Synthesis and anti-microbial screening of novel Schiff bases of 3-amino-2-methyl quinazolin 4-(3H)-one

Abstract
In the present study, novel Schiff bases were synthesized by condensation of 3-amino-2-methyl quinazolin-4-(3H)-ones with different aromatic aldehydes. The 3-amino-2-methyl quinazolin-4-(3H)-one was synthesized from anthranilic acid via the 2-methyl benzoxazin-4-one. The chemical structures of the synthesized compounds were confirmed by means of Infrared (IR), \textsuperscript{1}H-NMR, \textsuperscript{13}C-NMR, Mass spectral, and Elemental analysis. These compounds were screened for anti-bacterial (\textit{Staphylococcus aureus ATCC 9144}, \textit{Staphylococcus epidermidis ATCC 155}, \textit{Micrococcus luteus ATCC 4698}, \textit{Bacillus cereus ATCC 11778}, \textit{Escherichia coli ATCC 25922}, \textit{Pseudomonas aeruginosa ATCC 2853}, and \textit{Klebsiella pneumonia ATCC 11298}) and anti-fungal (\textit{Aspergillus niger ATCC 9029} and \textit{Aspergillus fumigatus ATCC 46645}) activities, using the paper disk diffusion technique. The minimum inhibitory concentrations (MIC) of the compounds were also determined by the agar streak dilution method. Most of the synthesized compounds exhibited significant anti-bacterial and anti-fungal activities. Among the synthesized compounds, 3-(4-hydroxy benzylideneamino)-2-methyl quinazolin-4(3H)-one 4g and 4c was found to exhibit the highest anti-bacterial activity and 3-(4-hydroxy-3-methoxy benzylideneamino)-2-methyl quinazolin-4(3H)-one 4k exhibited the highest anti-fungal activity.

Key words: 3-amino-2-methyl quinazolin-4-(3H)-one, anti-bacterial, anti-fungal, Schiff base

INTRODUCTION
Quinazolin-4-(3H)-ones have been reported to possess a wide range of biological activities such as anti-microbial,\cite{1,2} analgesic,\cite{6,7} anti-inflammatory,\cite{9} anti-convulsant,\cite{9,10} anti-cancer,\cite{11,12} anti-tubercular,\cite{13,14} anti-malarial,\cite{15} and anti-viral\cite{16,17} activities. Quinazolin-4-(3H)-ones, with substitution at the third position, has been reported to be associated with antimicrobial properties.\cite{18,19} The various substituents at the third position of quinazolin-4(3H)-one that have been reported, are various substituted phenyl ring moieties, bridged phenyl rings, heterocyclic rings, and the aliphatic system. In addition, in general Schiff bases, the presence of pharmacophores like –NO\textsubscript{2}, phenolic OH, –Cl, –CH\textsubscript{3} and –OCH\textsubscript{3} are reported to possess anti-microbial activities. These observations has led to the conception that a novel series of Schiff bases of 3-amino-2-methyl quinazolin-4-(3H)-ones 4a-4l have been synthesized using different aromatic aldehydes by condensation and their chemical structure is confirmed by IR, \textsuperscript{1}H-NMR, \textsuperscript{13}C-NMR, Mass spectral and Elemental analysis. These compounds have been screened for their anti-bacterial activity against four gram positive bacteria (\textit{Staphylococcus aureus ATCC 9144}, \textit{Staphylococcus epidermidis ATCC 155}, \textit{Micrococcus luteus ATCC 4698}, and \textit{Bacillus cereus ATCC 11778}), three gram negative bacteria (\textit{Escherichia coli ATCC 25922}, \textit{Pseudomonas aeruginosa ATCC 2853}, and \textit{Klebsiella pneumonia ATCC 11298}), and anti-fungal (\textit{Aspergillus niger ATCC 9029} and \textit{Aspergillus fumigatus ATCC 46645}) activities, using the paper disk diffusion technique. The minimum inhibitory concentrations (MIC) of the compounds were also determined by the agar streak dilution method.

MATERIALS AND METHODS
The melting points were taken in an open capillary tube and were uncorrected. The IR spectra of the compounds were recorded on an ABB Bomem FT-IR spectrometer MB 104 with KBr pellets. The \textsuperscript{1}H (300 MHz) and \textsuperscript{13}C-NMR (300 MHz) spectra were recorded on a Bruker 300 NMR spectrometer (with TMS for \textsuperscript{1}H and CDCl\textsubscript{3} for \textsuperscript{13}C as internal references). Mass spectra were recorded on a Shimadzu GC MS QP 5000.
Microanalyses were obtained with an elemental an Analyses system GmbH VarioEL V300 element analyzer. The purity of the compounds was checked by thin layer chromatography (TLC) on pre-coated SiO₂ gel (HF₆N₃ 200 mesh) aluminium plates (E Merck) using ethyl acetate : n-hexane (20 : 80) and visualized in an ultraviolet (UV) chamber. The reagent grade chemicals were purchased from S.D. Fine-Chem Limited, Mumbai, and Qualigens Fine Chemicals, Mumbai, and purified by either distillation or recrystallization, before use.

Chemistry
In the present study anthranilic acid 1 was treated with acetic anhydride to form 2-methyl benzoxazin-4-one 2, which further reacted with hydrazine hydrate resulting in 3-amino-2-methyl quinazolin-4-(3H)-one 3. Compound 3 was subjected to react with various aromatic aldehydes in the presence of ethanol as a solvent, to form schiff bases.

General Method of Synthesis (4a-4d)
The 3-amino-2-methyl quinazolin-4-(3H)-one 3 was prepared according to the reported literature.[18] Equimolar quantities (0.01 mol) of 3-amino 2-methyl quinazolin 4-(3H)-one and aromatic aldehydes were dissolved in 20 ml of ethanol, refluxed for eight hours, and then kept aside for three days. The product that separated out was filtered, dried, and recrystallized from absolute ethanol.

Anti-microbial Screening
The standard strains were procured from the American Type Culture Collection (ATCC), Rockville, USA, and the pathological strains were procured from the Department of Microbiology, CEEAL Analytical Lab, Chennai, India. All test compounds and standard drugs were dissolved in dimethyl formamide for screening the anti-microbial activity. All the synthesized compounds were screened for anti-bacterial and anti-fungal activities by the paper disk diffusion technique. The anti-bacterial activity of the compounds were evaluated against four gram positive bacteria (Staphylococcus aureus ATCC 9144, Staphylococcus epidermidis ATCC 155, Micrococcus luteus ATCC 4698, and Bacillus cereus ATCC 11778) and three gram negative bacteria (Escherichia coli ATCC 2592, Pseudomonas aeruginosa ATCC 2853, and Klebsiella pneumoniae ATCC 11298), using the nutrient agar medium (Hi-Media Laboratories, India). The anti-fungal activities of the synthesized compounds were evaluated against two fungi (Aspergillus niger ATCC 9029 and Aspergillus fumigatus ATCC 46645) using the Sabouraud dextrose agar medium (Hi-Media Laboratories, India). The minimum inhibitory concentrations (MIC) of the compounds were also determined by the agar streak dilution method.

Paper Disk Diffusion Technique
The sterilized[20] (autoclaved at 120°C for 30 min) medium (40 – 50°C) was inoculated (1 ml/100 ml of medium) with the suspension (10⁶ cfu/ml) of the microorganism (matched to the McFarland barium sulfate standard) and poured into a petridish to give a depth of 3 – 4 mm. The paper impregnated with the test compounds dissolved in dimethylformamide (100 µg/disk) and was placed on the solidified medium. The plates were pre-incubated for one hour at room temperature and incubated at 37°C for 24 and 48 hours for anti-bacterial and anti-fungal activities, respectively. Ciprofloxacin (100 µg/disk) and Ketoconazole (100 µg/disk) were used as the standards for anti-bacterial and anti-fungal activities, respectively. The observed zone of inhibition is presented in Table 1.

Minimum Inhibitory Concentration
The Minimum inhibitory concentration (MIC) of the compound was determined by the agar streak dilution method. A stock solution of the synthesized compound (100 µg/ml), in dimethylformamide, was prepared and graded quantities of the test compounds were incorporated in a specified quantity of molten sterile agar (nutrient agar for anti-bacterial activity and Sabouraud dextrose agar medium for anti-fungal activity). A specified quantity of the medium (40 – 50°C) containing the compound was poured into a petridish to give a depth of 3 – 4 mm, and allowed to solidify. A suspension of the microorganism were prepared, to contain approximately 10⁵ cfu/ml, and applied on the plates with serially diluted compounds in dimethylformamide, to be tested, and was incubated at 37°C for 24 and 48 hours for bacteria and fungi, respectively. The MIC was considered to be the lowest concentration of the test substance, exhibiting no visible growth of bacteria or fungi on the plate. The observed MIC is presented in Table 1.

RESULTS AND DISCUSSION
Chemistry
Infrared, ‘H-NMR, ‘C-NMR, Mass spectra, and Elemental analysis were consistent with the assigned structures. The optical activities of the compounds were not checked.

3-Amino 2-methyl Quinazolin-4(3H)-one (3)
Yield: 73%; m.p.141 – 143°C; IR (KBr, cm⁻¹): 3030 (Ar-CH), 2927 (CH in CH₂), 1716 (C=O), 1464 (C=C), 1332 (N-H). ‘H-NMR (CDCl₃) δ: 7.41-7.82 (m, 4H; C₆H₁₂, C₆H₁₂, Ar-H), 1.94 (s, 2H; -NH₂), 0.97 (s, 3H; -CH₃). ‘C-NMR (CDCl₃) δ: 164.2 (C₁), 161.7 (C₇), 133.6 (C₉), 128.2 (C₁₀), 127.6 (C₆′), 122.3 (C₅′), 18.9 (C₃). EI-MS m/z (M⁺): 175 (Calcd. for C₁₂H₁₀N₂O; C, 61.70; H, 5.18; N, 23.99. Found: C, 61.65; H, 5.18; N, 23.88 [Figure 1].

3-(Benzylideneamino)-2-methyl quinazolin-4-(3H)-one (4a)
Pale yellow crystal; Yield: 80%; m.p. 153 – 155°C; IR (KBr, cm⁻¹): 3018 (Ar-CH), 2972 (CH in CH₂), 1716 (C=O), 1464 (C=C), 1332 (N-H). ‘H-NMR (CDCl₃) δ: 7.41-7.82 (m, 4H; C₆H₁₂, C₆H₁₂, Ar-H), 1.94 (s, 2H; -NH₂), 0.97 (s, 3H; -CH₃). ‘C-NMR (CDCl₃) δ: 164.2 (C₁), 161.7 (C₇), 133.6 (C₉), 128.2 (C₁₀), 127.6 (C₆′), 122.3 (C₅′), 18.9 (C₃). EI-MS m/z (M⁺): 175 (Calcd. for C₁₂H₁₀N₂O; C, 61.70; H, 5.18; N, 23.99. Found: C, 61.65; H, 5.18; N, 23.88 [Figure 1].
Table 1: Anti-microbial activity of the synthesized compounds

| Compounds | S. aureus | S. epidermidis | M. luteus | B. cereus | E. coli | P. aeruginosa | K. pneumoniae | A. niger | A. fumigatus |
|-----------|-----------|---------------|-----------|-----------|--------|-------------|-------------|---------|-------------|
| 4a        | 15 (25.2) | 19 (20.4) | 13 (27.8) | 16 (19.2) | 18 (21.9) | 17 (19.8) | 14 (23.6) | 13 (29.1) | 11 (30.6) |
| 4b        | 19 (19.3) | 18 (21.2) | 20 (16.3) | 17 (15.3) | 18 (19.2) | 18 (18.6) | 15 (21.8) | 19 (17.9) | 16 (19.9) |
| 4c        | 21 (10.4) | 25 (9.8) | 23 (11.2) | 19 (12.1) | 21 (14.8) | 20 (10.8) | 22 (13.9) | 20 (13.3) | 19 (13.6) |
| 4d        | 20 (13.2) | 20 (17.6) | 17 (20.6) | 18 (16.7) | 17 (19.0) | 17 (19.7) | 17 (19.6) | 18 (21.3) | 17 (18.8) |
| 4e        | 19 (13.6) | 23 (14.8) | 20 (12.4) | 17 (17.1) | 20 (14.4) | 20 (12.6) | 24 (11.8) | 23 (13.8) | 18 (14.2) |
| 4f        | 22 (11.8) | 18 (20.2) | 17 (19.6) | 16 (21.2) | 18 (19.6) | 16 (18.6) | 20 (17.6) | 19 (20.2) | 18 (17.9) |
| 4g        | 24 (9.2) | 27 (10.2) | 24 (11.6) | 21 (9.6) | 23 (12.1) | 21 (11.8) | 25 (10.6) | 24 (13.1) | 19 (14.5) |
| 4h        | 20 (12.8) | 18 (18.6) | 20 (17.6) | 16 (20.2) | 22 (14.1) | 16 (21.4) | 22 (15.7) | 24 (12.8) | 17 (18.6) |
| 4i        | 22 (10.6) | 24 (10.4) | 21 (12.1) | 18 (13.7) | 22 (13.2) | 19 (13.4) | 22 (14.3) | 22 (14.1) | 15 (20.8) |
| 4j        | 19 (18.2) | 22 (13.8) | 19 (18.7) | 17 (18.6) | 20 (19.1) | 16 (20.8) | 17 (18.6) | 18 (16.9) | 17 (18.1) |
| 4k        | 21 (12.5) | 25 (10.3) | 22 (14.1) | 18 (10.6) | 21 (13.4) | 21 (11.8) | 23 (12.8) | 22 (12.2) | 20 (12.9) |
| 4l        | 17 (22.8) | 14 (24.0) | 18 (19.7) | 15 (20.7) | 19 (20.2) | 14 (21.6) | 16 (18.9) | 15 (21.8) | 13 (24.8) |

Ciprolfloxacin: 25 29 27 23 29 25 27 - -
Ketoconazole: - - - - - - - - 29 26
DMF: - - - - - - - - - -

C_{19}H_{13}N_{2}O_{2}, 128.9 (C_{19} and C_{19}), 128.6 (C_{9}), 127.1 (C_{1}), 19.8 (-CH_{2}).

EI-MS m/z (M+): 263 (Calcd. for C_{19}H_{13}N_{2}O_{2}: 263.29). Anal. Calcd. for C_{19}H_{13}N_{2}O_{2}: C, 72.99; H, 4.98; N, 15.96. Found: C, 72.95; H, 4.96; N, 15.92.

3-(4-Methoxybenzylideneamino)-2-methyl quinazolin-4-(3H)-one (4b)

Cream solid; Yield: 72%; m.p. 191 – 194°C; IR (KBr, cm^{-1}): 3046 (Ar-CH), 2912 (CH in CH_{2}), 1724 (C=O), 1514 (C=N), 1462 (C=C), 1124 (C-O). \(^{1}\)H-NMR (CDCl_{3} \delta): 8.07 (s, 1H; -N=CH_{2}), 6.81-7.92 (m, 8H; C\_6C\_6C\_6C\_6C\_6C\_6C\_6C\_6C\_6C\_6C\_6Ar-H), 3.70 (s, 3H; -OCH_{3}), 0.79 (s, 3H; -CH_{3}). \(^{13}\)C-NMR (CDCl_{3} \delta): 163.9 (C_{6}), 160.2 (C_{6}), 143.2 (-N=CH_{2}), 133.2 (C_{6}), 163.1 (C_{6}), 130.1 (C_{6} and C_{6}), 128.6 (C_{6}), 127.3 (C_{6}), 126.2 (C_{6}), 122.2 (C_{6}), 114.3 (C_{6} and C_{6}), 55.6 (-OCH_{3}), 20.2 (-CH_{3}). EI-MS m/z (M+): 293 (Calcd. for C_{19}H_{13}N_{2}O_{2}: 293.31). Anal. Calcd. for C_{19}H_{13}N_{2}O_{2}: C, 69.61; H, 5.15; N, 14.33. Found: C, 69.58; H, 5.14; N, 14.28.

3-(2-Hydroxybenzylideneamino)-2-methyl quinazolin-4-(3H)-one (4c)

Pale yellow solid; Yield: 66%; m.p. 173 – 175°C; IR (KBr, cm^{-1}): 3040 (Ar-CH), 2915 (CH in CH_{2}), 1722 (C=O), 1514 (C=N), 1457 (C=C) 1350,1205 (C-O). \(^{1}\)H-NMR (CDCl_{3} \delta): 7.99 (s, 1H; -N=CH_{2}), 6.78-7.88 (m, 8H; C\_6C\_6C\_6C\_6C\_6C\_6C\_6C\_6Ar-H), 5.41 (s, 1H; Ar-CH_{2}), 0.82 (s, 3H; -CH_{3}). \(^{13}\)C-NMR (CDCl_{3} \delta): 163.4 (C_{6}), 164.5 (C_{6}) 160.6 (C_{6}), 142.9 (N=CH_{2}), 135.7 (C_{6}), 132.2 (C_{6}), 130.3 (C_{6}), 128.6 (C_{6}), 127.4 (C_{6}), 122.1 (C_{6}), 121.3 (C_{6}), 118.2 (C_{6}), 116.2 (C_{6}), 20.1 (-CH_{3}). EI-MS m/z (M+): 279 (Calcd. for C_{19}H_{13}N_{2}O_{2}: 279.29). Anal. Calcd. for C_{19}H_{13}N_{2}O_{2}: C, 68.81; H, 4.69; N, 15.05. Found: C, 68.79; H, 4.61; N, 15.01.

3-(4-N,N-dimethylaminobenzylideneamino)-2-methyl quinazolin-4-(3H)-one (4d)

Bright yellow crystal; Yield: 68%; m.p. 187 – 190°C; IR (KBr, cm^{-1}): 3032 (Ar-CH), 2920 (CH in CH_{2}), 1720 (C=O), 1518 (C=N), 1453 (C=C). \(^{1}\)H-NMR (CDCl_{3} \delta): 8.02 (s, 1H; -N=CH_{2}), 6.75-7.89 (m, 8H; C\_6C\_6C\_6C\_6C\_6C\_6C\_6Ar-H), 2.86
3-(3-Nitrobenzylideneamino)-2-methyl quinazolin-4-(3H)-one (4e)

Cream solid; Yield: 65%; m.p. 190 – 194°C; IR (KBr, cm⁻¹): 3048 (Ar-CH), 2926 (CH in CH₂), 1715 (C=O), 1524 (C=N), 1522 and 1335 (N=O), 1450 (C=C). ¹H-NMR (CDCl₃): δ: 8.09 (s, 1H; -N=C=O), 7.41-7.92 (m, 7H; C₆H₅), 3.64; N, 15.07. Found: C, 73.63; H, 5.92; N, 18.31.

3-(4-Hydroxybenzylideneamino)-2-methyl quinazolin-4-(3H)-one (4k)

Cream solid; Yield: 76%; m.p. 164 – 166°C; IR (KBr, cm⁻¹): 3041 (Ar-CH), 2926 (CH in CH₂), 1718 (C=O), 1522 (C=N), 1448 (C=C). ¹H-NMR (CDCl₃): δ: 8.12 (s, 1H; -N=CH), 7.09-8.71 (m, 8H; C₆H₅), 13.58. Found: C, 66.06; H, 4.78; N, 13.62.

3-(3-Phenylallylideneamino)-2-methyl quinazolin-4-(3H)-one (4l)

Cream solid; Yield: 65%; m.p. 122 – 124°C; IR (KBr, cm⁻¹): 3042 (Ar-CH), 2922 (CH in CH₂), 1724 (C=O), 1514 (C=N), 1463 (C=C), 1132 (C-O). ¹H-NMR (CDCl₃): δ: 8.10 (s, 1H; -N=C=O), 7.38-7.92 (m, 4H; C₆H₅), 6.61 (s, 1H; Ar-H), 6.64 (s, 1H; C₆H₅), 3.82 (s, 3H; -OCH₃).

3-(4-Butenylideneamino)-2-methyl quinazolin-4-(3H)-one (4m)

Pale yellow crystal; Yield: 77%; m.p. 210 – 214°C; IR (KBr, cm⁻¹): 3032 (Ar-CH), 2924 (CH in CH₂), 1722 (C=O), 1514 (C=N), 1455 (C=C), 1352 and 1208 (C-O). ¹H-NMR (CDCl₃): δ: 7.99 (s, 1H; -N=C=O), 6.82-7.88 (m, 8H; C₆H₅), 13.58. Found: C, 70.57; H, 5.92; N, 18.29.

3-(3-Chlorobenzylideneamino)-2-methyl quinazolin-4-(3H)-one (4n)

Pale yellow powder; Yield: 75%; m.p. 155 – 157°C; IR (KBr, cm⁻¹): 3019 (Ar-CH), 2916 (CH in CH₂), 1728 (C=O), 1512 (C=N), 1458 (C=C). ¹H-NMR (CDCl₃): δ: 7.61 (s, 1H; -N=C=O), 7.14-7.88 (m, 9H; C₆H₅), 6.59-6.62 (d, 1H; J=7.2 Hz; C₆H₅), 5.61-5.63 (d, 1H; J=6.5 Hz; C₆H₅). EI-MS m/z (M⁺): 353.37. Anal. Calcd. for C₁₅H₁₂N₂O₄; C, 64.58; H, 5.42; N, 11.89. Found: C, 64.49; H, 5.38; N, 11.85.

3-(4-Hydroxy-3-methoxybenzylideneamino)-2-methylquinazolin-4(3H)-one (4p)

Cream solid; Yield: 65%; m.p. 122 – 124°C; IR (KBr, cm⁻¹): 3032 (Ar-CH), 2925 (CH in CH₂), 1722 (C=O), 1518 (C=N), 1455 (C=C), 1352 and 1208 (C-O). ¹H-NMR (CDCl₃): δ: 7.92 (s, 1H; -N=C=O), 7.42-7.82 (m, 4H; C₆H₅), 13.58. Found: C, 70.48; H, 4.01; N, 14.81.

3-(3-Nitrobenzylideneamino)-2-methyl quinazolin-4-(3H)-one (4i)

Yellow crystal; Yield: 75%; m.p. 222 – 225°C; IR (KBr, cm⁻¹): 3048 (Ar-CH), 2925 (CH in CH₂), 1715 (C=O), 1524 (C=N), 1518 and 1342 (N=O), 1452(C=O). ¹H-NMR (CDCl₃): δ: 8.12 (s, 1H; -N=C=O), 7.35-7.99 (m, 8H; C₆H₅), 1342 (C₆H₅), 129.4 (C₆H₅), 128.9 (C₆H₅), 127.6 (C₆H₅), 121.2 (C₆H₅), 13.58. Found: C, 66.06; H, 4.78; N, 13.62.

3-(4-Chlorobenzylideneamino)-2-methyl quinazolin-4-(3H)-one (4h)

Yellow crystal; Yield: 75%; m.p. 222 – 225°C; IR (KBr, cm⁻¹): 3048 (Ar-CH), 2926 (CH in CH₂), 1715 (C=O), 1524 (C=N), 1518 and 1342 (N=O), 1452(C=O). ¹H-NMR (CDCl₃): δ: 8.12 (s, 1H; -N=C=O), 7.35-7.99 (m, 8H; C₆H₅), 1342 (C₆H₅), 129.4 (C₆H₅), 128.9 (C₆H₅), 127.6 (C₆H₅), 121.2 (C₆H₅), 13.58. Found: C, 66.06; H, 4.78; N, 13.62.
Anti-microbial Screening

Most of the synthesized compounds exhibited moderate-to-potent anti-microbial activity against the tested microorganisms. Compounds 4g and 4k were found to possess significant anti-bacterial and anti-fungal activity when compared to the standard drug (Ciprofloxacin and Ketoconazole for anti-bacterial and anti-fungal, respectively). Compounds 4c, 4h, 4i, and 4l displayed moderate anti-microbial activity, whereas, the remaining compounds showed lesser activity. The MIC of the synthesized compounds was screened by the agar streak dilution method. All the synthesized compounds exhibited moderate-to-good anti-bacterial and anti-fungal activity, with an MIC range of 9.2 – 30.6 µg/ml. 3-(4-hydroxy benzylideneamino)-2-methyl quinazolin-4(3H)-one 4g was found to exhibit the highest anti-bacterial activity against S.aureus (MIC: 9.2 µg/ml), B.cereus (MIC: 9.6 µg/ml), E.coli (MIC: 12.1 µg/ml), and K.pneumoniae (MIC: 10.6 µg/ml). 3-(2-hydroxy benzylideneamino)-2-methyl quinazolin-4(3H)-one 4c was found to exhibit the highest anti-bacterial activity against S.epidermidis (MIC: 9.8 µg/ml), M.luteus (MIC: 11.2 µg/ml), and P.aeruginosa (MIC: 10.8 µg/ml). 3-(4-hydroxy-3-methoxy benzylideneamino)-2-methyl quinazolin-4(3H)-one 4k exhibited the highest anti-fungal activity against A.niger (MIC: 12.2 µg/ml) and A.fumigatus (MIC: 12.9 µg/ml). The synthesized compounds were active against all the tested microorganisms, with a range of MIC values for S.aureus (9.2 – 25.2 µg/ml), S.epidermidis (9.8 – 24.0 µg/ml), M.luteus (11.2 – 27.8 µg/ml), B.cereus (9.6 – 21.2 µg/ml), E.coli (12.1 – 21.9 µg/ml), P.aeruginosa (10.8 – 21.6 µg/ml), K.pneumoniae (10.6 – 23.6 µg/ml), A.niger (12.2 – 29.1 µg/ml), and A.fumigatus (12.9 – 30.6 µg/ml). The potent anti-microbial activity exhibited by 4c, 4g and 4k may be due to the incorporation of the electron-donating groups like phenolic OH (at either the second or fourth position of the phenyl ring in the 3-substituted quinazolin-4(3H)-ones) and –OCH₃. The interesting results we observed were both the electron donating as well as the electron withdrawing groups were found to increase the anti-microbial properties, whereas, the unsubstituted derivatives exhibited a lesser degree of activity. The compound 4g was found to possess anti-bacterial activity almost equivalent to the standard drug, but exhibited considerable anti-fungal activity.

CONCLUSION

In conclusion, the present study highlights the importance of aromatic imino substitution at the third position of the quinazolin-4(3H)-one ring features, responsible for the anti-microbial property, and therefore, may serve as a lead molecule to obtain clinically useful, novel entities, in the new millennium.

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