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A Clean, Benign, Energy Efficient One-Pot Multicomponent Synthesis and Bio-evaluation of Novel [1,2,4]Triazolo[1,5-*a*]quinolines

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ABSTRACT

In present work, a series of novel [1,2,4]triazolo[1,5-*a*]quinoline derivatives (**HP-101-110**) have been synthesized using multi-component reaction at room temperature in the presence of ammonium chloride as mild, cost effective green catalyst along with water as eco-friendly green solvent. The synthesis of 1,2,4-triazolo[1,5-*a*]quinolines **(HP-101-110)** was achieved by two step process. In first step, diversified Hantzsch pyridine reaction of an appropriate aromatic aldehyde, malononitrile, dimedone and benz hydrazide using ethanol as a solvent gives *N*-(2-amino-3-cyano-7,7-dimethyl-5-oxo-4-phenyl-5,6,7,8-tetrahydro-quinolin-1(4*H*)-yl)-4-hydroxybenzamide derivatives. In the second step, synthesis of the final product 2-(4-hydroxyphenyl)-8,8-dimethyl-6-oxo-5-phenyl-6,7,8,9-tetrahydro[1,2,4]triazolo[1,5-*a*]-quinoline-4-carbonitriles was achieved by the intramolecular cyclization of step 1 product.The structure of all the synthesized compounds (**HP101-110**) has been elucidated by FT-IR, ^{1}H & ^{13}C NMR, mass spectral data and elemental analyses.

KEYWORDS

Dimedone, Benz hydrazide, Triazolo-quinolines, Antimicrobial.

INTRODUCTION

The importance of 1,2,4-triazole and quinoline nuclei is well established in the field of pharmaceutical chemistry. The derivatives of triazole exhibit a variety of biological activities, including anti-inflammatory [1], antimicrobial [2], anti-thrombotic [3], antiviral [4] and anticonvulsant activities [5].

1,2,4-Triazole derived agents have been investigated as anticonvulsants [6], as 5-lipoxygenase inhibitors [7] or as anticancer drugs [8]. Platinum(II) complexes of 1,2,4-triazoles show antitumor activity similar to *cis*-platin [9]. Furthermore, ruthenium(III) complexes of 1,2,4-triazoles are promising as potential drugs in anticancer treatment as alternative to the approved platinum-based anticancer drugs [10]. 1,2,4-Triazoles such as rizatriptan as agents for acute treat-ment of migraine headaches are commercially available drugs [11]; however, they are also still a topic of intensive research [12].

In view of important biological and medicinal properties associated with triazoles and quinolines, it was thought worthwhile to incorporate both these scaffolds in a single molecular framework to further assess the biological profile. To achieve this, a design is initiated to synthesize triazolo-fused quinolines.

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In this work, ten novel analogues of 1,2,4-triazolo[1,5-*a*]quinoline **(HP-101-110)** are synthesized. The synthesis of 1,2,4-triazolo-[1,5-*a*]quinoline **(HP-101-110)** was achieved by two step process. In first step, diversified Hantzsch pyridine reaction of an appropriate aromatic aldehyde, malononitrile, dimedone and benz hydrazide using ethanol as a solvent gives *N*-(2-amino-3-cyano-7,7-dimethyl-5-oxo-4-phenyl-5,6,7,8-tetrahydro-quinolin-1(4*H*)-yl)-4-hydroxybenzamide derivatives. In the second step, synthesis of the final product 2-(4-hydroxyphenyl)-8,8-dimethyl-6-oxo-5-phenyl-6,7,8,9-tetrahydro[1,2,4]-triazolo[1,5-*a*]-quinoline-4-carbonitriles was achieved by the intra-molecular cyclization of step 1 product. The products were characterized by FT-IR, ^{1}H & ^{13}C NMR, mass spectra and elemental analyses.

EXPERIMENTAL

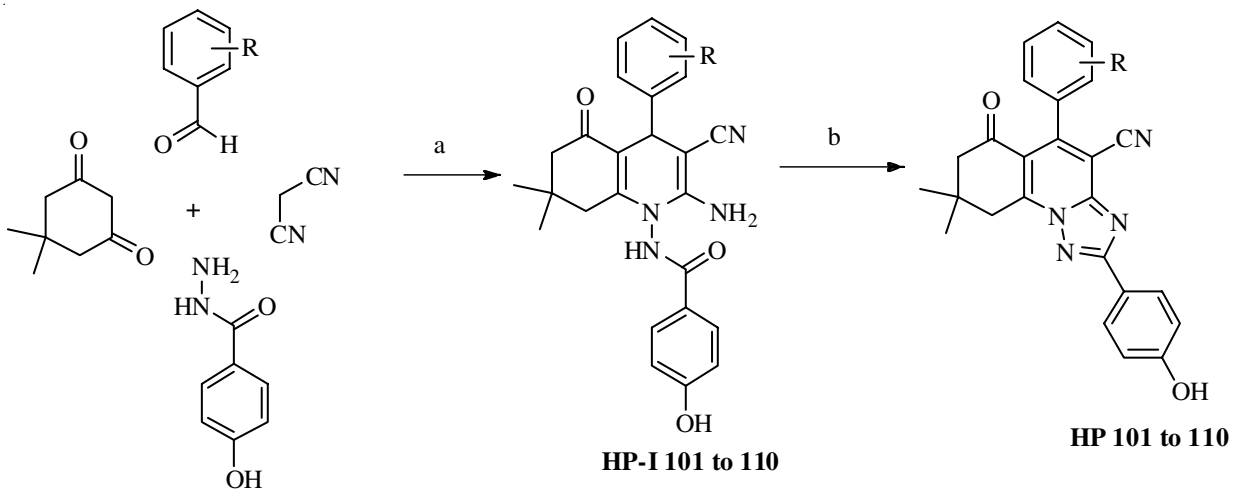
Melting points were determined in open capillary tubes and are uncorrected. Formation of the compounds was routinely checked by TLC on silica gel-G plates of 0.5 mm thickness and spots were located by iodine. IR spectra were recorded on IRAffinity-1S FTIR Spectrophotometer-Shimadzu using 'neat' sample. Mass spectra were recorded on Shimadzu GC-MS-QP-2010 model using Direct Injection Probe technique. ^{1}H NMR was determined in DMSO-d_6 solution on a Bruker Ac 400 MHz spectrometer. Elemental analysis of the all the synthesized compounds was carried out on Elemental Vario EL III Carlo Erba 1108 model and the results are in agreements with the structures assigned.

General synthetic procedure of *N*-(2-amino-3-cyano-7,7-dimethyl-5-oxo-4-phenyl-5,6,7,8-tetrahydroquinolin-1(4*H*)-yl)-4-hydroxybenzamides (HP-I-101-I-110): A mixture of aromatic aldehyde (1 mmol), malononitrile (1 mmol) and piperidine in ethanol was stirred for 5 min. After this benz hydrazides (1 mmol) and dimedone (1 mmol) were added and the resulting reaction mixture was stirred at room temperature for 40-60 min. The progress of the reaction being monitored by TLC using hexane:ethyl acetate 4:6. Upon completion of the reaction, solid was separated out. The reaction mixture was then filtered and dried solid product.

General synthetic procedure of 2-(4-hydroxyphenyl)-8,8-dimethyl-6-oxo-5-phenyl-6,7,8,9-tetrahydro[1,2,4]-triazolo[1,5-*a*]quinoline-4-carbonitriles (HP-101-110): A mixture of intermediate **HP-I** (1 mmol) and *N,N*-dimethyl-methylformamide 6 mL was heated at 120 ºC for 5 to 6 h. The progress of the reaction was monitored by TLC using $CHCl_3$: CH_3OH 9:1. After completion of the reaction, the reaction mass was allowed to cool at room temperature. The separated crystalline solid was filtered off and recrystallized from ethanol to give the pure product.

2-(4-Hydroxyphenyl)-8,8-dimethyl-6-oxo-5-phenyl-6,7,8,9-tetrahydro[1,2,4]triazolo[1,5-*a*]quinoline-4-carbonitrile (HP-101): Yield: 80%; m.p.: 178-180 ºC, *m.w.*: 408; R_f: 0.51. IR (KBr, ν_{max}, cm^{-1}): 3450 (O-H *str.*), 3125 (C-H *str.* arom. ring), 3030 (C-H *str.* CH_3), 2875 (C-H *str.* CH_2), 2366 (CN *str.*), 1741 (C=O *str.* carbonyl group), 1590 (C=N *str.* triazole ring), 1632 (C-C *str.* arom. ring), 1450, 1442, 1322 (C-H bending of -CH_2 and -CH_3), 742 (C-H bending of five adjacent hydrogen atom of monosubstituted aromatic ring); ^{1}H NMR (DMSO-d_6) δ ppm: 1.06 (s, 6H, H_a), 2.39 (s, 2H, H_b), 3.19 (s, 2H, H_c), 7.388-7.406 (dd, 2H, $H_{dd'}$, J = 7.4 Hz), 7.315-7.334 (t, 1H, $H_{e''}$, J = 7.01 Hz), 7.505-7.534 (d, 2H, $H_{ee'}$, J = 7.3 Hz), 7.913-7.932 (d, 2H, $H_{ff'}$, J = 7.5 Hz), 8.753-8.772 (d, 2H, $H_{gg'}$, J = 7.6 Hz), 9.202-9.230, (s, 1H); ^{13}C NMR (DMSO-d_6) δ ppm: 28.20, 35.65, 47.67, 52.92, 106.71, 116.87, 121.59, 125.89, 130.58, 134.35, 137.85, 148.09, 149.43, 153.29, 159.71, 170.32, 198.77; MS: *m/z* 408.16; Anal. calcd. (found) % for $C_{25}H_{20}N_4O_2$: C, 73.15 (73.29); H, 4.94 (4.88); N, 13.72 (13.84).

2-(4-Hydroxyphenyl)-8,8-dimethyl-6-oxo-5-(*p*-tolyl)-6,7,8,9-tetrahydro[1,2,4]triazolo[1,5-*a*]quinoline-4-carbonitrile (HP-102): Yield: 78%; m.p.: 202-204 ºC; *m.w.*: 422; R_f: 0.53; IR (KBr, ν_{max}, cm^{-1}): 3450 (O-H *str.*), 3323 (C-H *str.* arom. ring), 3033 (C-H *str.* CH_3), 2881 (C-H *str.* CH_2), 2355 (CN *str.*), 1749 (C=O *str.* carbonyl group), 1569 (C=N *str.* triazole ring), 1633 (C-C *str.* arom. ring), 1450, 1442, 1322 (C-H bending of -CH_2 and -CH_3), 846 (C-H bending of four adjacent hydrogen atom of *p*-substituted aromatic ring); ^{1}H NMR (DMSO-d_6) δ ppm: 1.09 (s, 6H, H_a), 2.23 (s, 2H, H_b), 3.19 (s,



Reagents and conditions: (a) Ethanol, piperidine, RT, 40-60 min; (b) DMF, 120°C, 5-6 h

Scheme-I

2H, H_c), 3.45 (s, 3H, $H_{d'}$), 7.342-7.452 (d, 2H, $H_{ee'}$, J = 6.9 Hz), 7.505-7.534 (d, 2H, $H_{ff'}$, J = 7.0 Hz), 7.913-7.932 (d, 2H, $H_{ff'}$, J = 7.5 Hz), 8.653-8.672 (d, 2H, $H_{gg'}$, J = 7.6 Hz), 9.230-9.236 (S, 1H); ^{13}C NMR (DMSO-d_6) δ ppm: 28.33, 36.22, 47.53, 53.10, 106.22, 117.12, 121,59, 125.63, 131.26, 135.26, 137.95, 148.23, 149.23, 153.26, 159.23, 171.59, 198.23; MS: *m/z* 422.17; Anal. calcd. (found) % for $C_{26}H_{22}N_4O_2$: C, 73.90 (73.29); H, 5.25 (5.69); N, 13.26 (13.81).

2-(4-Hydroxyphenyl)-5-(4-methoxyphenyl)-8,8-dimethyl-6-oxo-6,7,8,9-tetrahydro[1,2,4]triazolo[1,5-*a*]-quinoline-4-carbonitrile (HP-103): Yield: 86%; m.p.: 194-197 ºC; *m.w.*: 438; R_f: 0.56; IR (KBr, ν_{max}, cm^{-1}): 3450 (O-H *str.*), 3146 (C-H *str.* arom. ring), 3096 (C-H *str.* CH_3), 2796 (C-H *str.* CH_2), 2345 (CN *str.*), 1756 (C=O *str.* carbonyl group), 1560 (C=N *str.* triazole ring), 1629 (C-C *str.* arom. ring), 1446, 1445, 1364 (C-H bending of -CH_2 and -CH_3), 739 (C-H bending of four adjacent hydrogen atom of *p*-disubstituted aromatic ring); ^{1}H NMR (DMSO-d_6) δ ppm: 1.09 (s, 6H, H_a), 2.41 (s, 2H, H_b), 3.29 (s, 2H, H_c), 3.49 (s, 3H, H_d), 7.389-7.407 (dd, 2H, $H_{ee'}$, J = 7.2 Hz), 7.405-7.524 (d, 2H, $H_{ff'}$, J = 7.4 Hz), 7.914-7.934 (d, 2H, $H_{gg'}$, J = 6.9 Hz), 8.652-8.884 (d, 2H, $H_{hh'}$, J = 7.6 Hz). 9.225-9.236 (S, 1H); ^{13}C NMR (DMSO-d_6) δ ppm: 28.32, 36.45, 47.53, 52.42, 53.10, 106.25, 116.75, 120.99, 126.10, 131.45, 134.17, 136.22, 148.06, 149.26, 153.26, 159.16, 171.26, 198.77; MS: *m/z* 438.17; Anal. calcd. (found) % for $C_{26}H_{22}N_4O_3$: C, 71.22 (71.49); H, 5.06 (4.88); N, 12.78 (12.92).

5-(3,4-Dimethoxyphenyl)-2-(4-hydroxyphenyl)-8,8-dimethyl-6-oxo-6,7,8,9-tetrahydro[1,2,4]triazolo[1,5-*a*]-quinoline-4-carbonitrile (HP-104): Yield: 81%; m.p.: 187-189 °C; *m.w.*: 468; R_f: 0.58; IR (KBr, ν_{max}, cm^{-1}): 3450 (O-H *str.*), 3203 (C-H *str.* arom. ring), 3066 (C-H *str.* CH_3), 2772 (C-H *str.* CH_2), 2347 (C≡N *str.*), 1756 (C=O *str.* carbonyl group), 1555 (C=N *str.* triazole ring), 1629 (C-C *str.* arom. ring), 1446, 1445, 1378 (C-H bending of -CH_2 and –CH_3), 715-735 (C-H bending of three adjacent hydrogen atom of *m*-trisubstituted aromatic ring); ^{1}H NMR (DMSO-d_6) δ ppm: 1.12 (s, 6H, H_a), 2.65 (s, 2H, H_b), 3.12 (s, 2H, H_c), 3.49 (s, 3H, H_d), 3.64 (s, 3H, H_e), 6.910-6.928 (d, 2H, $H_{ff'}$, J = 6.9 Hz), 7.914-7.934 (d, 1H, $H_{e'}$, J = 6.9 Hz), 7.922-7.932 (d, 2H, $H_{hh'}$, J = 7.6 Hz), 8.210-8.223 (d, 2H, $H_{hh'}$), 9.225-9.236 (s, 1H); ^{13}C NMR (DMSO-d_6) δ ppm: 26.20, 34.80, 53.22, 55.93, 105.83, 117.63, 121.33, 130.12, 131.57, 146.83, 150.27, 152.42, 159.78, 170.42, 198.77; MS: *m/z* 468.80; Anal. calcd. (found) % for $C_{27}H_{24}N_4O_4$: C, 69.22 (69.52); H, 5.16 (5.22); N, 11.96 (11.96).

5-(2,5-Dimethoxyphenyl)-2-(4-hydroxyphenyl)-8,8-dimethyl-6-oxo-6,7,8,9-tetrahydro[1,2,4]triazolo[1,5-*a*]-quinoline-4-carbonitrile (HP-105): Yield: 78%; m.p.: 190-192 ºC; *m.w.*: 468; R_f: 0.60; IR (KBr, ν_{max}, cm^{-1}): 3450 (O-H *str.*), 3163 (C-H *str.* arom. ring), 3066 (C-H *str.* CH_3), 2815 (C-H *str.* CH_2), 2355 (CN *str.*), 1752 (C=O *str.* carbonyl group), 1578 (C=N *str.* triazole ring), 1512 (C-C *str.* arom. ring), 1446, 1445, 1362 (C-H bending of -CH_2 and –CH_3), 1210, 1010 (C-O *str.*) 810-845 (C-H bending of two adjacent hydrogen atom of *o*, *m* and *p*-trisubstituted aromatic ring); ^{1}H NMR (DMSO-d_6) δ ppm: 1.22 (s, 6H, H_a), 2.42 (s, 2H, H_b), 3.06 (s, 2H, H_c), 3.70-3.82 (s, 9H, $Hd_{ddd'''}$), 6.630-6.632 (s, 1H, H_f, J = 4.2 Hz), 7.093-7.111 (d, 2H, H_e, J = 3.9 Hz), 7.990-8.008 (d, 2H, $H_{gg'}$, J = 6.9 Hz), 8.765-8.788 (d, 2H, $H_{hh'}$, J = 7.6 Hz), 9.225-9.236 (s, 1H); ^{13}C NMR (DMSO-d_6) δ ppm: 27.92, 35.02, 47.52, 53.22, 56.10, 56.22, 56.48, 105.02, 107.21, 106.91, 117.09, 120.28, 121.03, 121.18, 130.03, 134.22, 142.09, 147.93, 152.63, 154.10, 160.22, 171.32, 198.05; MS: *m/z* 468.18; Anal. calcd. (found) % for $C_{27}H_{24}N_4O_4$: C, 69.22 (69.10); H, 5.16 (5.02); N, 11.96 (12.93).

2-(4-Hydroxyphenyl)-8,8-dimethyl-6-oxo-5-(3,4,5-trimethoxyphenyl)-6,7,8,9-tetrahydro[1,2,4]triazolo[1,5-*a*]-quinoline-4-carbonitrile (HP-106): Yield: 77%; m.p.: 196-199 ºC; *m.w.*: 498; R_f: 0.63; IR (KBr, ν_{max}, cm^{-1}): 3450 (O-H *str.*), 3209 (C-H *str.* arom. ring), 3042 (C-H *str.* CH_3), 2775 (C-H *str.* CH_2), 2362 (C≡N *str.*), 1746 (C=O *str.* carbonyl group), 1565 (C=N *str.* triazole ring), 1599 (C-C *str.* arom. ring), 1446, 1445, 1362 (C-H bending of -CH_2 and –CH_3), 1210, 1010, (C-O *str.*), 715-735 (C-H bending of three adjacent hydrogen atom of *m*-trisub-stituted aromatic ring); ^{1}H NMR (DMSO-d_6) δ ppm: 1.19 (s, 6H, H_a), 2.56 (s, 2H, H_b), 3.09 (s, 2H, H_c), 3.70-3.82 (s, 6H, $H_{dd'}$), 6.630-6.632 (s, 1H, H_f, J = 4.2 Hz), 7.0937-7.111 (d, 2H, $H_{ee'}$, J = 6.9 Hz), 7.993-8.010 (d, 2H, H_{gg}, J = 6.9 Hz), 8.765-8.783 (d, 2H, $H_{hh'}$, J = 7.6 Hz), 9.225-9.236 (S, 1H); ^{13}C NMR (DMSO-d_6) δ ppm: 28.39, 34.83, 46.93, 53.01, 55.83, 56.01, 106.07, 115.80, 117.08, 122.46, 123.13, 128.26, 146.10, 149.83, 153.26, 159.53, 171.06, 198.10; MS: *m/z* 498.19; Anal. calcd. (found) % for $C_{26}H_{23}N_5O_3$: C, 67.46 (68.10); H, 5.26 (5.02); N, 11.24 (12.93).

5-(4-Chlorophenyl)-2-(4-hydroxyphenyl)-8,8-dimethyl-6-oxo-6,7,8,9-tetrahydro[1,2,4]triazolo[1,5-*a*]quinoline-4-carbonitrile (HP-107): Yield: 83%; m.p.: 171-173 ºC; *m.w.*: 442; R_f: 0.59; IR (KBr, ν_{max}, cm^{-1}): 3450 (O-H *str.*), 3125 (C-H *str.* aromatic ring), 3030 (C-H *str.* CH_3), 2875 (C-H *str.* CH_2), 2366 (C≡N *str.*), 1741 (C=O *str.* carbonyl group), 1590 (C=N *str.* triazole ring), 1632 (C-C *str.* arom. ring), 1450, 1442, 1322 (C-H bending of -CH_2 and -CH_3), 742 (C-H bending of five adjacent hydrogen atom of monosubstituted aromatic ring); ^{1}H NMR (DMSO-d_6) δ ppm: 1.06 (s, 6H, H_a), 2.39 (s, 2H, H_b), 3.19 (s, 2H, H_c), 7.388-7.406 (dd, 2H, $H_{dd'}$, J = 7.4 Hz), 7.315-7.334 (t, 1H, $H_{e''}$, J = 7.01 Hz), 7.505-7.534 (d, 2H, $H_{ee'}$, J = 7.3 Hz), 7.913-7.932 (d, 2H, $H_{ff'}$, J = 7.5 Hz), 8.753-8.772 (d, 2H, $H_{gg'}$, J = 7.6 Hz), 9.225-9.236 (s, 1H); ^{13}C NMR (DMSO-d_6) δ ppm: 28.20, 35.65, 47.67, 52.92, 106.71, 116.87, 121.59, 125.89, 130.58, 134.35, 137.85, 148.09, 149.43, 153.29, 159.71, 170.32, 198.77; MS: *m/z* 442.12; Anal. calcd. (found) % for $C_{25}H_{19}N_4ClO_2$: C, 67.80 (67.29); H, 4.32 (4.88); N, 12.65 (12.81); Cl, 8.00 (7.99).

5-(3-Chlorophenyl)-2-(4-hydroxyphenyl)-8,8-dimethyl-6-oxo-6,7,8,9-tetrahydro[1,2,4]triazolo[1,5-*a*]quinoline-4-carbonitrile (HP-108): Yield: 85%; m.p.: 178-180 ºC; *m.w.*: 442; R_f: 0.61; IR (KBr, ν_{max}, cm^{-1}): 3456 (O-H *str.*), 3122 (C-H *str.* arom. ring), 3130 (C-H *str.* CH_3), 2875 (C-H *str.* CH_2), 2360 (C≡N *str.*), 1756 (C=O *str.* carbonyl group), 1591 (C=N *str.* triazole ring), 1611 (C-C *str.* aromatic ring), 1450, 1442, 1322 (C-H bending of -CH_2 and -CH_3), 690 (C-H bending of four adjacent hydrogen atom of *m*-disubstituted aromatic ring); ^{1}H NMR (DMSO-d_6) δ ppm: 1.22 (s, 6H, H_a), 2.28 (s, 2H, H_b), 3.06 (s, 2H, H_c), 7.388-7.406 (dd, 2H, $H_{dd'}$, J = 7.4 Hz), 7.998-8.331 (s, 1H, H_e, J = 4.01 Hz), 7.506-7.542 (d, 2H, H_e, J = 7.3 Hz), 7.913-7.932 (d, 2H, $H_{ff'}$, J = 7.3 Hz), 8.763-8.772 (d, 2H,

$H_{gg'}$, *J* = 7.6 Hz), 9.225-9.236 (s, 1H); ^{13}C NMR (DMSO-d_6) δ ppm: 28.24, 35.45, 48.67, 53.96, 105.71, 117.87, 121.56, 125.87, 130.58, 134.35, 137.85, 148.09, 149.43, 153.29, 159.71, 170.32, 198.77; MS: *m/z* 442.12; Anal. calcd. (found) % for $C_{25}H_{19}N_4O_2Cl$: C, 67.80 (67.29); H, 4.32 (4.88); N, 12.65 (12.81); Cl, 8.00 (7.98).

5-(4-Bromophenyl)-2-(4-hydroxyphenyl)-8,8-dimethyl-6-oxo-6,7,8,9-tetrahydro[1,2,4]triazolo[1,5-*a*]quinoline-4-carbonitrile (HP-109): Yield: 88%; m.p.: 186-188 ºC; *m.w.*: 486; R_f: 0.57; IR (KBr, ν_{max}, cm^{-1}): 3456 (O-H *str*.), 3022 (C-H *str* arom. ring), 3129 (C-H *str.* CH_3), 2865 (C-H *str.* CH_2), 2252 (C≡N *str.*), 1756 (C=O *str.* carbonyl group), 1581 (C=N *str* triazole ring), 1711 (C-C *str.* arom. ring), 1465, 1442, 1422 (C-H bending of -CH_2 and -CH_3), 845 (C-H bending of four adjacent hydrogen atom of *p*-disubstituted aromatic ring); ^{1}H NMR (DMSO-d_6) δ ppm: 1.29 (s, 6H, H_a), 2.39 (s, 2H, H_b), 3.18 (s, 2H, H_c), 7.553-7.562 (dd, 2H, $H_{dd'}$, *J* = 7.4 Hz), 7.756-7.776 (d, 2H, H_{ee}, *J* = 6.01 Hz), 6.668-6.789 (d, 2H, $H_{gg'}$, *J* = 7.3 Hz), 8.763-8.772 (d, 2H, $H_{hh'}$, *J* = 7.6 Hz), 9.239-9.252 (s, 1H); ^{13}C NMR (DMSO-d_6) δ ppm: 26.92, 26.42, 47.74, 54.09, 103.26, 115.12, 122.12, 127.63, 130.96, 135.23, 137.85, 148.09, 149.43, 153.23, 159.71, 170.32, 195.23; MS: *m/z* 486.07; Anal. calcd. (found) % for $C_{25}H_{19}N_4O_2Br$: C, 61.61 (61.29); H, 3.93 (4.09); N, 11.50 (12.81); Br, 16.40 (16.24).

5-(3-Bromophenyl)-2-(4-hydroxyphenyl)-8,8-dimethyl-6-oxo-6,7,8,9-tetrahydro[1,2,4]triazolo[1,5-*a*]quinoline-4-carbonitrile (HP-110): Yield: 82%; m.p.: 182-184 ºC; *m.w.*: 486; R_f: 0.65; IR (KBr, ν_{max}, cm^{-1}): 3442 (O-H *str*.), 3010 (C-H *str*. arom. ring), 3121 (C-H *str*. CH_3), 2865 (C-H *str*. CH_2), 2252 (C≡N *str*.), 1749 (C=O *str*. carbonyl group), 1581 (C=N *str*. triazole ring), 1723 (C-C *str*. arom. ring), 1464, 1442, 1422 (C-H bending of -CH_2 and -CH_3), 690-720 (C-H bending of four adjacent hydrogen atom of *m*-disubstituted aromatic ring); ^{1}H NMR (DMSO-d_6) δ ppm: 1.12 (s, 6H, H_a), 2.22 (s, 2H, H_b), 3.18 (s, 2H, H_c), 7.667-7.978 (d, 2H, $H_{dd'}$, *J* = 6.9 Hz), 7.456-7.561 (d, 2H, H_{ee}, *J* = 6.01 Hz), 6.668-6.789 (d, 2H, $H_{gg'}$, *J* = 7.3 Hz), 8.878-8.772 (d, 2H, $H_{hh'}$, *J* = 7.6 Hz), 9.239-9.252 (s, 1H); ^{13}C NMR (DMSO-d_6) δ ppm: 26.72, 26.42, 47.74, 52.09, 103.26, 116.12, 122.12, 129.63, 130.98, 135.23, 135.85, 148.09, 152.43, 153.23, 159.71, 170.32, 195.23; MS: *m/z* 486.07; Anal. calcd. (found) % for $C_{25}H_{19}N_4O_2Br$: C, 61.61 (61.22); H, 3.93 (4.50); N, 11.50 (11.81); Br, 16.40 (16.34).

Antimicrobial activity: All the synthesized compounds (**HP-101-110**) were tested for their antibacterial and antifungal activity (MIC) *in vitro* by broth dilution method [13,14] with two Gram-positive bacteria *Staphylococcus aureus* MTCC-96, *Streptococcus pyogenes* MTCC 443, two Gram-negative bacteria *Escherichia coli* MTCC 442, *Pseudomonas aeruginosa* MTCC 441 and three fungal strains *Candida albicans* MTCC 227, *Aspergillus niger* MTCC 282, *Aspergillus clavatus* MTCC 1323 taking ampicillin, chloramphenicol, ciprofloxacin, norfloxacin, nystatin and greseofulvin as standard drugs. The standard strains were procured from Microbial Type Culture Collection (MTCC) and Gene Bank, Institute of Microbial Technology, Chandigarh, India.

Serial dilutions of the test compounds and reference drugs were prepared in Mueller-Hinton agar. Drugs (10 mg) were dissolved in 1 mL DMSO. Further progressive dilutions with melted Mueller-Hinton agar were performed to obtain the required concentrations. In primary screening 1000, 500 and 250 μg mL^{-1} concentrations of the synthesized drugs were taken. The compounds found active in this primary screening were further tested in a second set of dilution at 200, 100, 50, 25, 12.5 and 6.25 μg mL^{-1} concentration against all microorganisms. The tubes were inoculated with 10^8 cfu mL^{-1} (colony forming unit/mL) and incubated at 37 ºC for 24 h. The MIC was the lowest concentration of the tested compound that yields no visible growth (turbidity) on the plate. To ensure that the solvent had no effect on the bacterial growth, a control was performed with the test medium supplemented with DMSO at the same dilutions as used in the experiments and it was observed that DMSO had no effect on the microorganisms in the concentrations studied.

RESULTS AND DISCUSSION

Novel [1,2,4]triazolo[1,5-*a*]quinoline derivatives (**HP-101-110**) were synthesized and characterized by FT-IR, ^{1}H NMR, ^{13}C NMR, mass spectra and elemental analyses. For **HP-101-110**, confirmatory bands for CN and carbonyl groups were observed at 2350-2150 and 1710-1680 cm^{-1}, respectively. Another characteristic C=N stretching band of triazole ring was observed at 1630-1610 cm^{-1}, which suggested the formation of desired products **HP-101-110**. ^{1}H NMR signals of a singlet for the methyl proton of quinoline ring at δ 1.05 to 1.20 ppm, a singlet for the methine proton of quinoline ring at δ 2.40 to 3.60 ppm and identical doublets for pyridine ring at δ 8.00 to 9.00 ppm. In ^{13}C NMR spectra, signal for methyl carbon of quinoline ring was observed at δ 20-30 ppm, signal for methine proton for quinoline ring were observed at δ 45-60 ppm. Signal for carbon of traizole was observed at δ 135-150 ppm indicates the involvement of triazole in cyclization process.

Biological activities: All the newly synthesized [1,2,4]-triazolo[1,5-*a*]quinoline derivatives (**HP-101-110**) were screened for their antibacterial activity against four bacterial strains: *E. coli*, *P. aeruginosa* as Gram-negative and *B. subtilus*, *S. aureus* as Gram-positive bacteria and three fungal strains *Candida albicans*, *Aspergillus niger* and *Aspergillus clavatus* MTCC 1323. The results obtained from antimicrobial susceptibility testing are shown in Table-1.

Conclusion

An atom-economical multi-component reactions at room temperature by stirring in the presence of ammonium chloride as mild, cost effective and green catalyst along with water as the eco-friendly green solvent to synthesize novel 1,2,4-triazolo[1,5-*a*]quinoline derivatives are reported. The results obtained from evaluation makes them promising tools for additional *in vivo* and *in vitro* evaluations for the development of lead with potential antimicrobial activity in the treatment of numerous dieses.

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TABLE-1
ANTIBACTERIAL AND ANTIFUNGAL ACTIVITY OF SYNTHESIZED COMPOUNDS **HP-101** TO **HP-110**

Compd. code	R	Minimal inhibition concentration (μg mL^{-1})						
		Gram-positive		Gram-negative		Fungal species		
		S.a.	*S.p.*	*E.c.*	*P.a.*	*C.a.*	*A.n.*	*A.c.*
HP-101	H	125	100	100	125	250	1000	250
HP-102	4-CH_3	250	500	250	250	250	200	200
HP-103	3-OCH_3	500	250	100	500	500	500	>1000
HP-104	3,4-OCH_3	125	125	250	200	500	>1000	1000
HP-105	2,5-OCH_3	250	500	250	500	>1000	>1000	>1000
HP-106	3,4,5-OCH_3	500	500	62.5	500	500	>1000	>1000
HP-107	4-Cl	500	62.5	250	62.5	1000	500	>1000
HP-108	3-Cl	100	250	62.5	500	1000	500	500
HP-109	4-Br	500	500	500	125	250	>1000	>1000
HP-110	3-Br	500	200	100	125	250	1000	250
Ampicillin		250	100	100	100	–	–	–
Chloramphenicol		50	50	50	50	–	–	–
Nystatin		–	–	–	–	100	100	100
Greseofulvin		–	–	–	–	500	100	100

S.a. = *Staphylococcus aureus* MTCC-96; *S.p.* = *Streptococcus pyogenes* MTCC 443; *E.c.* = *Escherichia coli* MTCC 442; *P.a.* = *Pseudomonas aeruginosa* MTCC 441; *C.a.* = *Candida albicans* MTCC 227; *A.n.* = *Aspergillus niger* MTCC 282; *A.c.* = *Aspergillus clavatus* MTCC 1323.

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