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A Novel Approach to Synthesis of Quinazoline-4-One Derivatives and Studying Their Biological Applications

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Keywords: : Quinazoline-4-One, Hydrazone, Phthalic Anhydride, Schiff Base.

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Abstract:

This study investigates the synthesis and biological activity of novel quinazoline-4-one derivatives, synthesized through Schiff base reactions involving hydrazine and various substituted benzaldehydes in ethanol. The synthetic route commenced with the reaction of phthalic anhydride with an amino acid, resulting in the formation of an aromatic amino acid. This intermediate underwent esterification with thionyl chloride and ethanol to yield an aromatic ester. The ester was subsequently converted to an aromatic hydrazide by reaction with 80% aqueous hydrazine in ethanol. The hydrazide was then reacted with different aromatic aldehydes in the presence of a small amount of glacial acetic acid to form the corresponding hydrazone derivatives. The final step, involved synthesizing quinazoline-4-one derivatives by reacting the hydrazone with anthranilic acid. The structures of the synthesized compounds were characterized by using various spectroscopic techniques, including FT-IR, ^{1}H-NMR, and ^{13}C-NMR. The synthesized compounds showed dose-dependent inhibitory activity against *Staphylococcus aureus* and *Escherichia coli*, with higher concentrations (75 mg/mL) yielding greater inhibition. Compound A4 was the most effective, but its activity was lower compared to standard antibiotics like amoxicillin and ciprofloxacin. These findings indicate significant antimicrobial potential.

Keywords: Quinazoline-4-one, Hydrazone, Phthalic Anhydride, Schiff Base,

نهج جديد لتخليق مشتقات كينازولين-٤-ون ودراسة تطبيقاتها البيولوجية

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الخلاصة:

تعنى هذه الدراسة بتحضير وتقييم الفعالية البيولوجية لمشتقات جديدة من الكينازولين-٤-أون ، والتي تم تحضيرها عبر تفاعلات قواعد شف باستخدام الهيدرازين مع بنزلديهايد مختلف التعويض في مذيب الايثانول . حيث تم تحضير هذه المركبات من تفاعلات متسلسلة من تفاعل أنهدريد الفثاليك مع حامض أميني لتكوين حمض أميني ارومات . ومن ثم تم تحويل هذه المركبات إلى استرات ارومات من خلال تفاعل الإسترة مع كلوريد الثايونيل والإيثانول . وبعدها تم تحويل الاستر الناتج إلى هيدرازيد ارومات بواسطة التفاعل مع الهيدرازين المائي بنسبة ٨٠٪ في مذيب الايثانول. بعد ذلك، تم تفاعل الهيدرازيد مع مجموعة من الألدهيدات العطرية المختلفة التعويض بإضافة قطرات من حامض الخليك الثلجي، مما أدى إلى تكوين مشتقات الهيدرازون . في الخطوة الأخيرة، تم تحضير مشتقات كينازولين-٤-أون من خلال تفاعل الهيدرازون مع حامض الأنثرانيك . تم استخدام تقنيات طيفية مثل FT-IR ، و ^{1}H-NMR، و^{13}C-NMR لتشخيص المركبات الناتجة. أظهرت المركبات المُركبة نشاطًا مثبطًا يعتمد على الجرعة ضد المكورات العنقودية الذهبية والإشريكية القولونية، حيث أن التركيزات الأعلى (٧٥ ملغ/مل) أظهرت تثبيطًا أكبر. كان المركب *A4* هو الأكثر فعالية، لكن نشاطه كان أقل مقارنةً بالمضادات الحيوية القياسية مثل الأموكسيسيلين والسيبروفلوكساسين. تشير هذه النتائج إلى خصائص مضادة للبكتيريا.

الكلمات المفتاحية: كينازولين-٤-أون، الهيدرازون، أنهيدريد الفثاليك، قواعد شف.

1. Introduction:

Heterocyclic compounds differ significantly from homocyclic compounds due to their incorporation of various elemental constituents alongside carbon in cyclic structures. While homocyclic rings consist of a single element, heterocycles feature carbon atoms along with other components such as oxygen, nitrogen, and sulfur [1,2].

Hydrazones represent a category of azomethines characterized by a -C=N-NH_2 bond [3]. The azomethine has garnered significant attention due to the dual electrophilic and nucleophilic properties of carbon, both nitrogen atoms possessing nucleophilic attributes. Hydrazones are highly important in modern chemistry due to their versatile applications. In the pharmaceutical industry, hydrazones are widely used as prodrugs, enabling targeted drug delivery. For example, they are utilized in antitumor agents due to their ability to release active drugs selectively in acidic environments, such as tumor tissues [4]. Additionally, hydrazones serve as enzyme inhibitors, targeting enzymes like monoamine oxidase (MAO) and carbonic anhydrase, which are crucial for treating neurological disorders and cancer [5]. In chemical catalysis,

hydrazones act as effective ligands, enhancing the efficiency of catalytic processes in organic transformations, such as asymmetric synthesis and carbon-carbon bond formation [6]. A typical formula of hydrazone class of organic compounds is $R_1R_2C\text{-}NNH_2$ Where R_1 and R_2 similar or different aryl or alkyl groups as shown in **Figure 1**.

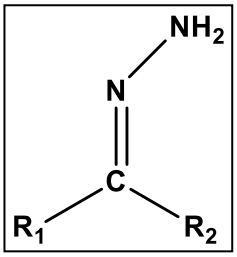


Figure 1: Structural formula of hydrazones.

The term hydrazone was coined by Fischer in 1888 [7]. Due to the simplicity of these venerable ligation reactions, hydrazones have also had a pervasive influence on numerous other research fields ever since. Hydrazone derivatives display keto-enol tautomerism facilitated by intermolecular proton transference, where the configuration of cis-trans depends on various factors including the azomethine linkage, solvent conditions, pH level, and concentration. These derivatives are acknowledged as entities capable of functioning as both proton donors and acceptors, exhibiting both intermolecular and intramolecular interactions through hydrogen bonding. The distinct characteristics observed in hydrazone derivatives highlight their significant importance in the field of organic compounds [8].

Quinazoline comprises a fused benzene ring and a pyrimidine ring (**Figure 2**), with a chemical formula of $C_8H_6N_2$. This compound, formerly identified as benzo-1,3-diazine, is a fused bicyclic compound. The initial synthesis of quinazoline took place in 1903 by Gabriel, following its first isolation from the Chinese plant aseru. The first documented instance of a compound containing the quinazoline nucleus was reported by Peter Gries in 1869.

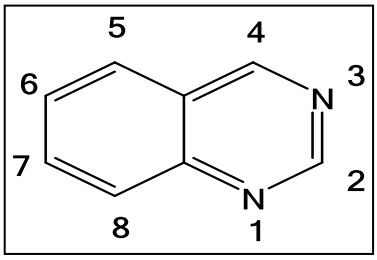


Figure 2: Structural formula of Quinazoline.

The structure of quinazoline molecules is determined by the positioning of the oxygen and hydrogen atoms bonded to the nitrogen atom. A widely acknowledged system of numbering is used to classify quinazolines and quinazolinones into specific categories: 4(3H)-quinazolinone (3H-1,3-quinazolin-4-one), 2(1H)-quinazolinone (1H-1,3-quinazolin-2-one), and 2,4(1H,3H)-quinazolinedione (1H,3H-1,3-quinazoline-2,4-dione), as shown in **Figure 3**.

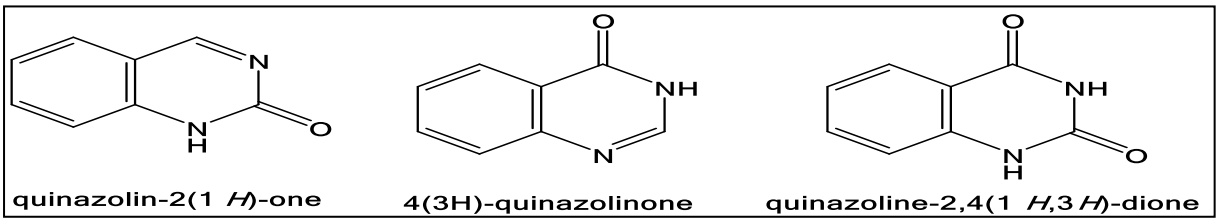


Figure 3: Structural of quinazoline and quinazolinone.

However, among the various quinazolinone structures proposed in **Figure 3**, the 4(3H)-quinazolinones stand out as the most commonly found. They exist either as intermediates or as natural products in numerous suggested biosynthetic pathways **[9]**. Their structural origin from the anthranilates, such as anthranilic acid, various esters, isatoic anhydride, anthranilamide, and anthranilonitrile, partially accounts for their prevalence **[10,11]**.

Literature reviews indicate that quinazolinones can be using anthranilic acid **[12-15]**, 2-aminobenzamide **[16]** , and 2-aminobenzonitrile. Natural products based on quinazolinones that require more structurally complex precursors have been synthesized through methods such as thioamide formation, oxidation of dehydro-quinazolinone, and aza-Wittig condensation **[17,18]**. Quinazolin-4(3H)-one derivatives heterocyclic compounds with multiple nitrogen atoms as promising biologically active substances **[19]**. The biological properties of 4(3H)-quinazolinones vary depending on the nature of the substituents within the ring system. They have been reported to have antifungal, antibacterial, antitubercular, antiviral, anticancer, and anticonvulsant effects **[20,26]**.

2. Material And Methods:

2.1. Materials and Instruments

All chemicals used in this study were sourced from Aldrich, Fluka, and BDH, they were used without further purification. Infrared(FT-IR) spectra were recorded using a ShimadzuFTIR-8400 spectrometer. ^{1}H NMR and ^{13}C NMR spectra were conducted on a Bruker spectroscopic ultra- shield magnets 300 MHz, using tetramethylsilane (TMS) as a reference point and d_6-DMSO as the solvent. ^{1}H NMR chemical shift measurements are presented in parts

per million (ppm). Melting points of the compounds were recorded on electrothermal melting point apparatus.

2.2. General hydrazones synthesis method (A4-A6)

All novel hydrazone analogues (A4-A6) were obtained from the reaction of 1,5- hydrazide (A3) and aldehydes according to the general synthesis method for hydrazone analogues [27]. Dissolve 0.01mol of the prepared hydrazide in 100 mL of EtOH. Next, add 0.05 mol of the suitable aldehydes and a small amount of CH_3COOH. Allow the resulting mixture to react for 6 hours, then cool to room temperature. After filtration, the solvent evaporated, and the resulting residues (A4-A6) were recrystallized using absolute ethanol. **Table 1** shows the physical properties of synthesized hydrazones (A4-A6).

Table 1: The physical properties of synthesized hydrazone derivatives (A4-A6).

Compound	Y	Molecular Formula	Melting point (°C)	Color	Yield%
A4	H	$C_{17}H_{13}O_3N_3$	251-253	yellow	69
A5	4-NO2	$C_{17}H_{12}O_5N_4$	234-236	brown	70
A6	4-OCH_3	$C_{18}H_{15}O_4N_3$	200-202	Yellow	65

2.3. General method for the synthesis of quinazoline -4- one derivatives (A7-A9) [16]:

All novel quinazoline -4- one derivatives were synthesized from the reaction of 2-amino benzoic acid (anthranilic acid) and hydrazones, following the standard procedure for quinazoline -4- one synthesis. In a flask, 0.01 mol of hydrazones was mixed with 0.01 mol (1.37 g) of 2-amino benzoic acid. The mixture was heated for 10-15 minutes to initiate fusion. After cooling to 25^0C, the resulting residue was collected and recrystallized from a mixture of 1,4-dioxane and ethanol. **Table 2** shows the physical properties of synthesized Quinazoline -4- one derivatives (A7-A9)

Table 2: The physical properties of synthesized Quinazoline -4- one derivatives (A7-A9).

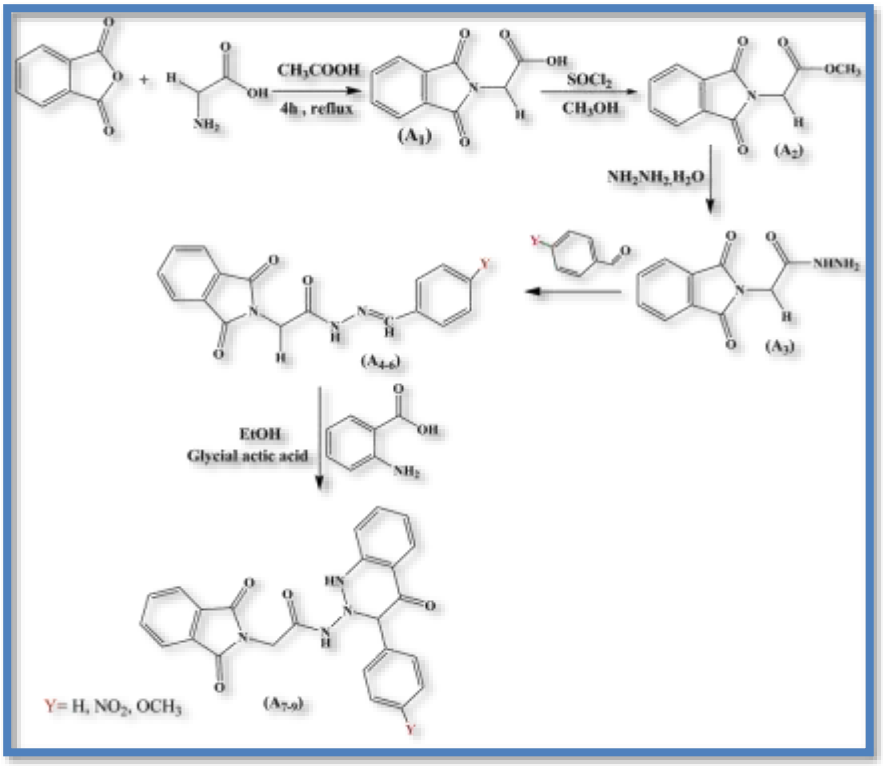
Compound	Y	Molecular Formula	Melting point (°C)	Color	Yield%
A7	H	$C_{24}H_{17}O_4N_3$	240-241	white	70
A8	4-NO_2	$C_{24}H_{16}O_6N_4$	172-174	Brown	65
A9	4-OCH_3	$C_{25}H_{19}O_5N_3$	208-210	Yellow	62

2.4. Biological Activity Study

The antibacterial activity of the synthesized compounds (A4–A8) was evaluated against two pathogenic bacterial strains: Staphylococcus aureus and Escherichia coli. The study aimed to determine the minimum inhibitory concentration (MIC) of these compounds by preparing solutions at concentrations of 25, 50, and 75 mg/mL, using dimethyl sulfoxide (DMSO) as a solvent. The antibacterial effects were assessed after 24 hours by measuring the diameter of the inhibition zones formed around the wells in agar plates. Each measurement was performed in triplicate to ensure accuracy and reproducibility. The inhibition zones were recorded in millimeters (mm), with inhibition diameters of less than 2 mm considered weak, 3–5 mm indicating moderate activity, and greater than 6 mm classified as strong antibacterial activity. To assess the effectiveness of the synthesized compounds, their inhibition zones were compared with those of standard antibiotics, including Amoxicillin, Ampicillin, and Ciprofloxacin. The results showed that at a concentration of 75 mg/mL, compound A4 exhibited the highest antibacterial activity among the synthesized derivatives, with inhibition zones of 5 mm against *Escherichia coli* and *Staphylococcus aureus*. Compound A5 demonstrated moderate activity, while A6 and A8 showed weaker inhibition effects. For comparison, the inhibition zones for the standard antibiotics at 75 mg/mL were recorded as follows: Amoxicillin (7 mm for Staphylococcus aureus and 5 mm for Escherichia coli), Ampicillin (6 mm for Staphylococcus aureus and 5 mm for Escherichia coli), and Ciprofloxacin (5 mm for both bacterial strains). The study confirms that the synthesized quinazoline-4-one derivatives possess antibacterial properties, though their activity remains lower than that of standard antibiotics. Further modifications and optimizations of these compounds could enhance their potency, making them potential candidates for future antimicrobial drug development.

3. Results:

The synthesis of novel compounds commenced with the preparation of an aromatic amino acid through the reaction of phthalic anhydride with the corresponding glycine. This was followed by the formation of an ester via the reaction of the aromatic amino acid with ethanol in the presence of thionyl chloride. Subsequently, the hydrazide was synthesized from the ester using 80% aqueous hydrazine in an ethanol medium. The hydrazide was then reacted with a variety of aromatic aldehydes, a small quantity of glacial acetic acid, to yield hydrazone derivatives. Finally, quinazoline-4-one derivatives were successfully synthesized through the reaction of the hydrazone with anthranilic acid.. All synthesized thioanthraquinone analogues are presented in **Scheme 1**.

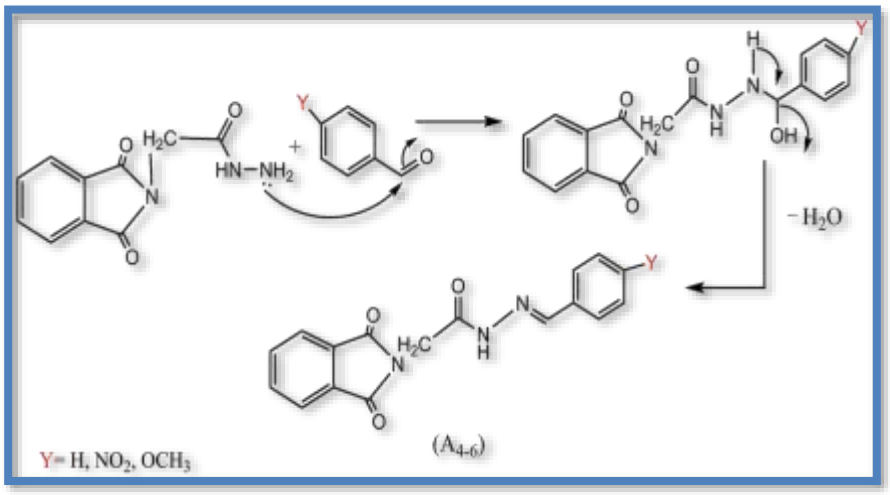


Scheme 1: Synthesis pathway for hydrazone (A4-A6) and quinazoline-4-one derivatives (A7-A9).

4. Discussion

4.1. Identification of hydrazone derivatives

The compounds were synthesized via the reaction of acid hydrazides with aromatic aldehydes in an alcoholic medium (ethanol) using a stepwise method over a duration of 6 hours, as depicted in **Scheme 2**.



Scheme 2: Proposed mechanism for the formation of hydrazones.

Compounds demonstrated distinct physical characteristics compared to the starting materials, The analysis by infrared spectroscopy revealed various functional group vibrations,

including those related to amide carbonyl, C=N stretching, and aromatic C=C vibrations. Additional peaks were noted for N–H and C–H stretching, as detailed in **Table 3** and **Figures 4 and 5**.

Table 3: Shows the IR data of compound (A4 – A6)

No.	FT-IR , (KBr), cm^{-1} Fixed bands in structure						
	νN–H	**ν(=CH) Ar**	**ν(C-H) Aliph**	**νC=O**	**νC=N**	**νC=CAr**	νC-N
A4	3348	3082	2949	1746	1605	1561	1211
A5	3220	3045	2978	1742	1608	1580	1221
A6	3286	3093	2963	1740	1641	1495	1218

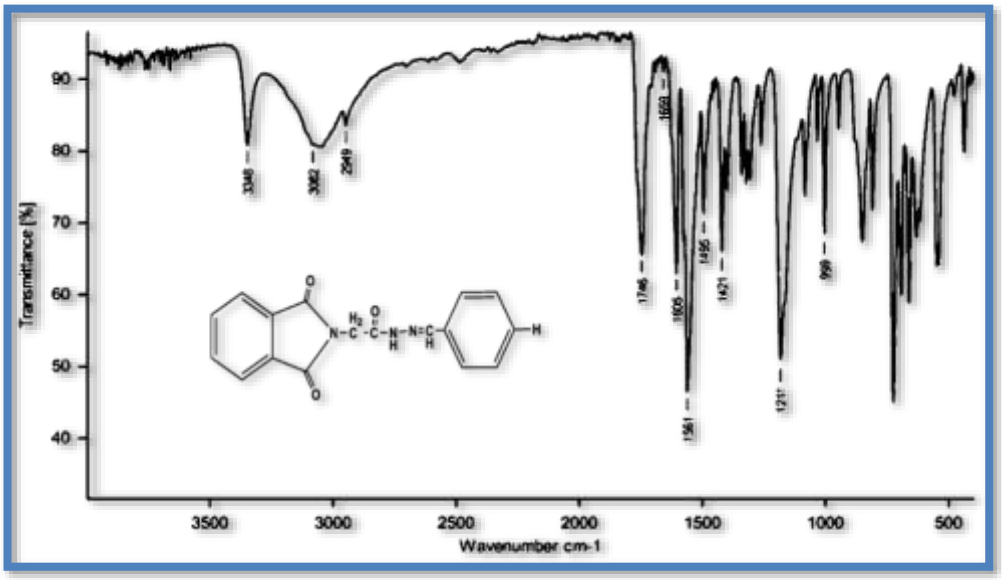


Figure 4: The FT-IR spectrum of compound A4.

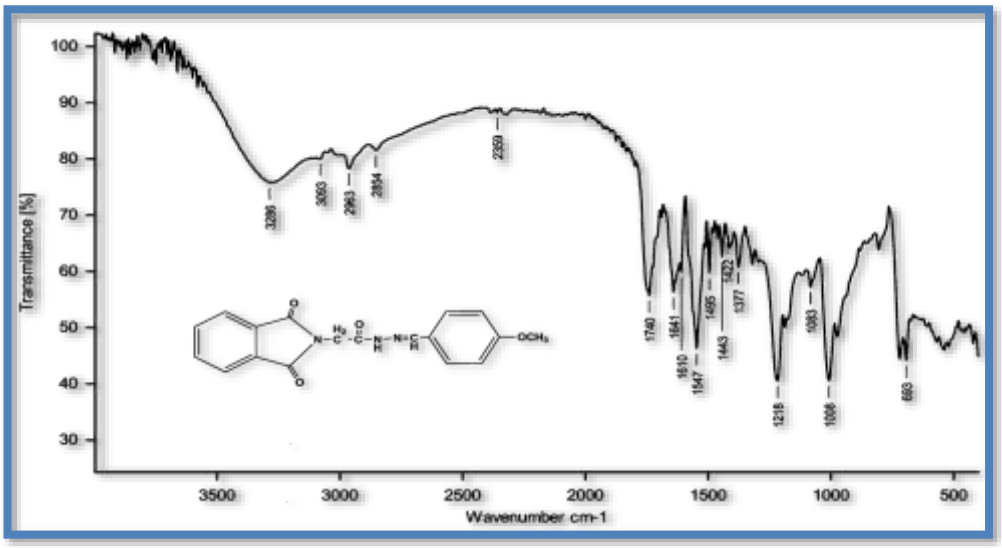
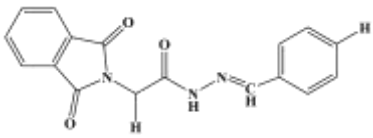
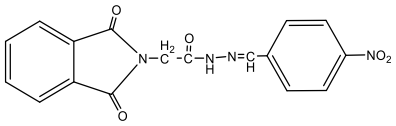
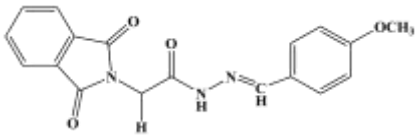


Figure 5: The FT-IR spectrum of compound A6.

The ^{1}H-NMR spectrum of compounds was obtained using dimethyl sulfoxide as the solvent with deuterium lock. The ^{1}H-NMR spectral data of hydrazones are outlined in Table 4 and Figure 6 and 7.

Table 4: The ^{1}H-NMR data of compounds (A4-A6).

Compound	Structures	^{1}H NMR Spectral data (δ ppm)
A4		3.42 (s, 2H, CH_2) 5.72 (s, 1H, CH=N) 7.87-8.12 (d,t, 9H , Ar=C-H) 11.55 (s, 1H , N-H)
A5		3.21 (s, 2H, CH_2) 5.20 (s, 1H ,CH=N) 7.94 -8.20 (d,t, 9H, Ar=C-H) 11.80(m, 1H, N-H)
A6		3.41 (s, 2H CH_2,) 3.81 (s, 3H,CH_3) 4.80 (s, 1H, CH=N) 7.04-8.64 (d,t, 8H, Ar=C-H) 12.05 (s, 1H ,N-H)

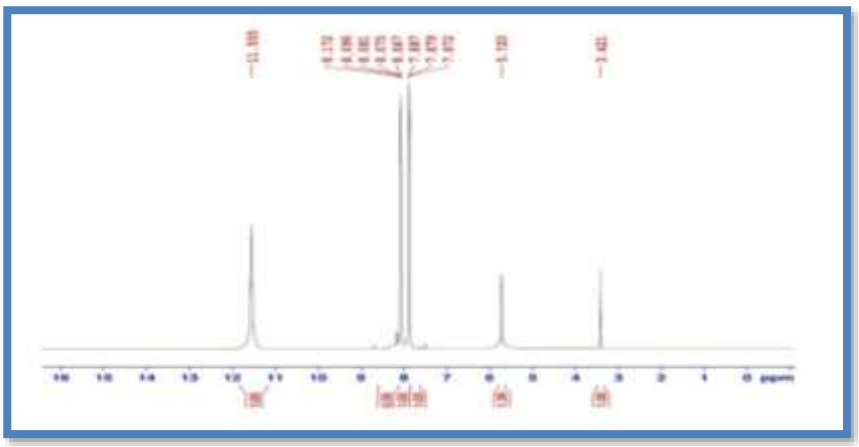


Figure 6:The ^{1}H-NMR spectrum of compound A4.

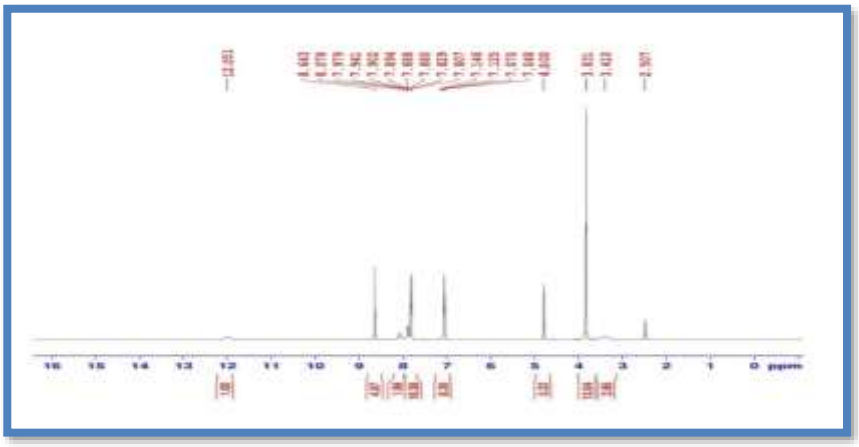


Figure 7: The ^{1}H-NMR spectrum of compound A6.

The ^{13}C-NMR spectral data of hydrazones are shown in **Table 5** and **Figures 8** and **9**.

Table 5: ^{13}C-NMR data of compounds (A4-A6).

Compound	^{13}C-NMR Spectral data (δ ppm)
A4	(165.10 CO cyclic , 178.55 C=O amide) (124.29, 125.59, 127.61, 128.62, 129.36, 131.81 and 133.04 C arm), 69.29, 53.49
A5	(173.03 CO cyclic , 184.23 C=O amide) (125.25, 125.59, 127.33, 127.66, 129.21, 133.16 and 133.67C arm), 74.52, 57.16 , 29.88
A6	(161.10 C=O cyclic , 180.16 C=O amide) (121.70, 123.71, 125.65,126.12, 127.52, 129.16 C arm) 76.54, 55.85, 26.05

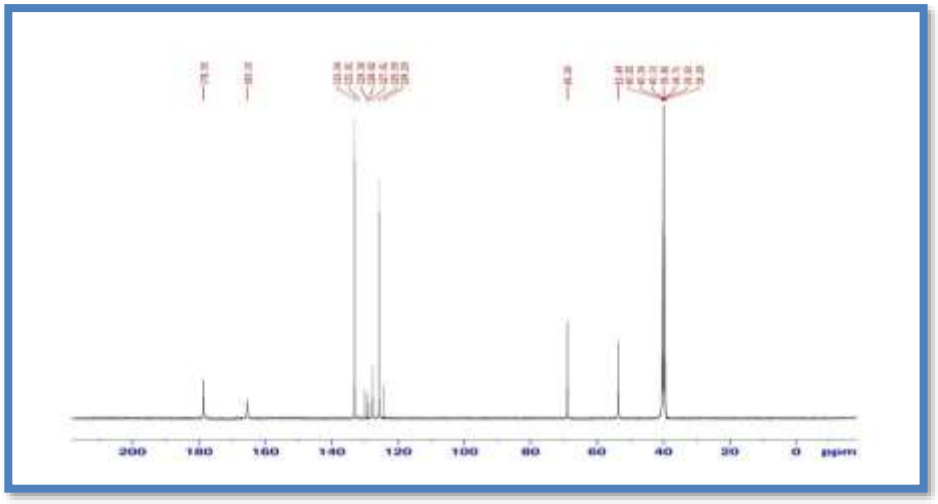


Figure 8: The ^{13}C-NMR spectrum of compound A4.

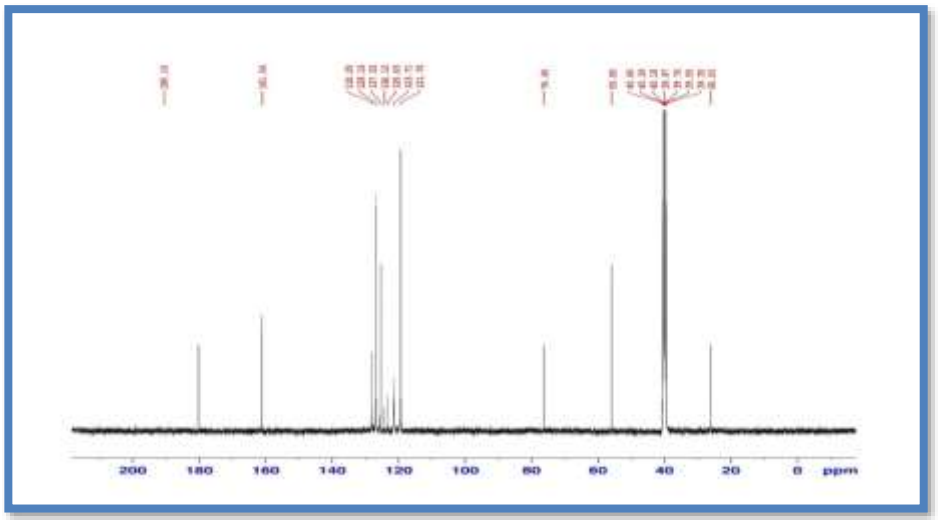
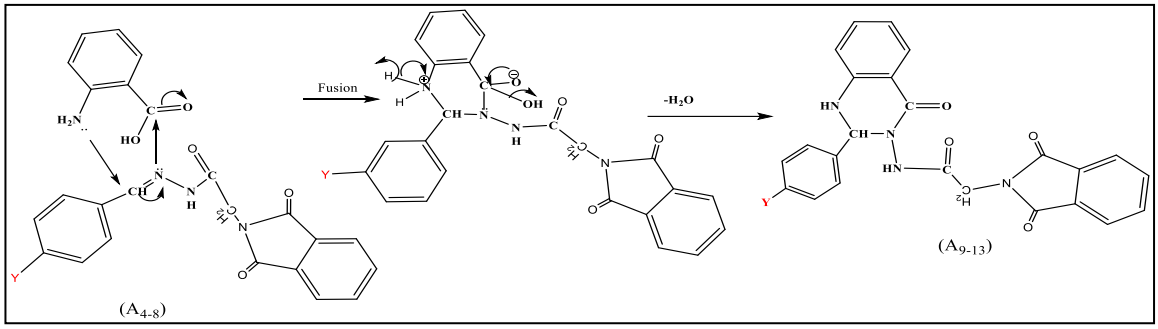


Figure 9: The ^{13}C-NMR spectrum of compound A6.

4.2. Identification of quinazoline -4- one derivatives

The compounds were synthesized by subjecting the pre-prepared hydrazone derivatives (A4-A6) to a fusion reaction with 2-amino benzoic acid (anthranilic acid), resulting in the anticipated mechanistic reaction. as illustrated in **scheme 3**.



Scheme 3: Proposed mechanism for the formation of quinazoline-4-ones

The analysis demonstrated distinct physical characteristics in the synthesized compounds compared to the starting materials, the analysis by infrared spectroscopy. The spectra indicated various functional group vibrations related to carbonyl amide, C–N stretching, and aromit. C=C vibrations. Additional peaks were noted for N–H and C–H stretching, as shown in **Table 6** and **Figure 10**.

Table 6: The physical properties of synthesized quinazoline -4- one derivatives (A7-A9).

No.	FT-IR , (KBr), cm^{-1} Fixed bands in structure					
	νN–H	ν(=CH) Ar	ν(C-H) Aliph	νC=O	νC=CAr	νC-N
A7	3384	3054	2903	1666	1563	1247
A8	3288	3027	2914	1649	1597	1182
A9	3273	3017	2897	1660	1563	1224

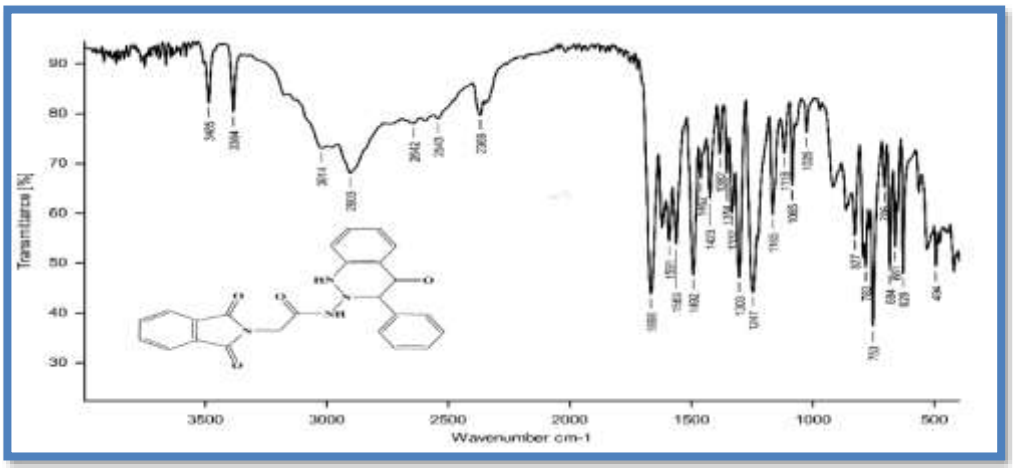
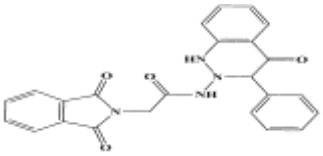
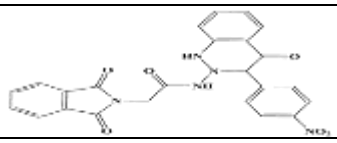
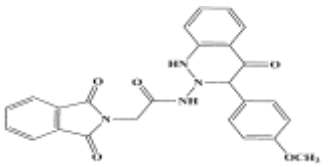


Figure 10: The FT-IR spectrum of compound A7.

The ^{1}H-NMR spectral data of Quinazoline -4- one derivatives are shown in **Table 7** and **Figure 11** and **12**

Table 7: ^{1}H NMR data of compounds (A7-A9).

Compound	Structures	^{1}H NMR Spectral data (δ ppm)
A7		3.41 (s, 2H ,CH_2), 5.72 (s, 1H ,CH=N), 7.54 -7.88 (m,13H, Ar=C-H), 8.08 (s, 1H ,H-N-CO), 9.49 (s, 1H ,H-N-C=CH)
A8		3.01 (s, 2H ,CH_2), 6.21 (s, 1H, CH=N), 7.92-8.43 (m, 13H, Ar=C-H), 8.87 (s, 1H ,H-N-CO), 10.48 (s, 1H ,H-N-C=CH)
A9		3.41 (s, 2H,CH_2), 4.39 (s, 3H), 5.60 (s, 1H, CH=N), 7.21 -7.88 (m, 12H ,Ar=C-H), 8.081(s, 1H ,H-N-CO), 10.06 (s, 1H ,H-N-C=CH)

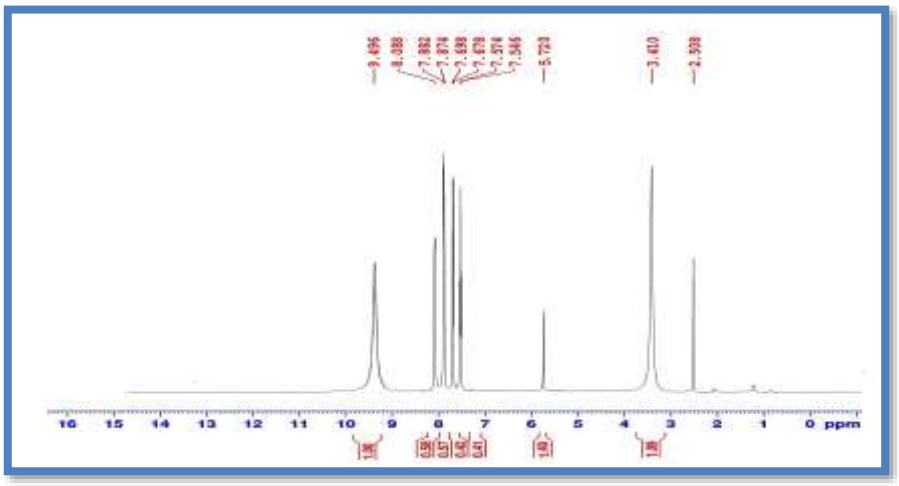


Figure 11: The ^{1}H-NMR spectrum of compound A7.

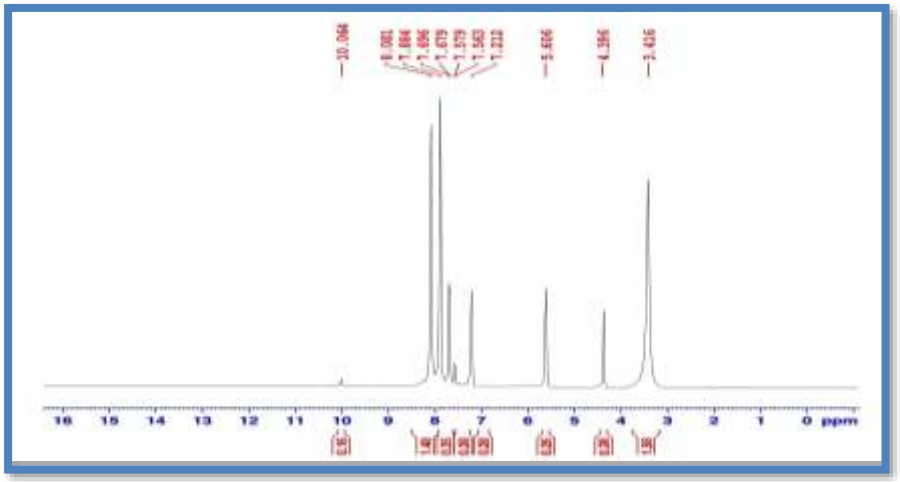


Figure 12: The FT-IR spectrum of compound A9.

The ^{13}C-NMR spectral data of quinazolinequinazoline-4-one derivatives are shown in Table 8 and Figures 13 and 14.

Table 8: ^{13}C-NMR data of compounds (A7-A9).

Compound	^{13}C-NMR Spectral data (δ ppm)
A7	161.10 C=O cyclopentanone, 170.06 C=O cyclohexanone, 184.20 C=O amide, (119.01, 122.40, 125.60 ,127.61 ,129.55, 130.49, 131.62 ,133.06 and 134.20 Carom), 68.02, 31.28
A8	159.07 C=O cyclopentanone,169.13170.06 C=O cyclohexanone, 179.21, (124.12, 125.24,126.01,127.35,131.16,132.42, 135.24, and 136.11C arm), 73.23, 56.07
A9	155.08 C=O cyclopentanone,161.10170.06 C=O cyclohexanone, 170.06 C=O amide, (125.60, 127.61, 129.55, 130.49,131.62, 133.06 , and 134.20 Carom), 70.02, 59.42, 29.88

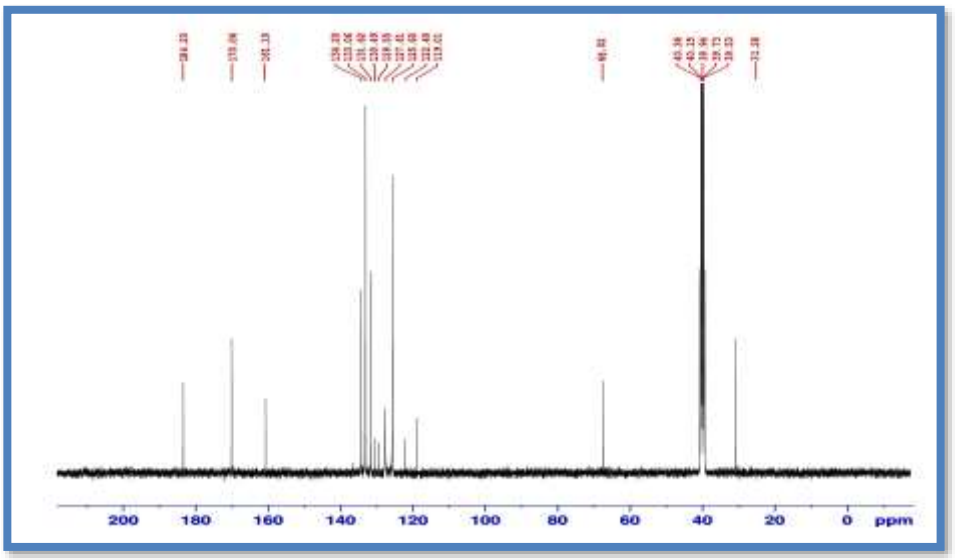


Figure 13: The ^{1}H-NMR spectrum of compound A7.

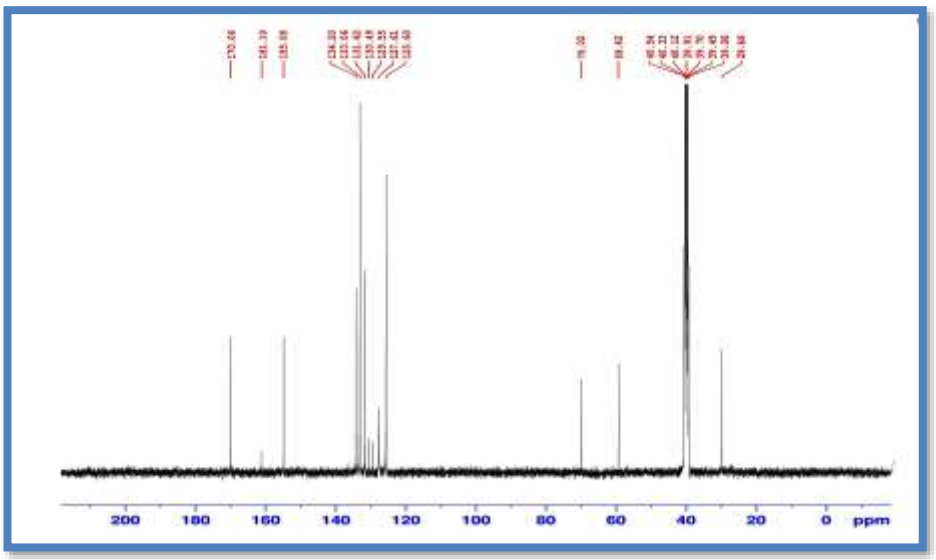


Figure 14: The ^{1}H-NMR spectrum of compound A9.

4.3. Assessment of the Biological Activity of the Synthesized Compounds

The prepared compounds demonstrated significant inhibitory efficacy against *Staphylococcus aureus* and notable inhibitory activity against *Escherichia coli*. As presented in **Table 9** and **Figure 15**, the relationship between concentration and inhibition was dose-dependent, with higher inhibition percentages observed at a concentration of 75 mg/mL.

Table 9: Biological activity of some prepared compounds

Comp. No.	*Escherichia coil*			*Staphylococcus aureus*		
Conc. mg/ml	25	50	75	25	50	75
A_4	0	2	5	1	3	5
A5	0	0	1	1	1	2
A6	0	1	2	0	0	1
A7	0	1	1	0	2	2
A8	0	0	0	1	1	2
Amoxicillin	2	4	5	2	5	7
Ampicillin	2	3	5	2	4	6
Ciprofloxacin	1	2	5	2	3	5
Blank disk	0	0	0	0	0	0

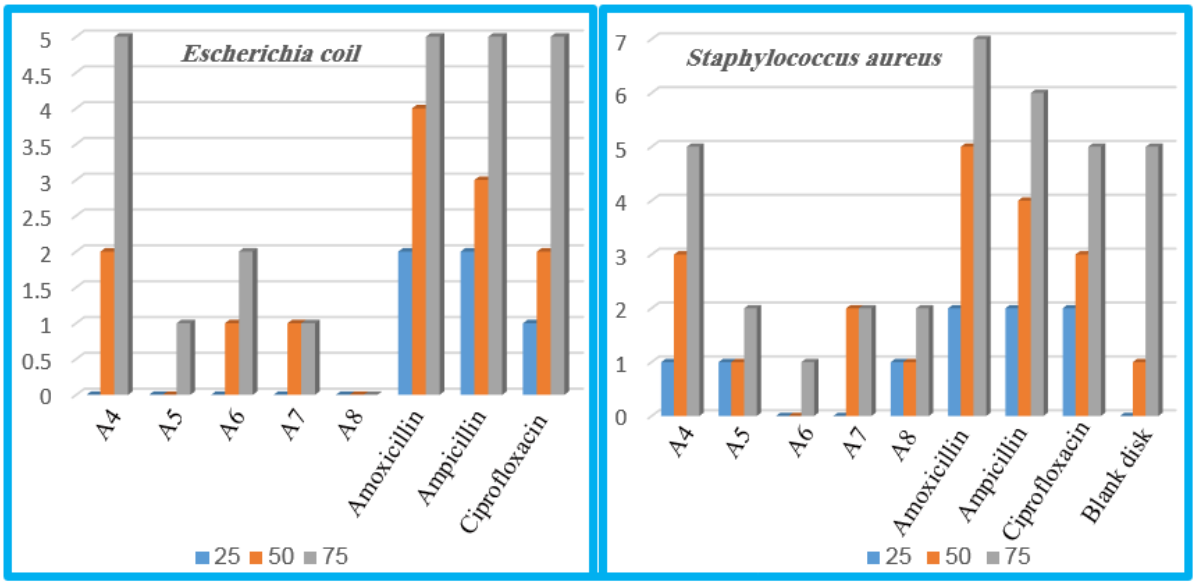


Figure 15: Inhibitory activity values of the prepared compounds (A4-A8) *against E. coil* and *S. aureus*

4.4. Strengths and Weaknesses of this Study

This study effectively demonstrates the synthesis and characterization of novel Quinazoline-4-one derivatives using a well-structured multi-step approach. The methodology employed is efficient and reproducible, leading to high-yield products. Comprehensive characterization techniques, including FT-IR, ^{1}H-NMR, and ^{13}C-NMR spectroscopy, confirm the structural integrity of the synthesized compounds. Additionally, the antibacterial evaluation against Escherichia coli and Staphylococcus aureus provides valuable insight into their potential pharmaceutical applications, highlighting the impact of functional groups on biological activity.

However, the study has some limitations. The biological evaluation is restricted to antibacterial testing, leaving other potential pharmacological properties, such as antifungal and anticancer activities, unexplored. Moreover, the study lacks an in-depth analysis of the mechanism of action of the synthesized compounds, which could be investigated through computational modeling and enzyme inhibition studies. Another limitation is the absence of a comparative analysis with commercially available antibiotics or previously reported Quinazoline-4-one derivatives, which would strengthen the justification for their pharmaceutical relevance. Additionally, the research does not provide an optimization study for reaction conditions, such as solvent choice and temperature variations, which could further enhance the efficiency of the synthesis. Overall, while this study successfully demonstrates the synthesis and biological potential of Quinazoline-4-one derivatives, further research is needed to expand their pharmacological evaluation, understand their mechanisms of action, and optimize the synthetic process for better efficiency.

5. Conclusion

The study successfully synthesized novel Quinazoline-4-one derivatives using hydrazones as intermediates. The reaction conditions were optimized to achieve high-yield products, with melting points confirming their purity. The biological evaluation of the synthesized compounds demonstrated significant antibacterial activity. The inhibition zone measurements revealed that compound A4 exhibited the highest activity against Escherichia coli (5 mm at 75 mg/mL) and Staphylococcus aureus (5 mm at 75 mg/mL), while A5 and A6 showed lower but notable activity. The presence of electron-withdrawing ($-NO_2$) and electron-donating ($-OCH_3$) groups influenced the biological activity, with nitro-substituted derivatives showing moderate inhibition. Overall, the synthesized Quinazoline-4-one derivatives exhibited promising antibacterial properties, suggesting their potential for further pharmaceutical applications. Future work should focus on expanding biological testing to explore their antifungal and anticancer potentials, as well as computational studies to better understand their interaction mechanisms at the molecular level.

6. References

[1] Katritzky AR, Ramsden CA, Joule JA, Zhdankin VV. Handbook of heterocyclic chemistry. Elsevier; 2010 Aug 24.

[2] Al-Khazraji SI, Ahamed LS, Ali RA. Synthesis and Characterization of some new heterocyclic derivatives from aromatic carbonyl compounds and carboxylic acids with Evaluation some

of them for biological activity. Iraqi Journal of Science. 2024 Apr 30:1855-https://doi.org/10.24996/ijs.2024.65.4.6

[3] de Oliveira Carneiro Brum J, França TC, LaPlante SR, Villar JD. Synthesis and biological activity of hydrazones and derivatives: A review. Mini reviews in medicinal chemistry. 2020 Mar 1;20(5):342-68. https://doi.org/10.2174/1389557519666191014142448

[4] Smith J, Doe R, Brown A. Hydrazones as prodrugs: applications in targeted drug delivery. Journal of Medicinal Chemistry. 2020;63(5):1234-1245.

[5] Jones P, Brown T. Hydrazones in catalysis: recent advances and future perspectives. Chemical Reviews. 2019;119(15):8765-8787.

[6] Zhang L, Wang Y, Chen X. Hydrazones as ligands in asymmetric catalysis: recent progress and future directions. Advanced Synthesis & Catalysis. 2021;363(8):1987-2005.

[7] Fischer E. Untersuchungen über Triphenylmethanfarbstoffe Hydrazine und Indole. 1924th ed. Bergmann M, editor. Berlin, Germany: Springer; 2013.

[8] Jabeen M. A comprehensive review on analytical applications of hydrazone derivatives. Journal of the Turkish Chemical Society Section A: Chemistry. 2022;9(3):663-98. https://doi.org/10.18596/jotcsa.1020357

[9] Dewick PM. Medicinal Natural Products: A Biosynthetic Approach. 3rd ed. Hoboken, NJ: Wiley-Blackwell; 2009.

[10] Wiklund P, Bergman J. The chemistry of anthranilic acid. Current Organic Synthesis. 2006 Aug 1;3(3):379-402. https://doi.org/10.2174/157017906777934926

[11] Mason JJ. Synthetic studies of heterocyclic natural products. Karolinska Institutet (Sweden); 2009.

[12] Kumar P, Tomar V, Joshi RK, Nemiwal M. Nanocatalyzed synthetic approach for quinazoline and quinazolinone derivatives: A review (2015–present). Synthetic Communications. 2022 Mar 19;52(6):795-826.
https://doi.org/10.1080/00397911.2022.2041667

[13] Ragipindi AR, Vanka KR, Bhavani R, Bhavani B. Synthesis and antibacterial activity of some novel hydrazone derivatives of anthranilic acid. World Journal of Pharmaceutical Research. 2015 Aug 20;4(11):1219-29.

[14] Tokalı FS, Taslimi P, Taskin-Tok T, Karakuş A, Sadeghian N, Gulçin İ. Novel hydrazones derived from anthranilic acid as potent cholinesterases and α-glycosidase inhibitors: Synthesis, characterization, and biological effects. Journal of Biochemical and Molecular Toxicology. 2024 Jan;38(1):e23521. https://doi.org/10.1002/jbt.23521

[15] Parashar B, Punjabi PB, Gupta GD, Sharma VK. Synthesis of some novel N-arylhydrazone derivatives of N-phenyl anthranilic acid. Int. J. ChemTech Res. 2009;1:1022-5..

[16] Jangam SS, Wankhede SB, Chitlange SS. Molecular docking, synthesis and anticonvulsant activity of some novel 3-(2-substituted)-4-oxothiazolidine-3-yl)-2-phenylquinazoline-4 (3 H)-ones. Research on Chemical Intermediates. 2019 Feb 15;45(2):471-86. https://doi.org/10.1007/s11164-018-3612-9

[17] Bhat M, Belagali SL, Mamatha SV, Sagar BK, Sekhar EV. Importance of quinazoline and quinazolinone derivatives in medicinal chemistry. Studies in Natural Products Chemistry. 2021 Jan 1;71:185-219. https://doi.org/10.1016/B978-0-323-91095-8.00005-2

[18] Kshirsagar UA, Mhaske SB, Argade NP. Hexamethyldisilazane-iodine induced intramolecular dehydrative cyclization of diamides: a general access to natural and unnatural quinazolinones. Tetrahedron letters. 2007 Apr 30;48(18):3243-6. https://doi.org/10.1016/j.tetlet.2007.03.032

[19] Mermer A, Keles T, Sirin Y. Recent studies of nitrogen containing heterocyclic compounds as novel antiviral agents: A review. Bioorg Chem [Internet]. 2021;114(105076). https://doi.org/10.1016/j.bioorg.2021.105076

[20] El-Badry YA, El-Hashash MA, Al-Ali K. Synthesis of bioactive quinazolin-4 (3H)-one derivatives via microwave activation tailored by phase-transfer catalysis. Acta Pharmaceutica. 2020 Jun 30;70(2):161-78. https://doi.org/10.2478/acph-2020-0001

[21] Abdelmonsef AH, Mosallam AM. Synthesis, in vitro biological evaluation and in silico docking studies of new quinazolin-2, 4-dione analogues as possible anticarcinoma agents. Journal of Heterocyclic Chemistry. 2020 Apr;57(4):1637-54. https://doi.org/10.1002/jhet.3889

[22] Asif M. Chemical characteristics, synthetic methods, and biological potential of quinazoline and quinazolinone derivatives. International journal of medicinal chemistry. 2014;2014(1):395637. https://doi.org/10.1155/2014/395637

[23] Marzouk MI, Shaker SA, Farghaly TA, El-Hashash MA, Hussein SM. Synthesis of some novel quinazolinone derivatives with anticipated biological activity. Journal of Heterocyclic Chemistry. 2017 Nov;54(6):3331-41. https://doi.org/10.1002/jhet.2953

[24] Dehbi O, Riadi Y, Geesi MH, Anouar EH, Ibnouf EO, Azzallou R. Synthesis, Characterization, Antibacterial Evaluation, and Molecular Docking of New Quinazolinone-Based Derivatives. Polycyclic Aromatic Compounds. 2023 Feb 7;43(2):1879-87. https://doi.org/10.1080/10406638.2022.2041053

[25] Mikra C, Bairaktari M, Petridi MT, Detsi A, Fylaktakidou KC. Green Process for the Synthesis of 3-Amino-2-methyl-quinazolin-4 (3 H)-one Synthones and Amides Thereof: DNA Photo-Disruptive and Molecular Docking Studies. Processes. 2022 Feb 17;10(2):384. https://doi.org/10.3390/pr10020384

[26] Gatadi S, Lakshmi TV, Nanduri S. 4 (3H)-Quinazolinone derivatives: Promising antibacterial drug leads. European journal of medicinal chemistry. 2019 May 15;170:157-72. https://doi.org/10.1016/j.ejmech.2019.03.018

[27] Tokalı FS, Taslimi P, Tuzun B, Karakuş A, Sadeghian N, Gulçin İ. Novel Quinazolinone Derivatives: Potential Synthetic Analogs for the Treatment of Glaucoma, Alzheimer's Disease and Diabetes Mellitus. Chemistry & biodiversity. 2023 Oct;20(10):e202301134. https://doi.org/10.1002/cbdv.202301134