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Synthesis, characterization, antimicrobial studies of certain s-triazine derived compounds and analogues

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ABSTRACT

Some novel compounds are synthesized using the substitution of chlorine in 2,4,6-trichloro-s-triazine by some moieties having structural as well as biological importance and not which are anti infective agents. In this manner 19 novel compounds are prepared and they are subjected to antibacterial and antifungal screening. Prior to this the synthesized compounds are duly characterized by IR and ^{1}H-NMR spectral analysis. These compounds reveal substantive antibacterial activities against some randomly chosen both gram +ve & gram-ve bacteria. The promising results are in support of the fact that the compounds are worth to be optimized for some novel drugs in future.

Keywords: Morpholine, substituted thiourea/urea, 4-amino-6-terbutyl-3-(methylthio)-1,2,4-triazin-5(4H)-one and Cyanuric chloride, Antimicrobial activity.

INTRODUCTION

In recent decades, problems of multi-drug resistant microorganisms have reached on alarming level in many countries around the world. A numbers of recent clinical reports describe the increasing occurrence of meticillin-resistant *S. aureus* and other antibiotic-resistant human pathogenic microorganisms in United State and European countries. Infections caused by those microorganisms pose a serious challenge to the medical community and the need for an effective therapy has led to a search for novel antimicrobial agents[1].

In this work, we report the synthesis and biological activity of some newly synthesized cyanuric chloride based derivatives.

Several derivatives of s-triazine show antimicrobial[2], antibacterial[3], and herbicidal activities.[4] They are also used for the treatment of HIV infection.[5,6] Cyanuric chloride derivatives are widely used in commercial chemicals, Some trisubstituted-1,3,5-triazines are also used as liposome[7]. Several investigators found s-triazine nucleus as potential therapeutic agents for diseases due to bacteria, malaria and cancer.[8] Trichlorotriazine derivatives have found extensive use in the synthesis of “activated” dyes, whiteners, herbicides and

pharmaceuticals. 1,3,5-Triazine derivatives also possess biological activities like antitubercular, antitumor[9], anti-inflammatory[10] and anthelmintic. 1,3,5-triazines represent a widely used lead structure with multitude of interesting applications in numerous field.[11]2,4,6-Trichloro-1,3,5-triazine (cyanuric chloride) is a heterocyclic organic compound commonly used for immobilization of proteins on various polymeric supports, such as cellulose and agarose, as well as for modification of proteins, liposome and natural polymers(e.g., chitosan and wool).1,3,5-Triazines are a class of compounds well known for a long time and still continue the object of considerable interest, mainly due to their applications in different fields, including the production of herbicides and polymer photo stabilizers.[12] Some s-triazines display important biological properties, for example hexamethyl melamine (HMM) and 2-amino-4-morpholino-s-triazine are used clinically due to their antitumor properties to treat lung breast and ovarian cancer, respectively.[13] Hydroxymethyl, Pentamethyl, Melamine is also the hydroxylated metabolite which corresponds to the major active form of HMM.[14] More recently, significant aromatase inhibitory activities were observed for s-triazines of 4,4'-(6-(1H-imidazole-1-yl)- 1,3,5-triazine-2,4-diyl)dimorpholine. It has been reported that s-triazine derivatives are used as templates for molecular imprinting and for the construction of three-helix bundle protein [15].

Cyanuric chloride is an essential organic intermediate of which three chlorines can be replaced by –NH2, –OH, –SH or –NHR step by step with high yield. Cyanuric chloride derivatives have been studied for decades, especially its amino derivatives. It is generally accepted that the first chlorine of cyanuric chloride can be easily substituted by NH2-group at 0–5°C, the second one at 40–50°C, and the third one typically above 80°C, which depends on the activity of amine nucleophiles [16].

Thiourea derivatives possess antibacterial [17], hypnotic antitubercular and possible anticonvulsant activities. It also represent a new class of human immuno deficiency virus type (HIV-1), non-nucleoside reverse transcriptase (NNRT) inhibitors [18], found as antagonist [19], and high density lipoprotein (HDL) elevating agents [20]. Over the last few years, the thiourea moiety has been of interest to design molecules as receptor antagonists, as natural product mimics or as synthetic intermediates to amidines or guanidines.[21] Thiourea not only confers antibacterial, antitubercular or antileprotic activity, but has also been reported to possess antifungal as well as antiviral properties.[22]

Urea derivatives are reported to possess antibacterial[23], antimicrobial antifungal, anticancer[24] and anticonvulsant[25] activities. Urea derivatives possess wide therapeutic activities such as antithyroidal[26], hypnotic and anesthetic[27], antibacterial[28], diuretic[29] and anthelmintics.

Morpholine derivatives find their wide spectrum of antimicrobial activity and exhibits anthelmintic, bactericidal and insecticidal activity.[30]

We planned to undertake the synthesis and characterization of some triazine derivatives carrying the above biodynamic heterocyclic systems with the hope to achieve enhanced biological activity.

MATERIALS AND METHODS

All the melting points were taken in open capillaries tube and are uncorrected. The purity of compounds was checked routinely by TLC (0.5 mm thickness) using silica gel – G coated Al – plates (Merck)and spots were visualized by exposing the dry plates in iodine vapours. IR spectra

were recorded on FTIR spectrophotometer using KBr or Nujol technique.^{1}H NMR spectra on a Varian 400 FT MHz NMR instrument at using $CDCl_3$ or DMSO-d_6 as solvent and TMS as internal reference.

Scheme:-

STEP-1

PREPARATION OF 4-(4,6-DICHLORO-1,3,5-TRIAZIN-2-YL)MORPHOLINE: (A)

To a stirred solution of cyanuric chloride (0.1 mole, 18.4 g.) in acetone (100 ml) at 0-5^{0}C, the solution of morpholine (0.1 mole, 8.7 ml) in acetone (15 ml) was added and pH being 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°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.

STEP-2

PREPARATION OF 6-tert-BUTYL-4-(4-CHLORO-6-MORPHOLINO-1,3,5-TRIAZIN-2-YLAMINO)-3-(METHYLTHIO)-1,2,4-TRIAZIN-5(4H)-ONE : (B)

To a stirred solution of (A) (0.1 mole,23.5 g) in acetone (150 ml) was added, the solution of 4-amino-6 *ter*-butyl-3-(methylthio)-1,2,4-triazine-5(4H)one(0.1 mole,21.4 g) in acetone (75 ml) was added drop wise maintaining the temperature at 40° C and the stirring was continued. The pH being 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°C during two 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.

STEP-3

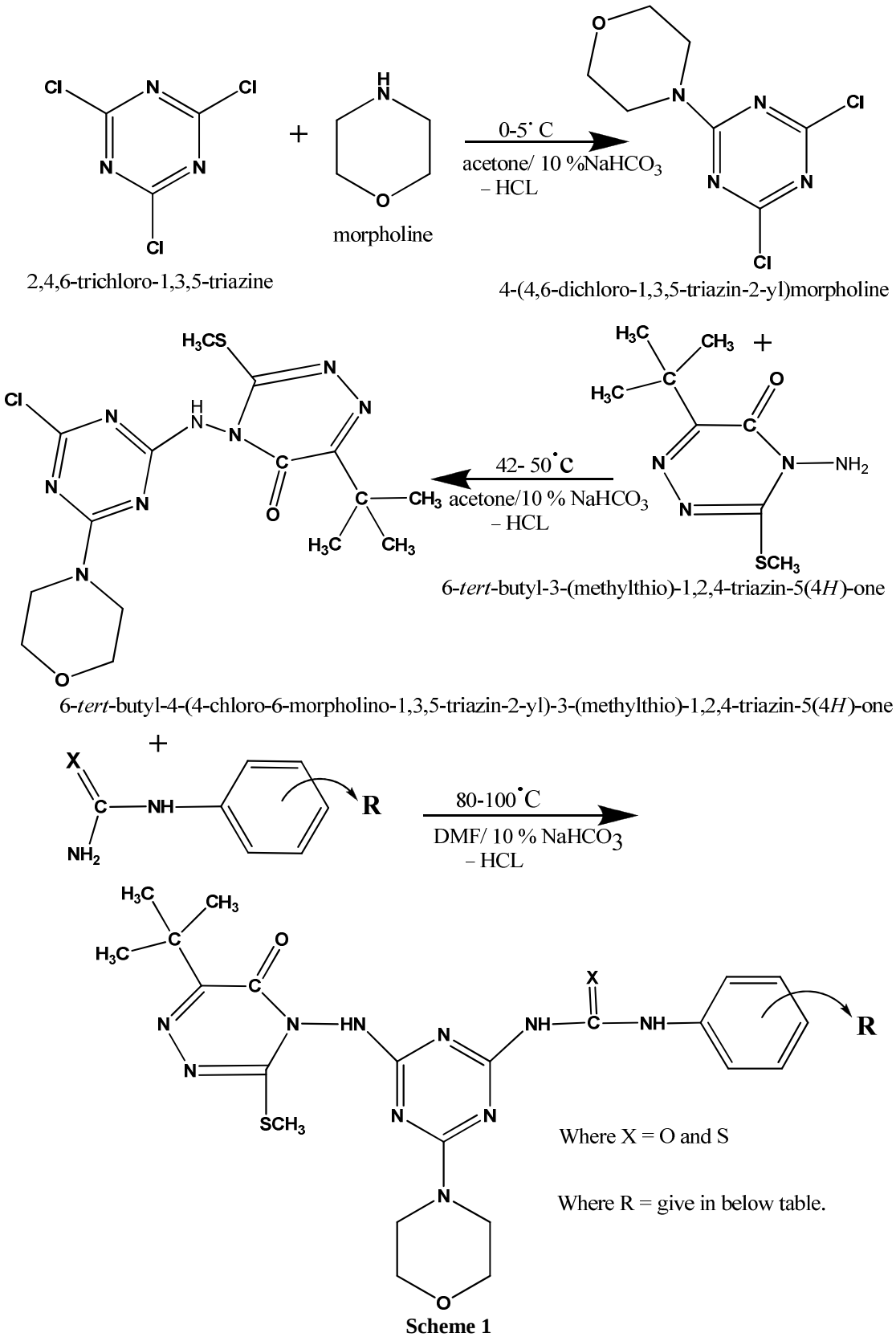
PREPARATION OF FINAL COMPOUND:-

A mixture of (B) (0.01 mole, 4.12g) and aryl urea/thiourea (0.01 mole) in DMF(20ml) was refluxed in oil bath. The temperature was gradually raised to 80-100^{0}C 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, add little charcoal in R.B.F. and then filter it into cold water. The solid product obtained was filtered and dried. The crude product was purified by recrystallization from absolute alcohol. Prepare all derivatives by this method. Analytical data are given table 1.

Compound (3a): Yield: 60.50%; m.p. 225^{0}C (dec.); **IR (KBr,cm^{-1}) :** 815 cm^{-1} (-C=N- s-triazine, 1060 cm^{-1}(-N-N-str),1132 cm^{-1}(-CH_2-O-CH_2-str),1320 cm^{-1} (-C-CH_3 str **),** 1400 cm^{-1}(>N-,3^0 amine), 1509 cm^{-1} (-NH-def), 1680 cm^{-1} (-C=O-),3339 cm^{-1} (-NH-str) **^{1}H-NMR: δ** 3.65(t,4H,-CH_2),3.59(t,4H,-CH_2 at –O-),2.50(s,3H, -SCH_3),1.25(s,9H,-C-CH_3),3.60(s,1H,-NH),10.28(s,1H,-NH in urea), 7.20-7.49 (m,5H, Ar-H),Elem.Anal. for$C_{22}H_{28}N_{10}O_3S$:cal. C,51.55%,H 5.51%,N 27.33%, and found C 51.50%,H 5.45%,N 27.30%.

Compound (3b): Yield: 58.10%; m.p. 90^{0}C (dec.); **IR (KBr,cm^{-1}) :** 807 cm^{-1} (-C=N- s-triazine, 1064 cm^{-1}(-N-N-str),1140 cm^{-1}(-CH_2-O-CH_2-str),1322 cm^{-1} (-C-CH_3 str **),** 1395 cm^{-1}(>N-,3^0 amine), 1500 cm^{-1} (-NH-def), 1695 cm^{-1} (-C=O-),3330 cm^{-1} (-NH-str), 2849.19 cm^{-1}(–OCH_3 str) **^{1}H-NMR: δ** 3.66(t,4H,-CH_2),3.62(t,4H,-CH_2 at –O-),2.54(s,3H, -SCH_3),1.26(s,9H,-C-CH_3),3.61(s,1H,-NH),10.36(s,1H,-NH in urea), 7.24-7.36(m,4H, Ar-H)3.46(s,3H,-OCH_3)

Elem.Anal. for $C_{23}H_{30}N_{10}O_4S$:cal. C,50.91%,H 5.57%,N 25.81%, and found C 50.88%,H 5.52%,N 25.77%.



Scheme 1

Table 1 Physical data of synthesized compounds

Sr. No.	X	R	Mol. Formula	Mol. Weight	M.P. °C	% Yield
3a	o	-H	$C_{22}H_{28}N_{10}O_3S$	512.58	225 ^{o}	60.50
3b	o	2 –OCH_3	$C_{23}H_{30}N_{10}O_4S$	542.61	90^o	58.10
3c	o	2 –CH_3	$C_{23}H_{30}N_{10}O_3S$	526.61	140^o	60.40
3d	o	4 - CH_3	$C_{23}H_{30}N_{10}O_3S$	526.61	140 ^{o}	59.30
3e	o	4 –OCH_3	$C_{23}H_{30}N_{10}O_4S$	542.61	145 ^{o}	61.20
3f	o	2 -Cl	$C_{22}H_{27}N_{10}O_3SCl$	547.01	135 ^{o}	59.20
3g	o	4 -Cl	$C_{22}H_{27}N_{10}O_3SCl$	547.01	180^o	60.25
3h	o	4 -F	$C_{22}H_{27}N_{10}O_3SF$	530.57	170 ^{o}	62.00
3i	o	4 -Br	$C_{22}H_{27}N_{10}O_3SBr$	591.48	190 ^{o}	70.00
4a	s	-H	$C_{22}H_{28}N_{10}O_2S_2$	528.65	260^o	60.50
4b	s	2 –OCH_3	$C_{23}H_{30}N_{10}O_3S_2$	558.69	110 ^{o}	59.80
4c	s	4 –OCH_3	$C_{23}H_{30}N_{10}O_3S_2$	558.69	115 ^{o}	60.05
4d	s	2 –CH_3	$C_{23}H_{30}N_{10}O_2S_2$	542.69	145 ^{o}	59.70
4e	s	4 - CH_3	$C_{23}H_{30}N_{10}O_2S_2$	542.69	100 ^{o}	60.24
4f	s	2 -Cl	$C_{22}H_{27}ClN_{10}O_2S_2$	563.09	112 ^{o}	60.05
4g	s	3 -Cl	$C_{22}H_{27}ClN_{10}O_2S_2$	563.09	105 ^{o}	59.22
4h	s	4 -Cl	$C_{22}H_{27}ClN_{10}O_2S_2$	563.09	140 ^{o}	60.12
4i	s	4 –NO_2	$C_{21}H_{26}N_{11}O_4S_2$	560.63	150 ^{o}	62.5
4j	s	α-Naphthyl	$C_{26}H_{30}N_{10}O_2S_2$	578.71	115 ^{o}	70.0

Compound (3c): Yield: 60.40%; m.p.140^{0}C (dec.); **IR (KBr,cm^{-1}) :** 817 cm^{-1} (-C=N- s-triazine, 1065 cm^{-1}(-N-N-str),1137 cm^{-1}(-CH_2-O-CH_2-str),1324 cm^{-1} (-C-CH_3 str **),** 1398 cm^{-1}(>N-,3^0 amine), 1504 cm^{-1} (-NH-def), 1692 cm^{-1} (-C=O-),3333 cm^{-1} (-NH-str) **^{1}H-NMR: δ** 3.75(t,4H,-CH_2),3.65(t,4H,-CH_2 at –O-),2.60(s,3H, -SCH_3),1.35(s,12H,-C-CH_3),3.70(s,1H,-NH),10.90(s,1H,-NH in urea), 7.34-7.89(m,4H, Ar-H),Elem.Anal. for $C_{23}H_{30}N_{10}O_3S$:cal. C,52.46%,H 5.74%,N 26.60%, and found C 52.43%,H 5.71%,N 26.58%.

Compound (3d): Yield: 59.30%; m.p.140^{0}C (dec.); **IR (KBr,cm^{-1}) :** 817 cm^{-1} (-C=N- s-triazine, 1065 cm^{-1}(-N-N-str),1137 cm^{-1}(-CH_2-O-CH_2-str),1324 cm^{-1} (-C-CH_3 str **),** 1398 cm^{-1}(>N-,3^0 amine), 1504 cm^{-1} (-NH-def), 1692 cm^{-1} (-C=O-),3333 cm^{-1} (-NH-str) **^{1}H-NMR: δ** 3.69(t,4H,-CH_2),3.59(t,4H,-CH_2 at –O-),2.51(s,3H, -SCH_3),1.28(s,12H,-C-CH_3),3.63(s,1H,-NH),10.31(s,1H,-NH in urea), 7.24-7.49(m,4H, Ar-H),Elem.Anal. for $C_{23}H_{30}N_{10}O_3S$:cal. C,52.46%,H 5.74%,N 26.60%, and found C 52.42%,H 5.70%,N 26.56%.

Compound (3e): Yield: 61.20%; m.p. 145^{0}C (dec.); **IR (KBr,cm^{-1}) :** 830 cm^{-1} (-C=N- s-triazine, 1050 cm^{-1}(-N-N-str),1190 cm^{-1}(-CH_2-O-CH_2-str),1315 cm^{-1} (-C-CH_3 str **),** 1385 cm^{-1}(>N-,3^0 amine), 1515 cm^{-1} (-NH-def), 1705 cm^{-1} (-C=O-),3344 cm^{-1} (-NH-str),2870 cm^{-1}(–OCH_3 str) **^{1}H-NMR: δ** 3.70(t,4H,-CH_2),3.65(t,4H,-CH_2 at –O-),2.45 (s,3H, -SCH_3),1.35(s,9H,-C-CH_3),3.69(s,1H,-NH),11.00(s,1H,-NH in urea), 7.45-7.76(m,4H, Ar-H)3.75(s,3H,-OCH_3) Elem.Anal. for $C_{23}H_{30}N_{10}O_4S$:cal. C,50.91%,H 5.57%,N 25.81%, and found C 50.87%,H 5.53%,N 25.79%

Compound (3f): Yield: 59.20%; m.p. 135^{0}C (dec.); **IR (KBr,cm^{-1}) :** 801 cm^{-1} (-C=N- s-triazine, 1055 cm^{-1}(-N-N-str),1147 cm^{-1}(-CH_2-O-CH_2-str),1334 cm^{-1} (-C-CH_3 str **),** 1388 cm^{-1}(>N-,3^0 amine), 1514 cm^{-1} (-NH-def), 1682 cm^{-1} (-C=O-),3345 cm^{-1} (-NH-str),717.86 cm^{-1}(-C-Cl-str)**^{1}H-NMR: δ** 3.75(t,4H,-CH_2),3.55(t,4H,-CH_2 at –O-),2.55

(s,3H, -SCH_3),1.38(s,9H,-C-CH_3),3.60(s,1H,-NH),11.31(s,1H,-NH in urea), 7.35-7.49(m,4H, Ar-H),Elem.Anal. for $C_{22}H_{27}N_{10}O_3SCl$:cal. C,48.30%,H 4.97%,N 25.60%, and found C 48.25%,H 4.95%,N 25.55%.

Compound (3g): Yield: 60.25%; m.p. 180^{0}C (dec.); **IR (KBr,cm^{-1}) :** 808 cm^{-1} (-C=N- s-triazine, 1065 cm^{-1}(-N-N-str),1127 cm^{-1}(-CH_2-O-CH_2-str),1314 cm^{-1} (-C-CH_3 str **),** 1402 cm^{-1}(>N-,3^0 amine), 1524 cm^{-1} (-NH-def), 1698 cm^{-1} (-C=O-),3400 cm^{-1} (-NH-str),727.16 cm^{-1}(-C-Cl-str)**^{1}H-NMR: δ** 3.70(t,4H,-CH_2),3.60(t,4H,-CH_2 at –O-),2.55 (s,3H, -SCH_3),1.25(s,9H,-C-CH_3),3.50(s,1H,-NH),10.01(s,1H,-NH in urea), 7.50-7.79(m,4H, Ar-H),Elem.Anal. for $C_{22}H_{27}ClN_{10}O_3S$: cal. C,48.30%,H 4.97%,N 25.60%, and found C 48.27%,H 4.92%,N 25.54%.

Compound (3h): Yield: 62.00%; m.p. 170^{0}C (dec.); **IR (KBr,cm^{-1}) :** 823 cm^{-1} (-C=N- s-triazine, 1070 cm^{-1}(-N-N-str),1120 cm^{-1}(-CH_2-O-CH_2-str),1320 cm^{-1} (-C-CH_3 str **),** 1415 cm^{-1}(>N-,3^0 amine), 1517 cm^{-1} (-NH-def), 1702 cm^{-1} (-C=O-),3305 cm^{-1} (-NH-str),1050 cm^{-1}(-C-F-str) **^{1}H-NMR: δ** 3.69(t,4H,-CH_2),3.59(t,4H,-CH_2 at –O-),2.51 (s,3H,-SCH_3),1.28(s,9H,-C-CH_3),3.63(s,1H,-NH),10.31(s,1H,-NH in urea),7.24-7.49(m,4H, Ar-H),Elem.Anal. for $C_{22}H_{27}FN_{10}O_3S$:cal. C,49.80%,H 5.13%,N 26.40%, and found C 49.75%,H 5.09%,N 26.36%.

Compound (3i): Yield: 70.00%; m.p. 190^{0}C (dec.); **IR (KBr,cm^{-1}) :** 821 cm^{-1} (-C=N- s-triazine, 1060 cm^{-1}(-N-N-str),1117 cm^{-1}(-CH_2-O-CH_2-str),1304 cm^{-1} (-C-CH_3 str **),** 1414 cm^{-1}(>N-,3^0 amine), 1509 cm^{-1} (-NH-def), 1688 cm^{-1} (-C=O-),3298 cm^{-1} (-NH-str), 690 cm^{-1}(-C-Br-str) **^{1}H-NMR: δ** 3.66(t,4H,-CH_2),3.52(t,4H,-CH_2 at –O-),2.45(s,3H, -SCH_3),1.22(s,9H,-C-CH_3),3.45(s,1H,-NH),10.61(s,1H,-NH in urea), 7.14-7.34(m,4H, Ar-H),Elem.Anal. for $C_{22}H_{27}BrN_{10}O_3S$:cal. C,44.67%,H 4.60%,N 23.68%, and found C 44.64%,H 4.55%,N 23.64%.

Compound (4a): Yield: 60.50%; m.p.260^{0}C (dec.); **IR (KBr,cm^{-1}) :** 821 cm^{-1} (-C=N- s-triazine, 1060 cm^{-1}(-N-N-str),1119 cm^{-1}(-CH_2-O-CH_2-str),1314 cm^{-1} (-C-CH_3 str **),** 1424 cm^{-1}(>N-,3^0 amine), 1500 cm^{-1} (-NH-def), 1110 cm^{-1} (-C=S-),3298 cm^{-1} (-NH-str), **^{1}H-NMR: δ** 3.66(t,4H,-CH_2),3.52(t,4H,-CH_2 at –O-),2.35(s,3H, -SCH_3),1.20(s,9H,-C-CH_3),3.40(s,1H,-NH),9.61(s,1H,-NH in thiourea), 7.14-7.34(m,5H, Ar-H),Elem.Anal. for $C_{22}H_{28}N_{10}O_2S_2$:cal. C,49.98%,H 5.34%,N 26.50%, and found C 49.90%,H 5.28%,N 26.35%.

Compound (4b): Yield: 59.80%; m.p. 110^{0}C (dec.); **IR (KBr,cm^{-1}) :** 817 cm^{-1} (-C=N- s-triazine, 1034 cm^{-1}(-N-N-str),1149 cm^{-1}(-CH_2-O-CH_2-str),1329 cm^{-1} (-C-CH_3 str **),** 1390 cm^{-1}(>N-,3^0 amine), 1492 cm^{-1} (-NH-def), 1100 cm^{-1} (-C=S-),3275 cm^{-1} (-NH-str), 2800 cm^{-1}(–OCH_3 str) **^{1}H-NMR: δ** 3.76(t,4H,-CH_2),3.69(t,4H,-CH_2 at –O-),2.44(s,3H, -SCH_3),1.18(s,9H,-C-CH_3),3.50(s,1H,-NH),9.50(s,1H,-NH in thiourea), 7.04-7.30(m,4H, Ar-H)3.56(s,3H,-OCH_3) Elem.Anal. for $C_{23}H_{30}N_{10}O_3S_2$:cal. C,49.45%,H 5.41%,N 25.07%, and found C 49.30%,H 5.32%,N 25.01%.

Compound (4c): Yield: 59.70%; m.p. 145^{0}C (dec.); **IR (KBr,cm^{-1}) :** 837 cm^{-1} (-C=N- s-triazine, 1080 cm^{-1}(-N-N-str),1147 cm^{-1}(-CH_2-O-CH_2-str),1314 cm^{-1} (-C-CH_3 str **),** 1400 cm^{-1}(>N-,3^0 amine),1524 cm^{-1} (-NH-def),1110 cm^{-1} (-C=S-),3322 cm^{-1} (-NH-str) **^{1}H-NMR: δ** 3.80(t,4H,-CH_2),3.72(t,4H,-CH_2 at –O-),2.50(s,3H, -SCH_3),1.18(s,12H,-C-CH_3),3.57(s,1H,-NH),9.90(s,1H,-NH in thiourea), 7.40-7.59(m,4H, Ar-H),Elem.Anal. for $C_{23}H_{30}N_{10}O_2S_2$:cal. C,50.90%, H 5.57%, N 25.81%, and found C 50.80%, H 5.42%,N 25.72%.

Compound (4d): Yield: 60.05%; m.p. 135^{0}C (dec.); **IR (KBr,cm^{-1}) :** 816 cm^{-1} (-C=N- s-triazine, 1024 cm^{-1}(-N-N-str),1147 cm^{-1}(-CH_2-O-CH_2-str),1311 cm^{-1} (-C-CH_3 str **),** 1356 cm^{-1}(>N-,3^0 amine), 2920 cm^{-1}(C-H stretching as –OCH_3),1510 cm^{-1}(-NH-def), 1113 cm^{-1} (-C=S-

),3255 cm^{-1} (-NH-str) **^{1}H-NMR: δ** 3.69(t,4H,-CH_2),3.62(t,4H,-CH_2,at–O-),2.51(s,3H,-SCH_3),3.46(s,3H,-OCH_3),1.28(s,9H,-C-CH_3),3.46(s,1H,-NH),9.25 (s,1H,-NH in thiourea) ,7.56-7.70(m,4H, Ar-H),Elem.Anal. for $C_{23}H_{30}N_{10}O_3S_2$:cal. C,49.45%,H 5.41%,N 25.07%, and found C 49.33%,H 5.33%,N 25.03%.

Compound (4e): Yield: 60.24%; m.p. 100^{0}C (dec.); **IR (KBr,cm^{-1}) :** 807 cm^{-1} (-C=N- s-triazine, 1056 cm^{-1}(-N-N-str),1137 cm^{-1}(-CH_2-O-CH_2-str),1320 cm^{-1} (-C-CH_3 str **),** 1390 cm^{-1}(>N-,3^0 amine),1537 cm^{-1} (-NH-def),1120 cm^{-1} (-C=S-),3343 cm^{-1} (-NH-str) **^{1}H-NMR: δ** 3.82(t,4H,-CH_2),3.80(t,4H,-CH_2 at –O-),2.57(s,3H, -SCH_3),1.26(s,12H,-C-CH_3),3.47(s,1H,-NH),9.65(s,1H,-NH in thiourea), 7.44-7.69(m,4H, Ar-H),Elem.Anal. for $C_{23}H_{30}N_{10}O_2S_2$:cal. C,50.90%, H 5.57%, N 25.81%, and found C 50.85%, H 5.45%,N 25.74%.

Compound (4f): Yield: 60.05%; m.p. 112^{0}C (dec.); **IR (KBr,cm^{-1}) :** 811 cm^{-1} (-C=N- s-triazine, 1045 cm^{-1}(-N-N-str),1155 cm^{-1}(-CH_2-O-CH_2-str),1344 cm^{-1} (-C-CH_3 str **),** 1402 cm^{-1}(>N-,3^0 amine), 1519 cm^{-1}(-NH-def),1123 cm^{-1}(-C=S-),3390 cm^{-1} (-NH-str),707 cm^{-1}(-C-Cl-str)**^{1}H-NMR: δ** 3.65(t,4H,-CH_2),3.60(t,4H,-CH_2 at –O-),2.59 (s,3H, -SCH_3),1.33(s,9H,-C-CH_3),3.62(s,1H,-NH),10.00(s,1H,-NH in thiourea),7.25-7.39(m,4H, Ar-H),Elem.Anal.for $C_{22}H_{27}ClN_{10}O_2S_2$:cal. C,46.93%,H 4.83%,N 24.87%, and found C 46.85%,H 4.80%,N 24.75%.

Compound (4g): Yield: 59.22%; m.p. 105^{0}C (dec.); **IR (KBr,cm^{-1}) :** 798 cm^{-1} (-C=N- s-triazine, 1023 cm^{-1}(-N-N-str),1150 cm^{-1}(-CH_2-O-CH_2-str),1349 cm^{-1} (-C-CH_3 str **),** 1422 cm^{-1}(>N-,3^0 amine), 1534 cm^{-1}(-NH-def),1118 cm^{-1}(-C=S-),3420 cm^{-1} (-NH-str),717 cm^{-1}(-C-Cl-str)**^{1}H-NMR: δ** 3.60(t,4H,-CH_2),3.40(t,4H,-CH_2 at –O-),2.49 (s,3H, -SCH_3),1.30(s,9H,-C-CH_3),3.52(s,1H,-NH),10.10(s,1H,-NH in thiourea),7.45-7.59(m,4H, Ar-H),Elem.Anal.for $C_{22}H_{27}ClN_{10}O_2S_2$:cal. C,46.93%,H 4.83%,N 24.87%, and found C 46.87%,H 4.76%,N 24.74%.

Compound (4h): Yield: 60.12%; m.p. 140^{0}C (dec.); **IR (KBr,cm^{-1}) :** 837 cm^{-1} (-C=N- s-triazine, 1042 cm^{-1}(-N-N-str),1160 cm^{-1}(-CH_2-O-CH_2-str),1330 cm^{-1} (-C-CH_3 str **),** 1414 cm^{-1}(>N-,3^0 amine), 1504 cm^{-1}(-NH-def),1129 cm^{-1}(-C=S-),3365 cm^{-1} (-NH-str),726 cm^{-1}(-C-Cl-str)**^{1}H-NMR: δ** 3.79(t,4H,-CH_2),3.62(t,4H,-CH_2 at –O-),2.49 (s,3H, -SCH_3),1.30(s,9H,-C-CH_3),3.76(s,1H,-NH),9.90(s,1H,-NH in thiourea),7.25-7.39(m,4H, Ar-H),Elem.Anal.for $C_{22}H_{27}ClN_{10}O_2S_2$:cal. C,46.93%,H 4.83%,N 24.87%, and found C 46.86%,H 4.84%,N 24.80%.

Compound (4i): Yield: 60.50%; m.p. 150^{0}C (dec.); **IR (KBr,cm^{-1}) :** 825 cm^{-1} (-C=N- s-triazine, 1054 cm^{-1}(-N-N-str),1150 cm^{-1}(-CH_2-O-CH_2-str),1320 cm^{-1} (-C-CH_3 str **),** 1433 cm^{-1}(>N-,3^0 amine), 1527 cm^{-1}(-NH-def),1131 cm^{-1}(-C=S-),3320 cm^{-1} (-NH-str),1550 cm^{-1}(-NO_2-str)**^{1}H-NMR:δ** 3.75(t,4H,-CH_2),3.70(t,4H,-CH_2 at –O-),2.54 (s,3H, -SCH_3),1.27(s,9H,-C-CH_3),3.72(s,1H,-NH),10.15(s,1H,-NH in thiourea), 7.50-7.85 (m,4H, Ar-H),Elem.Anal.for $C_{22}H_{27}ClN_{11}O_4S_2$:cal. C,46.06%,H 4.74%,N 26.86%, and found C 46.01%,H 4.68%,N 24.79%.

Compound (4j): Yield: 70.00%; m.p. 115^{0}C (dec.); **IR (KBr,cm^{-1}) :** 793 cm^{-1} (-C=N- s-triazine, 1057 cm^{-1}(-N-N-str),1145 cm^{-1}(-CH_2-O-CH_2-str),1327 cm^{-1} (-C-CH_3 str **),** 1426 cm^{-1}(>N-,3^0 amine),770 cm^{-1}(1:2:3 sub. benzene ring),1532 cm^{-1}(-NH-def),1120 cm^{-1}(-C=S-),3329 cm^{-1} (-NH-str), **^{1}H-NMR: δ** 3.80(t,4H,-CH_2),3.77(t,4H,-CH_2 at –O-),2.49(s,3H,-SCH_3),1.25(s,9H,-C-CH_3),3.57(s,1H,-NH),9.95(s,1H,-NH in thiourea), 7.55-7.75(m,7H,Ar-H),Elem.Anal.for $C_{26}H_{30}N_{10}O_2S_2$: cal.C,53.96%,H 5.23%, N24.20 %, and found C 53.90%,H 5.18%,N 24.14%.

Antimicrobial Activity

For the testing antimicrobial activity various microorganism were used for the study. The **broth dilution** method was used for this study. Following general procedure is adopted[31].The antimicrobial activity of all the compounds was studies at 1000 ppm concentration *in vitro*.The different types of microorganism used were some gram negative bacteria [*Escherichia coli, Pseudomonas aeruginosa*], gram positive bacteria [*Bacillus subtilis*, *Staphylococcus aureus*], fungus [*Candida albicans*].

80% DMSO are used as solvent to dissolve compound 3a to 3i and 4a to 4j to 10(µg/ml)

Sr. & Comp No.		Gram positive bacteria		Gram negative bacteria		Fungus
		S. aureus	*B. subtilis*	*E. coli*	*P. aeruginosa*	*C. albicans*
1.	3a	125-250	125-250	250-500	62.5-125	125-250
2.	3b	62.5-125	125-250	250-500	125-250	125-250
3.	3c	125-250	125-250	250-500	62.5-125	125-250
4.	3d	31.25-62.5	125-250	125-250	250-500	62.5-125
5.	3e	125-250	125-250	250-500	62.5-125	125-250
6.	3f	62.5-125	250-500	125-250	125-250	62.5-125
7.	3g	125-250	125-250	250-500	62.5-125	125-250
8.	3h	125-250	125-250	250-500	62.5-125	250-500
9.	3i	15.62-31.25	125-250	62.5-125	250-500	125-250
10.	4a	125-250	125-250	250-500	62.5-125	125-250
11.	4b	62.5-125	125-250	250-500	125-250	125-250
12.	4c	125-250	125-250	250-500	31.25-62.5	125-250
13.	4d	125-250	125-250	125-250	62.5-125	125-250
14.	4e	125-250	62.5-125	125-250	125-250	125-250
15.	4f	15.62-31.25	250-500	250-500	125-250	125-250
16.	4g	125-250	62.5-125	250-500	125-250	125-250
17.	4h	125-250	125-250	250-500	62.5-125	125-250
18.	4i	125-250	62.5-125	250-500	62.5-125	125-250
19.	4j	15.62-31.25	250-500	125-250	125-250	125-250
Ampicillin		250	100	100	100	------
Nystatin		---	---	---	---	100

CONCLUSION

A series of cyanuric chloride derivatives were prepared and tested for their *in vitro* antibacterial activity against the four strains of bacteria (gram +ve, gram –ve). Six compounds of the obtained series showed high *in vitro* antimicrobial activity. Compound (**3d, 3i, 4f, 4j**) showed excellent activity against *Staphylococcus aureus*. Compound (**4e, 4g, 4i**) showed good activity against *Bacillus subtillis*. Compound (**3i**) showed excellent activity against *Escherichia coli* and compound (**4c**) showed excellent activity against *P. aeruginosa*. Whereas compound (**3d, 3f**) show good activity against *C. albicans* .The presence of electron-withdrawing group on the aromatic ring in Series 3 and 4 in general increased the antimicrobial activity compared to compounds with electron-donating groups. Based upon the results, it will also be necessary to optimize the by substituting a series of electron-withdrawing groups on the aromatic ring and selectively modifying the above compound.

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