An efficient synthesis of new benzoalidrazide and 1, 3-thizane fused s-triazines as potential antiamicrobial 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-nitrobenzalidrazide and 6-(4-methoxyphenyl)-4-phenyl-6H-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, 1H-NMR, 13C-NMR, MASS Analysis.

Keywords: Cyanuric Chloride, 4-nitrobenzalidrazide, 6-(4-methoxyphenyl)-4-phenyl-6H-1, 3-thiazin-2-amine, Different thiourea derivatives and antiamicrobial 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 agents1. 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 inexorable increase and spread of multidrug-resistant strains.

The major problem in the use of these drugs is that resistance is likely to develop rapidly. Therefore, it is predicted that chemical entities with 1,3,5-thiazine fused, 6-(4-methoxyphenyl)-4-phenyl-6H-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 described 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-((5-(benzyl-1,3,4-thiadiazol-2-yl)amo)-6-((phenylamino)1,3,5-triazin-2-yl)amo)-6-((tert-butyl)-3(methylthio)-1,2,4-triazin-5(4H)-one derivatives30, 1-((4-(5-methyl-1,3,4-thiadiazol-2-yl)amo)-6-((4-phenylthiazol-2-yl)amo)-1,3,5-thiazin-2-yl)-3-phenylurea31, 4-((4-((5-benzyl-1,3,4-thiadiazol-2-yl)amo)-6-(phenyl amino)1,3,5-triazin-2-yl)amo)-6-((tert-butyl)-3-(methylthio)-1,2,4-triazin-5(4H)-one32. 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-2H-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
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 °C, 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 bicarbonate solution from time to time as per requirement of reaction condition. 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 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)

Reaction Scheme

Step 1:

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 °C, the pH was maintained neutral by the addition of 10% sodium bicarbonate solution from time to time as per requirement of reaction condition. The temperature was gradually raised to 45 °C 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-6H-1, 3-thiazin-2-amine (0.01 mol) in DMF (15mL) was refluxed in oil bath. The temperature was gradually raised to 80-100 °C during four hours, the pH being maintained neutral by the addition of 10% sodium bicarbonate 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.

Perkin–Elmer 2400 CHN analyzer. IR spectra of all compounds were recorded on a Perkin–Elmer FT-IR spectrophotometer in KBr. ¹HNMR spectra were recorded on Bruker Avance II-400 MHz and ¹³CNMR 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 quadrupole LCMS-6410 from Agilent Technology.
**Step 3:**

![Chemical Structure](image_url)

**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 -NO₂(1540.0), -C=O str. in amide (1591.0), -N-H deformation in -²²NH(1700.0), -C-H str. in -OCH₃(2831.4), -C-H str. in aromatic (3173.2), -N-H str. in -²²NH(3384.1).¹H NMR (400.0 MHz, DMSO-d₆, δH 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, -OCH₃).

**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 str. in aromatic ring(1330.1), -N=O str. in aromatic ring (1537), -C=O str. in amide(1606.7), -N-H deformation in -²²NH(1718.5), -C-H str. in -OCH₃(2815.1), -C-H str. in -CH₃(2924.1), -C-H str. in aromatic (3136.5), -N-H str. in -²²NH(3400.1).¹H NMR (400.0 MHz, DMSO-d₆, δH 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, -OCH₃). 2.18-2.28 (s, 3H, -CH₃).¹³C NMR(100MHz,DMSO-d₆,δC 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. °C | Yield % | Mol. Formula     | Calculated (Found) % |
|-------|-----------|---------|---------|------------------|----------------------|
|       |           |         |         |                  | C        | H        | N       |
| T1GE  | H         | 190     | 70.25   | C₃₄H₃₂N₁₀O₈S₂ | 57.94     | 4.00(3.98)| 19.87(19.81) |
| T2GE  | 2-CH₃     | 205     | 55.45   | C₃₅H₃₀N₁₀O₈S₂ | 58.48     | 4.21(4.16)| 19.49(19.45) |
| T3GE  | 4-CH₃     | 213     | 60.25   | C₃₅H₃₀N₁₀O₈S₂ | 58.48     | 4.21(4.13)| 19.49(19.44) |
| T4GE  | 2-OCH₃    | 210     | 65.70   | C₃₅H₃₀N₁₀O₈S₂ | 57.21     | 4.12(4.08)| 19.06(19.01) |
| T5GE  | 4-OCH₃    | 185     | 69.55   | C₃₅H₃₀N₁₀O₈S₂ | 57.21     | 4.12(4.10)| 19.06(19.03) |
| T6GE  | 3-N₂O     | 190     | 55.55   | C₃₅H₃₀N₁₀O₈S₂ | 54.47     | 3.63(3.60)| 20.55(20.50) |
| T7GE  | 3-Cl      | 200     | 58.60   | C₃₅H₃₂Cl₁₈N₈O₈S₂ | 55.24(55.20)| 3.68(3.62)| 18.95(19.80) |
| T8GE  | 4-Cl      | 165     | 71.15   | C₃₅H₃₂Cl₁₈N₈O₈S₂ | 55.24(55.21)| 3.68(3.66)| 18.95(18.88) |
| T9GE  | 4-F       | 188     | 60.50   | C₃₅H₂₂F₁₈N₈O₈S₂ | 56.50     | 3.77(3.72)| 19.38(19.36) |
| T10GE | 4-Br      | 170     | 68.60   | C₃₅H₂₂Br₁₈N₈O₈S₂ | 52.11     | 3.47(3.44)| 17.87(17.81) |
| T11GE | 2-N₂O     | 155     | 70.25   | C₃₅H₂₂N₁₀O₈S₂  | 54.47     | 3.63(3.61)| 20.55(20.52) |
| T12GE | 3-CH₃     | 220     | 67.80   | C₃₅H₂₂N₁₀O₈S₂  | 57.21     | 4.12(4.10)| 19.06(19.04) |
| T13GE | 3-CH₃     | 185     | 62.65   | C₃₅H₂₂N₁₀O₈S₂  | 58.48     | 4.21(4.17)| 19.49(19.44) |
| T14GE | 4-NO₂     | 215     | 66.75   | C₃₅H₂₂N₁₀O₈S₂  | 54.47     | 3.63(3.58)| 20.55(20.52) |
| T15GE | -Naphthyl | 225     | 69.85   | C₃₅H₃₀N₁₀O₈S₂  | 60.47     | 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 str. in aromatic ring(1348.0), -N=O- str. as -NO₂(1532.0), -C=O str. in amide(1596.0), -N-H deformation in -²²NH(1712.0), -C-H str. in -OCH₃(2843.4), -C-H str. in aromatic (3180.2), -N-H str. in -²²NH(3388.1).¹H NMR (400.0 MHz, DMSO-d₆, δH 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, -OCH₃), 2.14-2.20 (s, 3H, -CH₃).

**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 -NO₂(1536.0), -C=O str. in amide (1594.0), -N-H deformation in -²²NH(1701.0), -C-H str. in -OCH₃(2838.4), -C-H str. in aromatic (3177.2), -N-H str. in -²²NH(3382.1).¹H NMR (400.0 MHz, DMSO-d₆, δH ppm): 10.76 (s, 2H, -CS-NH), 9.16 (s, 1H, -CO-NH), 8.25 (s, 1H, -NH-NH-...
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 thioiourea (1111.0), -N=O- str. as -NO₂(1545.0), -C=O str. in amide (1595.0), -N-H deformation in -NO\(\text{\textsubscript{2}}\) NH(1709.0), -C=H str. in -OCH\(\text{\textsubscript{3}}\)(2842.4), -C-H str. in aromatic (3188.2), -N-H str. in -NO\(\text{\textsubscript{2}}\) NH(3380.1).\(^1\)\(^\text{H}\) NMR (400.0 MHz, DMSO-\(\text{d}_{\text{6}}, \delta_{\text{ppm}}\): 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\(\text{\textsubscript{3}}\)).

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 thioiourea (1135.0), -N=O- str. as -NO₂(1545.0), -C=O str. in amide (1600.0), -N-H deformation in -NO\(\text{\textsubscript{2}}\) NH(1711.0), -C=H str. in -OCH\(\text{\textsubscript{3}}\)(2828.4), -C-H str. in aromatic (3178.2), -N-H str. in -NO\(\text{\textsubscript{2}}\) NH(3380.1).\(^1\)\(^\text{H}\) NMR (400.0 MHz, DMSO-\(\text{d}_{\text{6}}, \delta_{\text{ppm}}\): 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\(\text{\textsubscript{3}}\)).

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 thioiourea (1145.0), -N=O- str. as -NO₂(1531.0), -C=O str. in amide(1580.0), -N-H deformation in -NO\(\text{\textsubscript{2}}\) NH(1716.0), -C=H str. in -OCH\(\text{\textsubscript{3}}\)(2839.4), -C-H str. in aromatic (3175.2), -N-H str. in -NO\(\text{\textsubscript{2}}\) NH(3388.1).\(^1\)\(^\text{H}\) NMR (400.0 MHz, DMSO-\(\text{d}_{\text{6}}, \delta_{\text{ppm}}\): 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\(\text{\textsubscript{3}}\)).

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 thioiourea (1128.0), -N=O- str. as -NO₂(1531.0), -C=O str. in amide(1599.0), -N-H deformation in -NO\(\text{\textsubscript{2}}\) NH(1725.0), -C=H str. in -OCH\(\text{\textsubscript{3}}\)(2846.4), -C-H str. in aromatic (3171.2), -N-H str. in -NO\(\text{\textsubscript{2}}\) NH(3389.1).\(^1\)\(^\text{H}\) NMR (400.0 MHz, DMSO-\(\text{d}_{\text{6}}, \delta_{\text{ppm}}\): 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\(\text{\textsubscript{3}}\)).

Compound T9GE: IR (KBr, cm⁻¹): -C≡N str. in s-triazine (787.5), -C-S-C str. in thiazole (831.5), -C=F str. In aromatic ring(1097.0), -C=S str. in thioiourea (1140.0), -N=O- str. as -NO₂(1536.0), -C=O str. in amide(1594.0), -N-H deformation in -NO\(\text{\textsubscript{2}}\) NH(1701.0), -C=H str. in -OCH\(\text{\textsubscript{3}}\)(2838.4), -C-H str. in aromatic (3177.2), -N-H str. in -NO\(\text{\textsubscript{2}}\) NH(3382.1).\(^1\)\(^\text{H}\) NMR (400.0 MHz, DMSO-\(\text{d}_{\text{6}}, \delta_{\text{ppm}}\): 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\(\text{\textsubscript{3}}\)).

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 thioiourea (1149.0), -N=O- str. as -NO₂(1543.0), -C=O str. in amide(1595.0), -N-H deformation in -NO\(\text{\textsubscript{2}}\) NH(1712.0), -C=H str. in -OCH\(\text{\textsubscript{3}}\)(2839.4), -C-H str. in aromatic (3179.2), -N-H str. in -NO\(\text{\textsubscript{2}}\) NH(3380.1).\(^1\)\(^\text{H}\) NMR (400.0 MHz, DMSO-\(\text{d}_{\text{6}}, \delta_{\text{ppm}}\): 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\(\text{\textsubscript{3}}\)).
NH(1696.0), -C-H str. in -OCH₃(2827.4), -C-H str. in aromatic (3165.2), -N-H str. in -2° NH(3380.1).¹¹H NMR (400.0 MHz, DMSO-d₆, δH 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, -OCH₃).

**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 -NO₂(1543.0), -C=O str. in amide(1578.0), -N-H deformation in -2° NH(1706.0), -C-H str. in -OCH₃(2825.4), -C-H str. in aromatic (3167.2), -N-H str. in -2° NH(3374.1).¹¹H NMR (400.0 MHz, DMSO-d₆, δH 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, -OCH₃).

### Table 2

| S.N. | Comp. | R= | 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-CH₃ | 125    | 500       | 250       | 500         | 125        | 500     | 500        |
| 3    | T3GE  | 4-CH₃ | 500    | 250       | 500       | 250         | 1000       | 500     | 500        |
| 4    | T4GE  | 2-OCH₃ | 250  | 62.5      | 500       | 1000        | >1000      | 250     | 250        |
| 5    | T5GE  | 4-OCH₃ | 62.5  | 125       | 250       | 62.5        | 1000       | 250     | 125        |
| 6    | T6GE  | 3-NO₂ | 250    | 500       | 250       | 500         | 125        | 500     | 500        |
| 7    | T7GE  | 3-Cl  | 62.5   | 500       | 250       | 500         | 500        | 1000    | 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-NO₂ | 250    | 250       | 500       | 125         | 1000       | 500     | >1000      |
| 12   | T12GE | 3-OCH₃ | 125  | 500       | 1000      | 500         | 125        | 500     | 500        |
| 13   | T13GE | 3-CH₃ | 250    | 500       | 1000      | 250         | 125        | 500     | 500        |
| 14   | T14GE | 4-NO₂ | 250    | 250       | 62.5      | 250         | 500        | 250     | 250        |
| 15   | T15GE | Naphthyl | 500  | 125       | 1000      | 500         | 250        | 1000    | 1000       |
| 16   | Ampicillin | 500  | 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 100-125 μg/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-6H-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, ¹¹H 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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References
1. Moustafa M A, Gineinah M M, Nasr M N, Arch Pharma, (2004) 337,427-433.
2. Demain A L, Sanchez S, J Antibiots, (2009) 62,5-16.
3. Krchnak V, Holliday M W, Solid phase heterocyclic chemistry Chem Rev, (2002) 102,61-92.
4. Da Silva C M, Da Silva D L, Modolo L V, Alves R V, De Resende M A, Martins C V B, De Fatima A, J Adv Res, (2011) 2,1-8.
5. Mohini Y, Prasad R B N, Karuna M S L, Med Chem Res, (2013) 22,4360-6.
6. Shi L, Tan S H, Li H Q, Song Y C, Zhu H L, Tan R X, Eur J Med Chem, (2007) 2,558-64.
7. Cheng L S, Tang J J, Luo H, Jin X J, Dai F, Yang Y, Qian Y P, Bioorg Med Chem Lett, (2010) 20, 2417-20.
8. Rollas S, Gulerman N, Erdeniz H, J Med Chem, (2002) 57, 171-4.
9. Bayrak H, Demirbas A, Demirbas N, Karaoglu S A, Eur J Med Chem, (2009) 44, 4362-6.
10. Kamble V U, Patil A S, Badami S P, J Incl Pheno Macro Chem, (2010) 68(3), 347-58.
11. Kaymakcioglu B, Elcin Oruc-Emre E, Unsalan S, Tabanca N, Khan S I, Earl D, Iscan G, Demirci F, Rollas S, Med Chem Res, (2012) 21, 3499-508.
12. Loncle C, Brunel J M, Vidal N, Dherbomez M, Letourneux Y, Eur J Med Chem, (2004) 39,1067-71.
13. Yamashita H, Ohno K, Amada Y, Hattori H, Funatsu Y O, Toya T, J Pharm Exp Ther, (2004) 308,127-33.
14. Rathod S P, Charjan A P and Rajput P R, Ras J Chem, (2010) 3,363-7.
15. Keerthi Kumar B, J Pharm Resi, (2011) 4,274-5.
16. Srikanth Jupudi et al Inter J Rese Pharm Chem, (2013) 3, 213-20.
17. Kalirajan R et al, J Chem Tech Rese, (2009) 1, 27-34.
18. Wang W, Zhao B, Chao X and Wenpeng W, Inter J Org Chem, (2012) 2, 117-20.
19. Meric A, Zerrin N and Ibrahim H, Med Chem Rese, (2014) 17, 30-41.
20. Beauchamp B, Hilpert and Wang, World Intellectual Property Organization, (2011) 165.
21. Levy S B, Marshall B, Nat Med, (2004) 10, S122-9.
22. Patel R V, Kumar P, Rajani D P, Panneconque C, DeClercq E, Chikhalia K H, Med Chem, (2012) 4, 1053-65.
23. Mishra A R, Singh S, J Agric Food Chem, (2000) 48, 5465-8.
24. Patel D H, Chikhalia K H, Shah N K, Patel D P, Kaswala P B, Buha V M, J Enzyme Inhib Med Chem, (2010) 25, 121-5.
25. Kumar G J, Bomma S S, Srihari E, Shrivastava S, Naidu V G M, Srinivas K, Rao V J, Med Chem Res, (2013) 22, 5973-81.
26. Liu B, Lee Y, Zou J, Petrazzi H M, Joseph R W, Chao W, Michelotti E L, Bukhtiyarova M, Springman E B, Dorsey B D, Bioorg Med Chem Lett, (2010) 20, 6592-6.
27. Dianzani C, Collino M, Gallicchio M, Fantozzi R, Samaritani S, Signore G, Menicagli R, J Pharm Pharmacol, (2006) 58,219-26.
28. Avupati V R, Yejella R P, Parala V R, Killari K N, Papasani V M R, Bioorg Med Chem Lett, (2013) 23, 5968-5970.
29. Bhat H R, Singh U P, Gahtori P, Ghosh S K, Gogoi K, Prakashe A, Singh R S, New J Chem, (2013) 37, 2654-62.
30. Malik G M, Patel T V, Journal of Asian Scientific Research, (2017) 7(6), 214-23.
31. Malik G M, Patel T V, International Journal of Advanced Research in Science, Engineering and Technology, (2017) 4, 6.
32. Malik G M, Patel T V, JUC (2018) 14(2), 76-83.