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Synthesis and Study Biological Activity of Some New Substituted Thiazolidin-4-one Derivatives

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Abstract

The microwave (MW) method was used to create a series of new thiazolidin-4-one derivatives containing benzothiazole and azo groups. Azoaldehyde derivative **A** was synthesized *via* the coupling reaction of 2-aminobenzothiazole diazonium ions and 2-hydroxybenzaldehyde. The resultant azoaldehyde **A** was then subjected to condensation reactions with the primary aromatic amines using the MW method to give azoimines derivatives **S1-S5**. Finally, compounds **S1-S5** were reacted with α-mercaptoacetic acid by the MW method to generate the thiazolidin-4-one derivatives **T1-T5**. The novel-produced compounds **T1-T5** were identified by FT-IR, ^{1}H NMR, and ^{13}C NMR spectroscopy. The DPPH was used to determine the antioxidant activity of the novel-produced compounds **T1-T5**. The obtained results for **T1** and **T5** were excellent as antioxidants in comparison with ascorbic acid, while in the antibacterial study, it was discovered that **T2**, **T3**, and **T5** were found to be more successful than *Gentamycin* as a control drug against *Staphylococcus aureus* in an antibacterial investigation, while **T3** was found to be more effective than the reference drug against *Escherichia coli*.

Keywords: 2-Aminobenzothiazole, Antibacterial, Antioxidant, Microwave irradiation, Thiazolidin-4-ones.

تحضير و دراسة النشاط البيولوجي لبعض مشتقات 4-ثيازوليدينون الجديدة المعوضة

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الخلاصة

تم استخدام طريقة الميكروويف (MW) لإنشاء سلسلة من مشتقات 4-ثيازوليدينون الجديدة التي تحتوي على مجموعتين البنزوثيازول و آزو. تم تصنيع مشتق أزوالديهيد **A** عن طريق تفاعل اقتران بين أيونات 2-أمينوبنزوثيازول ديازونيوم و 2-هيدروكسي بينزالديهايد. ثم، تم إدخال الأوزالدهيد الناتج **A** في تفاعل التكثيف مع الأمينات الاروماتية الأولية باستخدام طريقة الميكروويف ينتج مشتقات الآزوايمينات **S1-S5**. بعد ذلك، تم تفاعل المركبات **S1-S5** مع حمض α-mercaptoacetic بطريقة الميكروويف لتوليد مشتقات 4-ثيازوليدينون **T1-T5**. تم تحديد المركبات المنتجة حديثًا **T1-T5** بواسطة الطرائق الطيفية المتضمنة مطيافية الأشعة تحت الحمراء و الرنين النووي المغناطيسي للبروتون و الكاربون. تم استخدام DPPH لتحديد النشاط المضاد للأكسدة للمركبات المنتجة حديثًا **T1-T5**. كانت النتائج التي تم الحصول عليها لـ **T1** و **T5** ممتازة كمضادات للأكسدة مقارنة بحمض الأسكوربيك، بينما في الدراسة المضادة للبكتيريا، تم اكتشاف أن

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T2و **T3** و **T5** أكثر نجاحًا من *Gentamycin* كعقار تحكم ضد *Staphylococcus aureus* في فحص مضاد للجراثيم، بينما وجد أن **T3** أكثر فعالية من العقار المرجعي ضد *Escherichia coli*.

1. Introduction

Thiazolidinones are derived from thiazolidine and are an important class of heterocyclic compounds. There are a number of reported bioactive compounds with various heteroatoms, including oxygen, sulfur, and nitrogen [1]. On the other hand, 1,3-thiazolidin-4-ones have a five-member heterocyclic nucleus with a carbonyl group in position 2, sulfur in position 1, and nitrogen in position 3. Thiazolidin-4-ones are of great importance in both medical and pharmaceutical chemistry. A wide range of biological activities are given by this type of chemical, such as anti-HIV [2-5], antitumor [6, 7], antihypertensive [2, 8], antimicrobial [9, 10], antioxidant activity [11, 12], antihyperglycemic [2, 13], antidiabetic activity [2, 14, 15], anti-bacterial [2, 16], anti-fungal [2, 17, 18], anti-viral [2, 19], and anti-tuberculosis [2, 9, 20]. Microwave technology represents an actual shift in synthetic organic chemistry. This technique accelerates chemical reactions and produces relatively clean products. The Bolognese team has discovered that heating mercaptoacetic acid and benzylideneanilines in benzene at 33 °C in the microwave for just 10 minutes produces excellent yields of the thiazolidin-4-one heterocycles [21]. The majority of hospital acquired infections are caused by bacteria, which pose a serious risk to patient health and place a heavy strain on healthcare systems. *Escherichia coli*, methicillin-resistant *Staphylococcus aureus* (MRSA) [22], multidrug-resistant tuberculosis (MDR-TB), extended-spectrum lactamase-producing Enterobacteriaceae, and other dangerous bacteria have all arisen with various degrees of resistance to current therapeutic treatments [23]. Antioxidants with DPPH radical scavenging activity have gained popularity in recent years. Thiazolidinone compounds have been reported to have powerful antioxidant effects [24-28]. Because the core of benzothiazole [29-32] and thiazolidinone rings [33-35] is important in a wide range of pharmaceuticals with diverse biological activity, various compounds incorporating these moieties will be synthesized in this work.

2. Material and Methods

2.1. Chemicals and Instruments

Synthetic starting materials, reagents, and solvents were purchased by Sigma-Aldrich, GCC, S.D. Fine, BDH, Scharlau, Fluka, and Merck. The reactions have already been monitored by Silica TLC plates with an aluminum backing (0.2 mm, 60 F_{254}), and each pure component displayed a single spot. Cole Paramer MP-200D-120 Stuart Digital Melting Point Apparatus has been employed to measure melting points. FT-IR spectral data have been recorded on the SHIMADZU FTIR-8400S Infrared Spectrophotometer. ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectral data have been measured on a Varian-INOVA USA 500 MHz NMR spectrometer using DMSO-d_6 as solvent and TMS as an internal standard at Tehran University, Iran. Spectra processing was done with the NMR Manager 2022 Mestrelab Research, MestReNOVA 14.3.1-31739, employing the FID file. Chemical shifts were recorded as δ (ppm) adjacent to TMS, which was utilized as an internal standard. Coupling constants (*J*) were displayed in Hertz.

2.2. Preparation methods

2.2. *1. Synthesis of 5-(benzo[d]thiazol-2-yldiazenyl)-2-hydroxybenzaldehyde [**A**]* [36]

Concentrated H_2SO_4 (15 mL) was added to 2-aminobenzothiazole (54 mmol) and then cooled to 0 °C. To this solution, drop by drop, while stirring constantly, a cold solution of sodium nitrite (54 mmol) in distilled water (20 mL) was added. Whenever the addition has been completed, the resulting reaction is placed in an ice container for 1 hour. Then, the

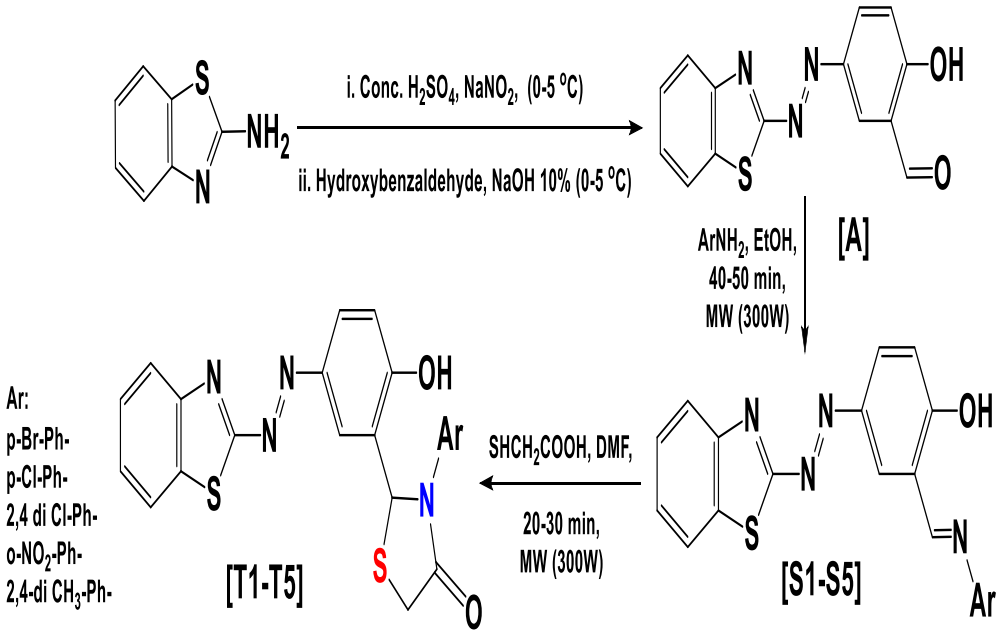
freezing-cold diazonium bisulfate solution was added drop by drop to the cool solution of 2-hydroxybenzaldehyde (54 mmol) that had been dissolved in NaOH (45 mL, 10%). This was done while shaking the mixture constantly. The result was a dark dye, and the solution was neutralized with dilute HCl. After the addition was completed, the mixture was quickly stirred. A solid was isolated and allowed to stay at room temperature for 30 minutes before being filtered and thoroughly rinsed with distilled water. Then the product was collected and purified by recrystallization from ethanol to yield **A** as a dark brown solid, yield 52%, m.p. 141-143 ºC, TLC (*n*-hexane/EtOAc, 1:2), Rf = 0.48.

*2.2.2. Synthesis of azoimines derivatives **S1-S5*** [37]

In a crucible, a mixture of appropriate aromatic amines (1 mmol) and aldehyde derivative **A** (1 mmol) in absolute ethanol (1 mL) was exposed to microwave irradiation at 300 W for 40 to 50 minutes. When the reaction had reached completion, as determined by TLC (*n*-hexane: EtOAc, 1:2), the solid crude material was recrystallized from ethanol to give the desired products **S1**-**S5**. The physical properties of compounds **S1**-**S5** are shown in Table 1.

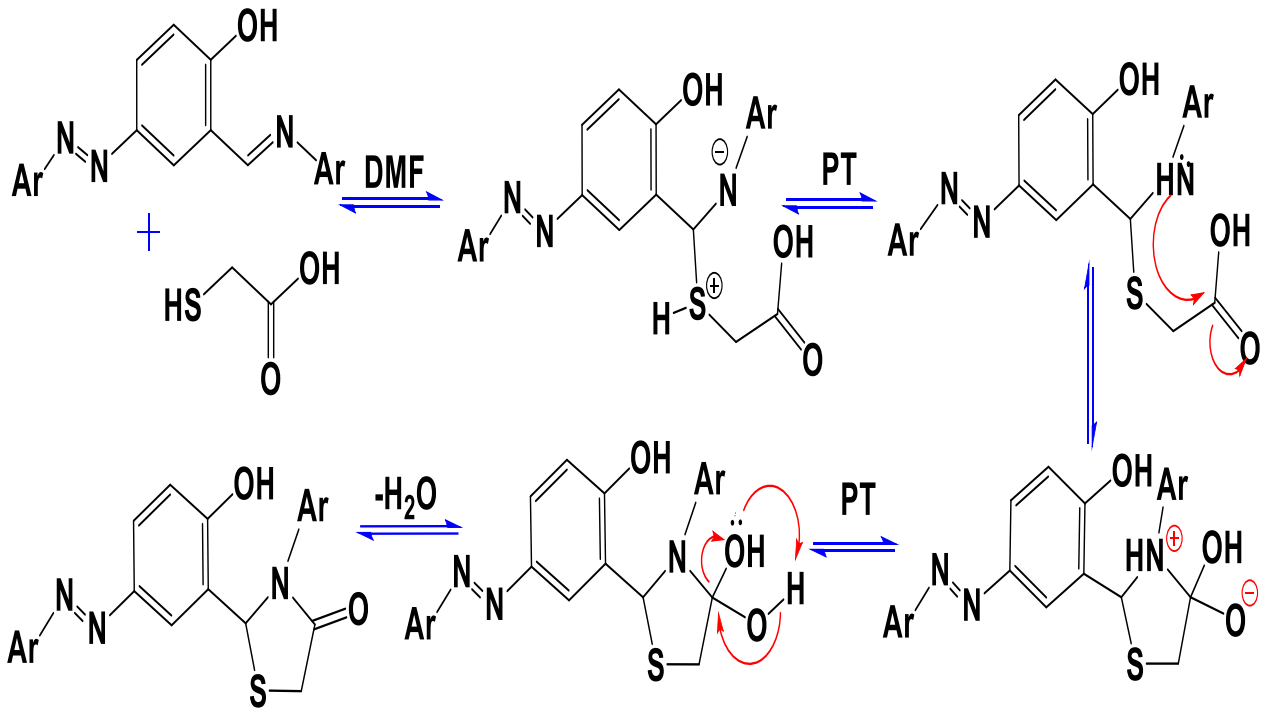
*2.2.3. Synthesis of thiazolidin-4-ones derivatives **T1-T5*** [21]

A mixture of mercaptoacetic acid (1 mmol) and Schiff bases **S1**-**S5** (1 mmol) in DMF (1 mL) was irradiated at 300 W for 20 to 35 minutes. The reaction was monitored by TLC (*n*-hexane:ethyl acetate, 1:3). The solid crude material was recrystallized from ethanol to afford the title products **T1**-**T5**. The physical properties of compounds **T1**-**T5** are shown in Table 1.



Scheme 1: Synthesis of thiazolidin-4-ones derivatives **T1-T5**

Scheme 2 shows the proposed chemical mechanism for ring closure, which leads to 1,3-thiazolidin-4-one in a solution of DMF [21].



Scheme 2: Mechanism of 1,3-thiazolidin-4-ones **T1-T5** formation in DMF

Table 1: The physical properties of all synthesized compounds

Compound No.	Color	R_f *n*-hexane/EtOAc (1:2)	m.p. (ºC)	Yield (%)
S1	Dark-Brown	0.73	173-175	80
S2	Brown	0.74	161-163	78
S3	Brown	0.73	176-178 [38]	81
S4	Green	0.78	121-123	82
S5	Brown	0.75	163-165 [38]	86
T1	Light-Brown	0.69	200-202	78
T2	Light-Brown	0.61	174-176	87
T3	Dark-Brown	0.62	197-199	81
T4	Dark-Green	0.64	207-209	90
T5	Light-Brown	0.60	138-138	90

2.3. Antibacterial activity

Using the agar diffusion technique [39], *Staphylococcus aureus* (Gram-positive) and *Escherichia coli* (Gram-negative) bacteria were employed to evaluate the antibacterial effect of the target 1,3-thiazolidin-4-one compounds **T1-T5**. In 1 mL of DMSO, 20 mg of each tested compound were resolved. The inhibition zone findings were compared to the reference antibiotic (Gentamycin) as a control drug. Figure 1 and Table 2 show the inhibition zone of each tested compound.

Table 2 : The antibacterial activity of thiazolidin-4-one derivatives **T1-T5**

Bacteria Type	***Staphylococcus Aureus* (G+)**	***Escherichia Coli* (G-)**
Compound No.	*Inhibitory zone (diameter) (mm)*	
T1	14	10
T2	19	12
T3	21	18
T4	13	11
T5	26	10
Gentamycin	18	15

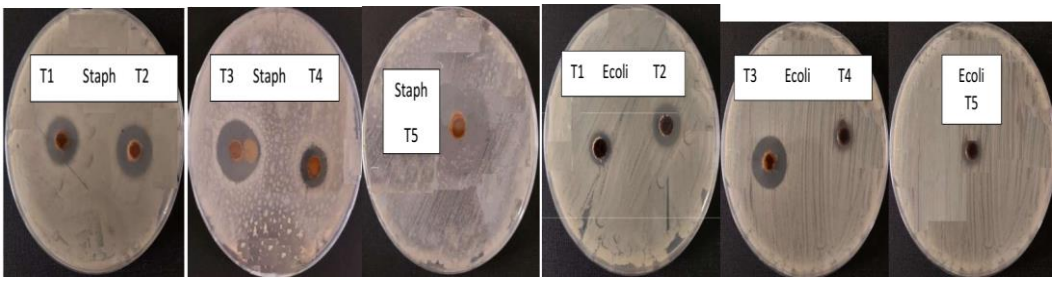


Figure 1: Inhibition zone of compounds **T1-T5** on gram-negative and gram-positive bacteria

2.4. Determination of antioxidant activity

The effectiveness of the synthesized compounds **T1-T5** at scavenging free radicals *in vitro* was studied employing the DPPH analysis with ascorbic acid serving as the standard solution. The samples (0.005 M) were prepared in 1 mL of methanol, then 20, 40, 60, 80, and 100 µL of the prepared compounds were taken and brought up to methanol (4 mL). DPPH (50 µ L, 0.004 M) in methanol (1 mL) was added to all tubes of samples, standard and control. The ascorbic acid (0.005 M) was prepared in methanol (1 mL) as a standard solution. The control was a mixture of methanol, DMSO, and a DPPH radical solution (0.005M). The mixture was vigorously mixed and let stand for 30 minutes at 25 ℃ in a darkened space [11]. The results of all tests and analyses were averaged across three replicates. Using a UV-M51 BEL Photonics spectrophotometer, the absorbance at 517 nm was measured, and the scavenging efficiency of each compound was calculated using the following equation [40]:

$$\% \text{ Scavenging } = \frac{\text{Ac} - \text{As}}{\text{Ac}} * 100$$

Which **Ac** is the absorbance of the control solution without a standard and sample, and **As** is the absorbance of the sample.

3. Results and discussion

3.1. Chemistry

The synthesis of thiazolidin-4-one derivatives **T1-T5** was done by an efficient method that included using microwave conditions (Scheme 1). The reaction is technically simple and generates the product quickly and with a high yield. In the ^{1}H NMR spectra, the signals that prove the formation of the thiazolidin-4-one ring are the hydrogens at positions 2 and 5 (Figure 2). For thiazolidin-4-ones **T1-T5**, the hydrogens **5a** and **5b** evidence a double doublet signal in the range of 3.61 to 3.94 ppm.

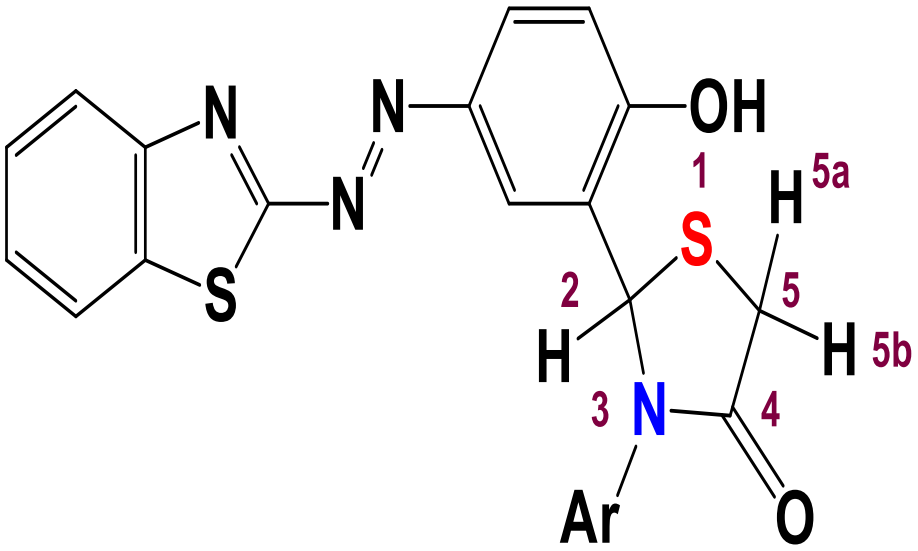


Figure 2: The general skeleton of the synthesized thiazolidine-4-one ring

Another characteristic signal is the hydrogen 2, belonging to the asymmetric carbon 2, which appears in the range of 6.5 to 6.6 ppm as singlet signals. Thiazolidin-4-one's distinctive peaks in the ^{13}C NMR spectra are carbons 2, 4, and 5. The carbonyl carbon 4 is the most deshielded signal in the spectrum at about 170.9-175.7 ppm. Methylene carbon 2 appears at 63.2-66.2 ppm and carbon 5 has a sign in the region of 33.1-34.8 ppm. Other signals are illustrated in detail:

2-(5-(Benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-3-(4-bromophenyl)thiazolidin-4-one (**T1**, $C_{22}H_{15}BrN_4O_2S_2$): ^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm): 9.65 (s, 1H, OH), 8.01-8.29 (m, 6H, $H_{arom.}$), 7.2-7.8 (m, 2H, $CH_{arom.}$), 7.18 (d, J = 8.1 Hz, 1H, $H_{arom.}$), 7.05 (d, J = 7.1 Hz, 1H, $H_{arom.}$), 6.87 (d, J = 7.4 Hz, 1H, $H_{arom.}$), 6.51 (s, 1H, $CH_{thiazolidin\text{-}4\text{-}one}$), 3.94-3.78 (m, 2H, $CH_{2thiazolidin\text{-}4\text{-}one}$). ^{13}C NMR (125 MHz, DMSO-d_6) δ (ppm): 171.46 ($C{=}O_{thiazole}$), 165.25 ($N{=}C\text{-}N_{benzothiazole}$), 156.63-114.61 (Ar-C), 66.25 (CH_2 or $CH_{thiazole}$) and 33.18 (CH_2 or $CH_{thiazole}$).

2-(5-(Benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-3-(4-chlorophenyl)thiazolidin-4-one (**T2** $C_{22}H_{15}ClN_4O_2S_2$) ^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm): 10.31 (s, 1H, OH), 8.17-8.10 (m, 2H, $H_{arom.}$), 8-7.95 (m, 1H, $H_{arom.}$) 7.65-7.6 (m, 2H, $H_{arom.}$), 7.43-7.41 (m, 4H, $H_{arom.}$), 7.22-7.19 (m, 1H, $H_{arom.}$), 7.02-6.99 (m, 1H, $H_{arom.}$), 6.56 (s, 1H, $CH_{thiazolidin\text{-}4\text{-}one.}$), 3.80-3.62 (m, 2H, $CH_{2thiazolidin\text{-}4\text{-}one}$). ^{13}C NMR (125 MHz, DMSO-d_6) δ (ppm): 171.0 ($C{=}O_{thiazole}$), 162.8 ($N{=}C\text{-}N_{benzothiazole}$), 153.2-112.9 (Ar-C), 66.0 (CH_2 or $CH_{thiazole}$) and 34.8 (CH_2 or $CH_{thiazole}$).

2-(5-(Benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-3-(2,4-dichlorophenyl)thiazolidin-4-one (**T3** $C_{22}H_{14}Cl_2N_4O_2S_2$) ^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm): 9.81 (s, 1H, OH), 8.21-8.17 (s, 1H, H_{arom}), 8.01-7.98 (s, 1H, H_{arom}), 7.62-7.60 (s, 1H, $H_{arom.}$), 7.51-7.45 (m, 2H, $H_{arom.}$), 7.35-7.33 (d, J = 4.6 Hz, 1H, $H_{arom.}$), 7.18-7.08 (m, 3H, $H_{arom.}$), 6.81 (d, J = 8.7 Hz, 1H, $H_{arom.}$), 6.61 (s, 1H, $CH_{thiazolidin\text{-}4\text{-}one}$), 3.90-3.85 (m, 2H, $CH_{2thiazolidin\text{-}4\text{-}one}$). ^{13}C NMR (125 MHz, DMSO-d_6) δ (ppm): 171.6 ($C{=}O_{thiazole}$), 167.4 ($N{=}C\text{-}N_{benzothiazole}$), 150.1-115.1 (Ar-C), 56.1 (CH_2 or $CH_{thiazole}$) and 34.9 (CH_2 or $CH_{thiazole}$).

2-(5-(Benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-3-(2-nitrophenyl)thiazolidin-4-one (**T4** $C_{22}H_{15}N_5O_4S_2$) ^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm): 9.80 (s, 1H, OH), 8.32-7.67 (m, 5H, $H_{arom.}$), 7.64-7.49 (m, 4H, $H_{arom.}$), 7.46 (s, 1H, $H_{arom.}$), 7.09-6.92 (d, J = 15.8 Hz, 2H, $H_{arom.}$), 6.55 (s, 1H, $CH_{thiazolidin\text{-}4\text{-}one}$), 3.78, 3.66 (m, 2H, $CH_{2thiazolidin\text{-}4\text{-}one}$). ^{13}C NMR (125 MHz, DMSO-d_6) δ (ppm): 171.1 ($C{=}O_{thiazole}$), 167.3 ($N{=}C\text{-}N_{benzothiazole}$), 154.3-114.1 (Ar-C), 64.7 (CH_2 or $CH_{thiazole}$) and 34.8 (CH_2 or $CH_{thiazole}$).

2-(5-(Benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-3-(2,4-dimethylphenyl)thiazolidin-4-one (**T5** $C_{24}H_{20}N_4O_2S_2$) ^{1}H NMR (500 MHz, DMSO-d_6) δ(ppm): 9.43 (s, 1H, OH), 8.01-7.99 (d, *J* = 7.9 Hz, 1H, $H_{arom.}$), 7.87-786 (d, *J* = 9.9 Hz, 1H, H_{arom}), 7.56-7.43 (m, 4H, H_{arom}), 7.29-7.26 (d, *J* = 5.5 Hz, 1H, $H_{arom.}$), 7.24- 7.16 (m, 1H, $H_{arom.}$), 7.07-7.02 (d, *J* = 18.5 Hz, 1H, $H_{arom.}$), 6.98-6.96 (d, *J* = 8.7 Hz, 1H, $H_{arom.}$), 6.51 (s, 1H, CH $_{thiazolidin-4-one}$), 3.94-3.86 (m, 2H, $CH_{2thiazolidin-4-one}$), 2.21 (m, 6H, CH_3). ^{13}C NMR (125 MHz, DMSO-d_6) δ(ppm): 171.6 ($C{=}O_{thiazole}$), 168.7 ($N{=}C{-}N_{benzothiazole}$), 152.6-112.1 (Ar-C), 64.7 (CH_2 or $CH_{thiazole}$) and 34.8 (CH_2 or $CH_{thiazole}$), 20.96 and 18.23 (2- and 4-CH_3).

The FT-IR spectral and analytical data of the synthesized compounds **A**, **S1-S5** and **T1-T5** are shown in Tables 3 and 4.

Table 3: FT-IR spectral data (cm^{-1}) of compounds **A** and **S1-S5**

Compound no.	A	S1	S2	S3	S4	S5
ν(O-H)	3269	3275	3375	3286	3325	2912
ν(C-H) aromatic	3059	3059	3063	3070	3097	2862
ν(C=O)	1651	-	-	-	-	-
ν(C=N) imine	-	1612	1616	1600	1620	1610
ν(C=N) benzothiazole	1589	1612	1600	1600	1620	1612
ν(C=C) aromatic	1566 1456	1551 1485	1543 1492	1531 1469	1504 1465	1512 1454
ν(N=N)	1435	-	-	-	1435	-
δ o.o.p (C-H) aromatic	748	748	752	744	748	756
Other bands (ν)	2928 2854 **(**C-H**)** aldehyde	1095 (C-Br) 2858 (CH_3)	2850 (CH_3) 1095 (C-Cl)	1030 (C-Cl)	1504 1249 (NO_2)	2912 2862 (CH_3)

Table 4: FT-IR spectral data (υ, cm-1) of thiazolidin-4-ones **T1-T5**

Compound No.	T1	T2	T3	T4	T5
ν(O-H)	3444	3298	3394	3113	3282
ν(C-H) aliphatic	2974 overlapped	2978 2928 overlapped	2978 overlapped	2970 2928 overlapped	2974 overlapped
νC-H) aromatic	3063	3056	3066 overlapped	3063	3066
ν(C=O)	1685	1689	1693	1685	1685
ν(C=N) thiadiazole	1612	1595	1589	1612	1647
ν(C=C) benzene	1531 1496 1462	1531 1492 1435	1519 1481	1535 1465 1446	1531 1516
ν(N=N)	1396	1400	1400	1404	1431
ν(C=S) thione form	756	756	756	756	756
Other bands (ν)	2974 (C-H) thiazolidine 1010 (C-Br)	2928 (C-H, thiazolidine) 1138 (C-Cl)	2978 (C-H) thiazolidine 1030 (C-Cl)	2928 (C-H) thiazolidine 1535, 1242 (NO_2)	2947 (C-H) thiazolidine

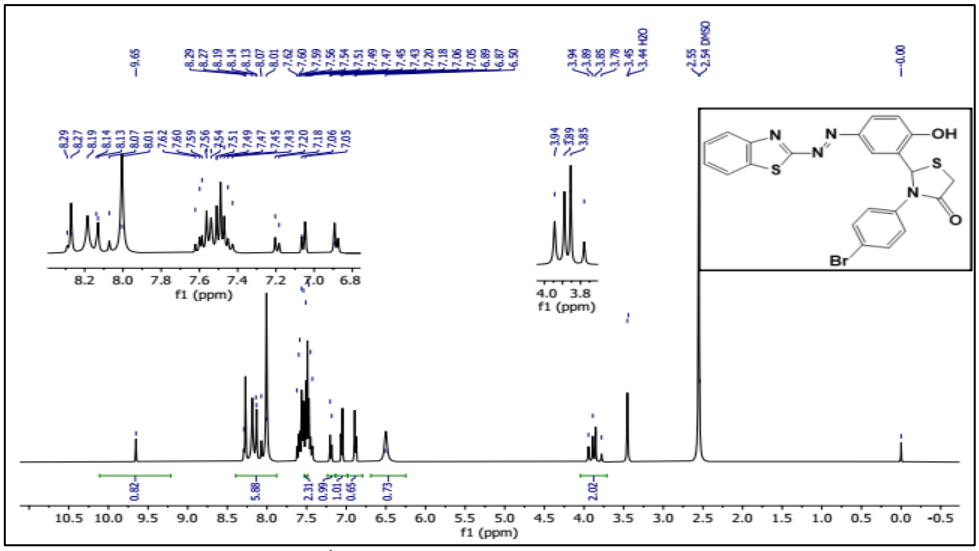


Figure 3: ^{1}H NMR spectrum of compound **T1**

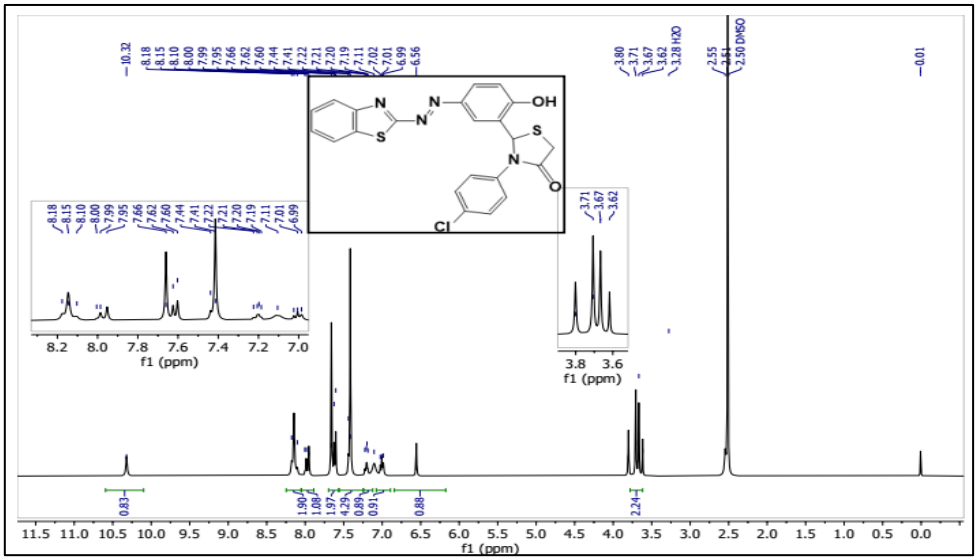


Figure 4: ^{1}H NMR spectrum of compound **T2**

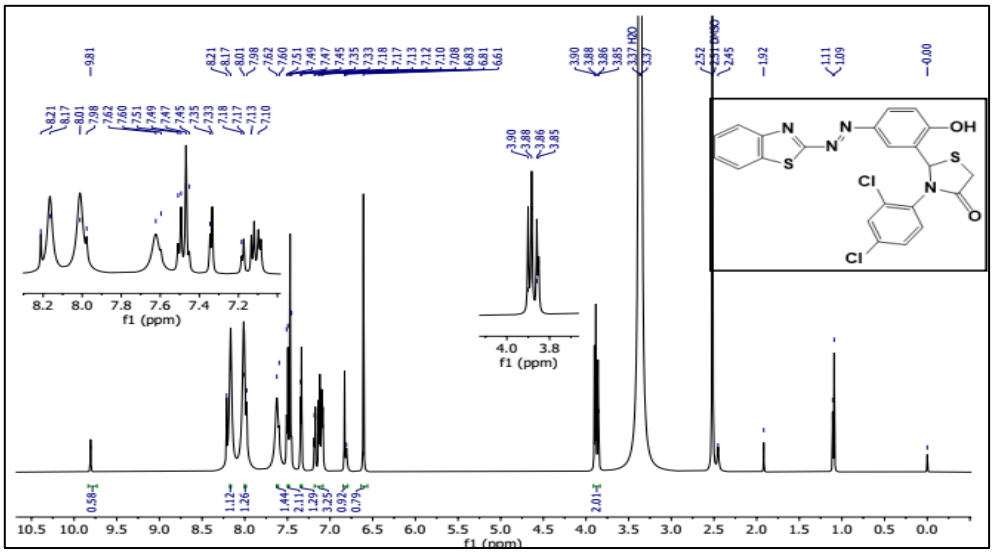


Figure 5: ^{1}H NMR spectrum of compound **T3**

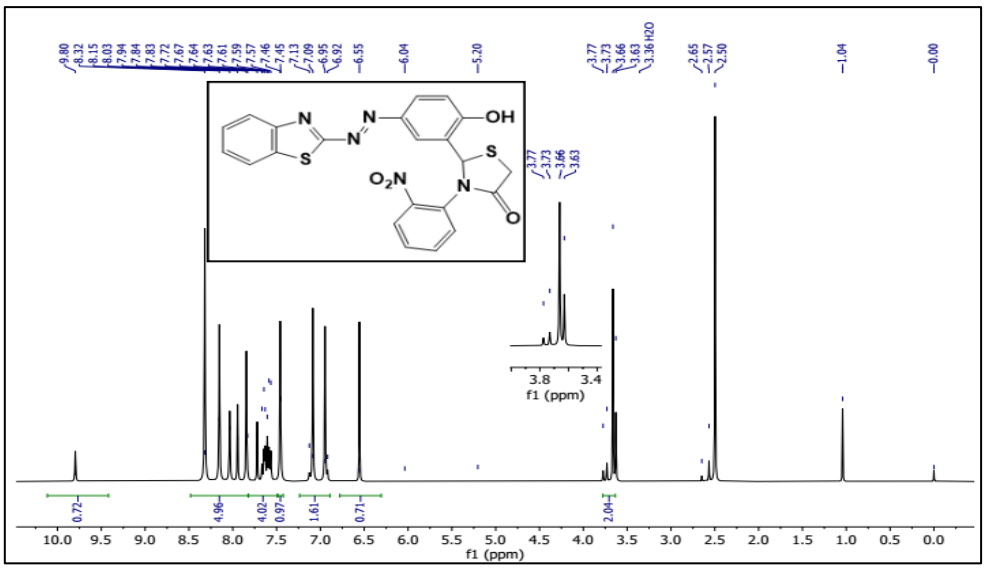


Figure 6: ^{1}H NMR spectrum of compound **T4**

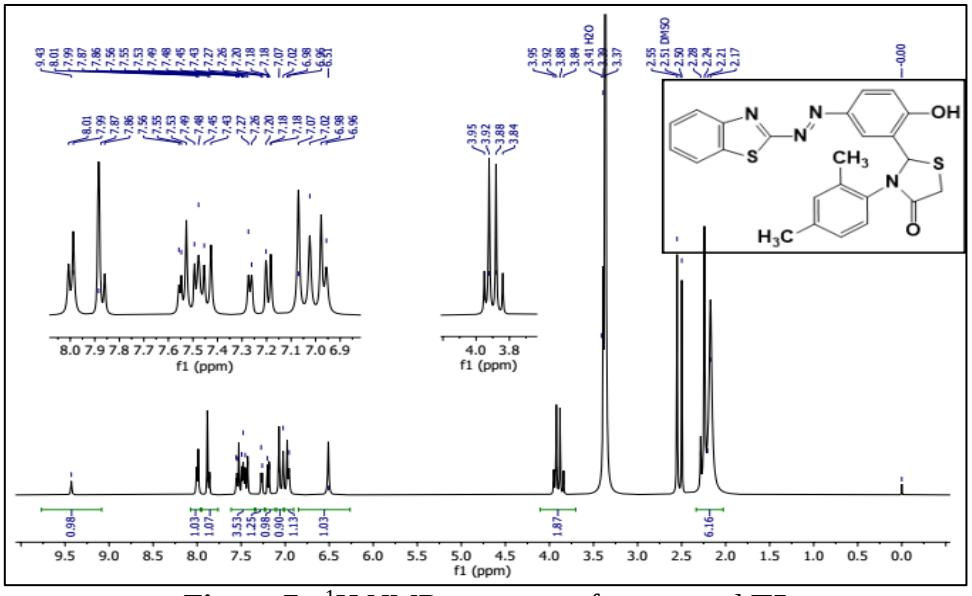


Figure 7: ^{1}H NMR spectrum of compound **T5**

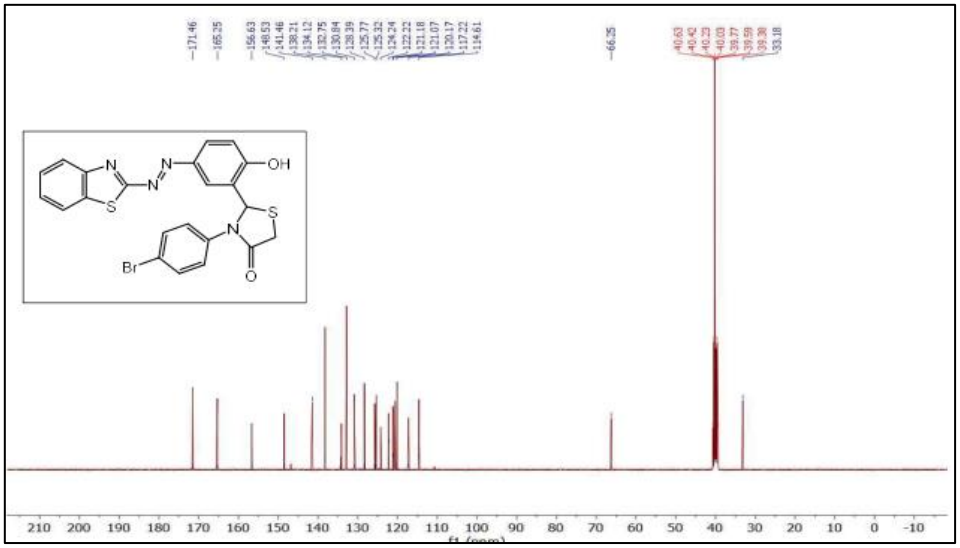


Figure 8: ^{13}C NMR spectrum of compound **T1**

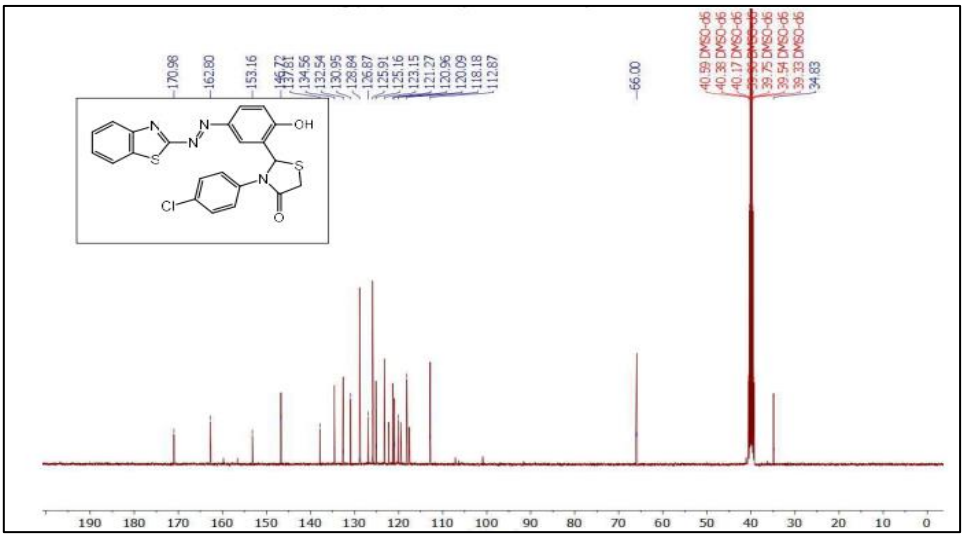


Figure 9: ^{13}C NMR spectrum of compound **T2**

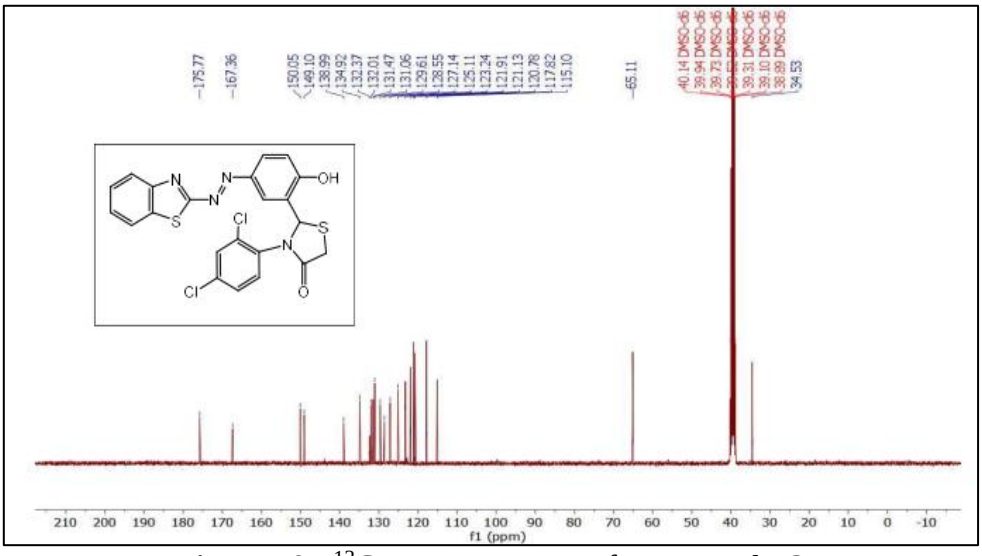


Figure 10: ^{13}C NMR spectrum of compound **T3**

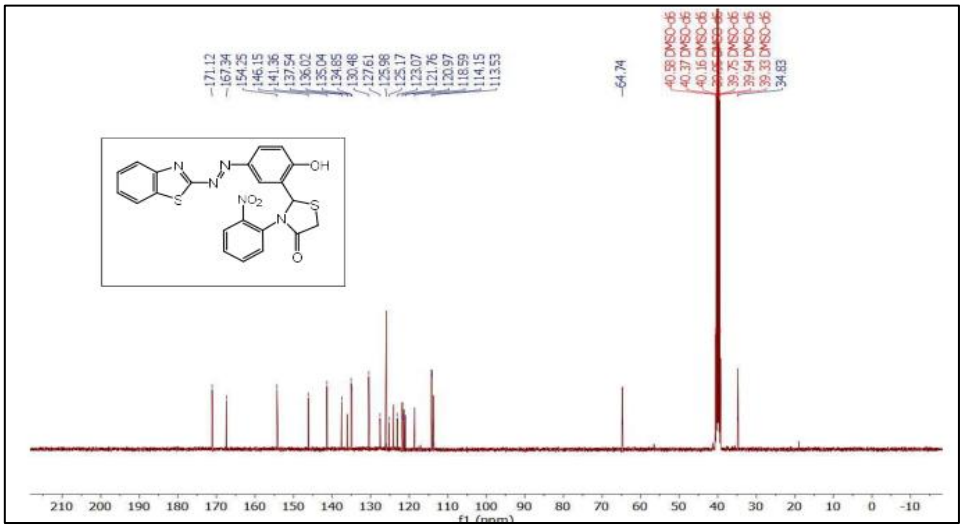


Figure 11: ^{13}C NMR spectrum of compound **T4**

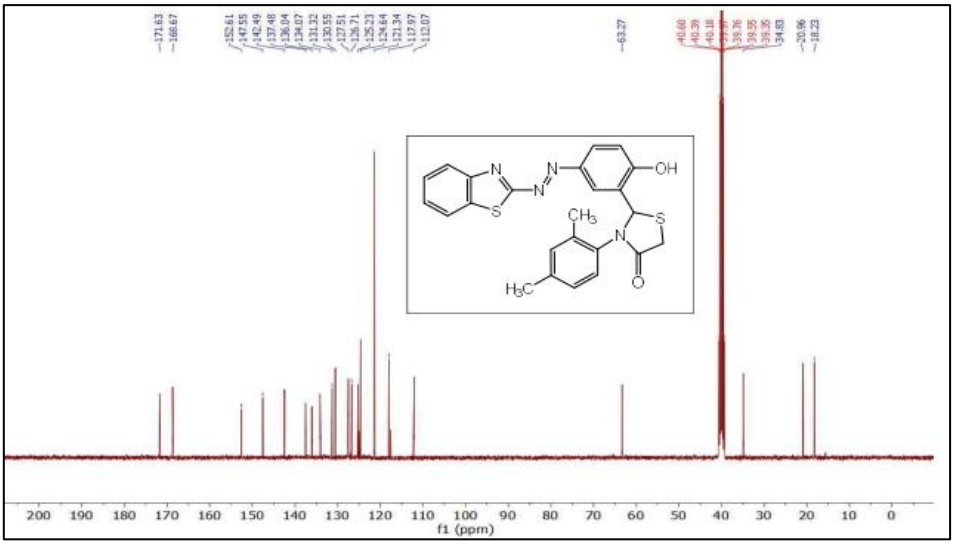


Figure 12: ^{13}C NMR spectrum of compound **T5**

3.2. Biological activity

3.2.1. Antibacterial activity

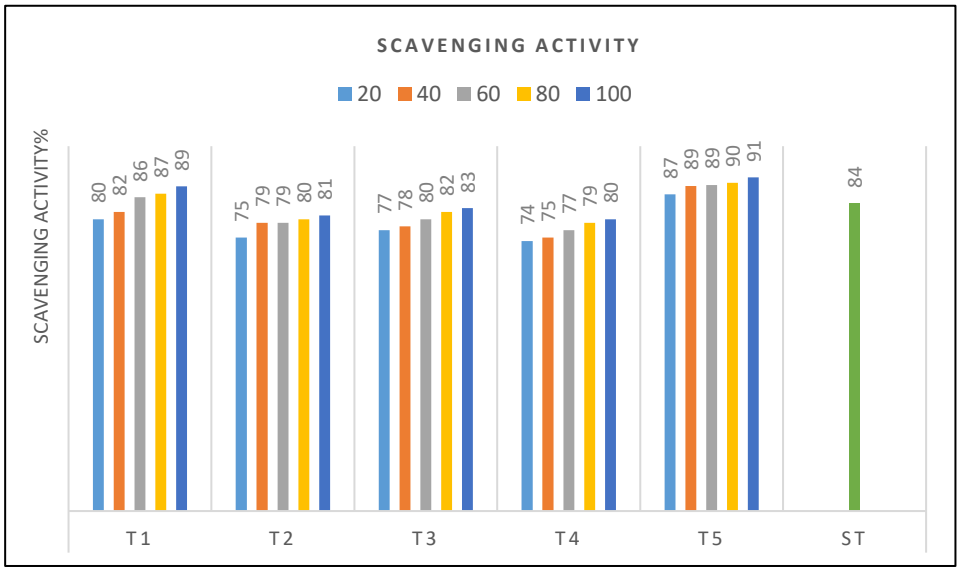
Using the diffusion method, the antibacterial activity of the produced compounds was evaluated against *Staphylococcus aureus* as a gram-positive bacteria and *Escherichia coli* as gram-negative bacteria. In an antibacterial study, it was discovered that the thiazolidin-4-one derivatives **T2**, **T3**, and **T5** were more effective than Gentamycin as a control medicine against *Staphylococcus aureus*, whereas compound **T3** was more effective than the reference drug against *Escherichia coli*.

3.2.2. DPPH assay:

The DPPH process is applied to study the antioxidant activity of the produced compounds. The ability of the studied compounds to convert the purple 1,1-diphenyl-2 picrylhydrazyl radical (DPP•) into its light, yellow reduced form (DPPH) served as a measure of their reducing abilities. At 517 nm, a decrease in violet color was measured, and the absorbance reduction corresponds to the antioxidant activity of the investigated substance. Compare the results using ascorbic acid as the control substance at concentrations of 20, 40, 60, 80, and 100 mg/mL. The results illustrate that the 100 mg/mL concentration provided an excellent outcome for all compounds. The DPPH radical scavenging abilities of compounds **T5** (91%) and **T1** (89%) are particularly strong, comparable to those of ascorbic acid (84%). Through SET and/or HAT types of antioxidant mechanisms, the studied compound's H• is transferred to the DPPH radical reagent's N• [41]. The hydrogens at the C2 and C5 locations of the thiazolidin-4-one ring, a five-membered heterocyclic ring, are two potential sites for H atom donation. The simple transfer of a H atom to the radicals must be the cause of this ring's antioxidant activity, and the hydrogen atom transfer (HAT) mechanism is the most popular one. The antioxidant effect of the thiazolidin-4-one derivatives is mainly due to resonance effects and tautomeric equilibrium [11, 12]. The scavenging activities of synthesized compounds T1-T5 are shown in Table 5 and Graph 1.

Table 5: Free radical-scavenging activity (%) for some of the prepared compounds **T1-T5**

Compounds	T1	T2	T3	T4	T5
Conc. mg/L	*Scavenging activity (%)*				
20	80	75	77	74	87
40	82	79	78	75	89
60	86	79	80	77	89
80	87	80	82	79	90
100	89	81	83	80	91
Ascorbic acid 50 µM	84.23				



Graph 1: Scavenging activity of thiazolidin-4-one derivatives **T1-T5** and reference standard vitamin C assessed by DPPH assay

4. Conclusion

This study gives important molecular insights that may be used to test the antibacterial activity of the thiazolidin-4-one ring and further improve its antioxidant properties.

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References

[1] R. A. Alfraiji and S. M. Al-Majidi, "Synthesis, characterization and evaluation of antimicrobial activity for new heterocyclic derivatives containing pentagonal, hexagonalrings", *Iraqi Journal of Science*, vol. 55, no. 4B, pp. 1694-1707, 2014.

[2] A. 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.

[3] V. Ravichandran, B. P. Kumar, S. Sankar, and R. Agrawal, "Predicting anti-HIV activity of 1, 3, 4-thiazolidinone derivatives: 3D-QSAR approach", *European Journal of Medicinal Chemistry*, vol. 44, no. 3, pp. 1180-1187, 2009.

[4] A. Rao, A. Chimirri, S. Ferro, A. M. Monforte, P. Monforte, and M. Zappalà, "Microwave-assisted synthesis of benzimidazole and thiazolidinone derivatives as HIV-1 RT inhibitors", *Arkivoc*, vol. 5, pp. 147-155, 2004.

[5] M. A. Pasha, S. Mondal, N. Panigrahi, G. Shetye, R. Ma, S. G. Franzblau, Y.-T. Zheng, and S. Murugesan, "One-pot synthesis of novel hydrazono-1, 3-thıazolıdın-4-one derivatives as anti-hiv and anti-tubercular agents: synthesıs, bıologıcal evaluatıon, molecular modelling and admet studıes", *Current HIV Research,* vol. 20, no. 3, pp. 255-271, 2022.

[6] E. D. Dincel, Ç. Akdağ, T. Kayra, E. D. Coşar, M. O. Aksoy, G. Akalın-Çiftçi, and N. Ulusoy-Güzeldemirci, "Design, synthesis, characterization, molecular docking studies and anticancer activity evaluation of novel hydrazinecarbothioamide, 1, 2, 4-triazole-3-thione, 4-thiazolidinone and 1,3,4-oxadiazole derivatives", *Journal of Molecular Structure,* vol. 1268, Article no. 133710, 2022.

[7] S. Kethireddy, S. Ketha, L. Eppakayala, and S. Chithaluri, "Anti-cancer docking investigations of Quinoxaline phenyl thiazolidinones", *Vietnam Journal of Chemistry,* vol. 60, no. 3, pp. 346-353, 2022.

[8] A. M. Farghaly, O. M. AboulWafa, Y. A. Elshaier, W. A. Badawi, H. H. Haridy, and H. A. Mubarak, "Design, synthesis, and antihypertensive activity of new pyrimidine derivatives endowing new pharmacophores", *Medicinal Chemistry Research,* vol. 28, no. 3, pp. 360-379, 2019.

[9] V. Kumar, P. Shetty, H . Anuradha, S. Chandra K, R. Ramu, S. M. Patil, A. Baliga, V. M. Rai, V. Udupi, and V. Poojary, "Potential fluorinated anti-mrsa thiazolidinone derivatives with antibacterial, antitubercular activity and molecular docking studies", *Chemistry and Biodiversity,* vol. 19, no. 2, p. e202100532, 2022.

[10] S. Şenkardeş, D. Kart, B. Bebek, M. G. Gündüz, and Ş. G. Küçükgüzel, "Synthesis, antimicrobial properties and in silico studies of aryloxyacetic acid derivatives with hydrazone or thiazolidine-4-one scaffold", *Journal of Biomolecular Structure and Dynamics*, vol. 41, no. 15, pp. 7421-7432, 2022.

[11] M. H. Shih and F. Y. Ke, "Syntheses and evaluation of antioxidant activity of sydnonyl substituted thiazolidinone and thiazoline derivatives", *Bioorganic & Medicinal Chemistry,* vol. 12, no. 17, pp. 4633-4643, 2004.

[12] M. Djukic, M. Fesatidou, I. Xenikakis, A. Geronikaki, V. T. Angelova, V. Savic, M. Pasic, B. Krilovic, D. Djukic, and B. Gobeljic, "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.

[13] M. R. Bhosle, J. R. Mali, S. Pal, A. K. Srivastava, and R. A. Mane, "Synthesis and antihyperglycemic evaluation of new 2-hydrazolyl-4-thiazolidinone-5-carboxylic acids having pyrazolyl pharmacophores", *Bioorganic and Medicinal Chemistry Letters,* vol. 24, no. 12, pp. 2651-2654, 2014.

[14] A. K. D. bin Ahmad Kamar, L. J. Yin, C. T. Liang, G. T. Fung, and V. R. Avupati, "Rhodanine scaffold: A review of antidiabetic potential and structure-activity relationships (SAR)", *Medicine in Drug Discovery,* vol. 15, p. 100131, 2022.

[15] K. I. Bhat, A. Apoorva, A. Kumar, and P. Kumar, "Synthesis and antidiabetic evaluation of some new coumarin coupled 4-thiazolidinone derivatives", *Research Journal of Pharmacy and Technology,* vol. 12, no. 11, pp. 5215-5218, 2019.

[16] H. T. Tandel, "Synthesis and antibacterial activity of coumarin containing 4-thiazolidinone derivatives", *International Journal of Research and Analytical Reviews,* vol. 7, no. 1, pp. 239-251, 2020.

[17] A. H. Makwana and H. R. Makwana, "Synthesis, characterization and biological evaluation of some novel thiazolidinone derivatives", *Journal of Advanced Scientific Research,* vol. 10, no. 04, pp. 91-95, 2019.

[18] M. A. Salem, S. Y. Abbas, M. A. S. El-Sharief, A. Y. Alzahrani, M. H. Helal, and H. K. Thabet, "Synthesis and antimicrobial activity of 4-methylthiazole and 4-thiazolidinone derivatives derived from 5-(aryldiazo) salicylaldehyde thiosemicarbazones", *Synthetic Communications*, vol. 51, no. 21, pp. 3325-3331, 2021.

[19] K. Kumar and B. Singh, "synthesis, characterization and anti-microbial activity of some 4-thiazolidinone conjugatives", *Asian Journal of Pharmaceutical Analysis,* vol. 10, no. 4, 195-200, 2020.

[20] R. Chintakunta and G. Subbareddy, "Synthesis docking studies, characterization and anti-tubercular activity of ofloxacin containing thiazolidinone derivatives", *Journal of Young Pharmacists,* vol. 14, no. 1, p. 77, 2022.

[21] A. Bolognese, G. Correale, M. Manfra, A. Lavecchia, E. Novellino, and V. Barone, "Thiazolidin-4-one formation, mechanistic and synthetic aspects of the reaction of imines and mercaptoacetic acid under microwave and conventional heating", *Organic and Biomolecular Chemistry,* vol. 2, no. 19, pp. 2809-2813, 2004.

[22] A. Hassoun, P. K. Linden, and B. Friedman, "Incidence, prevalence, and management of MRSA bacteremia across patient populations-a review of recent developments in MRSA management and treatment", *Critical Care,* vol. 21, no. 1, pp. 1-10, 2017.

[23] A. Cheddie, S. A. Shintre, A. Bantho, C. Mocktar, and N. A. Koorbanally, "Synthesis and antibacterial activity of a series of 2-trifluoromethylbenzimidazole-thiazolidinone derivatives", *Journal of Heterocyclic Chemistry,* vol. 57, no. 1, pp. 299-307, 2020.

[24] A. Geronikaki, E. Pitta, and K. Liaras, "Thiazoles and thiazolidinones as antioxidants", *Current Medicinal Chemistry,* vol. 20, no. 36, pp. 4460-4480, 2013.

[25] Archna, P. A. Chawla, G. Teli, S. Pathania, S. Singh, and V. Srivastava, "Exploration of antioxidant, anti-inflammatory and anticancer potential of substituted 4-thiazolidinone derivatives: synthesis, biological evaluation and docking studies", *Polycyclic Aromatic Compounds,* vol. 43, no. 1, pp. 597-618, 2023.

[26] Z. K. Al-Khazragie and B. K. Al-Salami, "Synthesis, antimicrobial, antioxidant, toxicity and anticancer activity of a new azetidinone, thiazolidinone and selenazolidinone derivatives based on sulfonamide", *Indonesian Journal of Chemistry,* vol. 22, no. 4, pp. 979-1001, 2022.

[27] G. Teli, P. Sharma, and P. A. Chawla, "Exploring the potential of substituted 4-thiazolidinone derivatives in the treatment of breast cancer: synthesis, biological screening and in silico studies", *Polycyclic Aromatic Compounds*, vol. 43, no. 7, pp. 6202-6234, 2023.

[28] J. Singh, P. A. Chawla, R. Bhatia, and S. Singh, "2,5-Disubstituted-4-thiazolidinones: synthesis, anti-inflammatory, free radical scavenging potentials and structural insights through molecular docking", *Letters in Organic Chemistry,* vol. 18, no. 12, pp. 957-968, 2021.

[29] M. Asif and M. Imran, "A mini-review on pharmacological importance of benzothiazole scaffold", *Mini-Reviews in Organic Chemistry,* vol. 18, no. 8, pp. 1086-1097, 2021.

[30] R. K. Yadav, R. Kumar, H. Singh, A. Mazumdar, B. Chauhan, and M. Abdullah, "Recent insights on synthetic methods and pharmacological potential in relation with structure of benzothiazoles", *Medicinal Chemistry,* vol. 19, no. 4, pp. 325-360, 2023.

[31] A. Kumar and A. K. Mishra, "Advancement in pharmacological activities of benzothiazole and its derivatives: An up to date review", *Mini Reviews in Medicinal Chemistry,* vol. 21, no. 3, pp. 314-335, 2021.

[32] A. M. Al-Azzawi and E. K. Jassem, "Synthesis and characterization of several new succinimides linked to phenyl azo benzothiazole or thiazole moieties with expected biological activity", *Iraqi Journal of Science,* vol. 57, no. 1C, pp. 534-544, 2022.

[33] S. A. Patil, S. A. Patil, T. Fariyike, K. O. Marichev, H. M. Heras Martinez, and A. Bugarin, "Medicinal applications of coumarins bearing azetidinone and thiazolidinone moieties", *Future Medicinal Chemistry,* vol. 13, no. 21, pp. 1907-1934, 2021.

[34] M. A. Iqbal, A. Husain, O. Alam, S. A. Khan, A. Ahmad, M. R. Haider, and M. A. Alam, "Design, synthesis, and biological evaluation of imidazopyridine-linked thiazolidinone as potential anticancer agents", *Archiv der Pharmazie,* vol. 353, no. 10, p. 2000071, 2020.

[35] M. Shirke, M. Gangthade, P. Chaskar, and R. Somani, "Synthesis, characterization and pharmacological evaluation of bifenyl based 4-thiazolidinones", *Indian Journal of Pharmaceutical Education and Research,* vol. 55, pp. 363-373, 2021.

[36] S. Prakash, G. Somiya, N. Elavarasan, K. Subashini, S. Kanaga, R. Dhandapani, M. Sivanandam, P. Kumaradhas, C. Thirunavukkarasu, and V. Sujatha, "Synthesis and characterization of novel bioactive azo compounds fused with benzothiazole and their versatile biological applications", *Journal of Molecular Structure*, vol. 1224, p. 129016, 2021.

[37] Y. Bekdemir and K. Efil, "Microwave assisted solvent-free synthesis of some imine derivatives", *Organic Chemistry International,* vol. 2014, p. 816487, 2014.

[38] R. T. H. Alasadi, N. Alhussein, and Z. H. Abood, "Synthesis and preliminary antibacterial activities of novel benzothiazoles", in *The 8th International Conference on Applied Science and Technology (ICAST 2020)*, Karbala, Iraq, 2020.

[39] R. Finn, "Theory of agar diffusion methods for bioassay", *Analytical Chemistry*, vol. 31, no. 6, pp. 975-977, 1959.

[40] W. C. Lee, R. Mahmud, S. Pillai, S. Perumal, and S. Ismail, "Antioxidant activities of essential oil of Psidium guajava L. leaves", *APCBEE Procedia*, vol. 2, pp. 86-91, 2012.

[41] M. Cuendet, K. Hostettmann, O. Potterat, and W. Dyatmiko, "Iridoid glucosides with free radical scavenging properties from Fagraea blumei", *Helvetica Chimica Acta*, vol. 80, no. 4, pp. 1144-1152, 1997.