

# CHEMISTRY & BIOLOGY INTERFACE

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## Synthesis, characterization and antimicrobial evaluation of N-(4-oxo-2phenyl/thiophenylquinazolin-3(4H)-yl)-1H-indole-2 or 3-carboxamide derivatives

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**Abstract:** A series of novel N-(4-oxo-2phenyl/thiophenylquinazolin-3(4H)-yl)-1H-indole-2 or 3-carboxamide derivatives were prepared and screened for their antimicrobial activities against different strains of bacteria and fungi. The most potent antibacterial and antifungal activity was exhibited by compound **5d** & **5h** with halogen substituted ring in the respective series compared to the compounds bearing other electron donating or withdrawing groups. The synthesized compounds were characterized with the help of spectroscopic techniques including IR, <sup>1</sup>H-NMR, <sup>13</sup>C-NMR and Mass spectra.

**Keywords:** Quinazolinone, carboxamide derivatives, antibacterial and antifungal activity

### Introduction:

Infectious diseases caused by microorganisms and their emergence to resistance pose a serious threat to present and future populations. [1-5] Thus there is an urgent need for new antimicrobial agents. Quinazolinone derivatives, one of the most active classes of compounds, possess a wide spectrum of biological activities [6-10] as antitumor [11-15], anti-inflammatory, [16-17] anticonvulsant, [18] antioxidants, [19] analgesic [20-22] and antimicrobial [23-30].

On the other hand, the indole framework represents a “privileged” structural motif commonly found in pharmaceutical drugs and natural products.[31] It is an important bicyclic heterocyclic nucleus and it is formed by the fusion of pyrrole and benzene ring at  $\alpha$ ,  $\beta$  position through sharing of one double bond [32-33]. Several substituted indole are reported in literature which show significant antibacterial, analgesic, anti-inflammatory, antipyretic, antitumor, anti-hypertensive, anti-depressant, antagonist, anti-emetic and antiviral

activity [34-40].

Looking to the medicinal importance of 4(3*H*)-quinazolinone and indole ring, we report both moieties in same molecule and try to develop potential bioactive hybrid molecules. The structures of the synthesized compounds were assigned on the basis of IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR, and Mass spectral data. These compounds were evaluated for their antifungal and antibacterial activity.

### Material and Method:

#### General Procedure:

All the reactions were monitored by thin layer chromatography over silica gel-G and basic alumina coated TLC plates and TLC was also performed using silica gel 60 F254 plates. The spot on TLC plates were developed by iodine vapours. The melting points were recorded on an electrically heated melting point apparatus and are uncorrected. IR spectra were recorded on Beckman Aculab-10, Perkin Elmer 881 and FT IR 8210 PC, Shimadzu spectrophotometers either on KBr discs or in neat and values are expressed in cm<sup>-1</sup>. Nuclear Magnetic Resonance (NMR) spectra were recorded on either Bruker Advance DRX-300 MHz or Bruker DRX 200 FT spectrometers using TMS (0.0ppm) as an internal reference. Chemical shifts ( $\delta$  in ppm) were reported relative to solvent peak (CHCl<sub>3</sub> in CDCl<sub>3</sub> at 7.23 ppm and DMSO in DMSO-*d*<sub>6</sub> at 2.49 ppm) or TMS. Signals were designated as follows: s, singlet; bs, broad singlet; d, doublet; dd, double doublet; t, triplet; m, multiplet and q, quartet. FAB mass spectra were recorded on JEOL SX 102/DA 6000 mass spectrometer using Argon/Xenon (6 KV, 10mA) as the FAB gas. EI mass spectra were recorded on JEOL JMS-D-300 spectrometer with ionization potential of 70 eV and ES mass on Quantro-II, micro mass.

#### Synthesis of 5-substituted Indol-2 or 3- methyl carboxylate (3)

On methylation of indole -2-carboxylic acid with methanol, sulphuric acid was added as acid catalyst. The reaction mixture was stirred at room temperature for 8-10 hrs. After completion of the reaction (Monitored by TLC), the solvent was evaporated on water bath and the crude product was obtained. It was purified by a column chromatography in a mixture of hexane and ethyl acetate (3:1). The solid crystalline compound obtained in good yield.

#### Synthesis of 5-substituted Indole-2 or 3-carbohydrazide (4)

A mixture of 5-substituted Indol-2 or 3- methyl carboxylate (3) (0.01 mole) and hydrazine hydrate (0.01mole) in absolute ethanol, (30ml) was heated under reflux condition for 5-7 hrs. After completion of reaction (Monitored by TLC) the reaction mixture was cooled at room temperature, precipitated solid was recrystallized in absolute ethanol. The crystalline compound 5-substituted Indole-2 or 3-carbohydrazide (4) was obtained in good yield.

#### Synthesis of N-(4-oxo-2-phenylquinazolin-3(4*H*)-yl)-1*H*-indole-2-carboxamide (5a)

2-Phenyl-3,1-benzoxazin-4-(4*H*)-one **1** (0.5 mol) was treated with Indole-2-carbohydrazide (4) equimolar proportion of (0.5 mol) using ethanol (25 ml) as a solvent. The resulting reaction mixture was refluxed for 4-6 hrs, after completion of the reaction was (Monitoring by TLC), the excess of solvent was distilled off on rotavapour and the resulting solid obtained was dried and recrystallized by rectified spirit, affording the corresponding compound (**5a**) as colourless crystalline solid in good yields.

Molecular Formula C<sub>23</sub>H<sub>16</sub>N<sub>4</sub>O<sub>2</sub>IR (KBr Solid), 3399, 3021, 1695, 1616, 1403, 1316, 1059; <sup>1</sup>H

NMR (300MHz, CDCl<sub>3</sub>):  $\delta$  7.26 (bs, 2NH), 7.53-7.60 (5H, m), 7.48 (1H, s), 7.70 (2H, d,  $J$  = 8.01 Hz), 7.85 (2H, t,  $J$  = 7.1 Hz), 8.25 (2H, d,  $J$  = 7.8 Hz), 8.32 (2H, dd,  $J$  = 7.2Hz), <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  117.2, 127.4, 127.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.7, 128.7, 128.9, 128.9, 130.4, 130.4, 132.8, 132.8, 136.7, 136.7, 136.7, 147.1, 147.1, 157.3, 159.8; MP 176-180 °C, ESMS:  $m/z$  381.2 [M + 1]<sup>+</sup> 380.

#### Synthesis of 2-(1*H*-indol-3-yl)-N-(4-oxo-2-phenylquinazolin-3(4*H*)-yl)acetamide(5b)

Molecular formula C<sub>24</sub>H<sub>18</sub>N<sub>4</sub>O<sub>2</sub>, IR (KBr Solid), 3360, 3025, 1680, 1520, 1433, 1320, 1050; <sup>1</sup>H NMR (300MHz, DMSO-d<sub>6</sub>):  $\delta$  4.05 (2H, s), 8.74 (1H, d  $J$  = 8.1, Hz), 8.08 (1H, d  $J$  = 7.8, Hz), 7.37 (2H, d  $J$  = 8.1, Hz), 7.57-7.70 (6H, m 5H Ar-H +1H indole ring), 7.52 (1H, t  $J$  = 7.8 Hz), 7.24 (1H, t,  $J$  = 9.0 Hz), 7.10 (1H, t,  $J$  = 7.2 Hz), 7.01 (1H, t,  $J$  = 7.2 Hz), 10.97 (2H, brs. NH) <sup>13</sup>C NMR (75 MHz, DMSO-d<sub>6</sub>):  $\delta$  51.9, 116.9, 118.8, 118.9, 120.3, 121.4, 121.5, 123.4, 124.5, 127.4, 129.0, 129.2, 129.4, 129.7, 131.1, 131.7, 132.6, 133.3, 134.9, 136.5, 141.6, 165.1, 167.7; MP 160-164 °C ESMS:  $m/z$  395.13 [M + 1]<sup>+</sup> 394.

#### Synthesis of 3-(1*H*-indol-3-yl)-N-(4-oxo-2-phenylquinazolin-3(4*H*)-yl)propanamide(5c)

Molecular formula C<sub>25</sub>H<sub>20</sub>N<sub>4</sub>O<sub>2</sub>, IR (KBr Solid), 3380, 3040, 1685, 1530, 1435, 1340, 1020; <sup>1</sup>H NMR (300MHz, DMSO-d<sub>6</sub>):  $\delta$  3.15 (2H, t  $J$  = 6.0 Hz), 3.6 (2H, t  $J$  = 6.0 Hz), 8.64 (1H, d  $J$  = 8.1Hz), 7.98 (1H, d  $J$  = 8.2 Hz), 7.47 (2H, d  $J$  = 7.6 Hz), 7.46-7.60 (6H, m 5H Ar-H +1H indole ring), 7.42 (1H, t  $J$  = 7.2 Hz), 7.14 (1H, t,  $J$  = 7.2 Hz), 6.95 (1H, t,  $J$  = 6.0 Hz), 6.88 (1H, t,  $J$  = 9.0 Hz), 11.97 (2H, brs. NH) <sup>13</sup>C NMR (75 MHz, DMSO-d<sub>6</sub>):  $\delta$  48.9, 115.9, 117.8, 117.9, 120.4, 121.5, 121.6, 123.7, 124.6, 128.3, 128.4, 129.2, 129.3, 129.6, 131.2, 131.8, 132.5, 133.4, 134.8, 134.9, 135.5, 140.6, 162.1, 164.7; MP 165-169 °C ESMS:  $m/z$  409.45 [M + 1]<sup>+</sup> 408.

#### Synthesis of 5-chloro-N-(4-oxo-2-phenylquinazolin-3(4*H*)-yl)-1*H*-indole-2-carboxamide(5d)

Molecular Formula C<sub>23</sub>H<sub>15</sub>ClN<sub>4</sub>O<sub>2</sub>IR (KBr Solid), 3410, 2990, 1702, 1616, 1503, 1320, 1070; <sup>1</sup>H NMR (300MHz, DMSO-d<sub>6</sub>):  $\delta$  7.50-7.64 (5H, m), 7.46 (1H, s), 7.76 (2H, d,  $J$  = 8.01Hz), 7.85(2H, t,  $J$  = 9.0Hz), 8.27(1H, d,  $J$  = 7.8Hz), 8.02 (1H, s) 8.23 (1H, dd,  $J$  = 7.2 Hz), 10.96 (2H, brs, NH) <sup>13</sup>C NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  116.6, 124.4, 124.7, 126.2, 126.6, 126.9, 127.5, 127.7, 127.8, 127.8, 128.8, 127.8, 131.6, 131.6, 132.5, 136.7, 136.7, 136.7, 144.2, 144.3, 148.3, 156.2, 162.3; MP 179-182 °C ESMS:  $m/z$  415.24 [M + 1]<sup>+</sup> 414.

#### Synthesis of N-(4-oxo-2-(thiophen-2-yl)quinazolin-3(4*H*)-yl)-1*H*-indole-2-carboxamide(5e)

2-(thiophen)-3,1-benzoxazin-4-(4*H*)-one **2** (0.5 mol) was treated with Indole-2-carbohydrazide (4) equimolar proportion of (0.5 mol) using ethanol (25 ml) as a solvent. The resulting reaction mixture was refluxed for 4-6 hrs, after completion of the reaction was (Monitoring by TLC), the excess of solvent was distilled off on rota vapour and the resulting solid obtained was dried and recrystallized by rectified spirit, affording the corresponding compound (**5e**) as colourless crystalline solid in good yield.

Molecular Formula C<sub>21</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub>S IR (KBr Solid), 3420, 2980, 1675, 1630, 1505, 1308, 1010; <sup>1</sup>H NMR (300MHz, DMSO-d<sub>6</sub>):  $\delta$  9.93 (2H, brs, NH), 8.19 (1H, d  $J$  = 9.0, Hz), 8.13 (1H, d  $J$  = 7.8, Hz), 7.83 (4H, t,  $J$  = 7.5 Hz, 2 Ar-H + 2 indole-H), 7.70 (1H, d  $J$  = 8.7 Hz, ), 7.50-7.39 (4H, m, 3H-thiophene +1H indole), 7.10 (1H, d  $J$  = 9.0, Hz) <sup>13</sup>C NMR (75 MHz, DMSO-d<sub>6</sub>):  $\delta$  114.0, 114.4, 121.0, 122.9, 122.9, 125.3, 126.2, 126.5, 127.6, 128.6, 129.2, 129.9, 129.9, 133.1, 133.1, 134.9, 148.8, 149.3, 152.4, 162.3, 163.0. MP 171-175 °C ESMS:  $m/z$

387.43 [M + 1]<sup>+</sup>386.

**Synthesis of 2-(1*H*-indol-3-yl)-N-(4-oxo-2-(thiophen-2-yl)quinazolin-3(4*H*)-yl)acetamide(5f)**

Molecular Formula C<sub>22</sub>H<sub>16</sub>N<sub>4</sub>O<sub>2</sub>S, IR (KBr Solid), 3420, 3120, 1675, 1545, 1450, 1316, 1105; <sup>1</sup>H NMR (300MHz, DMSO-d<sub>6</sub>): δ 10.83 (2H, brs, NH), 8.09 (1H, d *J* = 8.7, Hz), 7.98 (1H, d *J* = 9.0, Hz), 7.73 (4H, t, *J* = 7.2 Hz, 2 Ar-H+ 2 indole-H), 7.68 (1H, d *J* = 8.1 Hz, ), 7.58-7.43 ( 4H, m, 3H-thiophene +1H indole), 6.93. (1H, d *J* = 7.5, Hz) 3.81 (2H, s). <sup>13</sup>C NMR (75 MHz, DMSO-d<sub>6</sub>): δ 42.0, 112.4, 119.0, 121.9, 121.9, 124.2, 126.2, 126.3, 127.4, 128.6, 129.3, 129.7, 129.7, 133.3, 133.3, 134.8, 136.2, 147.6, 148.2, 156.4, 161.3, 162.0. MP 181-185 °C ESMS: m/z 401.45 [M + 1]<sup>+</sup>400.

**Synthesis of 3-(1*H*-indol-3-yl)-N-(4-oxo-2-(thiophen-2-yl)quinazolin-3(4*H*)-yl)propanamide(5g)**

Molecular Formula C<sub>23</sub>H<sub>16</sub>N<sub>4</sub>O<sub>2</sub>S, IR (KBr Solid), 3330, 3080, 1670, 1555, 1445, 1340, 1060; <sup>1</sup>H NMR (300MHz, DMSO-d<sub>6</sub>): δ 11.83 (2H, brs, NH), 8.43 (1H, d *J* = 9.0, Hz), 8.10 (1H, d *J* = 9.0, Hz), 7.87 (4H, t, *J* = 6.0 Hz, 2 Ar-H+ 2 indole-H), 7.62 (1H, d *J* = 9.0 Hz, ), 7.55-7.37(4H, m, 3H-thiophene +1H indole), 7.45 (1H, d *J* = 9.0, Hz) 2.62 (2H, t, *J* = 6.0 Hz), 3.11 (2H, t, *J* = 6.0 Hz). <sup>13</sup>C NMR (75 MHz, DMSO-d<sub>6</sub>): δ 44.1, 53.1, 113.4, 119.1, 120.8, 120.8, 123.4, 125.5, 125.8, 127.3, 127.3, 128.7, 128.7, 129.9, 132.3, 132.3, 133.8, 133.8, 135.1, 145.5, 157.3, 160.2, 164.0 MP 168-172 °C ESMS: m/z 415.28[M + 1]<sup>+</sup>414.

**Synthesis of 5-chloro-N-(4-oxo-2-(thiophen-2-yl) quinazolin-3(4*H*)-yl)-1*H*-indole-2-carboxamide(5h)**

Molecular Formula C<sub>21</sub>H<sub>13</sub>N<sub>4</sub>O<sub>2</sub>ClS IR (KBr Solid), 3268 NH, 3102(CH), 1706, 1432, 1460,

1208, 959 <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>): δ 7.58 (2NH, bs), 7.12-7.10 (m, 5H), 7.11 (s, 1H), 7.40 (d, *J* = 8.01 Hz, 2H), 7.10 (t, *J* = 9.00Hz, 2H), 7.83 (t, *J* = 7.1 Hz, 2H), 8.01 (m, 1H), 7.12 (dd, *J* = 7.2Hz, 1H), <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 111.8, 122.6, 123.4, 126.5, 126.5, 127.4, 127.4, 127.4, 128.7, 128.7, 128.7, 132.6, 132.6, 135.8, 135.8, 135.84, 146.3, 146.3, 149.2, 155.6, 166.3 MP 182-186 °C ESMS: m/z 421.17 [M + 1]<sup>+</sup>420.

**Biological evaluation:**

One of the purposes of the present work is to synthesize new heterocyclic compounds that might be of certain biological interest. All the newly synthesized quinazolinone derivatives were screened for their antimicrobial activity in vitro against various strains of microorganism to determine the “zone of inhibition” by Mueller - Hinton agar dilution methods (disc diffusion method). For antibacterial activity and antifungal activity streptomycin and fluconazole respectively, act as positive control however filter discs impregnated with 10μL of solvent (DMSO) were used as a negative control. Blank paper discs (Schleicher and Schuell, Spain) with a diameter of 8.0 mm were impregnated with 10μL of the tested concentration of the stock solutions. When a filter paper disc impregnated with a tested chemical is placed on agar, the chemical will diffuse from the disc into the agar. This diffusion will place the chemical in the agar only around the disc. The solubility of the chemical and its molecular size will measure the size of the area of chemical infiltration around the disc. If an organism is placed on the agar it will not grow in the area susceptible to the chemical around the disc. There is no growth around the disc; this area is known as “zone of inhibition” or “clear zone”. The zone inhibition diameters of disc diffusion were easily measured by slipping callipers of the National Committee for Clinical Laboratory Standards (NCCLS). The agar dilution method

is a very good alternative and faster method for antimicrobial activity in comparison to that of broth-based methods.

### Antibacterial Activity:

The in vitro antibacterial screenings of the newly synthesized compounds **5(a-h)** were individually performed against a panel of Gram positive bacteria (*Staphylococcus aureus*) and Gram negative bacteria (*E. coli* and *S. typhi*). The concentrations of 1mg/ml of tested samples were prepared by dissolving the compounds in DMSO and suspension of each sample spread on the nutrients agar medium. The plates were kept to stand at room temperature for two hours and then incubated. The organisms were grown in nutrient agar at 37 °C for 24 hours. Each sample was assayed in triplicate and the growth inhibition zones diameters were carefully measured in mm. The clear zone around the wells was measured as inhibition zones. The absence of a clear zone around the well was taken as inactivity.

### Antifungal Activity:

The antifungal activity of compounds **5(a-h)** was screened against *Candida albicans* by potato dextrose agar disk diffusion method and Fluconazole was used as standard drug. The test samples were dissolved in DMSO then 0.5 mL sample of each compound (1 mg/mL) plus 0.1 mL of the tested fungal suspension were mixed thoroughly with 20 mL of agar medium, which was maintained at 45°C. The inoculated medium was poured into sterile Petri-dishes, kept to solidify, and incubated at 25°C for seven days. Each sample was assayed in triplicate and the zone of inhibition was measured in millimetres.

### Result and Discussion:

#### Chemistry:

The devised synthetic route for the preparation of the final compounds **5a-h** is delineated in **scheme-1**. The reaction of anthranilic acid and benzoyl chloride or thiophene-2-carbonyl chloride in pyridine was carried out at reflux temperature to furnish **1** and **2** in quantitative yield (68%) and (65%) respectively. The compound **3** was obtained in moderate to good yield (77%) by the reaction of aromatic acids and methanol in presence of concentrate sulphuric acid at reflux temperature. The compound **4** was furnished by the reaction of compound **3** and hydrazine hydrate in ethanol at reflux temperature in quantitative yield (66%). The reaction of compound **4** and compound **1** or **2** in ethanol was carried out at reflux temperature to form **5** in good quantitative yield (74%). The aromatic acids were selected on the basis of their easy availability, low cost and their presence as substituent in various biologically active agents. The substitution patterns of R<sub>1</sub> and R<sub>2</sub> groups from **5a-h** are shown in **Table-1**. All the synthesized products were characterised by the IR, <sup>1</sup>H-NMR, <sup>13</sup>C-NMR and mass spectral data.

### 2.5 Synthesis N-(4-oxo-2phenyl/thiophenylquinazolin-3(4H)-yl)-1H-indole-2 or 3-carboxamide derivatives

The newly synthesized of N-(4-oxo-2phenyl/thiophenylquinazolin-3(4H)-yl)-1H-indole-2 or 3-carboxamide derivatives **5(a-h)** exerted important inhibitory activity against the growth of tested microorganism strains. The antibacterial antifungal data shown that all tested compounds of this investigation were found to exhibit moderate to good activity against all the tested pathogenic bacteria and Fungi as compared to the standard drug streptomycin and fluconazole respectively, presented in **Table-1**. The percentage zone of inhibition of all compounds **5(a-h)** were calculated by using following formula

$$\%I = \frac{\text{Control} - \text{Treatment(sample)}}{\text{Control}}$$

Scheme-1:

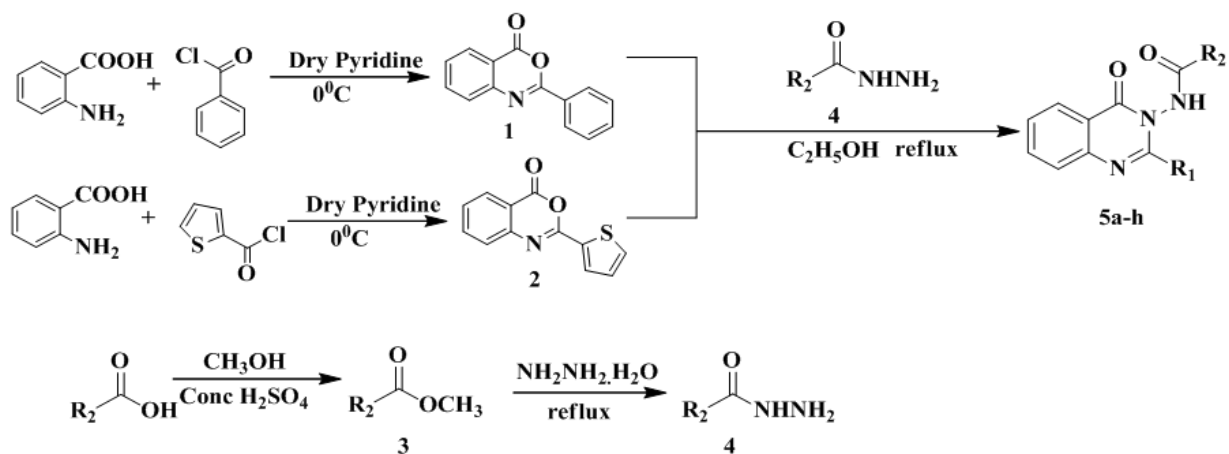


Table-1: Substitution Pattern of R groups in compound 5a-h.

| Compound 4 | R <sub>1</sub> Groups | R <sub>2</sub> Groups |
|------------|-----------------------|-----------------------|
| 5a         |                       |                       |
| 5b         |                       |                       |
| 5c         |                       |                       |
| 5d         |                       |                       |
| 5e         |                       |                       |
| 5f         |                       |                       |
| 5g         |                       |                       |
| 5h         |                       |                       |

The most potent antibacterial and antifungal activity was exhibited by compound **5d** & **5h** with halogen substituted ring in the respective series compared to the compounds bearing other electron donating or withdrawing groups. A close analysis of the screening results and structures of active compounds demonstrates that the halogen substitution of indole ring increased antimicrobial activity. The compound

**5d** & **5h** possesses active inhibition against all the tested strains and this may be attributed to the presence of chlorine in the compound. Hence, the replacement of 5-chloroindole nucleus by simple indole ring shows decrease in antimicrobial activity. Rest of the synthesized compounds exhibited moderate to good antimicrobial activity against all organisms.

**Table-1** Antibacterial and antifungal Activity of N-(4-oxo-2-phenyl/thiophenyl)quinazolin-3(4*H*)-yl)-1*H*-indole-2 or 3-carboxamide derivatives

| Sample                | Inhibition Zone(mm)    |                        |                         |    |
|-----------------------|------------------------|------------------------|-------------------------|----|
|                       | Bacteria               |                        | Fungus                  |    |
|                       | Gram Positive bacteria | Gram Negative bacteria | <i>Candida albicans</i> |    |
|                       | <i>S. aureus</i>       | <i>E. coli</i>         | <i>S. typhi</i>         |    |
| 5a                    | 14                     | 15                     | 09                      | 12 |
| 5b                    | 13                     | 08                     | 11                      | 08 |
| 5c                    | 12                     | 09                     | 08                      | 09 |
| 5d                    | 18                     | 20                     | 16                      | 17 |
| 5e                    | 16                     | 13                     | 13                      | 15 |
| 5f                    | 10                     | 12                     | 08                      | 09 |
| 5g                    | 08                     | 07                     | 06                      | 07 |
| 5h                    | 19                     | 18                     | 17                      | 16 |
| Control DMSO          | 00                     | 00                     | 00                      | 00 |
| Streptomycin(100 ppm) | 25                     | 25                     | 23                      | -  |
| Fluconazole 100 ppm   | -                      | -                      | -                       | 28 |

Con= 100 µg/ml of tested compound, 10µl was used for evaluation. For control 10µl each of streptomycin (100 µg/ml) and Fluconazole (100 µg/ml) was used. DMSO was used as control (10 µl).

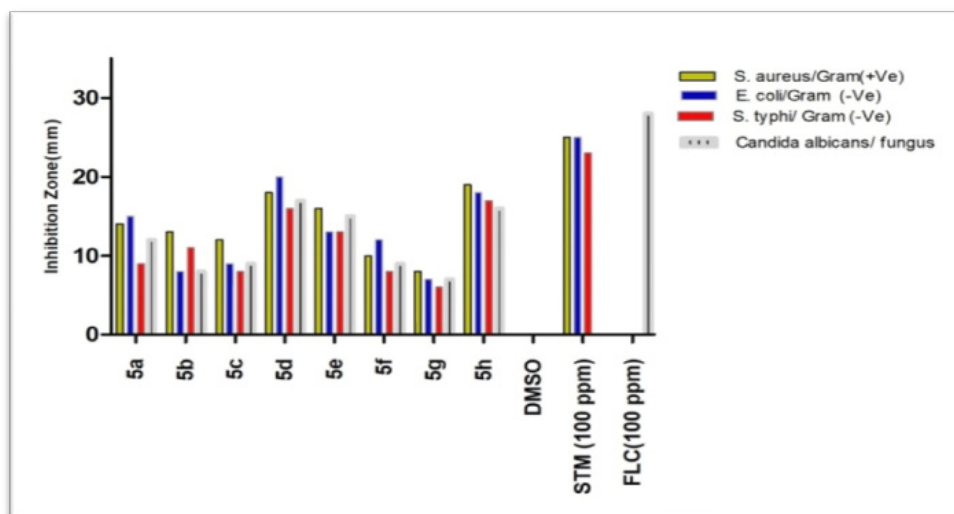


**Figure 1** The pictorial representation of antimicrobial activity of Quinazolinone derivatives **5(a-h)**

**Table-2** Antibacterial Activity of N-(4-oxo-2-phenyl/thiophenylquinazolin-3(4*H*)-yl)-1*H*-indole-2 or 3-carboxamide derivatives

| Compound              | % of Inhibition Zone(mm) |    |                |    |                 |    |
|-----------------------|--------------------------|----|----------------|----|-----------------|----|
|                       | <i>S. aureus</i>         | Sm | <i>E. coli</i> | Sm | <i>S. typhi</i> | Sm |
| 5a                    | 14                       |    | 15             |    | 09              |    |
| 5b                    | 13                       | 56 | 08             | 40 | 11              | 40 |
| 5c                    | 12                       | 52 | 09             | 32 | 08              | 48 |
| 5d                    | 18                       | 48 | 20             | 36 | 16              | 35 |
| 5e                    | 16                       | 72 | 13             | 80 | 13              | 70 |
| 5f                    | 10                       | 64 | 12             | 52 | 08              | 57 |
| 5g                    | 08                       | 40 | 07             | 48 | 06              | 35 |
| 5h                    | 19                       | 32 | 18             | 28 | 17              | 27 |
| Control DMSO          | 0                        | 76 | 0              | 72 | 0               | 74 |
| Streptomycin(100 ppm) | 25                       |    | 25             |    | 23              |    |

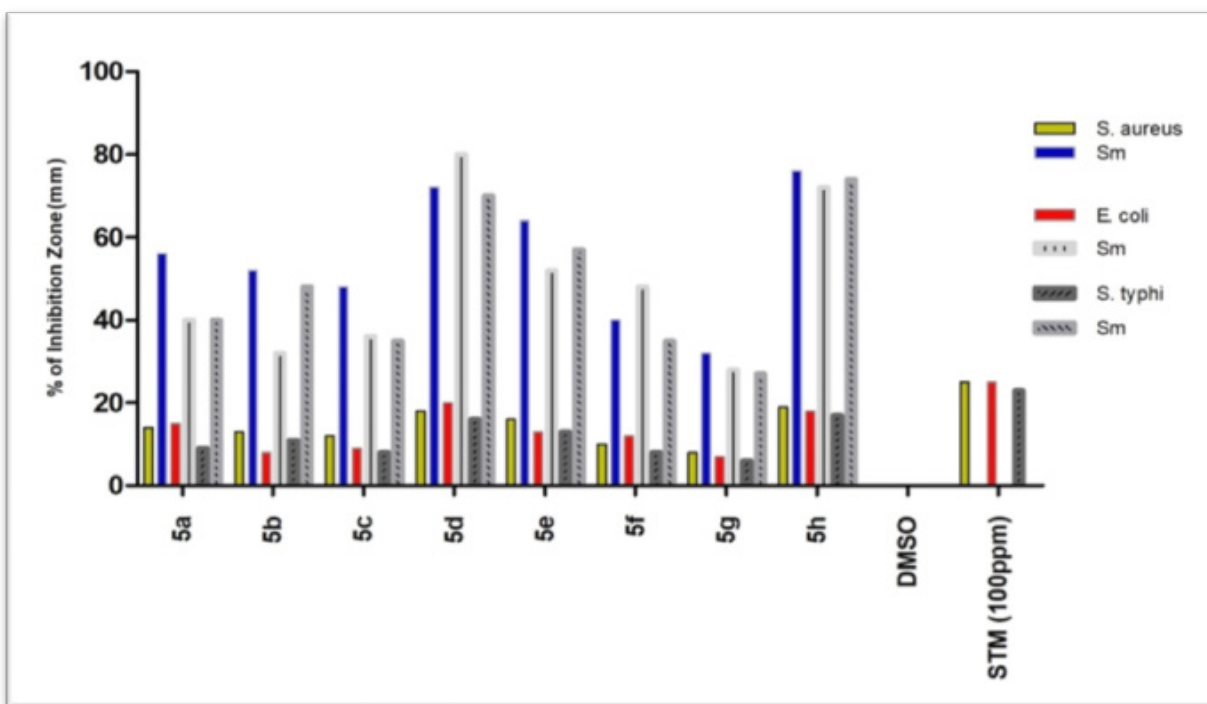
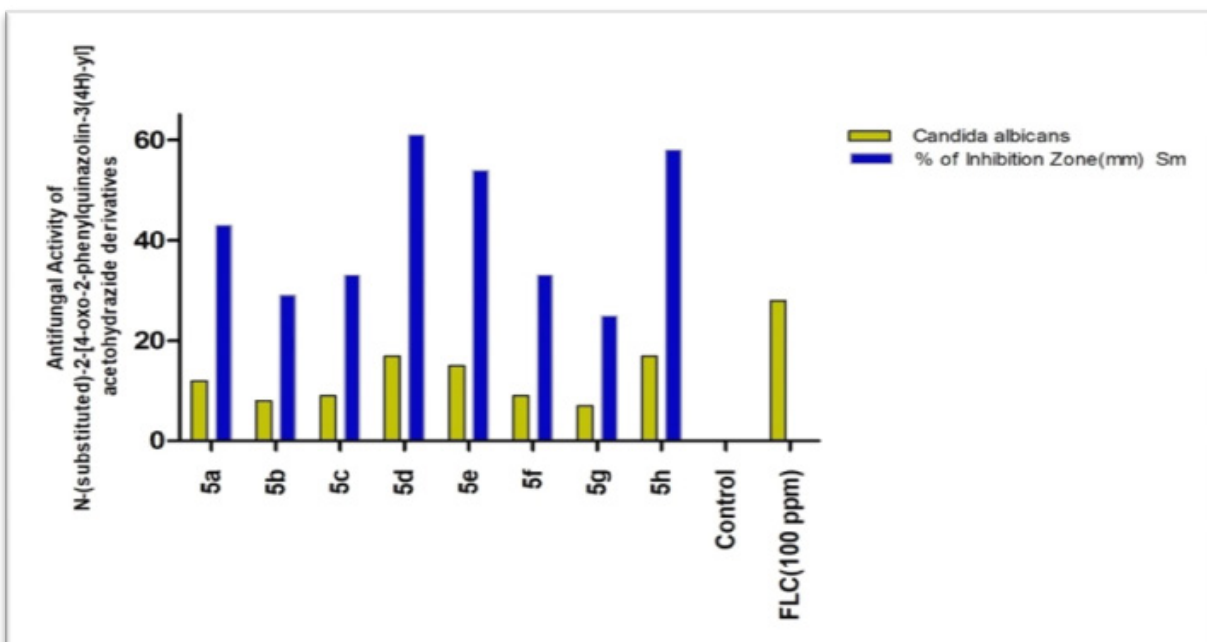
**Figure 2** The pictorial representation of antibacterial activity of Quinazolinone derivatives **5(a-h)**

**Table-3** Antifungal Activity of N-(4-oxo-2-phenyl/thiophenylquinazolin-3(4*H*)-yl)-1*H*-indole-2 or 3-carboxamide derivatives

| Compound            | <i>Candida albicans</i> | % of Inhibition Zone(mm) |
|---------------------|-------------------------|--------------------------|
|                     |                         | Fluconazole              |
| 5a                  | 12                      | 43                       |
| 5b                  | 08                      | 29                       |
| 5c                  | 09                      | 33                       |
| 5d                  | 17                      | 61                       |
| 5e                  | 15                      | 54                       |
| 5f                  | 09                      | 33                       |
| 5g                  | 07                      | 25                       |
| 5h                  | 17                      | 58                       |
| Control DMSO        | 0                       |                          |
| Fluconazole 100 ppm | 28                      |                          |

**Figure 3** The pictorial representation of antifungal activity of Quinazolinone derivatives **5(a-h)**

**Conclusion:**

The antimicrobial screening data represent that the newly synthesized compounds demonstrate moderately to good antimicrobial activities and it is significant to note that the new derivatives show more inhibitory effects than the original molecule (**1**). The new derivatives act as more powerful and potent bactericidal agents and fungicidal agents, thus killing more of the

bacteria and fungi than the original molecule (**1**). The  $\pi$ -electron delocalization over the new synthesized compounds raises the lipophilic character and favours its permeation through the lipid layer of the bacterial membranes. Due to their good biological activity, quinazolinone derivatives represent the rationale for the future development of new small molecules potentially useful as antimicrobial drugs.

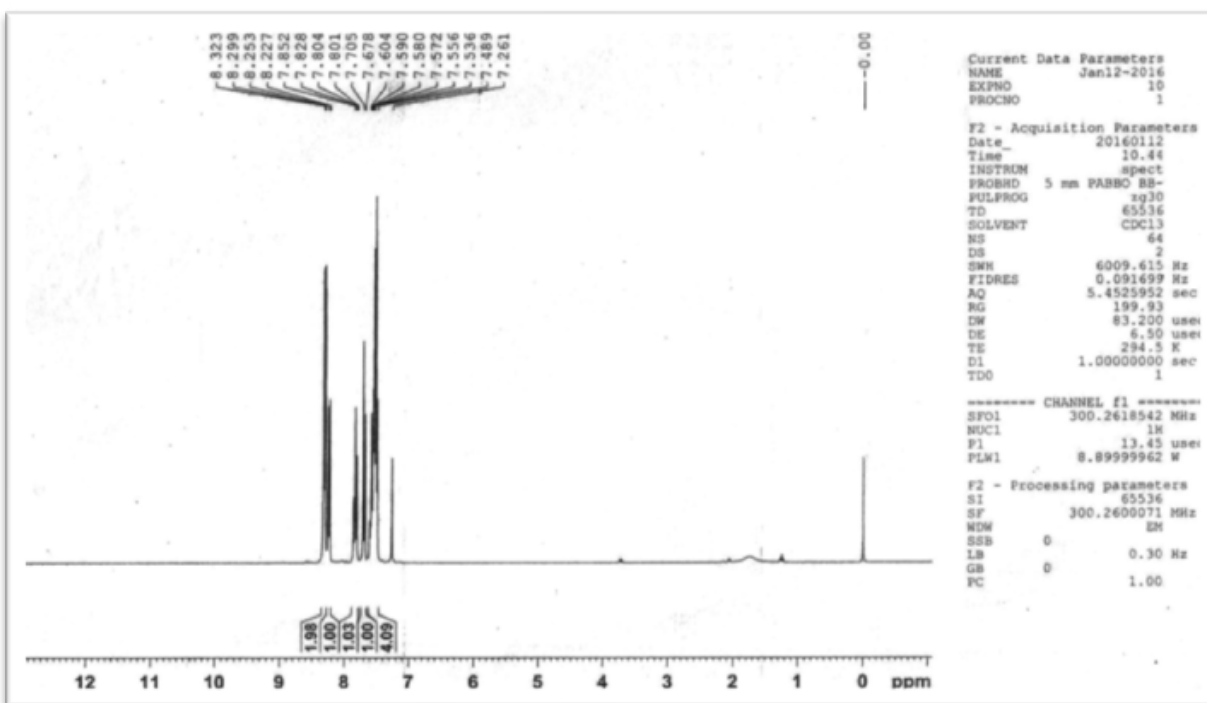
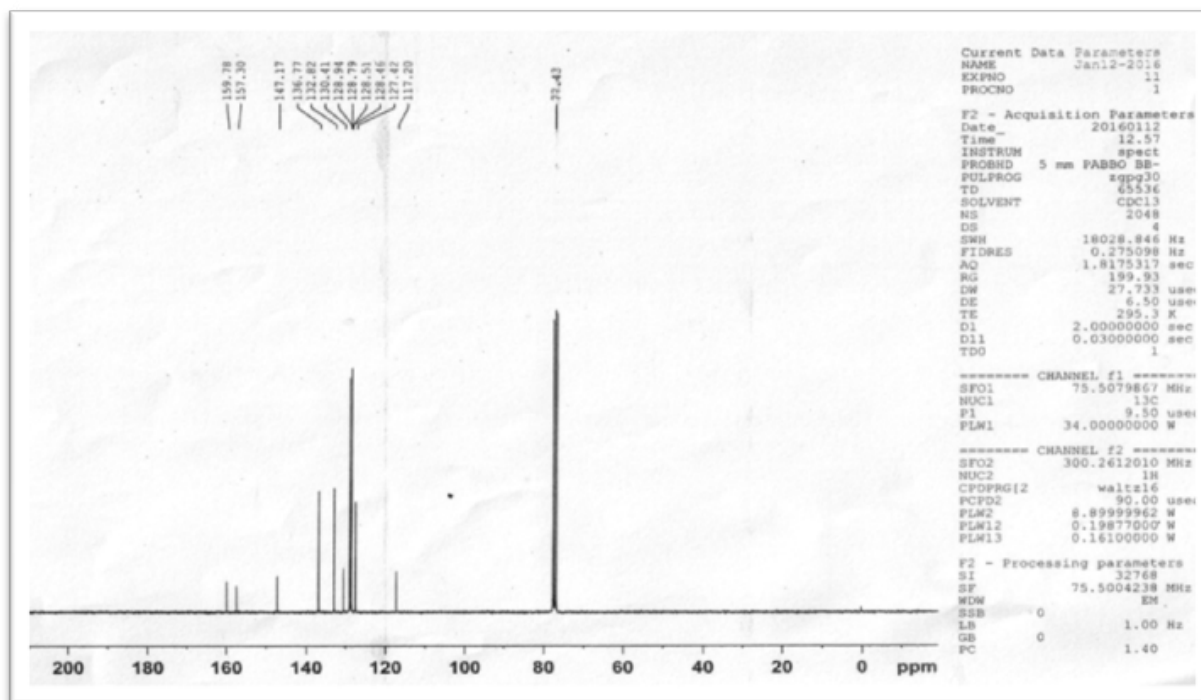
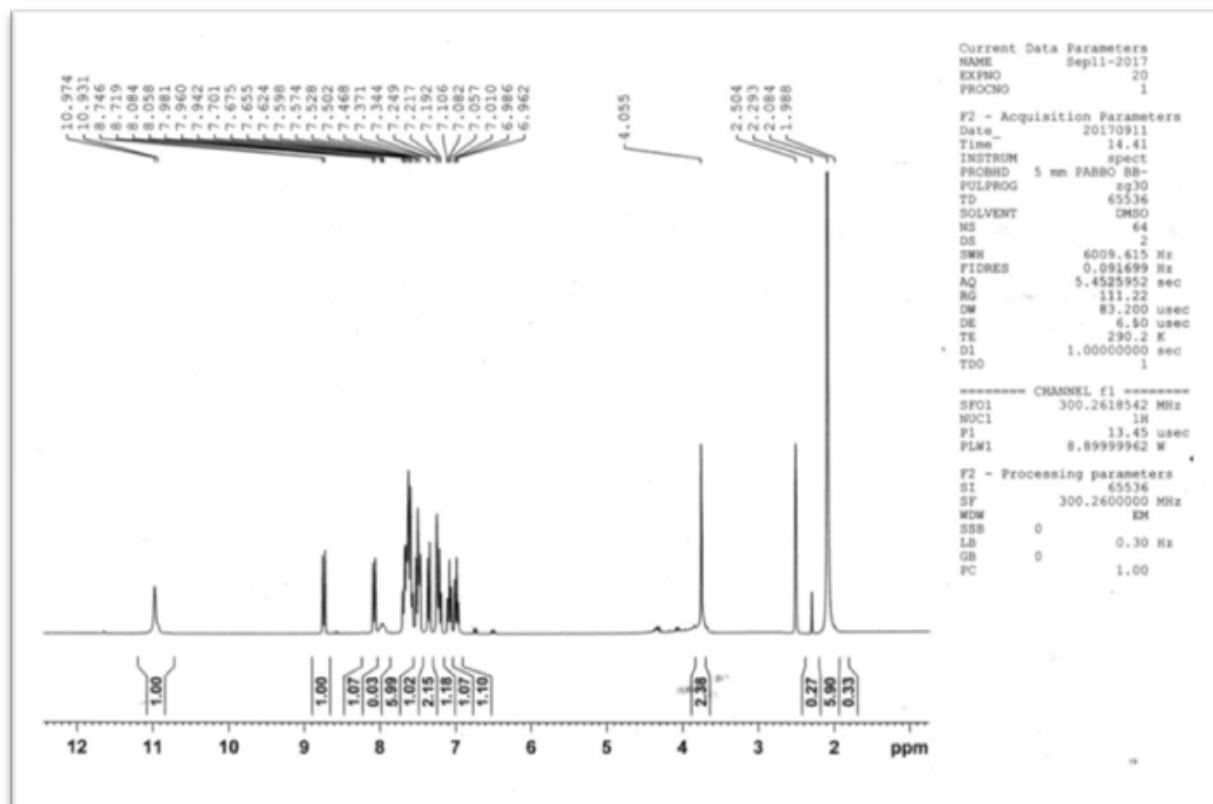
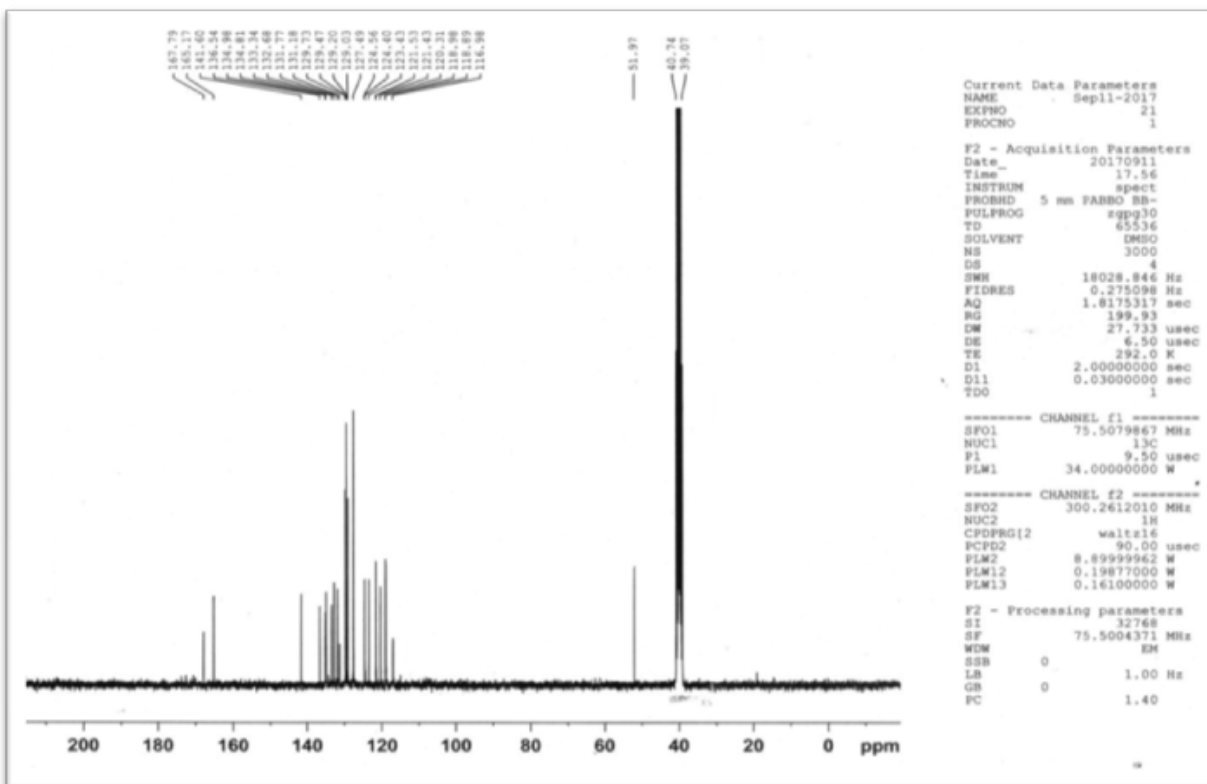
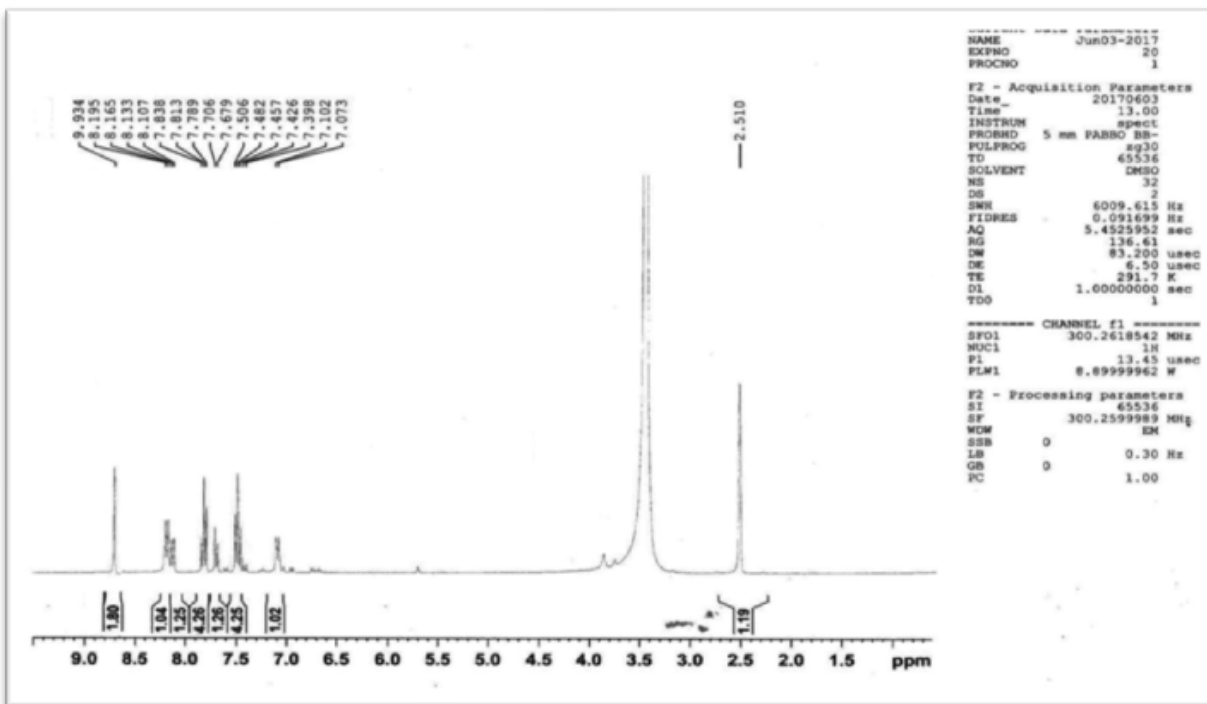
**Spectra of some selected compounds**

**Figure 1** Experimental  $^1\text{H}$  NMR spectrum of (**5a**) in  $\text{CDCl}_3$  solvent

Figure 2 experimental  $^{13}\text{C}$  NMR spectrum of (5a) in  $\text{CDCl}_3$  solventFigure 3 Experimental  $^1\text{H}$  NMR spectrum of (5b) in  $\text{DMSO-d}_6$  solvent

Figure 4 experimental  $^{13}\text{C}$  NMR spectrum of (5b) in DMSO- $d_6$  solventFigure 5 Experimental  $^1\text{H}$  NMR spectrum of (5b) in DMSO- $d_6$  solvent

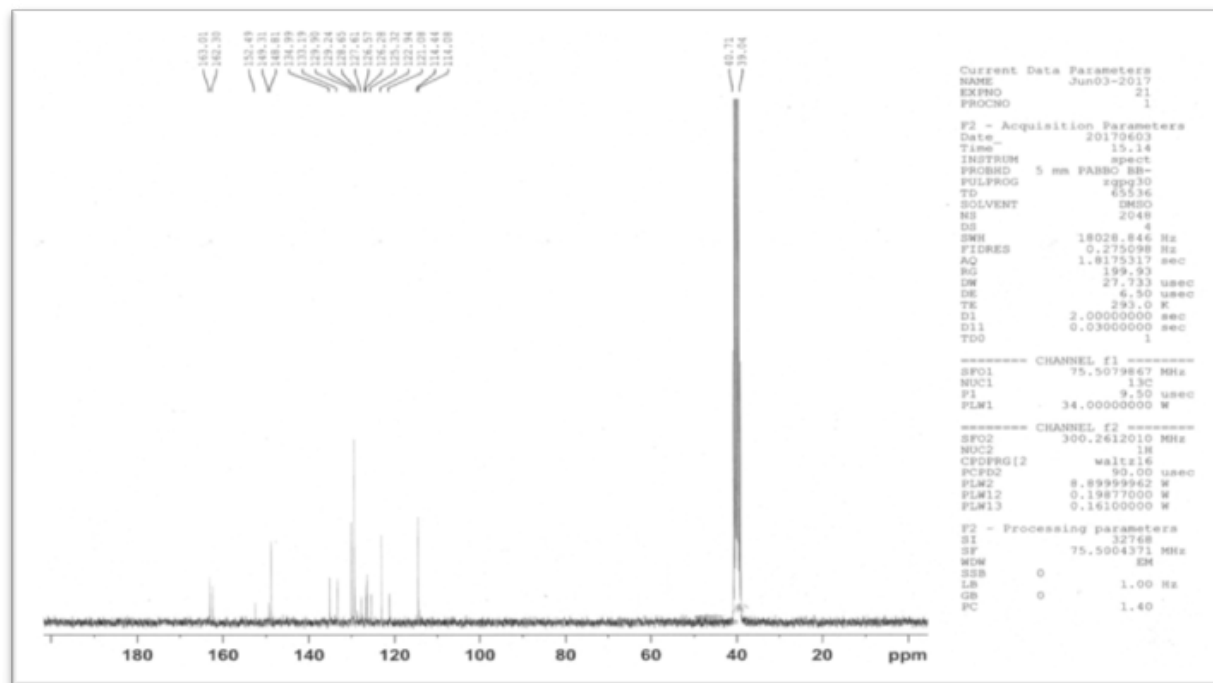


Figure 6 experimental  $^{13}\text{C}$  NMR spectrum of (5b) in DMSO- $d_6$  solvent

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