AMERICAN JOURNAL OF BIOSCIENCE AND CLINICAL INTEGRITY
https://biojournals.us/index.php/AJBCI
ISSN: 2997-7347

Article

Studying the bactericidal activity of some newly prepared oxazepine derivatives and characterizing these compounds

Dr.maan ziadan khalaf [1] Sraa Hussein Kreydie [2]

1. Education of Salah al-Din / Ministry of Education / Iraq.
2. College of Biomedical Informatics / University of Information Technology and Communications / Iraq.

*Correspondence: maanqqqq@gmail.com

Citation: Dr.maan ziadan khalaf, Sraa Hussein Kreydie. Studying the bactericidal activity of some newly prepared oxazepine derivatives and characterizing these compounds. American Journal Of Bioscience And Clinical Integrity 2026, 3(4), 21-28.

Received: 10th Jan 2026
Revised: 11th Feb 2026
Accepted: 24th Mar 2026
Published: 08th Apr 2026

Abstract: The present research focuses on the synthesis and structural investigation of a novel series of oxazepine derivatives obtained though a conventional sublimation-based approach. Interest in seven-membered heterocyclic systems arises from their recognized biological and pharmacological relevance, which has encouraged extensive exploration of their potential applications in medicinal and pharmaceutical sciences. The target compounds were synthesized via cyclization reactions involving 2-aminophenol and a set of chalcone intermediates. These chalcones were initially produced through condensation reactions between substituted scaffold of the study. The prepared derivatives exhibited satisfactory physicochemical properties, along with remarkable stability under standard laboratory conditions. The chemical structures of these compounds were confirmed and their purity assessed using several spectroscopic techniques, including Fourier transform infrared spectroscopy (FT-IR), proton nuclear magnetic resonance spectroscopy (1H-NMR), and carbon nuclear magnetic resonance spectroscopy (13C-NMR). Biological evaluation was also conducted to determine the antibacterial activity against representative Gram-negative (Escherichia coli) and Gram-positive (Staphylococcus aureus) bacteria. The experimental results showed variations in inhibition levels among the prepared molecules, with compound M8 exhibiting the highest activity against Gram-negative strains, followed by compound M10. The inhibitory effect against Gram-positive bacteria was less pronounced compared to the standard antibiotic used for comparison. Ciprofloxacin was used as a standard control, demonstrating higher antibacterial activity than all the prepared derivatives. However, the observed biological responses suggest that the prepared oxazepine compounds could be considered promising prototypical compounds for future development as antimicrobial agents.

Keywords: Oxazepine, Ciprofloxacin, Biological Activity.

1. Introduction:

Oxazepines are heptameric compounds called oxazepines if unsaturated but oxazepines if saturated [1,2]. They consist of five carbon atoms and two heteroatoms [3]. Isomers, depending on the position of the oxygen and nitrogen atoms in the heptameric structure [4]. Substituted seven-membered heterocyclics like oxazepine derivatives have received much attention in the recent years owing to their wide range of biological and pharmaceutical importance[5,6]. An appropriate substitution and functionalization of oxazepines have mproved potentially their pharmacological properties[7]. For example, some pyrrolo-based oxazepines and their derivatives3 have shown excellent biological activities[8] Many other oxazepine derivatives are known to be potential opioid analgesics and oxazepines erivatives are used as antihypertensive drugs and act as potential ACE inhibitors[9]. Many studies have shown that oxazepines can treat psychiatric disorders and many diseases [10]and have many medical and pharmaceutical applications. They also have anticancer activity, antioxidant activity, and activity against bacteria and microorganisms [11,12].

2. Experimental:

2.1. Material: All materials used were fully supplied by BDH, Fluka and Aldrich.

2.2.Devices: FT-IR 8400S disc 400-4000 cm-1 scale. 1H-NMR and 13C-NMR Bruker equipment operating at 300 MHZ.

2.3. synthesis of Oxazepine compounds (M_6-M_{10})[13]:

In a round-bottomed flask, 2-aminophenol (0.004 mol, 0.432 g) was solubillized in ethanol, while the chalcone derivatives (0.004 mol) were solubillized in 10 ml of ethanol. After that, the mix was agitated for 12 to 14 hours. Methanol was used to concentrate, filter, wash, and recrystallize the mix. The compounds' physical and chemical characteristics are listed in Table (1).

Table (1): physical properties of the compounds (M_6-M_{10})

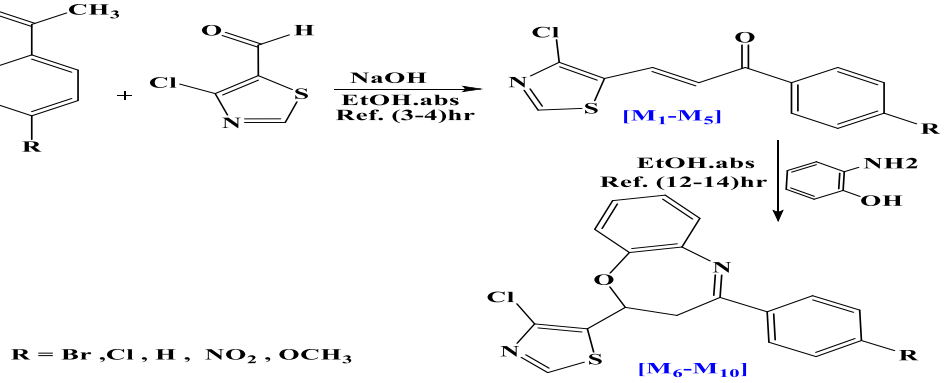
Comp No.	Ar	Molecular Formula/	Color	M.P (^{0}C)	R.T hr	R_f	Yield (%)
M_6	Br	$C_{18}H_{12}BrClN_2OS$	Orange	239-231	12	0.89	64
M_7	Cl	$C_{18}H_{12}Cl_2N_2OS$	Yellow	228-231	14	0.93	63
M_8	H	$C_{18}H_{13}ClN_2OS$	Light Brown	257-259	13	0.86	61
M_9	NO_2	$C_{18}H_{12}ClN_3O_3S$	Light yellow	216-218	14	0.94	59
M_{10}	OCH_3	$C_{19}H_{15}ClN_2O_2S$	Light yellow	257-260	12	0.87	65

2.4.Biological activity study:

The method for evaluating the antibacterial activity of compounds relies on a precise procedure that begins with the preparation of Mueller-Hinton agar (MHA) medium, followed by sterilization and pouring into Petri plates[14]. Next, two pure bacterial isolates are prepared: *Escherichia coli* and *Staphylococcus aureus*[15]. Bacterial suspensions are prepared by titrating the turbidity to 1.5×10^8 cells/mL. Compound solutions are then prepared in DMSO at concentrations of 0.1, 0.01, and 0.001 mg/mL. The medium is then inoculated with a cotton swab and evenly distributed. Using the agar well diffusion method, 40 µl of each solution is then added to the prepared wells[16]. The plates are incubated at 37°C for 24–48 hours, and the results are read to determine biological activity by comparing the diameter of the zone of inhibition surrounding the wells with that produced by standard antibiotics, such as ciprofloxacin[17].

3. Results and discussion:

The chains of compounds were prepared as shown in the scheme (1).



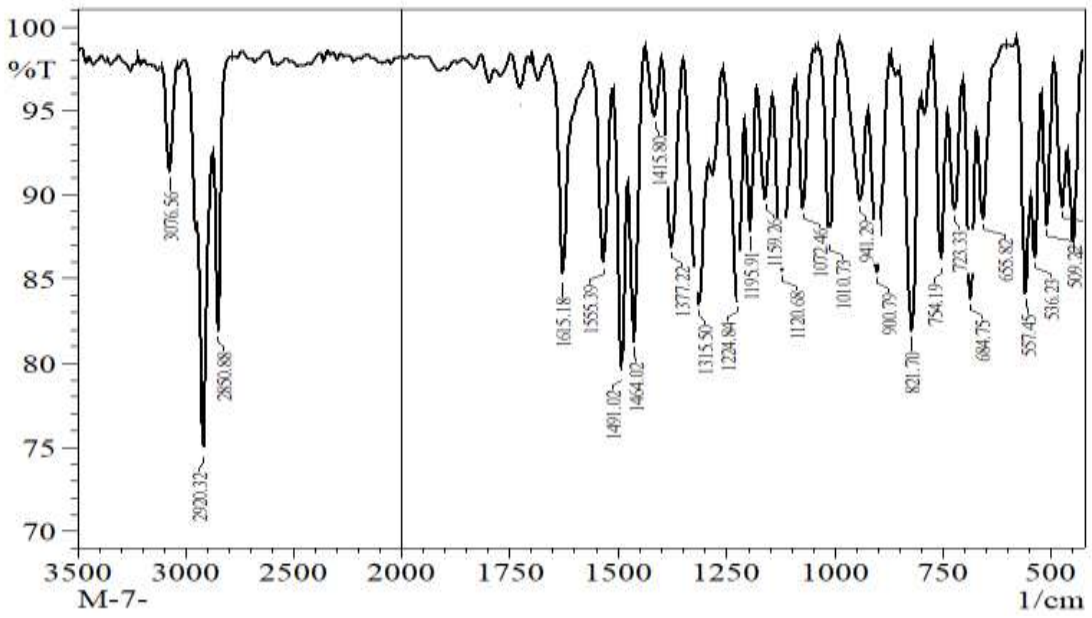
scheme (1): shown prepared compounds.

3.1. Characterization of Oxazepine derivatives [M_6-M_{10}]:

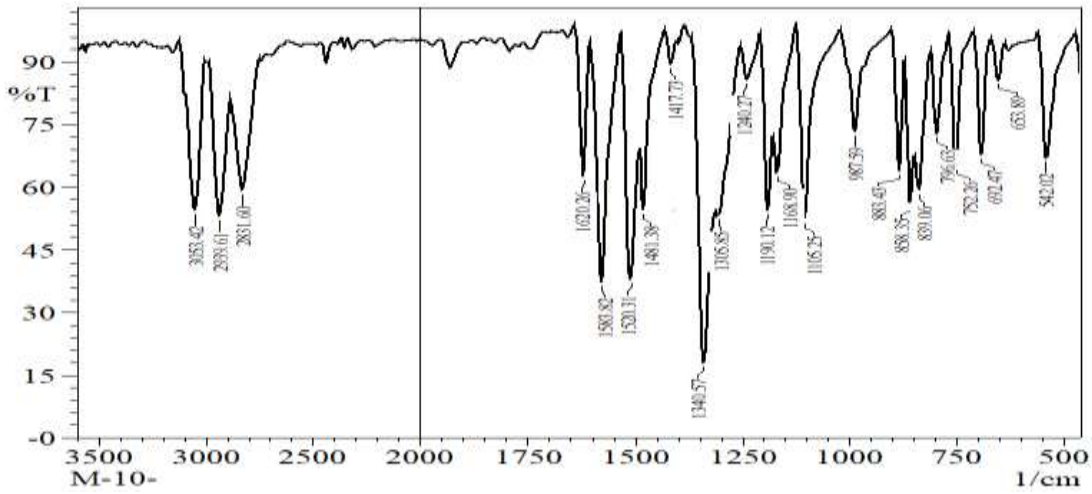
The compounds' infrared spectra [M_6-M_{10}] showed uptake lines in the (3083-3053) cm-1 area due to the elongation of the aromatic (C-H) link. Additionally, the elongation of the aliphatic (CH) link resulted in the appearance of two uptake lines in the span (2960-2920) cm-1 and (2831-2874) cm-1, while the elongation of the (C=N) link inside the seven-membered ring caused an uptake lines to arise in the span (1615-1623) cm-1. In addition to the formation of uptake lines at (1338-1377) cm-1 and (1224-1264) cm-1 due to the symmetric elongation, two uptake lines in the span of (1583-1548) cm-1 and (1491-1476) cm-1 were also seen as a result of the elongation of the aromatic (C=C) link. Additionally, as table (2) and figure 1 demonstrate, the asymmetrical sequential formation of the (C-O-C) link inside the seven-membered ring and the creation of an uptake lines in the span of (1209-1190) cm-1 are caused by the elongation of the (C-N) link [18].

Table (2): IR absorption spectra values of compounds (M_6-M_{10})

Comp. No.	Ar	IR (KBr) cm^{-1} ν (C-H) Arom.	ν(C-H) Aliph.	ν(C=N)	ν(C=C) Arom.	ν (C-O).	ν (C-N)	Others
M_6	Br	3056	2956 2859	1623	1567 1487	1367	1209	ν (C-Br)613
M_7	Cl	3076	2920 2850	1615	1555 1491	1377	1195	ν (C-Cl)723
M_8	H	3068	2931 2874	1618	1563 1481	1348	1197	---
M_9	NO_2	3083	2960 2852	1621	1548 1476	1338	1207	ν(NO_2) *asy*. (1520) *sym*. (1340)
M_{10}	OCH_3	3053	2939 2831	1620	1583 1481	1340	1190	---

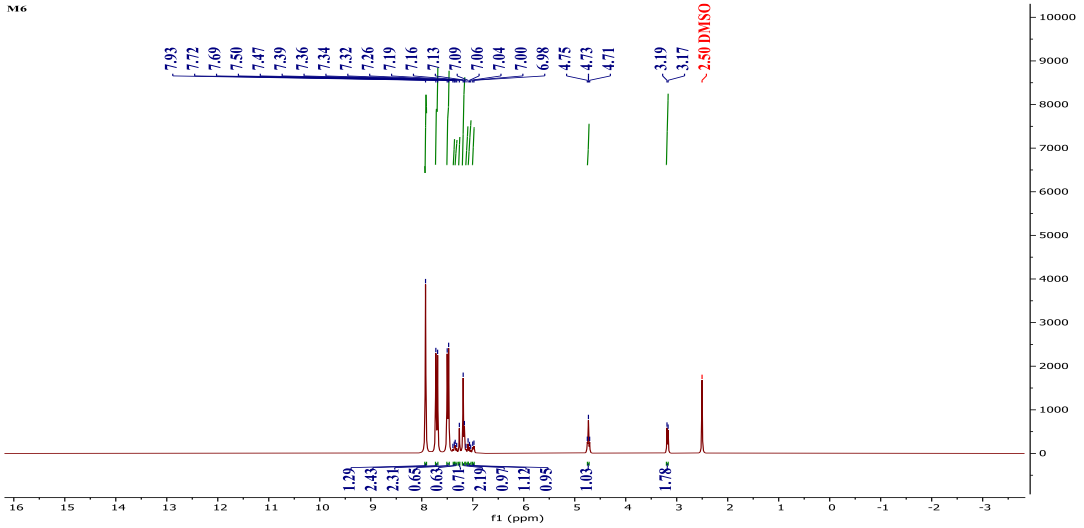


Fig(1): FT-IR of (M_7)



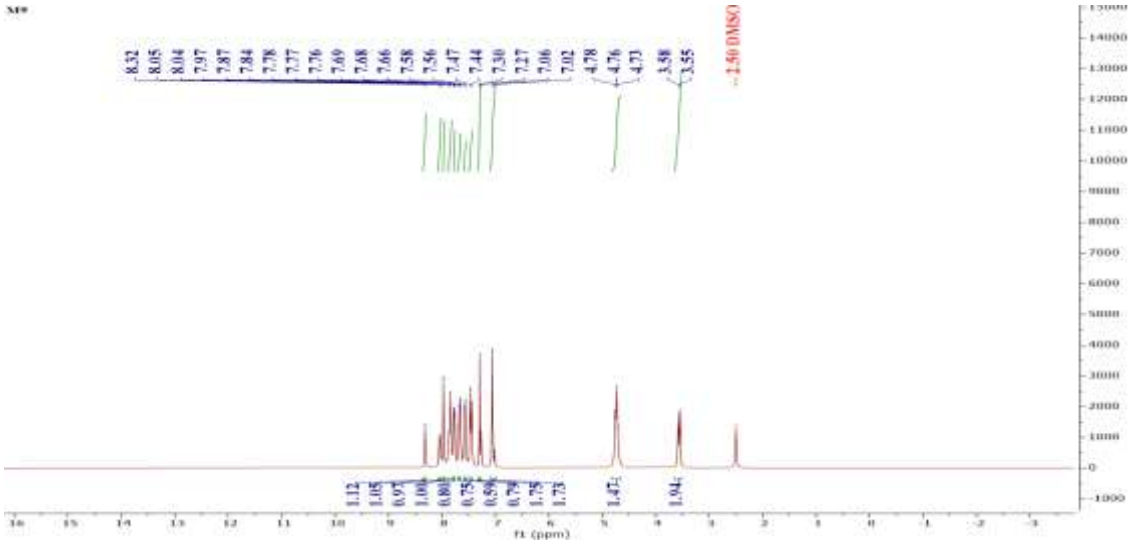
Fig(2): FT-IR of (M_{10})

Through 1H-NMR analysis of compound M_6, multiple signals were found that were attributed to hydrogen in the aromatic rings at the range (7.93-6.98) ppm, with a triple signal carrying two splits that was attributed to hydrogen (CH) at (4.75-4.71) ppm, and the presence of a double signal with one split at (3.19-3.17) ppm that was attributed to (CH2), in addition to the solvent signal at (2.50) ppm. As shown figure 3



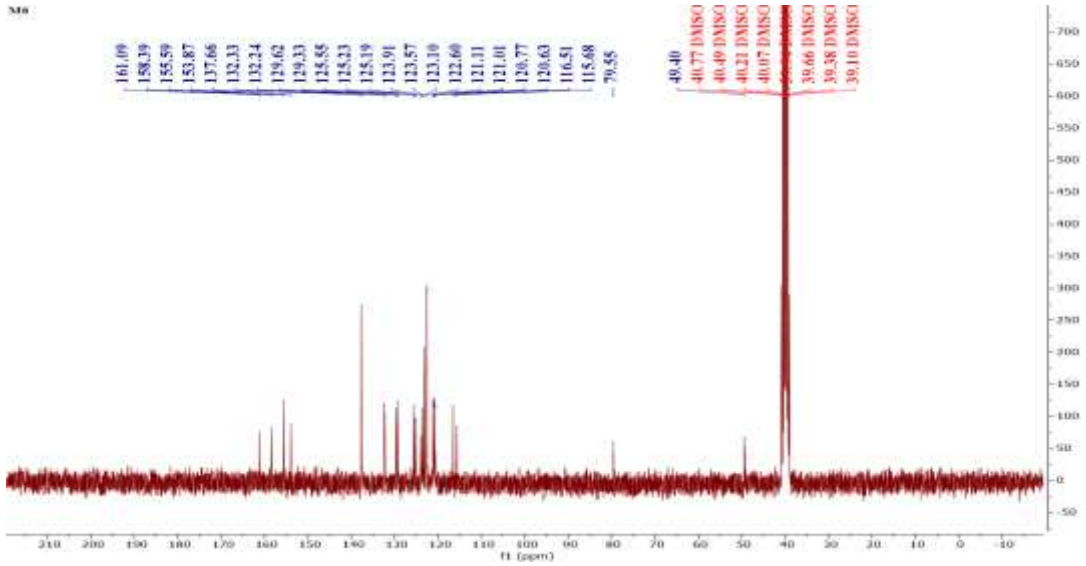
Fig(3): 1H-N.M.R of (M_6)

Through 1H-NMR analysis of compound M_9, multiple signals were found that were attributd to hydrogen in the aromatic rings in the range (8.32-7.02) ppm, with a triple signal carrying two spliets that was attributed to hydrogen (CH) at (4.78-4.73) ppm, and the presence of a double signal with one split at (3.58-3.55) ppm that was attributed to (CH2), in addition to the solvent signal at (2.50) ppm. As shown figure 4



Fig(4): 1H-N.M.R of (M_9)

The 13C-NMR spectrum of compound M_6 showed a signal that was included for azomethine in oxazepine (C=N) at (161.09) ppm, and a group of signals that were included for aromatic rings at (158.39-115.68) ppm, while the signal at (79.55) ppm was included for (CH), and the other signal at (49.40) ppm was included for the (CH2) group in the oxazepine ring. As shown figure 5



Fig(5): 13C-N.M.R of (M_6)

3.2. Evaluation of Biological Activity:

Due to the different properties of bacterial membranes, the prepared compounds exhibited different antibacterial effects[19]. The compounds exhibited the best antibacterial effects against Gram-negative bacteria, among which compound (M_8) showed the highest antibacterial activity against Gram-negative bacteria, with an inhibition diameter of (1.5 cm) at a high concentration of 0.1 mg/mL; followed by compound (M_{10}), with an inhibition diameter of (1.2 cm). In comparison, the antibiotics *ciprofloxacin* had inhibition diameters of

1.9 cm and 1.4 cm, respectively[20,21]. The antibacterial effects of the compounds on Gram-positive bacteria were not as good as those on Gram-negative bacteria. This inhibition was attributed to bacterial resistance to these compounds, against which the antibiotics showed activity, with the inhibition diameters of *ciprofloxacin* reaching 1.5 cm and 1.3 cm, respectively [22,23]. As shown in Table (3) and Figures .

Table (5): Biological effectiveness of compounds (inhibition in cm).

Comp. No.	*Escherichia coil*			*Staphylococcus aureus*		
Conc. mg/ml	0.1	0.01	0.001	0.1	0.01	0.001
M_6	0.6	0.9	0.5	0.6	0.3	0.4
M_7	0.8	0.2	0.7	0.5	0.3	0.3
M_8	1.5	0.5	0.5	0.7	0.5	0.8
M_9	1	0.4	0.4	0.8	0.4	0.2
M_{10}	1.2	0.6	0.3	0.5	0.5	0.5
Ciprofloxacin	3.5	3	2.1	3.8	3.2	2.7

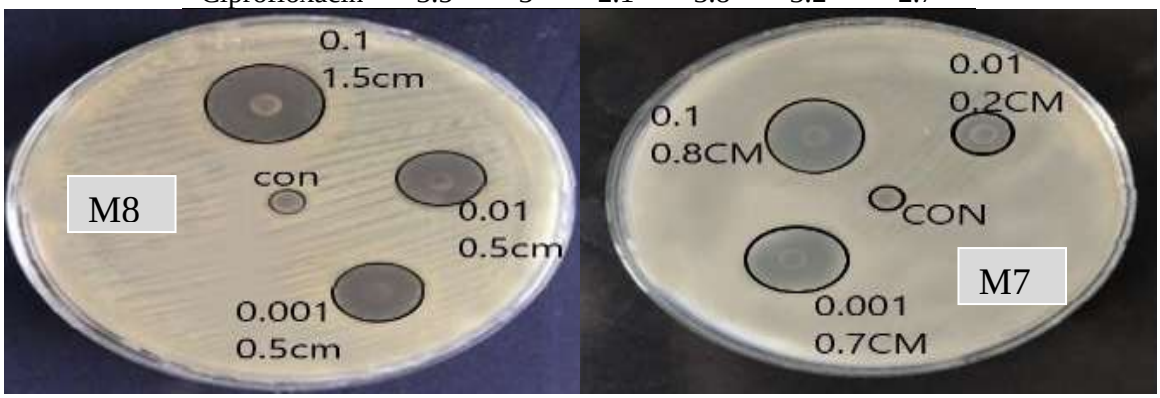


Fig 6: Efficacy of compounds (M7, 8) against Escherichia coli bacteria.

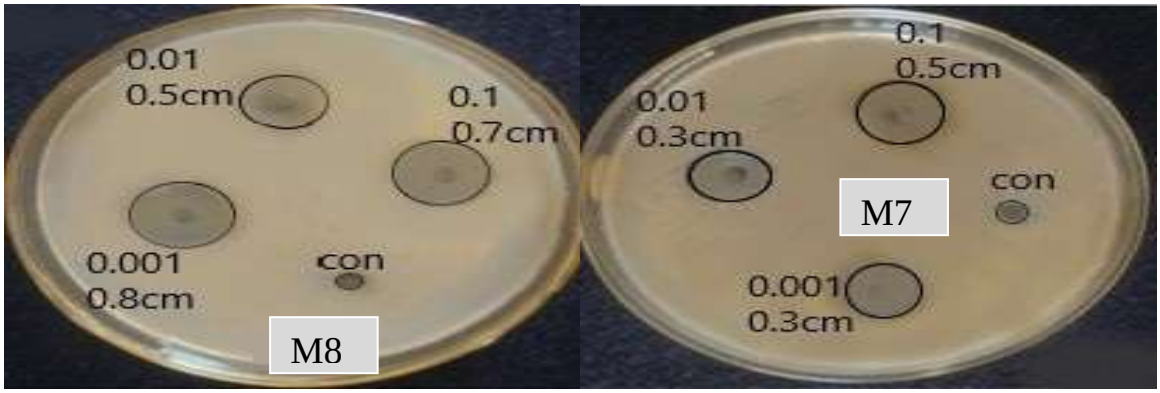


Fig 7: Efficacy of compounds (M7, M8) against Staphylococcus aureus bacteria.

4. Conclusions:

This sublimation process is an innovative, cost-effective, and time-efficient method for producing high-yield heterocyclic compounds. Spectrophotometric measurements confirmed the efficacy and accuracy of these products and demonstrated their high purity (using FT-IR spectroscopy, ^{1}H-N.M.R, and ^{13}C-N.M.R spectroscopy). These substances showed different degrees of action against two species of bacteria, despite their strong resistance to antibiotics. Additionally, they showed excellent stability in lab settings.

References:

[1] D. M. Najim, K. A. Al-Badrany, and M. K. Saleh, *Synthesis of Some New Oxazepine Compounds Derived from Cyanoethyl Acetate and Study Their Inhibitory Activity Against Some Pathogenic Bacterial Species*, Unpublished.

[2] F. M. Muhammad, B. A. Khairallah, and K. A. Albadrany, "Synthesis, characterization and antibacterial evaluation of novel 1,3-oxazepine derivatives using a cycloaddition approach," *Journal of Angiotherapy*, vol. 8, no. 3, pp. 1–5, 2024.
[3] A. S. T. Abdul Wahed, "Preparation and evaluation of bacterial activity and study of the crystalline properties of some 1,3-oxazepine-4,7-dione derivatives," *Central Asian Journal of Theoretical and Applied Sciences*, vol. 5, no. 2, pp. 15–26, 2024.
[4] S. A. Mohamed, M. S. Hussein, and K. A. Al-Badrany, "Synthesis and characterization of pyrazolines and oxazapine derivatives using chalcones as precursor and evaluation of their biological activity," *Samarra Journal of Pure and Applied Science*, vol. 4, no. 4, 2022.
[5] G. R. Newkome and P. W. Maudler, *Contemporary Heterocyclic Chemistry*. USA: John Wiley & Sons, 1982.
[6] A. G. Borel and F. S. Abbott, "Metabolic profiling of clobazam, a 1,5-benzodiazepine, in rats," *Drug Metabolism and Disposition*, vol. 21, no. 3, pp. 415–427, 1993.
[7] H. L. Yale and F. Sowinski, "Novel polycyclic heterocycles. II. Derivatives of 5,11-dihydrodibenz[b,e][1,4]oxazepine," *Journal of Medicinal Chemistry*, vol. 7, no. 5, pp. 609–614, 1964.
[8] W. Wan *et al.*, "Concise synthesis of ω-fluoroalkylated ketoesters," *Tetrahedron*, vol. 65, no. 21, pp. 4212–4219, 2009.
[9] C. V. C. Prasad *et al.*, "2,3-Benzodiazepin-1,4-diones as peptidomimetic inhibitors of γ-secretase," *Bioorganic & Medicinal Chemistry Letters*, vol. 14, no. 13, pp. 3535–3538, 2004.
[10] N. A. Al-Joboury, K. A. Al-Badrany, A. S. Hamed, and W. M. Aljoboury, "Synthesis of some new thiazepine compounds derived from chalcones and evaluation their biochemical and biological activity," *Biochemical & Cellular Archives*, vol. 19, no. 2, 2019.
[11] S. S. Jasim, M. M. Al-Tufah, and K. A. Al-Badrany, "Synthesis and antibacterial evaluation of some new 1,5-benzooxazepines derivatives," *Systematic Reviews in Pharmacy*, vol. 12, no. 3, pp. 270–285, 2021.
[12] B. A. Khairallah, F. M. Muhammad, J. N. Saleh, and M. J. Saleh, "Preparation, characterization, biological activity evaluation, and liquid crystallography study of new diazepine derivatives," *World of Medicine: Journal of Biomedical Sciences*, vol. 1, no. 7, pp. 65–76, 2024.
[13] A. B. Khalid, "Synthesis, characterization and biological study of some oxazepine derivatives from 2-acetylthiazole," *World of Medicine: Journal of Biomedical Sciences*, vol. 1, no. 8, pp. 40–48, 2024.
[14] B. A. Khairallah, F. M. Muhammad, J. N. Saleh, and M. J. Saleh, "Preparation, characterization, biological activity evaluation, and liquid crystallography study of new diazepine derivatives," *World of Medicine: Journal of Biomedical Sciences*, vol. 7, pp. 65–76, 2024.
[15] M. J. Saleh *et al.*, "Preparation and evaluation of the biological activity of a 2-amino pyran ring using a solid base catalyst," *Central Asian Journal of Medical and Natural Science*, vol. 4, pp. 130–138, 2024.
[16] A. W. A. S. Talluh, M. J. Saleh, and J. N. Saleh, "Preparation, characterisation and study of the molecular docking of some derivatives of the tetrazole ring and evaluation of their biological activity," *World of Medicine: Journal of Biomedical Sciences*, vol. 7, pp. 15–23, 2024.
[17] A. H. Dalaf, M. J. Saleh, and J. N. Saleh, "Green synthesis, characterization, and multifaceted evaluation of thiazolidinone derivatives: A study on biological and laser efficacy," *European Journal of Modern Medicine and Practice*, vol. 7, pp. 155–168, 2024.
[18] H. Al-Badrani, N. S. Ezzat, and Y. S. Al-Jawaheri, "Synthesis of oxazepino compound via electrophilic cyclization and evaluation of their biological activity," *Kimya Problemleri*, vol. 3, pp. 343–355, 2025.

[19] Z. Q. M. Hassan and M. G. Abdulkarim, "Synthesis, characterization, and biological activity evaluation of chalcones and pyrazole derivatives derived from indole," *Al-Yarmouk Journal*, vol. 2, pp. 42–52, 2023.
[20] F. M. Muhammad, B. A. Khairallah, and K. A. Albadrany, "Synthesis, characterization and antibacterial evaluation of novel 1,3-oxazepine derivatives using a cycloaddition approach," *Journal of Angiotherapy*, vol. 3, pp. 1–9, 2024.
[21] S. H. Abdullah, B. A. Khairallah, and K. A. Al-Badrany, "Preparation and characterization of some azetidine-2-one derivatives derived from benzothiazole-2-ol and evaluation of their biological activity," *Indian Journal of Heterocyclic Chemistry*, vol. 35, no. 1, 2025.
[22] S. H. Abdullah, M. M. Salih, and A. Al-Badrany, "Synthesis, characterization and antibacterial evaluation of novel thiazolidine derivatives," *Journal of Angiotherapy*, vol. 3, pp. 1–9, 2024.
[23] A. A. M. Al Rashidy, K. A. Al-Badrany, and G. M. Al Garagoly, "Spectrophotometric determination of sulphamethoxazole drug by new pyrazoline derived from 2,4-dinitrophenylhydrazine," *Materials Science Forum*, vol. 1002, 2020.