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SYNTHESIS, CHARACTERIZATION AND BILOGICAL EVALUATION OF 2,4,6-TRISUBSTITUTED 1,3,5-TRIAZINE DERIVATIVES

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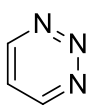
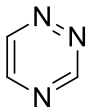
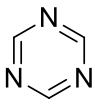
ABSTRACT
A new series of 2,4,6-trisubstituted 1,3,5-triazine derivatives were synthesized from 2,4,6-trichloro-1,3,5-triazine(Cyanuric Chloride) and 4-(4-aminophenyl)morpholin-3-one via regioselective reaction followed by reflux with substituted aryl amine in the presence of catalytic amount of triethyl amine. All the synthesized compounds were characterized by IR, ^{1}HNMR, Mass and Elemental Analysis. The newly synthesized compounds were also screened for their *in vitro* antimicrobial activity against standard drugs and some of them found to be remarkably active.

Keywords: 2,4,6-trichloro-1,3,5-triazine, 4-(4-aminophenyl)morpholin-3-one, Regioselective reaction, Antimicrobial activity.

1. INTRODUCTION
Triazines are six membered heterocyclic motifs containing three nitrogen atoms in their ring structure. They are widely explored and employed class of heteroaromatics due to their reactivity and various functionalization. The possible ring transformations make an ease of the synthesis of broad range of heterocyclic systems. In addition, the electrophilicity of the triazine ring allows the nucleophilic aromatic addition or substitution. Because of high reactivity, they can undergo further modifications through variety of possible pathways which make them important for developing bioactive compounds. As a result, triazines find wide applications in the synthesis of natural products or the design of new materials with some different properties like sensing, luminescent, liquid crystalline etc.
Depending on the located nitrogen in ring, triazines have three analogues as follows.


1,2,3-triazine


1,2,4-triazine


1,3,5-triazine

Literature study revealed that, 1,3,5-Triazine nucleus has gathered an extensive attention among chemists and researchers for a long time due to its significant biological activities and application in different fields [1]. They continue to be the object of considerable interest mainly due to their potent biological activities.
1,3,5-Triazine is a heterocyclic nucleus which exhibits numerous beneficial pharmacological effects, such as A2A antagonism [2], NF-κB inhibition [3],anti-bacterial [4-6], anti-malarial [7, 8] and anti-fungal effects [9]. Moreover, 1,3,5-triazine shows anti-cancer activity mediated via targeting various RTKs, such as EGFR [10], RET [11], VEGFR [12] and more importantly PI3K [13, 14] and mTOR [15, 16]. Many heterocyclic compounds containing s-Triazine nucleus are widely used as anti-protozoal [17], estrogen receptor modulators [18], cyclin dependent kinase modulators [19], antimicrobials [20], and antitumor [21].
Various 1,3,5-triazine morpholine-containing compounds show excellent inhibitory activity against PI3K/mTOR kinasesand are at various stages of drug development.

2. EXPERIMENTAL
2.1. Material and methods
All the chemicals used to synthesize library were purchased from CDH chemical, Delhi of AR grade and

were used as available without further purification. The progress of reaction was monitored by thin-layer chromatography (TLC) on silica gel-G plates (G60 F254 (Merck)) of 0.5 mm thickness, and the developed spots were made visualized with ultraviolet light (254 and 365 nm) and Iodine vapor. Melting points of the synthesized compounds were measured by open capillary method and are uncorrected. IR spectra were recorded on FTIR-8400 spectrophotometer (Shimadzu, Kyoto, Japan), using DRS probe KBr pallet method. 1H-NMR spectra of the synthesized compounds were recorded on a Bruker-Advance-II (400 MHz) spectrometer by using DMSO-d6 solvent. Chemical shift values are expressed in δ ppm by using TMS as an internal standard. Mass spectra were determined using a direct inlet probe on a QC-LCMS-QP 2010 mass spectrometer (Shimadzu, Kyoto, Japan).

2.2. Reaction scheme/synthetic pathway

The synthetic pathway for the targeted compounds (V3-a to V3-l) is shown in fig. 1a and physical parameters of synthesized products are shown in table 1.

The first step of synthesis involves the Regioselective reaction of 2,4,6-trichloro-1,3,5-triazine (Cyanuric Chloride) with 4-(4-aminophenyl)morpholin-3-one (Aromatic amine) to form 4-(4-((4,6-dichloro-1,3,5-triazin-2-yl)amino)phenyl)morpholin-3-one(INT-1). The second step is the synthesis of target molecule which is achieved by reflux of INT-1 with various substituted aryl amine in the presence of catalytic amount of triethyl amine.

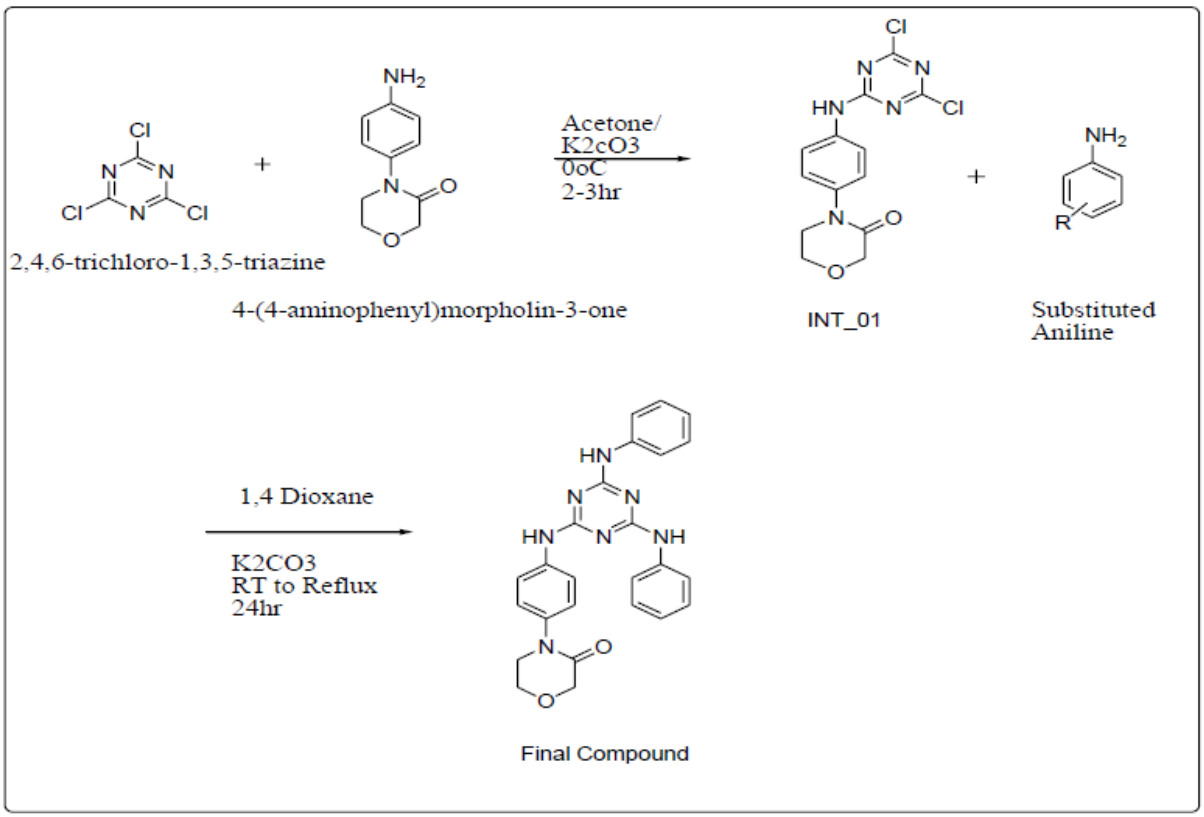


Fig. 1a: The synthetic pathway for the targeted compounds (V3-a to V3-l)

2.3. Experimental procedure

2.3.1. General synthesis of 4-(4-((4,6-dichloro-1,3,5-triazin-2-yl)amino)phenyl) morpholin -3-one(INT-01)

To a solution of 2,4,6-trichloro-1,3,5-triazine (10 g,0.054 mol) prepared in Acetone (150 mL), 4-(4-aminophenyl)morpholin-3-one (10.09 g, 0.054 mol) was added drop wise at 0°C. After complete addition, the resulting reaction mixture was stirred at this temperature. Then the catalytic amount of Potassium carbonate (5.48 g, 0.054mol) was added with constant stirring for about 2-3hr. The reaction mixture was then poured onto crushed ice, followed by neutralization with dilute HCl, and then filtered, dried, and recrystallized from Acetone to afford INT-1. Yield 88%, M.P. 259°C.

2.3.2. General synthesis of 4-(4-((4,6-bis (phenylamino)-1,3,5-traizin-2-yl)amino) phenyl)morpholin-3-one derivatives(V3-a to V3-l)

To a solution of 4-(4-((4,6-dichloro-1,3,5-triazin-2-yl) amino)phenyl)morpholin-3-one, INT-01 (0.01 mol) prepared in 1,4-dioxane (30 mL), the substituted Aniline derivative was added(2equivalent) and the reaction mixture was refluxed and stirred at RT for 24h. Potassium carbonate (2 equivalents) was used for neutralization of the reaction mixture. Progress of the reaction was monitored by TLC using toluene:acetone (8:2) as an eluent. The mixture was then poured onto crushed ice. The precipitates thus obtained were filtered off, dried and then recrystallized from THF to afford the desired compounds.

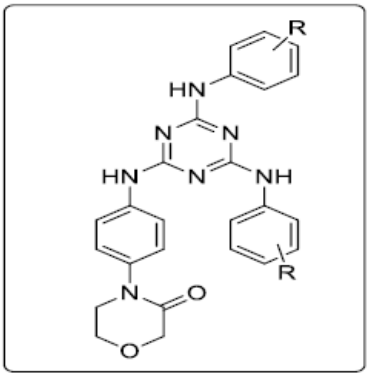


Table 1: Physical parameters of 4-(4-((4,6-bis(phenylamino)-1,3,5-triazin-2-yl)amino)phenyl) morpholin-3-one derivatives (V3-a to V3-l)

Code	Mol. Formula	'R' Substitution	Mol. Weight	% of Yield
V3-a	$C_{25}H_{21}N_7O_2Cl_2$	4-chloro	522.39	71
V3-b	$C_{27}H_{27}N_7O_4$	4-methoxy	513.55	62
V3-c	$C_{25}H_{19}Cl_4N_7O_2$	2,4-dichloro	591.28	65
V3-d	$C_{29}H_{31}N_7O_6$	2,4-dimethoxy	573.60	54
V3-e	$C_{27}H_{25}N_7O_2Cl_2$	3-chloro-2-methyl	550.44	63
V3-f	$C_{25}H_{21}F_2N_7O_2$	4-fluoro	489.48	70
V3-g	$C_{25}H_{21}Br_2N_7O_2$	4-bromo	611.29	81
V3-h	$C_{25}H_{21}N_9O_6$	4-nitro	543.49	65
V2-i	$C_{25}H_{19}N_{11}O_{10}$	2,4-dinitro	633.13	63
V3-j	$C_{27}H_{27}N_7O_2$	4-methyl	481.55	65
V3-k	$C_{27}H_{27}N_7O_2$	2-methyl	481.55	62
V3-l	$C_{25}H_{19}Br_2Cl_2N_7O_2$	4-bromo-2-chloro	676.93	65

2.4. Biological evaluation

All the synthesized compound were tested for their *in vitro* antimicrobial activity against Gram +ve strains, such as *Staphylococcus aureus* and *Bacillus subtilis*as well as Gram -ve strains, such as *Escherichia coli* and *Pseudomonas aeruginosa*by using ampicillin, chloramphenicol and tetracycline as standard drugs. *In vitro* antifungal activity was tested against three different fungal strains, such as *Candida albicans*, *Aspergillus flavus* and *Aspergillus Niger*. To prepare a solution with 2000 µg/mL of each target molecule, the target compounds (2 mg) were dissolved in DMSO (1 mL). An additional stepwise two-fold dilution in Muller-Hinton broth was carried out to achieve the Minimum concentrations of 1000, 500, 250, 125, 62.5, 31.25µg/mL concentrations. The control test was performed by using a medium supplemented with DMSO at the same dilutions used in the experiment to ensure that the solvent was not affecting the growth of bacteria.

Suspension of fresh bacterial and fungal culture was prepared in N-broth and potato dextrose broth respectively. In primary screening 1000 µg/mL, 500µg/mL, and 250 µg/mL concentrations of the synthesized drugs were taken. The active synthesized drugs found in this primary screening were furthertested in the second set of dilution at 125 µg/mL, 62.5 µg/mL, and 31.25µg/mL concentration against all microorganisms. The tubes were inoculated with 10^8 bacterial CFU/ mL and incubated at 37°C for 24 h. The MIC was reported.

3. RESULTS AND DISCUSSION

All the tri-substituted triazine derivatives were synthesized in simple way and in moderate to high yield. Newly synthesized compounds were characterized by spectral analysissuch as IR, NMR and Mass Spectra and structures were confirmed. The synthesized compounds were examined for their antibacterial and antifungal

activity. Most of the compound shown moderate to good activity. Among them, compound V3-f is most active against bacterial species and compound V3-h exhibited potent antifungal activity.

3.1. Spectral analysis of synthesized compounds

3.1.1. 4-(4-((4,6-bis((4-chlorophenyl)amino)-1,3,5-triazin-2-yl)amino)phenyl) morpholin-3-one (V3-a)

White Solid, Yield: 71%. IR (KBr, νmax, cm-1): 3496.55 (N-H stretching, primary or secondary amines), 3101.19, 3058.08 (C-H stretching aromatics), 2992.08, 2952.90, 2831.55 (C-H stretching, alkane), 1587.27, 1493.27, 1455.72, 1399.85 (C-C stretching in ring, aromatic), 1357.24, 1296.39, 1250.28 (C-N stretching, aromatic amines), 1183.27, 1145.49, 1113.04, 1033.12, 1004.88 (C-N stretching, aliphatic amines), 832.28, 759.62 (C-Cl stretching). 1H NMR (400 MHz, DMSO) in δ ppm: 3.705-3.730 (2H, t, -CH2-), 3.963-3.988 (2H, t, -CH2-), 4.198 (2H, s, -CH2-), 7.295-7.347 (6H, complex, Ar-H), 7.745-7.824 (6H, complex, -Ar-H), 9.461-9.489 (3H, s, -NH-). Elemental Analysis for $C_{25}H_{21}Cl_2N_7O_2$ is Cal. (%): C; 57.48, H; 4.05, Cl; 13.57, N; 18.77, O; 6.13. Found: C; 57.52, H; 4.09, Cl; 13.52, N; 18.73, O; 6.12.

3.1.2. 4-(4-((4,6-bis((4-methoxyphenyl)amino)-1,3,5-triazin-2-yl)amino)phenyl) morpholin-3-one (V3-b)

Off white solid, Yield: 62%. IR (KBr, νmax, cm-1): 3317.67, 3234.73, 3113.21, 3045.70, 2960.63, 2872.10, 2835.45, 1637.62, 1566.25, 1500.67, 1423.51, 1352.14, 1298.14, 1232.55, 1172.76, 1154.78, 1112.96, 1031.95. ^{1}H NMR (400 MHz, DMSO) in δ ppm: 3.708 (2H, c, -CH2-), 3.735 (6H, c, -OCH3), 3.958-3.970 (2H, t, -CH2-), 4.192 (2H, s, -CH2-), 6.859-6.880(4H, d, ortho Ar-H), 7.245-7.266(2H, d, Ar-H), 7.638- 7.777 (6H, d, -Ar-H), 9.050 (2H, singlet, -NH-), 9.208 (1H, s, -NH-). Elemental Analysis: Cal. (%): C; 63.15, H; 5.30, N; 19.09, O; 12.46. Found: C; 63.11, H; 5.35, N; 19.04, O; 12.42.

3.1.3. 4-(4-((4,6-bis((2,4-dichlorophenyl) amino)-1,3,5-triazin-2-yl)amino)phenyl) morpholin-3-one (V3-c)

White solid, Yield: 65%. IR (KBr, νmax, cm-1): 3492.53, 3475.78, 3121.58, 3054.26, 2994.29, 2955.62, 2834.73, 1591.42, 1496.28, 1456.73, 1355.27, 1298.02, 1248.29, 1153.48, 1125.72, 1030.87, 829.23, 762.78. ^{1}H NMR (400 MHz, DMSO) in δ ppm: 3.705-3.731 (2H, t, -CH2-), 3.962-3.987 (2H, t, -CH2-), 4.195 (2H, s, -CH2-), 7.268-7.310 (4H, complex, Ar-H), 7.337-7.353 (2H, doublet, Ar-H), 7.499-7.513 (2H, doublet, Ar-H) 7.787 (2H, singlet, -Ar-H), 9.460 (1H, singlet, -NH-), 9.483-9.497 (2H, multiplet, -NH-). Elemental Analysis: Cal.(%): C; 50.78, H; 3.24, Cl; 23.98, N; 16.58, O; 5.41. Found: C; 50.76, H; 3.21, Cl; 23.96, N; 16.63, O; 5.40.

3.1.4. 4-(4-((4,6-bis((2,4-dimethoxyphenyl) amino)-1,3,5-triazin-2-yl) amino) phenyl) morpholin-3-one (V3-d)

Off white solid, Yield: 54%.IR (KBr, νmax, cm-1): 3490.34, 3477.27, 3125.37, 3058.64, 2998.65, 2952.87, 2832.38, 1639.62, 1491.63, 1458.35, 1367.14, 1289.87, 1243.09, 1152.29, 1122.55, 1033.73. ^{1}H NMR (400 MHz, DMSO) in δ ppm: 3.710(2H, d, -CH2-), 3.737 (6H, s, -OCH3), 3.680(6H, s, -OCH3) , 3.948-3.960 (2H, t, -CH2-), 4.182 (2H, s, -CH2-), 6.859-6.880(4H, d, Ar-H), 7.235-7.256(2H, d, Ar-H), 7.638- 7.777 (2H, d, -Ar-H), 7.821(2H, s, Ar-H), 9.050 (2H, singlet, -NH-), 9.208 (1H, s, -NH-). Elemental Analysis: Cal. (%): C; 60.72, H; 5.45, N; 17.09, O; 16.74. Found: C; 60.82, H; 5.35, N; 17.04, O; 16.79.

3.1.5. 4-(4-((4,6-bis((3-chloro-2-methylphenyl) amino)-1,3,5-triazin-2-yl)amino)phenyl) morpholin-3-one (V3-e)

Off white solid, Yield: 63%.IR (KBr, νmax, cm-1): 3589.97, 3413.94 3191.33, 2974.66, 2922.39, 2850.37, 1728.06, 1538.10, 1447.11, 1378.52, 1345.95, 1308.17, 1249.90, 1160.20, 1071.22, 1015.67, 963.99, 834.52, 782.93. ^{1}H NMR (400 MHz, DMSO) in δ ppm: 3.709(2H, d, -CH2-), 3.293 (6H, s, -CH3), 3.938-3.950 (2H, t, -CH2-), 4.192 (2H, s, -CH2-), 6.869-7.819(10H, complex, Ar-H), 9.062 (2H, singlet, -NH-), 9.208 (1H, s, -NH-). Elemental Analysis: Cal. (%): C; 58.91, H; 4.58, N; 17.81, O; 5.81, Cl; 12.88. Found: C; 58.98, H; 4.50, N; 17.84, O; 5.75, Cl; 12.92.

3.1.6. 4-(4-((4,6-bis((4-fluorophenyl)amino)-1,3,5-triazin-2-yl)amino)phenyl) morpholin-3-one (V3-f)

White solid, Yield: 70%.IR (KBr, νmax, cm-1): 3490.27, 3113.83, 3057.45, 2996.26, 2955.27,

2835.38, 1587.35, 1494.72, 1455.38, 1358.24, 1295.98, 1254.46, 1190.45, 1147.49, 1120.27, 1037.39, 982.28, 859.62. ^{1}H NMR (400 MHz, DMSO) in δ ppm: 3.715-3.735 (2H, t, -CH2-), 3.933-3.958 (2H, t, -CH2-), 4.192 (2H, s, -CH2-), 7.395-7.457 (6H, complex, m- Ar-H), 7.795- 7.874 (6H, complex, ortho-Ar-H), 9.481-9.519 (3H, s, -NH-). Elemental Analysis: Cal. (%): C; 61.34, H; 4.32, F; 7.76, N; 20.03, O; 6.54. Found: C; 61.39, H; 4.38, F; 7.73, N; 19.99, O; 6.50.

3.1.7. 4-(4-((4,6-bis((4-bromophenyl)amino)-1,3,5-triazin-2-yl)amino)phenyl) morpholin-3-one (V3-g)

White solid, Yield: 81%. IR (KBr, νmax, cm-1): 3491.05, 3103.78, 3054.38, 2996.27, 2951.99, 2832.02, 1586.98, 1492.38, 1450.37, 1354.28, 1290.87, 1253.52, 1183.72, 1147.38, 1119.52, 1033.12, 1004.88, 982.28, 799.62. ^{1}H NMR (400 MHz, DMSO) in δ ppm: 3.709-3.733 (2H, t, -CH2-), 3.966-3.990 (2H, t, -CH2-), 4.198 (2H, s, -CH2-), 7.281-7.334 (6H, complex, Ar-H), 7.723- 7.804 (6H, complex, -Ar-H), 9.460-9.487 (3H, s, -NH-).Elemental Analysis: Cal. (%): C; 49.12, H; 3.46, Br; 26.14, N; 16.04, O; 5.23. Found: C; 49.19, H; 3.51, Br;26.07, N; 16.10, O; 5.19.

3.1.8. 4-(4-((4,6-bis((4-nitrophenyl)amino)-1,3,5-triazin-2-yl)amino)phenyl) morpholin-3-one (V3-h)

White solid, Yield: 65%. IR (KBr, νmax, cm-1): 3491.05, 3103.78, 3054.38, 2996.27, 2951.99, 2832.02, 1586.98, 1492.38, 1450.37, 1354.28, 1290.87, 1253.52, 1183.72, 1147.38, 1119.52, 1033.12, 1004.88.^{1}H NMR (400 MHz, DMSO) in δ ppm: 3.702-3.726 (2H, t, -CH2-), 3.961-3.986 (2H, t, -CH2-), 4.195 (2H, s, -CH2-), 7.391-7.454 (6H, complex, Ar-H), 7.793- 7.854 (6H, complex, -Ar-H), 9.460-9.487 (3H, s, -NH-). Elemental Analysis: Cal. (%): C; 55.25, H; 3.89, N; 23.19, O; 17.66. Found: C; 55.32, H; 3.80, N; 23.24, O; 17.69.

3.1.9. 4-(4-((4,6-bis((2,4-dinitrophenyl)amino)-1,3,5-triazin-2-yl)amino)phenyl) morpholin-3-one (V3-i)

White solid, Yield: 63%. IR (KBr, νmax, cm-1): 3495.28, 3475.09, 3128.76, 3053.32, 2996.78, 2950.54, 2830.38, 1566.98, 1490.36, 1460.26, 1363.52, 1325.63, 1291.63, 1155.72, 1121.38, 1037.27. ^{1}H NMR (400 MHz, DMSO) in δ ppm: 3.703-3.729 (2H, t, -CH2-), 3.961-3.986 (2H, t, -CH2-), 4.195 (2H, s, -CH2-), 7.266-7.315 (4H, complex, Ar-H), 7.732- 7.354 (2H, d, -Ar-H), 7.491-7.506 (2H, doublet, Ar-H) 7.896 (2H, singlet, -Ar-H), 9.460-9.487 (3H, s, -NH-). Elemental Analysis: Cal. (%): C; 47.40, H; 3.02, N; 24.32, O; 25.26. Found: C; 47.45, H; 3.15, N; 24.23, O; 17.17.

3.1.10. 4-(4-((4,6-bis(p-tolylamino)-1,3,5-triazin-2-yl)amino)phenyl)morpholin-3-one (V3-j)

Off white solid, Yield: 65%. IR (KBr, νmax, cm-1): 3277.65, 3129.51, 3115.26, 3058.70, 2958.67, 2852.10, 2833.65, 1634.62, 1545.25, 1496.67, 1423.56, 1296.14, 1253.29, 1173.29, 1149.32, 1112.89, 1038.32. ^{1}H NMR (400 MHz, DMSO) in δ ppm: 1.923(6H, s, -CH3), 3.708-3.735(2H, t, -CH2-), 3.938-3.968 (2H, t, -CH2-), 4.195 (2H, s, -CH2-), 6.799-6.810(4H, d, ortho Ar-H), 7.242-7.262(2H, d, Ar-H), 7.618- 7.745 (6H, d, -Ar-H), 9.053 (2H, singlet, -NH-), 9.218 (1H, s, -NH-). Elemental Analysis: Cal. (%): C; 67.34, H; 5.65, N; 20.36, O; 6.64. Found: C; 67.27, H; 5.74, N; 20.27, O; 6.67.

3.1.11. 4-(4-((4,6-bis(o-tolylamino)-1,3,5-triazin-2-yl)amino)phenyl)morpholin-3-one (V3-k)

Off white solid, Yield: 62%. IR (KBr, νmax, cm-1): 3279.33, 3130.51, 3115.26, 3057.70, 2958.67, 2852.10, 2833.65, 1633.62, 1545.25, 1496.67, 1423.56, 1296.14, 1253.29, 1171.29, 1149.32, 1112.89, 1037.32. ^{1}H NMR (400 MHz, DMSO) in δ ppm: 1.898(6H, s, -CH3), 3.710-3.734(2H, t, -CH2-), 3.931-3.968 (2H, t, -CH2-), 4.195 (2H, s, -CH2-), 6.799-7.462(8H, complex, Ar-H), 7.628- 7.735 (4H, complex, -Ar-H), 9.043 (2H, singlet, -NH-), 9.208 (1H, s, -NH-). Elemental Analysis: Cal. (%): C; 67.34, H; 5.65, N; 20.36, O; 6.64. Found: C; 67.27, H; 5.74, N; 20.27, O; 6.67.

3.1.12. 4-(4-((4,6-bis((4-bromo-2-chlorophenyl) amino)-1,3,5-triazin-2-yl)amino)phenyl) morpholin-3-one(V3-l)

Off white solid, Yield: 65%. IR (KBr, νmax, cm-1): 3490.45, 3472.78, 3118.34, 3055.09, 2996.56, 2955.62, 2835.34, 1586.43, 1496.65, 1452.55, 1357.48, 1294.38, 1250.66, 1158.26, 1127.37, 1035.87, 829.23, 762.78. ^{1}H NMR (400 MHz, DMSO)

in δ ppm: 3.715-3.739 (2H, t, -CH2-), 3.970-3.984 (2H, t, -CH2-), 4.203 (2H, s, -CH2-), 7.270-7.310 (4H, complex, Ar-H), 7.339-7.354 (2H, doublet, Ar-H), 7.501-7.513 (2H, doublet, Ar-H) 7.782 (2H, singlet, -Ar-H), 9.460 (1H, singlet, -NH-), 9.482-9.496 (2H, multiplet, -NH-). Elemental Analysis: Cal. (%): C; 44.15, H; 2.82, Br; 23.50, Cl; 10.42, N; 14.41, O; 4.70. Found: C; 44.23, H; 2.87, Br; 23.43, Cl; 10.45, N; 14.35, O; 4.67.

Table 2: Antibacterial activity of synthesized compounds V-3a to V-3l

Compound Code	Antibacterial activity			
	Minimum Inhibitory Concentration: µg/ml.			
	Gram +*ve*bacteria		Gram -*ve*bacteria	
	S. aureus	*B. subtilis*	*P. aeruginosa*	*E. coli*
V-3a	500	62.5	125	31.25
V-3b	-	250	-	250
V-3c	250	62.5	250	62.5
V-3d	250	250	-	125
V-3e	500	-	250	-
V-3f	**125**	**31.25**	**125**	**31.25**
V-3g	250	500	250	125
V-3h	125	62.5	250	62.5
V-3i	125	62.5	250	62.5
V-3j	-	250	-	250
V-3k	-	250	-	125
V-3l	250	125	250	125
Ampicillin	500	7.8	125	7.8
Chloramphenicol	125	3.9	125	3.95
Tetracycline	7.8	1.95	15.6	3.95

Table 3: Antifungal activity of synthesized compounds V-3a to V-3l

	Antifungal activity		
	Minimum Inhibitory Concentration: µg/ml.		
	Candida albicans	*Aspergillus flavus*	*Aspergillus Niger*
V-3a	125	250	125
V-3b	125	-	250
V-3c	-	-	125
V-3d	250	125	-
V-3e	-	-	125
V-3f	62.5	125	31.2
V-3g	125	250	125
V-3h	**31.2**	**31.2**	**31.2**
V-3i	31.2	62.5	-
V-3j	-	-	250
V-3k	250	250	-
V-3l	62.5	125	31.2
Nystatin	1.25	12.5	25
Griseofulvin	49.92	0.5	2.0

4. CONCLUSION

In summary, we have synthesized 2,4,6-trisubstituted 1,3,5-triazine derivatives. The synthesis was carried out in two steps by using cyanuric chloride as a starting material. The structures of synthesized compounds were confirmed by various spectroscopic techniques. The reaction is regioselective and the products were obtained in good to excellent yields without any further formation of any side products. It has gain significant importance for the synthesis of substituted 1,3,5

triazines. The present work is important for the synthesis of a wide variety of biologically active triazine heterocyclic derivatives.

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***Conflicts of interest*:**

There is no conflict of interest

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