An efficient synthesis of new benzohydrazide and 1, 3-thiazine fused s-triazines as potential antimicrobial agents

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Abstract
As a part of our endeavor toward the synthesis of new heterocyclic bioactive agents, some new substituted 1,3,5 triazine derivatives with 4-nitrobenzohydrazide and 6-(4-methoxyphenyl)-4-phenyl-6*H*-1,3-thiazin-2-amine and substituted thiourea were reacted and evaluated for their *in vitro* antimicrobial activity against Gram positive and Gram negative strains using a micro dilution procedure. Synthesized compounds T1GE to T15GE showed to be effective with MIC (µg/mL), among them T5GE, T8GE, T9GE and T14GE showed excellent activity against a panel of microorganisms. The newly synthesized compounds were characterized using IR, ^{1}H-NMR, ^{13}C-NMR, MASS Analysis.

Keywords: Cyanuric Chloride, 4-nitrobenzohydrazide, 6-(4-methoxyphenyl)-4-phenyl-6*H*-1, 3-thiazin-2-amine, Different thiourea derivatives and antimicrobial activity.

Introduction

After years of misuse and overuse of antibiotics, bacteria are becoming antibiotic resistant therefore recent efforts have been directed toward exploring novel antibacterial agents[1]. Since last two decades there are many antibiotics and chemotherapeutics available. The challenging therapeutic problems of the treatment of infectious diseases were still remains due to the inexorable increase and spread of multidrug-resistant strains. So as to diminish the speedy multidrug-resistance in pathogenic microbes, there is an appearance necessitate for the development of new module of antimicrobial agents.[2] For the development of drug resistance, new agents should rather consist of chemical characteristics that clearly differ from those of presented agents. Nowadays the new finding and commercial development of several therapeutic agents[3] afford consistently effective treatment for many infectious diseases which had previously caused widespread humanity and morbidity. In recent year in organic synthesis, the chemistry of substituted benzohydrazide derivatives are one of the important subjects. The major problem in the helpful antibacterial and antifungal treatment is increasing conflict of microorganisms to currently available antimicrobial drugs.[4-7] Benzohydrazide have been reported to possess various biological activities such as antileishmanial,[8] anti-inflammatory,[9] anticancer,[10] antimycobacterial,[11] anti-tumoral studies was reviewed by Rollas *et al.*[12] Thiazine derivatives are an important class of heterocyclic compounds reported to possess a wide spectrum of biological properties such as anticonvulsant,[13] anti-inflammatory,[14-16] anticancer,[17] antidiabetic,[18] analgesic,[19] immunotropic.[20] It has been reported that, s-triazine ring skeleton possesses a broad spectrum of biological and pharmaceutical activities, such as antimicrobial, antifungal, antibacterial, anticancer, anti HIV, anti-inflammatory, anti-tuberculosis, antimalarial etc.[21-29] Cyanuric chloride and various amines with good antibacterial properties were used. Therefore, it is predicted that chemical entities with 4-nitrobenzohydrazide, 6-(4-methoxyphenyl)-4-phenyl-6*H*-1, 3-thiazin-2-amine, different thiourea and s-triazine moieties would result in compounds of interesting biological activities. In view of these findings, we have attempted to incorporate all these four biologically active components together to give a confined structure as describe below in reaction scheme. All synthesized compounds for evaluating their antibacterial and antifungal activities.

Previously, we were also reported synthesis, characterization and antimicrobial evaluation of 4-((4-((5-benzyl-1,3,4-thiadiazol-2-yl)amino)-6-(phenylamino)1,3,5-triazin-2-yl)amino)-6-(*tert*-butyl)-3(methylthio)-1,2,4-triazin-5(4*H*)-one derivatives[30], 1-(4-((5-methyl-1,3,4-thiadiazol-2-yl-)amino)-6-((4-phenylthiazol-2-yl)amino-1,3,5-triazine-yl)-3-phenylurea[31], 4-((4-((5-benzyl-1,3,4-thiadiazol-2-yl)amino)-6-(phenyl amino) 1,3,5-triazin-2-yl)amino)-6-(tert-butyl)-3-(methylthio)-1,2,4-triazin-5(4H)-one[32], Keeping this in mind we have subsequently carried out the synthesis of s-triazine based 4-(benzo[*d*]thiazol-2-yl)aniline and 6-(4-methoxyphenyl)-4-phenyl-2*H*-1,3-oxazin-2-amine derivatives to explore the synthesis of more potential bioactive molecules in one framework.

Methods and Materials

All reactions except those in aqueous media were carried out by standard techniques for the exclusion of moisture. Melting points were determined on an electro thermal melting point apparatus and are reported uncorrected. TLC on silica gel plates were used for purity checking and reaction monitoring. Elemental analysis (% C, H, N) was carried out by a

Perkin–Elmer 2400 CHN analyzer. IR spectra of all compounds were recorded on a Perkin–Elmer FT-IR spectrophotometer in KBr. ^{1}HNMR spectra were recorded on Bruker Avance II-400 MHz and ^{13}CNMR spectra on Bruker Avance II-400, 100 MHz in DMSO-*d6* as a solvent and tetramethylsilane (TMS) as an internal standard. Mass spectra were recorded on triple quadrapole LCMS-6410 from Agilent Technology.

Preparation of 1-(4, 6-dichloro-1,3,5-triazin-2-yl)-3-phenylthiourea: (T1 to T15)

To the stirred solution of cyanuric chloride (0.01 mol) in acetone (25 mL) at 0-5 ºC, the solution of substituted phenyl thiourea (0.01 mol) in acetone (15 mL) was added and pH was maintained neutral by the addition of 10% sodium bi-carbonate solution from time to time as per requirement of reaction condition. The stirring was continued at 0-5 ºC 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 crude product was purified by crystallization from absolute alcohol to get title compound.

Preparation of 1-(4-chloro-6-(2-(4-nitrobenzoyl) hydrazinyl)-1, 3, 5-triazin-2-yl)-3-phenyl thiourea:(T1 to 15 G)

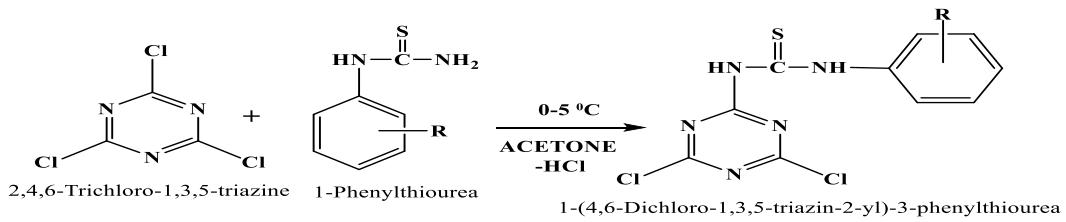
To a stirred solution of (T1 to 15) (0.01 mol) in DMF (25 mL), the solution of 4-nitrobenzohydrazide (0.01 mol) in DMF (15 mL) was added drop wise maintaining the temperature at 40 ºC, the pH was maintained neutral by the addition of 10% sodium bi-carbonate solution from time to time as per requirement of reaction condition. The temperature was gradually raised to 45 ºC during three hours. After the completion of reaction, the resultant content was poured into ice-cold water. The solid product obtained was filtered and dried. The crude product was purified by crystallization from absolute alcohol to get the title compound.

Preparation of 1-(4-((6-(4-methoxyphenyl)-4-phenyl-6H-1, 3-thiazin-2-yl) amino)-6-(2-(4-nitrobenzoyl) hydrazinyl)-1, 3, 5-triazin-2-yl)-3-phenylthiourea: (T1 to 15 GE)

A mixture of (T1G to 15G) (0.01 mol) and 6-(4-methoxyphenyl)-4-phenyl-6*H*-1, 3-thiazin-2-amine (0.01 mol) in DMF (15mL) was refluxed in oil bath. The temperature was gradually raised to 80-100 ºC during four hours, the pH being maintained neutral by the addition of 10% sodium bi-carbonate solution from time to time as per requirement of reaction condition. After the completion of reaction charcoal was added in R.B.F. and heated then mixture was filtered into cold water. The solid product obtained was filtered and dried. The crude product was purified by recrystallization from absolute alcohol.

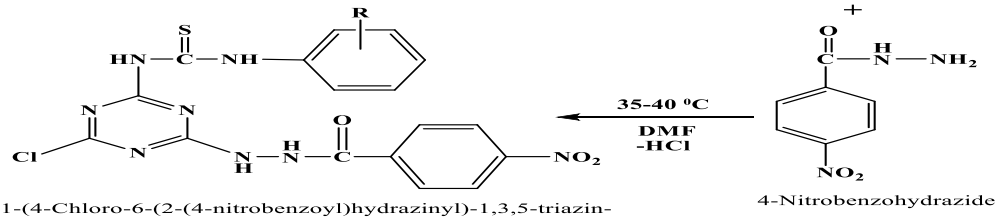
Reaction Scheme

Step 1:



2,4,6-Trichloro-1,3,5-triazine 1-Phenylthiourea 1-(4,6-Dichloro-1,3,5-triazin-2-yl)-3-phenylthiourea

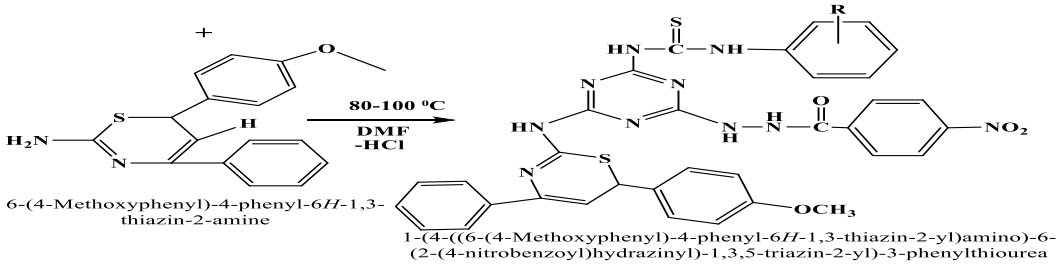
Step 2: (T1 to 15)



1-(4-Chloro-6-(2-(4-nitrobenzoyl)hydrazinyl)-1,3,5-triazin-2-yl)-3-phenylthiourea

(T1 to 15 G) **(G)** 4-Nitrobenzohydrazide

Step 3:



(E) **(T1 to 15GE)**

Compound T1GE: IR(KBr, cm^{-1}): -C=N str. in s-triazine (783.3),-C-S-C str. in thiazole (830.5), -C=S str. in thiourea (1148.0), -N=O- str. as $-NO_2$(1540.0), -C=O str. in amide (1591.0), -N-H deformation in -2^0 NH(1700.0), -C-H str. in $-OCH_3$ (2831.4), -C-H str. in aromatic (3173.2), -N-H str. in -2^0 NH(3384.1).^{1}H NMR (400.0 MHz, DMSO-d_6, δ_H ppm): 10.61 (s, 2H, -CS-NH), 9.11 (s, 1H, -CO-NH), 8.24 (s, 1H, -NH-NH-C), 6.90-8.32 (m, 18H, Ar), 6.88 (s, 1H, Ar=C-H), 5.11 (s, 1H, Ar-S-CH), 3.91 (s, 1H, -NH) , 3.70-3.80 (s, 3H, $-OCH_3$).

Compound T2GE: -C=N str. in s-triazine (785.1),-C-S-C- str. in thiazine (861.1), -C=S str. in thiourea (1121), -C-CH_3 str. in aromatic ring(1330.1), -N=O str. in aromatic ring (1537), -C=O- str. in amide(1606.7), -N-H deformation in -2^0 NH(1718.5), -C-H str. in $-OCH_3$ (2815.1), -C-H str. in $-CH_3$ (2924.1), -C-H str. in aromatic (3136.5), -N-H str. in -2^0 NH(3400.1).^{1}H NMR (400.0 MHz, DMSO-d_6, δ_H ppm): 10.68 (s, 2H, -CS-NH), 9.01 (s, 1H, -CO-NH), 8.19 (s, 1H, -NH-NH-C), 6.92-8.10 (m, 17H, Ar), 6.90(s, 1H, Ar=C-H), 5.07 (s, 1H, Ar-S-CH), 3.93 (s, 1H, -NH), 3.80-3.83 (s, 3H, $-OCH_3$), 2.18-2.28 (s, 3H, $-CH_3$).^{13}C NMR(100MHz,DMSO-d_6,$\delta_C$ppm):18.23,35.14,55.23,113.84,114.26(db),125.77,127.2(db),127.72,128.21(db),128.26,128.52,128.63 (db),130.01(db),130.57(db),132.64(db),133.40,134.24,136.08,137.84,143.94,151.35,159.3(db),165.25(db), 172.52,179.21(db).MS (EI): m/z: 718.5 (M+).

Table 1: Physicochemical data of the synthesized compounds T1GE to T15GE

S. No.	R	M.P. ^{O}C	Yield %	Mol. Formula	Calculated (Found) %		
					C	H	N
T1GE	H	190	70.25	$C_{34}H_{28}N_{10}O_4S_2$	57.94(57.90)	4.00(3.98)	19.87(19.81)
T2GE	2-CH_3	205	55.45	$C_{35}H_{30}N_{10}O_4S_2$	58.48 (58.42)	4.21 (4.16)	19.49 (19.45)
T3GE	4-CH_3	213	60.25	$C_{35}H_{30}N_{10}O_4S_2$	58.48 (58.46)	4.21 (4.13)	19.49 (19.44)
T4GE	2-OCH_3	210	65.70	$C_{35}H_{30}N_{10}O_5S_2$	57.21 (57.16)	4.12 (4.08)	19.06 (19.01)
T5GE	4-OCH_3	185	69.55	$C_{35}H_{30}N_{10}O_5S_2$	57.21 (57.18)	4.12 (4.10)	19.06 (19.03)
T6GE	3-NO_2	190	55.55	$C_{34}H_{27}N_{11}O_6S_2$	54.47 (54.43)	3.63(3.60)	20.55 (20.50)
T7GE	3-Cl	200	58.60	$C_{34}H_{27}ClN_{10}O_4S_2$	55.24(55.20)	3.68(3.62)	18.95 (18.90)
T8GE	4-Cl	165	71.15	$C_{34}H_{27}ClN_{10}O_4S_2$	55.24(55.21)	3.68(3.66)	18.95 (18.88)
T9GE	4-F	188	60.50	$C_{34}H_{27}FN_{10}O_4S_2$	56.50 (56.48)	3.77(3.72)	19.38 (19.36)
T10GE	4-Br	170	68.60	$C_{34}H_{27}BrN_{10}O_4S_2$	52.11 (52.09)	3.47(3.44)	17.87 (17.81)
T11GE	2-NO_2	155	70.25	$C_{34}H_{27}N_{11}O_6S_2$	54.47 (54.44)	3.63(3.61)	20.55 (20.52)
T12GE	3-OCH_3	220	67.80	$C_{35}H_{30}N_{10}O_5S_2$	57.21 (57.17)	4.12 (4.10)	19.06 (19.04)
T13GE	3-CH_3	185	62.65	$C_{35}H_{30}N_{10}O_4S_2$	58.48 (58.43)	4.21 (4.17)	19.49 (19.44)
T14GE	4-NO_2	215	66.75	$C_{34}H_{27}N_{11}O_6S_2$	54.47 (54.42)	3.63(3.58)	20.55 (20.52)
T15GE	-Naphthyl	225	69.85	$C_{38}H_{30}N_{10}O_4S_2$	60.47 (60.42)	4.01(3.99)	18.56 (18.53)

Compound T3GE: IR(KBr, cm^{-1}): -C=N str. in s-triazine (786.3),-C-S-C str. in thiazole (830.5), -C=S str. in thiourea (1143.0), -C-CH_3 str. in aromatic ring(1348.0), -N=O- str. as $-NO_2$ (1532.0), -C=O str. in amide(1596.0), -N-H deformation in -2^0 NH(1712.0), -C-H str. in $-OCH_3$ (2843.4), -C-H str. in aromatic (3180.2), -N-H str. in -2^0 NH(3388.1).^{1}H NMR (400.0 MHz, DMSO-d_6, δ_H ppm): 10.61 (s, 2H, -CS-NH), 9.12 (s, 1H, -CO-NH), 8.31 (s, 1H, -NH-NH-C), 6.98-8.23 (m, 17H, Ar), 6.90 (s, 1H, Ar=C-H), 5.13 (s, 1H, Ar-S-CH), 3.99 (s, 1H, -NH), 3.65-3.88 (s, 3H, $-OCH_3$), 2.14-2.20 (s, 3H, $-CH_3$).

Compound T4GE: IR(KBr, cm^{-1}): -C=N str. in s-triazine (789.3),-C-S-C str. in thiazole (839.5), -C=S str. in thiourea (1149.0), -N=O- str. as $-NO_2$(1536.0), -C=O str. in amide (1594.0), -N-H deformation in -2^0 NH(1701.0), -C-H str. in $-OCH_3$ (2838.4), -C-H str. in aromatic (3177.2), -N-H str. in -2^0 NH(3382.1).^{1}H NMR (400.0 MHz, DMSO-d_6, δ_H ppm): 10.76 (s, 2H, -CS-NH), 9.16 (s, 1H, -CO-NH), 8.25 (s, 1H, -NH-NH-

C), 6.84-8.11 (m, 17H, Ar), 6.78(s, 1H, Ar=C-H), 5.22 (s, 1H, Ar-S-CH), 3.89 (s, 1H, -NH), 3.70-3.81 (s, 6H, -OCH_3).

Compound T5GE: IR (KBr, cm^{-1}): -C=N str. in s-triazine (780.3),-C-S-C str. in thiazole (832.1), -C=S str. in thiourea (1111.0), -N=O- str. as -NO_2(1545.0), -C=O str. in amide (1595.0), -N-H deformation in -2^0 NH(1709.0), -C-H str. in -OCH_3 (2842.4), -C-H str. in aromatic (3188.2), -N-H str. in -2^0 NH(3380.1).^{1}H NMR (400.0 MHz, DMSO-d_6, δ_H ppm): 10.60 (s, 2H, -CS-NH), 9.12 (s, 1H, -CO-NH), 8.18 (s, 1H, -NH-NH-C), 6.71-8.08 (m, 17H, Ar), 6.89(s, 1H, Ar=C-H), 5.11 (s, 1H, Ar-S-CH), 3.91 (s, 1H, -NH), 3.65-3.88 (s, 6H, -OCH_3).

Compound T6GE: IR(KBr, cm^{-1}): -C=N str. in s-triazine (780.3),-C-S-C str. in thiazole (824.5), -C=S str. in thiourea (1135.0), -N=O- str. as -NO_2(1545.0), -C=O str. in amide (1600.0), -N-H deformation in -2^0 NH(1711.0), -C-H str. in -OCH_3 (2828.4), -C-H str. in aromatic (3178.2), -N-H str. in -2^0 NH(3380.1).^{1}H NMR (400.0 MHz, DMSO-d_6, δ_H ppm): 10.55 (s, 2H, -CS-NH), 9.14 (s, 1H, -CO-NH), 8.20 (s, 1H, -NH-NH-C), 6.78-8.24 (m, 17H, Ar), 6.90(s, 1H, Ar=C-H), 5.23 (s, 1H, Ar-S-CH), 3.98 (s, 1H, -NH), 3.61-3.91 (s, 3H, -OCH_3).

Compound T7GE: IR (KBr, cm^{-1}): -C-Cl str. In aromatic ring(753.0), -C=N str. in s-triazine (778.3),-C-S-C str. in thiazole (826.5), -C=S str. in thiourea (1145.0), -N=O- str. as -NO_2 (1531.0), -C=O str. in amide(1580.0), -N-H deformation in -2^0 NH(1716.0), -C-H str. in -OCH_3 (2839.4), -C-H str. in aromatic (3175.2), -N-H str. in -2^0 NH(3388.1).^{1}H NMR (400.0 MHz, DMSO-d_6, δ_H ppm): 10.61 (s, 2H, -CS-NH), 9.11 (s, 1H, -CO-NH), 8.27 (s, 1H, -NH-NH-C), 6.90-8.11 (m, 17H, Ar), 6.95 (s, 1H, Ar=C-H), 5.12 (s, 1H, Ar-S-CH), 3.90 (s, 1H, -NH), 3.70-3.86 (s, 3H, -OCH_3).

Compound T8GE: IR (KBr, cm^{-1}): -C-Cl str. In aromatic ring (751.0), -C=N str. in s-triazine (781.3),-C-S-C str. in thiazole (835), -C=S str. in thiourea (1128.0), -N=O- str. as -NO_2(1531.0), -C=O str. in amide(1599.0), -N-H deformation in -2^0 NH(1725.0), -C-H str. in -OCH_3 (2846.4), -C-H str. in aromatic (3171.2), -N-H str. in -2^0 NH(3389.1).^{1}H NMR (400.0 MHz, DMSO-d_6, δ_H ppm): 10.61 (s, 2H, -CS-NH), 9.43 (s, 1H, -CO-NH), 8.11 (s, 1H, -NH-NH-C), 6.71-8.45 (m, 17H, Ar), 6.90 (s, 1H, Ar=C-H), 5.15 (s, 1H, Ar-S-CH), 3.99 (s, 1H, -NH), 3.71-3.81 (s, 3H, -OCH_3).

Compound T9GE: IR (KBr, cm^{-1}): -C=N str. in s-triazine (787.3),-C-S-C str. in thiazole (831.5), -C-F str. In aromatic ring(1097.0), -C=S str. in thiourea (1140.0), -N=O- str. as -NO_2(1536.0), -C=O str. in amide(1594.0), -N-H deformation in -2^0 NH(1701.0), -C-H str. in -OCH_3 (2838.4), -C-H str. in aromatic (3177.2), -N-H str. in -2^0 NH(3382.1).^{1}H NMR (400.0 MHz, DMSO-d_6, δ_H ppm): 10.67 (s, 2H, -CS-NH), 9.02 (s, 1H, -CO-NH), 8.21 (s, 1H, -NH-NH-C), 6.98-8.38 (m, 17H, Ar), 6.91(s, 1H, Ar=C-H), 5.04 (s, 1H, Ar-S-CH), 3.93 (s, 1H, -NH), 3.75-3.82 (s, 3H, -OCH_3).

Compound T10GE: IR (KBr, cm^{-1}): -C=N str. in s-triazine (780.3),-C-S-C str. in thiazole (826.5), -C-Br str. In aromatic ring(1097.0), -C=S str. in thiourea (1149.0), -N=O- str. as -NO_2(1543.0), -C=O str. in amide(1595.0), -N-H deformation in -2^0 NH(1712.0), -C-H str. in -OCH_3 (2839.4), -C-H str. in aromatic (3179.2), -N-H str. in -2^0 NH(3380.1).^{1}H NMR (400.0 MHz, DMSO-d_6, δ_H ppm): 10.66 (s, 2H, -CS-NH), 9.11 (s, 1H, -CO-NH), 8.27 (s, 1H, -NH-NH-C), 6.74-8.22 (m, 17H, Ar), 6.76 (s, 1H, Ar=C-H), 5.13 (s, 1H, Ar-S-CH), 3.98 (s, 1H, -NH), 3.70-3.84 (s, 3H, -OCH_3).

Compound T11GE: IR(KBr, cm^{-1}): -C=N str. in s-triazine (781.3),-C-S-C str. in thiazole (826.5), -C=S str. in thiourea (1132.0), -N=O- str. as -NO_2(1523.0), -C=O str. in amide(1599.0), -N-H deformation in -2^0 NH(1723.0), -C-H str. in -OCH_3 (2830.4), -C-H str. in aromatic (3170.2), -N-H str. in -2^0 NH(3391.1).^{1}H NMR (400.0 MHz, DMSO-d_6, δ_H ppm): 10.54 (s, 2H, -CS-NH), 9.16 (s, 1H, -CO-NH), 8.43 (s, 1H, -NH-NH-C), 6.50-8.18 (m, 17H, Ar), 6.76 (s, 1H, Ar=C-H), 5.13 (s, 1H, Ar-S-CH), 3.87 (s, 1H, -NH), 3.81-3.89 (s, 3H, -OCH_3).

Compound T12GE: IR(KBr, cm^{-1}): -C=N str. in s-triazine (775.3),-C-S-C str. in thiazole (823.5), -C=S str. in thiourea (1154.0), -N=O- str. as -NO_2(1541.0), -C=O str. in amide(1576.0), -N-H deformation in -2^0 NH(1719.0), -C-H str. in -OCH_3 (2813.4), -C-H str. in aromatic (3165.2), -N-H str. in -2^0 NH(3311.1).^{1}H NMR (400.0 MHz, DMSO-d_6, δ_H ppm): 10.55 (s, 2H, -CS-NH), 9.17 (s, 1H, -CO-NH), 8.11 (s, 1H, -NH-NH-C), 6.78-8.45 (m, 17H, Ar), 6.76 (s, 1H, Ar=C-H), 5.07 (s, 1H, Ar-S-CH), 3.91 (s, 1H, -NH), 3.77-3.87 (s, 6H, -OCH_3).

Compound T13GE: IR(KBr, cm^{-1}): -C=N str. in s-triazine (792.3),-C-S-C str. in thiazole (826.5), -C=S str. in thiourea (1146.0), -N=O- str. as -NO_2(1541.0), -C=O str. in amide(1595.0), -N-H deformation in -2^0 NH(1712.0), -C-H str. in -OCH_3 (2845.4), -C-H str. in aromatic (3188.2), -N-H str. in -2^0 NH(3391.1).^{1}H NMR (400.0 MHz, DMSO-d_6, δ_H ppm): 10.71 (s, 2H, -CS-NH), 9.15 (s, 1H, -CO-NH), 8.11 (s, 1H, -NH-NH-C), 6.71-8.16 (m, 17H, Ar), 6.67(s, 1H, Ar=C-H), 4.96 (s, 1H, Ar-S-CH), 3.99 (s, 1H, -NH), 3.79-3.91 (s, 3H, -OCH_3), 2.17-2.31 (s, 3H, -CH_3).

Compound T14GE: IR(KBr, cm^{-1}): -C=N str. in s-triazine (795.3),-C-S-C str. in thiazole (822.5), -C=S str. in thiourea (1144.0), -N=O- str. as -NO_2(1541.0), -C=O str. in amide(1586.0), -N-H deformation in -2^0

NH(1696.0), -C-H str. in -OCH_3 (2827.4), -C-H str. in aromatic (3165.2), -N-H str. in -2^0 NH(3380.1).^{1}H NMR (400.0 MHz, DMSO-d_6, δ_H ppm): 10.76 (s, 2H, -CS-NH), 9.17 (s, 1H, -CO-NH), 8.29 (s, 1H, -NH-NH-C), 6.90-8.45 (m, 17H, Ar), 6.84 (s, 1H, Ar=C-H), 5.18 (s, 1H, Ar-S-CH), 3.84 (s, 1H, -NH), 3.67-3.97 (s, 3H, -OCH_3).

Compound T15GE: IR(KBr, cm^{-1}): -C=N str. in s-triazine (796.3),-C-S-C str. in thiazole (842.5), -C=S str. in thiourea (1156.0), -N=O- str. as -NO_2(1543.0), -C=O str. in amide(1578.0), -N-H deformation in -2^0 NH(1706.0), -C-H str. in -OCH_3 (2825.4), -C-H str. in aromatic (3167.2), -N-H str. in -2^0 NH(3374.1).^{1}H NMR (400.0 MHz, DMSO-d_6, δ_H ppm): 10.65 (s, 2H, -CS-NH), 8.94 (s, 1H, -CO-NH), 8.11 (s, 1H, -NH-NH-C), 6.76-8.30 (m, 20H, Ar), 6.88 (s, 1H, Ar=C-H), 5.14 (s, 1H, Ar-S-CH), 3.87 (s, 1H, -NH), 3.70-3.80 (s, 3H, -OCH_3).

Table 2

S.N.	Comp.	R=	Minimum Inhibitory Concentration (µg/mL)						
			Gram Negative Bacteria		Gram Positive Bacteria		FUNGAL SPECIES		
			E. coli	*P. aeruginosa*	*S. aureus*	*S. pyogenes*	*C. albicans*	*A. niger*	*A. clavatus*
1.	T1GE	H	250	>1000	250	500	**125**	500	>1000
2.	T2GE	2-CH_3	**125**	500	250	500	500	**125**	500
3.	T3GE	4-CH_3	500	250	500	250	1000	500	500
4.	T4GE	2-OCH_3	250	**62.5**	500	1000	>1000	**250**	**250**
5.	T5GE	4-OCH_3	**62.5**	**125**	250	**62.5**	1000	**250**	**125**
6.	T6GE	3-NO_2	250	500	250	500	**125**	500	500
7.	T7GE	3-Cl	**62.5**	500	250	500	500	500	1000
8.	T8GE	4-Cl	**62.5**	**125**	500	**62.5**	**250**	500	**125**
9.	T9GE	4-F	**125**	**125**	**62.5**	500	**250**	1000	500
10.	T10GE	4-Br	**125**	250	**62.5**	**125**	500	1000	500
11.	T11GE	2-NO_2	250	250	500	**125**	1000	500	>1000
12.	T12GE	3-OCH_3	**125**	500	1000	500	**125**	500	500
13.	T13GE	3-CH_3	250	500	1000	250	**125**	500	500
14.	T14GE	4-NO_2	250	250	**62.5**	250	500	**250**	**250**
15.	T15GE	Naphthyl	500	**125**	1000	500	500	250	1000
16.	Ampicillin		100	100	100	250	*	*	*
17.	Chloramphenicol		50	50	50	50	*	*	*
18.	Griseofulvin		*	*	*	*	500	100	100

Result and Discussion

Compounds T5GE, T7GE and T8GE exhibited excellent activity and T2GE, T9GE, T10GE and T12GE compounds exhibited good activity against *E. coli* as compared to Ampicillin. Compounds T5GE, T8GE, T9GE and T15GE exhibited good activity at 100-125 µg/mL activity and T4GE exhibited excellent activity as 62.5 µg/mL against *P. aeruginosa* as compared to Ampicillin. Compounds T9GE, T10GE and T14GE showed excellent activity at 62.5 µg/mL against *S. aureus* as compared to Ampicillin (MIC= 250 µg/mL). Compounds T10GE, T11GE exhibited good activity at 100-125µg/mL and compound T5GE and T8GE showed excellent activity at 62.5 µg/mL against *S. pyogenes* as compared to Ampicillin (MIC= 100 µg/mL).

Most of the compounds showed very good antifungal activity against *Candida albicans*, their MIC values were in the range between (100-500 µg/mL). As far as the anti-fungal activity are concerned for substituted thiourea derivatives of s-triazine compounds T1GE, T6GE, T12GE and T13GE showed excellent activity at 125 µg/mL and compounds T8GE and T9GE showed average activity at 250 µg/mL against *C. albicans* as compared to Griseofulvin (MIC= 500 µg/mL). Whereas T2GE, T4GE, T5GE and T14GE compounds showed good activity against *Aspergillus Clavatus* as compared to Griseofulvin (MIC= 100 µg/mL).

Conclusion

In this article we have report a series of 4-nitrobenzohydrazide and 6-(4-methoxyphenyl)-4-phenyl-6*H*-1, 3-thiazin-2-amine and substituted thiourea linked s-triazine showing better activity. T5GE showed better antifungal activity compared to standard. All the synthesized compounds have been established by elemental analysis, IR, ^{1}H NMR and mass spectral data. So, there is a future in doing more work on the synthesized compounds as some of them showed good activity against standard drugs.

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