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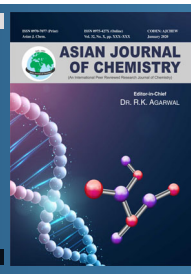

Synthesis, Characterization and Molecular Docking of 1,2,4-Triazole Derivatives as Potential Antimicrobial Agents

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In this study, a new series of (*E*)-*N*-(4-(3-(3,5-dialkylphenyl)acryloyl)phenyl)-2-(1*H*-1,2,4-triazol-1-yl)acetamide (**32-41**) was synthesized, characterized by FT-IR, ^{1}H NMR, ^{13}C NMR and Mass spectral analysis and evaluated for their *in vitro* antibacterial and antifungal activities. The docking study of the newly synthesized compounds was performed and results showed good binding mode in the active site of 1T9U protein. The zone of inhibition concentration was tested for the synthesized compounds against five bacterial and three fungal strains. Compounds **34** and **37** have good antibacterial activity. Compounds **3**, **4** and **6** shows moderate inhibition against the antifungal activity.

Keywords: 1,2,4-Triazole, Molecular docking, 1T9U Protein, Antibacterial activity, Antifungal activity.

INTRODUCTION

Microbial infections are the maximum distinguished loss of life-causing disease once an attack within the worldwide, because of their capacity to unfold quickly, blended with their toxicity and resistance closer to existing antibiotic drugs [1,2]. Those developments have emphasized the urgent need and venture for the development of more effective, potent and wide-spectrum antimicrobial novel drugs with practical bioavailability, no or fewer factor consequences to cure microbial infections [3]. In this context, drug discovery has obtained a considerable interest in a microbial target based totally on the synthesis of novel antimicrobial agents.

Heterocyclic molecules are a reliable source for discovering novel biologically active molecules. Among the heterocyclic compounds, 1,2,4-triazole derivatives represent one of the most interesting and essential classes of compounds [4]. The nitrogen-based heterocyclic system has been reportable to procedure numerous pharmacological applications [5]. Triazole that is famous for its effective antimicrobial activity has won extra involvement in the past many years [6,7]. As a result of their characteristics together with high biological activities, excessive efficiency, low toxicity, huge microbial spectrum and stereoselectivity, *etc.* [8]. Triazoles are attracting growing interest in the biological and pharmaceutical fields such as antibacterial [9,10], antifungal [11-13], antituberculosis [14], anticancer [15,16], herbicide [17], anti-inflammatory [18,19], anticonvulsant [20], antidiabetic [21], antimalarial [22] and antioxidant [23] activities. Additionally, amide along with an organic compound as a crucial biologically active group has higher anticancer, antibacterial and antiviral activities [24-26]. Besides these, amides are widely recognized for their therapeutic values. The chemistry of amides having a chloroacetyl group became additionally very charming and has received considerable attention now a day. *N*-Benzyl-β-chloropropionamide a very good anticonvulsant and turned into marketed below the alternate name Hibicon and Hydrane [27]. Triazole derivatives are given as fungicides in agrichemicals also as pharmaceutical applications for the treatment of topical and systematic fungal infections. The enormous use of triazole derivatives has generated significant issues regarding their distribution, free concentration and metabolism among the body, which is tormented by the ligand-protein interactions within the bloodstream [28]. In recent years, triazoles have received unique interest in drug discovery due to many drug molecules containing triazole groups such as tazobactam, cephalosporin and cefatrizine [29]. They may be clinically used for the treatment of microbial infections. Because of these above findings, it have been contemplated to layout and synthesize a new magnificence of heterocyclic derivatives

in which 1,2,4-triazole derivatives act as an antimicrobial agent.

EXPERIMENTAL

Performing TLC assessed the reactions and the purity of the products. All the reported melting points were taken in open capillaries and were uncorrected. FT-IR spectra were recorded in the ATR method on an Agilent Cary 630 FT-IR spectrophotometer and noteworthy absorption values (cm^{-1}) were listed. ^1H and ^{13}C NMR spectra were recorded at 400 MHz and 100 MHz, respectively on Brucker Avance II 400 NMR spectrometer using $CDCl_3$ as a solvent.

General procedure for synthesis of (*E*)-1-(4-aminophenyl)-3-(3,5-dialkylphenyl)prop-2-en-1-ones (12-21): The Claisen-Schmidt condensation reaction of equimolar quantities of aminoacetophenone (**1**, 0.01 mol) and substituted benzaldehyde (**2-11**, 0.01 mol) were stirred at room temperature in an ethanolic solution of potassium hydroxide for 2-3 h. The formed yellow crystals were filtered off, washed with distilled water, dried and recrystallized from ethanol.

General procedure for synthesis of (*E*)-2-chloro-*N*-(4-(3-(3,5-dialkylphenyl)acryloyl)phenyl)acetamide (22-31): The electrophilic substitution reaction of chloroacetyl chloride (0.01 mol) with the corresponding parent (*E*)-1-(4-aminophenyl)-3-(3,5-dialkylphenyl)prop-2-en-1-ones (**12-21**, 0.01 mol) in the presence of triethylamine as a base and dichloromethane (20 mL) as a solvent, was stirred at room temperature. The reaction process was monitored by TLC. After the completion, the reaction mixture was extracted with chloroform. The organic layer was separated and dried over-under vacuum. The crude product was collected and purified.

General procedure for synthesis of (*E*)-*N*-(4-(3-(3,5-dialkylphenyl)acryloyl)phenyl)-2-(1*H*-1,2,4-triazol-1-yl)acetamide (32-41): A mixture of (*E*)-2-chloro-*N*-(4-(3-(3,5-dialkylphenyl)acryloyl)phenyl)acetamide (**22-31**) (0.05 mol), potassium carbonate (0.01 mol) and 1,2,4-triazole (0.05 mmol) in dimethylformamide was refluxed. After completion of the reaction was monitored by TLC. The reaction was poured into ice-cold water. The product was washed and filtered with water and then recrystallized from ethanol.

Physical properties and spectral data

***N*-(4-(3-(3-chlorophenyl)acryloyl)phenyl)-2-(1*H*-1,2,4-triazol-1-yl)acetamide (32):** Yellow solid, yield: 72%, m.p.: 112-114 °C, m.w.: 366, FT-IR (KBr, ν_{max}, cm^{-1}): 3314 (NH), 3050 (Ar CH), 2925 (Ali CH), 1684 (amide C=O), 1660 (C=O), 1595 (C=N), 1530 (C=C). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 4.24 (s, 2H, CH_2), 7.26 (s, NH), 7.75 (d, CH), 7.59 (d, CH), 8.05 & 8.6 (s, triazole H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 188.7 (C=O), 161.9 (amide C=O), 151 (triazole C3), 141.8, 143.3 (triazole C5), ar C [140.8, 134.9, 130.2, 127.9, 126.8, 122.9, 119.4], 42.9 (CH_2). Elemental analysis for $C_{19}H_{15}N_4O_2Cl$ (%): C, 62.21; H, 4.12; N, 15.27.

***N*-(4-(3-(4-Chlorophenyl)acryloyl)phenyl)-2-(1*H*-1,2,4-triazol-1-yl)acetamide (33):** Yellow solid, yield: 70%, m.p.: 174-180 °C, m.w.: 366, FT-IR (KBr, ν_{max}, cm^{-1}): 3309 (NH), 3057 (Ar CH), 2953 (Ali CH), 1697 (amide C=O), 1655 (C=O), 1597 (C=N), 1529 (C=C). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 4.23 (s, 2H, CH_2), 7.26 (s, NH), 7.72 (d, CH), 7.57 (d, CH), 8.06 & 8.5 (s, triazole H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 188.61 (C=O), 164.08 (amide C=O), 151 (triazole C3), 141.31, 143.31 (triazole C5), ar C [140.87, 136.49, 134.52, 133.35, 129.2, 122.04, 119.41], 42.90 (CH_2). Elemental analysis for $C_{19}H_{15}N_4O_2Cl$ (%): C, 62.21; H, 4.12; N, 15.27.

***N*-(4-(3-(2,3-Dichlorophenyl)acryloyl)phenyl)-2-(1*H*-1,2,4-triazol-1-yl)acetamide (34):** Yellow solid, yield: 68%, m.p.: 158-162 °C, m.w.: 401, FT-IR (KBr, ν_{max}, cm^{-1}): 3274 (NH), 3047 (Ar CH), 2927 (Ali CH), 1696 (amide C=O), 1648 (C=O), 1593 (C=N), 1528 (C=C). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 4.23 (s, 2H, CH_2), 7.26 (s, NH), 7.43 (d, CH), 8.15 (d, CH), 8.04 & 8.48 (s, triazole H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 188.57 (C=O), 164.1 (amide C=O), 150.85 (triazole C3), 145.18 (triazole C5), ar C [141, 140.51, 135.63, 133.5, 127.41, 125.92, 119.42], 42.89 (CH_2). Elemental analysis for $C_{19}H_{14}N_4O_2Cl_2$ (%): C, 56.87; H, 3.52; N, 13.96.

***N*-(4-(3-(2,6-Dichlorophenyl)acryloyl)phenyl)-2-(1*H*-1,2,4-triazol-1-yl)acetamide (35):** Yellow solid, yield: 68%, m.p.: 118-120 °C, m.w.: 401, FT-IR (KBr, ν_{max}, cm^{-1}): 3301 (NH), 3072 (Ar CH), 2930 (Ali CH), 1682 (amide C=O), 1647 (C=O), 1575 (C=N), 1526 (C=C). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 4.23 (s, 2H, CH_2), 7.26 (s, NH), 7.43 (d, CH), 8.15 (d, CH), 8.04 & 8.48 (s, triazole H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 188.76 (C=O), 163.87 (amide C=O), 152.81 (triazole C3), 145.02 (triazole C5), ar C [141.73, 140.51, 137.71, 133.93, 131.42, 129.88, 128.8, 119.1, 113.9], 42.89 (CH_2). Elemental analysis for $C_{19}H_{14}N_4O_2Cl_2$ (%): C, 56.87; H, 3.52; N, 13.96.

***N*-(4-(3-(4-Fluorophenyl)acryloyl)phenyl)-2-(1*H*-1,2,4-triazol-1-yl)acetamide (36):** Yellow solid, yield: 72%, m.p.: 152-156 °C, m.w.: 350, FT-IR (KBr, ν_{max}, cm^{-1}): 3294 (NH), 3050 (Ar CH), 2948 (Ali CH), 1684 (amide C=O), 1660 (C=O), 1593 (C=N), 1532 (C=C). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 4.23 (s, 2H, CH_2), 7.26 (s, NH), 7.7 (d, CH), 7.34 (d, CH), 8.04 & 8.3 (s, triazole H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 188.7 (C=O), 165.3 (C=O), 162.85, 151.5 (triazole C3) 143.53 (triazole C5), ar C [140.77, 134.6, 131.1, 129.9, 121.3, 119.4, 116.06], 42.8 (CH_2). Elemental analysis for $C_{19}H_{15}N_4O_2F$ (%): C, 65.14; H, 4.32, N, 15.99.

***N*-(4-(3-(*p*-Tolyl)acryloyl)phenyl)-2-(1*H*-1,2,4-triazol-1-yl)acetamide (37):** Yellow solid, yield: 76%, m.p.: 172-178 °C, m.w.: 346, FT-IR (KBr, ν_{max}, cm^{-1}): 3310 (NH), 3016 (Ar CH), 2917 (Ali CH), 1667 (amide C=O), 1655 (C=O), 1597 (C=N), 1538 (C=C). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.39 (s, CH_3), 4.21 (s, 2H, CH_2), 7.26 (s, NH), 7.7 (d, CH), 7.34 (d, CH), 8.03 & 8.5 (s, triazole H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 189.1 (C=O), 164.14 (amide C=O), 151 (triazole C3), 144.9 (triazole C5), ar C [140.7, 134.8, 132.1, 129.7, 120.64, 119.4], 42.93 (CH_2), 21.55 (CH_3).Elemental analysis for $C_{20}H_{18}N_4O_2$ (%): C, 69.35; H, 5.24; N, 16.17.

***N*-(4-(3-(3-Methoxyphenyl)acryloyl)phenyl)-2-(1*H*-1,2,4-triazol-1-yl)acetamide (38):** Yellow solid, yield: 78%, m.p.: 128-132 °C, m.w.: 362, FT-IR (KBr, ν_{max}, cm^{-1}): 3282 (NH), 3053 (Ar CH), 2939 (Ali CH), 1697 (amide C=O), 1655 (C=O), 1593 (C=N), 1525 (C=C). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.85 (s, 3H, OCH_3), 4.29 (s, 2H, CH_2), 7.26 (s, NH), 7.7 (d, CH), 7.3 (d, CH), 8.03 & 8.56 (s, triazole H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 188.97 (C=O), 164.15 (amide C=O),

159.94, 151 (triazole C3), 144.76 (triazole C5), ar C [140.84, 136.2, 134.61, 129.96, 121.95, 119.4], 55.37 (OCH_3), 42.94 (CH_2). Elemental analysis for $C_{20}H_{18}N_4O_3$ (%): C, 66.29; H, 5.01; N, 15.46.

***N*-(4-(3-(4-Methoxyphenyl)acryloyl)phenyl)-2-(1*H*-1,2,4-triazol-1-yl)acetamide (39):** Yellow solid, yield: 78%, m.p.: 142-146 °C, m.w.: 362, FT-IR (KBr, ν_{max}, cm^{-1}): 3260 (NH), 3055 (Ar CH), 2929 (Ali CH), 1683 (amide C=O), 1654 (C=O), 1594 (C=N), 1529 (C=C). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.85 (s, 3H, OCH_3), 4.2 (s, 2H, CH_2), 7.26 (s, NH), 7.7 (d, CH), 7.3 (d, CH), 8.03 & 8.5 (s, triazole H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 189.03 (C=O), 164.09 (amide C=O), 161.74, 151 (triazole C3), 144.75 (triazole C5), ar C [140.58, 134.98, 131.61, 129.85, 127.5, 119.3], 55.43 (OCH_3), 42.91 (CH_2). Elemental analysis for $C_{20}H_{18}N_4O_3$ (%): C, 66.29; H, 5.01; N, 15.46.

***N*-(4-(3-(3,5-Dimethoxyphenyl)acryloyl)phenyl)-2-(1*H*-1,2,4-triazol-1-yl)acetamide (40):** Yellow solid, yield: 76%, m.p.: 162-166 °C, m.w.: 392, FT-IR (KBr, ν_{max}, cm^{-1}): 3255 (NH), 3097 (Ar CH), 2940 (Ali CH), 1683 (amide C=O), 1655 (C=O), 1589 (C=N), 1535 (C=C). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.74 (s, 6H, OCH_3), 4.2 (s, 2H, CH_2), 7.26 (s, NH), 7.7 (d, CH), 7.4 (d, CH), 8.06 & 8.2 (s, triazole H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 189.3 (C=O), 164.09 (amide C=O), 161.05, 151 (triazole C3), 145 (triazole C5), ar C [140.7, 134.8, 132.1, 129.9, 122.1, 119.48], 55.48 (OCH_3), 42.93 (CH_2). Elemental analysis for $C_{21}H_{20}N_4O_4$ (%): C, 64.28; H, 5.14; N, 14.28.

***N*-(4-(3-(3-Nitrophenyl)acryloyl)phenyl)-2-(1*H*-1,2,4-triazol-1-yl)acetamide (41):** Yellow solid, yield: 56%, m.p.: 138-142 °C, m.w.: 377, FT-IR (KBr, ν_{max}, cm^{-1}): 3261 (NH), 3090 (Ar CH), 2916 (Ali CH), 1667 (amide C=O), 1656 (C=O), 1594 (C=N), 1519 (C=C). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 4.24 (s, 2H, CH_2), 7.26 (s, NH), 7.7 (d, CH), 7.64 (d, CH), 8.08 & 8.52 (s, triazole H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 188.04 (C=O), 164.11 (amide C=O), 152.02 (triazole C3), 145.18 (triazole C5), ar C [141.64, 136.6, 134.09, 130.12, 124.28, 120, 119.5], 42.9 (CH_2).Elemental analysis for $C_{19}H_{15}N_5O_4$ (%): C, 60.47; H, 4.01; N, 18.56.

Molecular docking study: Molecular docking study is to predict the binding orientation of ligands to their protein and in turn expecting the binding affinity and strength of affiliation among the target and ligand. Molecular docking was completed among the active binding area of the energy minimized to stabilize the structure of 1T9U and the synthesized compounds the use of the CDOCKER docking protocol of the Discovery studio. CDOCKER is a grid-based molecular dynamic algorithm that employs the CHARMm force field using the ligand minimization tool [30].

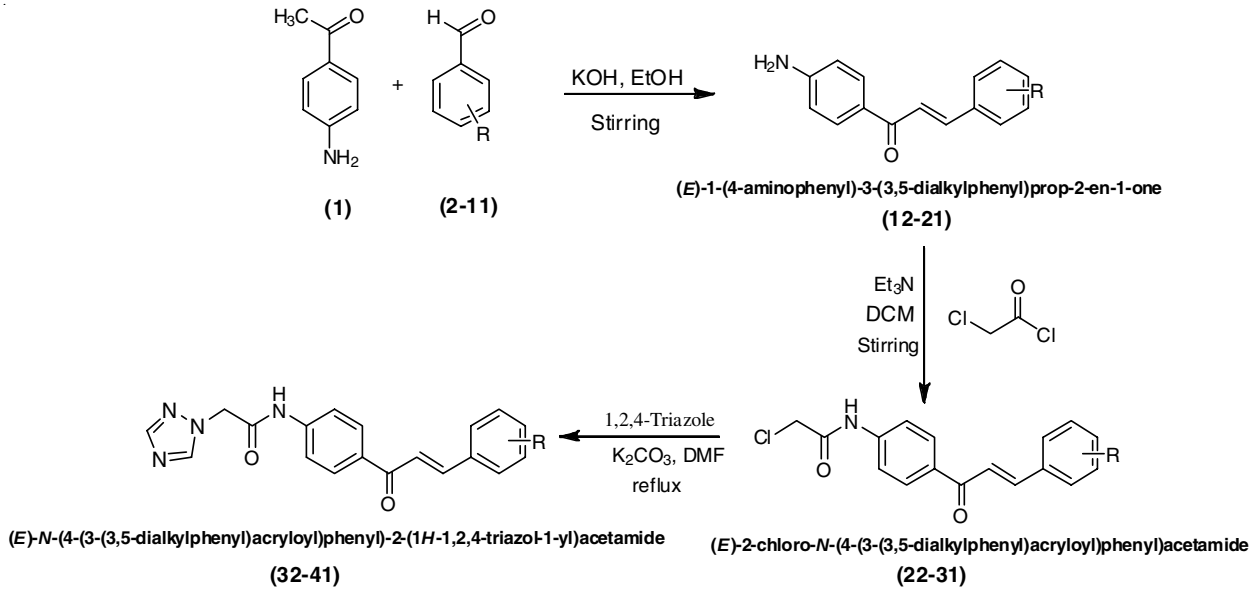
Molecular docking studies were finished through by Biovia discovery studio, 2016 software become utilized in performing this docking simulation study. The X-ray 3D crystal structure of bacterial multidrug efflux transporter AcrB (PDB ID: 1T9U) was retrieved from protein data bank with a good resolution of 3.5 Å [31]. After the docking process, the CDOCKER energy and CDOCKER interaction energy scores have been displayed within the output file. The best ligand was chosen, based on their lowest interaction energy and highly interacting amino acid residues. The interaction of the ligand molecule with the 1T9U protein and ligand poses have been analyzed and studied based on H-bonding poses to the receptor molecule and vander Waals interaction between the poses and receptor molecule. The unwanted water molecules, chains and co-factors were removed.

Antimicrobial activity: The *in vitro* antimicrobial activity was carried out by disc diffusion method [32,33]. The newly synthesized compounds were evaluated for their antibacterial activity towards a panel of pathogenic microorganisms, which includes three Gram-positive bacterial strains *Bacillus subtilis*, *Staphylococcus aureus*, *Proteus vulgaris* and two Gram-negative bacterial strains *Escherichia coli*, *Pseudomonas aeroginosa*. On the other hand, *Candida albicans*, *Candida parapsilosis* and *Candida tropicalis* had been chosen to study the antifungal activities of the synthesized compounds. The antibacterial and antifungal screening revealed that some of the examined compounds demonstrated fair to good antimicrobial activities relative to ciprofloxacin and fluconazole; standard potent antibacterial and antifungal, respectively.

The bacterial and fungal strains have been chosen based totally on their medical and pharmacological importance. Nutrient agar plates were prepared aseptically to get a thickness of 5-6 mm. The plates had been allowed to solidify and inverted to prevent condensate from falling on the agar surface. The plates were dried at 37 °C just before inoculation. The sterilized discs for the test drugs were placed in the petri dish at 37 ± 0.2 °C for about 18-24 h; after placing them in the refrigerator for 1 h to facilitate uniform diffusion. The average zone diameter of the plates was measured and recorded. All the synthesized compounds were tested for antibacterial and antifungal activities against the bacterial and fungal strains.

RESULTS AND DISCUSSION

A three-step synthetic route furnished the target compounds in good yields. General schematic representations are given in **Scheme-I**. The Claisen-Schmidt condensation reaction of equimolar quantities of 4-amino acetophenone and appropriate benzaldehyde in the presence of alcoholic KOH yielded (*E*)-1-(4-aminophenyl)-3-(3,5-dialkylphenyl)prop-2-en-1-ones (**12-21**). Then, various substituted (*E*)-2-chloro-*N*-(4-(3-(3,5-dialkylphenyl)acryloyl)phenyl)acetamide (**22-31**) were synthesized by the electrophilic substitution reaction of chloroacetyl chloride with the corresponding parent (*E*)-1-(4-aminophenyl)-3-(3,5-dialkylphenyl)prop-2-en-1-ones (**12-21**) in the presence of triethylamine as a base and dichloromethane as solvent, appreciable yields were obtained. Then condensation of (*E*)-2-chloro-*N*-(4-(3-(3,5-dialkylphenyl)acryloyl)phenyl)-acetamide (**22-31**) with 1,2,4-triazole in the presence of potassium carbonate in DMF furnished (*E*)-*N*-(4-(3-(3,5-dialkyl-phenyl)-acryloyl)phenyl)-2-(1*H*-1,2,4-triazol-1-yl)acetamide (**32-41**). The help of the melting points, elemental analysis, FT-IR, one-dimensional NMR (^{1}H and ^{13}C) and mass spectra supported the structures of all the newly synthesized compounds. In the FT-IR spectra of the targeted compounds **32-41** contained a stretching absorption peak at 3310-3250 assigned due to N-H stretch. The absorption peak for C=N was observed at 1593



Compd	32	33	34	35	36	37	38	39	40	41
R	3-Cl	4-Cl	2,3-diCl	2,6-diCl	4-F	4-CH_3	3-OCH_3	4-OCH_3	3,5-diOCH_3	4-NO_2

Scheme-I: Synthesis of (*E*)-*N*-(4-(3-(3,5-dialkylphenyl)acryloyl)phenyl)-2-(1*H*-1,2,4-triazol-1-yl)acetamide

cm^{-1}. The peak at 1680 and 1655 cm^{-1} was assigned due to amide C=O and chalcone C=O stretch, respectively. In the ^1H NMR spectrum showed two singlets at δ (ppm) 8.0 and 8.5 were assigned to CH protons of the 1,2,4-triazole ring, the singlet signal at δ 7.26 was assigned to NH proton. The singlet appeared at δ 4.2 due to CH_2 proton, the two doublet signal at δ 7.4 and 7.7 integrating for two protons were assigned for two olefin protons (CH=CH). In the ^{13}C NMR spectrum showed signals at δ (ppm) 188 and 164 corresponds to chalcone and amide carbonyl carbons, the signals at δ 151 and 144 represents C3 and C5 carbons of triazole ring, respectively.

Molecular docking studies: The synthesized compounds **32-41** were docked with 1T9U protein. The data obtained from the docking study is presented in Table-1. The docking results indicated the active pocket by forming hydrophobic interactions with amino acid residues. The compound **34** had shown hydrogen-bonding interaction with amino acid residues, respectively (Fig. 1). The halogen-substituted compounds **34**, **35** and **36** were more favourable for hydrophobic interactions as compared to the other substituted (NO_2, OCH_3, CH_3) compounds. The 4-F substitution in the benzyl ring of most active compound **36** fitted well into the hydrophobic pocket. The binding interactions for compound **34** are shown in Fig. 2.

TABLE-1
DOCKING RESULTS OF THE DESIGNED COMPOUNDS **32-41** TOWARDS 1T9U

Compounds	-CDOCKER energy (kcal/mol)	-CDOCKER interaction energy (kcal/mol)
32	4.297	30.957
33	3.01	33.898
34	11.535	30.991
35	6.631	31.446
36	7.858	27.624
37	3.923	30.06
38	6.017	30.743
39	6.148	30.531
40	5.522	34.663
41	6.818	31.772

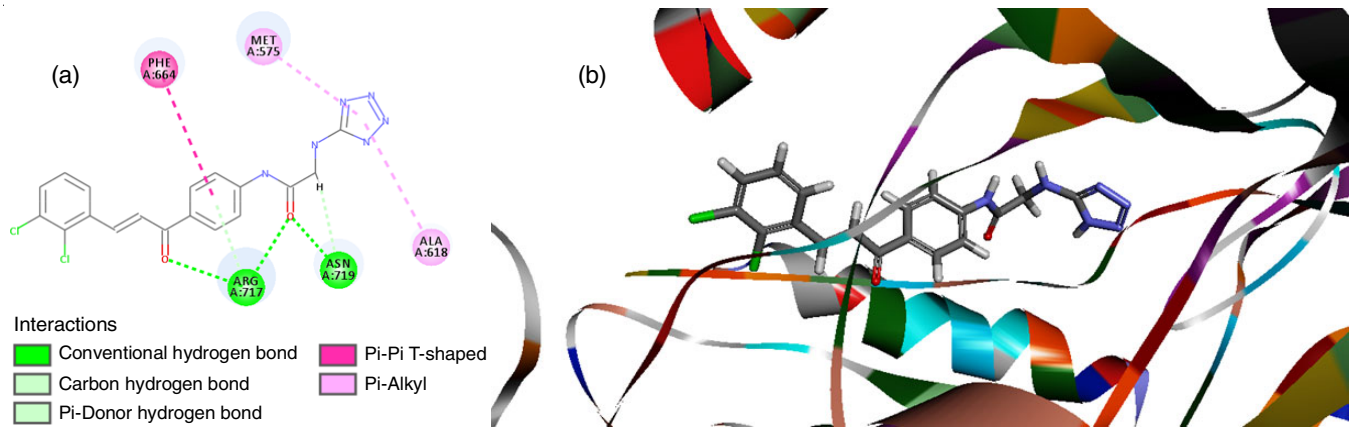


Fig. 1. 2D (a) and 3D (b) model of compound **34** docked with 1T9U protein

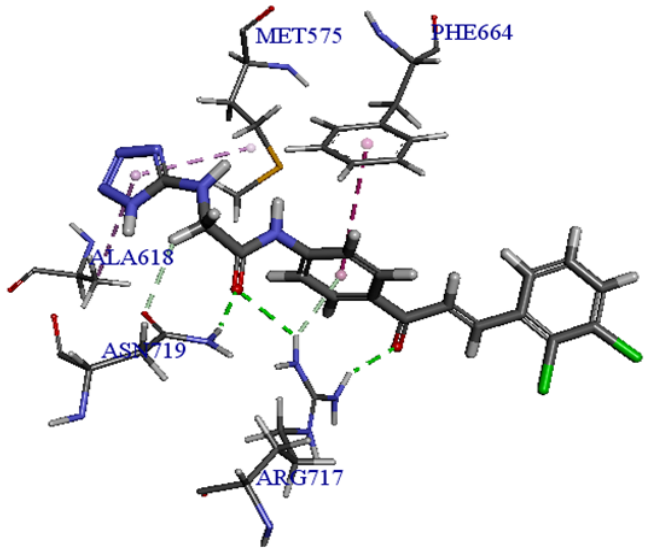


Fig. 2. Docking interactions of 1T9U protein with compound **34**

Antibacterial activity: Novel (*E*)-*N*-(4-(3-(3,5-dialkylphenyl)acryloyl)phenyl)-2-(1*H*-1,2,4-triazol-1-yl)acetamide (**32-41**) were tested for their antibacterial activity against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, *Proteus vulgaris* and *Pseudomonas aeruginosa*. Ciprofloxacin was used as a standard drug. The zone of inhibition values are shown in Table-2. Of the ten compounds, **32-41** tested for their antibacterial activity by the disc diffusion method. Compounds **38**, **39** and **40**, which have an electron-donating methoxy group attached to the phenyl ring exhibits moderate activity. The introduction of *para* fluoro substituted phenyl ring was found to enhance the antibacterial activity potency significantly. Thus, the compounds **33** and **34**, which have electron-withdrawing Cl, group attached to the phenyl ring exhibits excellent antibacterial activity against *Bacillus subtilis* and *E. coli*. Compounds **32** having a Cl group in the *meta* position shows better activity against *Staphylococcus aureus* and *E. coli*. Compound **35** did not promote activity against *E. coli* and *Proteus vulgaris*. The introduction of the nitro group was found to enhance the potency significantly. Whereas compounds **37**, which have methyl group at the *para* position of the phenyl ring did not have high activity against the all bacterial strains. Compounds **39** show better activity against the all bacterial strains, respectively.

Antifungal activity: The *in vitro* antifungal activity of (*E*)-*N*-(4-(3-(3,5-dialkylphenyl)acryloyl)phenyl)-2-(1*H*-1,2,4-triazol-1-yl)acetamide (**32-41**) was studied against the fungal strains *Candida albicans*, *Candida tropicalis*, *Candida parapsilosis*. Fluconazole was used as a standard drug. The zone of inhibition was reproduced in Table-2. Compounds **35**, **36** and **37** did not exhibit antifungal activity against *Candida tropicalis* and *Candida parapsilosis*. Further introduction of electron-withdrawing Cl functional group of the phenyl ring in compounds **32**, **33** and **34** better activity against *Candida albicans* and *Candida tropicalis*. Instead of Cl group attached at *ortho* and *meta* position of the phenyl ring in compound **34** exhibits excellent activity against the *Candida parapsilosis*. Compounds **38**, **39** and **40**, which contain electron-donating methoxy functional group, attached to the phenyl ring exhibits better activity against *Candida tropicalis* and *Candida parapsilosis*. Also, compound **41** which contains nitro group at the *para* position shows potent activity against *Candida albicans* and *Candida tropicalis*.

Conclusion

A three step synthetic route was furnished the target compounds (*E*)-*N*-(4-(3-(3,5-dialkylphenyl)acryloyl)phenyl)-2-(1*H*-1,2,4-triazol-1-yl)acetamide (**32-41**) in good yields. The compounds were characterized by their physical and analytical data. The docking research of synthesized compounds with 1T9U protein confirmed specific binding interactions and formed various hydrophobic interactions with active site residues. The *in vitro* antimicrobiological studies had been assess the antibacterial and antifungal potencies of the newly synthesized compounds. A close inspection of the diverse electron-donating (–CH_3, –OCH_3) and electron-withdrawing (–F, –Cl) functional group substituted in the phenyl ring of target compounds exerted good antibacterial and antifungal activities against the all bacterial and fungal species.

CONFLICT OF INTEREST

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

TABLE-2
ANTIBACTERIAL AND ANTIFUNGAL ACTIVITIES OF SYNTHESIZED COMPOUNDS **32-41** BY DISC DIFFUSION METHOD

Compounds	Zone of inhibition (mm)							
	Antibacterial activity					Antifungal activity		
	Bacillus subtilis	*Staphylococcus aureus*	*Escherichia coli*	*Pseudomonas aeruginosa*	*Proteus vulgaris*	*Candida albicans*	*Candida parapsilosis*	*Candida tropicalis*
32	19	23	20	23	–	12	12	10
33	28	23	26	23	18	18	10	16
34	23	20	21	22	21	16	13	14
35	18	19	–	20	-	10	–	14
36	21	21	18	18	20	14	10	–
37	18	18	18	21	20	11	–	10
38	19	22	24	22	20	16	11	12
39	18	22	19	22	20	12	10	10
40	24	23	21	21	20	12	09	15
41	20	18	22	21	18	16	10	14
Ciprofloxacin	32	28	28	24	26	–	–	–
Fluconazole	–	–	–	–	–	20	14	19

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