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GREEN SYNTHESIS, CHARACTERIZATION, AND MULTIFACETED EVALUATION OF THIAZOLIDINONE DERIVATIVES: A STUDY ON BIOLOGICAL AND LASER EFFICACY

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Abstract: This study involves the synthesis of thiazolidinone derivatives by reacting Schiff base derivatives with thioglycolic acid. The reactions were conducted using both conventional and microwave methods and characterized using determining melting points and purity, monitoring reaction progress and Rf values using thin-layer chromatography (TLC), and conducting infrared (FT-IR) spectroscopy, proton nuclear magnetic resonance (^{1}H-NMR) spectroscopy, and quantitative elemental analysis (C.H.N.). The biological activity of the synthesized compounds was evaluated by examining their effects on the growth of four types of antibiotic-resistant bacterial isolates: two Gram-negative strains (***Escherichia et al.***) and two Gram-positive strains (***Staphylococcus aureus*** and ***Staphylococcus epidermidis***). The standard antibiotic ***Ampicillin*** was used as a control sample. The synthesized compounds exhibited good inhibitory activity against the tested bacteria. Additionally, the laser activity of the synthesized compounds was measured using a helium-neon laser (visible laser). The compounds were irradiated for four different periods (15, 30, 45, and 60) seconds, and their physical properties were re-examined to observe any changes resulting from the laser irradiation.

Keywords: Thiazolidinone, Green Chemistry, Biological Activity, Laser Effectiveness.

1. Introduction

Thiazolidinone compounds are important in medical [1], and industrial fields [2], because they are heterocyclic compounds that contain sulfur and nitrogen [3], and have distinct optical and photochemical properties [4]. The researchers were interested in preparing thiazolidines [5, 6], as they used thioglycolic acid to obtain the thiazolidine 2-one ring while preserving the active carboxyl group [7]. Thiazolidinones are prepared by reacting Thiosemicarbazide with aldehydes or ketones [8]. Thiazolidinones are prepared by reacting Schiff bases with thioglycolic acid [9]. Thiazolidinedione compounds are biologically effective and important because they contain an atom of sulfur and nitrogen [10], which is why it has received wide attention from researchers, as well as their ability to resist many bacteria [11], fungi [12], and viruses [13]. A series of anti-diabetic agents have been developed and mainly studied the level of sugar in the blood and the extent to which the cell reduces its activities in resisting diabetes [14]. Obesity is genetically inherited, and this means that cells sometimes become resistant to insulin [15], as it has caused a breakthrough in anti-diabetic treatment by increasing sensitivity to insulin [16]. Therefore, they are also called “insulin sensitizers [17], and they have been used in treating diarrhea [18], and killing Parasites (Toxoplasma gondii) [19]. Thiazolidine-4-one compounds have a broad spectrum of biological activity [20], with a focus on thiazolidine because it is an anti-HIV [21], anti-diabetic [22], and diuretic compound Thiazolidinones are anti-inflammatory [23], anti-inflammatory [24], and anti-fungal [25]. Thiazolidinones are also inhibitors of

enzymes and modify metabolic pathways in cells [26]. Thiazolidinones have therapeutic potential against joint diseases [27], inflammation [28], anxiety diseases [29], and diabetes [30]. Thiazolidinediones are used in industrial fields, as they have the potential to develop Lasers and optical devices due to their electrical and optical properties, as well as their ability to multiply the frequency in laser devices [31]. Thiazolidinone molecules offer exceptional and promising adaptability because they exist at the convergence of biology and optics [32]. Their diverse range of biological functions make them very important in the search for new medical treatments, while their distinct optical qualities contribute to advances in laser and photonics technology [33].

2. Experimental part

2.1. Materials: All chemicals and reagents used in this study were supplied by companies Fluka.

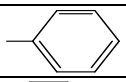
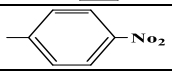
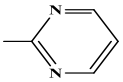
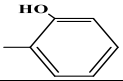
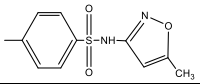
2.2. Synthesis of a series of thiazolidinedione derivatives by the traditional method (A_1-A_5)

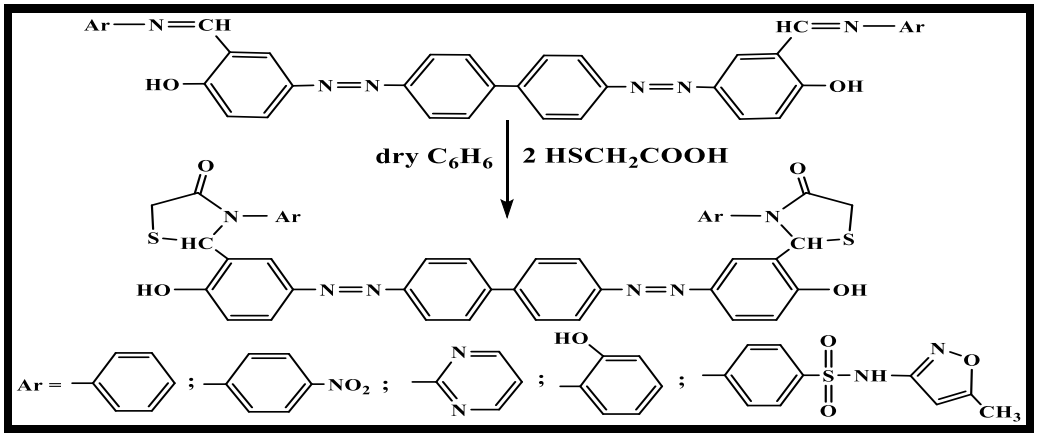
A mixture of (0.001 mol) of prepared Schiff bases, (0.002 mol, 0.14 ml) of thioglycolic acid, and (0.002 gm) of anhydrous zinc chloride was refluxed in (40 ml) of dry benzene with continuous stirring in a water bath for (9-12) hours. The completion of the reaction was confirmed using TLC. The solution was then cooled, the solvent evaporated, and the product filtered and recrystallized from ethanol to give a precipitate [34, 35], as in scheme (1). Table (1) provides some physical properties of the series of thiazolidinone derivatives (A_1-A_5),.

2.3. Synthesis of a series of thiazolidinedione derivatives by microwave method (A_1-A_5)

A mixture of (0.001 mol) of prepared Schiff bases and (0.002 mol, 0.14 ml) of thioglycolic acid in 10 ml of dry benzene was continuously stirred and placed in a microwave oven at 80°C and 400 W for (5-10) minutes. The completion of the reaction was confirmed using TLC. The solution was then cooled, the solvent evaporated, and the product filtered and recrystallized from ethanol to give a precipitate [36, 37], as in scheme (1). Table (1) provides some physical properties of the series of 4-thiazolidinedione derivatives (A_1-A_5).

Table (1): Some Physical Properties of the thiazolidinone derivatives (A1-A5) Prepared by the traditional and microwave methods.

Comp. No.	Ar	Molecular Formula/ M.Wt g/mol	Traditional Methods					Microwave Methods				
			Color	M.P. ^{0}C	T. Ref. h.	Yield %	R_f	Color	M.P. ^{0}C	T. Ref. min.	Yield %	R_f
A1		$C_{42}H_{32}N_6O_4S_2$ 748.88	Red	128-129	10	71	0.84	Red	128-129	5	89	0.84
A2		$C_{42}H_{30}N_8O_8S_2$ 838.87	Orange	151-153	12	49	0.51	Orange	151-153	10	88	0.51
A3		$C_{38}H_{28}N_{10}O_4S_2$ 752.83	Brown	194-196	9	80	0.79	Brown	194-196	8	95	0.79
A4		$C_{42}H_{32}N_6O_6S_2$ 780.87	Brown	141-142	12	67	0.90	Brown	141-142	10	92	0.90
A5		$C_{50}H_{40}N_{10}O_{10}S_4$ 1069.17	Green	177-179	10	70	0.80	Green	177-179	6	95	0.80



Scheme (1): Prepared compounds (A_1-A_5)

2.4. Evaluation of the Biological Activity of the Synthesized Compounds

The Muller-Hinton Agar medium was prepared by dissolving (39 gm) of it in (1 L) of distilled water. Four types of bacterial isolates were tested: two Gram-negative strains, ***Escherichia coli*** and ***Klebsiella pneumoniae***, and two Gram-positive strains, ***Staphylococcus aureus*** and ***Staphylococcus epidermidis***. Chemical solutions of the synthesized compounds were then prepared using DMSO as the solvent, with concentrations of (25, 50, 100) mg/ml for each solid derivative [38]. The Muller-Hinton Agar (MHA) medium was inoculated using a sterile cotton swab that had been dipped into tubes containing the diluted bacterial cultures. Excess inoculum was removed by pressing the swab against the inner walls of the tubes. The medium was then streaked in three directions to ensure uniform distribution of the inoculum. The plates were left for (10-15) minutes to allow absorption and drying [39, 40]. The Agar-well diffusion method was employed to evaluate the synthesized compounds. Following the inoculation of the bacterial isolates onto the agar medium, wells were created using the Cylinder metric method (according to the United States Pharmacopeia USP 35) with a cork borer. Into each well, (40 µl) of the synthesized compounds at the three different concentrations was introduced. The plates were incubated at (37 °C) for (24) hours [41]. Results were read after 24 hours and again at 48 hours to determine the sensitivity of the compounds, as indicated by the diameter of the inhibition zones around the wells. An increase in the diameter of the inhibition zones corresponds to an increase in the biological activity of the synthesized compounds. These results were compared with the inhibition zones of standard antibiotics [42]. Standard antibiotics such as ***Ampicillin*** were used as control samples, based on those used in Ministry of Health laboratories and adhering to World Health Organization protocols [43].

2.5. Measurement of Laser Activity of the Compounds

The laser activity of the synthesized compounds was measured using a helium-neon laser (visible laser). The compounds were irradiated for four different time intervals (15, 30, 45, and 60) seconds for each compound. The distance between the laser source and the sample was set at (10 cm), with a power of (1 mW) and a wavelength of (808 nm). The measurements were conducted at the Laser Laboratory, Department of Physics, College of Science, University of Tikrit. After irradiating the synthesized compounds, their physical properties were re-examined to observe any changes resulting from the laser irradiation [44].

3. Results and Discussion

3.1. Characterization of thiazolidinedione derivatives (A_1-A_5) by using UV-Vis and FT-IR

In the UV-Vis spectra of the synthesized compounds (A_1-A_5), ethanol (95%) was used as the solvent with concentrations ranging from (10^{-4}-10^{-5}) M. The compounds exhibited short wavelength maxima (λ_{max}) at (217-264) nm, corresponding to ($\pi \rightarrow \pi^*$) transitions, and long wavelength maxima (λ_{max}) in the range of

(291-356) nm, corresponding to (n→π*) electronic transitions [45]. Table (2) lists UV absorption values for the thiazolidinone derivatives (A_1-A_5).

In the IR spectra, the disappearance of the medium band at (1672-1622) cm^{-1}, attributed to the (C=N) group, and the appearance of a strong band at (1664-1670) cm^{-1}, attributed to the stretching of the amide carbonyl (C=O) bond, were observed. Additionally, a broad absorption band appeared in the range of (3402-3415) cm^{-1}, corresponding to the stretching of the (OH) bond. Aromatic (CH) stretching bands appeared in the range of (3039-3080) cm^{-1}, while aliphatic (CH) stretching bands appeared in the range of (2922-2987) cm^{-1}. Furthermore, bands in the range of (1486-1494 and 1569-1595) cm^{-1} were attributed to the aromatic (C=C) bond stretching, while the medium band in the range of (1413-1460) cm^{-1} was attributed to the (N=N) group. Other bands in the range of (1275-1282) cm^{-1} were attributed to (C-N) bond stretching and bands in the range of (742-785) cm^{-1} were attributed to (C-S) bond stretching. Table (2) which shows IR absorption results (cm^{-1}).

Table (2): UV/Vis., and FT-IR data of prepared compounds (A_1-A_5)

Comp No.	λ max$_1$ λ max$_2$ EtOH	IR (KBr) cm^{-1}							
		ν O-H	ν C-H Arom., Aliph.	ν C=O	ν C=C	ν N=N	ν C-N	ν C-S	Others
A22	244, 303	3404	3039, 2970	1664	1581, 1487	1413	1282	742	.....
A23	217, 291	3402	3068, 2968	1664	1593, 1494	1456	1280	744	ν (NO_2). 1548, 1350
A24	236, 342	3415	3047, 2987	1685	1569, 1487	1460	1278	748	
A25	245, 292	3410	3076, 2922	1690	1595, 1491	1442	1275	785	.....
A26	264, 356	3415	3080, 2936	1688	1587, 1486	1450	1281	765	ν (SO_2). 1359, 1181

3.2. Characterization of thiazolidinone derivatives (A_1, A_5) by used ^{1}H-NMR

When studying the ^{1}H-NMR spectrum of the compound (A_1) using a solvent (Chloroform-d), it was observed that a tetra signal appears at the chemical shift (3.80, 3.83, 3.85, 3.88) ppm due to the proton of two groups (CH_2) in the thiazolidinone ring, a single signal appeared at the chemical shift (7.02) ppm is attributed to the protons of two groups (CH) in the thiazolidinone ring, a multiple signal in the range (7.04-7.86) ppm is attributed to the protons of the aromatic rings, a single signal appeared at the chemical shift (7.87) ppm is attributed to the protons of two groups (OH), and a signal appears at the chemical shift (7.55) ppm is attributed to the protons of the solvent (Chloroform-d) [46], and as shown in Figure (4). In addition, the ^{1}H-NMR spectrum of the compound (A_5) using a solvent (Chloroform-d), it was observed that a single signal appeared at the chemical shift (2.30) ppm attributed to the protonation of the two groups (CH_3), a tetra signal appears at the chemical shift (3.80, 3.83, 3.85, 3.88) ppm due to the proton of two groups (CH_2) in the thiazolidinone ring, a single signal appeared at the chemical shift (6.09) ppm is attributed to the protons of two groups (CH) in the oxazole ring, a single signal appeared at the chemical shift (7.02) ppm is attributed to the protons of two groups (CH) in the thiazolidinone ring, a multiple signal in the range (7.04-7.85) ppm is attributed to the protons of the aromatic rings, a single signal appeared at the chemical shift

(7.86) ppm is attributed to the protons of two groups (NH), a single signal appeared at the chemical shift (7.87) ppm is attributed to the protons of two groups (OH), and a signal appears at the chemical shift (7.55) ppm is attributed to the protons of the solvent (Chloroform-d) [47], and as shown in Figure (5).

3.3. Elemental Analysis (C.H.N.S.) Measurement

Elemental analysis (C.H.N.S.) was conducted for some of the synthesized compounds to verify the accuracy and precision of their structural composition. The obtained elemental percentages were either consistent with or very close to the calculated values, confirming the correctness of the synthesized compound structures [48], as shown in Table (3).

Table (3): Elemental Analysis (C.H.N.S.) Results for Selected Synthesized Compounds

Comp. No.	Molecular Formula	Calculated				Found			
		C%	H%	N%	S%	C%	H%	N%	S%
A1	$C_{42}H_{32}N_6O_4S_2$	67.36	4.31	11.22	8.56	67.55	3.39	11.20	8.48
A2	$C_{42}H_{30}N_8O_8S_2$	60.14	3.60	13.36	7.64	60.25	3.66	13.50	7.60
A3	$C_{38}H_{28}N_{10}O_4S_2$	60.63	3.75	18.61	8.52	60.54	3.70	18.52	8.42
A4	$C_{42}H_{32}N_6O_6S_2$	64.60	4.13	10.76	8.21	64.69	4.08	10.70	8.25
A5	$C_{50}H_{40}N_{10}O_{10}S_4$	56.17	3.77	13.10	11.99	56.30	3.75	13.15	12.07

3.4. Green synthesis and traditional synthesis

All compounds were synthesized using both conventional and microwave methods, and the two methods were compared in terms of solvent use, catalyst requirements, reaction time, percentage yield, melting point, color, and solubility [49]. The microwave method produces a large yield and uses a small amount of solvent without the need for an auxiliary agent and in a very short time. Isolation of the prepared compounds was also easier using microwave technology. In terms of physical properties, such as color, melting point, and RF values, the compounds prepared by both methods were identical.

3.5. Evaluation of the Biological Activity of Synthesized Compounds

The biological activity of some synthesized compounds was assessed, as heterocyclic compounds are known for their varying biological activities against Gram-positive and Gram-negative bacteria. The impact of the synthesized compounds in this study was evaluated on four types of bacteria: ***Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus, Staphylococcus epidermidis.*** These bacteria were selected due to their medical importance, as they cause various diseases and exhibit different levels of antibiotic resistance [50]. The results indicate that the synthesized compounds exhibit inhibitory effects on the growth of both Gram-positive and Gram-negative bacteria, with varying degrees of inhibition, as shown in Table (4), Schemes (2, 3), and Figure (6).

Table (4): Antibacterial activity of the synthesized compounds (inhibition zone in mm).

Comp. No.	*E. Coil* mg/ml			*K. Pneumonia* mg/ml			*S. Aureus* mg/ml			*S. epidermidis* mg/ml		
	25	50	100	25	50	100	25	50	100	25	50	100
A_1	0	10	15	5	12	20	7	15	24	10	18	25
A_2	7	17	24	3	11	21	8	15	22	6	14	24
A_3	0	5	10	5	10	15	12	19	25	8	17	23

A_4	5	12	20	6	13	21	6	15	24	7	15	20
A_5	8	16	24	9	17	25	10	16	23	10	16	22
Ampicillin	7	17	22	6	12	20	7	14	24	10	14	24
Blank disk	0	0	0	0	0	0	0	0	0	0	0	0

3.6. Results of Laser Activity Measurement for Some Synthesized Compounds

In this study, the laser activity of certain synthesized compounds was measured by irradiating them with a Helium-Neon laser. Subsequently, the physical properties (color, melting point, and flow rate (Rf)) of the compounds were re-evaluated to observe any changes. The study revealed that within the time intervals of 15, 30, and 45 seconds, there were no changes in the physical properties of the chemical compounds [51]. These compounds retained their structural integrity and physical properties, showing no effects from laser irradiation during these periods. However, at the 60-second interval, significant changes were observed in the physical properties, with noticeable fluctuations in the melting points and altered flow rate (R*f*) values in thin-layer chromatography (TLC) [52]. Additionally, slight color changes were noted. These changes are likely due to the breaking of some bonds within the compounds, potentially leading to the formation of new compounds as a result of prolonged exposure to high-energy laser irradiation for 60 seconds [53]. The results of the laser activity measurement for some synthesized compounds are presented in Table (5).

Table (5): Laser Activity Measurement Results for Some Synthesized Compounds.

Comp No.	15 S			30 S			45 S			60 S		
	Color	M.P (^{0}C)	R*f*	Color	M.P (^{0}C)	R*f*	Color	M.P (^{0}C)	R*f*	Color	M.P (^{0}C)	R*f*
A1	Red	128-129	0.84	Red	128-129	0.84	Red	128-129	0.84	Light red	95-97	0.71
A2	Orange	151-153	0.51	Orange	151-153	0.51	Orange	151-153	0.51	Light orange	189-195	0.78
A3	Brown	194-196	0.79	Brown	194-196	0.79	Brown	194-196	0.79	Light brown	120-128	0.40
A4	Brown	141-142	0.90	Brown	141-142	0.90	Brown	141-142	0.90	Light brown	172-175	0.61
A5	Green	177-179	0.80	Green	177-179	0.80	Green	177-179	0.80	Light green	149-153	0.52

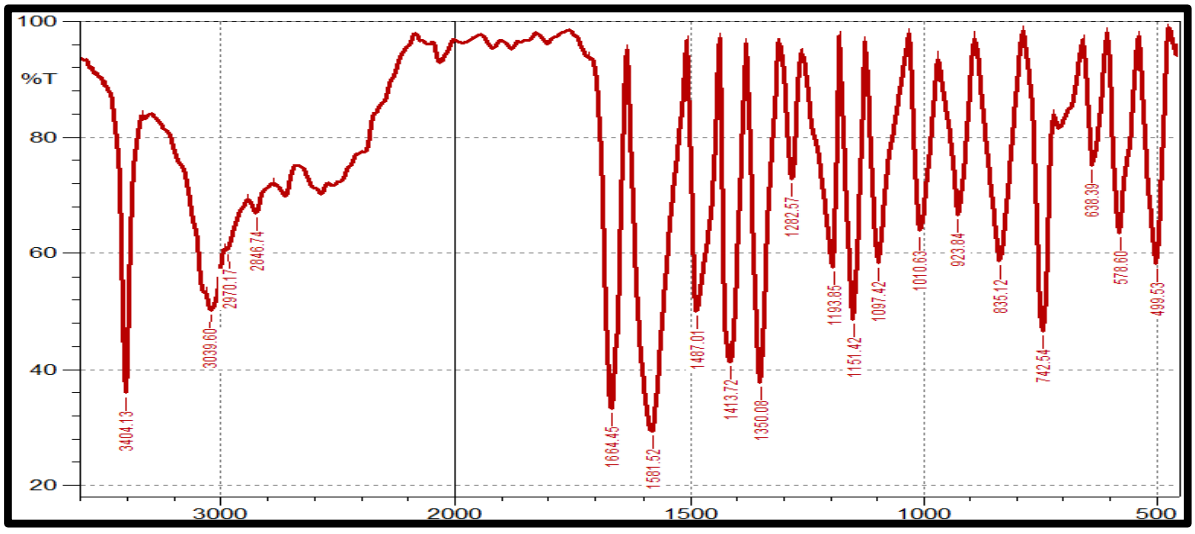


Figure (1): FT-IR spectrum of (A_1)

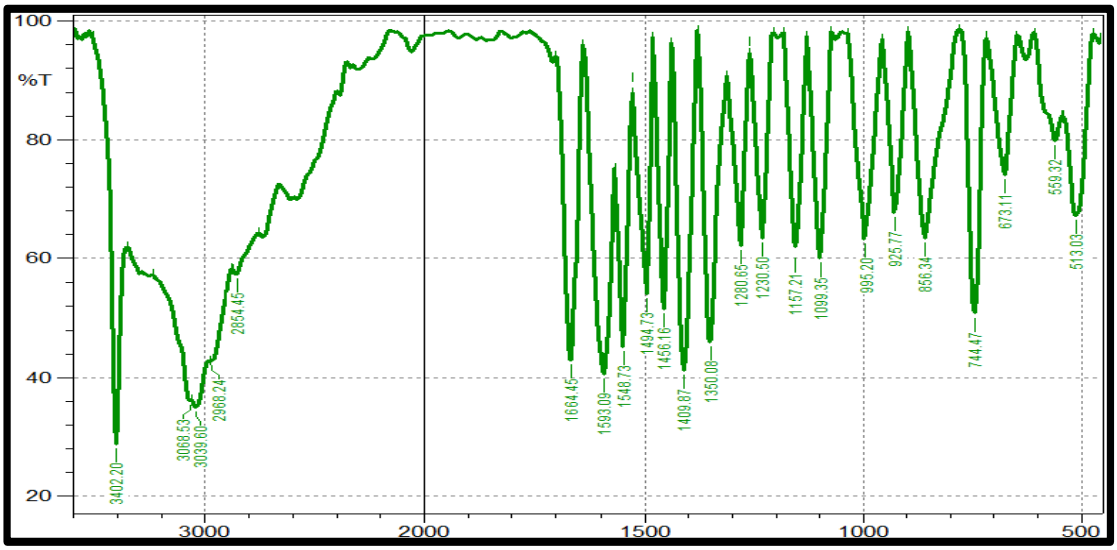


Figure (2): FT-IR spectrum of (A_2)

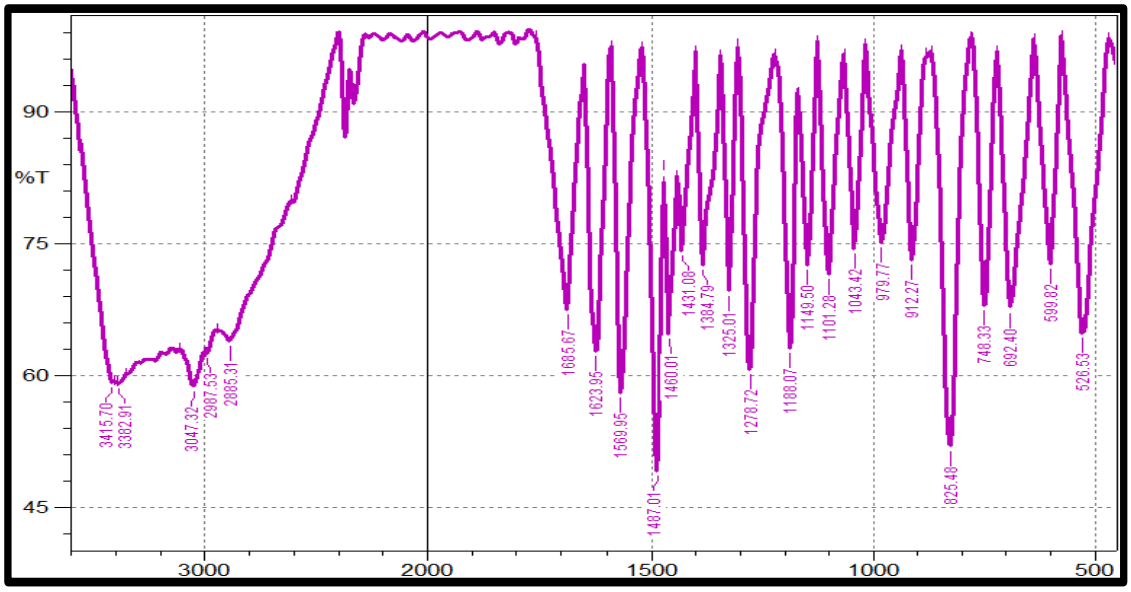


Figure (3): FT-IR spectrum of (A_3)

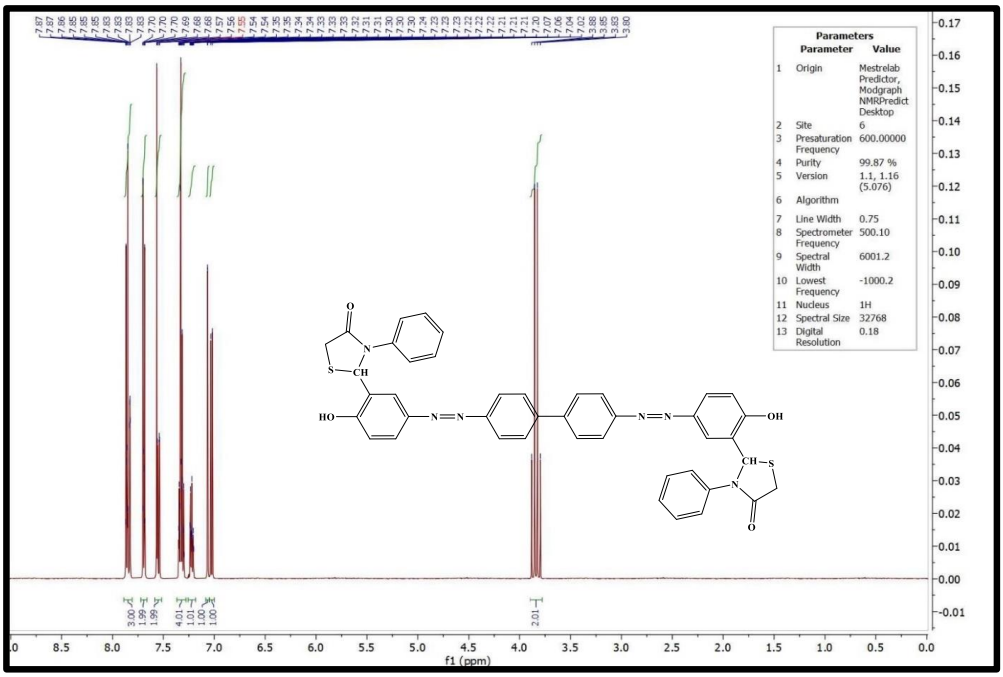


Figure (4): ^{1}H-NMR spectrum of (A_1)

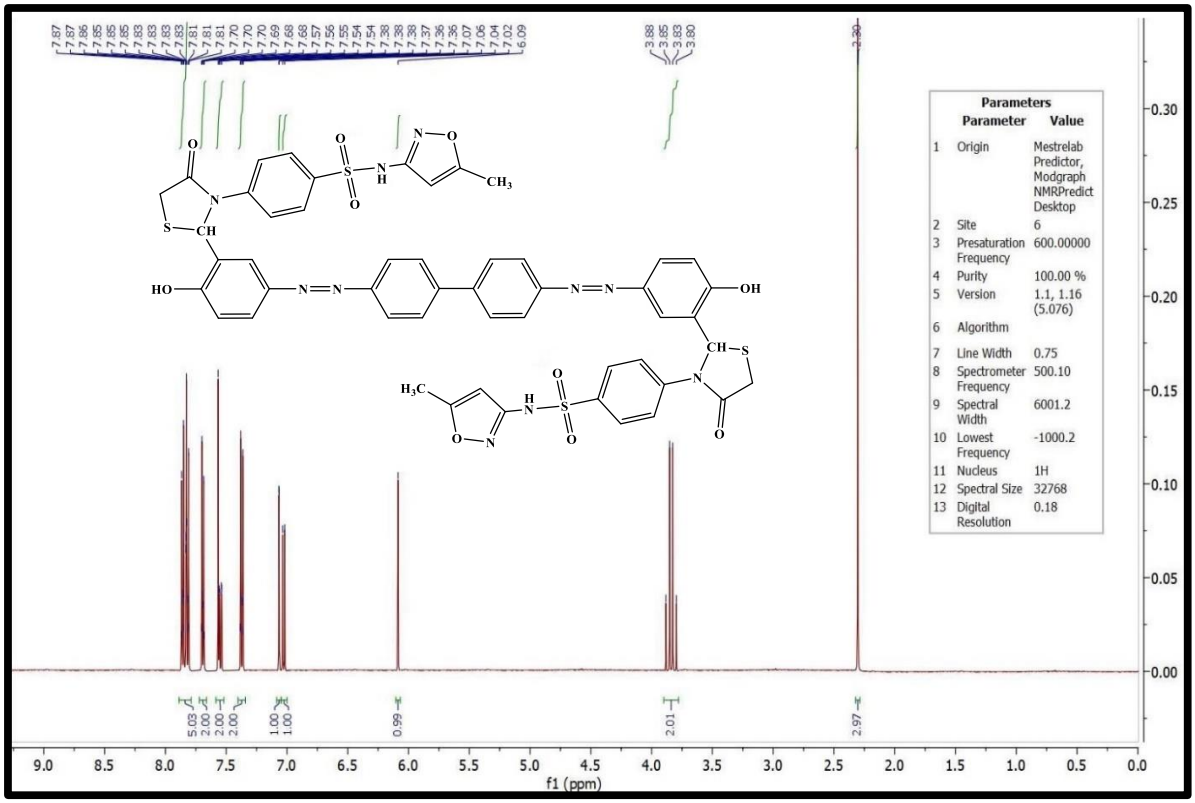
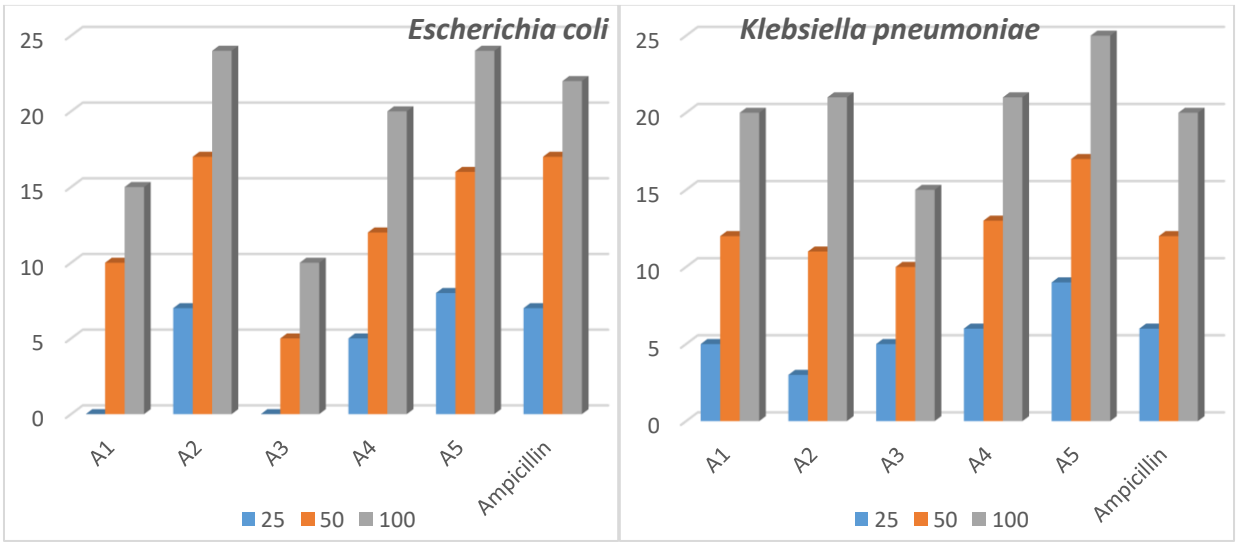
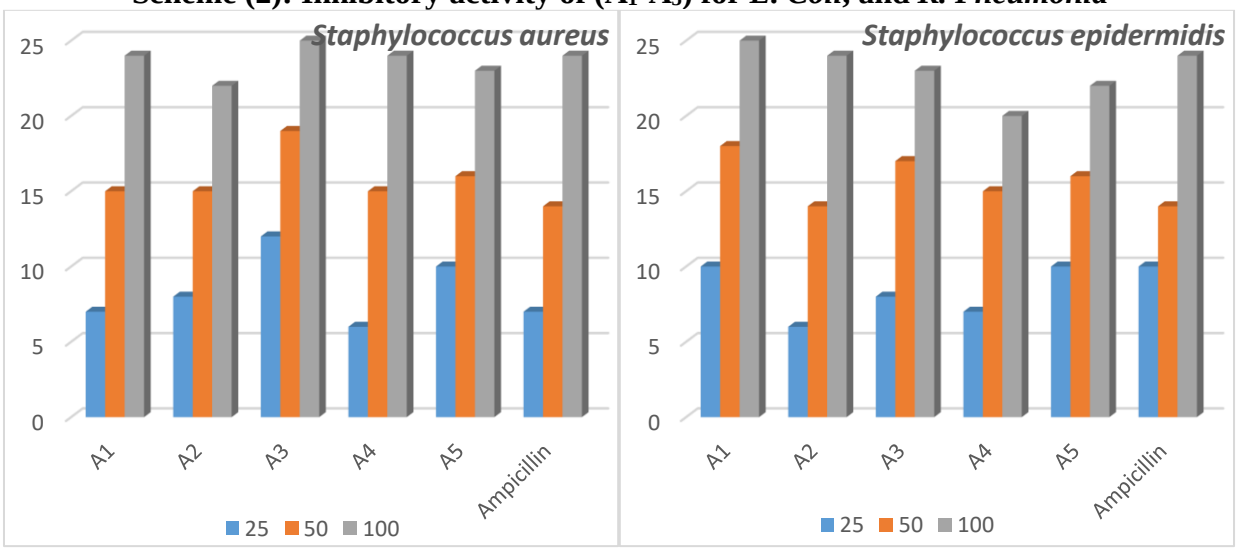


Figure (5): ^{1}H-NMR spectrum of (A_5)



Scheme (2): Inhibitory activity of (A_1-A_5) for *E. Coli*, and *K. Pneumonia*



Scheme (3): Inhibitory activity of (A_1-A_5) for *S. Aureus and S. Epidermidis*

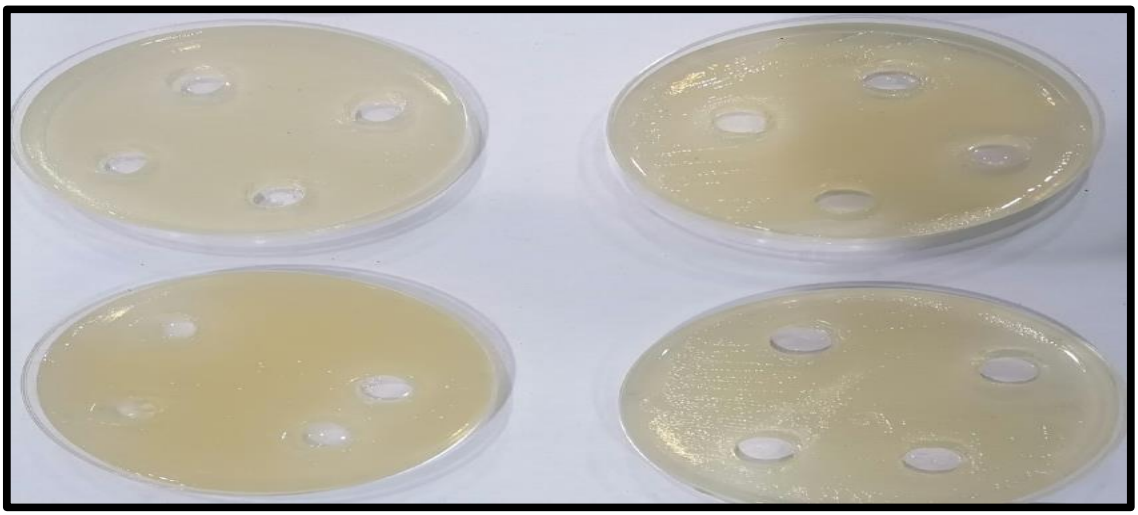


Figure (6): Evaluation of the Biological Activity of Synthesized Compounds

4. Conclusions

The microwave-assisted method for obtaining organic compounds yielded better results compared to the traditional method. This technique proved to be economical as it saved time, effort, solvents, and catalysts, while providing higher product yields. Thus, it can be concluded that microwave-assisted synthesis is a superior method, particularly for small-scale reactions. Additionally, the microwave method is less polluting to the laboratory environment and the broader ecosystem, as it uses fewer reactants, making it an environmentally friendly technique. The reaction of Schiff base derivatives with compounds containing suitable functional groups generally produces heterocyclic five-membered rings. The biological study revealed that the synthesized compounds exhibit antibacterial activity and are capable of inhibiting bacterial growth. These compounds demonstrated higher biological activity than their parent materials, which is significant since the initial materials are drugs used in medical fields. The synthesized compounds showed high stability when exposed to Helium-Neon laser radiation. Physical and spectroscopic measurements confirmed the accuracy and validity of the synthesized nanostructures.

5. Recommendations

- **Utilize Modern Green Techniques:** Expand the use of environmentally friendly techniques in laboratory preparations, such as microwave and ultrasonic methods, to increase the yield of study reactions.
- **Alternative Preparation Methods:** Employ other synthesis methods, such as melt methods, and compare them with traditional methods.
- **Study Liquid Crystalline Properties:** Investigate the liquid crystalline properties of the synthesized compound series.
- **Polymer Integration:** Explore the potential of integrating these compounds with natural polymers for use as materials to remove heavy ions from industrial water.
- **Develop New Pesticides:** Utilize the synthesized compounds to develop new pesticides for controlling various harmful organisms.
- **Kinetic and Thermodynamic Studies:** Conduct kinetic and thermodynamic studies of the synthesized derivatives.
- **Structure-Activity Relationship (SAR) Studies:** Investigate the relationship between structure and biological activity by calculating thermodynamic data and spatial configurations, utilizing them in modern software programs.

References

1. K. Jain, A. Vaidya, V. Ravichandran, S. K. Kashaw, and R. K. Agrawal, “Recent developments and biological activities of thiazolidinone derivatives: A review,” *Bioorganic and medicinal chemistry*, vol. 20, no, 11, pp. 3378-3395, 2012.
2. S. Cascioferro, B. Parrino, D. Carbone, D. Schillaci, E. Giovannetti, G. Cirrincione, and P. Diana, “Thiazoles, their benzofused systems, and thiazolidinone derivatives: versatile and promising tools to combat antibiotic resistance,” *Journal of medicinal chemistry*, vol. 63, no. 15, pp. 7923-7956, 2020.
3. S. P. Singh, S. S. Parmar, K. Raman, and V. I. Stenberg, “Chemistry and biological activity of thiazolidinones,” *Chemical Reviews*, vol. 81, no. 2, pp. 175-203, 1981.
4. H. Dalaf, “Synthesis and Characterization of Some Quartet and Quinary Hetero cyclic Rings Compounds by Traditional Method and Microwave Routes Method and Evaluation of Their Biological Activity,” *M.Sc. Thesis, Tikrit University*, Tikrit, Iraq: pp. 1-94, 2018.

5. D. Havrylyuk, B. Zimenkovsky, and R. Lesyk, "Synthesis and anticancer activity of novel nonfused bicyclic thiazolidinone derivatives," *Phosphorus, Sulfur, and Silicon*, vol. 184, no. 3, pp. 638-650, 2009.
6. H. Dalaf, and F. H. Jumaa, "Synthesis, Characterization of some 1,3-Oxazepane -4,7-Dione by Traditional and Microwave routes method and evaluation of their biological activity," *Al-utroha for Pure Science*. Vol. 8, 93-108, 2018.
7. M. Djukic, M. Fesatidou, I. Xenikakis, A. Geronikaki, V. T. Angelova, V. Savic, and L. Saso, "In vitro antioxidant activity of thiazolidinone derivatives of 1, 3-thiazole and 1, 3, 4-thiadiazole," *Chemico-Biological Interactions*, vol. 286, pp. 119-131, 2018.
8. H. Dalaf, F. H. Jumaa, and S. A. S. Jabbar, "Synthesis and Characterization of some 2, 3-dihydroquinozoline and evaluation of their biological activity," *Tikrit Journal of Pure Science*, vol. 23, no. 8, pp. 66-67, 2018.
9. K. Omar, A. Geronikaki, P. Zoumpoulakis, C. Camoutsis, M. Soković, A. Ćirić, and J. Glamočlija, Novel "4-thiazolidinone derivatives as potential antifungal and antibacterial drugs," *Bioorganic and medicinal chemistry*, vol. 18, no. 1, pp. 426-432, 2010.
10. F. M. Aqlan, A. S. Al-Bogami, N. F. Alqahtani, M. Y. Wani, and S. A. Khan, "Thiazolidinone: A structural motif of great synthetic and biological importance," *Journal of Molecular Structure*, vol. 1250, pp. 131771, 2022.
11. J. Salwa, L. H. Ali, H. D. Adil, S. A. Hossam, "Synthesis and Characterization of Azetidine and Oxazepine Compounds Using Ethyl-4-((4-Bromo Benzylidene) Amino) Benzoate as Precursor and Evalution of Their Biological Activity," *Journal of Education and Scientific Studies*, ISSN: 24134732. Vol. 16, no. 5, pp. 39-52, 2020.
12. Q. Abd, H. I. Ibrahim, H. M. Jirjes, and A. H. Dalaf, "Synthesis and Identification of new compounds have Antioxidant activity Beta-carotene, from Natural Auxin Phenyl Acetic Acid," *Research Journal of Pharmacy and Technology*, vol. 13, no. 1, pp. 40-46, 2020.
13. M. H. Shih, and F. Y. Ke, "Syntheses and evaluation of antioxidant activity of sydnonyl substituted thiazolidinone and thiazoline derivatives," *Bioorganic and medicinal chemistry*, vol. 12, no. 17, pp. 4633-4643, 2004.
14. H. Malipeddi, A. A. Karigar, V. R. Malipeddi, and M. S. Sikarwar, "Synthesis and antitubercular activity of some novel thiazolidinone derivatives," *Tropical Journal of Pharmaceutical Research*, vol. 11, no. 4, pp. 611-620, 2012.
15. H. Dalaf, and F. H. Jumaa, "Synthesis, Identification and Assess the Biological and Laser Efficacy of New Compounds of Azetidine Derived from Benzidine," *Muthanna Journal of Pure Science (MJPS)*, vol. 7, no. 2, pp. 12-25, 2020.
16. M. R. Shiradkar, M. Ghodake, K. G. Bothara, S. V. Bhandari, A. Nikalje, K. C. Akula, and P. J. Burange, "Synthesis and anticonvulsant activity of clubbed thiazolidinone–barbituric acid and thiazolidinone–triazole derivatives. *Arkivoc*, vol. 14, no. 14, pp. 58-74, 2007.
17. R. H. Saleh, W. M. Rashid, A. H. Dalaf, K. A. Al-Badrany, and O. A. Mohammed, "Synthesis of Some New Thiazolidinone Compounds Derived from Schiff Bases Compounds and Evaluation of Their Laser and Biological Efficacy," *Ann Trop and Public Health*, vol. 23, no. 7, 1012-1031, 2020.
18. R. B. Lesyk, B. S. Zimenkovsky, D. V. Kaminskyy, A. P. Kryshchyshyn, R. B. Havryluk, D. V. Atamanyuk, and D. V. Khyluk, "Thiazolidinone motif in anticancer drug discovery. Experience of DH LNMU medicinal chemistry scientific group," *Biopolymers and Cell*. 2011.

19. S. K. Manjal, R. Kaur, R. Bhatia, K. Kumar, V. Singh, R. Shankar, and R. K. Rawal, "Synthetic and medicinal perspective of thiazolidinones: A review," *Bioorganic Chemistry*, vol. 75, pp. 406-423, 2017.
20. A. Yass, M. M. Aftan, A. H. Dalaf, and F. H. "Synthesis and Identification of New Derivatives of Bis-1,3-Oxazepene and 1,3-Diazepine and Assess the Biological and Laser Efficacy for Them," *The Second International and The Fourth Scientific Conference of College of Science – Tikrit University*. Vol. P4, pp. 77-87, 2020.
21. F. Rahim, K. Zaman, H. Ullah, M. Taha, A. Wadood, M. T. Javed, and K. M. Khan, "Synthesis of 4-thiazolidinone analogs as potent in vitro anti-urease agents," *Bioorganic chemistry*, vol. 63, pp. 123-131, 2015.
22. D. Salih, A. H. Dalaf, M. A. Alheety, W. M. Rashed, and I. Q. Abdullah, "Biological activity and laser efficacy of new Co (II), Ni (II), Cu (II), Mn (II) and Zn (II) complexes with phthalic anhydride," *Materials Today: Proceedings*, vol. 43, pp. 869-874, 2021.
23. S. Bondock, W. Khalifa, and A. A. Fadda, "Synthesis and antimicrobial evaluation of some new thiazole, thiazolidinone and thiazoline derivatives starting from 1-chloro-3, 4-dihydronaphthalene-2-carboxaldehyde," *European journal of medicinal chemistry*, vol. 42, no. 7, pp. 948-954, 2007.
24. M. M. Aftan, M. Q. Jabbar, A. H. Dalaf, and H. K. Salih, "Application of biological activity of oxazepine and 2-azetidinone compounds and study of their liquid crystalline behavior," *Materials Today: Proceedings*, vol. 43, pp. 2040-2050, 2021.
25. Hu, Y. Wang, X. Wei, X. Wu, G. Chen, G. Cao, and X. Li, "Synthesis and biological evaluation of novel thiazolidinone derivatives as potential anti-inflammatory agents," *European journal of medicinal chemistry*, vol. 64, pp. 292-301, 2013.
26. M. M. Aftan, A. A. Talloh, A. H. Dalaf, and H. K. Salih, "Impact para position on rho value and rate constant and study of liquid crystalline behavior of azo compounds," *Materials Today: Proceedings*, vol. 45, pp. 5529-5534. 2021
27. S. Wang, Y. Zhao, G. Zhang, Y. Lv, N. Zhang, and P. Gong, "Design, synthesis and biological evaluation of novel 4-thiazolidinones containing indolin-2-one moiety as potential antitumor agent," *European journal of medicinal chemistry*, vol. 46, no. 8, pp. 3509-3518, 2011.
28. M. M. Aftan, M. A. Toma, A. H. Dalaf, E. Q. Abdullah, and H. K. Salih, "Synthesis and Characterization of New Azo Dyes Based on Thiazole and Assess the Biological and Laser Efficacy for Them and Study their Dyeing Application," *Egyptian Journal of Chemistry*, vol. 64, no. 6, pp. 2903-2911, 2021.
29. P. C. Lv, C. F. Zhou, J. Chen, P. G. Liu, K. R. Wang, W. J. Mao, and H. L. Zhu, "Design, synthesis and biological evaluation of thiazolidinone derivatives as potential EGFR and HER-2 kinase inhibitors," *Bioorganic and medicinal chemistry*, vol. 18, no. 1, pp. 314-319, 2010.
30. S. D. Khalaf, N. A. A. S. Ahmed, and A. H. Dalaf, "Synthesis, characterization and biological evaluation (antifungal and antibacterial) of new derivatives of indole, benzotriazole and thioacetyl chloride," *Materials Today: Proceedings*. vol. 47, no. 17, pp. 6201-6210, 2021.
31. V. Ravichandran, A. Jain, K. S. Kumar, H. Rajak, and R. K. Agrawal, "Design, Synthesis, and Evaluation of Thiazolidinone Derivatives as Antimicrobial and Anti-viral Agents," *Chemical biology and drug design*, vol. 78, no. 3, pp. 464-470, 2011.

32. H. Dalaf, F. H. Jumaa, and H. K. Salih, "Preparation, Characterization, Biological Evaluation and Assess Laser Efficacy for New Derivatives of Imidazolidin-4-one," *International Research Journal of Multidisciplinary Technovation*, vol. 3, no. 4, pp. 41-51, 2021.
33. S. Nirwan, V. Chahal, and R. Kakkar, "Thiazolidinones: Synthesis, reactivity, and their biological applications," *Journal of Heterocyclic Chemistry*, vol. 56, no, 4, pp. 1239-1253. 2019.
34. H. Dalaf, F. H. Jumaa, and H. K. Salih, "*MULTIDISCIPLINARY TECHNOVATION*. *Red*, vol. 15, no. A2, C44H36N10O8, 2021.
35. Kryshchyshyn, D. Kaminskyy, O. Karpenko, A. Gzella, P. Grellier, and R. Lesyk, "Thiazolidinone/ thiazole based hybrids–New class of antitrypanosomal agents. *European journal of medicinal chemistry*, vol. 174, pp. 292-308, 2019.
36. H. Dalaf, F. H. Jumaa, M. M. Aftana, H. K. Salih, and I. Q. Abd, "Synthesis, Characterization, Biological Evaluation, and Assessment Laser Efficacy for New Derivatives of Tetrazole," *In Key Engineering Materials*, Vol. 911, pp. 33-39, Trans Tech Publications Ltd, 2022.
37. R. P. de Siqueira, P. A. T. de Moraes Gomes, L. P. de Lima Ferreira, M. J. B. de Melo Rêgo, and A. C. L. Leite, "Multi-target compounds acting in cancer progression: Focus on thiosemicarbazone, thiazole and thiazolidinone analogues," *European Journal of Medicinal Chemistry*, vol. 170, pp. 237-260, 2019.
38. Y. Kh. Alasadi, F. H. Jumaa, A. H. Dalaf, S. M. Shawkat, and M. Gh. Mukhlif, "Synthesis, Characterization, and Molecular Docking of New Tetrazole Derivatives as Promising Anticancer Agents," *Journal of Pharmaceutical Negative Results*. Vol. 13, no. 3, pp. 513-522, 2022.
39. H. Dalaf, F. H. Jumaa, and I. A. Yass, "Synthesis, characterization, biological evaluation, molecular docking, assess laser efficacy, thermal performance and optical stability study for new derivatives of bis-1, 3-oxazepene and 1, 3-diazepine," *In AIP Conference Proceedings*, vol. 2394, no. 1, pp. 040037, AIP Publishing LLC, 2022.
40. X. C. Yang, P. L. Zhang, K. V. Kumar, S. Li, R. X. Geng, and C. H. Zhou, "Discovery of unique thiazolidinone-conjugated coumarins as novel broad spectrum antibacterial agents," *European Journal of Medicinal Chemistry*, vol. 232, pp. 114192, 2022.
41. Y. K. Alasadi, F. H. Jumaa, and A. H. Dalaf, "Synthesis, identification, antibacterial activity and laser effect of new derivatives of bis-1, 3-oxazepene-4, 7-dione and 1, 3-diazepine-4, 7-dione," *In AIP Conference Proceedings*, vol. 2394, no. 1, pp. 040019, AIP Publishing LLC, 2022.
42. R. H. Saleh, W. M. Rashid, A. H. Dalaf, K. A. Al-Badrany, and O. A. Mohammed, "Synthesis of some new thiazolidinone compounds derived from schiff bases compounds and evaluation of their laser and biological efficacy," *Ann Trop and Public Health*, vol. 23, no. 7, pp. 1012-1031, 2020.
43. A. Toma, D. A. Ibrahim, A. H. Dalaf, S. Q. Abdullah, M. M. Aftan, and E. Q. Abdullah, "Study the adsorption of cyclopentanone on to natural polymers," *In AIP Conference Proceedings*, vol. 2394, no. 1, pp. 040007, AIP Publishing LLC, 2022.
44. Oubella, A. E. El Mansouri, M. Fawzi, A. Bimoussa, Y. Laamari, A. Auhmani, and M. Y. A. Itto, Thiazolidinone-linked1, 2, 3-triazoles with monoterpenic skeleton as new potential anticancer agents: Design, synthesis and molecular docking studies," *Bioorganic Chemistry*, vol. 115, pp. 105184, 2021.
45. M. Hamad, Q. M. Atiyea, D. N. A. Hameed, and A. H. Dalaf, "Green synthesis of copper nanoparticles using strawberry leaves and study of properties, anti-cancer action, and activity against bacteria isolated from Covid-19 patients," *Karbala International Journal of Modern Science*, vol. 9, no. 1, pp. 12, 2023.

46. F. A. R. Ruiz, R. N. García-Sánchez, S. V. Estupiñan, A. Gómez-Barrio, D. F. T. Amado, B. M. Pérez-Solórzano, and V. V. Kouznetsov, "Synthesis and antimalarial activity of new heterocyclic hybrids based on chloroquine and thiazolidinone scaffolds," *Bioorganic and medicinal chemistry*, vol. 19, no. 15, pp. 4562-4573, 2011.

47. S. Jassim, A. H. Dalaf, and T. F. Abdullah, "Studying the Biological Activity and Properties of Copper Nanoparticles Prepared by Pulsed Laser Ablation in Liquid," *The Third International and The Fifth Scientific Conference for College of Science –Tikrit University*, vol. 1, no. 25, pp. 213-221, 2022.

48. J. Mohammed, A. M. Hamad, Q. M. Atiyea, W. A. Jwair, A. H. Dalaf, A. S. Jasim, S. M. Elsaigher, A. Ragab, and Z. H. S. Hassan, "In vitro Comparison of the Effect of Zinc Oxide Nanoparticles and Hibiscus sabdariffa Extract on Streptococcus mutans Isolated from Human Dental Caries," *The Third International and The Fifth Scientific Conference for College of Science –Tikrit University*, vol. 2, no. 2, pp. 5-14, 2022.

49. H. Dawood, and N. H. Ali, "Synthesis and characterization of some new Indazolone and Carbohydrazide derivatives from azachalcones," *Journal of Pharmaceutical Negative Results*, pp. 3178-3190, 2022.

50. Garnaik, and S. Dash, "Recent advances and potential antimicrobial activities of thiazolidinone derivatives: a review," *Asian Journal of Research in Chemistry*, vol. 7, no. 4, pp. 446-457, 2014.

51. R. S. Najm, Q. A. Shannak, and A. H. Dalaf, "Synthesis and Decoration of Aromatic Derivatives Nano Platelets by the Electric Method," *Azerbaijan Pharmaceutical and Pharmacotherapy Journal*, vol. 22, no. 2, pp. 92-97, 2023.

52. K. Salim, Q. M. Hassan, A. M. Jassem, H. A. Sultan, A. M. Dhumad, and C. A. Emshary, "An efficient ultrasound-assisted CH3COONa catalyzed synthesis of thiazolidinone molecule: theoretical and nonlinear optical evaluations of thiazolidinone-Schiff base derivative," *Optical Materials*, vol. 133, pp. 112917, 2022.

53. Kryshchyshyn-Dylevych, L. Radko, N. Finiuk, M. Garazd, N. Kashchak, A. Posyniak, and R. Lesyk, "Synthesis of novel indole-thiazolidinone hybrid structures as promising scaffold with anticancer potential," *Bioorganic and medicinal chemistry*, vol. 50, pp. 116453, 2021.