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Design, synthesis and antimicrobial screening of s-triazinyl derivatives containing 1,3,4-oxadiazole ring

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ABSTRACT

A series of Ten 2,4,6-trisubstituted s-triazines have been synthesized selectively with nucleophilic reagents such as 5-(4-flourophenyl)-1,3,4-oxadiazole-2-thiol, morpholin and different amines on the C-6 position of s-triazine ring. The title compounds were then examined for their in vitro microbial activity against 2 gram –Ve bacteria (E. Coli, P. Aeruginosa), 2 gram +Ve bacteria (S. Aerues, B. subtilis) and 2 fungal species (C. Albicans and A. niger). The most of the synthesized compounds have shown potent anti-bacterial and anti-fungal activities. Structure of final scaffolds has been affirmed by means of IR, 1H NMR, and elemental analysis.

Keywords: 1,3,4-oxadiazol, 2,4,6-trichloro-1,3,5-triazine, morpholine, anti fungal activity, anti bacterial activity.

INTRODUCTION

The rapidly expanding population of immune compromised patient results in a corresponding increase of diseases caused by bacteria, fungi and other yeast. Infection caused by these microorganisms pose a serious challenge to the medical community and highlight the importance and urgent need for new, more potent and selective non-traditional antimicrobial agent. The incidence of bacterial infections has increased dramatically in recent years. The widespread use of antibacterial and antifungal drugs and their resistance against bacterial and fungal infections has led to serious health hazards. The resistance of wide spectrum antibacterial agents has prompted discovery and modification towards new antifungal and antibacterial drugs.

The emergence of multi-drug resistant strains of bacteria is a problem of ever increasing significance. Consequently, the development of new antimicrobial agents will remain an important challenging task for medicinal chemists. There are two basic approaches to develop a new drug: (a) synthesis of analogues, modifications or derivatives of existing compounds for shortening and improving treatment and (b) searching for novel structures, that the bacteria has never been presented before. To pursue this goal, our research efforts are directed to synthesize new pharmacophores. Substituted 1,3,4-oxadiazoles are of considerable pharmaceutical importance, which is documented by several number of publications and patents. A large number of drugs used clinically have oxadiazole ring as a structural building block.

Literature survey reveals that 1,3,4-oxadiazoles have wide range of biological activities ranging from antibacterial, antifungal to anti-inflammatory. Derivatives of 1,3,4-oxadiazole with suitable substitution at 2,5-position have been reported to possess considerable pharmacological activities. 2-Amino-1,3,4-oxadiazole acts as muscle relaxant and also shows antimitotic activity.

Having an unique importance in heterocyclic compounds due to its wide range of therapeutic activities, 2,4,6-trichloro-1,3,5-triazine exhibited biological importance such as anti microbial, antiprotozoal, anticancer, antimalarial and antiviral. 2,4,6-trichloro-1,3,5-triazine is an inexpensive, commercially available reagent and the different reactivities of the substituent chlorine atoms, which are controlled by temperature makes its use more attractive. In a view of its adaptable chemistry, we are promoted for sequential introduction of various amine into the 1,3,5-triazine ring.

MATERIALS AND METHODS

All the melting points were recorded on Cintex melting point apparatus and are uncorrected. IR spectra in KBr were recorded on Schimadzu FTIR spectrophotometer in cm-1. 1HNMR spectra were recorded in CDCl3 or DMSO on a Bruker DRX-400 MHZ NMR instrument. Chemical shifts were reported in ppm using TMS as internal standard on δ scale. Completion of the reactions was monitored time to time by TLC using E-Merck 0.25 mm silica gel plates and toluene: acetone (8:2) as solvent system.

General Experimentation:-

General procedure to synthesis of 2-(4-Flourophenyl-1,3,4-oxadiazolyl)-5-thio-4-(morpholino)-6-(arylamino)-s-triazine:

Step – I:

(i) Synthesis of methyl 4-fluoro benzoate (1)

p- Flouro benzoic acid (0.1 mol) in 200 ml methanol and 5.0 ml con.sulfuric acid was refluxed for 12 hrs. Excess solvent distilled off and collect the product. Recrystallized from alcohol. The progress of reaction was monitored by TLC using toluene : acetone (8:2) as eluent.

B.P = 109-110 ^{0}C

(ii) Synthesis of 4-fluoro benzohydrazide -(2)

A mixture of methyl ester of 4-fluoro benzoate (0.1 mol) and hydrazine hydrate (0.2 mol) in methanol was heated for 14 hrs. and poured into ice. The product was filtered and washed with cold water. Crystallized from ethanol. The progress of reaction was monitored by TLC using toluene . acetone (8.2) as eluent.

M.P = 161-163°C

(iii) Synthesis of 5-(4-fluoropheneyl)-1,3,4-oxadiazole-2-thiol-(3)

The mixture of 4-fluoro benzohydrazide (0.1 mol), CS_2 (0.1 mol) and KOH solution (0.05 mol) in methanol (82 ml) was refluxed for 8 to 10 hours. After the completion of reaction the resultant mixture was poured in to crushed ice. Product was filtered, washed with water and recrystallized from alcohol. The progress of reaction was monitored by TLC using toluene : acetone (7:3) as eluent.

M.P = 195-197°C

Step – II: Synthesis of 2-(4-flourophenyl-1,3,4-oxadiazolyl)-5-thio-4,6-dichloro-s-triazine-(4)

To a stirred solution of cyanuric chloride (0.1 mol) in THF 100 ml at 0-5°c, The solution of 5-(4-Fluoropheneyl)-1,3,4-oxadiazole-2-thiol (0.1 mol) in THF (100 ml) was added drop-wise and pH was maintained neutral by the addition of 10 % $NaHCO_3$ solution. The stirring was continued at 0-5°C for 2 hours. After the completion of reaction the stirring was stopped and the solution was treated with crushed ice. The solid product obtained was filtered and dried. The progress of reaction was monitored by TLC using ethyl acetate . hexane (6.4) as eluent. The crude product was purified by crystallization from absolute alcohol.

M.P = 120-122°C

Step – III: Synthesis of 2-(4-flourophenyl-1,3,4-oxadiazolyl)-5-thio-4-(morpholino)-6-chloro- s-triazine: (5)

The solution of Morpholine (0.1 mol) in THF (100 ml) was added drop-wise to well stirred suspension of 2-(4-Flourophenyl-1,3,4-oxadiazolyl)-5-thio-4,6-dichloro-s-triazine. (0.1 mol) in THF (100 ml) maintaining the temp 40°C the pH was kept neutral by the addition of 10 % $NaHCO_3$ solution . The temperature was gradually raised to 45°C during 2 hours and futher maintained for 2 hr. After the completion of reaction the solution was poured in ice-cold water. The solid product was filtered and dried. The crude was purified by recrystalization from absolute alcohol.

M.P = 210-212°C

Step – IV: Synthesis of 2-(4-flourophenyl-1,3,4-oxadiazolyl)-5-thio-4-(morpholino)-6-(arylamino)-s-triazine: 6(a-j)

A mixture of 2-(4-Flourophenyl-1,3,4-oxadiazolyl)-5-thio-4-(morpholino)-6-chloro-s-triazine (0.005 mol) and aryl amine (0.005 mol) in dioxane (50.0 ml) was refluxed on heating mental with stirring at 100-110°C for 5 hours. The pH was adjusted to neutral by addition of 10 % $NaHCO_3$ solution. After the completion of reaction the content was added to ice-cold water. The product was filtered and dried the progress of reaction was monitored by TLC using ethylacetate. hexane (4.6) eluent.

Purificaton of all the synthesized compounds was achieved by recrystallization and purity of each compound was monitored by thin layer TLC.

2-(4-flourophenyl-1,3,4-oxadiazolyl)-5-thio-4-(morpholino)-6-(4-methyl-amino)-s-triazine (6a)

FTIR (KBr,cm^{-1}): 840 cm^{-1}(C=N in s-triazine), 3335 cm^{-1} (-NH- in amide), 1282 cm^{-1} (C-O in oxadiazole), 1531 cm^{-1} (C=N in oxadiazole), 1159 cm^{-1} (C-O in morpholine), 1114 cm^{-1} (C-N in morpholine), 1232 cm^{-1} (C-O-C in alkanyl ether), 1388 cm^{-1}(C-CH_3 in aromatic ring), ^{1}H-NMR (DMSO-d_6, δ, ppm): 2.24(s, 3H, CH_3), 3.43-3.64 (m, 8H,morpholine), 6.59-7.46 (m, 4H, Ar-H), 7.48-8.12 (m, 4H, Ar-H), 9.70(s, 1H, NH_2), mass(m/z); 466

2-(4-flourophenyl-1,3,4-oxadiazolyl)-5-thio-4-(morpholino)-6-(4-flouro-amino)-s-triazine (6b)

FTIR (KBr,cm^{-1}): 828 cm^{-1}(C=N in s-triazine), 3345 cm^{-1} (-NH- in amide), 1270 cm^{-1} (C-O in oxadiazole), 1548 cm^{-1} (C=N in oxadiazole), 1172 cm^{-1} (C-O in morpholine), 1107 cm^{-1} (C-N in morpholine), 1253 cm^{-1} (C-O-C in alkanyl ether), 1368 cm^{-1}(C-CH_3 in aromatic ring), ^{1}H-NMR (DMSO-d_6, δ, ppm): 2.15(s, 3H, CH_3), 3.35-3.52 (m, 8H, morpholine), 6.76-7.35 (m, 4H, Ar-H), 7.57-8.24 (m, 4H, Ar-H), 9.82(s, 1H, NH_2). mass(m/z); 469.4

2-(4-flourophenyl-1,3,4-oxadiazolyl)-5-thio-4-(morpholino)-6-(3-chloro-4-flouro-amino)-s-triazine (6c)

FTIR (KBr,cm^{-1}): 835 cm^{-1}(C=N in s-triazine), 3325 cm^{-1} (-NH- in amide), 1296 cm^{-1} (C-O in oxadiazole), 1519 cm^{-1} (C=N in oxadiazole), 1167 cm^{-1} (C-O in morpholine), 1127 cm^{-1} (C-N in morpholine), 1221 cm^{-1} (C-O-C in alkanyl ether), 1399 cm^{-1}(C-CH_3 in aromatic ring), ^{1}H-NMR (DMSO-d_6, δ, ppm): 2.29(s, 3H, CH_3), 3.41-3.60 (m, 8H, morpholine), 6.63-7.36 (m, 3H, Ar-H), 7.47-8.18 (m, 4H, Ar-H), 9.87(s, 1H, NH_2). mass(m/z); 503

2-(4-flourophenyl-1,3,4-oxadiazolyl)-5-thio-4-(morpholino)-6-(4-nitro-amino)-s-triazine (6d)

FTIR (KBr,cm^{-1}): 817 cm^{-1}(C=N in s-triazine), 3320 cm^{-1} (-NH- in amide), 1294 cm^{-1} (C-O in oxadiazole), 1548 cm^{-1} (C=N in oxadiazole), 1143 cm^{-1} (C-O in morpholine), 1124 cm^{-1} (C-N in morpholine), 1218 cm^{-1} (C-O-C in alkanyl ether), 1376 cm^{-1}(C-CH_3 in aromatic ring), ^{1}H-NMR (DMSO-d_6, δ, ppm): 2.31(s, 3H, CH_3), 3.36-3.54 (m, 8H, morpholine), 6.68-7.32 (m, 4H, Ar-H), 7.37-8.19 (m, 4H, Ar-H), 9.49(s, 1H, NH_2). mass(m/z); 496.4

2-(4-flourophenyl-1,3,4-oxadiazolyl)-5-thio-4-(morpholino)-6-(4-methoxy-amino)-s-triazine (6e)

FTIR (KBr,cm^{-1}): 823 cm^{-1}(C=N in s-triazine), 3315 cm^{-1} (-NH- in amide), 1264 cm^{-1} (C-O in oxadiazole), 1539 cm^{-1} (C=N in oxadiazole), 1141 cm^{-1} (C-O in morpholine), 1132 cm^{-1} (C-N in morpholine), 1213 cm^{-1} (C-O-C in alkanyl ether), 1368 cm^{-1}(C-CH_3 in aromatic ring), ^{1}H-NMR (DMSO-d_6, δ, ppm): 2.33(s, 3H, CH_3), 3.34-3.51 (m, 8H, morpholine), 6.73-7.23 (m, 4H, Ar-H), 7.30-8.17 (m, 4H, Ar-H), 9.84(s, 1H, NH_2). mass(m/z); 481.5

2-(4-flourophenyl-1,3,4-oxadiazolyl)-5-thio-4-(morpholino)-6-(3-methyl-amino)-s-triazine (6f)

FTIR (KBr,cm^{-1}): 828 cm^{-1}(C=N in s-triazine), 3347 cm^{-1} (-NH- in amide), 1296 cm^{-1} (C-O in oxadiazole), 1524 cm^{-1} (C=N in oxadiazole), 1169 cm^{-1} (C-O in morpholine), 1098 cm^{-1} (C-N in morpholine), 1238 cm^{-1} (C-O-C in alkanyl ether), , 1374 cm^{-1}(C-CH_3 in aromatic ring), ^{1}H-NMR (DMSO-d_6, δ, ppm): 2.28(s, 3H, CH_3), 3.38-3.59 (m, 8H, morpholine), 6.78-7.50 (m, 3H, Ar-H), 7.56-8.27 (m, 4H, Ar-H), 9.59(s, 1H, NH_2). mass(m/z); 465.5

2-(4-flourophenyl-1,3,4-oxadiazolyl)-5-thio-4-(morpholino)-6-(3-bromo-amino)-s-triazine (6g)

FTIR (KBr,cm^{-1}): 856 cm^{-1}(C=N in s-triazine), 3337 cm^{-1} (-NH- in amide), 1269 cm^{-1} (C-O in oxadiazole), 1544 cm^{-1} (C=N in oxadiazole), 1148 cm^{-1} (C-O in morpholine), 1130 cm^{-1} (C-N in morpholine), 1227 cm^{-1} (C-O-C in alkanyl ether), 1393 cm^{-1}(C-CH_3 in aromatic ring), ^{1}H-NMR (DMSO-d_6, δ, ppm): 2.14(s, 3H, CH_3), 3.31-3.49 (m, 8H, morpholine), 6.68-7.43 (m, 4H, Ar-H), 7.49-8.18 (m, 4H, Ar-H), 9.86(s, 1H, NH_2). mass(m/z); 530.7

2-(4-flourophenyl-1,3,4-oxadiazolyl)-5-thio-4-(morpholino)-6-(4-acetoxy-amino)-s-triazine FTIR (KBr,cm^{-1}): 843 cm^{-1}(C=N in s-triazine), 3313 cm^{-1} (-NH- in amide), 1292 cm^{-1} (C-O in oxadiazole), 1519 cm^{-1} (C=N in oxadiazole), 1167 cm^{-1} (C-O in morpholine), 1107 cm^{-1} (C-N in morpholine), 1249 cm^{-1} (C-O-C in alkanyl ether), ,

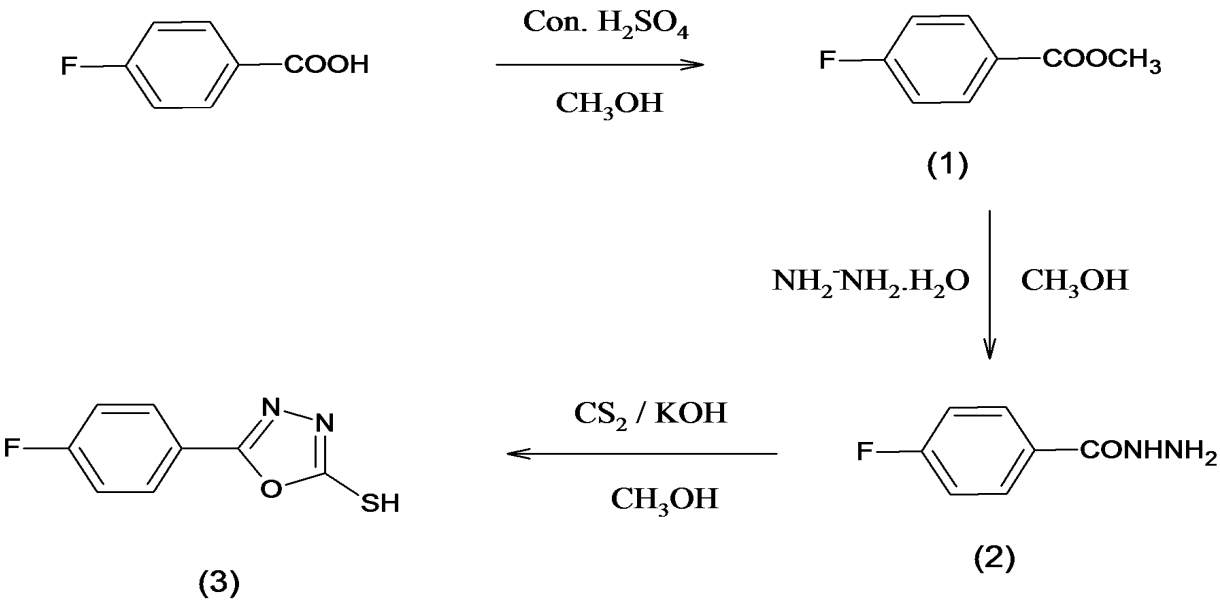
1380 cm^{-1}(C-CH_3 in aromatic ring), ^{1}H-NMR (DMSO-d_6, δ, ppm): 2.15(s, 3H, CH_3), 3.38-3.54 (m, 8H, morpholine), 6.64-7.39 (m, 4H, Ar-H), 7.45-8.10 (m, 4H, Ar-H), 9.73(s, 1H, NH_2). mass(m/z); 493.7

2-(4-flourophenyl-1,3,4-oxadiazolyl)-5-thio-4-(morpholino)-6-(3-chloro-amino)-s-triazine (6i)
FTIR (KBr,cm^{-1}): 836 cm^{-1}(C=N in s-triazine), 3327 cm^{-1} (-NH- in amide), 1273 cm^{-1} (C-O in oxadiazole), 1524 cm^{-1} (C=N in oxadiazole), 1169 cm^{-1} (C-O in morpholine), 1103 cm^{-1} (C-N in morpholine), 1250 cm^{-1} (C-O-C in alkanyl ether), 1406 cm^{-1}(C-CH_3 in aromatic ring), ^{1}H-NMR (DMSO-d_6, δ, ppm): 2.23(s, 3H, CH_3), 3.45-3.65 (m, 8H, morpholine), 6.67-7.38 (m, 3H, Ar-H), 7.44-8.05 (m, 4H, Ar-H), 9.59(s, 1H, NH_2). mass(m/z); 485.5

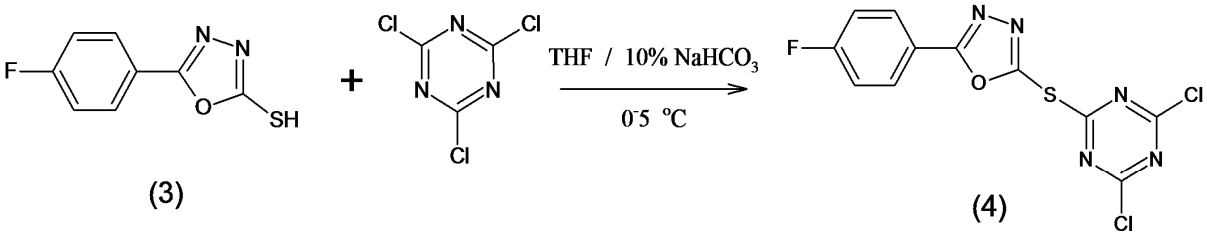
2-(4-flourophenyl-1,3,4-oxadiazolyl)-5-thio-4-(morpholino)-6-(4-chloro-amino)-s-triazine (6j)
FTIR (KBr,cm^{-1}): 849 cm^{-1}(C=N in s-triazine), 3318 cm^{-1} (-NH- in amide), 1273 cm^{-1} (C-O in oxadiazole), 1516 cm^{-1} (C=N in oxadiazole), 1168 cm^{-1} (C-O in morpholine), 1132 cm^{-1} (C-N in morpholine), 1254 cm^{-1} (C-O-C in alkanyl ether), , 1407 cm^{-1}(C-CH_3 in aromatic ring), ^{1}H-NMR (DMSO-d_6, δ, ppm): 2.16(s, 3H, CH_3), 3.42-3.63 (m, 8H, morpholine), 6.64-7.43 (m, 4H, Ar-H), 7.49-8.16 (m, 4H, Ar-H), 9.81(s, 1H, NH_2). mass(m/z); 489.9

Reaction Scheme:-
Synthesis of 2-(4-flourophenyl-1,3,4-oxadiazolyl)-5-thio-4-(morpholino)-6-(arylamino)-s-triazine.

Step - I

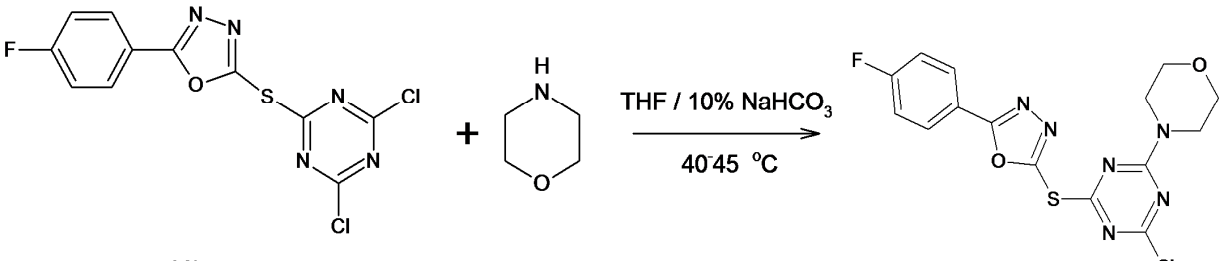


Step - II



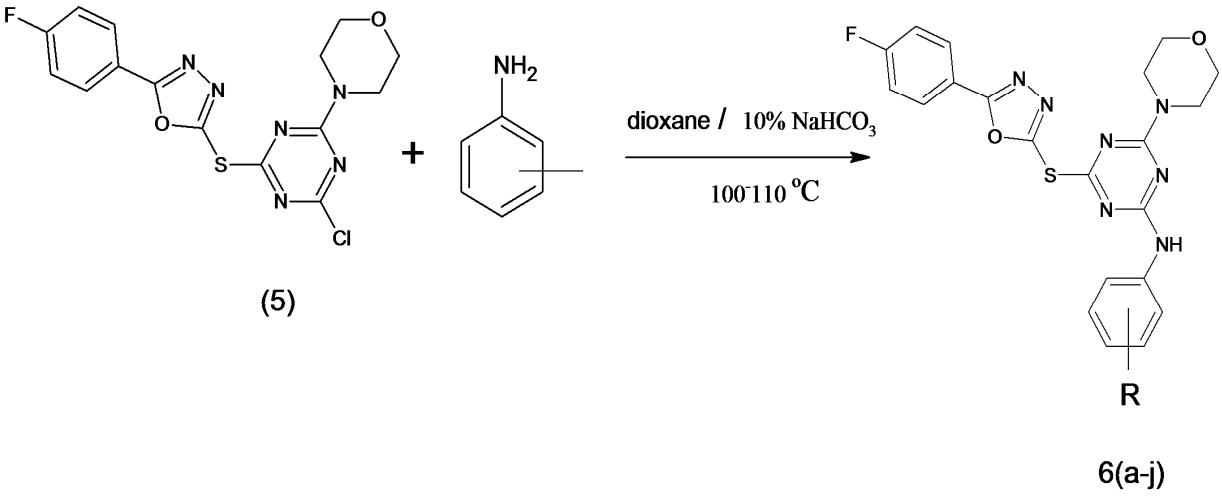
(3) (4)

Step - III



(4) (5)

Step - IV



(5) 6(a-j)

Sr. No.	Compound	Molecular Formula	M.W.	Appearance	M.P. (^{0}C)	R_f Value	% Yield	% of Carbon Found (Calc.)	% of Hydrogen Found (Calc.)	% of Nitrogen Found (Calc.)
1	6a	$C_{22}H_{20}FN_7O_2S$	465.5	Pale Yellow	149-151	0.58	80	56.62 (56.68)	4.26 (4.30)	20.98 (21.02)
2	6b	$C_{22}H_{17}F_2N_7O_2S$	469.4	White	176-178	0.55	81	53.54 (53.66)	3.55 (3.61)	20.73 (20.81)
3	6c	$C_{21}H_{16}F_2ClN_7O_2S$	503.9	White	165-167	0.62	75	49.92 (50.00)	3.10 (3.15)	19.36 (19.42)
4	6d	$C_{21}H_{17}FN_8O_4S$	496.4	White	231-233	0.54	72	50.67 (50.74)	3.44 (3.52)	22.46 (22.52)
5	6e	$C_{22}H_{20}FN_7O_3S$	481.5	Light brown	188-190	0.65	68	54.72 (54.83)	4.07 (4.11)	20.23 (20.29)
6	6f	$C_{22}H_{20}FN_7O_2S$	465.5	Light green	198-200	0.59	67	56.54 (56.62)	4.20 (4.25)	20.91 (20.98)
7	6g	$C_{21}H_{17}FBrN_7O_2S$	530.7	Light yellow	209-211	0.54	65	47.41 (47.48)	3.14 (3.17)	18.33 (18.44)
8	6h	$C_{23}H_{20}FN_7O_3S$	493.5	White	231-233	0.65	72	55.76 (55.81)	3.96 (4.02)	19.72 (19.77)
9	6i	$C_{21}H_{17}FClN_7O_2S$	485.5	White	183-185	0.62	70	51.78 (51.84)	2.84 (2.96)	20.08 (20.14)
10	6j	$C_{21}H_{27}FClN_7O_2S$	485.9	White	173-175	0.56	69	51.77 (51.84)	3.34 (3.42)	20.04 (20.13)

Antimicrobial activity:-

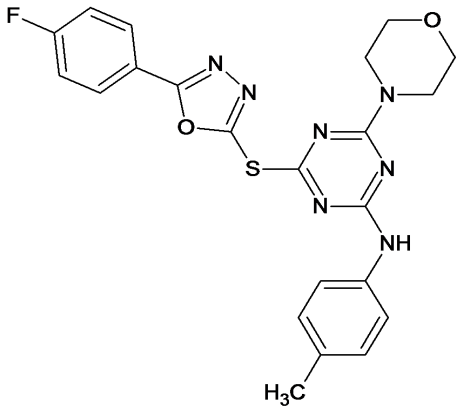
All the newly synthesized compounds were tested for their in vitro antibacterial and antifungal activity (MIC-minimum inhibitory concentration) by broth dilution method with two gram positive bacteria S. aureus and B. subtilis, 2 gram negative bacteria E. coli, P. aeruginosa and fungi species like C. albicans, A. niger organisms taking ciprofloxacin, ampicillin, chloramphenicol, norfloxacin, flucanazole, griseofulvin, and Nystatin as standard controll drug. Muller Hinton broth was used as nutrient medium to grow and dilute the drug suspension for test. DMSO was used as a diluent which is ineffective to the growth of microbes.

The above mentioned anti bacterial results revealed that the compound **6g** bearing 3-bromo aniline derivative to the basic s-triazine nucleus containing morpholine in addition to 5-(4-flouropheneyl)-1,3,4-oxadiazole-2-thiol linkage proved more beneficial compound compared to other analogues against Escherichia coli. The compounds **6c**, **6e**, **6f**, **6g**, **6h** and **6i** bearing 3-chloro-4-flouro-aniline, 4-methoxy aniline, 3-methyl aniline, 3-bromo aniline, 4-acetoxy aniline and 3-chloro aniline substituents respectively have shown the highest sensitivity against p. aeruginosa. Final s-triazine scaffolds **6b**, **6e**, **6g** and **6h** containing 4-flouro aniline, 4-methoxy aniline, 3-bromo aniline and 4-acetoxy aniline substituent respectively shown the best activity against S. aureus, whereas **6c** and **6j** having 3-chloro-4-flouro-aniline and 4-chloro aniline respectively proved as beneficial coupling agents to the final moiety for the best activity against B. subtilis. The biological screening results for fungal species revealed that compound **6j** bearing 4-chloro aniline constituent exhibited higher activity against both fungal species C. albicans and A. niger, in addition, the compounds **6g** and **6h** having 3-bromo aniline, 4-acetoxy aniline respectively exhibited similar minimum inhibitory concentration to that of compound **6j** bearing 4-acetoxy aniline against A. niger. In short, We made an attempt to increase the biological activity by increasing the volume of the substituents attached to the ring system led to different biological potency, depending on the nature, position and number of the atoms or groups introduced, whereas, high potency has been observed in the final scaffolds due to the presence of aniline systems with halogen, fluoro atom(s), methoxy group(s) . Due to the highest electronegativity, high thermal stability,and lipophilicity of F-atom, introduction of F substituents to biologically active aniline ring can affect their biological properties associated with lipophilicity, absorption, and transportation.

Minimum inhibitory concentration Comp. no.	R	Gram negative		Gram positive		Fungal species	
		E. coli	*P. aeruginosa*	*S. aureus*	*B. subtilis*	*C. albicans*	*A. niger*
6a	4-methyl-aniline	250	500	250	250	500	500
6b	4-flouro -aniline	50	100	50	100	50	250
6c	3-chloro-4-flouro-aniline	100	50	100	25	250	250
6d	4-nitro-aniline	50	100	250	100	250	500
6e	4-methoxy-aniline	100	50	50	50	100	250
6f	3-methyl-aniline	50	50	100	50	50	250
6g	3-bromo-aniline	25	50	50	50	100	100
6h	4-acetoxy-aniine	100	50	50	50	100	100
6i	3-chloro-aniline	50	50	100	100	100	250
6j	4-chloro-aniline	50	250	100	25	25	100
Ampicillin		100	100	250	100	-	-
Ciprofloxacin		25	25	50	50	-	-
Chloramphenicol		50	50	50	50	-	-
Norfloxacin		10	10	10	10	-	-
Griseofulvin				500		100	
Nystatin				100		100	
Flucanazole				10		10	

RESULTS AND DISCUSSION

2-(4-flourophenyl-1,3,4-oxadiazolyl)-5-thio-4-(morpholino)-6-(arylamino)-s-triazine (6) were obtained in 66-83% yield by converting 4-flouro benzoic acids to the methyl 4-flouro benzoate(1) and An ester intermediate was hydrazinolyzed with 99% hydrazine hydrate to afford 4-flouro benzohydrazide(2). which reacted with carbon disulfide and potassium hydroxide in ethanol followed by acidification furnished the corresponding 5-(4-fluoropheneyl)-1,3,4-oxadiazole-2-thiol (3) .Compound 4 2-(4-flourophenyl-1,3,4-oxadiazolyl)-5-thio-4,6-dichloro-s-triazine was prepared by the condensation of cyanuric chloride and 5-(4-fluoropheneyl)-1,3,4-oxadiazole-2-thiol (3) in THF at 0–5^{o}C, which reacts with morpholin in THF at 40–45^{o}C gave compound 2-(4-flourophenyl-1,3,4-oxadiazolyl)-5-thio-4-(morpholino)-6-chloro-s-triazine (5). Which reacts with arryl amino in 1,4-dioxane at refluxe tempature gave final compound 2-(4-flourophenyl-1,3,4-oxadiazolyl)-5-thio-4-(morpholino)-6-(arylamino)-s-triazine 6 (a-j)



Mass spectral data support the proposed structures. The mass spectrum showed various characteristic peaks. A peak at *m/z* 466 was assigned to the molecular ion

The FTIR spectrum showed absorption bands at 840 cm^{-1}(C=N stretching in s-triazine), 3335 cm^{-1} (-NH- stretching in amide), 1282 cm^{-1} (C-O stretching in oxadiazole), 1531 cm^{-1}(C=N stretching in oxadiazole), 1159 cm^{-1}(C-O) stretching in morpholine)1388 cm^{-1} ,1114 cm^{-1}(C-N) stretching in morpholine)1388 cm^{-1} (C-CH_3 stretching in aromatic ring) ,1232 cm^{-1}(C-O-C) stretching in alkanyl ether) respectively.

The ^{1}H-NMR spectrum of (6a-j) showed characteristic signals at 6.59 to 8.12 ppm which were assigned to the aromatic protons. A signal at 3.43-3.64 ppm was assigned to the morpholine proton. A signal at 2.24 ppm was assigned to the methyl proton, The singlet 9.70 ppm were assigned to the amino protons, respectively.

CONCLUSION

A series of trisubstituted s-triazine derivatives has been successfully synthesized and tested for their anti microbial activity. S-triazine nucleus is one of the active constituents present in many standard drugs, and is known to increase in pharmacological activity of the molecules as we have already reported its significant activity. The presence of morpholine moiety is also an instrumental in contributing the net biological activity. Herein, we have combined all these three potential unit, that is s-triazine nucleus, 1,3,4-oxadiazole, morpholine and various substituted aniline and moieties in one core and studied biological behavior of the resultant systems. Hence, it is concluded that, trisubstituted S-triazine are more active than mono and di-substituted S-triazine and thus, there is enough scope for further study in developing such compounds as a good lead activity. Overall conclusion placed for synthesized compounds is that most of the compounds shown very good promising activity as compared to standard drug for all representative panel of bacterial anf fungal strains.

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