, exhibited the highest efficacy in reducing dubas populations within the shortest time. Molecular studies revealed that all synthesized derivatives inhibited acetylcholinesterase (AChE), as confirmed by their interaction with the crystallographic structure of AChE (PDB ID:6xyu).

Keywords: Thiazine; Chalcone; Insecticide; Date palm

1. Introduction

Most of the organic insecticides that are now widely used have been found by systematically testing several random chemicals or by making derivatives of compounds that have already been shown to be effective. There has been little progress in the biochemical aspects of developing an antigen or enzyme antagonist with the characteristics needed for contact toxicity. However, the current level of understanding in this area seems sufficient to implement a project of this kind [1]. Thiazine is an organic chemical compound. The chemistry of thiazines has generated intensive scientific research worldwide [2]. Chemically, thiazine is a six-membered heterocyclic compound containing one nitrogen atom, a sulfur atom, and two double bonds [3]. Heterocyclic thiazine derivatives are significant because they are biological components of several biomolecules and medicines [4]. The six-membered ring of nitrogen and sulfur atoms of thiazines is thought to be crucial to their antifungal, anticonvulsant, antiviral, dye, and insecticidal properties. Chalcones are α,β-unsaturated ketones. Various critical biological compounds are collectively known as chalcones or chalconoids [5-7].

Pesticides designed to kill, injure, prevent, or reduce one or more insect species are known as insecticides [8]. Different methods of action are used by insecticides. Some pesticides cause nervous system disruption, whereas others may harm their exoskeletons and cause them to flee or be controlled by other methods [9].

In addition, insecticides are substances that either kill insects or prevent them from acting in unwanted or dangerous ways. Their composition and methods of action have been used to identify them [10]. Some insecticides, such as cholinesterase inhibitors, affect the nervous system of insects, while others act as growth regulators or endotoxins.

* Corresponding author: Abbas K. Abbas

The date palm insect, known as the Dubas insect, feeds on the sap. Adults, nymphs, and fruit clusters were tapped for their saps. It has become a serious pest on date palm farms in recent years. Due to the consumption of sap by the Dubas bug, honeydew is produced as a byproduct, which causes sooty mold to grow and reduces photosynthesis [11].

This study aimed to synthesize chalcone derivatives and evaluate their insecticidal efficacy against Dubas bugs on date palm trees.

2. Materials and Methods

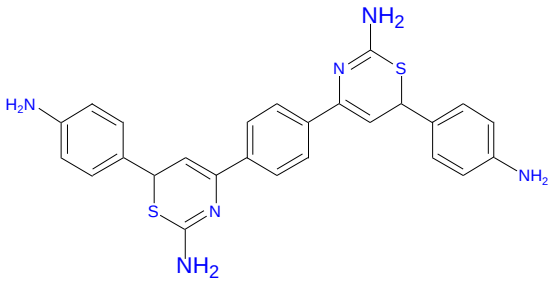
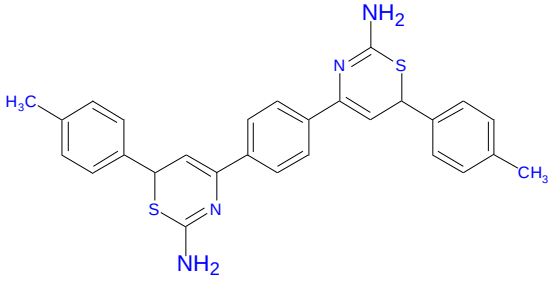
2.1. Synthesis of chalcone derivatives (A and B)

In an ice bath, 40 ml of ethanol was added to 15 g of sodium hydroxide dissolved in 200 ml distilled water and stirred for 20 min. Added acetophenone derivatives such as 0.02 mmol of 4-nitroacetophenone and 0.02 mmol of 4-methyl acetophenone, added 0.01 mmol of terephthalaldehyde, were to each solution with stirring for 12 hours [12]. These solutions were filtered and neutralized with HCl until the pH reached 7, dried, and recrystallized from ethanol to the target chemical compounds (A and B) [13].

2.2. Synthesis of thiazine derivatives (C and D)

A mixture of 0.001 mol of chalcone derivatives (A and B) was refluxed for 9 h with (0.152 g, 0.002 mol) thiourea dissolved in 50 ml EtOH and 10% sodium hydroxide [14], poured into 550 ml cold H_2O with stirring for an hour and then kept in the refrigerator for one day. The solutions were filtered, washed, and recrystallized using absolute ethanol [15].

Table 1 Physicochemical properties of thiazine derivatives (C and D).

Comp. No.	Chemical Structure	Molecular Weight	% Yelled	Color
C		484.6	76	Orange
D		482.6	74	Dark Yellow

3. Results and Discussion

The derivatives of chalcone compounds (A and B) were evaluated via spectroscopic techniques, such as FTIR and ^{1}HNMR. In the FTIR spectrum, the appearance of compounds (A and B) is shown by the carbonyl chalcone C=O stretching in 1708 and 1712 cm^{-1} [16], and the C=C of alkene detected at 1612 and 1622 cm^{-1} [17,18].

Table 2 FT-IR spectra of synthesized derivatives (A – D).

Comp. No.	NH_2	C-H Aromatic	C-H Aliphatic	C=O	C=C Aliphatic	C=C Aromatic
A	3326 + 3271	3073	---	1708	1612	1603
B	---	3088 + 3052	2916 + 2823	1712	1622	1602

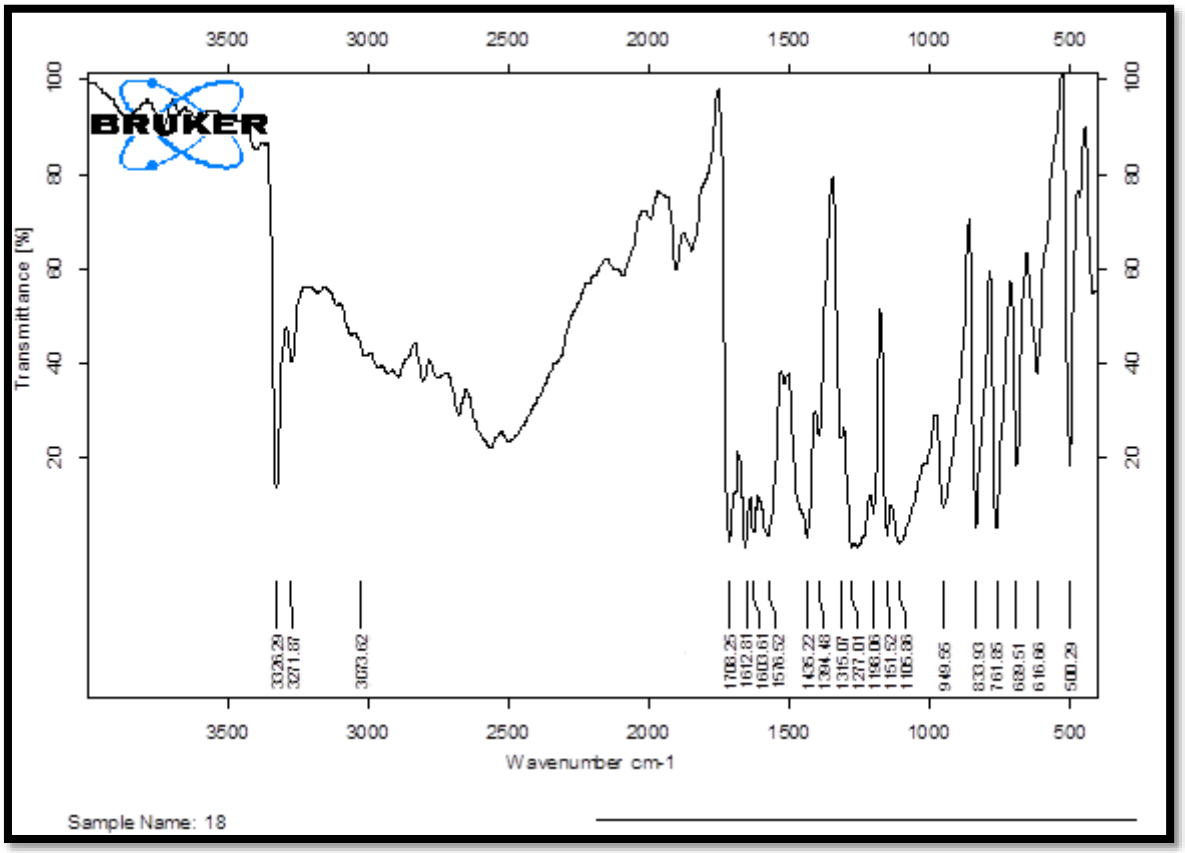


Figure 1 FT-IR spectrum of derivative (A)

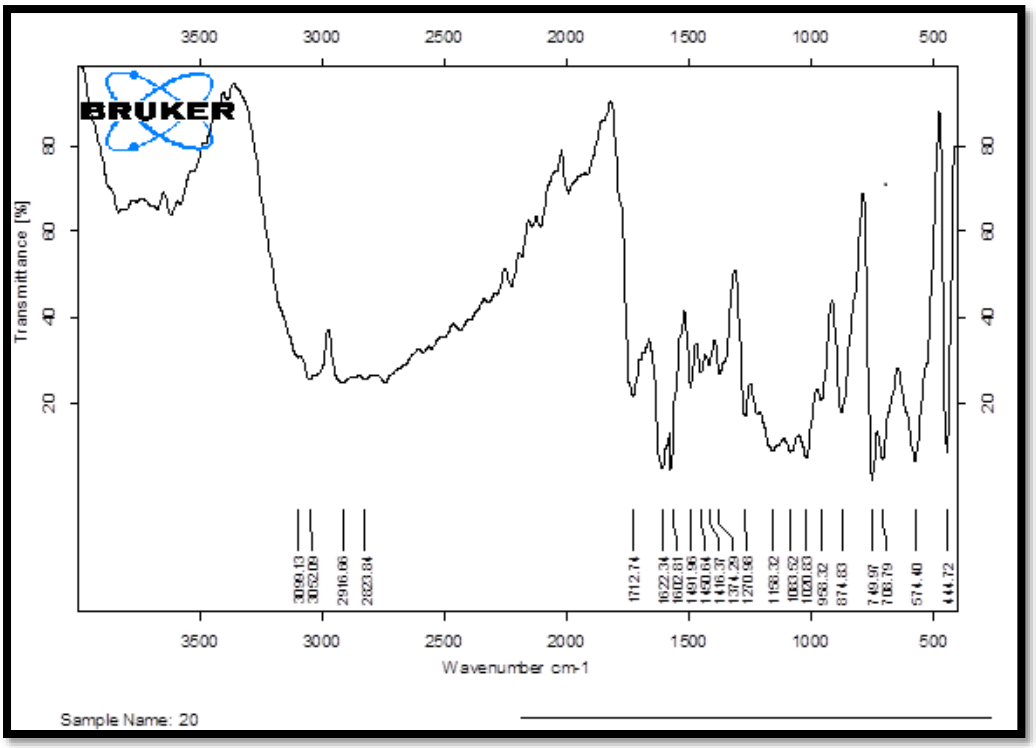


Figure 2 FT-IR spectrum of derivative (B).

Finally, the FTIR charts shown in figures (3-4) show that the compounds that were synthesized (C and D) disappeared in the carbonyl group and C=C of the alkene [17, 18], and new peaks of C=N were detected in the range of 1640 – 1649 cm^{-1} [22], and C=C of the aromatic ring was detected in the range of 1598 – 1600 cm^{-1} [19].

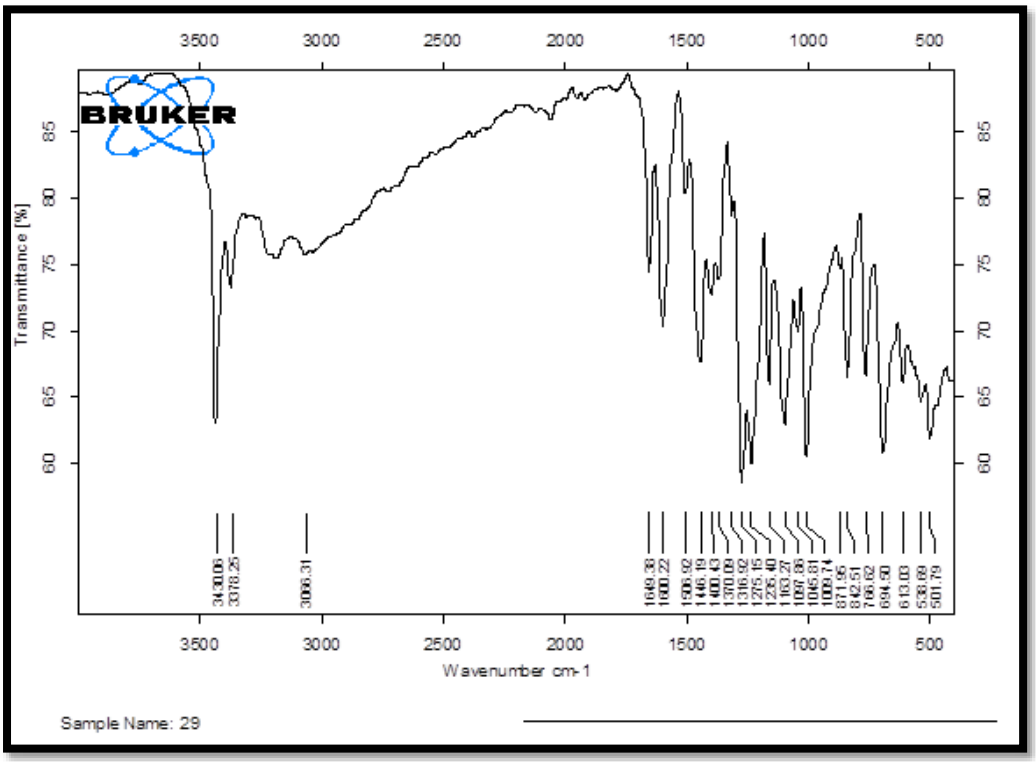


Figure 3 FT-IR spectrum of derivative (C).

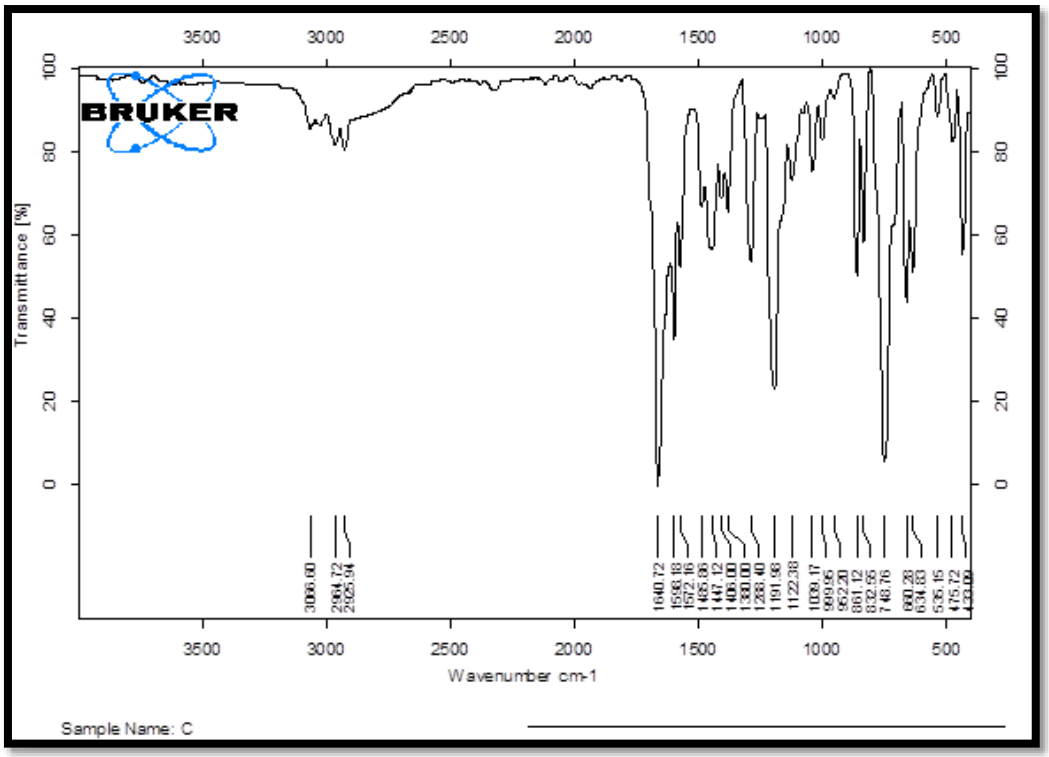


Figure 4 FT-IR spectrum of derivative (D).

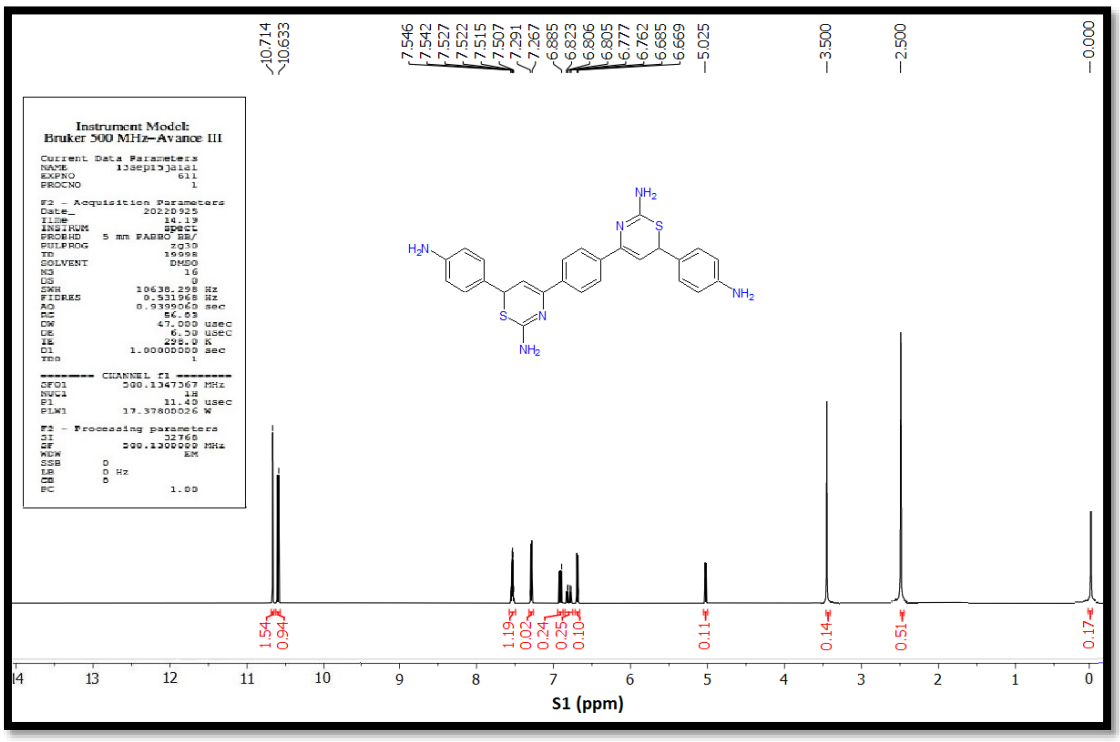


Figure 5 [1]HNMR spectrum of derivative (C).

The [1]HNMR for derivative C is shown in Figure 5, the protons of the amine group were detected at 10.7 ppm and 10.6 ppm, the protons of the aromatic ring detected a range at 7.5 – 6.6 ppm, and protons of HC-S detected at 5 ppm [20]. In derivative D shown in Figure 6, the protons of the amine group were detected at 10.5 ppm [21], the aromatic ring

protons detected a range of 7.7 – 6.8 ppm, and the protons of HC-S were detected at 4.8 ppm, and protons of the methyl group were detected at 2.2 ppm.

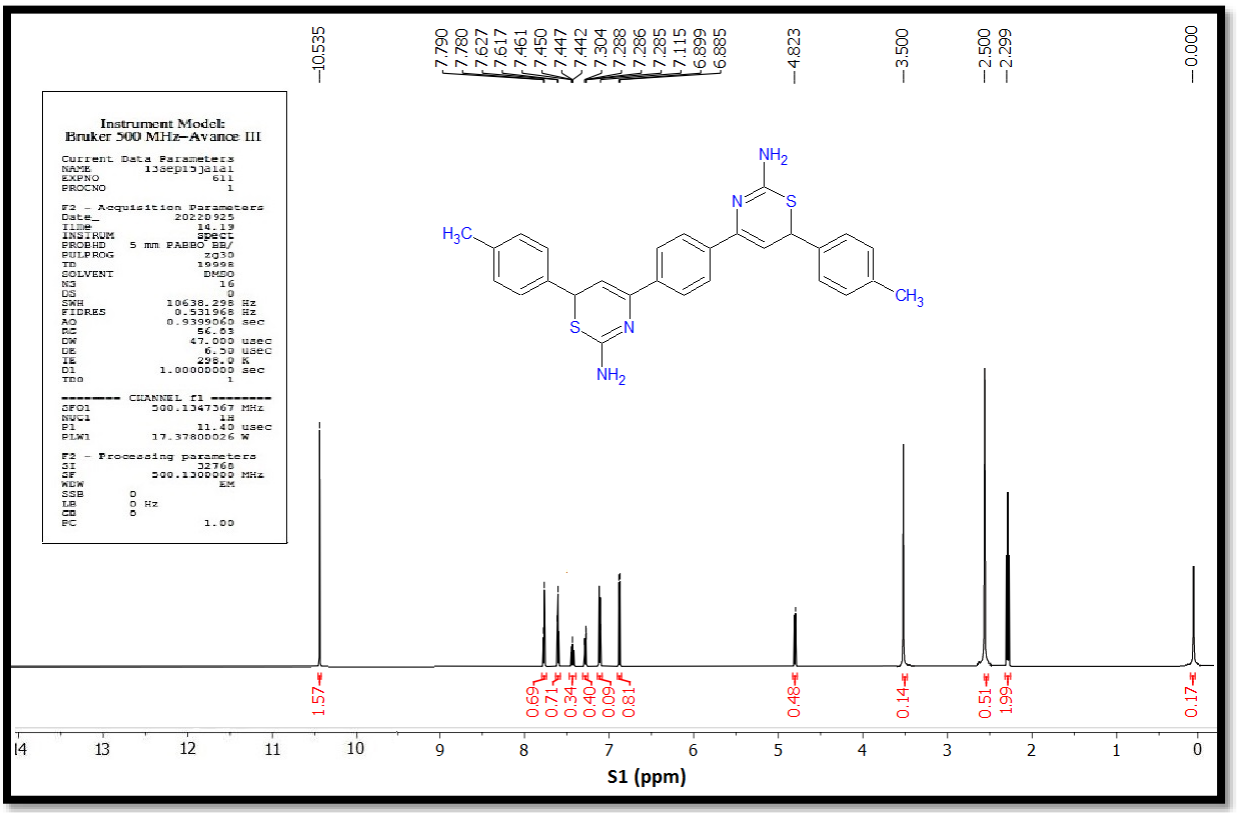


Figure 6 ^{1}HNMR spectrum of derivative (D).

3.1. Anti- Dubas activities

Derivatives C and D were used as pesticides in the spray method [22]; the concentrations of derivatives C and D were 5000, 6000, and 7000 ppm, respectively. This test was conducted in the Department of Plant Protection (Al Muthanna Agriculture Department) in the Al Muthanna Governorate.

Table 3 Anti-Dubas activity.

Compounds No.	**(ppm)**	**Note**	**L time (Sec.)**	**Mean n=10 for every concentration**	
C	5000	Killed Dubas	46	9	96 %
	6000		46	10	
	7000		41	10	
D	5000	Killed Duas	59	8	90 %
	6000		58	10	
	7000		49	10	

*L time (Sec.) is the time required to kill an insect, and Mean is the average number of insects killed.

Ten insects were used for each concentration. The synthesized compound C in 7000 ppm was the better compound that killed dubas insects in less time and was the better compound to kill all insects (n=10 dubas); compound C in 6000 ppm was the better concentration that killed dubas insects in less time than other concentrations and less than compound D in 7000. Compound D at 5000 ppm showed less activity than the other compounds at different concentrations.

To gain more insight into how ligands interact with the receptor. The synthesized derivatives were simulated against the crystallographic structure of acetylcholinesterase (AChE) (PDB ID:6xyu). Molecular docking is an important tool for exploring various possible interactions. The synthesized compounds demonstrated noticeable affinity by forming various interactions at the enzyme pocket, such as hydrogen bonding between the hydrogen of the free amine group and GLY402. In contrast, a -cation interaction was observed between the phenyl group of the derivative and ARG571. Multiple van de Waals interactions represented by methyl groups of compound D interactions were observed. The in-silico study of the derivatives correlated with experimental insecticide activity in which these derivatives could inhibit the activity of AChE enzyme of the earthworm and thus demolish the neurological system [23].

4. Conclusion

In conclusion, we synthesized novel derivatives of thiazine (C and D) and characterized them using FTIR and ^{1}H-NMR spectroscopy. Finally, evaluation of these compounds as anti-Dubas palm and killing Dubas revealed that the synthesized compound C at 7000 ppm was the best compound that killed Dubas insects in less time and was the best compound to kill all insects (n = 10 dubas). The synthesized derivatives were simulated against the crystallographic structure of acetylcholinesterase (AChE) (PDB ID:6xyu). All synthesized compounds had an inhibitory effect on the ACHE enzyme.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

This research was conducted with the ethical approval of the Al-Nahrain University, and Muthanna Agriculture Directorate, Ministry of Agriculture which granted permission to collect animal samples from the study area.

References

[1] Colovic MB, Krstic DZ, Lazarevic-Pasti TD, Bondzic AM, Vasic VM. Acetylcholinesterase inhibitors: pharmacology and toxicology. Curr Neuropharmacol. 2013;11(3):315-35.

[2] Asif M, Imran M. Antimicrobial Activities of Various Thiazine Based Heterocyclic Compounds: A Mini-Review. Mini Rev Org Chem. 2022;19(2):166-72.

[3] Choudhary S, Silakari O, Singh PK. Key updates on the chemistry and biological roles of the thiazine scaffold: a review. Mini Rev Med Chem. 2018;18(17):1452-78.

[4] Kalirajan R, Gaurav K, Pandiselvi A, Gowramma B, Sankar S. Novel thiazine substituted 9-anilinoacridines: Synthesis, antitumour activity and structure activity relationships. Anti-Cancer Agents Med Chem. 2019;19(11):1350-8.

[5] Jasim HA, Nahar L, Jasim MA, Moore SA, Ritchie KJ, Sarker SD. Chalcones: Synthetic chemistry, where nature leads. Biomolecules. 2021;11(8):1203.

[6] Elkanzi NA, Hrichi H, Alolayan RA, Derafa W, Zahou FM, Bakr RB. Synthesis of chalcones derivatives and their biological activities: a review. ACS Omega. 2022;7(32):27769-86.

[7] Freitas TSD, Xavier JDC, Pereira RL, Rocha JE, Muniz DF, da Silva PT, et al. Direct antibacterial and antibiotic resistance modulatory activity of chalcones synthesized from the natural product 2-hydroxy-3, 4, 6-trimethoxyacetophenone. FEMS Microbiol Lett. 2020;367(15):fnaa124.

[8] Sparks TC, Crossthwaite AJ, Nauen R, Banba S, Cordova D, Earley F, et al. Insecticides, biologics and nematicides: Updates to IRAC's mode of action classification-a tool for resistance management. Pestic Biochem Physiol. 2020; 167:104587.

[9] Al-Rawahi FG, Al-Antary TM, Sadder MT. Toxicity of three chemicals and neem insecticide against spring populations of dubas bug, de bergevin (Tropiduchidue: Homoptera) in Oman. FEB-FRESENIUS ENVIRON BULLETIN. 2018;8580.

[10] Mossa ATH, Mohafrash SM, Chandrasekaran N. Safety of natural insecticides: toxic effects on experimental animals. BioMed Res Int. 2018;2018.

[11] Al-Khatri SAH. 3. IPM of Dubas Bug. Date Palm Pests and Diseases. 2018;94.

[12] Arif R, Rana M, Yasmeen S, Khan MS, Abid M, Khan MS. Facile synthesis of chalcone derivatives as antibacterial agents: Synthesis, DNA binding, molecular docking, DFT and antioxidant studies. J Mol Struct. 2020; 1208:127905.

[13] Wijayanti LW, Swasono RT, Lee W, Jumina J. Synthesis and evaluation of chalcone derivatives as novel sunscreen agent. Molecules. 2021;26(9):2698.

[14] Ewies EF, El-Hag FA. Synthesis, reactions, and antimicrobial evaluations of new benzo [e][1, 3] thiazine derivatives. J Heterocycl Chem. 2020;57(1):163-72.

[15] Galai M, Rbaa M, Serrar H, Ouakki M, Ech-chebab A, Abousalem AS, et al. S-Thiazine as effective inhibitor of mild steel corrosion in HCl solution: Synthesis, experimental, theoretical and surface assessment. Colloids Surf A Physicochem Eng Asp. 2021;613:126127.

[16] da Cunha Xavier J, de Almeida-Neto FW, Rocha JE, Freitas TS, Freitas PR, de Araujo AC, et al. Spectroscopic analysis by NMR, FT-Raman, ATR-FTIR, and UV-Vis, evaluation of antimicrobial activity, and in silico studies of chalcones derived from 2-hydroxyacetophenone. J Mol Struct. 2021;1241:130647.

[17] Nogueira CES, de Oliveira MM, Teixeira AM, Bandeira PN, dos Santos HS, Ayala AP, et al. Crystal structure, FT-Raman and FTIR spectra and DFT calculations of chalcone (2E)-1-(4-aminophenyl)-3-(furan-2-yl) prop-2-en-1-one monohydrate. J Mol Struct. 2020;1212:128141.

[18] White R. Chromatography/Fourier transform infrared spectroscopy and its applications. CRC Press. 2020.

[19] Ozaki Y, Huck C, Tsuchikawa S, Engelsen SB, editors. Near-infrared spectroscopy: theory, spectral analysis, instrumentation, and applications. Berlin/Heidelberg: Springer; 2021.

[20] Emwas AH, Roy R, McKay RT, Tenori L, Saccenti E, Gowda GN, et al. NMR spectroscopy for metabolomics research. Metabolites. 2019;9(7):123.

[21] Gujar SK, Maheshwari S, Björkman-Burtscher I, Sundgren PC. Magnetic resonance spectroscopy. J Neuroophthalmol. 2005;25(3):217-26.

[22] Ibrahim AI, Hemeida AA, Abdelkader HS, Girgis AA, Abou-El-Einin H. Genetic variance between some Egyptian Date Palm cultivars using PCR-based markers with emphasis on the prevalence of Al wijam disease. Arch Phytopathol Plant Prot. 2011;44(8):732-42.

[23] Singh KD, Labala RK, Devi TB, Singh NI, Chanu HD, Sougrakpam S, Nameirakpam BS, Sahoo D, Rajashekar Y. Biochemical efficacy, molecular docking and inhibitory effect of 2, 3-dimethylmaleic anhydride on insect acetylcholinesterase. Sci Rep. 2017;7(1):12483.