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SYNTHESIS, PHARMACOLOGICAL EVALUATION AND COMPUTATIONAL STUDIES OF SOME NOVEL HYDRAZONE DERIVATIVES OF THIOPHENE CHALCONE AS ANTIMICROBIAL AND ANTIOXIDANT AGENTS

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ABSTRACT

The inevitable consequence of the widespread use of antimicrobial agents has been the emergence of antibiotic resistant pathogens, functioning an ever- increasing used for new drugs. In an effort to develop antimicrobial agents a series of hydrazones derivative of thiophene were synthesized from benzylidene hydrazine and various thiophene chalcones. Benzylidene hydrazine was reacted with various thiophene chalcones with varying substitution at benzaldehyde portion of chalcones in the presence of HCl and hydrazone derivatives were synthesized. The synthesized hydrazones were characterized on the basis of basis of physical, chemical tests and spectroscopic data and were evaluated for their antimicrobial activity against various bacterial and fungal strains using cup plate method using nutrient agar media and also for antioxidant activity using DPPH assay and Nitric oxide scavenging methods. Furthermore the assessment of structural similarity of the target compounds with various standard drugs was done. Evaluation of the compounds revealed remarkable antibacterial, antifungal and antioxidant activity.

Keywords: Hydrazone, Thiophene chalcones, Antimicrobial activity, Antioxidant activity, Computational studies.

1. INTRODUCTION

A dramatic increase in microbial infection and microorganisms resistant to multiple antimicrobial agents is a serious problem worldwide; especially gram positive bacteria which triggered a clear need for the discovery of new antibacterial rather than analogs of existing ones (Foroumadi et al., 2003; Papyne et al., 2004; Richet et al., 2001). Traditionally small molecules have been a reliable source for discovering novel biologically active compounds. Although a lot of work has been done on heterocycles, they remained an active area of research. Nitrogen and sulphur heterocyclic system families are very interesting due to their versatile pharmacological activities, such as antitumor, diuretics, fungicides, bactericides, antihelmintic, antiallergic, anti-ulcer and local analgesic (Kucukbay et al., 2004, 2003; Singh et al., 2000), especially in the sense of design of new drugs. Studies on thiophene and hydrazone like compounds have served as a feasible field of research in perusal of biologically active compounds. Hydrazones and molecules having hydrazide residues in their structures are capable of showing antifungal, antibacterial activities and in the treatment of tuberculosis infections (Abdel-Aziz, Abdel-Rahman, 2010; Banerjee et al., 2009).

On the other hand, an increasing interest in antioxidants, particularly in those intended to prevent the mischievous effects caused by free radicals in the human body is attracting one. The free radicals are also believed to be associated with carcinogenesis, mutagenesis, arthritis, diabetes, inflammation, cancer and genotoxicity (Buyukokuroglu et al., 2001; Kourounakis et al., 1999) due to oxidative stress, which arises as a result of imbalance between free radical generations. Thiophenes and hydrazones are also known to have considerable antioxidant activity and can be expressed by means of various *in vitro* models (Kumar et al., 2006; Padmashali, 2005).

Thus hydrazones of thiophene chalcone analogs might have antibacterial, antifungal and antioxidant activity. To test this idea we have synthesized 2-Benzylidene-1-(3-(4-substituted-phenyl)-1-(thiophen-2-yl) allylidene) hydrazine analogues [**TS1-TS6]** by reactions of benzylidene hydrazine [**6]** to thiophene chalcones [**3a-f]** in presence of acid and investigated in-vitro antibacterial, antifungal and antioxidant activities of synthesized compounds.

2. EXPERIMENTAL

2.1 Materials and Methods

All the reagents and chemicals were purchased from commercial sources (Thomas baker, Spectro chem, Lobe chemie etc.) Melting point of newly synthesized compounds was determined on Digital melting point apparatus and were found uncorrected. The solubility of synthesized compounds was tested in various solvents. IR spectra were recorded on a BRUKER ATR spectrometer. ^{1}H NMR spectra were measured in $CDCl_3$ and recorded on Bruker ADVANCE II 400 MHz NMR spectrometer. The λ_{max} was calculated by using UV-

Visible 1800 Shimadzu spectrophotometer. The progress of the reaction was monitored by thin layer chromatography (TLC) and spots were visualized in UV chamber.

2.2 Synthesis

2.2.1 General procedure for the synthesis of 3-(4-substitutedphenyl)-1-(thiophen-2-yl) prop-2-en-1-one [3a-3f] (Kalirajan et al., 2009)

To a solution of 2-acetylthiophene (0.015 mol, 1.71 ml) **[1]** in ethanol, 5ml 5% KOH was added dropwise with continuous stirring on an ice bath. To this equimolar amount of benzaldehyde **[2a]** or 4-nitrobenzaldehyde **[2b]** or 4-methoxybenzaldehyde **[2c]** or 4-methylbenzaldehyde **[2d]** or 4-cyanobenzaldehyde **[2e]** or 4-fluorobenzaldehyde **[2f]** was added dropwise and the mixture was stirred until it became cloudy. Then the mixture was poured slowly into 400 ml of ice water, the crude solid so obtained was filtered, washed with water, dried and purified by recrystallizing them from suitable solvents.

2.2.2 General procedure for the synthesis of 1-benzylidenehydrazine [6]

A mixture of benzaldehyde (0.04 mol, 4.28 ml) **[4]** and hydrazine hydrate (0.03 mol, 1.265 ml) **[5]** in ethanol in 250 ml round bottom flask was stirred on an ice bath, until it became cloudy. Then the mixture was poured slowly into 400 ml of ice water, the crude solid so obtained was filtered, washed with water, dried and purified by recrystallizing them from ethanol.

2.2.3 General procedure for the synthesis of 2-benzylidene-1-(3-(4-substituted- phenyl)-1-(thiophen-2-yl) allylidene) hydrazine analogues [TS_1-TS_6]

To a solution of 1-benzylidenehydrazine **[6]** in rectified spirit, compound **[3a or 3b or 3c or 3d or 3e or 3f]**, few drops of HCl was added and it was heated under reflux for 8 hours. The progress of the reaction was monitored by TLC. The solid formed after cooling was filtered off, dried and subjected to column chromatography with ethyl acetate/hexane and finally recrystallized by using suitable solvents.

a) 2-benzylidene-1-[(E)-3-phenyl-1-(thiophen-2-yl) allylidene] hydrazine [TS_1]

White powder (from ethanol), Yield: 82.14 %, M.pt. 236 ±2 ºC; IR (ν cm^{-1}): 1584.21 (C=N-N=C) ^{1}HNMR (400 MHz, $CDCl_3$, δ ppm): 8.27 (s, 1H CH=N), 7.88 and 7.24 (d, 1H CH),7.43 and 7.30 (d, 2H, Ar-H), 7.19 (d, 1H, C_4H_3S), 7.11 and 7.02 (t, 1H, C_6H_5), 7.10 and 7.10 (t, 2H, C_6H_5), 6.87 (t, 1H, C_4H_3S).

b) Synthesis of 2-benzylidene-1-[(E)-3-(4-nitrophenyl)-1-(thiophen-2-yl) allylidene] hydrazine [TS_2]

Pale yellow powder (from ethanol), Yield: 85.00 %, M.pt. 317±2 ºC; IR (ν cm^{-1}): 1528.96 (C=N-N=C), 1578.19 (Ar-NO_2); ^{1}HNMR (400 MHz, $CDCl_3$, δ ppm): 8.27 (s, 1H CH=N), 7.88 and 7.24 (d, 1H CH),7.43 and 7.30 (d, 2H, Ar-H), 7.19 (d, 1H, C_4H_3S), 7.11 and 7.02 (t, 1H, C_6H_5), 7.10 and 7.10 (t, 2H, C_6H_5), 6.87 (t, 1H, C_4H_3S).

c) Synthesis of 2-benzylidene-1-[(E)-3-(4-methoxyphenyl)-1-(thiophen-2-yl) allylidene] hydrazine [TS_3]

Yellow crystals (from methanol), Yield: 80.52 %, M.pt. 325±2 ºC; IR (ν cm^{-1}): 1515.11 (C=N-N=C), 1237.43 (OCH_3); ^{1}HNMR (400 MHz, $CDCl_3$, δ ppm): 8.13 (s, 1H CH=N), 7.82 and 7.12 (d, 1H CH),7.46 and 7.30 (d, 2H, Ar-H), 7.28 and 7.21(d, 1H, C_4H_3S), 7.12 (t, 1H, C_6H_5), 7.07 (t, 2H, C_6H_5), 6.60 (t, 1H, C_4H_3S), 6.60 (d, 2H, C_6H_5), 3.39 (s, 3H, OCH_3).

d) Synthesis of 2-benzylidene-1-[(E)-3-(methylphenyl)-1-(thiophen-2-yl) allylidene] hydrazine [TS_4]

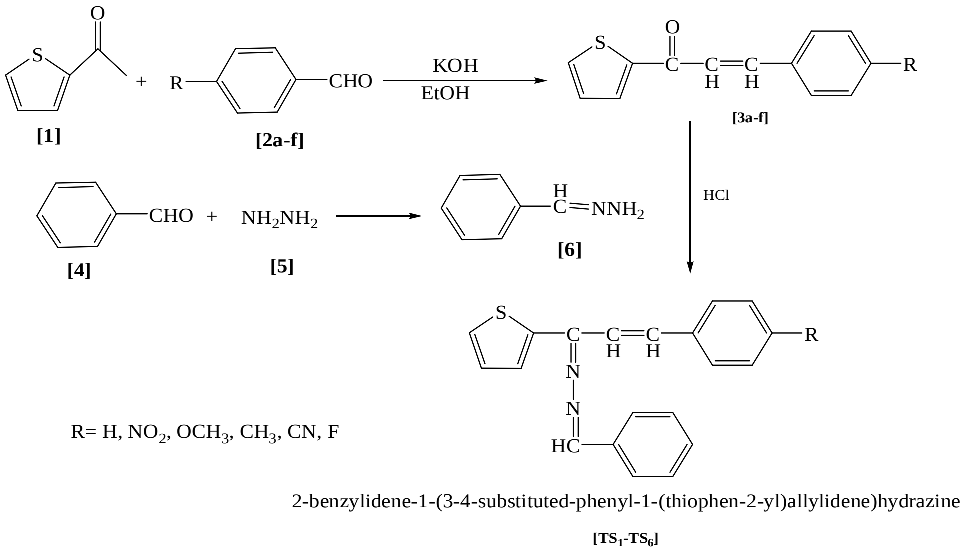
Off white powder (from ethanol), Yield: 75.36 %, M.pt. 283±2 ºC; IR (ν cm^{-1}): 1590.33 (C=N-N=C), 773.11 (CH_3); ^{1}HNMR (400 MHz, $CDCl_3$, δ ppm): 8.36 (s, 1H CH=N), 7.80 and 7.21 (d, 1H CH), 7.52 and 7.21 (d, 2H, Ar-H), 7.37 and 7.28 (d, 1H, C_4H_3S), 7.20 (t, 1H, C_6H_5), 7.19 (t, 2H, C_6H_5), 6.97 (t, 1H, C_4H_3S), 6.81 (d, 2H, C_6H_5), 2.13 (s, 3H, CH_3).

e) Synthesis of 2-benzylidene-1-[(E)-3-(cyanophenyl)-1-(thiophen-2-yl) allylidene] hydrazine [TS_5]

Pale yellow powder (from ethanol), Yield: 73.65 %, M.pt. 279±2 ºC; IR (ν cm^{-1}): 1519.50 (C=N-N=C), 1647.36 (C≡N); ^{1}HNMR (400 MHz, $CDCl_3$, δ ppm): 8.35 (s, 1H CH=N), 7.83 and 7.18 (d, 1H CH), 7.53, 7.45 and 7.29 (d, 2H, Ar-H), 7.33 and 7.24 (d, 1H, C_4H_3S), 7.17 (t, 1H, C_6H_5), 7.15 (t, 2H, C_6H_5), 6.96 (t, 1H, C_4H_3S).

f) Synthesis of 2-benzylidene-1-[(E)-3-(4-fluorophenyl)-1-(thiophen-2-yl) allylidene] hydrazine [TS_6]

White powder (from ethanol), Yield: 85.62 %, M.pt. 252±2 ºC; IR (ν cm^{-1}): 1532.65 (C=N-N=C), 1258.09 (C-F); ^{1}HNMR (400 MHz, $CDCl_3$, δ ppm): 8.24 (s, 1H CH=N), 7.71 and 7.09 (d, 1H CH), 7.42, 7.30 and 6.75 (d, 2H, Ar-H), 7.28 and 7.17 (d, 1H, C_4H_3S), 7.00 (t, 1H, C_6H_5), 6.96 (t, 2H, C_6H_5), 6.83 (t, 1H, C_4H_3S), 6.75 (d, 2H Ar-H).

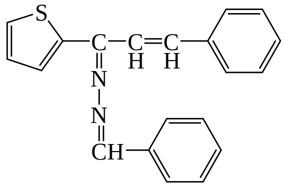
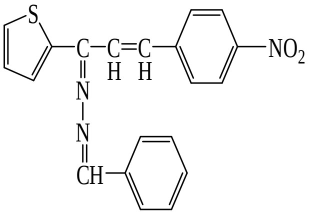
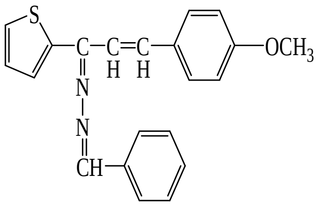


Scheme-1 Synthesis of 2-benzylidene-1-(3-(4-substituted-phenyl)-1-(thiophen-2-yl) allylidene) hydrazine analogues [TS_1-TS_6]

1.2.4 Physical Properties of Synthesized Compounds

Table 1 and 2 shows all the physical data like color, percentage yield, molecular formula, molecular weight, solubility, melting point, λ_{max}, R_f value of synthesized compounds.

Table-1 Physical data of various synthesized compounds

Compound	Chemical structure	Color	%age yield	Mol. Formula	Mol. weight
TS_1		White powder	82.14	$C_{20}H_{16}N_2S$	316.429
TS_2		Pale yellow powder	85.00	$C_{20}H_{15}N_3O_2S$	361.427
TS_3		Yellow crystals	80.52	$C_{21}H_{18}N_2OS$	346.456

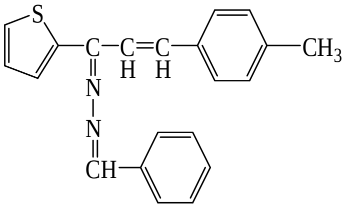
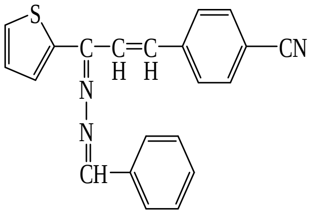
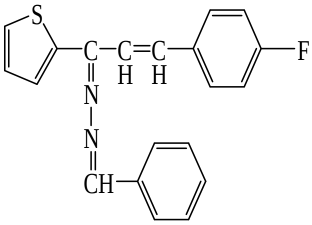
TS_4		Off white powder	75.36	$C_{21}H_{18}N_2S$	330.456
TS_5		Pale yellow powder	73.65	$C_{21}H_{15}N_3S$	341.439
TS_6		White powder	85.62	$C_{20}H_{15}FN_2S$	334.420

Table-2 Physical properties and UV-Visible analysis of various test compounds

Compound	Solubility	Melting point (°C)	λ_{max}	R_f value
TS_1	EtOH, MeOH, $CHCl_3$	236±2	253	0.45
TS_2	MeOH, $CHCl_3$	317±2	276	0.40
TS_3	EtOH, $CHCl_3$	325±2	240	0.60
TS_4	EtOH, MeOH, $CHCl_3$	283±2	248	0.56
TS_5	EtOH, MeOH, $CHCl_3$	279±2	237	0.31
TS_6	EtOH, MeOH, $CHCl_3$	252±2	269	0.43

TLC mobile phase- Ethyl acetate: Hexane (9:1)

3 PHARMACOLOGICAL EVALUATION

3.1 Antimicrobial activity

All the synthesized compounds were screened for their in-vitro antimicrobial activity against various bacterial strains; *Staphylococcus aureus, Streptococcus thermophilus* (Gram +ve bacteria) *Escherichia coli, Pseudomonas aeruginosa* (Gram –ve bacteria), fungal strain *Candida albicans* and yeast *Kluyveromyces marxianus* by Cup plate method using different concentrations (1600, 800, 400, 200, 100, 50, 25, 12.5, 6.5 µg/ml) of the test compounds. Ciprofloxacin (antibacterial) and Fluconazole (antifungal) was used as standards and DMF was used as control for all the strains. MIC (Minimum inhibitory concentration) was recorded for synthesized compounds as well as for standard and shown in Table-3 (IP, 1996; Panda, chowdary, 2008; Swamy, Agasimudin, 2008).

Table-3: Minimum inhibitory concentration (MIC) in µg/ml of synthesized compounds

Compound	**Minimum inhibitory concentration(MIC) in µg/ml**					
	EC	PA	SA	ST	CA	KM
TS1	50	21	31	42	10	25
TS2	200	50	20	28	35	100
TS3	12.5	28	12.5	15	50	25
TS4	25	30	25	12.5	20	12.5
TS5	50	100	50	19	12.5	50
TS6	100	30	38	37	45	100
Control	-	-	-	-	-	-
Fluconazole	-	-	-	-	12.5	6.25
Ciprofloxacin	6.25	12.5	6.25	6.25	-	-

EC- *Escherichia coli*; PA- *Pseudomonas aeruginosa*; SA- *Staphylococcus aureus*; ST- *Streptococcus thermophilus*; CA- *Candida albicans*; KM- *Kluyveromyces marxianus*

3.2 Antioxidant Activity

All the synthesized hydrazones are evaluated for their *in vitro* antioxidant activity by following methods

3.2.1 DPPH Assay

The anti-oxidant potential of any compound can be determined on the basis of its scavenging activity of the stable 1, 1-diphenyl-2-picryl hydrazyl (DPPH) free radical as described by Sadhu *et al* (Sadhu et al., 2003). DPPH is a stable free radical containing an odd electron in its structure and usually utilized for detection of the radical scavenging activity in chemical analysis. The aliquot of the different concentrations (5-500 µg/mL) of the test sample is added to 3 mL of a 0.004% ethanolic solution of DPPH. Absorbance at 517 nm is determined after incubation in dark for 30 min, and IC_{50} (Inhibitory concentration to scavenge 50% free radicals) is also determined. IC_{50} value denotes the concentration of sample required to scavenge 50% of the DPPH free radicals.

The equation used to measure free radical scavenging is:

$$\%DPPH\ Scavenging\ Activity = \frac{Control - Test}{Control} \times 100$$

The experiment is performed in triplicate and average absorption is noted for each concentration. Ascorbic acid is used as a positive control. Results are expressed as mean inhibitory concentration (IC_{50}). A lower value of IC_{50} indicates a higher free radical scavenging activity (Molyneux, 2004). % scavenging activity of the test compounds and standard are shown in Figure-1. Results are expressed as mean inhibitory concentration (IC_{50}) and shown in Table-4.

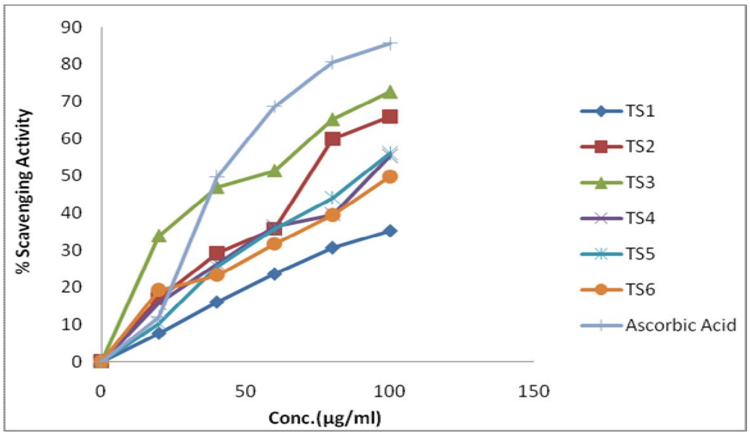


Figure-1 DPPH Radical Scavenging Activity of Test Compounds and Standard

3.2.2 Nitric Oxide Radical Scavenging Activity

Nitric oxide was generated from sodium nitroprusside and measured by the Greiss reaction according to the method of Marcocci. The chemical source of NO was sodium nitroprusside (5 mM) in 0.5 M phosphate buffer, pH 7.4, spontaneously generates nitric oxide in aqueous solution. Nitric oxide interacts with oxygen to produce stable products, leading to the production of nitrites (Marcocc et al., 1994).

About 1 ml sodium nitroprusside (5 mM) in 0.5 M phosphate buffer was mixed with 3.0 ml of different concentrations (20-100μg/ml) of the drugs dissolved in the suitable solvent systems and incubated at 25°C for 150min. Ascorbic acid was used as standard. The capability to scavenge the NO radical was calculated using the following equation

$$\%\ NO\ Scavenging\ Activity = \frac{Control - Test}{Control} \times 100$$

% scavenging activity of the test compounds is shown in Figure-2. Results are expressed as mean inhibitory concentration (IC_{50}) and shown in Table-4.

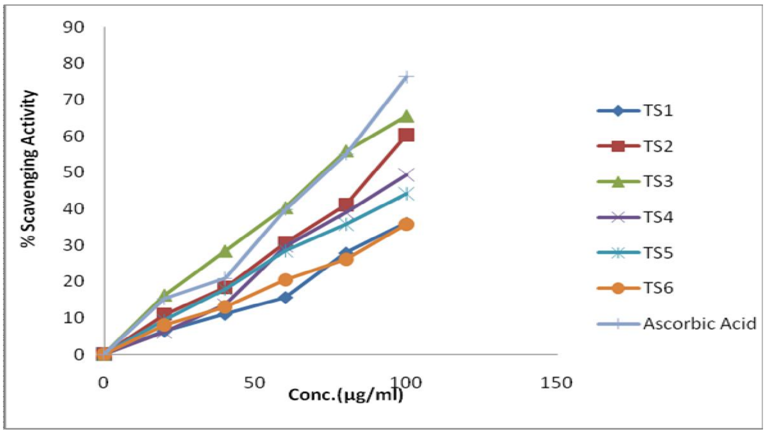


Figure-2 Nitric oxide scavenging activity of test compounds and standard

Table-4 IC_{50} (µg/ml) values of antioxidant activity of different synthesized compounds

Compound	**Nitric oxide scavenging activity (IC_{50} µg/ml)**	**DPPH Scavenging Activity (IC_{50} µg/ml)**
TS_1	129	150
TS_2	88	71
TS_3	70	52
TS_4	100	94
TS_5	110	88
TS_6	130	100
Ascorbic acid	70	40

3.3 Assessment of Structural Similarity of Target Compounds to Standard Drugs

Assessment of structural similarity of target compounds to standard drugs (Nikolova, 2003) involves the study of physiochemical and steric similarity between the standard drugs and new analogues designed. Assessment of structural similarity is a prerequisite for good spatial compatibility and effective binding to the site of action as lock and key model.

Several computational modules are available to predict molecular properties such as log P, polar surface area, molecular refractivity, ovality etc. this information can be related to prediction of biological activity for important drug targets. Therefore, we calculated a number of parameters for test compounds using Chem 3D ultra (version 8.0.3, Cambridge software) and compared them to the values obtained for standard compounds. The standard drugs used for assessment of similarity with target compounds are ticonazole, nifuroxazide (intestinal antiseptic), sertaconazole, pyridoxal salicyloyl hydrazone (antimycobacterial) and cefixime (Rollas, 2007; Singh et al., 1992). All the calculated parameters are given in Table-5.

The distance *di* of a particular target compound *i* could be presented according to the formula

$$di^2 = \sum_{j=1}^{n} \frac{(1 - X_{i,j}/X_{i,standard})^2}{n}$$

Where, $X_{i,j}$ is the value of molecular parameter *i* for compound *j*.

$X_{i,\,standard}$ is the value of same molecular parameter *i* for standard drug.

n is the total number of the considered molecular parameters.

Then the similarity of the compounds was calculated according to the formula

Similarity (%) = (1-R) × 100

Where R= quadratic mean (also known as the root mean square) and can be calculated as

$$\textbf{R}= \sqrt{di^2}$$

The %age similarity between test compound and standard drugs was given in Table-6.

Table -5: Calculation of Various Molecular Parameters of the Target Compounds

Compound	SAS[a]	MS[b]	SEV[c]	Ovality	MR[d]	MTI[e]	WI[f]	BI[g]	MW[h]	Log P
TS_1	566.478	303.62	250.305	1.58063	98.830	9182	1170	305884	304.418	4.8605
TS_2	601.753	325.329	269.737	1.61143	99.9	12482	1713	572204	349.410	4.7117
TS_3	607.67	328.894	275.436	1.60654	105.293	11612	1523	470214	334.444	4.7341
TS_4	597.153	322.626	267.175	1.60824	103.871	10475	1335	379995	318.445	5.3476
TS_5	596.175	320.087	263.579	1.61006	104.568	11759	1523	470214	329.428	4.8938
TS_6	574.102	307.661	253.953	1.58642	99.0465	9977	1335	379995	322.408	5.0186
Std.1	539.906	298.138	277.813	1.4479	97.2836	8131	1271	346539	387.718	4.2753
Std.2	616.258	346.62	319.63	1.53322	113.61	12978	1886	605751	437.779	5.5133
Std.3	484.294	243.229	188.922	1.52722	---	6563	981	272224	275.222	---
Std.4	530.952	281.057	236.329	1.52042	80.3531	8198	1156	387032	303.319	---
Std.5	650.956	361.159	337.033	1.54205	105.886	13778	2067	856808	427.505	---

Where,

[a] Connolly Solvent Accessible Surface Area	Std.1 - Ticonazole
[b] Connolly Molecular Surface Area	Std.2- Sertaconazole
[c] Connolly Solvent Excluded Volume	Std.3- Nifuroxazide
[d] Molar Refractivity	Std.4- Pyridoxal salicyloyl hydrazide
[e] Molecular Topological Index	Std.5- Cefoxitin
[f] Wiener Index	
[g] Balaben Index	
[h] Molecular Weight	

Table-6 %age Similarity of target compounds with standard drugs

Compound	Ticonazole (1-R)100	Sertaconazole (1-R)100	Nifuroxazide (1-R)100	Pyridoxal salicyloyl hydrazide (1-R)100	Cefoxitin (1-R)100
TS_1	89.18	74.29	65.63	88.88	61.77
TS_2	69.54	89.62	45.16	70.49	84.57
TS_3	78.96	74.45	56.77	73.51	80.28
TS_4	85.60	80.61	64.87	84.38	75.16
TS_5	74.79	83.36	57.50	78.06	79.71
TS_6	79.72	71.75	69.16	87.84	74.14

4. RESULTS AND DISCUSSION

Synthesis of hydrazone derivatives of thiophene chalcones (TS1-TS6) were carried out through base catalyzed claisen-schmidt condensation of 2-acetylthiophene with substituted benzaldehyde in ethanol using at room temperature. The chalcones were obtained in high yields (>80%). Followed by subsequent treatment of thiophene chalcones derivatives with benzylidene hydrazine in the presence of HCl yielded 2-Benzylidene-1-(3-(4-substituted-phenyl)-1-(thiophen-2-yl) allylidene) hydrazine derivatives (TS1-TS6). Which were purified by crystallization technique. The final yield of the derivatives was in the range of 75-86% (Table 1). The compounds have been characterized by UV, IR and ^{1}H-NMR.

Comparison of the compounds activity with that of standard antibiotic ciprofloxacin (for antibacterial activity) and fluconazole (for antibacterial activity) is effectively represented in the Table 3. Almost all compounds demonstrate the significant activity against all micro organisms, but only TS_1 was more active than fluconazole. While studying MIC against fungal strains, compound TS_5 was as active as fluconazole. TS_1 was most active against *C. albicans* as compared to any other bacterial and fungal strain. TS_1, TS_3, and TS_5 were moderately active against *K. marxianus*. TS_3 was least active against *C. albicans*. TS_1, TS_2 and TS_6 were more active against *P. aeruginosa* than *E. coli*. TS_2, TS_3, TS_4 and TS_5 were more active against *S. aureus* as compared to *P. aeruginosa*. TS_2, TS_6 were least active against *E. coli*. TS_3, TS_4 were most active against *S. thermophilus*. TS_4, TS_5, TS_6 were more active against *S. thermophilus* than *S. aureus*. It was found that compounds containing methyl and methoxy group were more active against all bacterial and fungal strains. Structure and biological activity relationship of these compounds showed that presence of electron donating group such as $–OCH_3$ and $–CH_3$ on aromatic ring enhanced the activity compared to unsubstituted aromatic ring.

While studying antioxidant activity by using DPPH method TS_2, TS_3 were the most active compounds (Table 4). TS_3 was as active as Ascorbic acid by NO method. TS_6 and TS_1 were least active compounds. TS_4 and TS_5 showed moderate antioxidant activity by both methods. While studying antioxidant activity by Nitric oxide scavenging method TS_2 and TS_3 were most active compounds. It was found that nitro and methoxy group enhanced the antioxidant activity of the synthesized compounds.

Assessment of structural similarities of target compounds with standard drugs showed that all compounds have good percentage similarity. All the synthesized compounds showed good structural similarity with ticonazole, sertaconazole and pyridoxal salicyloyl hydrazide as compared to other standard drugs. It was found that synthesized compounds have least similarity to nifuroxazide. Least structural similarity of target compounds to nifuroxazide was due to the absence of thiophene moiety in the standard compound.

5. CONCLUSION

We have synthesized new hydrazone derivatives from thiophene chalcone and evaluated for their antimicrobial (antibacterial and antifungal) activity and antioxidant activity. It has been found that the presence of methyl and methoxy group on phenyl group enhanced antimicrobial activity of the test compounds and the presence of nitro and methoxy group enhanced the antioxidant activity of the synthesized compounds. All the synthesized compounds showed good structural similarity with ticonazole, sertaconazole and pyridoxal salicyloyl hydrazide as compared to other standard drugs. It was found that synthesized compounds have least similarity to nifuroxazide.

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