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Synthesis, Characterization and Biological Studies of Novel Series of Triazolyl Schiff Bases Bearing Thiazole Moiety and their S-Derivatives

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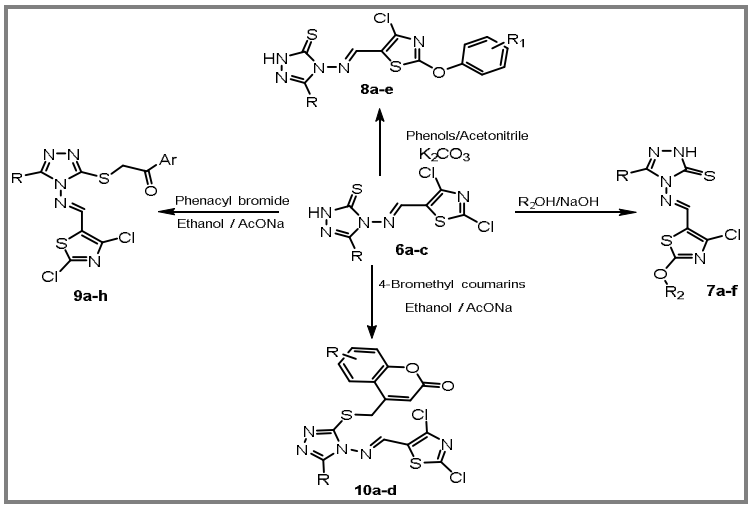
ABSTRACT

The condensation of 5-substituted-3-mercapto-1,2,4-triazoles with 2,4-dichloro-1,3-thiazole in ethanol solvent containing catalytic amount of sulfuric acid afforded novel series of 5-substituted-{[(2,4-dichloro-1,3-thiaol-5-yl)methylidene]amino-1,2,4-triazole-3(4H)-thiones (6). These compounds (6) were further derivatized through substitution of the chlorine atom at the 2nd position of thiazole ring with aliphatic alcohols/phenols and through substitution on SH group of 1,2,4-triazole moiety with phenacyl bromides/4-bromomethylcoumarins to afford novel series of alkoxy-(7)/phenoxy-(8 / and S-substituted (9/10) Schiff base derivatives respectively. The structures of the newly synthesized compounds were confirmed by their 1H-NMR, IR, Mass spectral and analytical data. All the new compounds were screened for their antibacterial and antioxidant activities.

Graphical Abstract



Novel series of Schiff bases of 1,2,4-triazole bearing 1,3-thiazole derivatives.

Keywords: Antibacterial activity, Antioxidant activity, Schiff bases, S-alkyl derivatives, 1, 2, 4-Triazoles.

INTRODUCTION

The Chemistry of 1,2,4-triazole and its derivatives has gained great attention in drug discovery research due to their prominent chemotherapeutical values such as antifungal [**1, 2**], antibacterial [**2-4**], anticancer [**4**], anti-tubercular, anti-inflammatory [**5**] and antioxidant [**6, 7**] properties. The 1, 2, 4-triazole core is also known to be one of the key pharmacophores in a variety of biologically active compounds found in many drugs such as anastrozole, etizolam, ribavirin and triazolam [**8**]. In addition, some mercapto/thione-substituted 1, 2, 4-triazoles possessing broad spectrum of biological activities including antioxidant activity were reported [**9, 10**]. Furthermore, 4-amino-3-mercapto-1,2,4-triazole moiety played a vital role in the synthesis of bioactive drugs such as imidazothiadiazoles, triazolothiadiazepines, trazolothiadiazines, triazolodithiazines or triazolyl-Schiff/Mannich bases and their S-derivatives [**11-13**].

Schiff base derivatives have been extensively documented not only because they serve as synthons for the synthesis of many bioactive compounds, but also, they exhibit potent biological properties such as antibacterial, antifungal [**14, 15**], anthelmintic [**16**], antipyretic, analgesic [**17**], anti-inflammatory [**17, 18**], antiglycation, and antidepressant [**19**]. On the other hand, the 1,3-thiazole moiety has been used as privileged scaffold in drug discovery possibly due to its toxophoric unit (S-C=N), which constitutes the major component of many biologically active drugs with good pharmacological value such as antimicrobial [**20**], antioxidant [**21**], antiprotozoal [**22**] and anti-inflammatory[**23**] properties.

Promoted by these observations and in continuation of our research to discover new bioactive compounds [**10-12, 29**] a novel series of Schiff bases of 1,2,4-triazole bearing 1,3-thiazole derivatives have been synthesized (Scheme 1) and evaluated for their biological activity.

MATERIALS AND METHODS

The melting points of the synthesized compounds were determined on Innovative DTC-967A apparatus and are uncorrected. The IR-spectra (in KBr pellets) were recorded on Shimadzu FT-IR prestige-21 Spectrophotometer or on Perkin Elmer Spectrum RX 1 FT-IR Spectrometer and are expressed in cm^{-1}. The mass spectra were recorded on Shimadzu LC-MS-8030 mass spectro-photometer operating at 70 eV. ^{1}H-NMR spectra were recorded on a Bruker AVNCE II 400 MHz instrument in DMSO-d_6 or $CDCl_3$ as a solvent and TMS as an internal standard. Syntronics Spectrophotometer-106 was used to measure the absorbance for DPPH scavenging activity assay. The completions of the reaction as well as the purity of the compounds were checked by TLC using silica gel plates (Merck) with hexane: ethyl acetate (4:6) as mobile phase.

General procedure: The synthesis of novel series of triazolyl Schiff bases bearing thiazole moiety and their s-derivatives were shown in Scheme 1.

Synthesis of 5-substituted-4-{[(2,4-dichloro-1,3-thiazol-5-yl)methylidene]amino}-1,2,4-triazole-3(4H)-thiones (6a-c): Equimolar amounts (0.01mol) of 5-substitued-4-amino-3-mercapto-1,2,4-triazoles (2) and 2,4-dichloro-1,3-thiazole-5-carbaldehyde (4) were condensed for 4-5 hours under reflux on a water bath in ethanol solvent (20 mL) containing catalytic amount of conc. H_2SO_4 (0.2 mL). On cooling, the solid product separated was collected by filtration, washed thoroughly with cold water and dried to give pure product.

Synthesis of 5-sbstituted-4-{[(2-alkoxy-4-chloro-1,3-thiazol-5-yl)methylidene]amino}-1,2,4-triazole-3(4H)-thiones (7a-f): The Schiff bases **(6a-c)** (0.005 mol) were dissolved in an appropriate alcohol (40 mL) (methanol, ethanol, n-propanol), then added at room temperature an aqueous KOH (0.5 g in 5 mL H_2O). The reaction mixture was further stirred at room temperature for 6h, and the resulting reaction mass was poured and stirred into ice cold water (50 mL). The solid separated after

addition of some drops of conc. HCl was collected by filtration, washed with cold water to give pure product. The spectral data for few selected compounds prepared according to this procedure are given below.

Synthesis of 5-sbstituted-4-{[(4-chloro-2-phenoxy-1,3-thiazol-5-yl)methylidene]amino}-1,2,4-triazole-3(4H)-thiones (8a-e): To a solution of Schiff bases (6a-c) (0.025mol) in acetonitrile (80 mL) was added anhydrous potassium carbonate (0.05 mol, 6.9 g) and stirred at room temperature for 10 min. A solution of substituted phenol (0.025mol) in 10 mL of acetonitrile was then added, and further stirred at room temperature for 10h. The resulting reaction mixture was poured into ice-cold water, followed by the addition of few drops of conc. HCl. The separated solid was collected by filtration, washed with cold water, dried and recrystallized from ethanol.

Synthesis of S-substituted-4-{[(2,4-dichloro-1,3-thiazol-5-yl)methylidene]amino}-1,2,4-triazole-3(4H)-thiones (9a-h and 10-d): To equimolar amount of Schiff's base (6a-c) and phenacylbromide or 4-bromomethylcoumarins (0.01mol) in ethanol (50 mL) was added sodium acetate in a catalytic amount. The solution was stirred at room temperature for 1-4 hours. The solid separated was collected by filtration, dried and recrystallized from ethanol.

Antibacterial activity: The agar well diffusion method [24] was used for antibacterial activity study against four bacterial isolates, namely *Staphylococcus aureus* (MTCC 9660), *Enterococcus faecalis* (MTCC 2729) (Gram-positive bacteria*), Chromo bacterium violaceum* (MTCC 2656) and *Escherichia coli* (MTCC 443) (Gram-negative bacteria). Prepared Muller-Hinton Agar media was poured onto sterile Petri plates and allowed to solidify, 20 µL of the suspension containing individual bacterial strain ($5x10^5$ CFU mL^{-1}) that was grown for 24 h in nutrient broth were aseptically inoculated on the above Petri plates using a sterile cotton swab. Aseptically, 6mm holes were punched in the inoculated media, and then 25 µL of test solution prepared by dissolving 1 mg test sample 1 mL^{-1} DMSO were added to them along with the control (DMSO) and standard drug streptomycin prepared in the same way as the test sample. After incubation for 24 h at 37°C, the zones of inhibition were measured in mm. The tests were carried out in triplicate and the results were presented as their rounded mean value (Table 4).

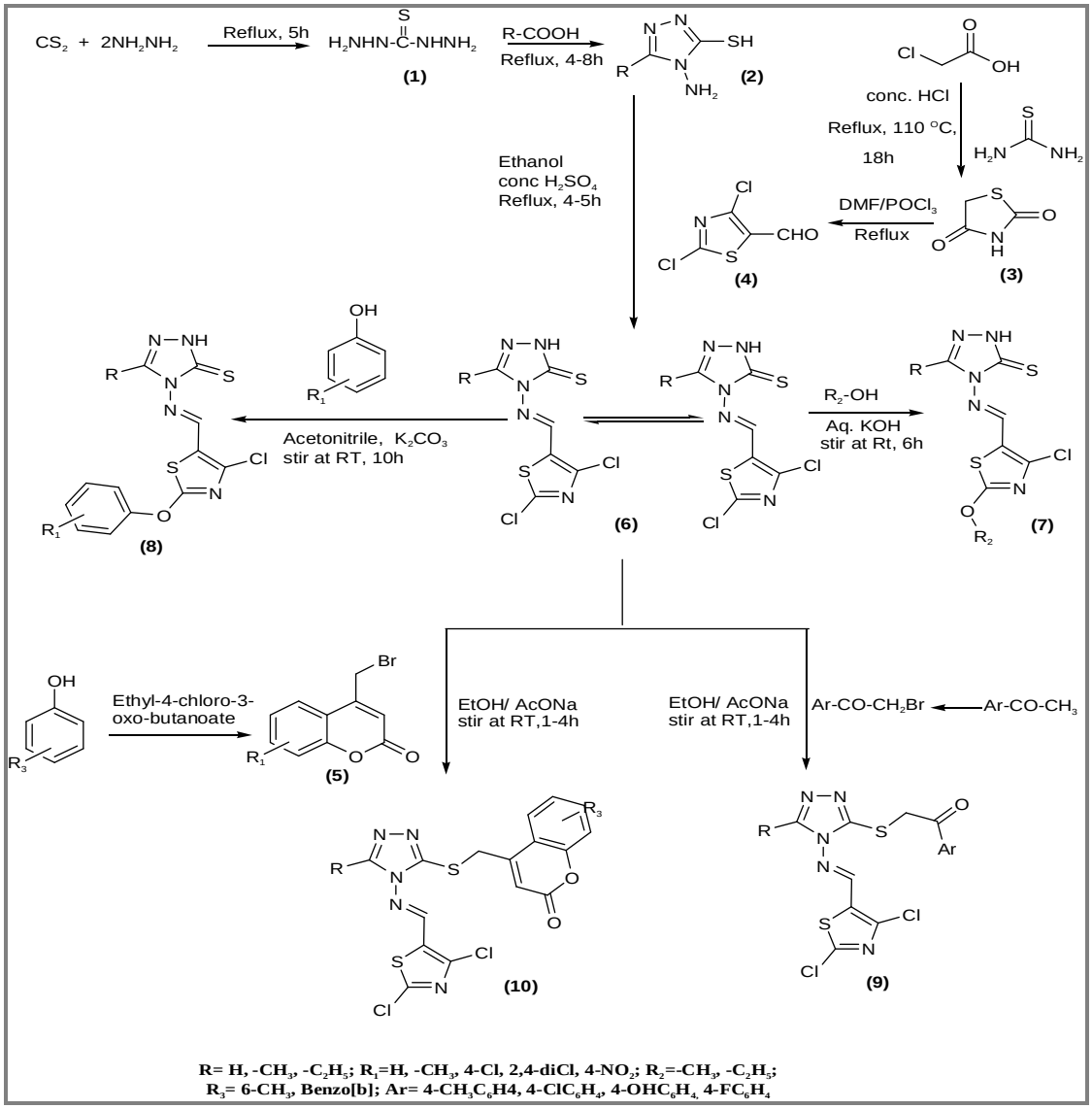
Antioxidant activity: The antioxidant activity of the newly synthesized compounds was performed using stable 2, 2-diphenyl-1-picryhydrazyl radical (DPPH) using the modified method of Mensor*et.al* [25]. The stock solution of test compounds (1 mg mL^{-1}) was prepared in DMSO and 0.3 mM DPPH was prepared in ethanol, 150 µL of each test sample was taken in a test tube, diluted upto 2.5 mL with ethanol so that the final concentration was 60 µL mL^{-1}. Then, 1 mL DPPH solution was added to each test sample, mixed well and incubated at room temperature for half an hour, after which the absorbance of stable DPPH radical was measured at 518 nm against the absorbance of the control (A_c) prepared in the same way as the sample solution, except that 150 µL of test sample was replaced by DMSO solvent. Butylated hydroxy anisole (BHA) was used as standard and was prepared in the same way as the test samples. The DPPH free radical scavenging activity was calculated as follows: % radical scavenging activity = $[(A_c-A_s)/A_c] \times 100$, where A_c was the absorbance of the control, A_s was the absorbance of test compounds. Each experiment was repeated thrice, and the results were expressed as their mean values (Table 5).

RESULTS AND DISCUSSION

5-Substituted-4-amino-3-mercapto-1,2,4-triazoles **(**2) were synthesized by refluxing at 120°C an appropriate carboxylic acid with thiocarbohydrazide (1) for 4-8h [26, 27]. The latter compound (1) was in turn prepared by refluxing the mixture of carbon disulfide with hydrazine hydrate [28]. 2.4-Dichloro-1, 3-thiazole-5-carbaldehyde (4) was obtained starting from 1,3-thiazolidine-2,4-dione (3) as reported in our previous paper [29]. 4-Bromomethylcoumarins (5) were prepared by the Pechmann cyclization of substituted phenols with ethyl-4-bromo-3-oxobutanoate [30]. The latter product was

synthesized by bromination of ethylacetoacetate in dry diethyl ether following literature procedure [31] with little modification. The required phenacylbromides were afforded by bromination of different acetophenones.

Novel series of Schiff bases (6) were synthesized by refluxing on water bath the mixture of triazole (2) and thiazole (4) in ethanol medium containing catalytic amount of conc. H_2SO_4. These Schiff bases (6) further underwent the base-catalyzed nucleophilic substitution of the chlorine atom located at the 2nd position of the 1,3-thiazole ring with alcohols/phenols when stirred at room temperature under suitable solvent to afford novel series of alkoxy/phenoxy derivatives(7/8). New series of S-substituted Schiff bases (9/10) were synthesized under selective S-alkylation of compounds (6) with different phenacylbromides/4-bromomethylcoumarins in ethanol solvent containing catalytic amount of sodium acetate (Scheme 1).



Scheme 1. Synthesis of novel series of triazolyl Schiff bases bearing thiazole moiety and their s-derivatives

The structures of these newly synthesized compounds were confirmed by their ^{1}H-NMR, IR, mass spectral data and elemental analysis. The characterization data of the newly synthesized compounds is given in table 1, 2 and 3. The IR spectrum of {[(2,4-dichlorothiazol-5-yl)methylidene]amino}-5-ethyl-

1,2,4-triazole-3(4H)-thione **(**6e) showed characteristic bands for thione (C=S) and C=N at 1280 and 1581 cm^{-1} respectively. The bands at 3111 and 2973 cm^{-1} are assigned to NH and C-H stretching respectively. The C=C absorption band appeared at 1506 cm^{-1} while the C-Cl band was seen at 785cm^{-1}. In the ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of the same compound (6e) the methyl (CH_3-) protons appeared as triplet centered at ð, 1.26 ppm integrating for three protons. Methylene (-CH_2-CH_3) protons resonated as quartet centered at ð, 2.73 ppm integrating for two protons. The signal due to HC=N was seen as a singlet at ð, 11.06 ppm integrating for one proton, and the NH proton came into resonance as a singlet at ð, 13.78 ppm integrating for one proton. Further, the mass spectrum of this compound **(**6e**)** showed molecular ion peak at m/z 306 (M^+-1) which is in agreement with its molecular formula $C_8H_7Cl_2N_5S_2$.

Similarly, the formation of alkoxy-/phenoxy-derivatives **(**7 and 8**)** was also confirmed by Spectral data. As a typical example, the IR spectrum of 4-{[(4-chloro-2-ethoxythiazol-5-yl) methylidene] amino}-1,2,4-triaole-3(4H)-thione **(**7b**)** showed the absorption bands at 1236cm^{-1} and at 3111 cm^{-1} corresponding to C=S and NH stretching mode respectively.The ^{1}H-NMR spectrum of the same compound **(**7b**)** showed a triplet at ð, 1.41 ppm integrating for three protons for methyl (CH_3) group while oxymethylene (-OCH_2) protons resonated as a quartet centered at ð, 4.53 ppm integrating for two protons. The signal due to HC=N proton came into resonance as a singlet at ð, 10.27 ppm and the NH/SH proton resonated as a broad singlet at ð, 13.91 ppm integrating for one proton each. The signal for triazole-5H proton appeared atð, 8.66 ppm. The mass spectrum of this compound **(7b)** showed molecular ion peak at (m/z): 287.8 M^+-1) which is in conformity with its molecular formula $C_8H_8ClN_5OS_2$. Chlorine isotopic peak was observed at m/z=289.8 M^++1) in the ratio 3:1 thereby confirming the formation of the product.

Further, the formation of S-alkylated derivatives **(**9 and 10**)** rather than N-alkylated derivatives was confirmed by the absence of both NH and C=S bands in their IR spectra thereby indicating the involvement of thiol tautomer in a selective S-alkylation reaction. The IR spectrum of 2-[(4-{[(2,4-dichlorothiazol-5-yl)methylidene]amino}-*4H*-1,2,4-triazole-3-yl)sulfanyl]-1-(4-methylphenyl) etha-none **(**9a**)** showed characteristic bands at 1682 cm^{-1} and at 1603cm^{-1} for C=O and C=N stretching respectively. The absorption bands at 1513 $cm^{-1}$is assigned for C=C stretching frequency. The C-H and C-Cl stretching frequencies were seen at 3121, 3058, 2908 cm^{-1} and 780 cm^{-1} respectively. The selective S-alkylated compounds (9 and 10) were further confirmed by studying their ^{1}H-NMR spectra. The appearance of signal between 4.5 to 5.0 ppm for S-CH_2C=O protons and the absence of any signal in the region above 5.0 to 5.5 ppm for N-CH_2C=O clearly indicated the selective S-alkylation reaction that the reaction took place at sulfur atom rather than on the nitrogen atom. In a typical example, ^{1}H-NMR spectrum of compound **(**9a**)** showed a singlet at ð,2.40 ppm for three proton of methyl (CH_3) group. Two protons of methylene (SCH_2) group resonated as a singlet at ð, 4.92 ppm. Four aromatic protons appeared as two doublets centered at ð, 7.37 ppm (J=8.08 Hz) and at ð, 7.94 ppm (J=8.16 Hz)integrating for two protons each. The HC=N proton appeared as a singlet at a ð, 9.48 ppm while the signal due to triazole-5H proton resonated as a singlet at ð, 9.04 ppm integrating for one proton. The mass spectrum of this compound (9a**)** showed molecular ion peak at m/z 409.90 (M^+-1) consistent with its molecular formula $C_{15}H_{11}Cl_2N_5OS_2$. The cluster of isotopic peaks were seen at m/z=411.90 (M^++1), m/z=413.90 (M^++3).

Table 1. Characterization data of compounds 6a-e

Compd. No.	R	m.p (°C) (Yield %)	Molecular formula (Mol. Wt.)	Colour and Crystal nature	Elemental analysis found (Calculated) (%)		
					C	H	N
6a	H	177-179 (75)	$C_6H_3Cl_2N_5S_2$ (280.16)	Yellow Amorphous solid	25.47 (25.72)	1.12 (1.08)	25.04 (25.00)
6b	CH_3	178-180 (41)	$C_7H_5Cl_2N_5S_2$ (294.18)	Yellow Amorphous solid	28.74 (28.58)	1.62 (1.71)	23.72 (23.81)
6c	C_2H_5	180-182 (87)	$C_8H_7Cl_2N_5S_2$ (308.21)	Yellow Amorphous solid	31.08 (31.18)	2.36 (2.29)	22.89 (22.72)

Table 2. Characterization data of compounds **7a-f** and **8a-e**

Compd. No.	R	R_1/R_2	M.p (^oC) (Yield %)	Molecular formula (Mol. Wt.)	Colour and Crystal nature	Elemental analysis found (Calculated) (%)		
						C	H	N
7a	H	CH_3	78-80 (61)	$C_7H_6ClN_5OS_2$ (275.74)	Gray Amorphous solid	30.58 (30.49)	2.24 (2.19)	25.39 (25.40)
7b	H	C_2H_5	140-142 (99)	$C_8H_8ClN_5OS_2$ (289.77)	Golden Amorphous solid	33.22 (33.16)	2.67 (2.78)	24.26 (24.17)
7c	H	nC_3H_7	176-178 (66)	$C_9H_{10}ClN_5OS_2$ (303.79)	Golden Amorphous solid	35.54 (35.58)	3.36 (3.32)	23.04 (23.05)
7d	CH_3	CH_3	138-140 (30)	$C_8H_8ClN_5OS_2$ (289.77)	Pale yellow Amorphous solid	33.14 (33.16)	2.74 (2.78)	24.18 (24.17)
7e	C_2H_5	CH_3	168-170 (99)	$C_8H_7Cl_2N_5S_2$ (308.21)	Yellow Amorphous solid	31.18 (31.18)	2.28 (2.29)	22.69 (22.72)
7f	C_2H_5	C_2H_5	148-150 (58)	$C_{10}H_{12}ClN_5OS_2$ (317.82)	Gray Amorphous solid	37.72 (37.79)	3.86 (3.81)	22.16 (22.04)
8a	H	4-CH_3	168-170 (63)	$C_{13}H_{10}ClN_5OS_2$ (351.83)	Gray Amorphous solid	44.62 (44.38)	2.96 (2.86)	19.82 (19.91)
8b	H	4-Cl	168-170 (98)	$C_{12}H_7Cl_2N_5OS_2$ (372.25)	Gray Amorphous solid	38.69 (38.72)	1.94 (1.90)	18.88 (18.81)
8c	H	2,4-Cl_2	158-160 (97)	$C_{12}H_6Cl_3N_5OS_2$ (406.70)	Yellow Amorphous solid	35.48 (35.44)	1.52 (1.49)	17.28 (17.22)
8d	C_2H_5	H	178-180 (31)	$C_{14}H_{12}ClN_5OS_2$ (365.86)	Gray Amorphous solid	45.84 (45.96)	3.36 (3.31)	19.08 (19.14)
8e	C_2H_5	2,4-Cl_2	198-200 (61)	$C_{14}H_{10}Cl_3N_5OS_2$ (434.75)	Gray Amorphous solid	36.62 (38.68)	2.44 (2.32)	16.24 (16.11)

Table 3. Characterization data of S-substituted Schiff bases **9**a-h and **10**a-d

Compd. No.	R	Ar/R_3	M.p (^oC) (Yield %)	Molecular formula (Mol. Wt.)	Colour and Crystal nature	Elemental analysis found (Calculated) (%)		
						C	H	N
9a	H	4-CH_3 C_6H_4	186-188 (99)	$C_{15}H_{11}Cl_2N_5OS_2$ (412.32)	White Amorphous solid	43.58 (43.69)	2.72 (2.69)	17.04 (16.99)
9b	H	4-Cl C_6H_4	178-180 (73)	$C_{14}H_8Cl_3N_5OS_2$ (432.74)	White Amorphous solid	38.92 (38.86)	1.88 (1.86)	16.06 (16.18)
9c	H	4-F C_6H_4	128-130 (89)	$C_{14}H_8Cl_2FN_5OS_2$ (416.28)	Yellow Amorphous solid	40.36 (40.39)	1.98 (1.94)	16.84 (16.82)
9d	H	4-OCH_3 C_6H_4	178-180 (94)	$C_{15}H_{11}Cl_2N_5O_2S_2$ (428.32)	White Amorphous solid	42.12 (42.06)	2.64 (2.59)	16.38 (16.35)
9e	C_2H_5	4-Cl C_6H_4	118-120 (52)	$C_{16}H_{12}Cl_3N_5OS_2$ (460.79)	Pale yellow Amorphous solid	41.76 (41.70)	2.60 (2.62)	15.24 (15.20)
9f	C_2H_5	4-F C_6H_4	80-82 (65)	$C_{16}H_{12}Cl_2FN_5OS_2$ (444.33)	Yellow Amorphous solid	43.32 (4325)	2.76 (2.72)	15.73 (15.76)
9g	C_2H_5	4-CH_3 C_6H_4	189-191 (56)	$C_{17}H_{15}Cl_2N_5OS_2$ (440.37)	White Amorphous solid	46.32 (45.37)	3.48 (3.43)	15.96 (15.90)
9h	C_2H_5	4-OCH_3 C_6H_4	80-82 (52)	$C_{17}H_{15}Cl_2N_5O_2S_2$ (456.37)	Pale yellow Amorphous solid	44.69 (44.74)	3.38 (3.31)	15.42 (15.35)
10a	H	6-CH_3	178-180 (98)	$C_{17}H_{11}Cl_2N_5O_2S_2$ (452.34)	Gray Amorphous solid	45.16 (45.14)	247 (2.45)	15.44 (15.48)
10b	C_2H_5	6-CH_3	187-189 (88)	$C_{19}H_{15}Cl_2N_5O_2S_2$ (480.39)	White Amorphous solid	47.48 (47.50)	3.18 (3.15)	14.52 (14.58)
10c	C_2H_5	Benzo[h]	188-190 (85)	$C_{22}H_{15}Cl_2N_5O_2S_2$ (516.42)	White Amorphous solid	51.12 (51.17)	2.98 (2.93)	13.64 (13.56)
10d	H	Benzo[h]	168-170 (92)	$C_{20}H_{11}Cl_2N_5O_2S_2$ (488.37)	White Amorphous solid	49.04 (49.19)	2.34 (2.27)	14.42 (14.34)

Antibacterial activity: Agar well diffusion method was used for antibacterial activity evaluation. The results (Table 4) showed that compound 6a had greater antibacterial activity than standard Streptomycin against *S. aureus* and *E.coli*. Similarly, compound 7e showed significant activity against *Staphylococus aureus* and *C. violaceum*, while compound 9f displayed promising activity against *C.*

violaceum. The substitution of the chlorine atom in compound 6a with alcohols/phenols to give compound 7a, 7b, 7e/8a, 8b, 8c resulted in a decrease in activity against all tested bacterial stains. Similarly, S-alkylation reaction of this compound 6a to give compound 9a-d and 10a, 10d, decreased the activity against all tested bacterial strains. These observations prove the need of such chlorine atom at the 2nd positions of thiazole ring and free NH/SH in compound 6a for its activity against all tested bacterial strains. However, the same substitution reaction of the chlorine atom or SH group in compound 6c caused the variation in activity for *S aureus* and *C. violaceum*, while they have decreased or caused the complete loss of activity against *E. fcecalis* and *E. coli*.

Table 4. Antibacterial activity data of compounds 6a-c/7a-f/8a-c/9a-h and 10a-d

Compd. No.	Diameter zone of inhibition (mm) at 1mg mL^{-1}			
	Gram-positive bacteria		Gram-negative bacteria	
	S. aureus (MTCC 9760)	*E. faecalis* (MTCC 2729)	*C. violaceum* (MTCC 2656)	*E. coli* (MTCC 443)
6a	31	12	22	12
6b	15	-	15	09
6c	13	11	16	11
7a	14	-	08	09
7b	15	-	14	10
7c	13	-	12	-
7d	11	-	13	08
7e	21	-	18	09
7f	13	-	17	-
8a	09	11	13	-
8b	13	-	15	09
8c	09	-	15	10
8d	14	-	15	10
8e	14	-	13	-
9a	10	-	10	-
9b	14	-	11	-
9c	15	12	10	-
9d	18	-	12	09
9e	11	-	09	-
9f	09	-	24	-
9g	09	-	10	-
9h	10	-	17	-
10a	09	-	10	-
10b	14	-	13	-
10c	13	-	18	-
10d	15	-	13	-
Streptomycin	27	20	27	11
DMSO	-	-	-	-

Antioxidant activity: The DPPH radical scavenging assay was used to investigate the antioxidant activities. The results **(**Table 5**)** showed that compounds **(**6a, 7a, 7b, 7d and 7e**)** exhibited good DPPH

Table 5. DPPH scavenging activity of compounds 6a-c/7a-f/8a-e/9a-h and 10a-d

Compd. No.	Percentage DPPH inhibition (%)	Compd. No.	Percentage DPPH inhibition (%)	Compd. No.	Percentage DPPH inhibition (%)
6a	50.3±0.60	8a	18.6±0.17	9e	08.3±0.12
6b	41.5±0.42	8b	37.7±0.36	9f	14.0±0.20
6c	34.4±0.38	8c	27.3±0.28	9g	08.3±0.14
7a	51.2±0.53	8d	26.1±0.20	9h	17.6±0.10
7b	55.8±0.58	8e	-	10a	-
7c	46.0±0.30	9a	-	10b	-
7d	58.4±0.64	9b	06.01±012	10c	-
7e	61.5±0.72	9c	16.8±0.16	10d	-
7f	32.0±0.28	9d	-	BHA	90.2±0.86

free radical scavenging activity comparable to the standard BHA. These results revealed the need of substitution of the chlorine atom at the 2nd position of thiazole moiety with either methoxy or ethoxy groups for enhancing the antioxidant activity. Further, this activity was in general decreased by the substitution of the same atom with bulkier groups such as phenol derivatives to give compound 8a-e and completely lost by nucleophilic substitution on SH groups to give compound 9 and 10 thereby indicating the necessity of free NH/SH group for antioxidant activity.

APPLICATION

The 1,2,4-triazole and its derivatives are of great interest due to their pharmacological properties. The synthesized compounds are checked whether they are active substrates or not for antibacterial, and antioxidant properties. Agar well diffusion method was used for antibacterial activity evaluation. The results (Table 4) above showed that compound 6a had greater antibacterial activity than standard Streptomycin against *S. aureus and E. coli.* Similarly, compound 7e showed significant activity against *Staphylococus aureus and C. violaceum*, while compound 9f displayed promising activity against *C. violaceum*.The DPPH radical scavenging assay was used to investigate the antioxidant activities. The results (Table 5)aboveshowed that compounds (6a, 7a, 7b, 7d & 7e) exhibited good DPPH free radical scavenging activity comparable to the standard BHA.

CONCLUSION

All the newly synthesized novel series of triazolyl Schiff bases bearing thiazole moiety and their s-derivatives have shown good antibacterial and antioxidant activity, when compared with the standard drug. Compound 6a showed greater antibacterial activity than standard *Streptomycin against S. aureus and E. coli.* Compounds 6a, 7a, 7b, 7d and 7e displayed good DPPH radical scavenging activity comparable to that of standard BHA.

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