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Synthesis, Characterisation and antimicrobial activity of Quinoline and Pyrazoline derivatives.

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Abstract

The present investigation is in the interest of some synthesized novel derivatives 1-[3-(6-chloro-2-methyl-4-phenyl quinoline-3-yl)-4,5-dihydro-1H-pyrazol-1-yl]ethanone 3(a-j) and 6-chloro-2-methyl-3-[5-1H-pyrazol-3-yl]-4- phenyl quinoline 4 (a-j). The core nucleus quinoline scaffold is incorporated with biological active heterocycle pyrazoline/pyrazole and benzene ring.. The characterization of the synthesised compounds reported is based on IR, 1H NMR, ^{13}C NMR and mass spectral data. All the synthesised compounds were screened for their antibacterial activity on four bacteria (two Gram positive Species Bacillus subtilis, Staphylococcus aureus and two Gram negative species, Escherichia coli, Salmonella typhi) and antifungal activity on two fungi species (Aspergillusniger, Aspergillusfumigatus). Ciprofloxacin is used as bacterial standards and Amphotericin B is used as fungal standards for references to evaluate the efficacy of the tested compounds. Amongst the biological evaluated synthesised compounds 3d,4d and 5b exhibited most potent antimicrobial activity. It was observed that the presence of electron withdrawing group like chloro,fluoro and alkoxy at 6 position of quinoline and in the aromatic ring remarkably enhanced the antimicrobial activity.

Keywords: Quinoline,pyrazoline, Ciprofloxacin,Amphotericin B and antimicrobial.

Introduction

With the rise of the difficult-to-eradicate infectious diseases, the need for new antimicrobial agents is urgently needed. A promising strategy for the development of new antimicrobial drugs is the synthesis of molecular hybrids containing two or more covalently joined antimicrobial pharmacophores within a single molecule [1-3].Heterocyclic compounds have gained a lot of attention because of their numerous significant medical and biological uses. Research interest on heterocyclic compounds is rapidly increasing due to the extensive synthetic study and functional utility.Particularly, the nitrogen based heterocycles are omnipresent and play pivotal role in medicinal chemistry[4-9].

Amongst the various N-heterocycles, Quinoline derivatives have attracted considerable interest for many years due to their chemical reactivity and biological activity[10-13]. Literature surveys revealed that these derivatives possesses anti-inflammatory [14,15], antimicrobial [16,17],antimalarial[18,19], antioxidant [20,21], antitumor [22,23], antiprotozoal[24], antituberculosis[25,26] and antiulcer activity [27] as well as, A3 adenosine receptor antagonists [28]. On the other hand, pyrazole derivatives are known to exhibit diverse biological activities including anti-inflammatory [29] anticancer [30] and antimicrobial [31,32] activity.On the other hand 2-Pyrazoline derivatives have been reported to exhibit various pharmacological activities such as antimicrobial ,[33] anti-inflammatory [34],antihypertensive, anti-tumor [35,36] and anticonvulsant [37]. In addition, pyrazolines are also reported to possess cytotoxic properties against human lung tumor cell line (A549)[38].

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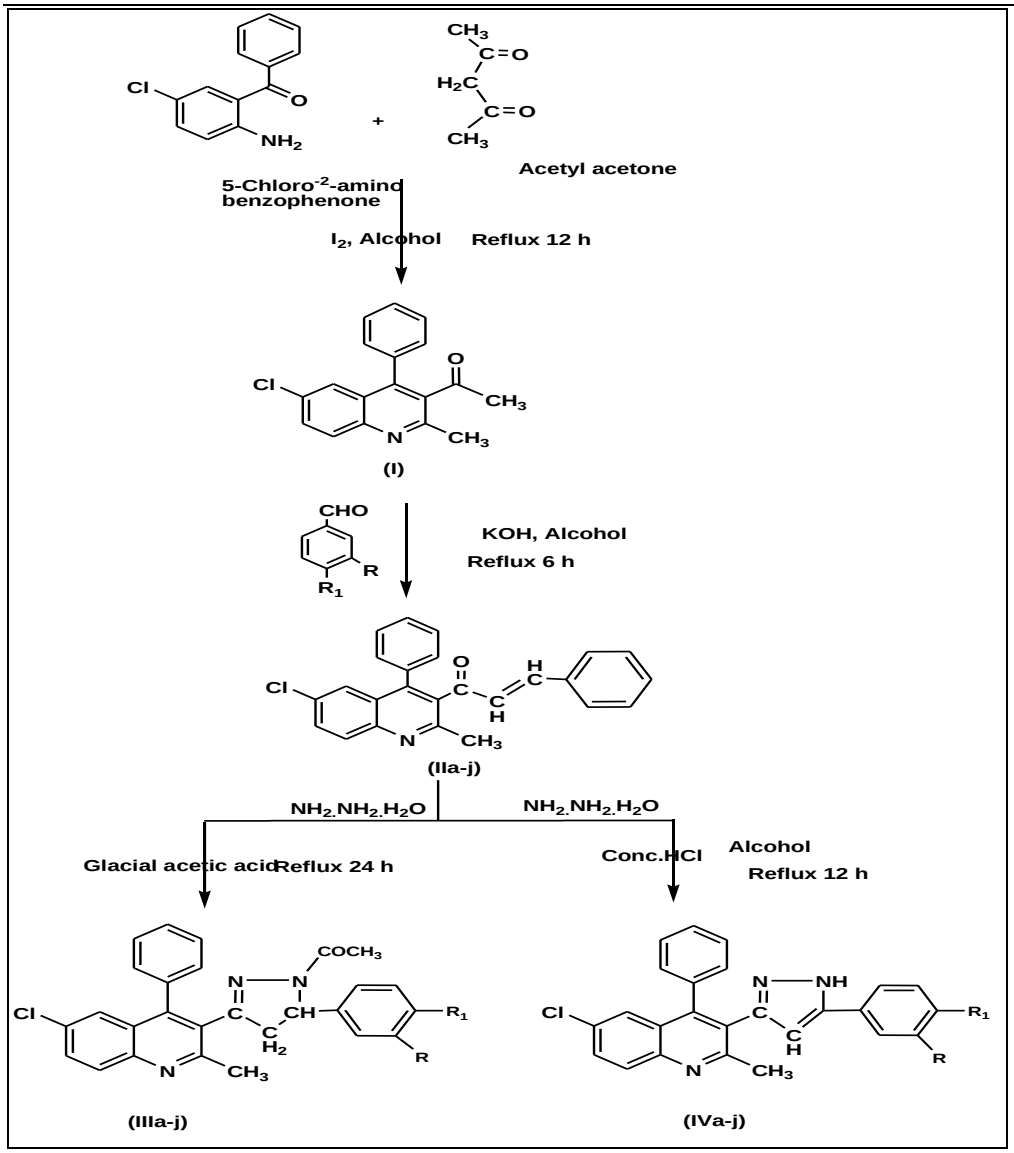
In the light of the above mentioned facts and our interest in designing new biologically active molecules, our efforts were directed towards the synthesis of new heterocyclic compounds containing quinoline and pyrazole moieties with anticipated biological activities.

Materials and Methods

Chemicals, Methods and Structural Studies

All the chemicals and solvents were of laboratory reagent grade and used as received from Sigma Aldrich and SD fine. Melting points were determined in open capillaries and are uncorrected. The purity of the compounds was checked by TLC using silica gel-G coated aluminum plates (Merck) and spots were visualized by exposing the dry plates to iodine vapors. The IR (KBr) spectra were recorded on a Perkin-Elmer spectrometer on FT-IR spectrometer. The 1H NMR (DMSO-d6) spectra recorded on a Bruker (400 MHz) and the chemical shifts were expressed in ppm (δ scale) downfield from TMS. Mass spectral data were recorded by electron impact method on JEOL GCMATE II GC-MS mass spectrometer. Elemental analysis was carried out using Flash EA 1112 series elemental analyzer. All the compounds gave C, H and N analysis within±0.5% of the theoretical values.



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Procedure for the preparation of 3-ace tyl quinoline (I):

Into a clean round bottom flask introduced 5-chloro-2-amino benzophenone (2.31 gms, 0.01 mol), acetyl acetone (1 ml, 0.01 mol), Iodine (100 mg) and 15 ml alcohol. The mixture was refluxed for 12 h, cooled and the separated solid product was collected by filtration, washed with alcohol and dried. The obtained product was recrystallized from ethanol, melting point was 152 ^{o}C and yield was 85 %.

IR (KBr) (ƛmax in cm-1): 1577(C=C); 1616(C=N);3013(Ar C-H);

^{1}H-NMR (400 MHz,**$CDCl_3$, δ ppm):** 7.3-8.0 (m, 8H of Ar-H), 2.6 (s, 3H of CH_3), 2.0 (s, 3H of -$COCH_3$).

Analysis: Calcd for C_{18} $H_{14}ClNO$ (295),C, 73.10; H, 11.99; N,4.74; O,5.41.
Found C, 73.08; H, 11.97; N,4.71; O,5.38.

General procedure for the preparation of chalcones (II a-j):

Equimolar quantity of 3-acetyl quinoline and appropriate aldehydes (0.01 mol), were introduced into a round bottomed flask containing 10 ml alcohol, then added 10 ml of 2 N potassium hydroxide and the contents were refluxed for 6 h, cooled and poured onto ice cold water. The separated solid was collected by filtration and dried.

2A

1-(6-Chloro-2-methyl-4-phenylquinoline-3-yl)-3-(3,4-dimethoxyphenyl) prop-2-en-1-one

IR (KBr) (ƛmax in cm-1):1617(C=N); 1700(C=O); **^{1}H-NMR (**400 MHz,**$CDCl_3$, δ ppm):** 8.0-8.1 (d, 1H of CH=CH), 6.8-7.7 (m, 11H of Ar-H),6.4-6.5 (d, 1H of CH=CH), 3.7-3.9 (d, 6H of 2 x OCH_3), 2.7 (s, 3H of CH_3).

Mass Spectra (m/z): Molecular weight of the sample is 444 and molecular ion peak was appeared as M+ at 444.
Analysis: Calcd for C_{27} $H_{22}ClNO_3$ (443),C, 73.05; H, 5; Cl,7.9;N,3.16;O,10.81.
Found C, 73.02; H, 4.8; N,7.72;Cl,7.5;N,3.13;O,10.80.

2B

1-(6-Chloro-2-methyl-4-phenylquinoline-3-yl) -3-(3-hydroxyphenyl) prop-2-en-1-one

IR (KBr) (ƛmax in cm-1): 1624(C=N); 1701(C=O);
^{1}H-NMR ($CDCl_3$, δ ppm): 8.7-8.8 (d, 1H of OH), 7.7 (d, 1H of CH), 6.8-7.7 (m, 12H of Ar-H), 6.4-6.6 (d, 1H of =CH).,mol mass 400
Analysis: Calcd for $C_{25}H_{18}ClNO_2$ (400),C, 75.09; H, 4.54; Cl,8.87; N,3.50 ;O,8.

Found C, 75.05; H, 4.34; Cl,8.83; N,3.48;O,7.97.

2C

1-(6-Chloro-2-methyl-4-phenylquinoline-3-yl) -3-(4-ethxylphenyl) prop-2-en-1-one

IR (KBr) (ƛmax in cm-1): 1634(C=N); 1705(C=O);

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^{1}H-NMR (CDCl$_3$, δ ppm): 2.61 (q 2H of CH_2), 1.9(t, 3H of CH_3), 6.8-7.7 (m, 12H of Ar-H), 6.4-6.6 (d, 1H of =CH), 7.7(d,1H of =CH),2.53(s,3H of CH_3).
Analysis: Calcd for $C_{27}H_{22}ClNO$ (412),C, 78.73; H, 5.38; N,3.40; Cl,8.61; O,3.88.
Found C, 78.71; H, 5.35; N,3.38;Cl,8.59; O,3.88

2D

1-(6-Chloro-2-methyl-4-phenylquinoline-3-yl) -3-(4-fluorophenyl) prop-2-en-1-one

IR (KBr) (λmax in cm-1):1617(C=N); 1700(C=O);
^{1}H-NMR (CDCl$_3$, δ ppm): 6.8-7.7 (m, 12H of Ar-H), 6.4-6.6 (d, 1H of =CH), 7.7(d,1H of =CH),2.53(s,3H of CH_3).
Analysis: Calcd for $C_{25}H_{17}ClFNO$ (402),C, 74.42; H, 4.26; N,3.49;Cl,8.82; O,3.98;F;4.73
Found C,74.40; H, 4.23; N,3.45; Cl,8.80; O,3.96; F;4.70.

2E

1-(6-Chloro-2-methyl-4-phenylquinoline-3-yl-3-(3-ethoxy-4-hydroxyphenyl) prop-2-en-1-one

IR (KBr) (λmax in cm-1): 1624(C=N); 1701(C=O);
^{1}H-NMR (CDCl$_3$, δ ppm): 4.09 (q 2H of CH_2), 1.82(t, 3H of CH_3), 6.8-7.7 (m, 11H of Ar-H), 6.4-6.6 (d, 1H of =CH), 7.7(d,1H of =CH),2.53(s,3H of CH_3),5.35(s,1H of OH).
Analysis: Calcd for $C_{27}H_{22}ClNO_3$ (443), C, 73.05; H, 5; Cl,7.99; N,3.16; O,10.81.
Found C, 73.02; H, 4.8; Cl,7.5;N,3.13;O,10.80.nb

2F

1-(6-Chloro-2-methyl-4-phenylquinoline-3-yl)-3-(4-methoxyphenyl) prop-2-en-1-one

IR (KBr) (λmax in cm-1): 1634(C=N); 1705(C=O);
^{1}H-NMR (CDCl$_3$, δ ppm):8.0-8.1 (d, 1H of CH=CH), 6.8-7.7 (m, 12H of Ar-H),6.4-6.5 (d, 1H of CH=CH), 3.83 (s,3H of OCH_3), 2.7 (s, 3H of CH_3).
Analysis: Calcd for $C_{26}H_{20}ClNO_2$ (413), C, 75.45; H, 4.87; Cl,8.57; N,3.38; O,7.73.
Found C, 75.42; H, 4.85; Cl,8.55; N,3.35; O,7.71.

2G

1-(6-Chloro-2-methyl-4-phenylquinoline-3-yl) -3-(4-methylphenyl) prop-2-en-1-one

IR (KBr) (λmax in cm-1):1617(C=N); 1700(C=O);

^{1}H-NMR (CDCl$_3$, δ ppm): 6.8-7.7 (m, 12H of Ar-H), 6.4-6.6 (d, 1H of =CH), 7.7(d,1H of =CH),2.53(s,3H of CH_3),2.34(s,1H of CH_3).
Analysis: Calcd for $C_{26}H_{20}ClNO$ (398), C, 78.48; H, 5.67; Cl,8.91; N,3.52; O,4.02.
Found C, 78.46; H, 5.65; Cl,8.90; N,3.50; O,4.0.

2H

1-(6-Chloro-2-methyl-4-phenylquinoline-3-yl)-3-(4-ethoxy-3-methylphenyl) prop-2-en-1-one

IR (KBr) (λmax in cm-1): 1624(C=N); 1701(C=O);

^{1}H-NMR (CDCl$_3$, δ ppm): 4.09 (q 2H of CH_2), 1.82(t, 3H of CH_3), 6.8-7.7 (m, 11H of Ar-H), 6.4-6.6 (d, 1H of =CH), 7.7(d,1H of =CH),2.53(s,3H of CH_3).
Analysis: Calcd for $C_{27}H_{22}ClNO_2$ (429), C, 75.78; H, 5.18; Cl,8.26; N,3.27; O,7.48

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Found C, 75.76; H, 5.16; Cl,8.24; N,3.25; O,7.46.

2I

1-(6-Chloro-2-methyl-4-phenylquinoline-3-yl) -3-(4-hydroxy-3-methoxyphenyl) prop-2-en-1-one

IR (KBr) (ƛmax in cm-1): 1634(C=N); 1705(C=O);
^{1}H-NMR ($CDCl_3$, δ ppm):6.8-7.7 (m, 11H of Ar-H),6.4-6.5 (d, 1H of CH=CH), 7.7(d,1H of =CH),3.83 (s,3H of OCH_3),2.53(s,3H of CH_3), 5.35(s,1H of OH).
Analysis: Calcd for $C_{26}H_{20}ClNO_3$ (429), C, 72.64; H, 4.69; Cl,8.25; N,3.26; O,11.17.
Found C, 72.62; H, 4.67; Cl,8.22; N,3.24; O,11.15.

2J

1-(6-Chloro-2-methyl-4-phenylquinoline-3-yl) -3-(3-chlorophenyl) prop-2-en-1-one

IR (KBr) (ƛmax in cm-1): 1624(C=N); 1701(C=O);

^{1}H-NMR ($CDCl_3$, δ ppm):2.53(s,3H of CH_3), 6.8-7.7 (m, 11H of Ar-H),6.4-6.5 (d, 1H of CH=CH), 7.7(d,1H of =CH).
Analysis: Calcd for $C_{25}H_{17}Cl_2NO$ (418), C, 71.78; H, 4.10; Cl,16.95; N,3.35; O,3.82..
Found C, 71.76; H, 4.08; Cl,16.93; N,3.33; O,3.80

General Procedure for the preparation of pyrazolines (III a-j):

Into a clean round bottomed flask containing 5 ml of glacial acetic acid, introduced appropriate chalcones (**II a-j**) (0.001 mol), and the hydrazine hydrate (0.001 mol) was added drop by drop with continuous stirring for 10 min, then the reaction mixture was refluxed for 24 h, cooled, poured onto crushed ice with continuous stirring, the obtained solution was kept in the refrigerator for 24 h to complete the precipitation. The separated solid product was collected by filtration and dried.

3A

1-[3-(6-Chloro-2-methyl-4-phenylquinolin-3-yl) -5-(3,4-dimethoxyphenyl)-4,5-dihydro-1*H*- pyrazol-1-yl] ethanone

IR (KBr) (ƛmax in cm-1): 1577(C=C); 1616(C=N); 1690(C=O).
^{1}H-NMR ($CDCl_3$, δ ppm): 6.7-8.0 (m, 11H of Ar-H), 6.5-6.6 (d, 1H of CH), 6.3-6.4 (1H, d, 1H of CH_2), 5.2-5.4 (1H, d, 1H of CH_2), 3.8-3.9 (d, 6H of 2x OCH_3), 2.7-2.8 (s, 3H of CH_3), 2.3 (s, 3H of $COCH_3$).

MassSpectra (m/z): Molecular weight of the sample is 500 and molecular ion peak was appeared as M+ at 500.
Analysis: Calcd for $C_{29}H_{26}ClN_3O_3$ (500), C, 69.83; H, 5.86; Cl,6.87; N,8.14; O,9. 30.
Found C, 69.81; H, 5.83; Cl,6.85; N,8.12; O,9.28.

3B

1-[3-(6-Chloro-2-methyl-4-phenylquinolin-3-yl)-5-(3-hydroxyphenyl)-4,5-dihydro-1*H*-pyrazol-1-yl] ethanone

IR (KBr) (ƛmax in cm-1): 1577(C=C); 1616(C=N); 1690(C=O)
^{1}H-NMR (DMSO d_6, δ ppm): 9.2-9.3 (s, 1H of OH), 6.7-8.0 (12H, m, 12H of Ar-H), 6.5-6.6 (d, 1H of CH), 6.3-6.4 (1H, d, 1H of CH_2), 5.2-5.4 (1H, d, 1H of CH_2), 2.5-2.6 (3H, s, 3H of CH_3), 2.4 (3H, s, 3H of $COCH_3$).

MassSpectra (m/z): Molecular weight of the sample is 456 and molecular ion peak was appeared as M+ at 456.

Analysis: Calcd for $C_{27}H_{22}ClN_3O_2$ (456), C, 71.25; H, 5.55; Cl,7.51; N,8.90; O,6.78.
Found C, 71.23; H, 5.53; Cl,7.50; N,8.88; O,6.75.

3C

1-[3-(6-Chloro-2-methyl-4-phenylquinolin-3-yl)-5-(4-ethoxyphenyl)-4,5-dihydro-1*H*-pyrazol-1-yl] ethanone

IR (KBr) (λmax in cm-1): 1577(C=C); 1616(C=N); 1690(C=O)

^{1}H-NMR (DMSO d_6, δ ppm): 4.09 (q 2H of CH_2), 1.9(t, 3H of CH_3), 6.8-8.09 (m, 12H of Ar-H),2.53(s,3H of CH_3),2.4 (3H, s, 3H of $COCH_3$),4.9(t,Hof CH), 3.19-3.44(dd ,2H of CH_2).

Analysis: Calcd for $C_{29}H_{26}ClN_3O$ (468), C, 72.06; H, 6.05; Cl,7.09; N,8.40; O,6.40.
Found C, 72.064H, 6.03; Cl,7.07; N,8.38; O,6.38.

3D

1-[3-(6-Chloro-2-methyl-4-phenylquinolin-3-yl)-5-(4-fluorophenyl)-4,5-dihydro-1*H*- pyrazol-1-yl] ethanone

IR (KBr) (λmax in cm-1): 1577(C=C); 1616(C=N); 1690(C=O)

^{1}H-NMR (DMSO d_6, δ ppm): 6.8-8.09 (m, 12H of Ar-H),2.53(s,3H of CH_3),2.4 (3H, s, 3H of $COCH_3$),4.9(t,Hof CH), 3.19-3.44(dd ,2H of CH_2).

Analysis: Calcd for $C_{27}H_{21}ClFN_3O$ (458), C, 70.95; H, 5.32; Cl,7.48; F4.01;N,8.87; O,3.38.
Found C, 70.93; H, 5.30; Cl,7.45; F4.0;N,8.85; O,3.35.

3E

1-[3-(6-Chloro-2-methyl-4-phenylquinolin-3-yl)-5-(3-ethoxy-4-hydroxyphenyl)-4,5-dihydro-1*H*- pyrazol-1-yl] ethanone

IR (KBr) (λmax in cm-1): 1577(C=C); 1616(C=N); 1690(C=O)

^{1}H-NMR (DMSO d_6, δ ppm): 4.09 (q 2H of CH_2), 1.82(t, 3H of CH_3), 5.35(s,1H of OH)6.8-8.09 (m, 11H of Ar-H),2.53(s,3H of CH_3),2.04 (3H, s, 3H of $COCH_3$),4.9(t,H of CH), 3.19-3.44(dd ,2H of CH_2).

Analysis: Calcd for $C_{29}H_{26}ClN_3O_3$ (500), C, 69.83; H, 5.86; Cl,6.87; N,8.14; O,9. 30.
Found C, 69.81; H, 5.83; Cl,6.85; N,8.12; O,9.28.

3F

1-[3-(6-Chloro-2-methyl-4-phenylquinolin-3-yl) -5-(4-methoxyphenyl)-4,5-dihydro-1*H*- pyrazol-1-yl] ethanone

IR (KBr) (λmax in cm-1): 1577(C=C); 1616(C=N); 1690(C=O)

^{1}H-NMR ($CDCl_3$, δ ppm): 6.8-8.09 (m, 12H of Ar-H), 3.83 (s,3H of OCH_3), 2.04 (3H, s, 3H of $COCH_3$),2.53(s,3H of CH_3),4.9(t,H of CH), 3.19-3.44(dd ,2H of CH_2).

Analysis: Calcd for $C_{28}H_{24}ClN_3O_2$ (470), C, 71.67; H, 5.81; Cl,7.29; N,8.05; O,6.58.
Found C, 71.65; H, 5.80; Cl,7.27; N,8.03; O,6.56.

3G

1-[3-(6-Chloro-2-methyl-4-phenylquinolin-3-yl) -5-(4-methylphenyl)-4,5-dihydro-1*H*-pyrazol-1-yl] ethanone

IR (KBr) (λmax in cm-1): 1577(C=C); 1616(C=N); 1690(C=O)

^{1}H-NMR (CDCl$_3$, δ ppm): 6.8-8.08 (m, 12H of Ar-H), 2.53(s,3H of CH_3),2.34(s,1H of CH_3),2.04 (3H, s, 3H of $COCH_3$),4.9(t,H of CH), 3.19-3.44(dd ,2H of CH_2).

Analysis: Calcd for $C_{28}H_{24}ClN_3O$ (454), C, 74.11; H, 6.00; Cl,7.54; N,8.94; O,3.40.
Found C, 74.09; H, 5.98; Cl,7.52; N,8.92; O,3.38.

3H

1-[3-(6-Chloro-2-methyl-4-phenylquinolin-3-yl) -5-(4-ethoxyphenyl)-4,5-dihydro-1*H* - pyrazol-1-yl] ethanone

IR (KBr) (λmax in cm-1): 1577(C=C); 1616(C=N); 1690(C=O)

^{1}H-NMR (CDCl$_3$, δ ppm): 4.09 (q 2H of CH_2), 1.82(t, 3H of CH_3), 6.8-8.1(m, 11H of Ar-H), 2.53(s,3H of CH_3),2.04 (3H, s, 3H of $COCH_3$),4.9(t,H of CH), 3.19-3.44(dd ,2H of CH_2).

Analysis: Calcd for $C_{29}H_{26}ClN_3O_2$ (484), C, 72.06; H, 6.05; Cl,7.09; N,8.40; O,6.40.
Found C, 72.03; H, 6.03; Cl,7.07; N,8.38; O,6.37.

3I

1-[3-(6-Chloro-2-methyl-4-phenylquinolin-3-yl)-5-(4-hydroxy-3-methoxyphenyl)-4,5-dihydro-1*H*- pyrazol-1-yl] ethanone

IR (KBr) (λmax in cm-1): 1577(C=C); 1616(C=N); 1690(C=O)

^{1}H-NMR (CDCl$_3$, δ ppm):6.8-8.01 (m, 11H of Ar-H),3.83 (s,3H of OCH_3),2.53(s,3H of CH_3),5.35(s,1H of OH),2.04 (3H, s, 3H of $COCH_3$),4.9(t,H of CH), 3.19-3.44(dd ,2H of CH_2).

Analysis: Calcd for $C_{28}H_{24}ClN_3O_3$ (486), C, 69.38; H, 5.62; Cl,7.06; N,8.37; O,9.56.
Found C, 69.36; H, 5.60; Cl,7.04; N,8.35; O,9.54.

3J

1-[3-(6-Chloro-2-methyl-4-phenylquinolin-3-yl)-5-(3-chlorophenyl)-4,5-dihydro-1*H*-pyrazol-1-yl] ethanone

IR (KBr) (λmax in cm-1): 1577(C=C); 1616(C=N); 1690(C=O)

^{1}H-NMR (CDCl$_3$, δ ppm):2.53(s,3H of CH_3),6.8-8.01 (m, 12H of Ar-H),2.04 (3H, s, 3H of $COCH_3$),4.9(t,H of CH), 3.19-3.44(dd ,2H of CH_2).

Analysis: Calcd for $C_{27}H_{21}Cl_2N_3O$ (474), C, 68.57; H, 5.14; Cl,14.46; N,8.57; O,3.26.
Found C, 68.55; H, 5.12; Cl,14.44; N,8.55; O,3.24.

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Table-1

Sl No	Compound Code	R	R_1	Molecular Formula	Molecular Weight	Melting Point (°C)	Yield %
1	IIIa	$-OCH_3$	$-OCH_3$	$C_{29}H_{26}ClN_3O_3$	500	142-144	50
2	IIIb	-OH	-H	$C_{27}H_{22}ClN_3O_2$	456	270-272	60
3	IIIc	-H	$-C_2H_5$	$C_{29}H_{26}ClN_3O$	468	190-192	72
4	IIId	-H	-F	$C_{27}H_{21}ClFN_3O$	458	100-102	79
5	IIIe	$-OC_2H_5$	-OH	$C_{29}H_{26}ClN_3O_3$	500	144-146	71
6	IIIf	-H	$-OCH_3$	$C_{28}H_{24}ClN_3O_2$	470	170-172	76
7	IIIg	-H	$-CH_3$	$C_{28}H_{24}ClN_3O$	454	150-152	73
8	IIIh	-H	$-OC_2H_5$	$C_{29}H_{26}ClN_3O_2$	484	130-132	69
9	IIIi	$-OCH_3$	-OH	$C_{28}H_{24}ClN_3O_3$	486	150-152	71
10	IIIj	-Cl	-H	$C_{27}H_{21}Cl_2N_3O$	474	160-162	65

General procedure for the preparation pyrazoles (IV a-j):

Into a clean round bottomed flask containing 5 ml alcohol, introduced appropriate chalcones (**II a-j**) (0.001 mol), hydrazine hydrate (0.004 mol) and Conc. HCl (0.5 ml) and the contents were refluxed for 12 h, cooled and pour it into crushed ice with continuous stirring. The solid separated was collected by filtration and washed with water and dried.

4A

6-chloro-2-methyl-3-[5-(3,4-dimethoxyphenyl)-1*H*-pyrazol-3-yl]-4-phenylquinoline

IR (KBr) (λmax in cm-1): 1568(C=C); 1658 (C=N);3056(N-H (pyrazole))

^{1}H-NMR ($CDCl_3$, δ ppm):5.9(broad s,1H of NH), 6.8-7.9(m, 1H of CH and 11H of Ar-H),3.7-3.9 (s, 6H of 2 x OCH_3), 2.7 (s, 3H of CH_3).

Analysis: Calcd for $C_{27}H_{22}ClN_3O_2$ (456), C, 71.25; H, 5.55; Cl,7.51; N,8.90; O,6.78.
Found C, 71.23; H, 5.53; Cl,7.50; N,8.88; O,6.76.

4B

6-chloro-2-methyl-3-[5-(3-hydroxyphenyl) -1*H*-pyrazol-3-yl]-4-phenylquinoline

IR (KBr) (λmax in cm-1):1577(C=C); 1616(C=N); 3049(N-H (pyrazole)

^{1}H-NMR ($CDCl_3$, δ ppm): 8.7-8.8 (d, 1H of OH), 6.4-8 (m, 1H of CH and 11H of Ar-H), 3.8(s,3H of OCH_3),5.9(broad s,1H of NH),2.7 (s, 3H of CH_3).

Analysis: Calcd for $C_{25}H_{18}ClN_3O$ (412), C, 72.79; H, 5.18; Cl,8.28; N,9.82; O,3.74.
Found C, 72.77; H, 5.15; Cl,8.25; N,9.80; O,3.71.

4C

6-chloro-2-methyl-3-[5-(4-hydroxy-3-methoxyphenyl)-1*H*-pyrazol-3-yl]-4-phenylquinoline

IR (KBr) (λmax in cm-1): 1572(C=C); 1650(C=N); 3053(N-H (pyrazole)

^{1}H-NMR ($CDCl_3$, δ ppm): 2.61 (q 2H of CH_2), 1.9(t, 3H of CH_3), 6.8-8.01 (m, 12H of Ar-H), 2.53(s,3H of CH_3),5.9(broad s,1H of NH).

Analysis: Calcd for $C_{26}H_{20}ClN_3O_2$ (442), C, 70.81; H, 5.28; Cl,7.74; N,9.12; O,6.99.

Found C, 70.80; H, 5.26; Cl,7.72; N,9.10; O,6.97.

4D

6-chloro-2-methyl-3-[5-(4-fluorophenyl) -1*H*-pyrazol-3-yl]-4-phenylquinoline

IR (KBr) (ƛmax in cm-1): 1568(C=C); 1658 (C=N);3056(N-H (pyrazole))

^{1}H-NMR ($CDCl_3$, δ ppm): 6.8-7.9 (m, 12H of Ar-H), 2.53(s,3H of CH_3),5.9(broad s,1H of NH).

Analysis: Calcd for $C_{25}H_{17}ClFN_3$ (414), C, 72.64; H, 4.92; Cl,8.25;F,4.42; N,9.77.
Found C, 72.64; H, 4.92; Cl,8.25;F,4.42; N,9.77.

4E

6-chloro-2-methyl-3-[5-(4-ethoxyphenyl)-1*H*-pyrazol-3-yl]-4-phenylquinoline

IR (KBr) (ƛmax in cm-1):1577(C=C); 1616(C=N); 3049(N-H (pyrazole)

^{1}H-NMR ($CDCl_3$, δ ppm): 4.09 (q 2H of CH_2), 1.82(t, 3H of CH_3), 6.8-7.7 (m, 11H of Ar-H), 2.53(s,3H of CH_3),5.9(broad s,1H of NH).

Analysis: Calcd for $C_{27}H_{22}ClN_3O$ (440), C, 73.75; H, 5.75; Cl,7.78; N,9.92; O,3.51
Found C, 73.73; H, 5.73; Cl,7.76; N,9.90; O,3.49

4F

6-chloro-2-methyl-3-[5-(4-methoxyphenyl)-1*H*-pyrazol-3-yl]-4-phenylquinoline

IR (KBr) (ƛmax in cm-1): 1572(C=C); 1650(C=N); 3053(N-H (pyrazole)

^{1}H-NMR ($CDCl_3$, δ ppm):6.8-8.09 (m, 12H of Ar-H),3.83 (s,3H of OCH_3), 2.7 (s, 3H of CH_3),5.9(broad s,1H of NH).

Analysis: Calcd for $C_{26}H_{20}ClN_3O$ (426), C, 73.38; H, 5.47; Cl,8.02; N,9.51; O,3.62
Found C, 73.36; H, 5.45; Cl,8.00; N,9.50; O,3.61

4G

6-chloro-2-methyl-3-[5-(4-methoxyphenyl) -1*H*-pyrazol-3-yl]-4-phenylquinoline

IR (KBr) (ƛmax in cm-1): 1568(C=C); 1614(C=N); 3056(N-H (pyrazole)

^{1}H-NMR ($CDCl_3$, δ ppm): 6.8-7.7 (m, 12H of Ar-H), 2.53(s,3H of CH_3),2.34(s,1H of CH_3), 5.9(broad s,1H of NH).

Analysis: Calcd for $C_{26}H_{20}ClN_3O$ (426), C, 73.38; H, 5.47; Cl,8.02; N,9.51; O,3.62
Found C, 73.36; H, 5.45; Cl,8.00; N,9.50; O,3.61

4H

6-chloro-2-methyl-3-[5-(3-ethoxy-4-hydroxy phenyl)-1*H*-pyrazol-3-yl]-4-phenylquinoline

IR (KBr) (ƛmax in cm-1):1577(C=C); 1616(C=N); 3049(N-H (pyrazole)

^{1}H-NMR ($CDCl_3$, δ ppm): 4.09 (q 2H of CH_2), 1.82(t, 3H of CH_3), 6.8-7.7 (m, 11H of Ar-H), 2.53(s,3H of CH_3),5.9(broad s,1H of NH),5.35(s,1Hof OH)

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Analysis: Calcd for $C_{27}H_{22}ClN_3O_2$ (428), C, 71.25; H, 5.55; Cl,7.51; N,8.90; O,6.78.
Found C, 71.23; H, 5.53; Cl,7.50; N,8.88; O,6.76.

4I

6-chloro-2-methyl-3-[5-(4-ethylphenyl) -1*H*-pyrazol-3-yl]-4-phenylquinoline

IR (KBr) (ƛmax in cm-1): 1572(C=C); 1650(C=N); 3053(N-H (pyrazole)

^{1}H-NMR ($CDCl_3$, δ ppm):6.8-7.7 (m, 11H of Ar-H),3.83 (s,3H of OCH_3),2.53(s,3H of CH_3),5.35(s,1H of OH),5.9(broad s,1H of NH).

Analysis: Calcd for $C_{27}H_{22}ClN_3$ (424), C, 76.44; H, 5.96; Cl,8.06; N,9.95;
Found C, 76.42; H, 5.94 Cl,8.03; N,9.93.

4J

6-chloro-2-methyl-3-[5-(3-chlorophenyl)-1*H*-pyrazol-3-yl]-4-phenylquinoline

IR (KBr) (ƛmax in cm-1): 1568(C=C); 1614(C=N); 3056(N-H (pyrazole)

^{1}H-NMR ($CDCl_3$, δ ppm):5.9(broad s,1H of NH),2.53(s,3H of CH_3),6.8-7.7 (m, 11H of Ar-H),

Analysis: Calcd for $C_{25}H_{17}Cl_2N_3$ (430), C, 68.96; H, 4.74; Cl,15.88; N,9.41;
Found C, 68.94; H, 4.72; Cl,15.85; N,9.38;

Table-2

Sl No	Compound Code	R	R_1	Molecular Formula	Molecular Weight	Melting Point (°C)	Yield %
1	IVa	$-OCH_3$	$-OCH_3$	$C_{27}H_{22}ClN_3O_2$	456	110-112	75
2	IVb	-OH	-H	$C_{25}H_{18}ClN_3O$	412	140-142	78
3	IVc	$-OCH_3$	-OH	$C_{26}H_{20}ClN_3O_2$	442	104-106	79
4	IVd	-H	-F	$C_{25}H_{17}ClFN_3$	414	100-102	74
5	IVe	-H	$-OC_2H_5$	$C_{27}H_{22}ClN_3O$	440	124-126	72
6	IVf	-H	$-OCH_3$	$C_{26}H_{20}ClN_3O$	426	170-172	78
7	IVg	-H	$-CH_3$	$C_{26}H_{20}ClN_3$	410	130-132	75
8	IVh	$-OC_2H_5$	-OH	$C_{27}H_{22}ClN_3O_2$	428	124-126	76
9	IVi	-H	$-C_2H_5$	$C_{27}H_{22}ClN_3$	424	110-112	70
10	IVj	-Cl	-H	$C_{25}H_{17}Cl_2N_3$	430	154-156	75

Biological Activities

Antimicrobial Activity The antibacterial activities of compounds 4(a-f) and 5(a-c), were carried out using the cup plate diffusion method [66-67]. This method depends on the diffusion of the antibiotic from a cavity through the solidified agar layer in a petri dish to an extent such that the growth of the addedmicroorganism is prevented in a circular zone around the cavity containing a solution of the antibiotic. For antibacterial activity, antibacterial species used are two Gram negative species, Escherichia coli (ATCC 9637), Salmonella typhi (ATCC 6539) and two Gram

positive species, Bacillus subtilis (ATCC 6633), Staphylococcus aureus (ATCC 29737). Two fungal strains Aspergillusniger (ATCC 16509), Aspergillusfumigatus (ATCC16406) were used for antifungal activity. Solution of each compound at a concentration of 1000µg/ml in DMSO was prepared and the inhibition zone diameter in millimeter was used as the criterion for measuring the microbial activity after 24h for bacteria and 72h for fungi. Ciprofloxacin is used as bacterial standards and Amphotericin B is used as fungal standards for references to evaluate the efficacy of the tested compounds under the same conditions. DMSO used as control and solvent to prepare compound solutions. Measurements of results are shown inTable -3

Table-3

	Gram Positive		Gram negative		Antifungal Activity	
Compound No	***Bacillus Subtilis***	***Staphylococcus aureus***	***Escheric-hia Coli***	***Salmonella Typhi***	***A. fumigates***	***A. Niger***
3a	29±0.29	21±0.24	31±0.236	21±0.213	32±0.167	28±0.230
3b	22±0.166	17±0.167	21±0.145	18±0.132	23±0.153	19±0121
3c	26±0.233	----	21±0.147	17±0.305	20±0.331	25±0.261
3d	29±0.29	29±0.241	27±0.203	28±0.305	33±0.152	31±0.251
3e	27±0.12	16±0.233	23±0.205	15±0.143	22±0.155	28±0.214
3f	23±0.066	19±0.296	28±0.276	23±0.215	28±0.283	25±0.221
3g	23±0.067	21±0.24	22±0.153	21±0.142	22±0.145	19±0.261
3h	18±0.202	18±0.305	19±0.134	19±0.216	28±0.210	17±0.275
3i	22±0.176	22±0.153	20±0.128	17±0.202	27±0.186	21±0.192
3j	26±0.173	19±0.297	28±0.283	24±0.145	33±0.231	29±0.176
4a	23±0.066	15±0.140	23±0.192	21±0.0.153	21±0.197	
4b	29±0.203	24±0.185	32±0.173	25±0.305	24±0.264	14±0.213
4c	23±0.145	19±0.133	26±0.243	24±0.264	19±0.152	16±0.197
4d	19±0.173	22±0.186	17±0.166	21±0.275	24±0.192	21±0.204
4e	28±0.305	19±0.203	24±0.135	23±0.281		13±0.198
4f	23±0.067	21±0.251	13±0.261	26±0.247	22±0.201	21±0.214
4g	20±0.153	13±0.20	26±0.033	17±0.194	19±0.296	28±0.216
4h	27±0.116	22±0.145	21±0.145	18±0.178	21±0.152	25±0.186
4i	25±0.033	17±0.184	18±0.214	21±0.201	25±0.115	17±0.179
4j	17±0.29	16±0.175	19±0.231	16±0.172	32±0.241	29±0.302
Ciproflaxcin						
	32	30	34	32		
Amphotericin B					34	36

Results and Discussion

Chemistry

In the present investigation chalcones,2(a-j) are obtained by the condensation of 1-(6-Chloro-2-methyl-4-phenyl-quinolin-3-yl)-ethanone with various disubstitutedbenzene. In solvent.The IR spectrum of all chalcones exhibited a strong carbonyl absorption around 1700cm^{-1}corresponding

to α, β unsaturated carbonyl group.[1]H NMR spectrum of compound 2b has shown a, singlet at δ2.75 (s,3H) due to methyl protons. The deshielded protons present on the α, β carbons of the chalcones appeared at *δ* 6.75 and δ 7.10(2H, -CH=CH-) respectively. The structural elucidation of the compound is also explained from ^{13}C NMR spectral data.The^{13}C NMR of 2b shows peak at δ24.05 due to methyl group and peak at196.36 is encountered for the carbonyl carbon of α, β unsaturatedketone.

. The 1H NMR spectrum of one of the target compound (3b), singlet at 2.90 due to three protons of methyl group. The existence of methylenic protons of pyrazoline ring as dd, clearly indicates the magnetic non-equivalence of these two protons, which have chemical shift at δ3.44-2.51centered at δ 3.47 and δ3.19-3.735centered at δ 3.22, the CH proton appeared as triplet at δ 4.93- 4.96 centered at δ 4.94 due to vicinal coupling with two protons of methylene.The^{13}C NMR spectrum of the compound (3b) has shown peaks at *δ*26 due to carbon of methyl group, *δ*42.93 corresponding to methylinic carbon atom of pyrazoline ring, *δ* 46 due to CH of pyrazoline ring. The disappearance of the^{13}C peak at δ 198 confirms the cyclisation mechanism to form pyrazoline ring. Furthermore, the mass spectrum of (3b) has exhibited molecular ion peak at m/z 456.

Similarly spectrum of the compound (4b) has shown peaks at *δ* 25.82 due to methyl group, . The 1H NMR spectrum of one of the target compound (4b) has,broad singlet at δ 5.7-5.9 corresponds to pyrazole NH, singlet at 2.90 due to three protons of methyl group. The ^{13}C NMR Spectrum of the compound (4b) has shown peaks at *δ*26 due to carbon of methyl group, ,*δ* 46 due to CH of pyrazole ring. The disappearance of the^{13}C peak at δ 198 confirms the cyclisationmechanism to form pyrazole ring. Furthermore, the mass spectrum of (4b) has exhibited molecular ion peak at m/z 412 corresponding to the molecular weight of the compound .

Antimicrobial Activity

All the synthesised compounds were subjected for antimicrobial activity. In vitro antibacterial activities of the synthesized compounds were evaluated utilizing Bacillus subtilis, Staphylococcus aureus, Escherichia coli and Salmonella typhi, antifungal activity against *Aspergillusniger*and *Aspergillusfumigatus*by cup plate method. The bioactivity of the synthesised compounds depicts that activity depends on the nature of the substituent. The electronic nature of the substituent groups leads to significant discrepancy in antimicrobial activity. The presence of chloro group on the aromatic ring at 5th position of quinolinering and alsothe presence of chloro and flouro at the phenyl ring amplified the antimicrobial activity of the compounds compared to electron donating CH3 group.The OCH_3substituent which has greater negative inductive effect than OH also showed good antibacterial activity.They showed good activity against gram –ve bacteria. The pyrazolines displayed higher antimicrobial activity than pyrazoles**. 3d** has exhibited highest antimicrobial activitywhile remaining compounds showed moderate activity.. All the test were performed in triplicate. Obtained bioactivity results were compared with commercially available drugs, Ciprofloxacin and AmphotericinB.The preliminary in vitro antifungal and antibacterial screening of the compounds 3(a-j) and 4(a-j) revealed that most of the compounds showed potent activity but However, none of the compounds exhibited zone of inhibition more than that of standard.

Conclusion

The synthesis of **3(a-j)** was prepared by cyclocondensation of chalcones**2 (a-j)** with hydrazine hydrate in acetic acid, similarly **4 (a-j)** were obtained by the cyclocondensation of chalcones with hydrazine hydrate in Hydrochloric acid.
The structures of synthesisedquinoline –pyrazolederivatives were confirmed by their IR,1H NMR, 13C NMR, Mass spectral and analytical data. Synthesised compounds **3a ,3d and 4d,** have shown maximum zone of inhibition against *Bacillus subtilis*(ATCC 6633), *Staphylococcus aureus*(ATCC 29737), *Escherichia coli* (ATCC 9637), and *Salmonella typhi*(ATCC 6539) rest of the compounds showed moderate to less activity.

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