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Synthesis of Substituted 5-Phenyltriazolylquinazolinylamino Nicotinic Acid Esters, Screened their Antibacterial Activity and Molecular Docking Studies

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Quinazolines and imidazoles are substantial attention because of the several varieties of their biological activities. Substituted 5-phenyl-[1,2,4]triazolo[4,3-c]quinazolin-3-yl)amino)nicotinates were synthesized from anthranilamide as starting material by cyclization with benzaldehyde gave 2-phenyl-2,3-dihydroquinazolin-4(1*H*)-one, then followed by treated with Lawesson's reagent and hydrazine hydrate to produce hydrazine by replaced the sulfur atom. 5-Phenyl-[1,2,4]triazolo[4,3-*c*]quinazolin-3-amine obtained by cyclization of hydrazine compound with cyanogen bromide, followed by amidation with substituted 6-fluoronicotinates in the presence of DIPEA in DMSO solvent to get corresponding the title compounds. These compounds further evaluated for their *in vitro* antibacterial activity studies and molecular docking studies. Some of the newly synthesized compounds were found to possess excellent growth inhibition activity compared to commercial standards drugs like penicillin-G and streptomycin. All the synthesized compounds were confirmed by their elemental analysis, infrared, ^{1}H, ^{13}C NMR and mass spectral data.

Keywords: Quinazolines, Anthranilamide, Antibacterial activity, Molecular docking.

INTRODUCTION

Fused heterocycles like quinazolines are significant attention because of the various range of their biological activities [1]. The derivatives of quinazoline have more substantial attention since from the discovery of gefitinib for lung cancer as front-line drug. Some of the drugs like vandetanib, erlotinib and icotinib are significant antitumor agents which are containing quinazoline moiety. One of the drugs, Iressa known as gefitinib was synthetic compound containing anilinoquinazoline which acts as tyrosine kinase inhibitor (TKI) receptor shown antitumor activity [2]. Derivatives of 2,3,8-trisubstituted-4-(3*H*)-quinazoline were synthesized and studied their anticonvulsant activity by E1-Azab & El-Tahir [3]. Few compound's imidazole containing quinazoline were synthesized and evaluated for the hypotensive activities *in vivo* [4].

Some quinazoline molecules are already resolute many beneficial activities like, anticancer [5,6], antiinflammation [7], antimicrobial [8,9], CNS depressant [10,11] and anticonvulsant [3,12]. Thus, we approach to synthesize triazole moiety connected with quinazoline cores forthcoming direction of applications in the field of biology and medicine.

EXPERIMENTAL

Melting points using accessible capillary were measured and are uncorrected. The procurement of mass spectral data was made using a commercial ion trap mass spectrometer LCQ. The ^{1}H NMR spectra were recorded by a Varian spectrophotometer (400 MHz, $CDCl_3$, DMSO-d_6), all the starting materials were procured at Sigma-Aldrich, USA. The reaction development was checked by thin-layer chromatography using 0.25 mm silica gel plates.

Synthesis of 2-phenylquinazolin-4(3*H*)-one (2): To a solution of anthranilamide (5 mmol) dissolved in 20 mL of anhydrous DMF, benzaldehyde (5 mmol) was added. To a resulting mixture while stirring, iodine (6 mmol) and anhydrous potassium carbonate (5 mmol) was added and then heated at 60-80 ºC for 6 h. The mixture was poured into crushed ice water in (200 mL). The precipitated product was filtered, washed with hypo solution and then recrystallized from methanol.

Synthesis of (10Z)-1-(2-phenylquinazolin-4-(3*H*)-ylidene)hydrazine (4): To a compound **2** (0.01 mmol) in toluene (10 mL), added Lawesson's reagent (0.0058 mol) was refluxed for 3 h than removed the solvent under vacuum, collected crude

(**3**) (0.0074 mmol), which was directly used to next step. To this added methanol dissolved, hydrazine hydrate (0.058 mmol) was added and the reaction mass was heated up to 12-14 h. The reaction mixture cooled and the solvent distilled out under *vacuo*. After few hours solid separated, filtered and washed with water to get the compound **4**.

Synthesis of 5-phenyl[1,2,4]triazolo[4,3-*c*]quinazolin-3-amine (5): Compound **4** (2.0 mmol) taken in to a round bottom flask dissolved in dioxane solvent (20 mL) then added slowly Na_2CO_3 solution (10 %, 10 mL). A solution of cyanogen bromide (2.4 mmol) in dioxane (10 mL) dropped slowly at 5-10 ºC. The stirring was continued for 12-14 h and the confirmation of reaction was checked by TLC and then the solution was distilled out in order to obtain the residue. The residue was purified by recrystallization with methanol to get corresponding compound **5**. Yield: 67%; Light yellow; m.p.: 257-259 ºC. IR (KBr, ν_{max}, cm^{-1}): 3424, 3385 (NH_2); ^{1}H NMR ($CDCl_3$) δ ppm: 4.66 (s, 2H, -NH_2), 7.57- 7.601 (m, 3H, Ar-H), 7.64-7.66 (m, 1H, Ar-H), 7.78- 7.83 (m, 1H, Ar-H), 8.05- 8.07 (d, *J* = 7.5 Hz, 1H, Ar-H), 8.37- 8.40 (d, 1H, Ar-H), 8.43- 8.46 (m, 2H, Ar-H); ^{13}C NMR ($CDCl_3$) δ ppm: 116.54, 122.54, 127.23, 129.56, 129.70, 129.90, 130.90, 132.23, 135.22, 143.09, 144.94, 145.76, 160.09; MS (ESI): *m/z* [(M+1)$^+$]: 262. HRMS *m/z* calcd. for $C_{15}H_{11}N_5$ [(M+H)$^+$]: 262.0132; found: 262.0136.

Synthesis of substituted 6-(5-phenyl[1,2,4]triazolo[4,3-*c*]-quinazolin-3-ylamino)nicotinate 7(a-h): Compound **5** (0.01 mol) dissolved in DMSO (25 mL) was added to substituted 6-fluoronicotinic acid esters (**6a-f**) (0.01 mol) and cooled to 10 ºC. To this reaction mixture, slowly added a diisopropyl ethylamine (0.03 mol) solution and then slowly raise the temperature to 110 ºC for 8 h, the reaction mixture was monitored by TLC. After completion of reaction poured into ice-cold water extract with chloroform. The collected organic layers were removed under vacuum to get the final compound, which was purified by column chromatography (mobile phase: 3:7 ethyl acetate:petroleum ether).

Methyl-6-(5-phenyl[1,2,4]triazolo[4,3-*c*]quinazolin-3-ylamino)nicotinate (7a): Yield: 62%; yellow solid; m.p.: 201-202 °C. IR (KBr, ν_{max}, cm^{-1}): 3415 (NH), 3024 (Ar-CH), 1748 (C=O), 1652 (C=N); ^{1}H NMR (DMSO-d_6) δ ppm: 3.9 (s, 3H, -OCH_3), 6.9 (d, 1H, Ar-H), 7.48 (m, 3H, Ar-H), 7.62 (m, 1H, Ar-H), 7.80 (m, 1H, Ar-H), 7.90 (d, 1H, Ar-H), 8.10 (d, *J* = 7.5 Hz, 1H, Ar-H), 8.38-8.42 (m, 3H, Ar-H), 8.58-8.60 (m, 1H, Ar-H), 10.13 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 52.08, 113.39, 116.54, 119.37, 122.54, 127.23, 129.56, 129.70, 129.90, 130.90, 132.23, 135.22, 140.08, 145.33, 145.76, 147.91, 150.22, 151.63, 159.59, 164.04; MS (ESI): *m/z* [(M+H)$^+$]: 397. HRMS *m/z* calcd. for $C_{22}H_{16}N_6O_2$[(M+H)$^+$]: 397.0135; found: 397.0137.

Ethyl-6-(5-phenyl[1,2,4]triazolo[4,3-*c*]quinazolin-3-ylamino)nicotinate (7b): Yield:57%; yellow solid; m.p.187-189 ºC; IR (KBr, ν_{max}, cm^{-1}): 3410 (NH), 3032 (Ar-CH), 1737 (C=O), 1654 (C=N); ^{1}H NMR (DMSO-d_6) δ ppm: 2.21 (t, *J* = 6.0 Hz, 3H, -CH_3), 4.62 (q, 2H, -CH_2), 6.97 (d, *J* = 7.5 Hz, 1H, Ar-H), 7.20-7.23 (m, 2H, Ar-H), 7.37-7.42 (m, 3H, Ar-H), 7.60-7.65 (m, 2H, Ar-H), 7.78-7.83 (m, 2H, Ar-H), 8.14 (d, *J* = 7.5 Hz, 1H, Ar-H), 8.65 (m, 1H, Ar-H), 9.53 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 14.72, 61.27, 113.56, 116.53, 119.24, 122.53, 127.22, 129.55, 129.89, 129.91, 130.90, 132.22, 133.23, 135.20, 140.72, 145.32, 145.74, 147.90, 151.22, 154.58, 165.73; MS (ESI): *m/z* [(M+H)$^+$]: 411. HRMS *m/z* calcd. for $C_{23}H_{18}N_6O_2$ [(M+H)$^+$]: 411.0152; found: 411.0154

Isopropyl 6-((5-phenyl[1,2,4]triazolo[4,3-*c*]quinazolin-3-yl)amino)nicotinate (7c): Yield: 20%; yellow solid; m.p: 195-197 ºC; IR (KBr, ν_{max}, cm^{-1}): 3306 (NH), 3034 (Ar-CH), 1745 (C=O), 1684 (C=N); ^{1}H NMR (DMSO-d_6) δ ppm: 1.31-1.45 (m, 6H, -2CH_3), 3.68 (s, 1H, -CH), 6.81 (s, 1H, Ar-H), 7.22-8.16 (m, 10H, Ar-H), 8.72 (s, 1H, Ar-H), 9.81 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 22.54, 70.42, 113.80, 116.53, 119.23, 122.53, 127.22, 129.55, 129.71, 129.90, 130.89, 132.22, 135.21, 141.40, 145.32, 145.75, 147.90, 150.91, 152.29, 154.57, 165.88; MS (ESI): *m/z* [(M+H)$^+$]: 422; HRMS *m/z* calcd. for $C_{24}H_{20}N_6O_2$ [(M+H)$^+$]: 422.0153; found: 422.0156

***tert*-Butyl 6-((5-phenyl[1,2,4]triazolo[4,3-*c*]quinazolin-3-yl)amino)nicotinate (7d):** Yield: 58%; Light yellow; m.p: 205-207 ºC; IR (KBr, ν_{max}, cm^{-1}): 3402 (NH), 3012 (Ar-CH), 1706 (C=O), 1628 (C=N); ^{1}H NMR (DMSO-d_6) δ ppm: 1.40 -1.63 (m, 9H, -3CH_3), 6.81 (s, 1H, -Ar-H), 7.32- 8.06 (m, 10H, Ar-H), 8.35 (s, 1H, Ar-H), 10.42 (s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ ppm: 28.42, 81.44, 114.07, 116.52, 119.35, 122.52, 127.22, 129.55, 129.72, 129.91, 130.89, 132.22, 135.22, 142.15, 145.32, 145.75, 147.90, 150.63, 153.37, 154.58, 163.90; MS (ESI): *m/z* [(M+H)$^+$] 435.12. HRMS *m/z* calcd. for $C_{25}H_{22}N_6O_2$ [(M+H)$^+$]: 435.0125; found: 435.0127.

Phenyl 6-((5-phenyl[1,2,4]triazolo[4,3-*c*]quinazolin-3-yl)amino)nicotinate (7e): Yield: 60%; yellow solid; m.p: 201-203 ºC; IR (KBr, ν_{max}, cm^{-1}): 3312 (NH), 3032 (Ar-CH), 1724 (C=O), 1653 (C=N); ^{1}H NMR (DMSO-d_6) δ ppm: 6.73 (s, 1H, Ar-H), 7.05- 7.10 (m, 3H, Ar-H), 7.15- 7.23 (m, 2H, Ar-H), 7.30 (s, 1H, Ar-H), 7.35- 7.40 (m, 2H, Ar-H), 7.53 (s, 1H, Ar-H), 7.60- 7.64 (m, 2H, Ar-H), 7.71 (s, 1H, Ar-H), 7.94 (d, *J* = 15.8 Hz, 2H, Ar-H), 8.05 (s, 1H, Ar-H), 8.85 (s, 1H, Ar-H), 9.65 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 114.07, 116.52, 119.35, 120.81, 122.53, 125.28, 127.24, 129.54, 129.72, 129.84, 129.92, 130.90, 132.22, 135.21, 142.15, 145.32, 145.75, 147.90, 150.63, 151.02, 153.38, 154.58, 164.90; MS (ESI): *m/z* [(M+H)$^+$]: 452.15. HRMS *m/z* calcd. for $C_{27}H_{18}N_6O_2$ [(M+H)$^+$]:452.0156; found: 452.0159.

Benzyl-6-(5-phenyl[1,2,4]triazolo[4,3-*c*]quinazolin-3-yl)amino)nicotinate (7f): Yield: 5%; yellow solid; m.p.210-212 ºC. IR (KBr, ν_{max}, cm^{-1}): 3394 (NH), 3037 (Ar-CH), 1732 (C=O), 1659 (C=N); ^{1}H NMR (DMSO-d_6) δ ppm: 4.38 (s, 2H, -CH_2), 6.88 (d, *J* = 7.5 Hz, 1H, Ar-H), 7.28-7.32 (m, 5H, Ar-H), 7.39-7.46 (m, 1H, Ar-H), 7.54-7.57 (d, *J* = 7.5 Hz, 2H, Ar-H), 7.62-7.65 (m, 2H, Ar-H), 7.78-7.83 (m, 2H, Ar-H), 7.97 (d, *J* = 7.5 Hz, 1H, Ar-H), 8.23 (d, *J* = 1.4 Hz, 1H, Ar-, H), 8.62 (m, 1H, Ar-H), 10.21 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 66.88, 113.56, 116.53, 119.22, 122.53, 127.22, 128.15, 128.16, 128.30, 129.55, 129.80, 129.91, 129.89, 130.91, 132.22, 135.21, 137.07, 140.72, 145.31, 145.75, 147.90, 151.22, 154.57, 165.43; MS (ESI): *m/z* [(M+H)$^+$] 473. HRMS *m/z* calcd. for $C_{28}H_{20}N_6O_2$ [(M+H)$^+$]: 473.0180; found: 473.0183.

4-Chlorobenzyl-6-(5-phenyl[1,2,4]triazolo[4,3-*c*]quinazolin-3-yl)amino)nicotinate (7g): Yield:70%; yellow

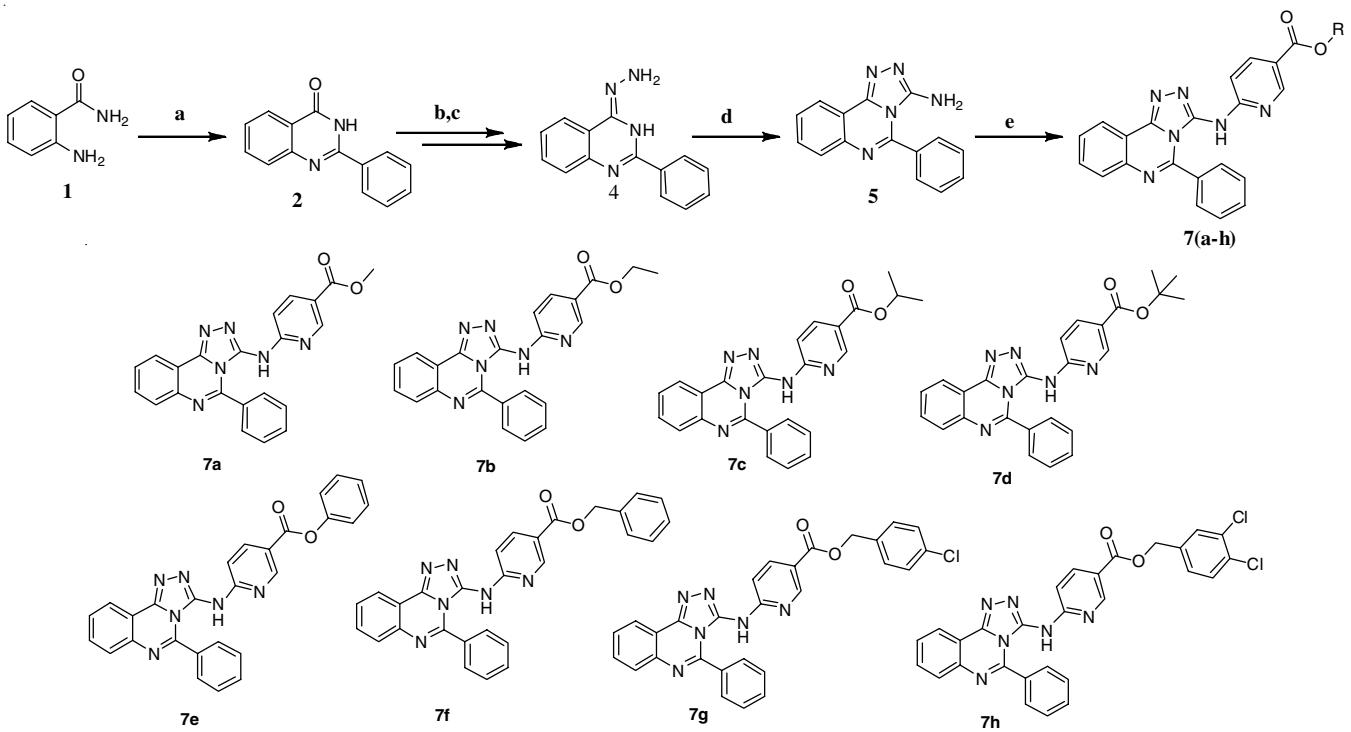
solid; m.p.154-156 ºC. IR (KBr, ν_{max}, cm^{-1}): 3410 (NH), 3042 (Ar-CH), 1730 (C=O), 1661 (C=N); ^{1}H NMR (DMSO-d_6) δ ppm: 5.34 (s, 2H, -CH_2), 6.90 (d, *J* = 7.5 Hz, *J* = 7.5 Hz, 1H, Ar-H), 7.23-7.26 (m, 2H, Ar-H), 7.32-7.39 (s, 2H, Ar-H), 7.44-7.49 (m, 2H, Ar-H), 7.57-7.62 (d, *J* = 7.5 Hz, 2H, Ar-H), 7.69-7.74 (m, 2H, Ar-H), 7.89-7.93 (m, 2H, Ar-H), 8.12 (d, 1H, Ar-H), 8.27 (d, 1H, Ar-H), 8.73 (m, 1H, Ar-H), 10.36 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 66.90, 113.56, 116.53, 119.23, 122.53, 127.22, 128.68, 129.26, 129.55, 129.71, 129.91, 130.89, 132.22, 134.21, 135.20, 135.24, 140.72, 145.32, 145.74, 147.90, 151.21, 151.22, 154.58, 165.43; MS (ESI): *m/z* (M+1) 507, (M+3) 509. HRMS *m/z* calcd. for $C_{28}H_{19}ClN_6O_2$ [(M+H)$^+$]: C, 66.34; H, 3.78, N, 16.58; found: C, 66.31; H, 3.75; N, 16.56.

3,4-Dichlorobenzyl-6-(5-phenyl[1,2,4]triazolo[4,3-*c*]-quinazolin-3-yl)amino)nicotinate (7h): Yield:68 %; yellow solid; m. p.164-166 ºC. IR (KBr, ν_{max}, cm^{-1}): 3412 (NH), 3042 (Ar-CH), 1735 (C=O), 1663 (C=N); ^{1}H NMR (DMSO-d_6) δ ppm: 5.32 (s, 2H, -CH_2), 6.92 (d, *J* = 7.5 Hz, 1H, Ar-H), 7.23-7.26 (m, 2H, Ar-H), 7.32 (s, 1H, Ar-H), 7.42-7.46 (m, 2H, Ar-H), 7.52-7.60 (d, *J* = 7.5 Hz, 2H, Ar-H), 7.65-7.70 (m, 2H, Ar-H), 7.80-7.85 (m, 2H, Ar-H), 8.14 (d, *J* = 7.5, 1H, Ar-H), 8.29 (d, 1H, Ar-H), 8.75 (m, 1H, Ar-H), 10.4 (s, 1H, NH). ^{13}C NMR (DMSO-d_6) δ ppm: 66.70, 113.56, 116.52, 119.24, 122.53, 127.22, 127.51, 129.05, 129.54, 129.69, 129.89, 129.91, 130.89, 130.94, 131.76, 131.84, 132.22, 135.21, 138.39, 140.72, 145.32, 145.75, 147.90, 151.22, 154.58, 165.42; MS (ESI): *m/z* [(M+1)$^+$] 541, [(M+3)$^+$] 543. HRMS *m/z* calcd. for $C_{28}H_{18}ClN_6O_2$ [(M+H)$^+$]: 543.0874; found: 543.0878.

RESULTS AND DISCUSSION

The synthesis of derivatives of 5-phenyl[1,2,4]triazolo-[4,3-*c*]quinazolin-3-ylamino)nicotinates (**7a-h**) are shown in **Scheme-I**. *o*-Amino benzamide (**1**) cycli-zation took place with benzaldehyde gave 2-phenyl-2,3-dihydroquinazolin-4(1*H*)-one (**2**), which was treated with Lawesson's reagent to produce corresponding compound thione **3**. Compound **3** was treated with hydrazine hydrate to form hydrazine **4** by replaced the sulfur atom. Compound (10Z)-1-(2-phenylquinazolin-4-(3*H*)-ylidene)hydrazine (**4**) underwent cyclization with cyanogen bromide under reflux conditions to yield 5-phenyl-[1,2,4]triazolo[4,3-*c*]-quinazolin-3-amine (**5**) and followed by amidation with substituted 6-fluoronicotinates (**6**) in the presence of DIPEA in DMSO solvent to get corresponding title 6-(5-phenyl[1,2,4]triazolo-[4,3-*c*]quinazolin-3-ylamino)nicotinate (**7a-h**) derivatives.

The IR spectrum of 5-phenyl[1,2,4]triazolo[4,3-*c*]quinazolin-3-amine (**5**) showed the characteristic IR band doublet at 3424, 3385 cm^{-1} which indicated the presence of NH_2 group. The title compounds 6-(5-phenyl[1,2,4]triazolo[4,3-*c*]quinazolin-3-ylamino)nicotinate **(7a-h)** showed the characteristic IR bands at 3415 cm^{-1} for the presence of N–H, aromatic -C-H shows at 3024 cm^{-1} C=O and CN group characteristic bands at 1748 and 1652 cm^{-1}. The intermediate 5-phenyl[1,2,4]triazolo-[4,3-*c*]quinazolin-3-amine **(5a)** and 6-(5-phenyl[1,2,4]triazolo-[4,3-*c*]quinazolin-3-ylamino)nicotinate **(7a-h)** products were further confirmed by proton–NMR spectral data. The ^{1}H NMR spectrum of compound 5-phenyl[1,2,4]triazolo[4,3-*c*]quinazolin-3-amine (**5**) showed at 4.66 ppm indicating that the NH_2 group and multiple signals such as multiplet and doublet from the range δ 7.52 -8.46 indicates the presence of aromatic protons. The ^{1}H NMR spectrum of 6-(5-phenyl[1,2,4]-triazolo-[4,3-*c*]-quinazolin-3-ylamino)nicotinate (**7a**) showed a singlet signal 10.13 δ ppm due to NH signal, three protons of methyl ester appeared at chemical shift value of 3.9 δ ppm, remaining chemical shift in the aromatic region resonated at δ 6.9 (d, 1H), 7.48 (m,



Scheme-I: (a) Benzaldehyde, I_2 in DMF, (b) Lawesson's reagent, (c) Hydrazine hydrate, (d) CNBr, (e) 6-flouro nicotinic acid derivatives, DIPEA in DMSO

3H), 7.62 (m, 1H), 7.80 (m, 1H), 7.90 (d,1H), 8.10 (d, 1H), 8.38-8.42 (m, 3H) and 8.58-8.60 (m, 1H) indicates aromatic protons.

In ^{13}C NMR spectra, the chemical shift value δ 164.0 ppm indicates the characteristic signals of quinazoline carbon which is present between two nitrogen atoms at δ 159.5 ppm represents the aromatic carbon which attached to methoxy group, at δ 151.9, 150.0 ppm, respectively indicates that triazolo[4,3-*c*]-quinazolin-3-ylamino carbon, which are attached to nitrogen atoms remaining chemical shifts at δ 147.9, 145.7, 145.3, 140.0, 132.2, 130.9, 129.9, 129.7, 128.8, 127.2, 116.5 ppm, indicates that remaining carbons of aromatic rings, peak at δ 113.3 ppm represents aromatic carbon attached to methoxy group and another -OCH_3 group appears at δ 52.0 ppm. Similarly, compound **7a** also confirmed by the ESI-Mass $[M+H]^+$ peak observed at *m/z* 262.

The chemical structure of synthesized compounds **4a-j** was confirmed by IR, NMR, mass and elemental (C, H and N) analysis. From the IR spectrum, the sharp bands at 3326 cm^{-1}, indicates the presence of-NH group and a sharp band at 1565 cm^{-1} shows the C=N. From the ^1H NMR spectrum, the appearance of signal at δ 6.82 ppm indicates a isoxazole proton and a multiple signal at δ 6.80-8.56 ppm indicates the presence of aromatic protons. The singlet at δ 4.18 ppm shows -O-CH_2-protons, 3.98 quartet signal indicates CH-protons and signal at δ 1.78 ppm indicates methyl protons. Mass spectrum of the title compounds were determined by molecular ion peak at *m/z* of corresponding molecular weights.

Antibacterial screening: The antibacterial screening of all the newly synthesized **7a-h** derivatives were evaluated for *in vitro* antibacterial activity against two representative Gram-positive bacterial strains like *Bacillus sphericus* (MTCC 11), *Staphylococcus epidermidis* (MTCC 2639) and Gram-negative bacterial strains like *Klebsiella pneumonia* (MTCC 3384), *Escherichia coli* (MTCC 443) species using standard drugs penicillin-G and streptomycin. The investigation of bacterial screening revealed that almost all the compounds are active and showing moderate to excellent antibacterial activity. Among them, compounds **7d** and **7e** displayed good to excellent inhibition activity. Specifically, compound containing 3,4-dichloro group on the phenyl ring (**7h**) has shown superior inhibition activity against all the four cell lines than commercial standard drugs (Table-1).

Molecular docking studies: A molecular docking study (Table-2) where compound **7h** was docked in the binding site of ABC transporter–substrate binding domain. The docking study was done by using AUTODOCK 4.2 version and the images are being rendered using Schrodinger's maestro v9.5 visualizer interface docking values for antimicrobial studies. The active compounds **7a-h** from antibacterial studies further supported by docking studies through molecular interactions with Gram-positive and Gram-negative bacteria. Molecular docking studies revealed that compounds **7d**, **7e** and **7h** showed better docking scores than remaining molecules when compared to all the compounds **7h** displayed the best docking score of -9.19. Thus the 2D and 3D interaction diagram of the ligand **7h** with the complex protein is shown in Fig. 1. Crystal structure of *S. aureus* MURB was taken from protein data bank PDB ID: 1HSK and binding site has been recognized inside 2.3 Å distance from co-crystal ligand. The multi-step Schrödinger's protein partition tool has been used for final preparation of receptor model. The synthesized compounds **7a-h** were selected by means of 2D-sketcher and prepared for docking with Ligprep, module of Schrödinger. A total of 10 conformations were generated for all compounds.

TABLE-1
ANTIBACTERIAL SCREENING

Compound	Zone of inhibition (diameter in millimeter)			
	Gram-positive bacteria		Gram-negative bacteria	
	BS	SE	KP	EC
7a	15(30)	14(30)	22(30)	21(30)
7b	14(30)	13(30)	21(30)	22(30)
7c	13(30)	12(30)	20(30)	19(30)
7d	20(30)	17(30)	27(30)	26(30)
7e	21(30)	17(30)	27(30)	25(30)
7f	18(30)	15(30)	21(30)	20(30)
7g	19(30)	14(30)	23(30)	24(30)
7h	22(30)	19(30)	31(30)	28(30)
Pencillin-G	22(30)	18(30)	–	–
Streptomycin	–	–	30(30)	28(30)
DMSO	0	0	0	0

BS = *Bacillus sphericus*; SE = *Staphylococcus epidermidis*; KP = *Klebsiella pneumonia*; EC = *Escherichia coli*

Conclusion

In this work, substituted 5-phenyl[1,2,4]triazolo[4,3-*c*]-quinazolin-3-yl)amino)nicotinates were synthesized from anthranilamide as precursor material by cyclization with benzal-dehyde gave 2-phenyl-2,3-dihydroquinazolin-4(1*H*)-one, then followed by treated with Lawesson's reagent and

TABLE-2
MOLECULAR DOCKING VALUES

Compound	Binding energy (kcal/mol)	Inhibition constant (nM)	Number of hydrogen bonds	Residues involved in hydrogen bonding	Run
7a	-8.59	506.61	3	VAL A:75, GLU A:72, GLU A:171	5
7b	-8.33	788.13	3	VAL A:75, GLU A:72, GLU A:171	5
7c	-8.43	662.73	7	VAL A:75, GLU A:72, GLU A:171	3
7d	-9.16	182.78	3	VAL A:75, GLU A:72, GLU A:171	8
7e	-9.08	221.71	0	0	9
7f	-8.14	1.07 uM	2	VAL A:75, GLU A:171	3
7g	-8.65	454.80	2	VAL A:75, GLU A:171	1
7h	-9.19	187.48	1	HIS A:196	4

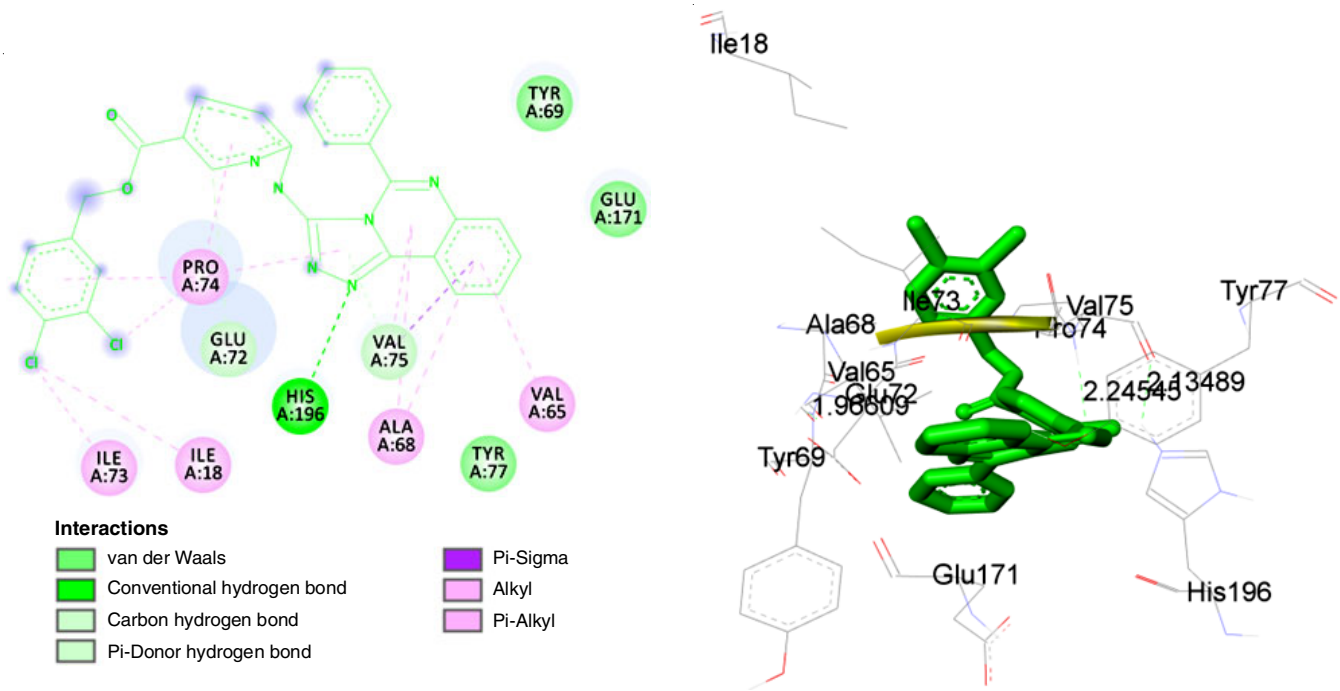


Fig. 1. 2D and 3D Interaction diagrams for ligand **7h** with *S. aureus* MURB

hydrazine hydrate to produce hydrazine by replaced the sulfur atom. 5-Phenyl[1,2,4]triazolo[4,3-*c*]quinazolin-3-amine obtained from cyclization of hydrazine compound with cyanogen bromide, followed by amidation with substituted 6-fluoro-nicotinates in the presence of DIPEA in DMSO solvent to get corresponding title compounds. These compounds further evaluated for their *in vitro* antibacterial activity studies and molecular docking studies. Some of the newly synthesized compounds were found to possess excellent growth inhibition activity compared to commercial standards drugs like streptomycin and Penicillin-G. All the synthesized compounds were confirmed by their elemental analysis, IR, NMR and mass spectral data.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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