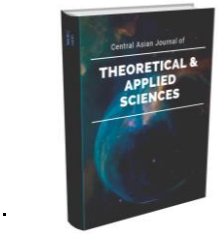

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*Article*

# Synthesis and Characterization of New Derivatives of 2,3-Dihydroquinazolin-4-one and Evaluation of their Antibacterial Activity

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**Abstract:** The present study included the synthesis of heterogeneous compounds of hydroquinazoline by reacting the prepared hydrazones with 2-aminophenol in the presence of ethanol as a solvent. The structures of the formed compounds were confirmed by physical and spectroscopic methods such as infrared spectra and proton and carbon nuclear magnetic resonance spectra (1H, 13C-NMR). The biological activity was evaluated using two types of bacterial isolates known for their resistance to antibiotics, namely Gram-negative Escherichia coli (Gram -ve) and Gram-positive Staphylococcus aureus (Gram +ve), and compared with the antibiotic as a control factor (Controls) Ciprofloxacin. The results showed good inhibitory activity for two types of used bacteria and high effectiveness and selectivity.

**Keywords:** Hydrazones, 2,3-Dihydroquinazolin-4-one, Biological activity.

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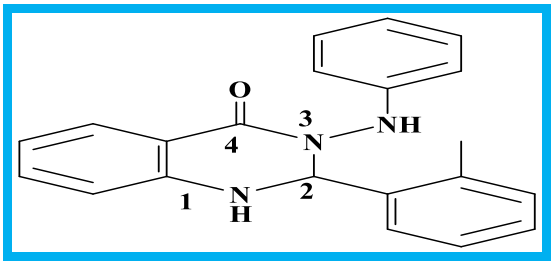
## 1. Introduction

**Heterocyclic** compounds are cyclic compounds that have at least one of three distinct types of atoms forming nitrogen, oxygen, and sulfur rings. A large proportion of them are composed of carbon atoms [1]. Heterocyclic compounds are used in medicine, drugs, polymer additives, and dyes. They are the building blocks of many pharmaceuticals. Heterocyclic compounds include many physiologically active substances including antibiotics [2]. **2,3-Dihydroquinazolin-4-one** They are hexagonal cyclic compounds containing two nitrogen atoms and a carbonyl group. When they contain a carbonyl group at the -4 position, they are called dihydroquinazoline -4-one, as shown in the figure below.



Hydroquinazoline compounds are of biological and medical importance and are closely related to medicinal chemistry. They are used to prepare many drugs, such as 1,2-dihydroquinazoline derivatives used as insecticides and bacterial inhibitors [4]. It has anti-inflammatory, central nervous system sedative, antidepressant and antibacterial effects [5], and can treat hepatitis virus infection [6].

## 2. Materials and Methods

Experimental

**Material**: Materials from Fluka, Oxford, and Aldrich were used in this study.

### Synthesis of 2,3-Dihydroquinazolin-4-one derivatives [$S_{23}$-$S_{27}$] [7,8]

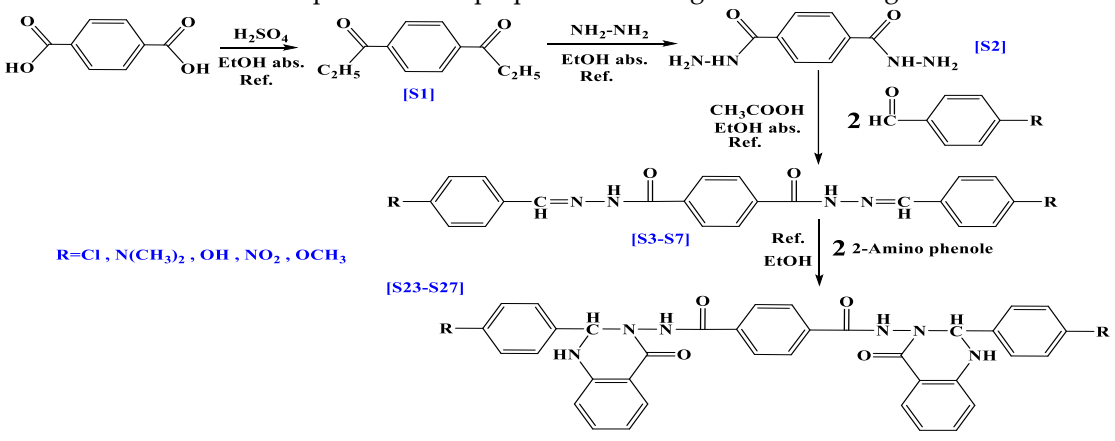
Dissolve (0.001 mol) hydrazone [S7-S3] in 15 mL of absolute ethanol, add (0.002 mol, 0.274 g) anthranilic acid dissolved in (20 mL) of absolute ethanol, stir the mixture (10-12 h) and confirm the reaction by TLC, cool the mixture, wash with sodium bicarbonate solution (10%), filter, wash with cold water and recrystallize with absolute ethanol to obtain the dried product. As in Table1

### Biological activity study

The medium and additional solutions are autoclaved for 15 minutes at 1.5 pressure and 121°C to sanitize them. An electric oven set to 180°C is used to sterilize the glassware required to prepare the culture medium and solutions for three hours. This procedure involves sterilizing the solutions impacted by high temperatures using membrane filters with 0.45 and 0.22 micron diameters[9–14]. The culture medium is made in accordance with the manufacturer's instructions, sterilized for fifteen minutes in an incubator, chilled, and then transferred onto a sterile Petri dish. The susceptibility of bacterial isolates to chemicals is tested using this medium[15–20]. Shape, size, color, texture, odor, lactose fermentation on pasta agar, mannitol fermentation on mannitol agar, and microscopic analysis following staining were among the features used to identify the isolates cultured on culture media. After that, Gram stain is seen using a light microscope with an oil-based lens at 100x magnification to see the bacterial cells' size, shape, and clumping behavior as well as how they respond to the stain[21–25].

## 3. Results

The derivatives of the compounds were prepared according to the following scheme:




**Scheme 1:** Path of the prepared compounds

### 3.1. Characterization of 2,3-Dihydroquinazolin-4-one derivatives (S23-S27)

When studying the infrared spectrum of 2,3-dihydroquinazoline derivatives, it was noted that the azomethine band disappeared and an absorption band appeared in the range (3351-3232) cm-1 due to the stretching of the (NH) bond, and the appearance of an absorption band in the range (3058-3028) cm-1 due to the stretching of the aromatic

(CH) bond, as well as the appearance of two absorption bands in the range (2949-2916) cm-1 and (2885-2840) cm-1 due to the stretching of the aliphatic (CH) bond, and an absorption band appeared in the range (1670-1654) cm-1 due to the stretching of the carbonyl bond (C=O) in 3,2-dihydroquinazoline ring, an absorption band appeared in the range (1647-1631) cm-1 due to the stretching of the amide (C=O) bond, as well as the appearance of two absorption bands in the range (1579-1533) cm-1 and (1502-1459) cm-1 due to the stretching of the aromatic (C=C) bond, and the appearance of an absorption band in the range (1269-1224) cm-1 due to the stretching of the (C-N) bond[26] . as in Table 2 and Figure1,2 When studying the 1H-NMR spectrum of the compound [S25] using the solvent (DMSO-d6), a single signal was observed at the chemical shift (5.45) ppm attributed to the protons of the (C-H) group and numbered (8) in the hexagonal ring, and the spectrum showed the appearance of a single signal at the chemical shift (5.98) ppm attributed to the proton of the (N-H) group in the formed hexagonal ring and numbered (7), and the spectrum showed multiple signals at the chemical shifts (6.87-7.77) ppm attributed to the (C-H-Ar) group numbered (5,1,6,9,3,4,10) respectively, and a single signal at the chemical shift (9.92) ppm attributed to the protons of the (OH) group and numbered (11), and a single signal at the chemical shift (11.78) ppm attributed to To the proton of the amide group (N-H) and numbered (2), and a signal at chemical shift (2.49) ppm was attributed to the protons of the solvent (DMSO-d6) . As shown in Figure 3 When studying the 13C-NMR spectrum of the compound [S25], a signal was observed at the chemical shift (71.74) parts per million, which was attributed to the (C-H) group numbered (5) in the formed hexagonal ring. The spectrum also showed signals at the chemical shifts (160.34, 149.16, 145.21, 136.68, 135.96, 129.46, 128.15, 127.44, 125.50, 124.08, 120.44, 116.30) parts per million, which were attributed to the carbon atoms of the benzene ring (C-H-Ar) numbered (15, 10, 12, 2, 8, 5, 13, 1, 6, 7, 14, 9), respectively. The appearance of a signal at the chemical shift (165.63) ppm is due to the (C=O) group numbered (4) in the formed hexagonal ring, and a signal appeared in the spectrum at the chemical shift (162.60) ppm due to the carbon atom of the (C=O) group numbered (3), in addition to the appearance of a multiple signal in the range (40.62-39.36) ppm which is due to the carbon atoms of the solvent (DMSO-d6) . As shown in Figure 4

### 3.2. Evaluation of the biological effectiveness of the prepared compound

Some of the compounds prepared in this study were tested against two types of flexible bacteria: Staphylococcus aureus (Gram-positive bacteria) and Escherichia coli (Gram-negative bacteria)[27-30]. The test was performed on Petri dishes by diffusion method. Concentrations of some compounds (0.1, 0.01, 0.001 mg/ml) were prepared in Petri dishes using Mueller-Hunten agar medium, the diameter of the inhibition zone was measured in centimetres and the results were compared with the antibiotic ciprofloxacin [31-33] for comparison, for example. Compound S24 has the highest inhibitory effect on E. coli, with an inhibitory diameter of (1.5) cm, while compound S27 has the highest inhibitory effect on Staphylococcus aureus, with a diameter of (4.5) cm [34-35] . As in Table 3 and Figures 6 and 7

**Table 1 :** Physical Properties of the Prepared Compounds

| Comp. No. | R | Molecular Formula/ M.Wt g/mol | Color | M.P. | R.T hour | $R_f$ | Yield(%) |
|---|---|---|---|---|---|---|---|
| **S23** | Cl | $C_{36}H_{26}Cl_2N_6O_4$ 677 | Off white | 320-322 | 10 | 0.87 | 71 |
| **S24** | $N(CH_3)_2$ | $C_{40}H_{38}N_8O_4$ 694 | Drak yellow | 306-308 | 10 | 0.90 | 76 |
| **S25** | OH | $C_{36}H_{28}N_6O6$ 640 | Off white | 299-301 | 12 | 0.91 | 55 |
| **S26** | $NO_2$ | $C_{36}H_{26}N_8O_8$ 698 | Light Brown | 267-269 | 10 | 0.82 | 65 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **$S_{27}$** | $OCH_3$ | $C_{38}H_{32}N_6O_6$ 668 | White | 313-315 | 11 | 0.72 | 64 |

**Table 2 :** FT-IR Spectrum of the Prepared Compounds

| Comp. No. | R | IR (KBr) $cm^{-1}$ νN-H | νC-H Aliph. | νC=O νC=O | νC=C Arom. | νC-H Arom. | νC-N | Others |
|---|---|---|---|---|---|---|---|---|
| **$S_{23}$** | Cl | 3297<br>3245 | 2916<br>2840 | 1669<br>1644 | 1566<br>1485 | 3058 | 1231 | ν (C- Cl) 771 |
| **$S_{24}$** | $N(CH_3)_2$ | 3308<br>3256 | 2943<br>2885 | 1668<br>1647 | 1579<br>1482 | 3036 | 1250 | --- |
| **$S_{25}$** | OH | 3351<br>3238 | 2936<br>2860 | 1654<br>1631 | 1553<br>1459 | 3028 | 1241 | ν (OH) 3382 |
| **$S_{26}$** | $NO_2$ | 3319<br>3232 | 2949<br>2874 | 1670<br>1639 | 1550<br>1502 | 3055 | 1224 | ν($NO_2$) *asy*. (1516)<br>*sym*. (1375) |
| **$S_{27}$** | $OCH_3$ | 3323<br>3259 | 2947<br>2866 | 1656<br>1633 | 1533<br>1489 | 3051 | 1269 | ν (C-O) 1344 |

**Table 3** : Inhibitory Activity of the Prepared Compounds on the Growth of a Number Gram-Negative and Gram-Positive Bacteria (Inhibition Diameter Measured ib cm)

| Comp. No. | E. Coil Conc. mg/ml | | | Staph. Aureus Conc. mg/ml | | |
|---|---|---|---|---|---|---|
| | 0.001 | 0.01 | 0.1 | 0.001 | 0.01 | 0.1 |
| **$S_{23}$** | 1.8 | 1.3 | 1.6 | 0.5 | 1.2 | 1.7 |
| **$S_{24}$** | 1 | 1.2 | 1.5 | 0.9 | 1.3 | 1.9 |
| **$S_{25}$** | 0.4 | 0.9 | 1.2 | 1.3 | 1.6 | 2. 5 |
| **$S_{26}$** | 0.2 | 1 | 1.3 | 1 | .16 | 2 |
| **$S_{27}$** | 0.5 | 0 | 0.7 | .05 | 3.5 | 4.5 |
| Ciprofloxacin | 2 | 2.5 | 3 | 2.1 | 2.8 | 3.4 |

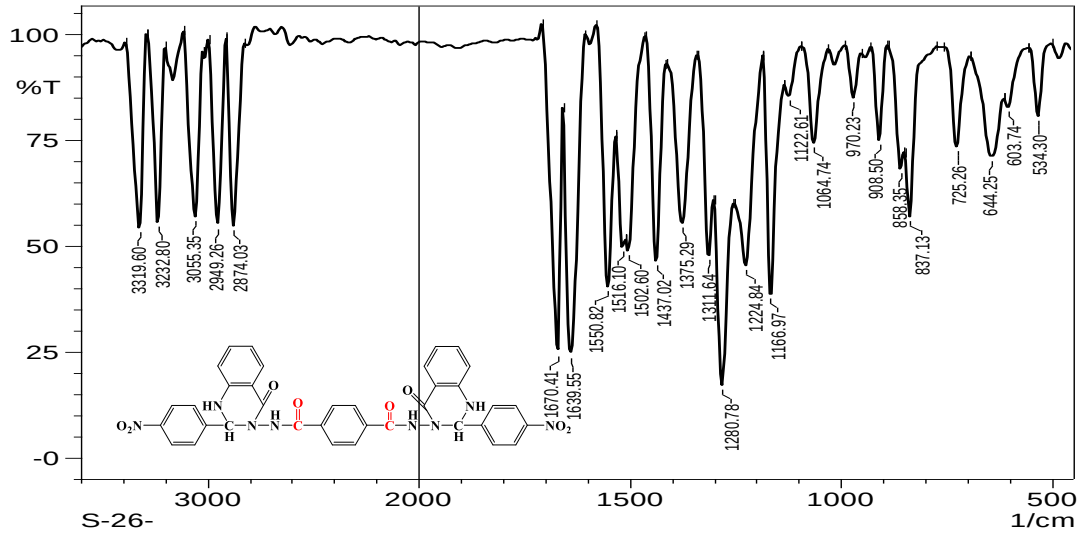



**Figure 1** : FT-IR of S26

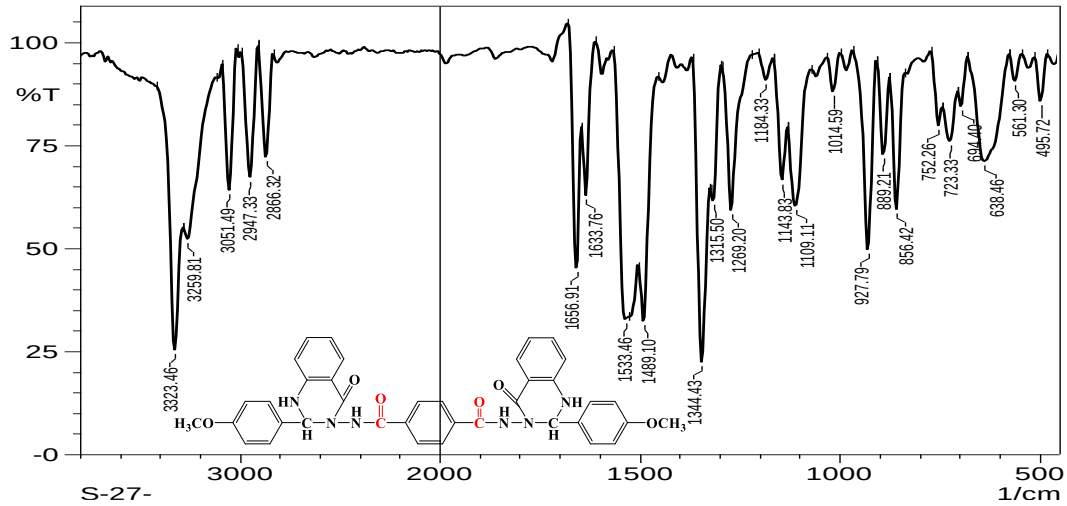



**Figure 2** : FT-IR of S27

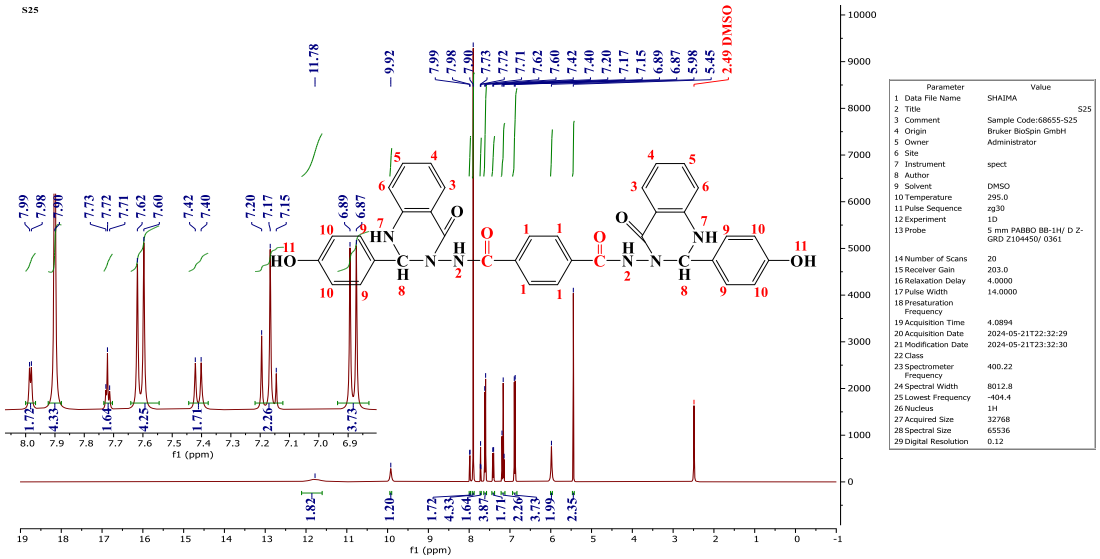



**Figure 3** : 1H-NMR of S25

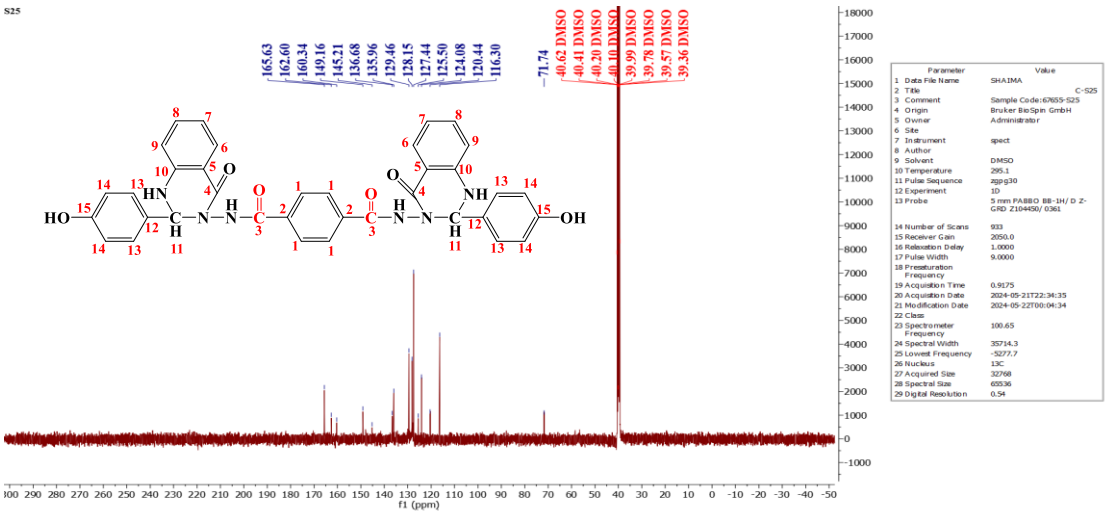



**Figure 4** : 13C-NMR of S25


**Figure 5** : Compounds (S27) have Inhibitory effect on Escherichia coli.

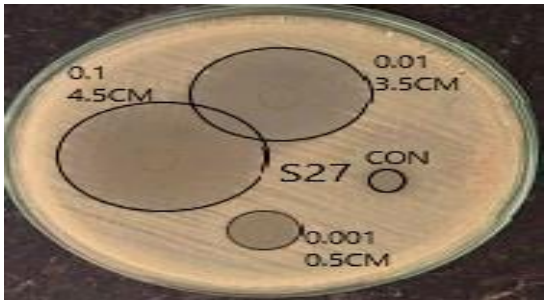



**Figure 6 :** Compounds (S27) have inhibitory effect Staphylococcus Aureus

## 4. Conclusion

The reaction of the (C=N) group in intermediates such as hydrazones with 2-aminophenol gives hexagonal rings of hydroquinoline precursors. These compounds showed good yields and high purity as confirmed by spectroscopic measurements such as infrared proton and carbon NMR spectra. They also showed high activity against the used bacteria compared to the used antibiotic .

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