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Synthesis, characterization and antimicrobial activity of 7-methoxy quinoline-4- substituted 1, 2, 3-triazole derivatives

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ABSTRACT

A series of 7-methoxy quinoline-4-substituted 1, 2, 3-triazoles have been synthesized by 1, 3-dipolar cycloaddition reaction of 4-azido-7-methoxy quinoline **2** with acetyl acetone and ethyl acetoacetate, respectively. The reaction of **2** with acetyl acetone afforded 1-(1-(7-methoxyquinolin-4-yl)-5-methyl-1H-1, 2, 3-triazol-4-yl) ethanone **3** and with ethyl acetoacetate afforded ethyl 1-(7-methoxyquinolin-4-yl)-5-methyl-1H-1, 2, 3-triazol-4-carboxylate **5**. Compound **3** upon condensation with aromatic aldehydes gave 1-aryl (1-(7-methoxyquinolin-4-yl)-5-methyl-1H-1, 2, 3-triazol-4-yl) prop-2-en-1-ones **4a-f**. Compound **5** is converted into its hydrazide **6** which upon further reaction with different aromatic aldehydes furnished Schiff's bases, N-{1-arylmethylene}-1-(7-methoxy quinolin-4-yl)-5-methyl -1H-1,2,3-triazol-4-carbohydrazides **7a-f**. The structure of newly synthesized 1, 2, 3-triazole derivatives have been characterized by IR, ¹H NMR, ¹³C NMR and Mass spectral data. The synthesized compounds have been screened for antimicrobial activities.

Keywords: 1,3-Dipolar cycloaddition, 4-azido-7-methoxyquinoline, 1,2,3-triazoles, antimicrobial activities and MIC.

INTRODUCTION

The quinoline nucleus is an important class of heterocyclic compounds found in many synthetic and natural products with a wide range of pharmacological activities, such as antiviral [1], anticancer [2], antibacterial [3, 4], analgesic [5], antifungal [6], antiobesity [7], anti-inflammatory [8], and antiplasmodial [9] activity, which can be well illustrated by the large number of drugs in the market containing this heterocyclic class. The 1,2,3-triazole ring system has been the subject of considerable research interest mainly due to its usefulness in synthetic organic chemistry and also because of the pharmacological properties associated with some of its derivatives. Hence the synthesis of 1,2,3-triazoles incorporated with quinoline moiety is of very importance and they possess many biological activities [10]. Prompted by these observations and in search of new antimicrobial agents, herein we reported the synthesis of novel series of 1,2,3-triazolyl quinolines.

MATERIALS AND METHODS

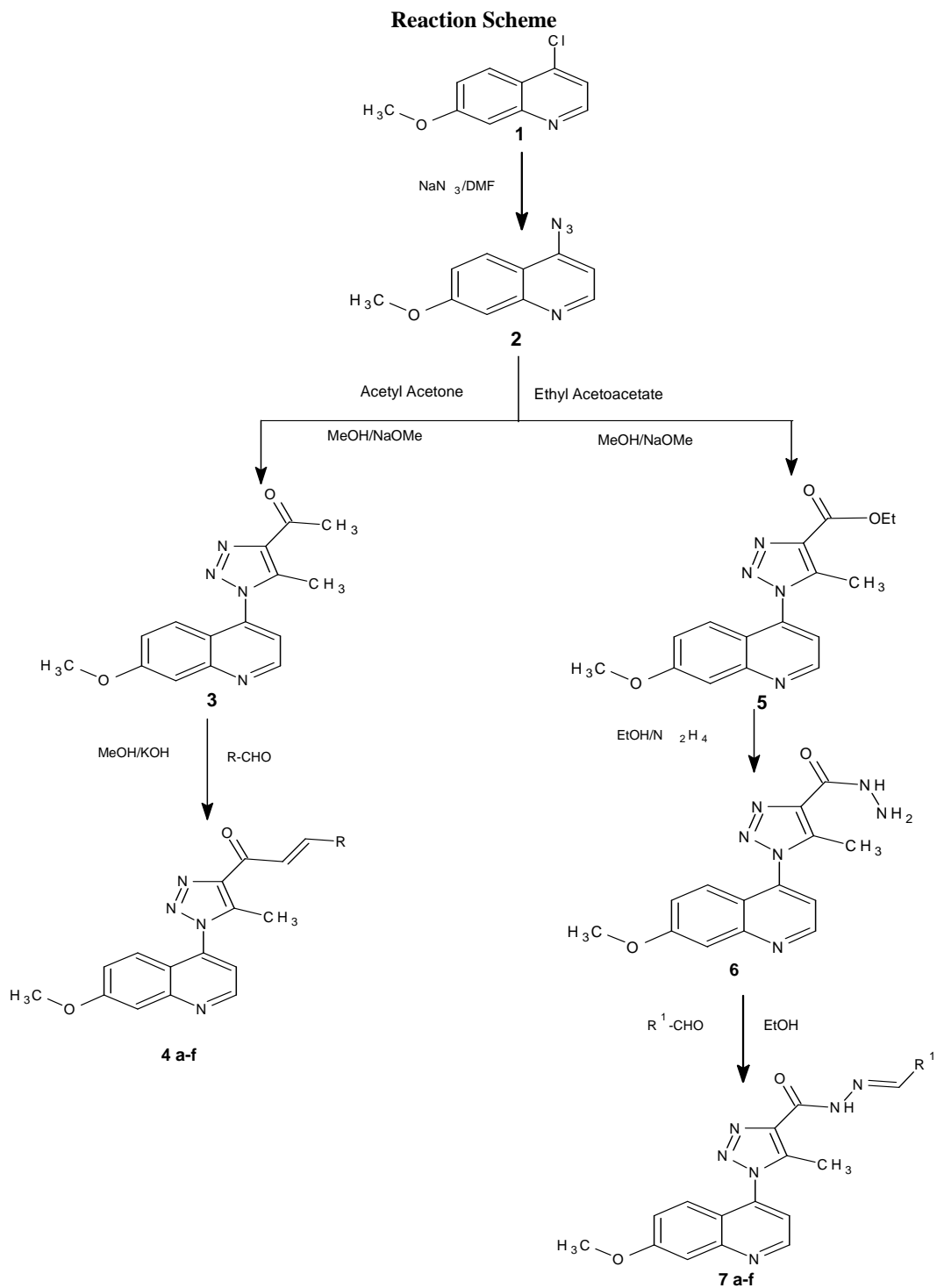
Melting points were determined in open capillary tubes and were uncorrected. The IR spectra (in KBr pellets) were recorded on a JASCO FT/IR-4100 spectrophotometer. ^1H NMR and ^{13}C NMR spectra were recorded in CDCl_3 at 300MHz on Varian spectrometer using TMS as internal standard. Chemical shift values are given in δ scales. Mass spectra were recorded on LC/MSD Trap XCT spectrometer. Elemental analyses were performed on a Flash EA 1112 series CHNS-O Analyzer. The completion of the reaction was checked by thin layer chromatography (TLC) on silica gel coated aluminium sheets (silica gel 60 F254). Commercial grade solvents and reagents were used without further purification.

Synthesis of 4-azido-7-methoxy quinoline (2)

To a solution of 4-chloro-7-methoxy quinoline **1**, (0.025 mol), in DMF (20 ml), sodium azide (0.025 mol) was added and the reaction mixture was stirred at 90-100 $^{\circ}\text{C}$ for 2 hr. After completion of the reaction, the reaction mixture was poured onto cold water and obtained precipitate was collected by filtration and recrystallized using methanol. Yield 85%, m melting point 112-115 $^{\circ}\text{C}$.

Synthesis of 1-(1-(7-methoxyquinolin-4-yl)-5-methyl-1H-1,2,3-triazol-4-yl)ethanone (3)

An equimolar quantity of 4-azido-7-methoxy quinoline **2**, (0.0049 mol) and acetyl acetone (0.0049 mol) was taken in ethanol (20 ml) and cooled to 0 $^{\circ}\text{C}$. To this, sodium ethoxide (0.01 mol) was added under inert atmosphere and the whole reaction mixture was stirred at ambient temperature for 8 hr. After completion of the reaction, the mixture was poured onto ice-cold water and neutralized with acetic acid. The obtained solid was filtered, washed with water and recrystallized from ethanol. Yield 80%, melting point 60-64 $^{\circ}\text{C}$. IR (KBr) cm^{-1} : 1075(-OCH₃), 3069(Ar-H), 1621(C=O). ^1H NMR(CDCl_3) δ : 2.22 (s, 3H, CH₃), 2.55 (s, 3H, CH₃), 3.98 (s, 3H, OCH₃), 7.14-7.15 (d, 1H, methoxyquinoline), 7.20-7.22 (d, 1H, methoxyquinoline), 7.30 (s, 1H, methoxyquinoline), 7.46-7.53 (d, 1H, methoxyquinoline), 9.04-9.06 (d, 1H, methoxyquinoline).



4a; R = 4-F-C₆H₄

4b; R = 4-Cl-C₆H₄

4c; R = 2-Cl-6-F-C₆H₃

4d; R = 3,4-(OCH₃)₂-C₆H₃

4e; R = 4-OCH₃-C₆H₄

4f; R = 3-CH₃-C₆H₄

7a; R' = C₆H₅

7b; R' = 4,5-(OCH₃)₂-2-NO₂-C₆H₂

7c; R' = Biphenyl

7d; R' = 2-OH-3-OCH₃-C₆H₃

7e; R' = 2-OCH₃-Naphthyl

7f; R' = 2-OH-C₆H₄

Synthesis of 1-aryl (1-(7-methoxyquinolin-4-yl)-5-methyl-1H-1, 2, 3-triazol-4-yl) prop-2-en-1-ones (4a-f)

An equimolar quantity of compound **3** (0.0035 mol) and substituted aromatic aldehydes in methanol (20ml) was cooled to 10 °C and to this the aqueous solution of potassium hydroxide (0.5g in 3 ml water) was added and then stirred for 12 hr at room temperature. After the completion of the reaction, it was poured on to ice-cold water. The separated solid was filtered, washed with water and recrystallized from methanol.

Characterization of synthesized compounds.

6.5.1. (E)-3-(4-Fluorophenyl)-1-(7-methoxyquinoline-4-yl)-5-methyl-1H-1,2,3-triazol-4-yl)prop-2-en-1-one (4a), Yield 80%, melting point 222-225°C. IR (KBr) cm^{-1} : 3073, 3231(Ar-H), 1671(C=O), 1617(C=C), 978(C-F). ^1H NMR(CDCl_3) δ : 2.52 (s, 3H, CH_3), 3.98 (s, 3H, OCH_3), 7.08–7.13 (m, 2H, 4-fluorophenyl), 7.25–7.26 (d, 1H, methoxyquinoline), 7.28–7.30 (d, 2H, 4-Fluorophenyl), 7.56 (s, 1H, methoxyquinoline), 7.69–7.70 (d, 1H, methoxyquinoline), 7.73-7.74 (d, 1H, methoxyquinoline), 8.01-8.06 (2d, 2H, $\text{CH}=\text{CH}$), 9.02–9.04 (d, 1H, methoxyquinoline). ^{13}C NMR: 183.8, 161.6, 151.6, 150.5, 143.6, 142.7, 140.07, 130.7, 130.6, 123.2, 122.45, 122.43, 122.17, 118.7, 116.38, 116.17, 115.88, 107.83, 55.69, 9.87. LCMS: 423.1(M+1). Anal. calcd. for $\text{C}_{22}\text{H}_{17}\text{FN}_4\text{O}_2$: C-68.03, H-4.41, N-14.43, found: C-68.01, H-4.40, N-14.42%.

(E)-3-(4-Chlorophenyl)-1-(7-methoxyquinoline-4-yl)-5-methyl-1H-1,2,3-triazol-4-yl)prop-2-en-1-one (4b)

Yield 81%, melting point 215-218°C. IR (KBr) cm^{-1} : 3072, 3229(Ar-H), 1664(C=O), 1617(C=C), 822(C-Cl). ^1H NMR(CDCl_3) δ : 2.55 (s, 3H, CH_3), 4.01 (s, 3H, OCH_3), 6.9–7.14 (m, 2H, 4-chlorophenyl), 7.14–7.15 (d, 1H, methoxyquinoline), 7.18–7.20 (d, 1H, methoxyquinoline), 7.30 (s, 1H, methoxyquinoline), 7.47-7.58 (d, 1H, methoxyquinoline), 8.08-8.13 (2d, 2H, $\text{CH}=\text{CH}$), 9.04–9.06 (d, 1H, methoxyquinoline). ^{13}C NMR: 183.4, 161.5, 150.6, 150.1, 143.0, 142.6, 140.05, 131.4, 130.9, 130.6, 130.4, 123.1, 122.4, 122.3, 122.1, 118.5, 116.3, 116.1, 115.3, 107.8, 55.6, 9.7. LCMS: 405.1 (M+1), Anal. calcd. for $\text{C}_{22}\text{H}_{17}\text{ClN}_4\text{O}_2$: C-65.27, H-4.23, N-13.84, found: C-65.24, H-4.25, N- 13.82%.

(E)-3-(2-Chloro-6-fluorophenyl)-1-(7-methoxyquinoline-4-yl)-5-methyl-1H-1,2,3-triazol-4-yl)prop-2-en-1-one (4c)

Yield 75%, melting point 160-162°C. IR (KBr) cm^{-1} : 3052, 3219(Ar-H), 1660(C=O), 1615(C=C), 829(C-Cl), 989(C-F). ^1H NMR(CDCl_3) δ : 2.56 (s, 3H, CH_3), 4.01 (s, 3H, OCH_3), 7.11–7.14 (d, 2H, 2-chloro-6-fluorophenyl), 7.26 (s, 1H, methoxyquinoline), 7.27–7.29 (d, 1H, methoxyquinoline), 7.30–7.31 (d, 1H, methoxyquinoline). 7.6 (s, 1H, 2-chloro-6-fluorophenyl), 7.45-7.53 (d, 1H, methoxyquinoline), 8.15-8.38 (2d, 2H, $\text{CH}=\text{CH}$), 9.05–9.06 (d, 1H, methoxyquinoline). ^{13}C NMR: 184.3, 161.7, 150.3, 143.6, 140.3, 139.3, 136.7, 136.6, 133.9, 130.7, 129.3, 125.98, 125.93, 122.3, 122.2, 118.8, 116.3, 115.0, 114.7, 107.7, 55.7, 9.9. LCMS: 388.9 (M+1). Anal. calcd. for $\text{C}_{22}\text{H}_{16}\text{ClFN}_4\text{O}$: C-62.49, H-3.81, N- 13.25, found: C-62.5, H-3.80, N- 13.23%.

(E)-3-(3,4-dimethoxyphenyl)-1-(7-methoxyquinoline-4-yl)-5-methyl-1H-1,2,3-triazol-4-yl)prop-2-en-1-one (4d)

Yield 85%, melting point 180-182°C. IR (KBr) cm^{-1} : 3073, 3231(Ar-H), 1663(C=O), 1621(C=C). ^1H NMR(CDCl_3) δ : 2.48 (s, 3H, CH_3), 3.98 (3s, 9H, OCH_3), 7.0-7.1 (d, 1H, 3,4-dimethoxyphenyl), 7.2 (s, 1H, 3,4-dimethoxyphenyl), 7.19-7.24 (2d, 2H, methoxyquinoline and

dimethoxyphenyl), 7.56 (s, 1H, methoxyquinoline), 7.28–7.30 (d, 1H, methoxyquinoline), 7.78–7.80 (d, 1H, methoxyquinoline), 8.04–8.06 (2d, 2H, CH=CH), 9.04–9.02 (d, 1H, methoxyquinoline). ¹³C NMR: 183.8, 154.5, 152.7, 151.6, 150.5, 143.6, 142.7, 140.07, 131.8, 130.8, 130.7, 130.6, 130.4, 123.2, 122.45, 122.43, 122.17, 118.7, 110.2, 109.8, 55.7, 55.9, 55.6, 9.9. LCMS; 431.2(M+1). Anal. calcd. for C₂₄H₂₂N₄O₄: C-66.97, H-5.15, N- 13.02, found: C-66.98, H-5.14, N- 13.0%.

(E)-3-(4-methoxyphenyl)-1-(7-methoxyquinoline-4-yl)-5-methyl-1H-1,2,3-triazol-4-ylprop-2-en-1-one (4e)

Yield 82%, melting point 160-163^oC. IR (KBr) cm⁻¹: 3072, 3160(Ar-H), 1681(C=O), 1618(C=C). ¹H NMR(CDCl₃) δ: 2.5 (s, 3H, CH₃), 4.0 (s, 6H, OCH₃), 7.03–7.05 (d, 2H, 4-methoxyphenyl), 7.18–7.20 (d, 1H, methoxyquinoline), 7.28–7.30 (d, 1H, methoxyquinoline), 7.6 (s, 1H, methoxyquinoline), 7.68–7.70 (d, 2H, 4-methoxyphenyl), 7.72–7.69 (d, 1H, methoxyquinoline), 8.01–8.06 (2d, 2H, CH=CH), 9.01–9.03 (d, 1H, methoxyquinoline). ¹³C NMR: 183.7, 153.5, 152.6, 151.6, 150.5, 143.4, 142.3, 140.1, 131.8, 130.8, 130.5, 130.6, 130.4, 126.1, 122.5, 122.4, 122.0, 118.3, 110.1, 109.8, 55.8, 55.9, 9.9. LCMS: 401.3(M+1). Anal. calcd. for C₂₃H₂₀N₄O₃: C-68.99, H-5.03, N- 13.99, found: C-68.98, H-5.03, N- 13.97%.

(E)-1-(1-(7-methoxyquinoline-4-yl)-5-methyl-1H-1,2,3-triazol-4-yl)-3-m-tolylprop-2-en-1-one (4f)

Yield 79%, melting point 174-176^oC. IR (KBr) cm⁻¹: 3064, 3219(Ar-H), 1671(C=O), 1605(C=C). ¹H NMR(CDCl₃) δ: 2.49 (2s, 6H, CH₃), 3.98 (s, 3H, OCH₃), 7.0 (s, 1H, 3-methylphenyl), 7.14–7.15 (d, 1H, 3-methylphenyl), 7.18–7.19 (t, 1H, 2-methylphenyl), 7.19–7.21 (d, 1H, methoxyquinoline), 7.27–7.29 (d, 1H, methoxyquinoline), 7.32 (s, 1H, methoxyquinoline), 7.38–7.40 (d, 1H, 3-methylphenyl), 7.75–7.78 (d, 1H, methoxyquinoline), 8.013–8.09 (2d, 2H, CH=CH), 9.04–9.06 (d, 1H, methoxyquinoline). ¹³C NMR: 182.3, 160.6, 151.6, 150.2, 143.1, 141.7, 140.07, 131.8, 130.9, 130.6, 130.4, 130.1, 123.2, 122.45, 122.4, 122.17, 117.7, 116.4, 115.9, 107.8, 55.7, 22.1, 9.9. LCMS: 385.2(M+1). Anal. calcd. for C₂₃H₂₀N₄O₂: C-71.86, H-5.24, N- 14.57, found : C-71.85, H-5.23, N- 14.55%.

Synthesis of ethyl 1-(7-methoxyquinolin-4-yl)-5-methyl-1H-1, 2, 3-triazol-4-carboxylate (5)

The mixture of 4-azido-7-methoxy quinoline **2**, (0.0033 mol) and ethyl acetoacetate, (0.0033 mol) in ethanol (20 ml) was cooled to 0 ^oC and to this sodium ethoxide (0.005 mol) was added under inert atmosphere and stirred at 20^oC for 5 hr. Progress of the reaction was monitored by TLC (ethyl acetate/n-hexane, 9:1, v/v). After completion of the reaction, the mixture was poured on to ice-cold water and neutralized with acetic acid. The precipitated solid was filtered, washed with water and recrystallized from ethanol. Yield 75%, melting point 160-163^oC. IR (KBr) cm⁻¹: 3230, 3073(Ar-H), 1645(C=O). ¹H NMR(CDCl₃) δ: 1.28 (t, 3H, CH₃), 2.55 (s, 3H, CH₃), 4.0 (s, 3H, OCH₃), 4.28 (q, 2H, CH₂), 7.12–7.14 (d, 1H, methoxyquinoline), 7.22–7.24 (d, 1H, methoxyquinoline), 7.30 (s, 1H, methoxyquinoline), 7.42–7.48 (d, 1H, methoxyquinoline), 9.04–9.06 (d, 1H, methoxyquinoline).

Synthesis of 1-(7-methoxyquinolin-4-yl)-5-methyl-1H-1,2,3-triazole-4-carbohydrazide (6)

An Equimolar mixture of compound **5** (0.003 mol) and hydrazine hydrate (0.003 mol) in ethanol (25ml) was heated under reflux for 8 hr. After completion of the reaction the reaction mixture was allowed to cool and the crystals separated were filtered and recrystallized from ethanol. Yield 82%, melting point 192-195^oC. IR (KBr) cm⁻¹: 3232, 3071(Ar-H), 3307(NH₂), 1640(C=O). ¹H NMR(CDCl₃) δ: 2.58 (s, 3H, CH₃), 4.0 (s, 3H, OCH₃), 4.3 (s, 2H, NH₂), 7.13–

7.14 (d, 1H, methoxyquinoline), 7.20–7.22 (d, 1H, methoxyquinoline), 7.26 (s, 1H, methoxyquinoline), 7.45–7.52 (d, 1H, methoxyquinoline), 9.04–9.06 (d, 1H, methoxyquinoline), 9.50 (s, 1H, NH).

General procedure for synthesis of 1-(7-methoxy quinolin-4-yl)-5-methyl-1H-1,2,3-triazole-4-carbohydrazide (7a-f)

An Equimolar quantity of compound **6** and suitable aromatic aldehydes in methanol was refluxed for about 3–4 h in the presence of 1 ml of glacial acetic acid. The solid separated after cooling resulting was filtered, washed with cold methanol and recrystallized using methanol.

(E)-N-benzylidene-1-(7-methoxyquinolin-4-yl)-5-methyl-1H-1,2,3-triazole-4-carbohydrazide (7a)

Yield 79%, melting point 218–220°C. IR (KBr) cm^{-1} : 3432 (NH), 3232, 3072 (Ar-H), 1675(C=O). ^1H NMR (CDCl_3) δ : 2.55 (s, 3H, CH_3), 4.0 (s, 3H, OCH_3), 7.22–7.44 (m, 5H, phenyl), 7.58–7.59 (d, 1H, methoxyquinoline), 7.82–7.83 (d, 1H, methoxyquinoline), 7.83 (s, 1H, methoxyquinoline), 7.83–7.84 (d, 1H, methoxyquinoline), 8.29 (s, 1H, =CH), 9.05–9.04 (d, 1H, methoxyquinoline), 10.28 (s, 1H, NH). ^{13}C NMR: 161.7, 156.9, 151.7, 150.6, 148.2, 139.6, 139.2, 137.5, 133.5, 130.5, 128.7, 127.8, 126.4, 125.2, 123.2, 122.3, 118.7, 116.45, 108.0, 55.7, 9.3. LCMS: 387.2(M+1). Anal. calcd. for $\text{C}_{21}\text{H}_{18}\text{N}_6\text{O}_2$: C-65.27, H-4.70, N- 21.75, found: C- 65.25, H-4.67, N- 21.74%.

(E)-N-(4,5-dimethoxy-2-nitrobenzylidene)-1-(7-methoxyquinolin-4-yl)-5-methyl-1H-1,2,3-triazole-4-carbohydrazide (7b)

Yield 78%, melting point 134–136°C. IR (KBr) cm^{-1} : 3445(NH), 3222, 3083(Ar-H), 1625(C=O). ^1H NMR(CDCl_3) δ : 2.57(s, 3H, CH_3), 4.0–4.08 (3s, 9H, OCH_3), 7.28–7.26 (d, 1H, 2-nitro-4,5-dimethoxyphenyl), 7.30–7.31 (d, 1H, 2-nitro-4,5- dimethoxyphenyl), 7.33–7.34(d, 1H, methoxyquinoline), 7.62–7.63 (d, 1H, methoxyquinoline), 7.66 (d, 1H, methoxyquinoline), 7.77 (s, 1H, methoxyquinoline), 8.98 (s, 1H, =CH), 9.06–9.07 (d, 1H, methoxyquinoline), 10.54 (s, 1H, NH). ^{13}C NMR:160.2, 156.4, 151.2, 150.4, 147.4, 145.3, 140.2, 139.2, ,138.0, 132.2, 130.1, 128.3, 126.3, 123.1, 120.8, 117.4, 115.8, 109.6, 107.8, 56.2, 56.2, 9.4. LCMS:492.3(M+1), Anal. calcd. for $\text{C}_{23}\text{H}_{21}\text{N}_7\text{O}_6$: 56.21, H-4.31, N- 19.95, found: C-56.17, H-4.30, N- 19.91%.

(E)-N-(biphenyl-2-yl methylene)-1-(7-methoxy quinolin-4-yl)-5-methyl-1H-1,2,3-triazole-4-carbohydrazide (7c)

Yield 81%, melting point 203–206°C. IR (KBr) cm^{-1} : 3350(NH), 3230, 3062(Ar-H), 1658(C=O). ^1H NMR(CDCl_3) δ : 2.57 (s, 3H, CH_3), 4.01(s, 3H, OCH_3), 7.25–7.64 (m, 9H, biphenyl), 7.65–7.66 (d, 1H, methoxyquinoline), 7.66(s, 1H, methoxyquinoline), 7.67–7.69 (d, 1H, methoxyquinoline), 7.91–7.93 (d, 1H, methoxyquinoline), 8.32 (s, 1H, =CH), 9.06–9.07 (d, 1H, methoxyquinoline), 10.31(s, 1H, NH). ^{13}C NMR:160.8, 156.6, 151.4, 150.6, 147.8, 140.4, 139.8, 136.3, 134.8, 131.0, 130.6, 129.8, 128.6, 128.0, 127.7, 127.2, 127.0, 123.4, 121.8, 120.4, 118.7, 116.6, 107.6, 55.7, 9.3. LCMS: 463.4(M+1). Anal. calcd. for $\text{C}_{27}\text{H}_{22}\text{N}_6\text{O}_2$: C-70.12, H-4.79, N- 18.72, found: C-70.11, H-4.78, N- 18.74%.

(E)-N-(2-hydroxy-3-methoxybenzylidene)-1-(7-methoxyquinolin-4-yl)-5-methyl-1H-1,2,3-triazole-4-carbohydrazide (7d)

Yield 75%, melting point 129–131°C. IR (KBr) cm^{-1} : 3444 (NH), 3340(OH), 3260, 3073 (Ar-H), 1693 (C=O). ^1H NMR (CDCl_3) δ : 2.55 (s, 3H, CH_3), 4.0 (2s, 6H, OCH_3), 6.89–6.91 (d, 1H, methoxyquinoline), 6.94–6.94 (d, 1H, 2-hydroxy-3-methoxyphenyl), 6.96–6.98 (d, 1H,

methoxyquinoline), 7.23 (s, 1H methoxyquinoline), 7.26–7.27 (d, 1H, methoxyquinoline), 7.29–7.31 (t, 1H, 2-hydroxy-3-methoxyphenyl), 7.58–7.59 (d, 1H, 2-hydroxy-3-methoxyphenyl), 8.49 (s, 1H, = CH), 9.05–9.06 (d, 1H, methoxyquinoline), 10.33 (s, 1H, NH), 10.98 (s, 1H, OH). ¹³C NMR: 160.9, 156.8, 152.5, 151.9, 148.0, 147.1, 145.2, 139.4, 135.2, 130.4, 130.0, 126.2, 122.1, 120.8, 119.4, 118.6, 116.4, 115.1, 108.1, 56.2, 55.8, 9.3. LCMS: 433.1(M+1). Anal. calcd. for C₂₂H₂₀N₆O₄: C-61.10, H-4.66, N- 19.43, found C-61.10, H-4.64, N- 19.41%.

(E)-N-((6-methoxynaphthalen-2-yl) methylene)-1-(7-methoxyquinolin-4-yl)-5-methyl-1H-1,2,3-triazole-4-carbohydrazide (7e)

Yield 80%, melting point 240–243^oC. IR (KBr) cm⁻¹: 3480 (NH), 3215, 3063(Ar–H), 1621(C=O). ¹H NMR (CDCl₃) δ: 2.57 (s, 3H, CH₃), 3.9 (2s, 6H, OCH₃), 7.18–7.19 (d, 1H, methoxy-naphthyl), 7.26–7.27 (d, 1H, methoxy-naphthyl), 7.27–7.29 (d, 1H, methoxyquinoline), 7.30–7.31 (d, 1H, methoxy-naphthyl), 7.76–7.77 (d, 1H, methoxyquinoline), 7.78–7.79 (d, 1H, methoxyquinoline), 8.01 (s, 1H, methoxy-naphthyl), 8.07–8.08 (d, 1H, methoxy-naphthyl), 8.09 (s, 1H methoxy-naphthyl), 8.10 (s, 1H, methoxyquinoline), 8.37 (s, 1H, = CH), 9.04–9.06 (d, 1H, methoxyquinoline), 10.34 (s, 1H, NH). ¹³C NMR: 160.8, 159.7, 156.6, 153.0, 152.3, 148.2, 139.1, 138.4, 137.8, 137.0, 131.2, 130.0, 130.5, 130.0, 129.6, 128.1, 127.8, 123.1, 118.2, 116.2, 105.3, 105.8, 55.6, 55.8, 9.3. LCMS: 467.3(M+1). Anal. calcd. for C₂₆H₂₂N₆O₃: C-66.94, H-4.75, N- 18.02, found: C-6.92, H-4.75, N-18.00%.

(E)-N-(2-hydroxy benzylidene)-1-(7-methoxy quinolin-4-yl)-5-methyl-1H-1,2,3-triazole-4-carbohydrazide (7f)

Yield 71%, melting point 235–236^oC. IR (KBr) cm⁻¹: 3400 (NH), 3300 (OH), 3260, 3078 (Ar–H), 1670 (C=O). ¹H NMR (CDCl₃) δ: 2.57 (s, 3H, CH₃), 4.0 (s, 1H, OCH₃), 6.98–6.99 (d, 1H, methoxyquinoline), 7.12–7.13 (d, 1H, methoxyquinoline), 7.30 (s, 1H, methoxyquinoline), 7.32–7.33 (d, 1H, methoxyquinoline), 7.29–7.31 (m, 4H, 2-hydroxy-phenyl), 8.26 (s, 1H, = CH), 9.05–9.06 (d, 1H, methoxyquinoline), 10.29 (s, 1H, NH), 10.92 (s, 1H, OH). ¹³C NMR: 161.3, 159.8, 151.6, 150.2, 148.8, 148.0, 139.4, 138.2, 133.2, 130.1, 129.7, 127.5, 123.4, 121.8, 122.6, 118.3, 117.6, 116.4, 108.2, 55.7, 9.3. LCMS: 403.2(M+1), Anal. calcd. for C₂₁H₁₈N₆O₃: C-62.68, H-4.51, N- 20.88, found: C-62.66, H-4.50, N- 20.86%.

Antimicrobial activity

The antimicrobial activity for newly synthesized compounds was carried out using agar well diffusion method [12, 13, 14]. The bacterial strains were collected from different infectious status of patients who had not administered any antibacterial drugs for at least two weeks with the suggestions of an authorized physician. The *In vitro* antimicrobial activity was carried out against 24 h old culture of four bacterial strains namely *Bacillus subtilis*, *streptococcus haemolyticus* as Gram positive and *Pseudomonas aeruginosa*, *Klebsiella pneumonia* as Gram negative. The antifungal activity was carried out against two fungal strains *aspergillus niger* and *candida albicans*. The compounds were tested at 50 µg/mL concentration against both bacterial and fungal strains. DMSO was used as a vehicle. Ciprofloxacin (50 µg in 100µl) and Fluconazole (50 µg in 100µl) were used as standard drugs for comparison of antibacterial and antifungal activities respectively. The zone of inhibition was compared with standard drug after 24 h of incubation at 37^oC for antibacterial activity and 72 h at 25^oC for antifungal activity. The results are recorded in **Table 1**.

Minimum Inhibitory Concentrations (MIC)

The MIC of all synthesized compounds was determined by a micro dilution method [15]. The respective clinical strain was spread separately on the medium. The wells were created using a stainless steel sterilized cork borer under aseptic conditions. The synthesized compounds at different concentrations viz. 10, 20, 30, 40 and 50 µg was dissolved respectively in 25, 50, 75, 100 and 125 µL of DMSO and loaded into corresponding wells. The standard drug Ciprofloxacin (50 µg in 100µl) and Fluconazole (50 µg in 100µl) which were used as standard drugs for comparison of antibacterial and antifungal activities respectively were also loaded into wells. The zone of inhibition was compared with standard drug after 24 h of incubation at 37°C for antibacterial activity and 72 h at 25°C for antifungal activity. The results are recorded in mm in **Table 2**.

Table 1 Anti-microbial activity of synthesized compounds.

Compound 50 µg in 100µL	Zone of inhibition in (mm)					
	Antibacterial activity				Antifungal Strains	
	<i>B.subtilis</i>	<i>streptococcus haemolytius</i>	<i>Pseudomonas aeruginosa</i>	<i>Klebsiella pneumoniae</i>	<i>A.niger</i>	<i>C.albicans</i>
4a	20	18	19	19	19	18
4b	20	21	19	20	19	18
4c	18	19	18	21	20	18
4d	19	17	19	20	19	19
4e	21	19	19	19	18	18
4f	19	18	18	19	18	20
7a	21	18	20	18	20	19
7b	21	18	20	18	20	19
7c	19	18	18	19	20	20
7d	18	18	18	19	20	20
7e	20	20	21	17	19	19
7f	18	20	20	18	19	19
Ciprofloxaci ^a	21	20	20	20	-	-
Fluconazole ^b	-	-	-	-	21	20
Control	0	0	0	0	0	0

^a Standard antibacterial drug – Ciprofloxacin, ^b Standard anti fungal drug – Fluconazole Control : DMSO (Dimethyl sulphoxide)

Table 2 Minimum Inhibitory Concentration (MIC) of synthesized compounds.

Compound 10-50 (µg)	MIC (µg/µL)					
	Antibacterial strains				Antifungal Strains	
	<i>B.subtilis</i>	<i>streptococcus haemolytius</i>	<i>Pseudomonas aeruginosa</i>	<i>Klebsiella pneumoniae</i>	<i>A.niger</i>	<i>C.albicans</i>
4a	40	40	30	40	30	30
4b	30	30	30	30	30	30
4c	40	40	30	40	40	20
4d	30	30	40	30	40	40
4e	30	20	40	30	40	30
4f	40	40	30	30	30	40
7a	40	40	30	30	40	40
7b	30	40	30	30	40	40
7c	40	40	40	40	30	30
7d	30	30	30	30	30	20
7e	40	40	40	40	30	40
7f	30	40	30	40	40	40
Control DMSO	0	0	0	0	0	0

Control : DMSO (Dimethyl sulphoxide)

On the basis of the observed zone of inhibition values, the entire tested compounds were emerged as active against all tested microorganisms. The compound **4b** against *streptococcus haemolytius*, **4c** against *Klebsiella pneumoniae* and **7e** *Pseudomonas aeruginosa* have shown

more significant antibacterial activities compared with standard *Ciprofloxacin*. Few synthesized compounds are co-relating in case of antifungal activity carried out against selected strains with compared to standard drugs *Fluconazole*. A careful analysis of the antimicrobial activity data of the compounds suggested that these synthesized compounds exhibited potent antibacterial activity.

RESULTS AND DISCUSSION

4-Chloro-7-methoxy quinoline **1** was prepared in good yield according to literature procedure [11]. The synthesis of new quinolines containing triazole derivatives showed in **Scheme 1**. The reaction of **1** with sodium azide in *N, N*-dimethylformamide yielded 4-azido-7-methoxy quinoline **2** which is used as a key intermediate for the synthesis of target molecules. Compound **2** when treated with acetyl acetone in presence of sodium ethoxide in ethanol at 0°C yielded 1-(1-(7-methoxyquinolin-4-yl)-5-methyl-1H-1,2,3-triazol-4-yl)ethanone **3** which upon further reaction with different aromatic aldehydes gave the corresponding chalcones **4a-f**. The reaction of 4-azido-7-methoxy quinoline **2** with ethyl acetoacetate in presence of sodium ethoxide in ethanol at 20°C yielded ethyl 1-(7-methoxyquinolin-4-yl)-5-methyl-1H-1, 2, 3-triazol-4-carboxylate **5**. The triazole carboxylate **5** upon treatment with hydrazine hydrate in ethanol at 80°C gave the corresponding 1-(7-methoxyquinolin-4-yl)-5-methyl-1H-1,2,3-triazole-4-carbohydrazide **6** which when treated with different aromatic aldehydes, furnished the corresponding Schiff bases **7a-f**.

CONCLUSION

A novel series of Substituted quinolone derivatives were synthesized. The structures of the synthesized compounds were established by IR, 1H NMR, 13C NMR and Mass spectroscopic data. All the synthesized compounds were screened for their in-vitro antibacterial activity against gram-positive and gram-negative bacteria as compared with the standard. In summary, preliminary results indicate that some of the newly synthesized title compounds exhibited promising antibacterial activities.

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