Indian Journal of Chemistry
Vol. 60B, December 2021, pp. 1601-1606

# Synthesis, antioxidant and antibacterial activities of quinoline incorporated 2,4,5-trisubstituted imidazole derivatives

B Somashekara[a,b] & G R Vijayakumar*[a]

[a] Department of Chemistry, University College of Science, Tumkur University, Tumkur 572 103, India

[b] Department of Chemistry, Smt. Indira Gandhi Government First Grade Women's College, Sagar 577 401, India

E-mail: vijaykumargr18@gmail.com

*Received 31 July 2020; accepted (revised) 4 August 2021*

A series of quinoline incorporated 2,4,5-trisubstituted imidazole derivatives (**4a-h** and **5a-f**) have been synthesized. The structures of the synthesized compounds have been established by FT-IR, $^1$H NMR and mass spectral analysis. The prepared compounds have been evaluated for their *in vitro* antioxidant activity by DPPH method and antibacterial activity against *Bacillus subtilis*, *Escherichia coli*, *Bacillus megaterium* and *Salmonella typhi* bacterial strains at 500 µg/mL concentration. The compounds **4a**, **4e** and **4d** exhibit good antioxidant activity. Among the synthesized compounds, **4a** has shown significant antibacterial activity against all the three tested microorganisms.

**Keywords**: 2-Chloroquinoline, 2-hydroxyquinoline, antioxidant, antibacterial

Present scenario imidazole based scaffolds are very important synthetic intermediates for the synthesis of useful chemical compounds to tackle various diseases. The imidazole ring is an essential part of many natural compounds such as histidine and histamine. Imidazole and its derivatives have occupied a unique place in the field of medicinal and agrochemical industries. Currently using drugs have made up of imidazole ring as a core moiety. Imidazole containing molecules i.e. tioconazole, sertaconazole, clotrimazole and bifonazole are effective antifungal drugs, whereas metronidazole and nimorazole are antibacterial drugs. Imidazole derivatives found to possess various pharmacological properties such as antioxidant[1,2], anticancer[3,4], anti-inflammatory[5], antimicrobial[6-8], protein tyrosine phosphatase inhibitor[9], kinase inhibitor[10], α-glucosidase inhibitor[11,12], antimalarial[13], anticonvulsant[14], antiviral[15] and antitubercular[16].

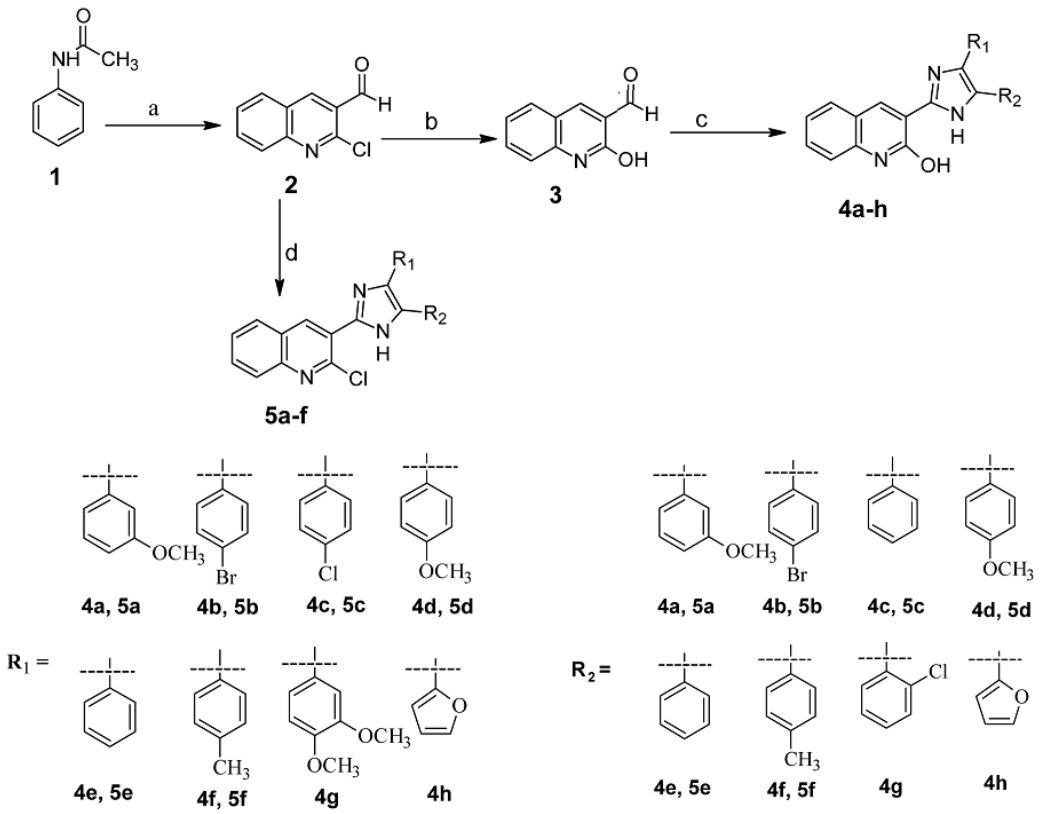
On the other hand, quinoline derivatives have gained considerable attention because of their wide range of applications. The quinoline is found in many naturally occurring alkaloids. Quinine is an antimalarial drug and has been isolated from the bark of cinchona trees. Many synthetic drugs used for the treatment of malaria such as chloroquin, plasmoquin and atebrin containing quinoline as an essential component. Quinoline ring is also present in commercially available dye cyanin. Apart from the above quinoline derivatives have been found to possess other biological activities such as antibacterial[17,18], antifungal[19], anticancer[20,21], anti-inflammatory[22,23], antihypertensive[24], antiviral[25,26], inhibits the enzymes such as α-amylase[27] and glucosidase[28,29].

The major problem of existing antimicrobial drugs for the treatment of microbial diseases is due to their side effects and also some microorganisms acquiring resistance against present drugs. In order to overcome this current situation, it is necessary to search for the new antimicrobial agents. Considering the bio-profile of imidazole and quinoline derivatives a series of quinoline containing 2,4,5-trisubstituted imidazole derivatives were synthesized and evaluated for their antioxidant and antibacterial activities.

## Results and Discussion

### Chemistry

In the present work a series of quinoline containing substituted imidazole derivatives have been synthesized. The synthetic route for the final targeted compounds is shown in the reaction Scheme I. Intermediate 2-chloroquinoline-3-carbaldehyde (**2**) was synthesized using Vilsmeier-Haack reagent from acetanilide. 2-Hydroxy-quinoline-3-carbaldehyde (**3**) was prepared by heating the 2-chloroquinoline-3-carbaldehyde (**2**) with 70% acetic acid. The title compounds were successfully achieved by the condensation of 2-chloroquinoline-3-carbaldehyde or




**Reaction Conditions:** (a) $POCl_3$, DMF/reflux, (b) 70% $CH_3COOH$/reflux, (c) and (d) substituted benzil, $CH_3COONH_4$, $CH_3COOH$/reflux

Scheme I — Preparation of quinoline incorporated imidazole derivatives **4a-h** and **5a-f**

2-hydroxyquinoline-3-carbaldehyde, substituted benzil and $CH_3COONH_4$ in presence of acetic acid. All the synthesized quinoline-imidazoles were characterized by spectral analysis. The compound **4a** showed FT-IR stretching frequencies of 3327.6 $cm^{-1}$ for N-H bond, 1605.4 $cm^{-1}$ for C=C and 1579.4 $cm^{-1}$ for C=N bonds of imidazole ring. The $^1H$ NMR spectrum of the compound **4a** in DMSO-$d_6$ solvent showed two singlet at (δ 3.70 and 3.73 ppm) corresponds to $-OCH_3$ group, singlet at δ 12.29 ppm for -OH and singlet at δ 12.41 ppm for imidazole NH. The aromatic protons of the compound **4a** were appeared in the range 6.85 to 8.81 ppm. The structure **4a** was further confirmed by mass spectral data which showed *m/z* value at 424.34 and which corresponds to M+1 ion. Similarly, all other compounds **4b-h** and **5a-f** was characterized.

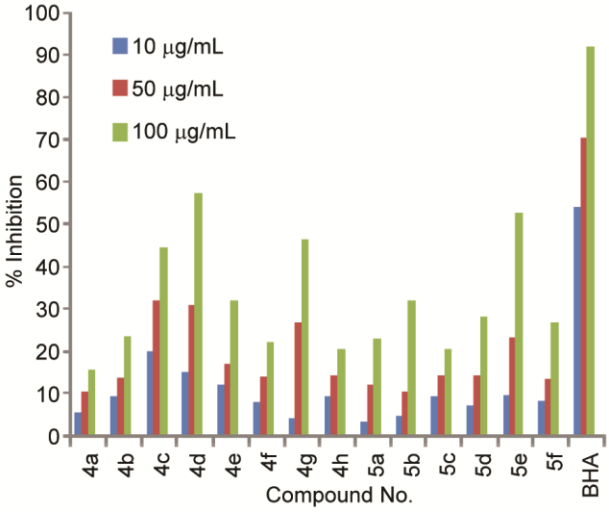



Figure 1 — Antioxidant activity of compounds **4a-h** and **5a-f**

## Antioxidant activity

Antioxidant activity of the synthesized quinoline incorporated 2,4,5-trisubstituted imidazole derivatives **4a-h** and **5a-f** were carried out using DPPH free radical scavenging assay method. Among the synthesized compounds 4**d** with methoxy group **4c** and **4g** with chloro group showed good antioxidant activity. The compound **5e** with benzene ring showed significant activity. The antioxidant activity results of (**4a-h**) and (**5a-f**) is given in Figure 1.

**Antibacterial activity**

Antibacterial activity of the synthesized compounds **4a-h** and **5a-f** were determined using agar diffusion method. The compounds **4b, 4d** and **4e** exhibited considerable antibacterial activity against *Bacillus subtilis*, *Escherichia coli*, *Bacillus megaterium* and *Salmonella typhi* bacterial strains at 500 µg/mL concentration as compared with drug ciprofloxacin. Among **5a-f** series, **5a**, **5c**, **5d** and **5e** exhibited considerable activity against all the tested bacterial strains. Results of the antibacterial study are given in Table I.

**Materials and Methods**

All reagents used in the preparation of quinoline containing 2,4,5-trisubstituted imidazole derivatives were purchased from Sigma-Aldrich, USA. Solvents were purchased from S. D. Fine chemicals, India. The progress of the reaction and purity of the samples were checked by TLC using mobile phase petroleum ether and ethyl acetate (7:3). For TLC stationary phase, silica gel coated aluminium sheets (silica gel 60 F254) procured from MERCK, India were employed. UV light is used to visualize the compounds spot on TLC plates. Column chromatography was used to purify the crude products and yields were recorded after the isolation. FT-IR spectra of the products were obtained on a JASCO FT-IR-4100 spectrophotometer using KBr pellet method. $^1$H NMR were recorded using JEOL 500 MHz NMR instrument by using TMS as internal standard and chemical shift values are expressed in δ (ppm) scale. Melting points of the synthesized compounds were recorded by open capillary method by using Mvtec melting point apparatus and are uncorrected.

Table I — Antibacterial activity of compounds **4a-h** and **5a-f** at 500 µg/mL concentration

| Compd | Zone of inhibition (mm) | | | |
|---|---|---|---|---|
| | *S. typhi* | *B. substilis* | *B. megaterium* | *E. coli* |
| **4a** | 4.5 ±0..2 | * | * | * |
| **4b** | 3.1±0.1 | 4.4±0.4 | 4.7±0.1 | 3.3±0.2 |
| **4c** | * | * | * | * |
| **4d** | 8.1±0.5 | 5.2±0.4 | 5.1±0.1 | 6.1±0.1 |
| **4e** | 4.8±0.2 | 4.1±0.2 | 3.2±0.3 | 3.0±0.2 |
| **4f** | * | * | * | * |
| **4g** | * | * | * | * |
| **4h** | * | * | * | * |
| **5a** | 5.2±0.3 | 4.8±0.7 | 4.6±0.1 | 5.7±0.3 |
| **5b** | * | * | * | * |
| **5c** | 7.3±0.6 | 6.5±0.1 | 7.2±0.6 | 6.3±0.3 |
| **5d** | 3.2±0.4 | 5.3±0.5 | 3.3±0.4 | 5.7±0.6 |
| **5e** | 5.7±0.2 | 8.1±0.2 | 6.8±0.8 | 5.7±0.1 |
| **5f** | * | * | * | * |
| [a] **Ciprofloxacin** | 27.1±0.1 | 25.4±0.2 | 27.0±0.3 | 31.4±0.4 |

[a] Reference standard ciprofloxacin at 25 µg/mL concentration
*Compounds not showed inhibition at tested concentration

**Experimental Section**

2-Chloroquinoline-3-carbaldehyde **2** and 2-hydroxyquinoline-3-carbaldehyde **3** were synthesized as per the previously reported literature[30].

**General synthetic procedure for the preparation of quinoline incorporated 2,4,5-trisubstituted imidazole derivatives**

Mixture of 2-hydroxyquinoline-3-carbaldehyde or 2-chloroquinoline-3-carbaldehyde (20 mmol), substituted benzil (20 mmol), $CH_3COONH_4$ (100 mmol) and 100 mL of glacial acetic acid was refluxed for 8-13 h in a three necked round bottom flask. The progress of the reaction was monitored by TLC using mobile phase petroleum ether and ethyl acetate (7:3). After completion of the reaction, the mixture was poured into ice cold water. The solid compound precipitated was filtered and dried. The crude product was purified by column chromatography using petroleum ether and ethyl acetate.

**2-Chloroquinoline-3-carbaldehyde, 3**: Off white solid. Mol. formula: $C_{10}H_6ClNO$. Yield 72%. m.p.146-148°C. FT-IR (KBr): 3059.5 (Ar-H), 1685.5 (C=O), 1614.1 cm$^{-1}$ (C=C); $^1$H NMR (500 MHz, DMSO-$d_6$): δ 7.75 (t, *J* = 7.2 Hz, 1H, ArH), 8.00 (t,*J* = 7.2 Hz, 1H, ArH), 8.05 (d, *J* = 8.3 Hz, 1H, ArH), 8.30 (d, *J* = 8.3 Hz, 1H, ArH), 9.01 (s, 1H, ArH), 10.39 (s, 1H, -CHO); MS: *m/z* Calcd 191.61. Found: 192.16 [M+1].

**2-Hydroxyquinoline-3-carbaldehyde, 4**: Off white solid. Mol. formula: $C_{10}H_7NO_2$. Yield 85%. m.p.248-250°C. FT-IR (KBr): 3362.3 (O-H), 3057.9 (Ar-H), 1685.5 (C=O), 1619.9 cm$^{-1}$ (C=C); $^1$H NMR (500 MHz, DMSO-$d_6$): δ 7.23 (m, 1H, ArH), 7.36 (d, *J* = 8.5 Hz, 1H, ArH), 7.66 (m, 1H, ArH), 7.92 (m, 1H, ArH), 8.51 (s, 1H, ArH) 10.24 (s, 1H, -CHO), 12.23 (s, 1H, -OH); MS: *m/z* Calcd 173.16. Found: 174.16 [M+1].

**3-[4,5-bis(3-Methoxyphenyl)-1*H*-imidazol-2-yl] quinolin-2-ol, 4a**: Pale yellow solid. Mol. formula: $C_{26}H_{21}N_3O_3$. Yield 78%. m.p.192-193°C. FT-IR

(KBr): 3374.8 (N-H), 3058.6 (Ar-H), 1651.7 (C=C), 1571.7 (C=N), 1418.4 $cm^{-1}$ (C-O); $^1$H NMR (500 MHz, DMSO-$d_6$): δ 3.76 (s, 3H, -$OCH_3$), 3.79 (s, 3H, -$OCH_3$), 6.84 (d, *J* = 7.5 Hz, 1H, ArH), 6.87 (d, *J* = 8.5 Hz, 1H, ArH), 7.08 (m, 1H, ArH), 7.13 (d, *J* = 7.5 Hz, 1H, ArH), 7.27 (m, 6H, ArH), 7.53 (m, 1H, ArH), 7.75 (d, *J* = 7.5 Hz, 1H, ArH), 9.01 (s, 1H, ArH), 10.70 (s, 1H, OH), 12.03 (s, 1H, NH); MS: *m/z* Calcd 423.46. Found: 424.12 [M+1].

**3-[4,5-bis(4-Bromophenyl)-1*H*-imidazol-2-yl] quinolin-2-ol, 4b**: Brown solid. Mol. formula: $C_{24}H_{15}Br_2N_3O$. Yield 81%. m.p.226-228°C. FT-IR (KBr): 3419.2 (N-H), 3061.4 (Ar-H), 1586.2 (C=C), 1575.6 (C=N), 1421.3 $cm^{-1}$ (C-O); $^1$H NMR (500 MHz, DMSO-$d_6$): δ 6.99 (d, *J* = 9.0 Hz, 1H, ArH), 7.30 (m, 1H, ArH), 7.44 (m, 2H, ArH), 7,52 (m, *2*H, ArH), 7.58 (m, 1H, ArH), 7.64 (dd, *J* = 6.9 Hz, 2.1 Hz, 2H, ArH), 7.87 (m, 2H, ArH), 7.94 (d, *J* = 6.9 Hz, 1H, ArH), 8.80 (s, 1H, ArH), 12.41 (s, 1H, OH), 12.42 (s, 1H, NH); MS: *m/z* Calcd 521.21. Found: 522.15 [M+1].

**3-[4-(4-Chlorophenyl)-5-phenyl-1*H*-imidazol-2-yl] quinolin-2-ol, 4c**: Pale yellow solid. Mol. formula: $C_{24}H_{16}ClN_3O$. Yield 84%. m.p.221-223°C. FT-IR (KBr): 3451.2 (N-H), 3055.7 (Ar-H), 1617.0 (C=C), 1573.6 (C=N), 1418.4 $cm^{-1}$ (C-O); $^1$H NMR (500 MHz, DMSO-$d_6$): δ 7.26 (m, 6H, ArH), 7.50 (m, 3H, ArH), 7.58 (m, 3H, ArH), 7.94 (m, 1H, ArH), 8.81 (s, 1H, ArH), 12.36 (s, 1H, OH), 12.42 (s, 1H, NH); MS: *m/z* Calcd 397.85. Found: 398.07 [M+1].

**3-[4,5-bis(4-Methoxyphenyl)-1*H*-imidazol-2-yl] quinolin-2-ol, 4d**: Pale brown solid. Mol. formula: $C_{26}H_{21}N_3O_3$**.**Yield 85%. m.p.206-208°C. FT-IR (KBr): 3418.2 (N-H), 3030.5 (Ar-H), 1611.2 (C=C), 1571.7 (C=N), 1421.2 $cm^{-1}$ (C-O); $^1$H NMR (500 MHz, DMSO-$d_6$): δ 3.76 (s, 3H, -$OCH_3$), 3.80 (s, 3H, -$OCH_3$), 6.80 (m, 4H, ArH), 7.27 (m, 1H, ArH), 7.43 (d, *J* = 8.5 Hz, 2H, ArH), 7.55 (m, 2H, ArH), 7.65 (d, *J* = 7.9 Hz, 2H, ArH), 7.74 (d, *J* = 7.5 Hz, 1H, ArH) 8.96 (s, 1H, ArH), 10.34 (s, 1H, OH), 11.87 (s, 1H, NH); MS: *m/z* Calcd 423.46. Found: 424.12 [M+1].

**3-(4,5-Diphenyl-1*H*-imidazol-2-yl)quinolin-2-ol, 4e**: Yellow solid. Mol. formula: $C_{24}H_{17}N_3O$. Yield 88%. m.p.281-283°C. FT-IR (KBr): 3321.8 (N-H), 3050.2 (Ar-H), 1615.1 (C=C), 1567.8 (C=N), 1416.5 $cm^{-1}$ (C-O); $^1$H NMR (500 MHz, DMSO-$d_6$): δ 7.27 (m, 2H, ArH), 7.34 (m, 3H, ArH), 7.42 (t, *J* = 7.6 Hz, 3H, ArH), 7.51 (m, 2H, ArH), 7.58 (m, 3H, ArH), 7.93 (d, *J* = 7.6 Hz, 1H, ArH), 8.81 (s, 1H, ArH), 12.30 (s, 1H, OH), 12.43 (s, 1H, NH); MS: *m/z* Calcd 363.41. Found: 362.20 [M-1].

**3-[4,5-bis(4-Methylphenyl)-1*H*-imidazol-2-yl] quinolin-2-ol, 4f**: Pale yellow solid. Mol. formula: $C_{26}H_{21}N_3O$. Yield 78%. m.p.240-241°C. FT-IR (KBr): 3341.1 (N-H), 3052.8 (Ar-H), 1615.1 (C=C), 1568.8 (C=N), 1418.4 $cm^{-1}$ (C-O); $^1$H NMR (500 MHz, DMSO-$d_6$): δ 2.31 (s, 3H, -$CH_3$), 2.34 (s, 3H, -$CH_3$), 7.14 (d, *J* = 8.3 Hz, 2H, ArH), 7.23 (d, *J* = 7.6 Hz, 3H, ArH), 7.28 (m, 2H, ArH), 7.37 (d, *J* = 8.3 Hz, 2H, ArH), 7.42 (d, *J* = 8.3 Hz, 1H, ArH), 7.57 (m, 1H, ArH), 7.92 (d, *J* = 7.6 Hz, 1H, ArH), 8.79 (s, 1H, ArH), 12.20 (s, 1H, OH), 12.42 (s, 1H, NH); MS: *m/z* Calcd 391.46. Found: 392.11 [M+1].

**3-[5-(2-Chlorophenyl)-4(3,4-dimethoxyphenyl)-1*H*-imidazol-2-yl]quinolin-2-ol, 4g**: Brown solid. Mol. formula: $C_{26}H_{20}ClN_3O_3$. Yield 80%. m.p.255-258°C. FT-IR (KBr): 3542.6 (N-H), 3052.8 (Ar-H), 1614.1 (C=C), 1587.1 (C=N), 1417.4 $cm^{-1}$ (C-O); $^1$H NMR (500 MHz, DMSO-$d_6$): δ 3.55 (s, 3H, -$CH_3$), 7.73 (s, 3H, -$CH_3$), 6.90 (m, 2H, ArH), 7.04 (m, 1H, ArH), 7.28 (d, *J* = 7.8 Hz, 1H, ArH), 7.44 (m, 1H, ArH), 7.57 (m, 3H, ArH), 7.92 (d, *J* = 7.8 Hz, 3H, ArH), 8.79 (s, 1H, ArH), 12.37 (s, 1H, OH), 12.39 (s, 1H, NH); MS: *m/z* Calcd 457.90. Found: 458.00 [M+1].

**3-[4,5-Di(furan-2-yl)-1*H*-imidazol-2-yl]quinolin-2-ol, 4h**: Brown solid. Mol. formula: $C_{20}H_{13}N_3O_3$; Yield:76%. m.p.248-250°C. FT-IR (KBr): 3417.1 (N-H), 3056.0 (Ar-H), 1605.4 (C=C), 1579.4 (C=N), 1427.1 $cm^{-1}$ (C-O); $^1$H NMR (500 MHz, DMSO-$d_6$): δ 7.30 (t, *J* = 7.4 Hz, 2H, ArH), 7.45 (d, *J* = 8.1 Hz, 2H, ArH), 7.62 (m, 2H, ArH), 7.81 (m, 2H, ArH), 7.95 (d, *J* = 7.3 Hz, 2H, ArH), 8.82 (s, 1H, ArH), 12.41 (s, 1H, OH), 12.54 (s, 1H, NH); MS: *m/z* Calcd 343.33. Found: 344.06 [M+1].

**3-[4,5-bis(3-Methoxyphenyl)-1*H*-imidazol-2-yl]-2-chloroquinoline, 5a**: Pale yellow solid. Mol. formula: $C_{26}H_{20}ClN_3O_2$. Yield 65%. m.p.179-180°C. FT-IR (KBr): 3383.5 (N-H), 3064.3 (Ar-H), 1600.6 (C=C), 1590.0 (C=N), 746.3 $cm^{-1}$ (C-Cl); $^1$H NMR (500 MHz, DMSO-$d_6$): δ 3.69 (s, 3H, -$OCH_3$), 3.75 (s, 3H, -$OCH_3$), 6.84 (m, 1H, ArH), 6.96 (dd, *J* = 9.0 Hz, 2.1 Hz, 1H, ArH), 7.09 (d, *J* = 7.6 Hz, 2H, ArH), 7.18 (d, *J* = 7.6 Hz, 2H, ArH), 7.25 (t, *J* = 7.9 Hz 1H, ArH), 7.37 (t, *J* = 7.9 Hz, 1H, ArH), 7.74 (t, *J* = 7.6 Hz, 1H, ArH), 7.90 (t, *J* = 7.6 Hz, 1H, ArH), 8.05

(d, *J* = 8.3 Hz, 1H, ArH), 8.15 (d, *J* = 7.6 Hz, 1H, ArH), 8.85 (s, 1H, ArH), 12.91 (s, 1H, NH); MS: *m/z* Calcd 441.9. Found: 442.34 [M+1].

**3-[4,5-bis(4-Bromophenyl)-1*H*-imidazol-2-yl]-2-chloroquinoline, 5b**: Brown solid. Mol. formula: $C_{24}H_{14}Br_2ClN_3$. Yield 60%. m.p.232-235°C. FT-IR (KBr): 3330.5 (N-H), 3051.6 (Ar-H), 1609.1 (C=C), 1584.3 (C=N), 738.1 $cm^{-1}$ (C-Cl); $^1$H NMR (500 MHz, DMSO-$d_6$): δ 7.29 (d, *J* = 7.6 Hz, 1H, ArH), 7.44 (dd, *J* = 11 Hz, 8.3 Hz, 2H, ArH), 7.55 (m, 2H, ArH), 7.65 (d, *J* = 9.0 Hz, 1H, ArH), 7.87 (m, 5H, ArH), 7.94 (d, *J* = 6.9 Hz, 1H, ArH), 8.80 (s, 1H, ArH), 12.43 (s, 1H NH); MS: *m/z* Calcd 539.64. Found: 540.83 [M+1].

**2-Choro-3-[4-(4-chlorophenyl)-5-phenyl-1*H*-imidazol-2-yl]quinoline, 5c**: Pale yellow solid. Mol. formula: $C_{24}H_{15}Cl_2N_3$. Yield 65%. m.p.162-163°C. FT-IR (KBr): 3418.2 (N-H), 3063.4 (Ar-H), 1617.0 (C=N), 1600.6 (C=N), 748.2 $cm^{-1}$ (C-Cl); $^1$H NMR (500 MHz, DMSO-$d_6$): δ 7.31 (m, 2H, ArH), 7.41 (m, 4H, ArH), 7.50 (m, 1H, ArH), 7.64 (m, 3H, ArH), 7.78 (m, 1H, ArH), 7.96 (d, *J* = 7.9 Hz, 1H, ArH), 8.04 (d, *J* = 8.4 Hz, 1H, ArH), 9.25 (d, *J* = 10.2 Hz, 1H, ArH), 10.38 (s, 1H, NH); MS: *m/z* Calcd 416.2. Found: 418.24 [M+2].

**3-[4,5-bis(4-Methoxyphenyl)-1*H*-imidazol-2-yl]-2-chloroquinoline, 5d**: Pale yellow solid. Mol. formula: $C_{26}H_{20}ClN_3O_2$. Yield 65%. m.p.148-150°C. FT-IR (KBr): 3418.2 (N-H), 3052.8 (Ar-H), 1613.2 (C=C), 1573.6 (C=N), 756.9 $cm^{-1}$ (C-Cl); $^1$H NMR (500 MHz, DMSO-$d_6$): δ 3.80 (s, 3H, -$OCH_3$), 3.81 (s, 3H, -$OCH_3$), 7.26 (m, 1H, ArH), 6.88 (m, 1H, ArH), 6.99 (m, 3H, ArH), 7.33 (d, *J* = 8.3 Hz, 1H, ArH), 7.48 (m, 2H, ArH), 7.88 (m, 2H, ArH) 8.14 (m, 2H, ArH), 8.84 (s, 1H, ArH), 12.89 (s, 1H, NH); MS: *m/z* Calcd 441.90. Found: 442.34 [M+1].

**2-Choro-3-[4,5-diphenyl-1*H*-imidazol-2-yl] quinoline, 5e**: Pale yellow solid. Mol. formula: $C_{24}H_{16}ClN_3$. Yield 68%. m.p.186-188°C. FT-IR (KBr): 3428.8 (N-H), 3062.4 (Ar-H), 1617.0 (C=C), 1582.3 (C=N), 748.2 $cm^{-1}$ (C-Cl); $^1$H NMR (500 MHz, DMSO-$d_6$): δ 7.26 (m, 1H, ArH), 7.33 (t, *J* = 7.6 Hz, 2H, ArH), 7.40 (m, 1H, ArH), 7.46 (m, 2H, ArH), 7.53 (m, 2H, ArH), 7.59 (d, *J* = 6.9 Hz, 2H, ArH), 7.74 (t, *J* = 7.9 Hz, 1H, ArH), 7.90 (m, 1H, ArH), 8.04 (d, *J* = 7.6 Hz, 1H, ArH), 8.15 (d, *J* = 7.6 Hz, 1H, ArH), 8.86 (s, 1H, ArH), 12.90 (s, 1H, NH); MS: *m/z* Calcd 381.85. Found: 382.29 [M+1].

**3-[4,5-bis(4-Methylphenyl)-1*H*-imidazol-2-yl]-2-chloroquinoline, 5f**: Pale yellow solid. Mol. formula: $C_{26}H_{20}ClN_3$. Yield 65%. m.p.163-165°C. FT-IR (KBr): 3397.0 (N-H), 3063.4 (ArH), 1616.5 (C=C), 1584.2 (C=N), 747.3 $cm^{-1}$ (C-Cl); $^1$H NMR (500 MHz, DMSO-$d_6$): δ 2.31 (s, 3H, -$CH_3$), 2.33 (s, 3H, -$CH_3$), 7.21 (d, *J* = 67.5 Hz, 4H, ArH), 7.44 (d, *J* = 19.3 Hz, 4H, ArH), 7.73 (t, *J* = 7.2 Hz, 1H, ArH), 7.89 (t, *J* = 7.9 Hz, 1H, ArH), 8.03 (d, *J* = 8.3 Hz, 1H, ArH), 8.14 (d, *J* = 8.3 Hz, 1H, ArH), 8.84 (s, 1H, ArH), 12.78 (s, 1H, NH); MS: *m/z* Calcd 409.91. Found: 410.36 [M+1].

## Antioxidant activity

The antioxidant activity study of **4a-h** and **5a-f** were carried out by using DPPH method reported by Sunil *et al*.[31] The different concentration of stock solutions (10, 50 and100 µg/mL) of synthesized compounds were prepared by using methanol. 0.1 mM 1,1-diphenyl-2-picryl hydrazyl [DPPH] in methanol was added to the above stock solutions and mixed uniformly. The resulting solution was kept in dark for 20 minutes at room temperature. Then the absorbance of the test solution was measured at 517 nm taking a reference standard BHA. The percentage inhibition was calculated by the following formula.

$$\% \text{ Inhibition} = \frac{(\text{Control OD} - \text{Sample OD})}{\text{Control OD}} \times 100$$

## Antibacterial activity

Antibacterial activity on *Escherichia coli*, *Bacillus subtilis*, *Bacillus megaterium* and *Salmonella typhi* was performed for **4a-h** and **5a-f** by using agar well diffusion method described by Perez *et al*.[32] taking ciprofloxacin as a standard. Initially the bacterial cultures were incubated at 37°C for 18 h in a media. The agar plates in the media were prepared and on each agar plate previously incubated culture was spread uniformly. Then plates were allowed to keep it for 20 min and wells were filled with 500 µg/mL concentration of synthesized compounds. The diameter of zone inhibition (in mm) was recorded after the plates were incubated at 37°C for 24 h.

## Conclusions

In this study, we have reported a series of 2-hydroxyquinoline and 2-chloro-quinoline incorporated 2,4,5-trisubstituted imidazole derivatives through one-pot multi-component synthesis using 2-hydroxy quinoline-3-carbaldehyde (for **4a-h**) or 2-chloroquinoline-3-carbaldehyde (for **5a-f**), ammonium acetate and substituted benzil in the presence acetic acid with good yield. The yields in the

range 61 to 88 % were obtained. All the synthesized quinoline containing imidazoles were characterized by FT-IR, $^1$H NMR and Mass spectra of analysis. The synthesized compounds exhibited good antioxidant activity at 10, 50, 100 µg/mL concentrations. It is found that antioxidant activity increases with the increase in compound concentration. Among the tested compounds the compounds **4c**, **4g** and **5e** exhibited significant antioxidant activity. Antibacterial activity of compounds **4a-h** and **5a-f** against *Bacillus subtilis*, *Escherichia coli*, *Bacillus megaterium* and *Salmonella typhi* bacterial strains at 500 µg/mL concentration indicated that the compounds **5a-f** series exhibited considerable antibacterial activity against tested bacterial strains.

## Supplementary Information

Supplementary information is available in the website http://nopr.niscair.res.in/handle/123456789/60.

## Acknowledgement

The authors are thankful to the Principal and the staff of Smt. Indira Gandhi Government First Grade Women's College, Sagar and Tumkur University administration for their support and encouragement. Authors also thank Skanda Life Science Bangalore for needful assistance for carrying out biological activity.

## References

1 Harshad B, Maja M & Valentina P, *Karbala Int J Modern Sci*, 4 (2018) 200.
2 Jayaraman J, Venugopal T, Nagarajan R, Kanagarathinam S & Marimuthu V P, *Med Chem Res*, 21 (2012) 1850.
3 Yusuf O, Ilhan I, Zerri I & Gulsen A, *Eur J Med Chem*, 45 (2010) 3320.
4 Katharia M, Bernhard B, Sabastian S, Marcus R, Ralaf F, Rainer S & Thamos M, *Eur J Med Chem*, 118 (2016) 9.
5 Mohd A, Iftikhar A, Wasim A, Khan S A & Ishrar A, *Indian J Chem*, 50B (2011) 207.
6 Sunil C, VikasV, Devinder K & Ashwani K, *Synthetic Commun*, 49 (2019) 1427.
7 Xian-Yu S, Mei-Yu L, Chun-Yan Z, Gui-Lin Z, Ming-Yue L, Bo-Tao J, Chun-Yuan P & Xin W, *J Braz Chem Soc*, 29 (2018),701.
8 Ivan H R T, Ali H R A-D, Ahmad M A & Mohammad F A-M, *J Saudi Chem Soc*, 20 (2016) S509.
9 Ling Z, Yu L, Quing M W & Cheng-He Z, *Bioorg Chem*, 88 (2019) 102900.
10 Dae-Kee K, Sun-Hee J, Ho-Soon L & Purushoottam M D, *Eur J Med Chem*, 44 (2009) 568.
11 Faryal C, Sadia N, Muhammad A, Mariya A-R, Bakhat J, Munawar A M & Misbahul A K, *Bioorg Chem*, 82 (2019) 267.
12 Sadia N, Faryal C, Munawar A M, Muhmmad A, Sujhla H & Misbahul A K, *Bioorg Chem*, 76 (2018) 365.
13 Rajesh K S, Ashish B & Ravi K, *Der Pharmacia Lettre*, 8 (2016) 188.
14 Asif H, Nadeem S, Sarafroz M D, Yasmin K, Rasid M & Niyaz A, *Acta Poloniae Pharmaceutica-Drug Res*, 68 (2011) 657.
15 Yuki O, Nariko S-T, Madoka K, Ailwabu, Manashi O, Tadashi W, Fumihiro K, Takayuki H, Masahiro F & Noriaki M, *Bioorg Med Chem*, 27 (2019) 218.
16 Jyoti P, Vinod K T, Shyam S V, Vinita C, Bhatnagar S, Sinha S, Gaikwad A N & Rama P T, *Eur J Med Chem*, 44 (2009) 3350.
17 Sun N, Du R L, Zheng Y Y, Huang B H, Guo Q, Zhang R F, Wong KY& Lu Y J, *Eur J Med Chem*, 135 (2017) 1.
18 Nisheeth C D, Bonny Y P & Bharati P D, *Med Chem Res*, 26 (2017) 109.
19 Musiol R, Serda M, Hensel-Bielowka S & Polanski J, *J Curr Med Chem*, 17 (2010) 1960.
20 Selim M R, Zahran M A, Belal A, Mostafa M S, Shedid S A, Mehany A B M, Elhagli G A M & Ammar Y A, *Anticancer Agents Med Chem*, 19 (2019) 439.
21 Murat B, Owen T, Chritopher R G, Selina K S, Greg M A, Glenn M M, Belamy B C, Naresh K & David St C B, *Molecules*, 21 (2016) 916.
22 Mukherjee S & Pal M, *Curr Med Chem*, 20 (2013) 4386.
23 Ling-Ling T, Xin-Ling Z & Guang-Zhen M, *Biomed Res*, 27 (2016) 1060.
24 Muruganantham N, Sivakumar R, Anbalagan N, Gunasekaran V & Leonard J T, *Biol Pharm Bull*, 27 (2004) 1683.
25 Rami M, Jiantao Z, Peter T, Naoya K, Shreya S B, Yanmei H, Rajesh K & Jun W, *J Med Chem*, 62 (2019) 4074.
26 Zemtsova M N, Zimichev A V, Trakhtenberg P L, Klimochkin Y N, Leonova M V, Balakhnin S M, Bormotov N I, Serova O A & Belanov E F, *Pharm Chem J*, 45 (2011) 267.
27 Muhammad T, Muhammad T J, Syahrul I, Manikandan S, Sridevi C, Hayat U, Fazal R, Faha K, Jahidul I M & Khalid M K, *Bioorg Chem*, 74 (2017) 179.
28 Nikookar H, Mohammadi K M, Imamparst S, Faramarzi M A, Ranjbar P R, Mahdavi M & Larijani B, *Bioorg Chem*, 77 (2018) 280.
29 Muhammad T, Nor H I, Syahrul I, Abdul W, Fazal R, Muhammad A & Ashfaq U R, *Med Chem Commun*, 6 (2015) 1826.
30 Mustapha C M, Bapu R T, Dnyaneshwar S, Raghunatha P & Ramesh Y, *Heterocycl Letters*, 5 (2015) 251.
31 Sunil K, Dinesh K, Manjusha, Kamal S, Nidhan S & Bhoodev V, *Acta Pharm*, 58 (2008) 215.
32 Perez C, Pauli M & Bazerque O, *Acta Biol Med Exp*, 15 (1990) 113.