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Synthesis and Characterization and Biological Study of Some Oxazepine Derivatives from 2-Acetylthiazole

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Abstract

This study involved the preparation of different α-β unsaturated compounds by reacting 2-acetylthiazole with different aromatic benzaldehyde substituents (E1-E5) and reacting compounds (E1-E5) with 2-aminophenol. The minimal medium with 10% NaOH was then examined for the inhibitory activity against E. coli and Gram-positive Staphylococcus aureus using some spectroscopic methods. : H1-NMR, 13C-NMR, and TLC techniques were used to confirm the effectiveness of the prepared compounds.

Keywords: Chalcone, Oxazepines, biological activity.

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1. Introduction

Chalcone is composed of two aromatic rings connected by an α-β-unsaturated carbonyl system, which is a derivative of 1,3-diphenyl-2-propen-1-one [1-3]. Nucleophilic addition reactions form a colored crystalline compound that is insoluble in water but soluble in organic solvents. The importance of these compounds lies in the successive presence of two functional groups, the double bond and the carbonyl group [4-7]. **Oxazepines** are heptameric compounds called oxazepines if unsaturated but oxazepines if saturated [8,9]. They consist of five carbon atoms and two heteroatoms [10]. Isomers, depending on the position of the oxygen and nitrogen atoms in the heptameric structure [11]. Many studies have shown that oxazepines can treat psychiatric disorders and many diseases [12]and have many medical and pharmaceutical applications. They also have anticancer activity, antioxidant activity, and activity against bacteria and microorganisms [13,14]

2. Materials and Methods:

2.1. Chemicals used: Utilized were chemicals produced by BDH Thomas, Fluka, Merck, and Aldrich.

2.2. Preparation of Chalcone [15]

(2-acetylthiazole) (0.007 mol, 1 g) was dissolved in ethanol (10 ml), a solution of (10% NaOH) (10 ml) was added, and stirred for 10 minutes, then (0.007 mol) aromatic aldehyde was added and dissolved in (10 ml of absolute ethanol) and the mixture was stirred in a water bath at a temperature of (20-40 °C) for (2-3) hours and the mixture was left in the refrigerator overnight and then added to crushed ice to form a precipitate that was filtered, collected and recrystallized from ethanol. As in Table 1

2.3. Preparation of Oxazepine .[16]

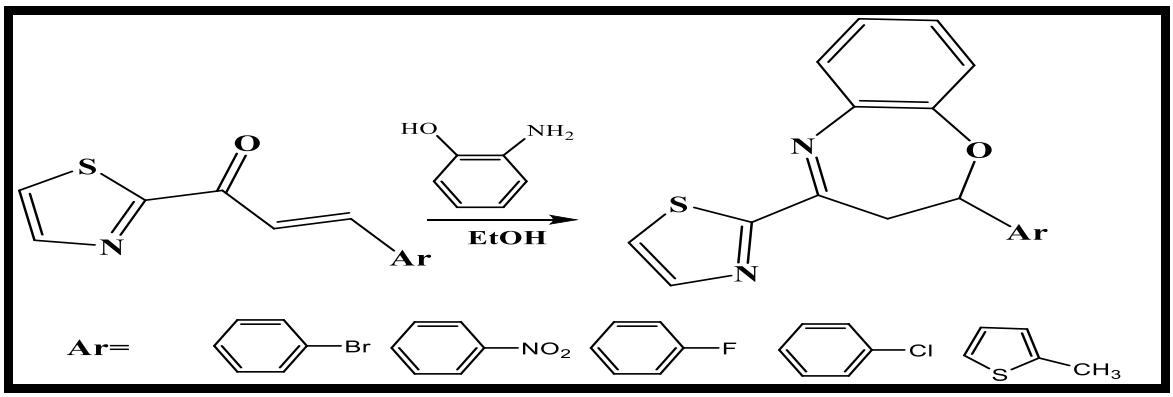
Dissolve an equal amount of one of the chalcones (0.00257 mol, ~0.691 g) in (10 mL) of absolute ethanol and add an excess of aminophenol dissolved in (5 mL) of ethanol and stir for (10) minutes, then add 5 mL of 10% sodium hydroxide solution, stir continuously, heat for (5-8) hours, then concentrate the solution, cool, add to crushed ice, add dilute hydrochloric acid dropwise to neutralize, use a TLC plate to follow the reaction process, as shown in Table 1.

.2.4. study of Biological activity

Dissolve Mueller Hinton agar (39 g) in (1 L) of distilled water, then heat and dissolve it using a magnetic stirrer, then sterilize it using an autoclave at a temperature of (121 °C). °C) and a pressure of (1.5 bar) for 2 hours, then cool to 50 °C, then pour into Petri dishes and freeze at room temperature[17,18]. Two types of bacterial isolates were tested. 1 Gram-negative strain [Gr-ve] E. coli, 1 Gram-positive strain [Gr+ve] Gold Staphylococcus aureus[19,20]. Two colonies of pure bacterial isolates of both Gram-positive and Gram-negative bacteria were transferred from the solid culture medium to test tubes containing (5 ml) distilled water using heat-sterilized holders. The tubes were incubated at 30 °C. (37°C) for (16-20) hours, then diluted with physiological solution until the turbidity reaches a level similar to the standard turbidity to obtain a cell count of approximately (1.5 x 108) cells/ml[21-25].

3. Results and discussions

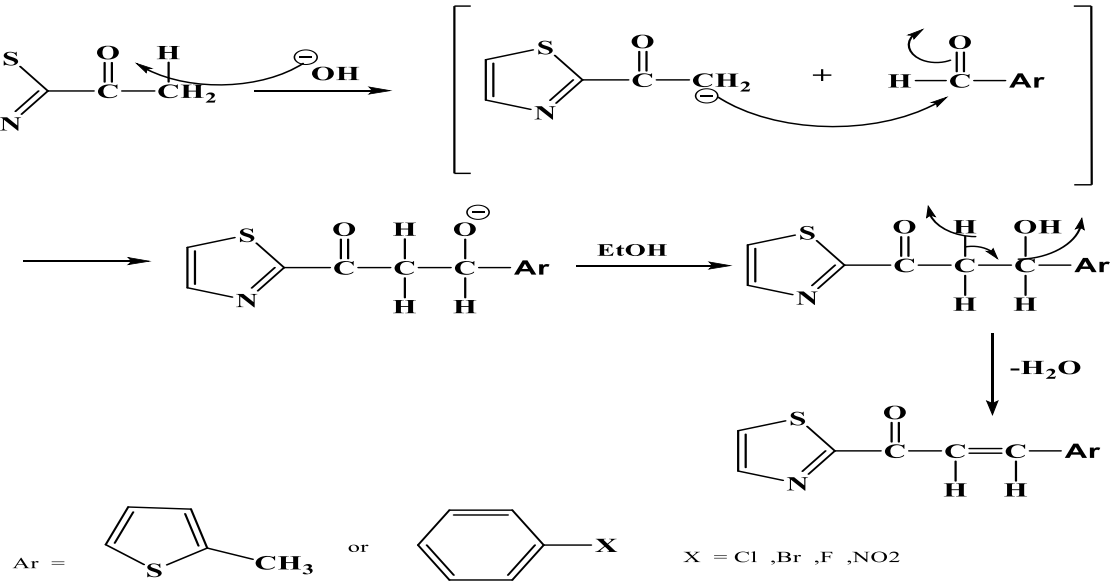
The following Scheme shows the preparation of azetidine derivatives.



Scheme 1: Shows the path of the prepared compounds.

3.1. Characterization of Chalcone.

Proposed mechanism for the following reaction:



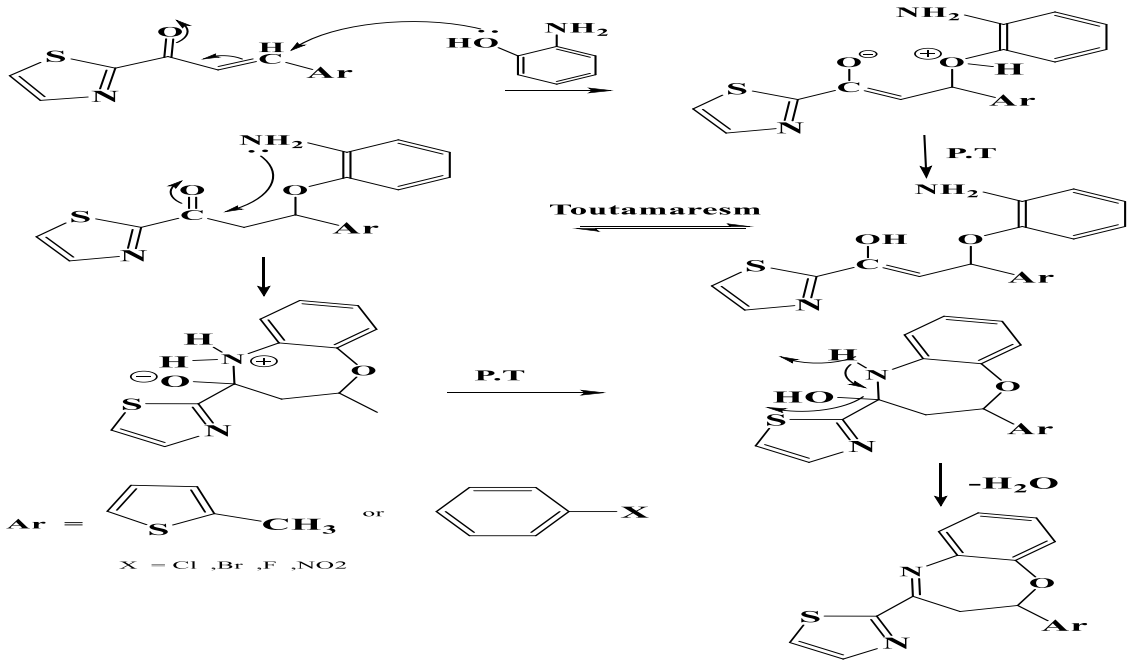
Scheme (2): shows the mechanism of formation of chalcone compounds (E1-E5)

When studying the 1H-NMR spectrum of compound [E4], a double signal was observed at ppm (6.82-6.85) attributed to α (=CH) and a double signal at ppm (7.04-7.06) attributed to β (=CH). A multiple signal at ppm (7.26-7.86) was attributed to the aromatic rings[26]. As in Figure 1

The 13C-NMR spectrum of compound [E4] using the solvent (DMSO-d6) showed a signal at the ppm position (187.55) attributed to the carbonyl carbon (C=O), at the ppm position (120.37) a signal attributed to the carbon of the (α-CH) group adjacent to the benzene ring at the point (144.45), a signal attributed to the carbon of the (β-CH) group of the alkene group appeared at the ppm position (144.45), and at the ppm position multiple signals attributed to the aromatic carbons appeared at (128.16-142.86), as shown in Figure 2

3.2. Characterization of Oxazepine.

Proposed mechanism for the following reaction:



Scheme (3): Shows the mechanism of formation of oxazepine rings (E11-E15)

The 1H-NMR spectrum of the compound (E11) showed a double signal at (2.96, 2.99) ppm attributed to (CH_2) of the oxazepine ring, a triple signal at (3.74-3.79) ppm attributed to (-CH) of the oxazepine ring, and the signals at the position (7.04-7.97) ppm belong to the aromatic system[27], as in Figure 3.

When studying the 13C-NMR spectrum of compound (E11), a signal was observed at ppm (21.61) due to carbon (CH2) of the oxazepine ring, a signal at ppm (75.11) due to carbon (-CH- O) in the oxazepine ring, a signal at ppm (162.97) due to carbon (C=N) of the oxazepine ring, and signals at ppm (113.34-144.80) due to the aromatic system, as in Figure 4.

3.2. Evaluation of the Biological Activity of Prepared Compounds

Compounds with heterocyclic rings have different biological activities against Gram-positive and Gram-negative bacteria[28,29]. The bioavailability of some of the prepared compounds was evaluated in this study on two types of bacteria: Escherichia coli (negative) and Staphylococcus aureus. These bacteria were chosen for their medical importance, as they cause a range of diseases. They have varying degrees of resistance to antibiotics. The bioavailability of the prepared compounds was evaluated using the etching method (26) and the inhibition level (zone of inhibition) was measured. The results showed that the prepared compounds could inhibit the growth of antibiotics[30-33]. The bacteria bind to Gram-positive and Gram-negative staining types in different proportions. Using the antibiotic ampicillin as a control group, compounds (E1, E4, and E11) had significant inhibitory effects on E. coli infection, and compounds (E14, E12, and E5) had significant inhibitory effects on Staphylococcus aureus[34,35]. The relationship is directly related to the concentration used and the inhibitory effect of the compound. The highest degree of inhibition occurs at a concentration of 0.01 mg/ml[36-38]. as shown in the table2

Table (1): Some physical properties of for Prepared compounds (E1-E15).

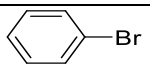
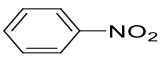
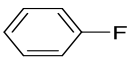
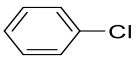
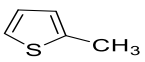
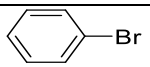
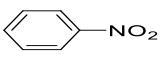
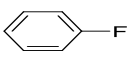
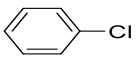
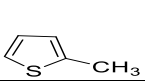
Comp. No.	Ar	Molecular Formula	m.p. °C	Yield%	Color
E1		$C_{12}H_8BrNOS$	107-110	94	off white
E2		$C_{12}H_8N_2O_3S$	119-121	79	Dark brown
E3		$C_{12}H_8FNOS$	114-116	75	Light Yello
E4		$C_{12}H_8ClNOS$	125-127	80	Light brown
E5		$C_{10}H_9NOS_2$	94-96	68	Dark brown
Comp. No.	**Ar**	**Molecular Formula**	**m.p. °C**	**Yield%**	Color
E11		**$C_{18}H_{13}BrN_2OS$**	**205-207**	**68**	Brown
E12		**$C_{18}H_{13}N_3O_3S$**	**270-272**	**71**	Dark brown
E13		**$C_{18}H_{13}FN_2OS$**	**159-161**	**62**	Dark brown
E14		**$C_{18}H_{13}ClN_2OS$**	**144-146**	**74**	Liaghtbro wn
E15		**$C_{17}H_{14}N_2OS_2$**	**154-156**	**55**	Brown

Table (2): Biological efficacy of produced substances and control methods (measured in millimeters of inhibition).

Comp. No	Conc. mg/ml	*Staphylococcus aureus*	*Escherichia coil*
E1	**0.01**	**31**	15
	0.001	21	13
	0.0001	10	9
E4	0.01	26	26
	0.001	19	17
	0.0001	13	16
E5	0.01	10	Niz
	0.001	8	6
	0.0001	5	10
E11	0.01	15	28
	0.001	13	17
	0.0001	12	16
E12	0.01	Niz	10
	0.001		0
	0.0001		0
E14	0.01	Niz	13
	0.001		12
	0.0001		12
Ampicillin	For every focus.	16	15

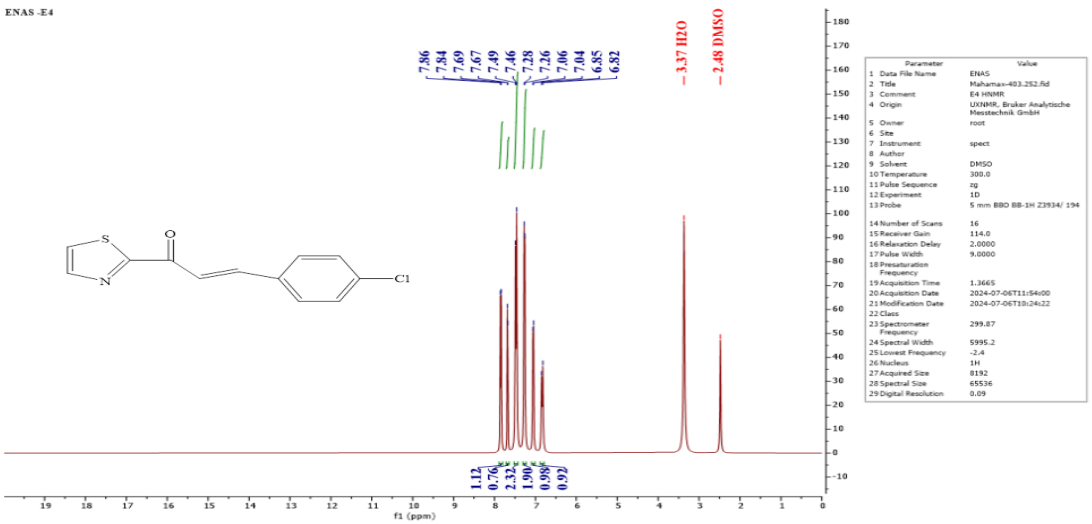


Figure (1): 1-H NMR spectra of the substance (E4).

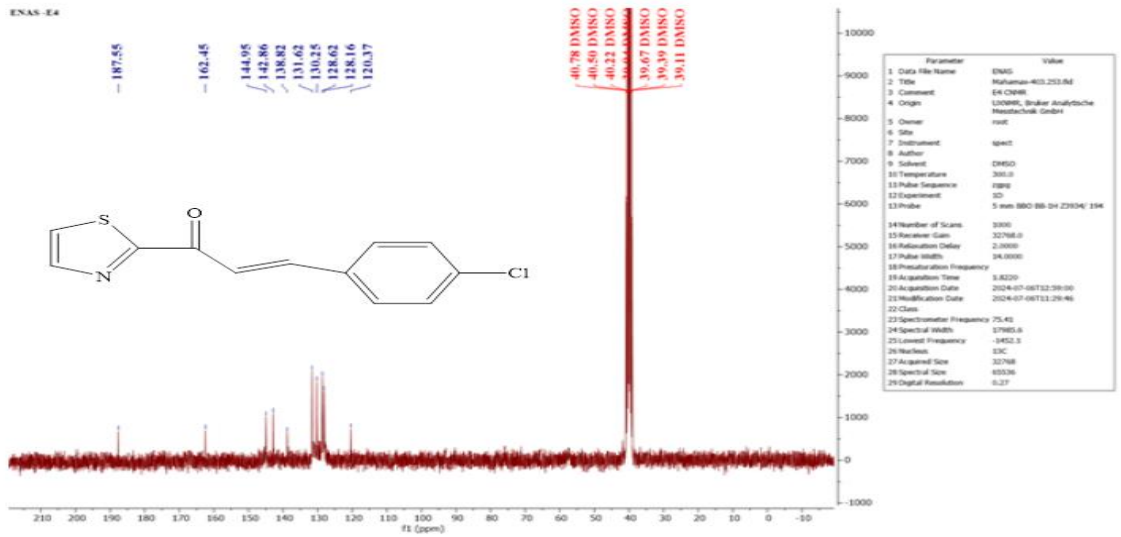


Figure (2): 13C- NMR spectra of the substance (E4).

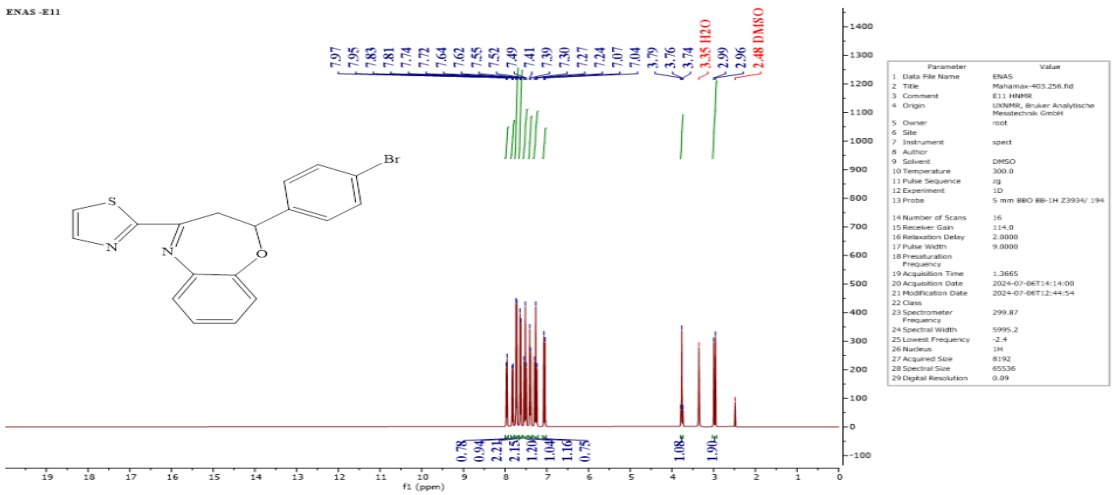


Figure (3): 1-H NMR spectra of the substance (E11).

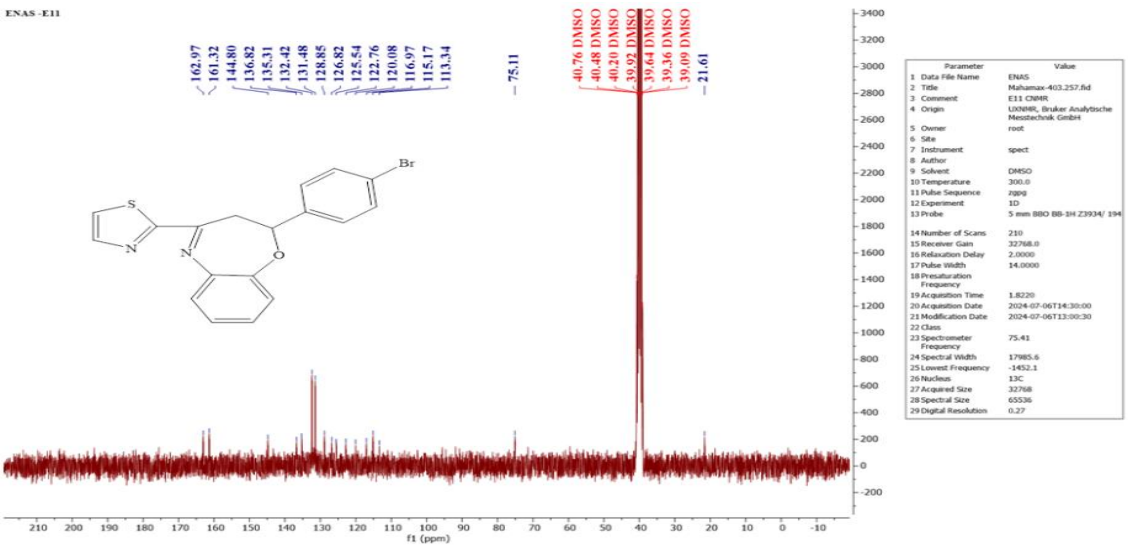


Figure (4): 13C- NMR spectra of the substance (E11).

4. Conclusions

The prepared compounds showed high purity as proven by spectroscopic measurements such as proton and carbon nuclear magnetic resonance spectra and showed varying effectiveness against the two types of bacteria used, as some of them showed effectiveness against the first type and others showed effectiveness against the second type.

References:

1. Al-Joboury, N. A., Al-Badrany, K. A., Hamed, A. S., & Aljoboury, W. M. (2019). SYNTHESIS OF SOME NEW THIAZEPINE COMPOUNDS DERIVED FROM CHALCONES AND EVALUATION THERE BIOCHEMICAL AND BIOLOGICAL ACTIVITY. Biochemical & Cellular Archives, 19(2).
2. Al-Tufah, M. M., Jasim, S. S., & Al-Badrany, K. A. (2020). Synthesis and Antibacterial Evaluation of some New Pyrazole Derivatives. Prof.(Dr) RK Sharma, 20(3), 178.
3. Al-Joboury, M. R., & Al-Badrany, A. (2018). Synthesis of Some New pyrazoline Compounds Derived from chalcones Compounds and Study Their biological activity. journal of kerbala university, 14(3), 58-67.
4. Mohamed, S. A., Al-Badrany, K. A., & Huseen, M. S. (2022). Preparation and Study of Biological Activity of Pyrimidine Compounds Derived from 2-Acetylpyridine. Vegueta. Anuario de la Facultad de Geografía e Historia, 22(8).
5. AL-Garagoly, G. M., AL-Rashidy, A. A., & AL-Badrany, K. A. (2019). Spectrophotometric Determination of Sulfanilamide in Pure and Synthetic Sample by New Derivative from Pyrazoline Derived from 2, 4-Dinitro Phenyl Hydrazine. Diyala Journal for Pure Science, 15(4).
6. Al-Sabawy, S. M. I. (2024). SYNTHESIS AND CHARACTERIZATION AND BIOLOGICAL STUDY OF SOME CYCLOHEXENONE DERIVATAVES FROM 2-ACETYL PYROL. EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE, 4(7), 321-329.
7. Saleh, M. J., Saleh, J. N., Al-Badrany, K., Dalaf, A. H., Najm, R. S., & Talluh, A. W. A. S. (2024). 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, 5(4), 130-138.
8. Najim, D. M., Al-badrany, K. A., & Saleh, M. K. Synthesis of some new oxazepine compounds derived from cyanoethyl acetate and study their inhibitory activity against some pathogenic bacterial species. Unpublished.
9. Muhammad, F. M., Khairallah, B. A., & Albadrany, K. A. (2024). Synthesis, characterization and Antibacterial Evaluation of Novel 1, 3-Oxazepine Derivatives Using A Cycloaddition Approach. Journal of Angiotherapy, 8(3), 1-5.
10. Abdul Wahed, A. S. T. (2024). 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, 5(2), 15-26.
11. Mohamed, S. A., Hussein, M. S., & Al-badrany, K. A. (2022). 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, 4(4).
12. Al-Joboury, N. A., Al-Badrany, K. A., Hamed, A. S., & Aljoboury, W. M. (2019). SYNTHESIS OF SOME NEW THIAZEPINE COMPOUNDS DERIVED FROM CHALCONES AND EVALUATION THERE BIOCHEMICAL AND BIOLOGICAL ACTIVITY. Biochemical & Cellular Archives, 19(2).

13. Jasim, S. S., Al-tufah, M. M., & Al-badrany, K. A. (2021). Synthesis and antibacterial evaluation of some New 1, 5-Benzooxazepines derivatives. Syst Rev Pharm, 12(3), 270-285.
14. Khairallah, B. A., Muhammad, F. M., Saleh, J. N., & Saleh, M. J. (2024). Preparation, Characterization, Biological Activity Evaluation, and Liquid Crystallography Study of New Diazepine Derivatives. World of Medicine: Journal of Biomedical Sciences, 1(7), 65-76.
15. Al-Badrany, K. A., Jasim, S. S., & Al-Tufah, M. M. (2020). Synthesis of some of the compounds of Chalcones and pyrozoline containing phthalimide unit and evaluation their biological activity of some of them. Samarra Journal of Pure and Applied Science, 2(4).
16. Al-Joboury, M. R., & Al-Badrany, A. (2018). Synthesis of Some New pyrazoline Compounds Derived from chalcones Compounds and Study Their biological activity. journal of kerbala university, 14(3), 58-67.
17. Talluh, A. W. A. S., Saleh, M. J., & Saleh, J. N. (2024). 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, 1(7), 15-23.
18. Dalaf, A. H., Saleh, M. J., & Saleh, J. N. (2024). GREEN SYNTHESIS, CHARACTERIZATION, AND MULTIFACETED EVALUATION OF THIAZOLIDINONE DERIVATIVES: A STUDY ON BIOLOGICAL AND LASER EFFICACY. European Journal of Modern Medicine and Practice, 4(7), 155-168.
19. Saleh, M. J., Saleh, J. N., & Al-Badrany, K. (2024). PREPARATION, CHARACTERIZATION, AND EVALUATION OF THE BIOLOGICAL ACTIVITY OF PYRAZOLINE DERIVATIVES PREPARED USING A SOLID BASE CATALYST. EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE, 4(7), 25-32.
20. Saleh, J. N., & Khalid, A. (2023). Synthesis, characterization and biological activity evaluation of some new pyrimidine derivatives by solid base catalyst AL2O3-OBa. Central Asian Journal of Medical and Natural Science, 4(4), 231-239.
21. Talluh, A. W. A. S., Saleh, J. N., & Saleh, M. J. (2024). Preparation, Characterization and Evaluation of Biological Activity and Study of Molecular Docking of Some New Thiazoli-dine Derivatives.
22. Talluh, A. W. A. S., Saleh, M. J., Saleh, J. N., Al-Badrany, K., & mohammed saleh Al-Jubori, H. (2024). Preparation, characterization, and evaluation of the biological activity of new 2, 3-dihydroquinazoline-4-one derivatives. EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE, 4(4), 326-332.
23. Talluh, A. W. A. S. (2024). Preparation, Characterization, Evaluation of Biological Activity, and Study of Molecular Docking of Azetidine Derivatives. Central Asian Journal of Medical and Natural Science, 5(1), 608-616.
24. Al-Joboury, W. M., Al-Badrany, K. A., & Asli, N. J. (2022, November). N-alkylation of substituted 2-amino benzothiazoles by 1, 4-bis (bromo methyl) benzene on mixed oxides at room temperature and study their biological activity. In AIP Conference Proceedings (Vol. 2394, No. 1). AIP Publishing.
25. Al-Joboury, W. M., Al-Badrany, K. A., & Asli, N. J. (2021). Synthesis of new azo dye compounds derived from 2-aminobenzothiazole and study their biological activity. Materials Today: Proceedings, 47, 5977-5982.
26. Al-Joboury, N. A., Al-Badrany, K. A., Hamed, A. S., & Aljoboury, W. M. (2019). SYNTHESIS OF SOME NEW THIAZEPINE COMPOUNDS DERIVED FROM CHALCONES AND EVALUATION THERE BIOCHEMICAL AND BIOLOGICAL ACTIVITY. Biochemical & Cellular Archives, 19(2).

27. Farah M. Muhammad, Bushra A. Khairallah, K. A. Albadrany. (2024). Synthesis, characterization and Antibacterial Evaluation of Novel 1,3-Oxazepine Derivatives Using A Cycloaddition Approach, Journal of Angiotherapy, 8(3), 1-9, 9506

28. Saleh, M. J., & Al-Badrany, K. A. (2023). Preparation, characterization of new 2-oxo pyran derivatives by AL2O3-OK solid base catalyst and biological activity evaluation. Central Asian Journal of Medical and Natural Science, 4(4), 222-230.

29. Muhammad, F. M., Khairallah, B. A., Saleh, M. J., & Saleh, J. N. (2024). Preparation and Characterization of New Rings of Oxazine Derivatives and Studying Their Biological and Laser Effectiveness and Molecular Docking. Central Asian Journal of Theoretical and Applied Science, 5(4), 190-201.

30. Sattar Talluh, A. W. A., Saleh, J. N., Saleh, M. J., & Saleh Al-Jubori, H. M. (2024). Preparation and Characterization of New Imidazole Derivatives Derived From Hydrazones and Study of their Biological and Laser Efficacy. Central Asian Journal of Theoretical and Applied Science, 5(4), 202-211.

31. Saleh, M. M., Saleh, J. N., Rokan, F. F., & Saleh, M. J. (2024). Synthesis, Charactarizit and evaluation of bacterial efficacy and study of molecular substrates of cobalt (II) complex [Co (2-(benzo [d] thiazol-2-yloxy) acetohydrazide)(H2O)(Cl2)]. Central Asian Journal of Medical and Natural Science, 5(4).

32. Talluh, A. W. A. S., Saleh, M. J., Saleh, J. N., & Al-Jubori, H. M. S. (2024). Synthesis and Characterization of Some New Imine Graphene Derivatives and Evaluation of Their Biological Activity. Central Asian Journal of Medical and Natural Science, 5(4), 272-290.

33. Owed, A.I., Al – Jubouri, A.A., & Al-Samarrai, S.Y. (2024). A nano-sensor for copper oxide was manufactured and developed using a new organic precipitant via green chemistry methods. Sensors and Machine Learning Applications.

34. Shannak, Q. A., Najim, T. M., & Madab, D. I. (2022). Evaluation of the level of vitamin D3 in the blood serum of patients infected with COVID-19 in Al-Amiriya city. Technium BioChemMed, 3(2), 127-135.

35. Shannak, M. Q. A., Othman, I. A. W., Rasheed, M. K., & Mahmood, S. K. (2018). Synthesis and Characterization of New Some Binuclear Complexes for Some Transition Element Metals with Schiff Base ligand Derived from 1-Chloro-2-(2-Chloroethoxy) Ethane. Eurasian Journal of Analytical Chemistry, 13, 339-346.

36. Najm, R. S., Shannak, Q. A., & Dalaf, A. H. (2023). Synthesis and Decoration of Aromatic Derivatives Nano Platelets by the Electric Method. Azerbaijan Pharmaceutical and Pharmacotherapy Journal, 22(2), 92-97.

37. Shannak, Q. A., Madab, D. I., Mohammed, S., & Alhiti, M. A. (2021). Effects of Ascorbic Acid Supplement and Furdivita extraction on Hematological Parameters, liver function tests and histopathological changes in Rabbits liver. Annals of the Romanian Society for Cell Biology, 25(6), 5432-5441.

38. Mahmood Mahdy Saleh, Amenah l. Al-Nassiry, Jamil Nadhem Saleh, & Mohammed Jwher Saleh. (2024). Preparation and Diagnosis of New Complexes for Hg (II) With 4-Amino Acetanilide And (Dppp) As A Ligand And Study Of The Bacterial Efficacy And Molecular Docking Of The Prepared Complexes. Central Asian Journal of Theoretical and Applied Science, 5(4), 364-373.