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# THE BIOLOGICAL ASSESSMENT AND SYNTHESIS OF NOVEL N-HETEROCYCLIC CARBENE DERIVATIVES

A. M. Shirode<sup>1</sup>, P. R. Kamble<sup>2</sup>**Article History: Received: 10.05.2023****Revised: 29.05.2023****Accepted: 09.06.2023****Abstract**

Nitrogen-based compounds 4(3H)-quinazolinone and imidazole have a heterocyclic skeleton and a variety of biological functions, such as fungicidal, anticonvulsant, antibacterial, anticancer, antimalarial, and anti-inflammatory properties. The research into novel therapeutics based on the quinazolinone containing Imidazolium-based Metal N-Heterocyclic Carbene analogues core accelerated. The most significant breakthroughs in the synthesis of quinazolinone containing Imidazolium-based Metal N-Heterocyclic Carbene analogues, a scaffold that is highly valued for its therapeutic potential in the treatment of a number of ailments produced a range of promising outcomes. Novel quinazolinone-containing Imidazolium-based Metal N-Heterocyclic Carbene analogues have been produced, spectrum data was used to characterize it, and they have been investigated for their effectiveness as antibacterial agents against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, and *Pseudomonas aeruginosa*, as well as their antifungal activity against *Candida albicans* and *Aspergillus niger*. However, the same group of compounds also demonstrated strong in vitro antifungal activity against *Candida albicans* and *Aspergillus niger*. Compounds TM4a and TM4g showed good antibacterial activity in vitro against *S. aureus*, *B. subtilis*, *E. coli*, and *P. aeruginosa*.

**Keywords:** 4(3H)-quinazolinone, Imidazolium based Ionic liquids, N- Heterocyclic Carbene analogues.

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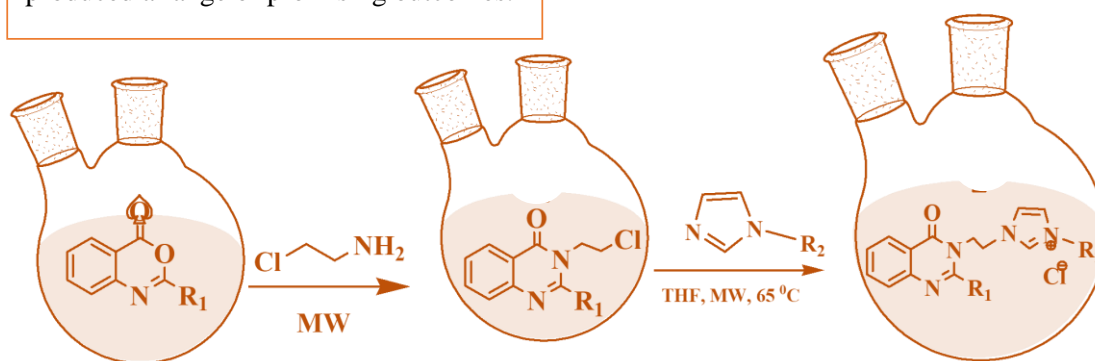
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# NOVEL N-HETEROCYCLIC CARBENE

The most significant breakthroughs in the synthesis of quinazolinone containing Imidazolium-based Metal N-Heterocyclic Carbene analogues, a scaffold that is highly valued for its therapeutic potential in the treatment of a number of ailments produced a range of promising outcomes.

Heterocyclic skeleton and a variety of biological functions, such as fungicidal, anticonvulsant, antibacterial, anticancer, antimalarial, and anti-inflammatory properties

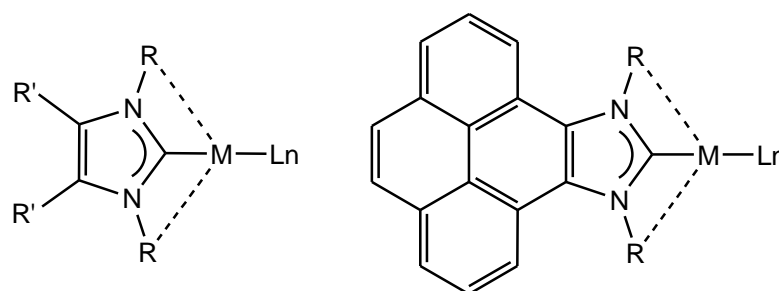


**Graphical Abstract:** Synthesis of novel n-heterocyclic carbene derivatives

## 1. Introduction:

Heterocycles containing nitrogen are a highly extensive and prevalent class of molecules found in heterocyclic compounds of all kinds. The diversity of heterocyclic molecules opens up a number of chemical pathways for examining their therapeutic potential. Researchers have found that the revered class of nitrogen-containing heterocyclic skeletons like quinazolinone, imidazole, thiazole, triazole, and indole exhibit a wide range of biological effects, including anti-inflammatory, antimicrobial, anti-tubercular, anticancer, and antiviral activity [1–8]. Researchers have focused their attention mostly on imidazole-based ionic liquids because this structure is

common to many different medication families, including antifungal, antibacterial, and diuretic ones[9]. NHCs are ionic liquids that include these ligands, while metal NHC complexes are ionic liquids that have coordinated metals. The synthesis and characterisation of novel N-heterocyclic carbene (NHC) transition metal complexes (**Figure 1**) have grown swiftly over the past two decades, and their application in medicine and a variety of catalytic processes has been fascinating[10–14]. Ionic liquids have proven to be effective catalysts for the Suzuki coupling, Michael oxidation, and the Diels-Alder reaction also numerous other synthetic processes[15,16].



**Figure 1:** Metal-NHC Complex

These complexes exhibit potent activity against micro-organisms like bacteria, fungi also show potency against cancer effects when viewed from a medicinal chemistry perspective, with antimicrobial activity being one of the most actively researched [17–22]. Some exemplary N-heterocyclic carbene (NHC) that exhibit important biological activity mention by many researchers in their research papers as Barnard and co-workers was reported a thorough analysis of the mitochondrial pathway and the cell death brought on by Au NHC complexes[23]. Arnaud Gautier and a colleague discuss recent developments in the identification of abnormal N-heterocyclic carbenes, acyclic diamino carbenes, and carbenes associated with metals such as palladium, nickel, platinum, gold, silver, and copper that exhibited antiproliferative activity [13]. Kascatan-Nebioglu and colleague discuss NHC-silver complexes when applied against a variety of infections, including resistant microorganisms recovered from lung tissue of cystic fibrosis patients, NHC-silver complexes were found to have stronger antibacterial activity than the commonly employed silver antimicrobials[24]. Wukun Liu and colleague discuss metal–NHC complexes (metals such as palladium, nickel, platinum, gold, silver, and copper and Ru)

as antitumor agents[25,26]. More ever S. Aher and colleague discuss the medical and pharmacological approaches to the anticancer effects of metal NHC complexes[27].

Antibacterial and antifungal illnesses are quite common in all countries. Since the resistance developed by the bacteria makes the antimicrobial medications now in use ineffective, ongoing efforts are performed to synthesize new antimicrobial agents.

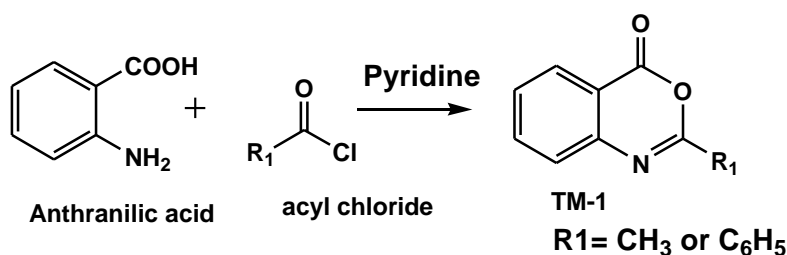
## 2. Experimental Work:

**2.1. Materials:** All of the chemicals used were of Laboratory Reagent (LR) Grade purity. The synthesized compounds were identified using the melting point (Physical Constant), TLC (chromatography), FT-IR (spectroscopy), and NMR (spectroscopy). The spots were found by treating iodine in an iodine chamber while using Silica Gel G that was put on crystal clear glass plates for thin-layer chromatography. Physical constants (M.P., uncorrected) were measured in straightforward capillary tubes submerged in liquid paraffin. All microwave reactions employed the "Ragatch Scientific Microwave System," which included automatic power settings from 140 W to 700 W. TLC was used to monitor the reactions development throughout the first minute. Commercial vendors provide all the chemicals required.

## 2.2. Synthetic Strategy:

### 2.2.1 Scheme for Synthesis of Benzoxazinone (TM1)

Benzoxazinone (**Figure 2**) synthesized when acyl chlorides are used to treat anthranilic acid.



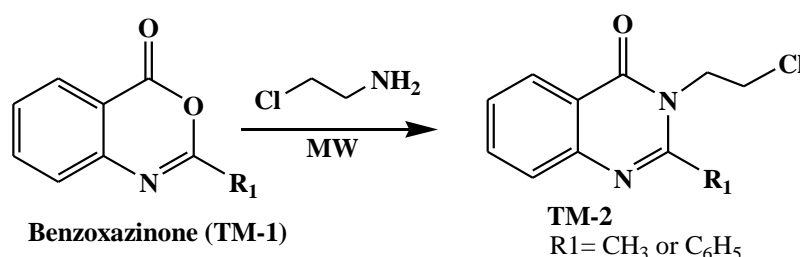
**Figure 2:** Chemical Reaction (Step-1)

#### Procedure Step-1:

Anthranilic acid (0.1mol) and pyridine 30 ml in RBF (100 ml) while stirring slowly at room temperature. At 0 °C acyl chloride had been added, the above mixture was agitated for another 30 to 45 minutes at room temperature before being left alone for an hour. The resulting pasty material was treated with sodium hydrogen carbonate solution after being mixed with 50ml of water. When the precipitate stopped bubbling, it was filtered and rinsed with water. Once drying, the resultant crude benzoxazinone was recrystallized with the diluted ethyl alcohol yields white to light brown product.

### 2.2.2 Scheme for Synthesis of TM-2 [3-(2-chloroethyl)-2-substitutedquinazolin-4(3H)-one]

Reaction of benzoxazinone (TM-1) (**Figure 3**) with amine which yield 3-(2-chloroethyl)-2-substitutedquinazolin-4(3H)-one.



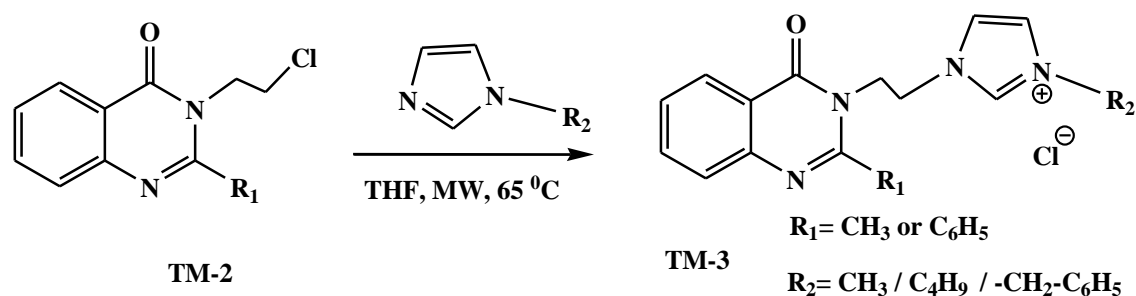
**Figure 3:** Chemical Reaction (Step-2)

#### Procedure Step-2:

The aminoethyl chloride pyridines were added to the above TM-1 solution from step 1, and they were then microwave irradiated at the 240 watt for the identified duration of time varying from 12-18min. After cooling, the reaction mixture was combined with ice cold water. The synthesized crude product was filtered, then washed in ice-cold water and dried. Absolute ethanol carried out for the recrystallization of a white to light brown colour crude product. TLC, M. P., and IR spectroscopy were used to verify the TM2 products.

### 2.2.3 Scheme for Synthesis of TM-3 (3-Substituted-1-[2-(2-Substituted-4-oxoquinazolin-3(4H)-yl) ethyl]-1H-imidazol-3-ium chloride)

Reaction of TM-2 with various N- substituted imidazole yields TM-3 (**Figure 4**).



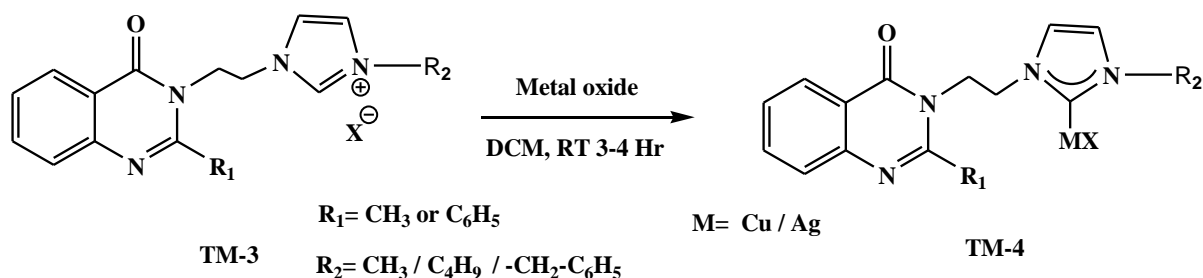
**Figure 4:** Chemical Reaction (Step-3)

### Procedure Step-3:

N-substituted imidazole and TM-2 were dissolved in a solution of 1:1 mol equivalence in THF and then refluxed using microwave at 240 watt and 65 °C. THF was decanted after cooling the reaction mixture. In order to obtain hygroscopic white to light brown powder, the sticky solid was purified by being washed three times in 20 ml of acetone.

### 2.2.4 Scheme for Synthesis of Metal-NHC Complex TM-4

Reaction of TM-3 with various Metal oxide yields TM-4 (*Figure 5*).



**Figure 5:** Chemical Reaction (Step-4)

### Procedure Step-4:

Metal oxide and Imidazolium salts (TM-3) (0.6:1 mol equivalence) were mixed in DCM for three to four hours in the dark. DCM was filtered out of the reaction mixture and vacuum-reduced. In order to precipitate Metal-NHCs, n-pentane was added to the mixture and agitated in the dark. To create metal complexes as a fine powder, the solvents were decanted, and any remaining solvent was evaporated under low pressure. Other way of TM-4 preparation was metal halide and Imidazolium salts (TM-3) (1:1 mol equivalence) were mixed in THF for three to four hours at temp below 20 °C in the dark. Then follow the remaining procedure as mention above.

## 3. Pharmacological Evaluation:

### 3. 1. The Antimicrobial Properties

**Antibacterial Action:** The Imidazolium-based metal N-heterocyclic carbene analogues that were synthesised had their antibacterial properties tested. Common gram-positive and gram-negative bacteria, including *Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, and *Escherichia coli*, were examined to determine the minimum inhibitory

concentrations (MIC) of all synthesised compounds. As a benchmark, ciprofloxacin was used to compare the activity.

**Antifungal Action:** All synthetic metal N-heterocyclic carbene analogues were tested for their antifungal efficacy against the two different fungi strains *Candida albicans* and *Aspergillus niger* to determine the minimum inhibitory concentrations (MIC). As a benchmark, fluconazole was used to

compare the activity. Tables No. 1 and 2 for antibacterial and antifungal, respectively, indicate the MIC values also zone of inhibition showed in Table no. 3 for antibacterial and antifungal activity.

#### Procedure for antimicrobial activity:

The recognized method for routinely assessing the antibiotic susceptibility of microorganisms is agar disk-diffusion testing. The Clinical and Laboratory Standards Institute (CLSI) now publishes a number of permitted and recognized standards for identifying bacteria and fungi. The well-known method involves inoculating agar plates

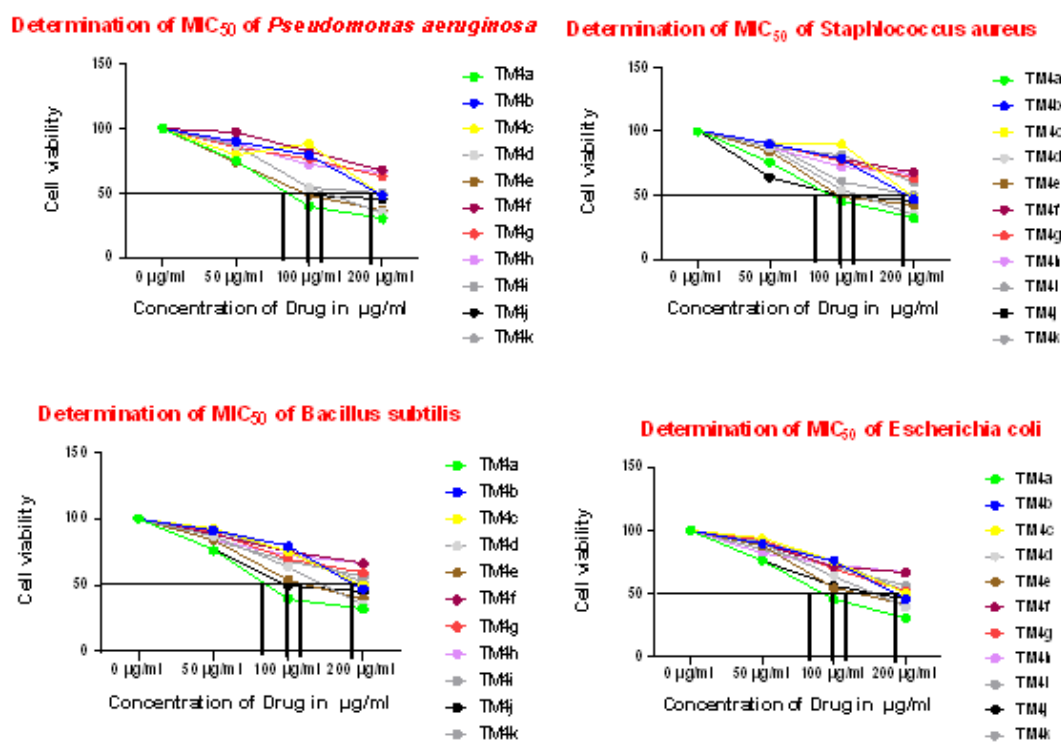
with a standardized inoculum of the test microorganism. The next step performed to apply TM4a to TM4l to filter paper discs before setting them on the agar surface at concentrations of 50, 100, and 200 micrograms/ml. Incubation of the Petri plates takes place under the proper conditions. The sizes of the inhibitory growth zones are then determined. An antimicrobial medication that diffuses into the agar normally an antimicrobial medication that diffuses into the agar inhibits the test microorganism's germination and development. A Motic 2.0 microscope was used to perform additional testing on the Petri dishes.

**Table 1:** Antibacterial activity of synthesized metal N-heterocyclic carbene analogues

Metal N-heterocyclic carbene analogues	Conc.(µg/ml)			
	Gram-(+ve) <i>Staphylococcus aureus</i>	Gram-(+ve) <i>Bacillus subtilis</i>	Gram(-ve) <i>Pseudomonas aeruginosa</i>	Gram(-ve) <i>Escherichia coli</i>
<b>TM4A</b>	100	125	100	120
<b>TM4B</b>	140	160	160	145
<b>TM4C</b>	125	140	180	125
<b>TM4D</b>	105	120	125	110
<b>TM4E</b>	130	140	175	130
<b>TM4F</b>	135	155	175	135
<b>TM4G</b>	120	125	130	110
<b>TM4H</b>	145	165	185	140
<b>TM4I</b>	125	140	180	125
<b>TM4J</b>	110	135	125	100
<b>TM4K</b>	130	140	175	130
<b>TM4L</b>	135	155	175	135
<b>CIPROFLOXACIN</b>	50	50	50	50

**Table 2:** Antifungal Activity of synthesized metal N-heterocyclic carbene analogues

Metal N-heterocyclic carbene analogues	Conc.(µg/ml)	
	<i>Candida albicans</i>	<i>Aspergillus niger</i>
TM4A	110	100
TM4B	140	145
TM4C	125	120
TM4D	100	100
TM4E	130	135
TM4F	135	140
TM4G	115	125
TM4H	130	140
TM4I	135	145
TM4J	150	160
TM4K	165	170
TM4L	165	175
FLUCONAZOLE	50	50



**Figure 6:** Determination of MIC50

**Table 3:** Values of Zone of Inhibition

Synthesized	Zone of Inhibition (in mm)
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derivative code	Gram <sub>+</sub> ve		Gram <sub>-</sub> ve		Fungi	
	<i>S. aureus</i> ,	<i>B. subtilis</i>	<i>P. aeruginosa</i>	<i>E. coli</i>	<i>C. albicans</i>	<i>A. Niger</i>
TM4A	20	18	21	18	16	28
TM4B	10	8	12	8	8	8
TM4C	8	21	10	8	12	14
TM4D	15	7	17	7	9	12
TM4E	8	9	19	9	9	8
TM4F	9	7	7	7	8	8
TM4G	16	18	18	15	20	18
TM4H	8	8	8	8	10	8
TM4I	12	14	14	8	8	21
TM4J	9	12	10	7	15	7
TM4K	9	8	8	9	8	9
TM4L	8	8	8	7	9	7
<b>Ciprofloxacin</b>	25	27	22	20	--	--
<b>Fluconazole</b>	--	--	--	--	25	20

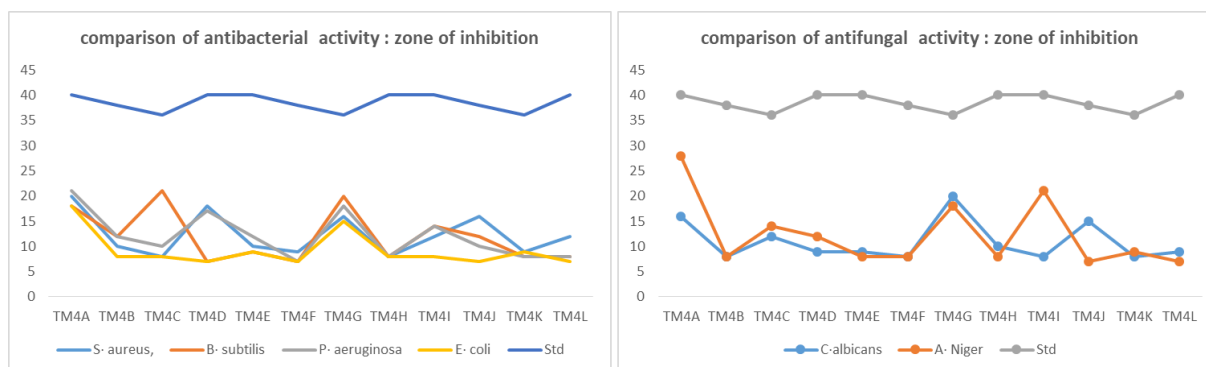
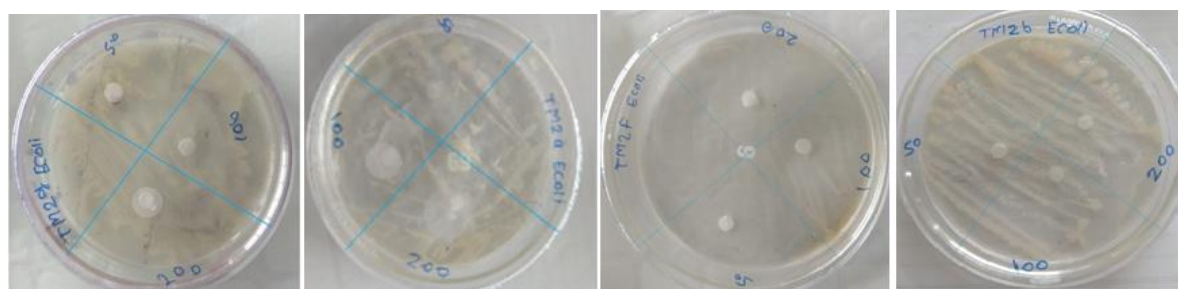


Figure 7: Zone of inhibition



Based on the results, synthesized analogue were moderately active against this bacterial strains. The most potent derivatives were TM4a, TM4d, and TM4g found effective on species *S. aureus*, TM4a, TM4c, and TM4g found effective on *B. subtilis*, and TM4a and TM4g found effective on *E. coli*. While TM4a and TM4g were the most effective derivative found effectiveness on species *C. albicans*, and TM4a, TM4g and TM4i are the most active against *A. niger*.



## 4. RESULTS AND DISCUSSION:

**4.1 Physical Properties of compounds:** Table No.4 represents the % yield and R<sub>f</sub> value of all synthesized derivatives. The prepared TLC was used to carefully monitor the reactions.

**Table 4:** Physical Properties of compounds

Sr. No.	R <sub>1</sub> substituent	R <sub>2</sub> substituent	M substituent	Codes	Physical constant (°C)	% Yield	R <sub>f</sub>
1.	-CH <sub>3</sub>	-CH <sub>3</sub>	Ag	TM4A	98-102	70	0.78
2.	-CH <sub>3</sub>	-C <sub>4</sub> H <sub>7</sub>	Ag	TM4B	102-104	60	0.68
3.	-CH <sub>3</sub>	-CH <sub>2</sub> -C <sub>6</sub> H <sub>5</sub>	Ag	TM4C	110-112	64	0.55
4.	-CH <sub>3</sub>	-CH <sub>3</sub>	Cu	TM4D	92-94	85	0.69
5.	-CH <sub>3</sub>	-C <sub>4</sub> H <sub>7</sub>	Cu	TM4E	101-103	85	0.75
6.	-CH <sub>3</sub>	-CH <sub>2</sub> -C <sub>6</sub> H <sub>5</sub>	Cu	TM4F	106-108	54	0.60
7.	-C <sub>6</sub> H <sub>5</sub>	-CH <sub>3</sub>	Ag	TM4G	120-122	55	0.55
8.	-C <sub>6</sub> H <sub>5</sub>	-C <sub>4</sub> H <sub>7</sub>	Ag	TM4H	129-131	50	0.65
9.	-C <sub>6</sub> H <sub>5</sub>	-CH <sub>2</sub> -C <sub>6</sub> H <sub>5</sub>	Ag	TM4I	112-114	40	0.78
10.	-C <sub>6</sub> H <sub>5</sub>	-CH <sub>3</sub>	Cu	TM4J	118-120	58	0.70
11.	-C <sub>6</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>7</sub>	Cu	TM4K	135-137	60	0.67
12.	-C <sub>6</sub> H <sub>5</sub>	-CH <sub>2</sub> -C <sub>6</sub> H <sub>5</sub>	Cu	TM4L	119-121	64	0.59

### 4.2 Characterization of Compound I-VIII:

For synthesized analogues (TM4A-TM4L) were verified by IR, <sup>1</sup>NMR and mass spectroscopic techniques.

**FT-IR Characterization-** Sharp peaks in the target molecule sequence TM4A-TM4L ranged from 850 to 700 cm<sup>-1</sup>, which is indicative of aromatic C-H bending, and 1510-1350 cm<sup>-1</sup>, which results from (C-N) imidazole functional group. Metal complexes showed a strong peak at 900-880 cm<sup>-1</sup>. Intense vibrations and a recognizable peak are produced by the metal's bond with the carbene center at 2130-2090 cm<sup>-1</sup>. The peak at 2230-2200 cm<sup>-1</sup> that corresponds to C-N, the aliphatic chain's C-H stretching at between 2950 - 2850 cm<sup>-1</sup>, and the sharp signal from carbonyl's C=O in the region of 1700-1630 cm<sup>-1</sup> was observed.

**<sup>1</sup>H NMR Characterization-** <sup>1</sup>H NMR spectroscopy was used to confirm that the

synthetic compound series TM4a-TM4L had been successfully synthesized. In <sup>1</sup>H NMR spectra for conformation of the aliphatic and aromatic proton, a distinctive singlet resonance peak at 9-11 ppm was seen, which disappeared with metalation in the organic structure of carbene salts.

**<sup>13</sup>C NMR Characterization-** <sup>13</sup>C NMR spectra with a response peak at 130-160 ppm corresponding to carbene carbon (NCHN) salts were also used to confirm the synthesis of the TM3 series. Whereas during metalation in complex TM4, this distinctive signal of carbene carbon was moved to a down field and show up around 160-190 ppm.

### Spectral analysis of synthesized TM:

**3-(2-(1,2-dihydro-1-methylimidazol-3-yl)ethyl)-2-methylquinazolin-4(3H)-one silver chloride (TM4A)** IR (cm<sup>-1</sup>): 3180 (C-H) Ar., 2920 (C-H alkane) 2220 (C-N str.), 2115 (C-X str.) 1693.56 (C=O),

1645(C=N), 1490 (C-N imidazole bending), 785 (C-H bending); <sup>1</sup>H NMR (DMSO): δ 9.7 (1H, s, Carbene) 7.4- 7.9 (4H, m, H-Ar), 4.8 (1H, s, CH) 3.3 (2H, t, ethylene bridge) 2.85 (2H, t, ethylene bridge) 0.9 (3H, s, CH<sub>3</sub>); MS: m/z . 411

**3-(2-(1-butyl-1,2-dihydroimidazol-3-yl)ethyl)-2-methylquinazolin-4(3H)-one silver chloride (TM4B)** IR (cm<sup>-1</sup>): 3170 (C-H) Ar., 2922 (C-H alkane) 2225 (C-N str.), 2129 (C-X str.) 1694 (C=O), 1640 (C=N), 1480 (C-N imidazole bending), 795 (C-H bending); <sup>1</sup>H NMR (DMSO): δ 9.7 (1H, s, Carbene) 7.4- 7.9 (4H, m, H-Ar), 4.8 (1H, s, CH) 3.3 (2H, t, ethylene bridge) 2.85 (2H, t, ethylene bridge), 2.55(2H, t, CH<sub>2</sub>) 1.43 (2H, m, CH<sub>2</sub>), 0.9 (3H, s, CH<sub>3</sub>); MS: m/z .453

**3-(2-(1-benzyl-1,2-dihydroimidazol-3-yl)ethyl)-2-methylquinazolin-4(3H)-one silver chloride (TM4C)** IR (cm<sup>-1</sup>): 3185 (C-H) Ar., 2915 (C-H alkane) 2204 (C-N str.), 2120 (C-X str.) 1690 (C=O), 1640 (C=N), 1495 (C-N imidazole bending), 786 (C-H bending); <sup>1</sup>H NMR (DMSO): δ 9.7 (1H, s, Carbene) 7.4- 7.9 (4H, m, H-Ar), 4.8 (1H, s, CH) 3.3 (2H, t, ethylene bridge) 2.85 (2H, t, ethylene bridge), 3.87 (2H, t, CH<sub>2</sub>), 7.0- 7.2 (5H, m, H-Ar), 1.43 (2H, m, CH<sub>2</sub>), 0.9 (3H, s, CH<sub>3</sub>); MS: m/z .486

**3-(2-(1,2-dihydro-1-methylimidazol-3-yl)ethyl)-2-methylquinazolin-4(3H)-one copper chloride (TM4D)** IR (cm<sup>-1</sup>): 3180 (C-H) Ar., 2920 (C-H alkane) 2220 (C-N str.), 2100 (C-X str.) 1693.56 (C=O), 1645(C=N), 1490 (C-N imidazole bending), 785 (C-H bending); <sup>1</sup>H NMR (DMSO): δ 9.7 (1H, s, Carbene) 7.4- 7.9 (4H, m, H-Ar), 4.8 (1H, s, CH) 3.3 (2H, t, ethylene bridge) 2.85 (2H, t, ethylene bridge) 0.9 (3H, s, CH<sub>3</sub>); MS: m/z . 367

**3-(2-(1-butyl-1,2-dihydroimidazol-3-yl)ethyl)-2-methylquinazolin-4(3H)-one copper chloride (TM4E)** IR (cm<sup>-1</sup>): 3170 (C-H) Ar., 2922 (C-H alkane) 2225 (C-N str.), 2109 (C-X str.) 1694 (C=O), 1640 (C=N), 1480 (C-N imidazole bending), 795 (C-H bending); <sup>1</sup>H NMR

(DMSO): δ 9.7 (1H, s, Carbene) 7.4- 7.9 (4H, m, H-Ar), 4.8 (1H, s, CH) 3.3 (2H, t, ethylene bridge) 2.85 (2H, t, ethylene bridge), 2.55(2H, t, CH<sub>2</sub>) 1.43 (2H, m, CH<sub>2</sub>), 0.9 (3H, s, CH<sub>3</sub>); MS: m/z .409

**3-(2-(1-benzyl-1,2-dihydroimidazol-3-yl)ethyl)-2-methylquinazolin-4(3H)-one copper chloride (TM4F)** IR (cm<sup>-1</sup>): 3185 (C-H) Ar., 2915 (C-H alkane) 2204 (C-N str.), 2105 (C-X str.) 1690 (C=O), 1640 (C=N), 1495 (C-N imidazole bending), 786 (C-H bending); <sup>1</sup>H NMR (DMSO): δ 9.7 (1H, s, Carbene) 7.4- 7.9 (4H, m, H-Ar), 4.8 (1H, s, CH) 3.3 (2H, t, ethylene bridge) 2.85 (2H, t, ethylene bridge), 3.87 (2H, t, CH<sub>2</sub>), 7.0- 7.2 (5H, m, H-Ar), 1.43 (2H, m, CH<sub>2</sub>), 0.9 (3H, s, CH<sub>3</sub>); MS: m/z .443

**3-(2-(1,2-dihydro-1-methylimidazol-3-yl)ethyl)-2-phenylquinazolin-4(3H)-one silver chloride (TM4G)** IR (cm<sup>-1</sup>): 3190 (C-H) Ar., 2912 (C-H alkane) 2215 (C-N str.), 2119 (C-X str.) 1694 (C=O), 1665 (C=N), 1485 (C-N imidazole bending), 776 (C-H bending); <sup>1</sup>H NMR (DMSO): δ 9.7 (1H, s, Carbene) 7.4- 7.9 (4H, m, H-Ar), 4.8 (1H, s, CH) 3.3 (2H, t, ethylene bridge) 2.85 (2H, t, ethylene bridge), 3.87 (2H, t, CH<sub>2</sub>), 7.2- 7.6 (5H, m, H-Ar), 1.43 (2H, m, CH<sub>2</sub>), 2.47 (3H, s, CH<sub>3</sub>); MS: m/z .473

**3-(2-(1-butyl-1,2-dihydroimidazol-3-yl)ethyl)-2-phenylquinazolin-4(3H)-one silver chloride (TM4H)** IR (cm<sup>-1</sup>): 3175 (C-H) Ar., 2925 (C-H alkane) 2230 (C-N str.), 2112 (C-X str.) 1684 (C=O), 1635(C=N), 1498 (C-N imidazole bending), 787 (C-H bending); <sup>1</sup>H NMR (DMSO): δ 9.7 (1H, s, Carbene) 7.4- 7.9 (4H, m, H-Ar), 4.8 (1H, s, CH) 3.3 (2H, t, ethylene bridge) 2.85 (2H, t, ethylene bridge), 3.87 (2H, t, CH<sub>2</sub>), 7.0- 7.2 (5H, m, H-Ar), 2.55(2H, t, CH<sub>2</sub>) 1.43 (2H, m, CH<sub>2</sub>), 1.43 (2H, m, CH<sub>2</sub>), 0.9 (3H, s, CH<sub>3</sub>); MS: m/z .515

**3-(2-(1-benzyl-1,2-dihydroimidazol-3-yl)ethyl)-2-phenylquinazolin-4(3H)-one silver chloride (TM4I)** IR (cm<sup>-1</sup>): 3174 (C-H) Ar., 2923 (C-H alkane) 2234 (C-N

str.), 2105 (C-X str.) 1704 (C=O), 1649 (C=N), 1497 (C-N imidazole bending), 781 (C-H bending); <sup>1</sup>H NMR (DMSO): δ 9.7 (1H, s, Carbene) 7.4- 7.9 (4H, m, H-Ar), 4.8 (1H, s, CH) 3.3 (2H, t, ethylene bridge) 2.85 (2H, t, ethylene bridge), 3.87 (2H, t, CH<sub>2</sub>), 7.0- 7.2 (5H, m, H-Ar), 1.43 (2H, m, CH<sub>2</sub>); MS: m/z .549

**3-(2-(1,2-dihydro-1-methylimidazol-3-yl)ethyl)-2-phenylquinazolin-4(3H)-one copper chloride (TM4J)** IR (cm<sup>-1</sup>): 3190 (C-H) Ar., 2912 (C-H alkane) 2215 (C-N str.), 2109 (C-X str.) 1694 (C=O), 1665 (C=N), 1485 (C-N imidazole bending), 776 (C-H bending); <sup>1</sup>H NMR (DMSO): δ 9.7 (1H, s, Carbene) 7.4- 7.9 (4H, m, H-Ar), 4.8 (1H, s, CH) 3.3 (2H, t, ethylene bridge) 2.85 (2H, t, ethylene bridge), 3.87 (2H, t, CH<sub>2</sub>), 7.2- 7.6 (5H, m, H-Ar), 1.43 (2H, m, CH<sub>2</sub>), 2.47 (3H, s, CH<sub>3</sub>); MS: m/z .429

**3-(2-(1-butyl-1,2-dihydroimidazol-3-yl)ethyl)-2-phenylquinazolin-4(3H)-one copper chloride (TM4K)** IR (cm<sup>-1</sup>): 3175 (C-H) Ar., 2925 (C-H alkane) 2230 (C-N str.), 2091 (C-X str.) 1684 (C=O), 1635(C=N), 1498 (C-N imidazole bending), 787 (C-H bending); <sup>1</sup>H NMR (DMSO): δ 9.7 (1H, s, Carbene) 7.4- 7.9 (4H, m, H-Ar), 4.8 (1H, s, CH) 3.3 (2H, t, ethylene bridge) 2.85 (2H, t, ethylene bridge), 3.87 (2H, t, CH<sub>2</sub>), 7.0- 7.2 (5H, m, H-Ar), 2.55(2H, t, CH<sub>2</sub>) 1.43 (2H, m, CH<sub>2</sub>), 1.43 (2H, m, CH<sub>2</sub>), 0.9 (3H, s, CH<sub>3</sub>); MS: m/z .471

**3-(2-(1-benzyl-1,2-dihydroimidazol-3-yl)ethyl)-2-phenylquinazolin-4(3H)-one copper chloride (TM4L)** IR (cm<sup>-1</sup>): 3174 (C-H) Ar., 2923 (C-H alkane) 2234 (C-N str.), 2095 (C-X str.) 1704 (C=O), 1649 (C=N), 1497 (C-N imidazole bending), 781 (C-H bending); <sup>1</sup>H NMR (DMSO): δ 9.7 (1H, s, Carbene) 7.4- 7.9 (4H, m, H-Ar), 4.8 (1H, s, CH) 3.3 (2H, t, ethylene bridge) 2.85 (2H, t, ethylene bridge), 3.87 (2H, t, CH<sub>2</sub>), 7.0- 7.2 (5H, m, H-Ar), 1.43 (2H, m, CH<sub>2</sub>); MS: m/z .505.

## 5. CONCLUSION

In the current research, novel metal-NHC complex were created using microwave irradiation techniques. With microwave irradiation approach, good yields were quickly produced. The compound structures were identified using FTIR, <sup>1</sup>HNMR, mass. When exposed to test the synthesised quinazolinone compounds, all of the examined organisms were shown to have modest antibacterial activity. The synthesised compounds TM4a, TM4c, TM4d, and TM4g good antibacterial abilities were specifically directed against *Staphylococcus aureus*. *Bacillus subtilis*. TM4a, TM4g potent antifungal abilities were specifically directed against *Candida albicans*, *Aspergillus niger*.

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### ABBREVIATIONS:

NaH: Sodium Hydride; THF: Tetrahydrofuran, TLC: Thin layer chromatography; NMR: Nuclear Magnetic Resonance Spectroscopy; IR: Infrared Spectroscopy; Str.: Stretching vibrations; µg/mL: Microgram per mililiter; g: gram; MIC: minimum inhibitory concentration; Gram +ve: Gram positive; Gram -ve: Gram negative; *S.Aureus*: *Staphylococcus aureus*; *E.coli*: *Escherichia coli*; *C.albicans*:*Candida Albicans*; *A.niger*:*Aspergillus niger*.

### References:

1. Khan I, Ibrar A, Ahmed W, Saeed A. Synthetic approaches, functionalization and therapeutic potential of quinazoline and quinazolinone skeletons: The advances continue. Eur J Med Chem. 2015;90:124–69.

2. Gupta T, Rohilla A, Pathak A, Akhtar MJ, Haider MR, Yar MS. Current perspectives on quinazolines with potent biological activities: A review. *Synth Commun.* 2018;48(10):1099–127.
3. Chavan BB, Bhalawane PP, Kolsure AK, Chabukswar AR. Synthesis and evaluation of some new 4,6-disubstituted quinazoline derivatives for antimicrobial and antifungal activities. *Asian J Biomed Pharm Sci.* 2014;4(33):43–6, 4 pp.
4. Ahmed MF, Belal A, Youns M. Design, synthesis, molecular modeling and anti-breast cancer activity of novel quinazolin-4-one derivatives linked to thiazolidinone, oxadiazole or pyrazole moieties. *Med Chem Res.* 2015;24(7):2993–3007.
5. Chawla A, Batra C. Recent Advances of Quinazolinone Derivatives As Marker for Various Biological Activities. *Int Res J Pharm.* 2013;4(3):49–58.
6. Shalini K, Sharma P, Kumar N. Imidazole and its biological activities: A review. *Chem Sin.* 2010;1(3):36–47.
7. Ganguly S, Vithlani VV, Kesharwani AK, Kuhu R, Baskar L, Mitramazumder P, Sharon A, Dev A. Synthesis, antibacterial and potential anti-HIV activity of some novel imidazole analogs. *Acta Pharm.* 2011;61(2):187–201.
8. Romero DH, Heredia VET, García-Barradas O, López MEM, Pavón ES. Synthesis of Imidazole Derivatives and Their Biological Activities. *J Chem Biochem.* 2014;2(2).
9. Anderson EB, Long TE. Imidazole- and imidazolium-containing polymers for biology and material science applications. *Polymer (Guildf).* 2010;51(12):2447–54.
10. Jensen TR, Schaller CP, Hillmyer MA, Tolman WB. Zinc N-heterocyclic carbene complexes and their polymerization of d,l-lactide. *J Organomet Chem.* 2005;690(24–25):5881–91.
11. Sitalu K, Babu BH, Latha JNL, Lakshmana Rao A. Synthesis, characterization and antimicrobial activities of copper derivatives of NHC-II complexes. *Pakistan J Biol Sci.* 2017;20(2):82–91.
12. Jahnke MC, Ekkehardt Hahn F. CHAPTER 1: Introduction to N-Heterocyclic Carbenes: Synthesis and Stereoelectronic Parameters. Vols. 2017-Janua, RSC Catalysis Series. 2017. 1–45 p.
13. Gautier A, Cisnetti F. Advances in metal-carbene complexes as potent anti-cancer agents. *Metallomics.* 2012;4(1):23–32.
14. Hopkinson MN, Richter C, Schedler M, Glorius F. An overview of N-heterocyclic carbenes. *Nature.* 2014;510(7506):485–96.
15. Li Y, Hindi K, Watts KM, Taylor JB, Zhang K, Li Z, Hunstad DA, Cannon CL, Youngs WJ, Wooley KL. Shell crosslinked nanoparticles carrying silver antimicrobials as therapeutics. *Chem Commun.* 2010;46(1):121–3.
16. Melaiye A, Sun Z, Hindi K, Milsted A, Ely D, Reneker DH, Tessier CA, Youngs WJ. Silver(I)-imidazole cyclophane gem-diol complexes encapsulated by electrospun tectophilic nanofibers: Formation of nanosilver particles and antimicrobial activity. *J Am Chem Soc.* 2005;127(7):2285–91.
17. Riduan SN, Zhang Y. Imidazolium salts and their polymeric materials for biological applications. *Chem Soc Rev.* 2013;42(23):9055–70.

18. Khupse ND, Kumar A. Ionic liquids: New materials with wide applications. *Indian J Chem - Sect A Inorganic, Phys Theor Anal Chem.* 2010;49(5-6):635-48.
19. Marrucho IM, Branco LC, Rebelo LPN. Ionic liquids in pharmaceutical applications. *Annu Rev Chem Biomol Eng.* 2014;5:527-46.
20. Migowski P, Dupont J. Catalytic applications of metal nanoparticles in imidazolium ionic liquids. *Chem - A Eur J.* 2007;13(1):32-9.
21. Wilkes JS, Levisky JA, Wilson RA, Hussey CL. Dialkylimidazolium Chloroaluminate Melts: A New Class of Room-Temperature Ionic Liquids for Electrochemistry, Spectroscopy, and Synthesis. *Inorg Chem.* 1982;21(3):1263-4.
22. Erdmenger T, Paulus RM, Hoogenboom R, Schubert US. Scaling-up the synthesis of 1-butyl-3-methylimidazolium chloride under microwave irradiation. *Aust J Chem.* 2008;61(3):197-203.
23. Barnard PJ, Berners-Price SJ. Targeting the mitochondrial cell death pathway with gold compounds. *Coord Chem Rev.* 2007;251(13-14 SPEC. ISS.):1889-902.
24. Kascatan-Nebioglu A, Panzner MJ, Tessier CA, Cannon CL, Youngs WJ. N-Heterocyclic carbene-silver complexes: A new class of antibiotics. *Coord Chem Rev.* 2007;251(5-6):884-95.
25. Liu W, Gust R. Update on metal N-heterocyclic carbene complexes as potential anti-tumor metallodrugs. *Coord Chem Rev.* 2016;329(September):191-213.
26. Liu W, Gust R. Metal N-heterocyclic carbene complexes as potential antitumor metallodrugs. *Chem Soc Rev.* 2013;42(2):755-73.
27. Aher SB, Muskawar PN, Thenmozhi K, Bhagat PR. Recent developments of metal N-heterocyclic carbenes as anticancer agents. *Eur J Med Chem.* 2014;81:408-19.