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SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL SCREENING OF NEW IMIDAZOLIUM CONTAINING SILVER-N-HETEROCYCLIC CARBENE ANALOGUES

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Abstract

A new series of quinazolinone-containing silver N-heterocyclic carbene (NHC) complexes have been synthesised by combining the appropriate N-substituted imidazolium salt with silver oxide in DCM. The proposed structures for the novel compounds have been confirmed by 1H-NMR,13C-NMR, FT-IR. To assess their antimicrobial efficacy against gram-negative E. coli and gram-positive S.aureus bacterial strains as well as C.albicans fungal species, their Minimum Inhibition Concentration (MIC) values have been determined. Among the novel synthesized analogues moderately active derivatives were **P-3a, P-3d, P-4a** and **P-4d** found effective on species S.aureus, B.subtilus,P.aeruginosa and E. coli also found effectiveness on species C. albicans, A. niger.These findings indicated all of the substances inhibited the growth of all bacterial and fungal strains and several complexes had good antimicrobial effects.The increasing applications of ILs in the pharmaceuticals and new drug development fascinating researchers in recent years. This research covers the medical and pharmacological approach, as well as other significant applications of ILs in a variety of sectors.

Keywords: Imidazole based ionic liquid, N-substituted Imidazolium salt , Quinazolinone, Silver N- Heterocyclic Carbene Complexes.

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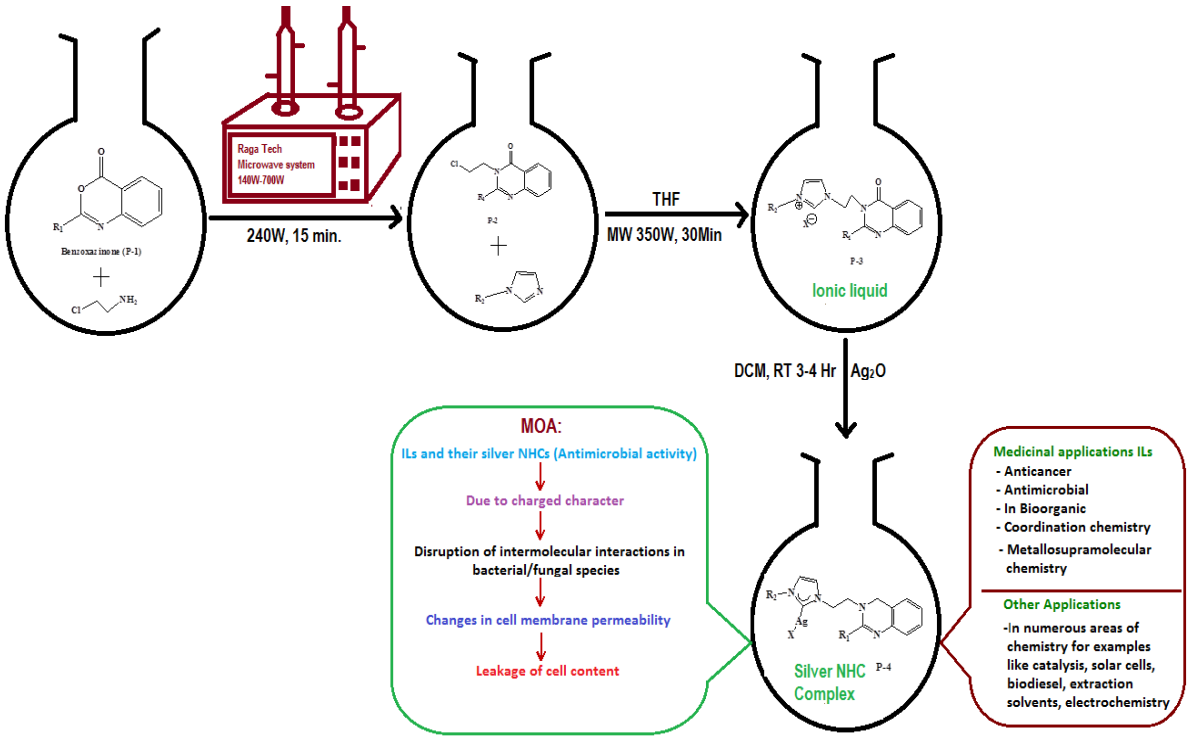


Graphical Abstract: Ioinc liquids and thier Silver NHC

1. Introduction:

Infections caused by bacterial and fungal have become a global health concern due to a lack of adequate and effective antimicrobial medications, particularly in immunocompromised patients [1]. methicillin-resistant S.aureus (MRSA) is a common cause of hospital acquired illness (nosocomial infection) [2]. Human being is at a high risk of illness without antibiotics, hence antimicrobial medications have established a crucial role in healthcare.The conventional therapy with antibiotics is inadequate in case of drug-resistant pathogen like MRSA, P. aeruginosa, B. cepacia and many more. In such cases, the silver N-heterocyclic carbenes (Ag–NHCs) can be a suitable substitute. Major breakthroughs in the development of medicinal drugs with more potency than organic compounds have been made with the approval of Silver sulfadiaizine for burn related infection [3].

The ionic liquids (ILs) have outstanding applications in numerous filed of chemistry for examples like catalysis, solar cells, biodiesel, extraction solvents, electrochemistry, medicinal applications and many more[4-10]. Novel analogues of ILs find extraordinary significance as anticancer, antimicrobial applications out of which mainly antibacterial agents as a medicinal agents[11]. The potential ILs are being studied worldwide for their antimicrobial and cytotoxic activities[12][13]. ILs and their analogues comprise of antimicrobial activity owed to their charged character leading to disruption of intermolecular interactions in bacterial species leading to changes in cellular-membrane permeability and leakage of cellular contents[14-16]. Silver (Ag) and gold (Au) based metal- NHC complexes exhibits predominant bactericidal properties[17]. The drug Silver Sulfadiazine (SSD) approved in 1973 used for the treatment of major burns with broad spectrum activity against gram-positive and gram-negative bacteria in USA[18]. Ag-NHC complexes have been shown to have numerous medical applications, mainly antimicrobial activity[19][20].

Heteroaromatic analogues (NHC) with N-atoms have fascinated researcher for synthesis of Ag-complexes predominatly with antimicrobial activity.

Quinazoline and quinazolinone are amazing heterocyclic molecules in medicinal chemistry because of their diverse biological applications[21-23]**.** Quinazoline derivatives shown extended spectrum of biological actions like antimalarial, antimicrobial, anti-inflammatory, anticonvulsant, anti-diabetic, antihypertensive, anticancer and dihydrofolate reductase inhibitory[24][25]. Another promising heterocyclic scaffold is imidazole and its analogues, which have a broader range of pharmacological actions like anti-cancer, anti-microbial, anti-inflammatory, and many more[26]. Nowadays microwave-assisted synthesis technique is used in synthetic chemistry community, with multiple benefits over conventional techniques as it is eco-friendly, accelerated reaction times, and increased yields. The aim of this research is to design a new set of innovative Ionic liquids and Quinazolinone containing Imidazolium based silver-N-heterocyclic carbene analogues using a microwave-assisted approach. Additionally, the antifungal and antibacterial properties of the newly produced ionic liquids and Silver NHCs were evaluated.

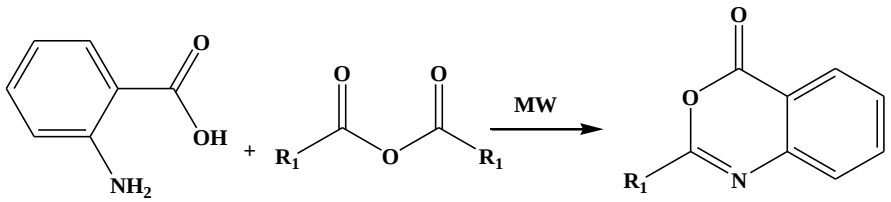
2. Experimental Work:

2.1 Materials: All the chemicals were procured from commercial suppliers and utilised without being purified. Synthesized analogues were confirmed by melting point, Thin layer chromatography subsequently undergone spectral analysis with FT-IR spectroscopy, GC-MS as well as NMR . After performing thin-layer chromatography with Silica Gel-G on the glass plates, the spots were seen by exposing them to iodine. The melting points were determined using thiels's tube having capillary filled with podered compound. All microwave procedures were completed using a "Ragatch Scientific microwave System" with a power setting range of 140 W to 700 W.

2.2 Synthetic Pathway:

2.2.1 Scheme for synthesis of step-1: P-1 (Benzoxazinone)

P-1 is produced by treating anthranilic acid with several anhydrides like propionic anhydride, valeric anhyride .



Anthranilic acid **anhydride** **Benzoxazinone (P-1)**

R_1=C_2H_5,C_4H_9

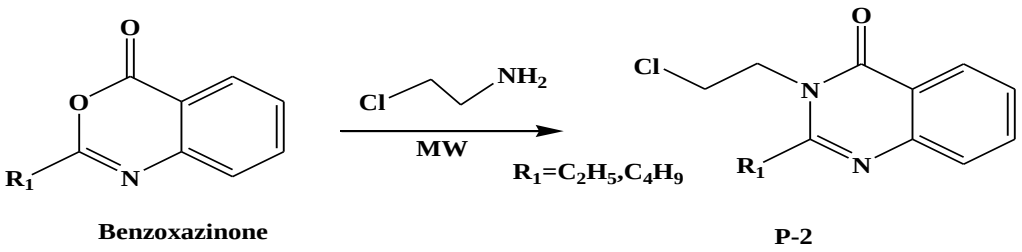
Figure 1: Anthranilic acid with anhydride (step-1)

Various anhydrides and antranilic acid were mixed and the mixture was microwaved at the 240 watt for about 15 min . The reaction mixture was mixed with cold water after cooling. The crude product was filtered, rinsed in cold water, and dried at 100^0 Celsius. The crude porduct was recrystallized from absolute ethanol and dried at 100^0C to obtain light brown colored amorphous powder.

2.2.2 Step-2 Synthesis of (P-2)

Reaction of various amines with P-1 (benzoxazinone) yields corresponding quinazolin-4-one derivatives.

Chemical Reaction Step-2



Benzoxazinone **P-2**

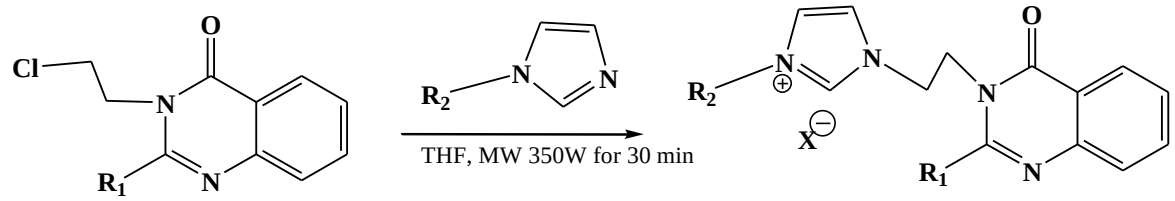
Figure 2: Formation of product P-2 (Step-2)

In above reaction, the product P-1 (benzoxazinone), the chloroethylamine were added in 1:1 ratio to pyridine (5 ml) and treated under microwave irradiation at 240 watt for about 15 min. After cooling, the reaction mixture was mixed into cold water. The crude product (P-2) was filtered, rinsed with cold water, and dried at 100^0 C. The crude porduct was then recrystallized from absolute ethanol and dried at 100^0C to obtain light grey to white colored amorphous powder.

2.2.3 Step-3 Synthesis of P-3:

Reaction of P-2 with several N- substituted imidazole Yeilds P-3.

Chemical Reaction step-3b



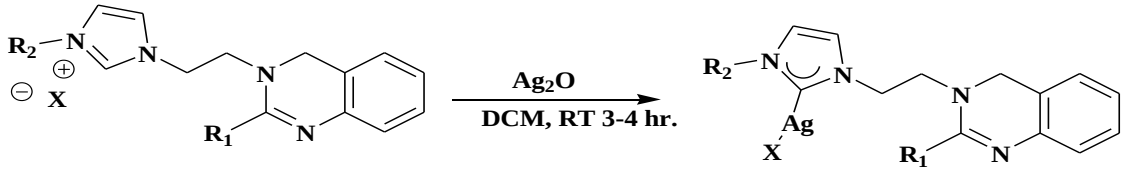
P-2 **$R_1=C_2H_5,C_4H_9$** **R2=-CH_3,-C_4H_9,-CH_2-C_6H_5** **P-3**

Figure 3: Formation of product P-3 (Step-3)

N-substituted imidazole and the derivative P-2 were taken in 1:1 mol equivalent and disoolved in THF and then refluxed for 48 hours at 65ºC. THF was decanted after cooling the reaction mixture. In order to obtain hygroscopic white powder, the sticky solid was purified by being washed three times in 20 mL of acetone.

2.2.4 Step-4 Syntheis of Silver-NHC Complex P-4

Reaction of P-3 with various silver oxide yields P-4.



$R_1=C_2H_5,C_4H_9$ **R2=-CH_3,-C_4H_9,-CH_2-C_6H_5**

P-3 **P-4**

Figure 4: Synthesis of Silverl-NHC Complex (Step-4)

In the dark conditions, the silver oxide and imidazolium salts (P-3) (0.6:1 mol equivalence) were mixed in DCM and stirred for 3-4 hours at room temp. The solvent DCM was vacuum-reduced to 4-5 ml after being filtered out of the reaction mixture. n-Pentane was introduced to the mixture and stirred in the dark to precipitate the Ag-NHC complex. The solvent has been decanted and any remaining solvent was evaporated at low pressure using a rotary evaporator to produce Ag-NHC complexes.

3. Pharmacological Evaluation:

3.1 Antimicrobial Study: These synthesised compounds were screened for antimicrobial profile, exhibiting substantive antimicrobial activity. Two types of pathogens were taken for antimicrobila study siuch as bacteria and fungi. Four bacterial strains were used consisting two gram-positive and two gram-negative strains, wheres two fungal strains wrere used antifungal activity. For antibacterial action 2 gram-positive and gram negetive bacteria used. For antifungal action 2 fungal strains are used. The biological results obtained from the antibacterial activity are given in Table 1.

3.2 Method performed for antimicrobial activity:

Broth or agar dilution method is another name for Tube well method, which is one of the common methods for evaluating antimicrobial activity in vitro. This method involves preparing a series of dilutions of the antimicrobial agent in a liquid broth or a solid agar medium and inoculating each dilution with a standard amount of the test microorganism. Following incubation, the antimicrobial agent's minimum inhibitory concentration (MIC) that inhibits visible growth of the microorganism is determined and reported. The MIC is a measure of an antimicrobial agent's potency and efficacy. Agar plates are inoculated with a standardised inoculum of the test microorganism in this well-known procedure. Then, **P-3a** to **P-3f** and **P-4a** to **P-4f** are applied to filter paper discs and placed on the agar surface at concentrations of 50, 100, and 200 microgram/ml. The Petri plates are incubated using the suitable parameters. An antimicrobial medication that diffuses into the agar generally inhibits the germination and development of the test microorganism, and the diameters of the inhibitory growth zones are then noted. The Petri dishes were further examined using a Motic 2.0 microscope.

3.3 Microbiological Assays:

3.3.1 Antimicrobial Evaluation:

All synthesized compounds were evaluated for antibacterial activity using the agar dilution technique.. Two typical species of microorganism S. aureus, B. subtilis (gram-positive) and two species of organisms P.aeruginosa, E. coli (gram-negative) were tested. The synthesized compounds were compared agianst the reference stanndard antibacterial Ciprofloaxacin and antifungal Fluconazole. The MICs of different substituted triazole derivatives were determined. Also, these compounds were checked against fungi C.albicans and A. niger.

Table 1: Minimum inhibitory concentrations (MIC) of substituted triazole derivatives.

Product code	**R_1 group**	**R_2 group**	**Conc.(µg/ml)**					
			gram-positive		gram-negative		fungi	
			S.aureus,	*B.subtilis*	*P. aeruginosa*	*E.coli*	*C.albicans*	*A.Niger*
P-3a	**C_2H_5**	**$-CH_3$**	108	110	112	105	112	108
P-3b	**C_2H_5**	**$-C_4H_9$**	205	210	215	210	220	210
P-3c	**C_2H_5**	**$-CH_2C_6H_5$**	200	215	210	212	210	212
P-3d	**C_4H_9**	**$-CH_3$**	100	105	102	104	106	108
P-3e	**C_4H_9**	**$-C_4H_9$**	220	230	215	220	220	225
P-3f	**C_4H_9**	**$-CH_2C_6H_5$**	215	220	210	212	215	220
P-4a	**C_2H_5**	**$-CH_3$**	100	105	104	102	108	110
P-4b	**C_2H_5**	**$-C_4H_9$**	208	214	215	215	210	220
P-4c	**C_2H_5**	**$-CH_2C_6H_5$**	205	215	208	205	225	230
P-4d	**C_4H_9**	**$-CH_3$**	100	101	102	104	108	110
P-4e	**C_4H_9**	**$-C_4H_9$**	208	214	215	215	210	215
P-4f	**C_4H_9**	**$-CH_2C_6H_5$**	212	210	208	220	210	215
Ciprofloxacin			50	50	50	50	-	-
Fluconazole			-	-	-	-	75	75

Standard drug Ciprofloxacin was taken for comparing of antibacterial activity while standard drug Fluconazole was taken antifungal activity. All synthesized compounds were tested for antibacterial and antifungal activities.. When these derivatives were exposed to the test organism, they found moderately effective. In novel synethsized series of imidazolium containing ILs and silver-N-heterocyclic carbene analogues the most effective compounds **were P-3a, P-3d** and **P-4a,P-4** respetively against these strains of bacteria and fungi.

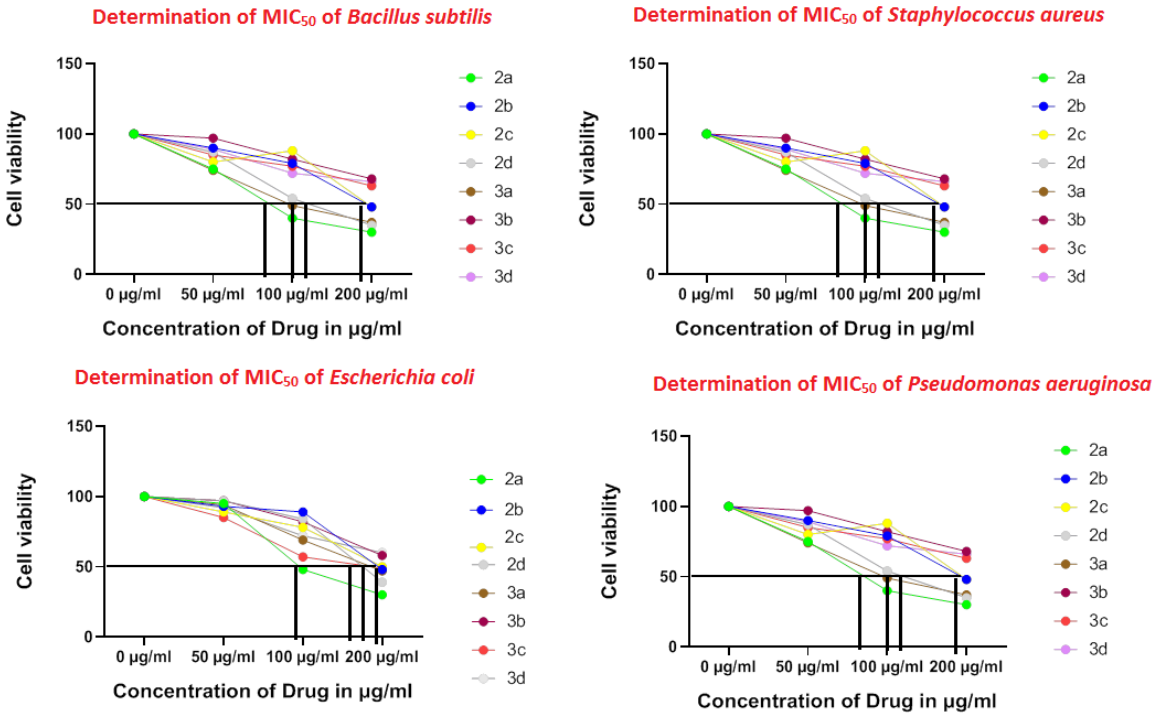


Figure 5: Determination of MIC_{50} values

While Table 2 indicates the zone of inhibition of synthesized compounds, the results show that synthesized analogues were moderately active against the tested bacterial species.

Table 2: Values of Zone of Inhibition

Product code	R_1 group	R_2 group	Zone of Inhibition (in mm)					
			gram-positive		gram-negative		fungi	
			S. aureus	*B. subtilis*	*P. aeruginosa*	*E. coli*	*C. albicans*	*A. Niger*
P-3a	C_2H_5	$-CH_3$	20	24	21	21	13	16
P-3b	C_2H_5	$-C_4H_9$	11	12	11	12	12	12
P-3c	C_2H_5	$-CH_2C_6H_5$	12	11	10	10	15	13
P-3d	C_4H_9	$-CH_3$	16	18	20	19	17	12
P-3e	C_4H_9	$-C_4H_9$	12	10	13	11	15	16
P-3f	C_4H_9	$-CH_2C_6H_5$	9	10	8	11	18	12
P-4a	C_2H_5	$-CH_3$	24	23	21	22	13	10
P-4b	C_2H_5	$-C_4H_9$	10	13	10	13	14	14
P-4c	C_2H_5	$-CH_2C_6H_5$	09	12	09	12	13	16
P-4d	C_4H_9	$-CH_3$	21	23	21	23	12	12

P-4e	**C_4H_9**	**$-C_4H_9$**	12	11	12	11	15	13
P-4f	**C_4H_9**	**$-CH_2C_6H_5$**	09	12	09	12	17	12
Ciprofloxacin			40	36	38	40	--	--
Fluconazole			--	--	--	--	25	20

The most potent derivatives were **P-3a, P-3d, P-4a**, and **P-4d**, which were proven effectiveness on species S.aureus, B.subtilus, P.aeruginosa, and E. coli, as well as C. albicans and A. niger.

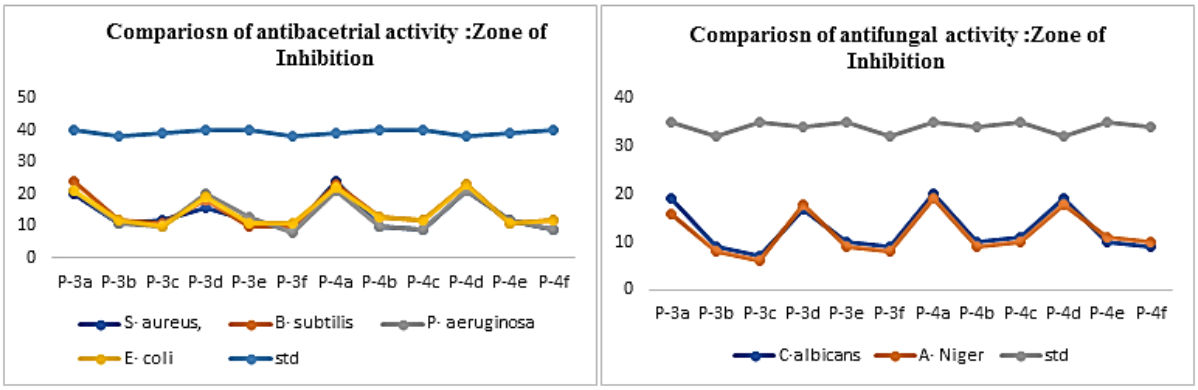


Figure 6: Comparison of Zone of Inhibition

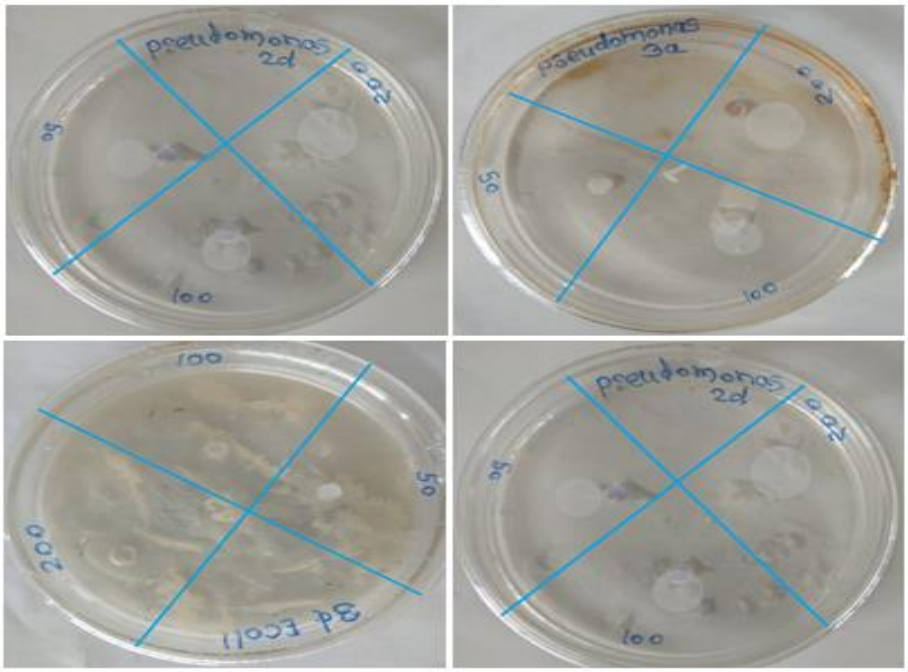


Figure 7: Anti-bacterial and anti-fungal Activities with Zone of Inhibition

4. Results And Discussion:

4.1 Physical Properties of compounds:

Table 3 represents the melting points, % yield and Rf value of all synthesized derivatives. The capillary method was used to determine physical constants (M.P), and prepared TLC was used to carefully monitor the reactions.

Table 3: Physical properties melting points,Rf values and yield of compounds

Product Code	R_1	R_2	Rf Value	% Yield	M.P
P-3a	$-C_2H_5$	$-CH_3$	0.52	64	178
P-3b	$-C_2H_5$	$-C_4H_9$	0.65	70	186
P-3c	$-C_2H_5$	$-CH_2C_6H_5$	0.72	58	192
P-3d	$-C_4H_9$	$-CH_3$	0.82	72	210
P-3e	$-C_4H_9$	$-C_4H_9$	0.92	78	220
P-3f	$-C_4H_9$	$-CH_2C_6H_5$	075	82	190
P-4a	$-C_2H_5$	$-CH_3$	0.56	77	194
P-4b	$-C_2H_5$	$-C_4H_9$	0.71	71	212
P-4c	$-C_2H_5$	$-CH_2C_6H_5$	0.62	65	220
P-4d	$-C_4H_9$	$-CH_3$	0.91	60	240
P-4e	$-C_4H_9$	$-C_4H_9$	0.84	65	182
P-4f	$-C_4H_9$	$-CH_2C_6H_5$	0.68	75	174

4.2 Characterization of Compound:

The structures of newly synthesized analogues **(P-3a -P-4f)** were verified by FT-IR, 1HNMR, 13C NMR and HR-MS spectroscopic techniques. The desired product of series **P-3a- P-4f** displayed intense peaks in the 870–690 cm-1 and 1500–1310 cm^{-1} ranges, respectively, which are caused by aromatic C–H bending and the $C–N_{imid}$ functional group, respectively. The vibrations become stronger and exhibit a distinctive peak due to the silver bonding with the carbene centre at 2100-2080cm^{-1}.Charactertics peak for -CN stretching observed at 2250-2210cm^{-1}. A significant peak was observed in the region of 2980–2820cm^{-1} for the C–H stretching of an aliphatic chain. Intense signals in the region 1710-1680cm-1 was observed by the C=O carbonyl group. A strong peak around 890–860cm^{-1} had been observed in Ag-NHCs but not in N-Heterocyclic salts, indicating that the metal has been incorporated into the organic structure of salts.

The successful synthesis of the compounds **P-3a-P-4f** has been confirmed using 1H NMR spectroscopy. A unique singlet resonance signal at 9.30-11ppm in 1H NMR spectra related to the conformation of aromatic and aliphatic proton vanished with silver metalation in the organic structure of carbene salts.. This peak in compound **P-4a-P-4f** disappears, indicating that the carbene proton has been utilised for silver(Ag)-metalation to produce Ag-NHC complexes.Through 13C NMR spectra, the effective synthesis of the **P-3a–P-4f** series was also confirmed and the peak at 130–150 ppm corresponds to carbene carbon for NHC salts (**P-3a–P-3f**). But when silver was added to the complex (**P-4a-P-4f**), the carbene carbon shows distinctive resonance which was moved downfield signal at 180-190 ppm.

4.3 Spectral Analysis of compounds:

2-ethyl-3-(2-(1,2-dihydro-1-methylimidazol-3-yl) ethyl) quinazolin-4(3H)-one chloride salt: (P-3a)

Compound P3-a: IR (cm^{-1}): 3160 cm^{-1} (Ar-str),2980 cm^{-1},(-CH str), 2240 cm^{-1} (-CNstr), 1706 (-C=O str), 1500 cm^{-1} (-C–N_{imid} bending), 780 cm^{-1}(Ar C-H bending) MS: 318 [M.]; 1H NMR (ppm) $DMSO_4$: 7.4-7.9 (4H, multiplet, Ar-H), 4.8(1H,singlet,-CH),3.81 (1H,singlet,CH) 3.68 (2H, triplet,CH_2- X),3.48 (2H, triplet, CH_2- X), 1.4 (2H,triplet,CH_2) 0.9(3H, triplet,CH_3).

13C NMR(ppm) $DMSO_4$:154 (1-C,Imine),161(1-C,Amide),140(1C-carbene),120-133(1-Benzene),24.3(1-C, aliphatic)

3-(2-(1-butyl-1,2-dihydroimidazol-3-yl)ethyl)-2-ethylquinazolin-4(3H)-one chloride salt: (P-3b)

Compound II: IR (cm^{-1})3160 cm^{-1} (Ar-str),2980 cm^{-1},(-CH str), 2240 cm^{-1} (-CNstr), 1706 (-C=O str), 1500 cm^{-1} (-C–N_{imid} bending), 780 cm^{-1}(Ar C-H bending) MS: 326[M.]; 1H NMR (ppm) $DMSO_4$: 7.4-7.9 (H, multiplet, Ar-H), 4.8(1H,singlet,-CH),3.81 (1H,singlet,CH) 3.68 (2H, triplet,CH_2- X),3.48 (2H, triplet, CH_2- X), 2.55(triplet,CH_2),1.4 (2H,triplet,CH_2),

1.33 (4H,multiplet,CH_2),0.96(triplet,CH_3), 0.9(3H, triplet,CH_3), 13C NMR(ppm) $DMSO_4$:154 (1-C,Imine),161(1-C,Amide),140(1C-carbene),120-133(1-Benzene),24.3(1-C, aliphatic)

3-(2-(1-benzyl-1,2-dihydroimidazol-3-yl)ethyl)-2-ethylquinazolin-4(3H)-one chloride salt: (P-3c)

Compound III: IR (cm^{-1}): 3160 cm^{-1} (Ar-str),2980 cm^{-1},(-CH str), 2240 cm^{-1} (-CNstr), 1706 (-C=O str), 1500 cm^{-1} (-C–N_{imid} bending), 780 cm^{-1}(Ar C-H bending) MS: 360.4[M.]; 1H NMR (ppm) $DMSO_4$: 7.6-7.9 (4H, multiplet, Ar-H), 7.3-7.5 (5H, multiplet, Ar-H), 4.8(1H,singlet,-CH),3.81 (1H,singlet,CH) 3.68 (2H, triplet,CH_2-X),3.48 (2H, triplet, CH_2- X), 1.4 (2H,triplet,CH_2) 0.9(3H, triplet,CH_3). 13C NMR(ppm) $DMSO_4$:154 (1-C,Imine),161(1-C,Amide),140(1C-carbene),120-133(1-Benzene),24.3(1-C, aliphatic)

2-butyl-3-(2-(1,2-dihydro-1-methylimidazol-3-yl)ethyl)quinazolin-4(3H)-one chloride salt: (P-3d)

Compound IV: IR (cm^{-1}): 3160 cm^{-1} (Ar-str),2980 cm^{-1},(-CH str), 2240 cm^{-1} (-CNstr), 1706 (-C=O str), 1500 cm^{-1} (-C–N_{imid} bending), 780 cm^{-1}(Ar C-H bending) MS: 312.4[M.]; 1H NMR (ppm) $DMSO_4$: 7.4-7.9 (4H, multiplet, Ar-H), 4.8(1H,singlet,-CH),3.81 (1H,singlet,CH) 3.68 (2H, triplet,CH_2- X),3.48 (2H, triplet, CH_2- X), 2.47(3H,singlet,CH_3), 1.4 (2H,triplet,CH_2) 0.9(3H, triplet,CH_3). 13C NMR(ppm) $DMSO_4$:154 (1-C,Imine),161(1-C,Amide),140(1C-carbene),120-133(1-Benzene),24.3(1-C, aliphatic)

2-butyl-3-(2-(1-butyl-1,2-dihydroimidazol-3-yl)ethyl) quinazolin-4(3H)-one chloride salt: (P-3e)

Compound V: IR (cm^{-1}): 3160 cm^{-1} (Ar-str),2980 cm^{-1},(-CH str), 2240 cm^{-1} (-CN str), 1706 (-C=O str), 1500 cm^{-1} (-C–N_{imid} bending), 780 cm^{-1}(Ar C-H bending) MS: 354[M.]; 1H NMR (ppm) $DMSO_4$: 7.4-7.9 (4H, multiplet, Ar-H), 4.8(1H,singlet,-CH),3.81 (1H,singlet,CH) 3.68 (2H, triplet,CH_2- X),3.48 (2H, triplet, CH_2- X), 2.55 (3H,singlet,CH_3), 1.3 (6H,multiplet,CH_2) 0.96(3H, triplet,CH_3). 13C NMR(ppm) DMSO4:154 (1-C,Imine),161(1-C,Amide),140(1C-carbene),120-133(1-Benzene),24.3(1-C, aliphatic)

3-(2-(1-benzyl-1,2-dihydroimidazol-3-yl)ethyl)-2-butylquinazolin-4(3H)-one chloride salt(P-3f)

Compound VI: IR (cm^{-1}): 3160 cm^{-1} (Ar-str),2980 cm^{-1},(-CH str), 2240 cm^{-1} (-CNstr), 1706 (-C=O str), 1500 cm^{-1} (-C–N_{imid} bending), 780 cm^{-1}(Ar C-H bending) MS: 388 [M.]; 1H NMR (ppm) $DMSO_4$: 7.6-7.9 (4H, multiplet, Ar-H), 7.3-7.5 (5H, multiplet, Ar-H), 4.8(1H,singlet,-CH),3.81

(1H,singlet,CH) 3.68 (2H, triplet,CH_2-X),3.32 (2H, triplet, CH_2- X), 1.4 (2H,triplet,CH_2) 0.9(3H, triplet,CH_3). 13C NMR(ppm) $DMSO_4$:154 (1-C,Imine),161(1-C,Amide),140(1C-carbene),120-133(1-Benzene),24.3(1-C, aliphatic)

2-ethyl-3-(2-(1,2-dihydro-1-methylimidazol-3-yl)ethyl)quinazolin-4(3H)-one silver chloride: (P-4a)

Compound VII: IR (cm^{-1}): 3160 cm^{-1} (Ar-str),2980 cm^{-1},(-CH str), 2240 cm^{-1} (-CN str), 1706 (-C=O str), 1500 cm^{-1} (-C–N_{imid} bending), 780 cm^{-1}(Ar C-H bending) MS: 440 [M.]; 1H NMR (ppm) $DMSO_4$: 7.4-7.9 (4H, multiplet, Ar-H), 4.8(1H,singlet,-CH),3.81 (1H,singlet,CH) 3.68 (2H, triplet,CH_2- X),3.48 (2H, triplet, CH_2-X),0.9(3H, triplet,CH_3).13C NMR(ppm) $DMSO_4$:154 (1-C,Imine),161(1-C,Amide) 120-133(1-Benzene),24.3(1-C, aliphatic), 13C NMR(ppm) $DMSO_4$: 180 (1C-carbene),154 (1-C,Imine),161(1-C,Amide),120-133(1-Benzene),24.3(1-C, aliphatic)

3-(2-(1-butyl-1,2-dihydroimidazol-3-yl)ethyl)-2-ethylquinazolin-4(3H)-one silver chloride salt: (P-4b)

Compound VIII: IR (cm^{-1}): 3160 cm^{-1} (Ar-str),2980 cm^{-1},(-CH str), 2240 cm^{-1} (-CNstr), 1706 (-C=O str), 1500 cm^{-1} (-C–N_{imid} bending), 780 cm^{-1}(Ar C-H bending) MS: 468.2 [M.]; 1H NMR (ppm) $DMSO_4$: 7.4-7.9 (H, multiplet, Ar-H), 4.8(1H,singlet,-CH),3.81 (1H,singlet,CH) 3.68 (2H, triplet,CH_2- X),3.48 (2H, triplet, CH_2- X), 2.55(triplet,CH_2), 1.33 (4H,multiplet,CH_2),0.96(triplet,CH_3), 0.9(3H, triplet,CH_3), 13C NMR(ppm) $DMSO_4$: 180 (1C-carbene),154 (1-C,Imine),161(1-C,Amide),120-133(1-Benzene),24.3(1-C, aliphatic)

3-(2-(1-benzyl-1,2-dihydroimidazol-3-yl)ethyl)-2-ethylquinazolin-4(3H)-one silver chloride salt: (P-4c)

Compound IX: IR (cm^{-1}): 3160 cm^{-1} (Ar-str),2980 cm^{-1},(-CH str), 2240 cm^{-1} (-CNstr), 1706 (-C=O str), 1500 cm^{-1} (-C–N_{imid} bending), 780 cm^{-1}(Ar C-H bending) MS: 502.5[M.]; 1H NMR (ppm) $DMSO_4$: 7.6-7.9 (4H, multiplet, Ar-H), 7.3-7.5 (5H, multiplet, Ar-H), 4.8(1H,singlet,-CH),3.81 (1H,singlet,CH) 3.68 (2H, triplet,CH_2-X),3.48 (2H, triplet, CH_2- X),0.9(3H, triplet,CH_3). 13C NMR(ppm) $DMSO_4$: 180 (1C-carbene),154 (1-C,Imine),161(1-C,Amide),120-133(1-Benzene),24.3(1-C, aliphatic)

2-butyl-3-(2-(1,2-dihydro-1-methylimidazol-3-yl)ethyl)quinazolin-4(3H)-one silver chloride salt: (P-4d)

Compound X: IR (cm^{-1}): 3160 cm^{-1} (Ar-str),2980 cm^{-1},(-CH str), 2240 cm^{-1} (-CNstr), 1706 (-C=O str), 1500 cm^{-1} (-C–N_{imid} bending), 780 cm^{-1}(Ar C-H bending) MS: 454.2[M.]; 1H NMR (ppm) $DMSO_4$: 7.4-7.9 (4H, multiplet, Ar-H), 4.8(1H,singlet,-CH),3.81 (1H,singlet,CH) 3.68 (2H, triplet,CH_2- X),3.48 (2H, triplet, CH_2- X), 2.47(3H,singlet,CH_3), 1.4 (2H,triplet,CH_2) 0.9(3H, triplet,CH_3). 13C NMR(ppm) $DMSO_4$: 180 (1C-carbene),154 (1-C,Imine),161(1-C,Amide),120-133(1-Benzene),24.3(1-C, aliphatic)

2-butyl-3-(2-(1-butyl-1,2-dihydroimidazol-3-yl) ethyl) quinazolin-4(3H)-one silver chloride salt: (P-4e)

Compound XI: IR (cm^{-1}): 3160 cm^{-1} (Ar-str),2980 cm^{-1},(-CH str), 2240 cm^{-1} (-CNstr), 1706 (-C=O str), 1500 cm^{-1} (-C–N_{imid} bending), 780 cm^{-1}(Ar C-H bending),MS: 496.2[M.]; 1H NMR (ppm) $DMSO_4$: 7.4-7.9 (4H, multiplet, Ar-H), 4.8(1H,singlet,-CH),3.81 (1H,singlet,CH) 3.68 (2H, triplet,CH_2- X),3.48 (2H, triplet, CH_2- X), 2.55 (3H,singlet,CH_3),0.96(3H, triplet,CH_3). 13C NMR(ppm) $DMSO_4$: 180 (1C-carbene),154 (1-C,Imine),161(1-C,Amide),120-133(1-Benzene),24.3(1-C, aliphatic)

3-(2-(1-benzyl-1,2-dihydroimidazol-3-yl)ethyl)-2-butylquinazolin-4(3H)-one silver chloride salt(P-4f)

Compound XII: IR (cm^{-1}): 3160 cm^{-1} (Ar-str),2980 cm^{-1},(-CH str), 2240 cm^{-1} (-CN

str), 1706 (-C=O str), 1500 cm^{-1} (-C–N_{imid} bending), 780 cm^{-1}(Ar C-H bending) MS: 530.4 [M.]; 1H NMR (ppm) $DMSO_4$: 7.6-7.9 (4H, multiplet, Ar-H), 7.3-7.5 (5H, multiplet, Ar-H), 4.8(1H,singlet,-CH),3.81 (1H,singlet,CH) 3.68 (2H, triplet,CH_2-X),3.32 (2H, triplet, CH_2- X),0.9(3H, triplet,CH_3). 13C NMR (ppm) $DMSO_4$: 180 (1C-carbene),154 (1-C,Imine),161(1-C,Amide),120-133(1-Benzene),24.3(1-C, aliphatic).

5. Conclusion:

In the current study, microwave synthesised ILs and Ag(I)NHCs with imidazole cores fused with quinazolinone; these analogues have been synthesized in sufficient yields. All of these compounds were shown moderate anti-bacterial activity and anti-fungal activity. Although the mechanism of antimicrobial action is unknown, there is being observed that the antimicrobial capacity of Ag-carbene complexes against specific bacteria and fungi changes with ligand type.According to the findings, all synthesized analogues were moderately potent towards all bacterial species tested. The most effective derivatives were P-3a, P-3d, and P-4a,P-4d tested against bacetrial starins S.aureus, B.subtilis, and E.coli derivatives against fungal strains C.albicans and A.niger. With this studies extensive research on new Au and Ag-NHC complexes beneficial metal containing agents and other therapeutic applications is also being initiated.

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Conflict of Interest: The authors declare no conflict of interest.

Abbreviations:

IR: Infrared Spectroscopy; **FTIR:** Fourier transformed Infrared Spectroscopy; **NMR:** Nuclear Magnetic Resonance Spectroscopy; **Str**.: Stretching vibrations; **M.P**: Melting Point; **TLC**: Thin layer chromatography; **THF**: Tetrahydro furan, **NaH**: Sodium Hydride;**µg/mL**: Microgram per mililiter; **g:** gram; MIC: minimum inhibitory concentration; **Gram +ve:** Gram positive; **Gram -ve:** Gram-negative; ***S-aureus****: Staplylococcous aureus;* ***E.coli****: Escherichia coli;* ***C.albicans:****Candida Albicans;****A.niger****:Aspergilus niger.*

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