Synthesis, Spectral Characterization and Pharmacological Screening of 1-methylene-4-(5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-yl)thiosemicarbazide Derivatives

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ABSTRACT: Recently a series of 1-methylene-4-(5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-yl) thiosemicarbazide derivatives were synthesized and their pharmacologically evaluated for antimicrobial activities. The purpose of this study was to evaluate the potency of the title compounds on bacterial and fungal activities by varying the substituted in the 1-methylene-4-(5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-yl)thiosemicarbazide derivatives. All compounds of this series showed promising antimicrobial activities. It was found that some of these compounds possess marked antifungal and antibacterial properties comparable in efficiency to the reference drug Flukanazole and Ciprofloxacin respectively. In present study the structures of compounds were confirmed by UV, IR, ^{1}H NMR.

Keywords: 1-methylene-4-(5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-yl) thiosemicarbazide derivatives; antibacterial agents; antifungal agents; *S. aureus; B. subtilis; E. coli; K. pneumoniae; C. albican; A. niger* and UV, IR, ^{1}H NMR spectroscopy.

INTRODUCTION

Antimicrobials reduce or completely block the growth and multiplication of bacteria. This has made them unique for the control of deadly infectious diseases caused by a variety of pathogens. The interesting properties of many of these heterocycles have increased the need for rapid syntheses of new, potentially useful sulfur-nitrogen heterocycles. They have transformed our ability to treat infectious diseases such as pneumonia, meningitis, tuberculosis, malaria and AIDS. Derivatives of 1-methylene-4-(5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-yl) thiosemi- carbazide condensed nucleus system found to have diverse pharmacological activities[1] such as fungicidal, insecticidal, bactericidal, herbicidal, anti-tumor[2], anti-inflammatory[3], CNS stimulant properties[4]. They also find applications as dyes, lubricants and analytical reagents[5], antiviral agents[6]. Examples of such compounds bearing the 1,3,4-thiadiazole moieties are a powerful azole antifungal agent[7]. Also, a number of 1,3,4-thiadiazoles showed antibacterial properties similar to those of well-known sulfonamide drugs[8]. The thiadiazole nucleus with N–C–S linkage exhibits a large number of biological activities[1]. Prompted by these findings and in continuation of our efforts in synthesizing various condensed bridge bioactive molecules, bearing multifunctional and pharmaceutically active groups[9-10], herein, we reported the synthesis and *in vitro* antimicrobial activity of 1-methylene-4-(5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-yl)thiosemicarbazide erivatives derivatives.

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CHEMISTRY

This study synthesized first step is represented by compounds (1) which displays an electron donating NH_2 group on phenyl ring and halogen in *para* position on benzoic acid. Found to normally employed to obtain bicyclic 4-(phenylamino) benzoic acid (1) in the presence of potassium carbonate and catalyse by copper in isoamyl alcohol solvent. Elimination of hydrogen Chloride under goes to the reaction Mechanism of Nucleophilic Aromatic Substitution reactions[11]. Cyclization of the further intermediate product was obtained in heating with polyphosphoric acid

in normal condition. The involved mechanism of reaction attack of Nucleophilic Addition Reaction[12] followed by dehydrocyclisation of the intermediate and tautomaric form to loss a water molecule to yield 5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-amine (2). Compound 4-(5-(4-(phenylamino) phenyl)-1,3,4-thiadiazol-2-yl)thiosemicarbazide (3) was synthesized by the conversion of the 5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-amine into their corresponding carbon disulphide in presence of alcoholic NaOH to obtain the sodium salts, followed by the addition of the hydrazine hydrate gives the thiosemicarbazide compound, which involved the reported reaction mechanism of Nucleophilic Addition Reaction[13]. The condensation of thiosemicarbazide with aromatic and heterocyclic aldehydes gave the title compounds 1-substituted-4-(5-(4-(phenylamino) phenyl)-1,3,4-thiadiazol-2-yl)thiosemicarbazide derivatives (4a–f). Reaction mechanism of this step undergoes to Nucleophilic Addition Reaction[14]. Substitution with a bulky group on diphenyl amine did result in a slight increase in activity. Unsubstitution of diphenylamine and substitution with a halogen entire the compound produced better lipophilicity and enhanced the antifungal activity[15]. Electron-withdrawing as well as electron-donating groups showed similar results. Carried out physico-Chemical and thermodynamic properties requirement of drug design, are shown in Table 2, 3.

MATERIALS AND METHODS

Preparation of 4-(phenylamino) benzoic Acid[16] (1)

This Reaction undergoes – Ullmann condensation: In a flat bottomed flask, mixture of *p*-chlorobenzoic acid 10 g (0.064 mol) aniline 5.84 ml (0.064 mol) and copper powder 0.2 g in 60 ml isoamylalcohol, dry potassium carbonate 10 g was slowly added and the contents were allowed to reflux for 6 h on an oil bath. After completion of reaction isoamylalcohol was removed by steam distillation and the mixture poured into 1: l of hot water and acidified with concentrated hydrochloric acid. Precipitate formed was filtered, washed with hot water and collected. The crude acid was dissolved in aqueous sodium hydroxide solution, boiled in the presence of activated charcoal and filtered. On acidification of the filtrate with concentrated hydrochloric acid, light yellowish precipitate was obtained which was washed with hot water and recrystallized from aqueous methanol to give a light yellow product, 80% yield, m.p. 183 °C.

Preparation of 5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-amine [17] (2)

In a ground mixture of the 4-(phenylamino)benzoic acid 5.54 g. (0.026 mol) and thiosemicarbazide 2.4 g. (0.026 mol) was added in portions over 0.5 h to polyphosphoric acid (10 times the weight of carboxylic acid) to vigorously stirred at 80-90 °C, the mixture was stirred at this temperature for 2-4 h. The mixture was kept at this temperature for a further 0.5 h and cooled, water/ice was added, and the mixture was finally basified with NH_3 (0.88 g/mL). The solids isolated by filtration were washed with water and air-dried to obtained slightly coffee colored solid and recrystallized by ethanol. It found 60% yield, m.p. 212 °C.

Preparation of 4-(5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-yl) thiosemicarbazide[18](3)

3.76 g (0.014 mol.) 5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-amine was taken in 15 ml of dimethyl formamide (DMF) in a flat bottem flask. To this sodium hydroxide (0.014 mol.), carbon disulphide (0.014 mol.) were added. The mixture was stirred at 15-20 °C for 1 h, to the stirred mixture was added hydrazine hydrate (0.014) mol and stirred continue for 1 h more at 60 °C. On adding water, a pale yellow solid separated out which was recrystallized from DMF- Ethanol. The pale yellow colored product obtained, yield 78%, melting point 251 °C.

Preparation of 1-benzylidene-4-(5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-l)thiosemicarbazide[19](4a)

In a dry flat bottom flask 3.42 g. 4-(5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-yl)thiosemicarbazide was taken in 35 ml of ethanol. This solution was added an equimolar quantity of the appropriate benzaldehyde in a small quantity of alcohol. Then added few drops of glacial acetic acid, stirring was done for 5 min. Immediate precipitation occurred and solid was filtered, dried and recrystallized from hot ethanol.

Preparation of 1-(2-hydroxybenzylidene)-4-(5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-yl)thiosemicarbazide (4b)

In a dry flat bottom flask 3.42 g. 4-(5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-yl)thiosemicarbazide was taken in 35 ml of

ethanol. This solution was added an equimolar quantity of the appropriate *o*-hydroxybenzaldehyde in a small quantity of alcohol. Then added few drops of glacial acetic acid, stirring was done for 2 min. Immediate precipitation occurred and solid was filtered, dried and recrystallized from hot ethanol.

Preparation of 1-(*p*-chlorobenzylidene)-4-(5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-yl)thiosemicarbazide (4c)

In a dry flat bottom flask 3.42 g. 4-(5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-yl)thiosemicarbazide was taken in 35 ml of ethanol. This solution was added an equimolar quantity of the appropriate *p*-Chlorobenzaldehyde in a small quantity of alcohol. Then added few drops of glacial acetic acid, Stirring was done for 10 min. Immediate precipitation occurred and solid was filtered, dried and recrystallized from hot ethanol.

Preparation of 1-(*p*-(dimethylamino) benzylidene)-4-(5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-yl)thiosemicarbazide (4d)

In a dry flat bottom flask 3.42 g. 4-(5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-yl)thiosemicarbazide was taken in 35 ml of ethanol. This solution was added an equimolar quantity of the appropriate *p*-(dimethylamino) benzaldehyde in a small quantity of alcohol. Then add few drops of glacial acetic acid, stirring was done for 4 min. Immediate precipitation occurred and solid was filtered, dried and recrystallized from hot ethanol.

Preparation of 1-(3-phenylallylidene)-4-(5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-yl)thiosemicarbazide (4e)

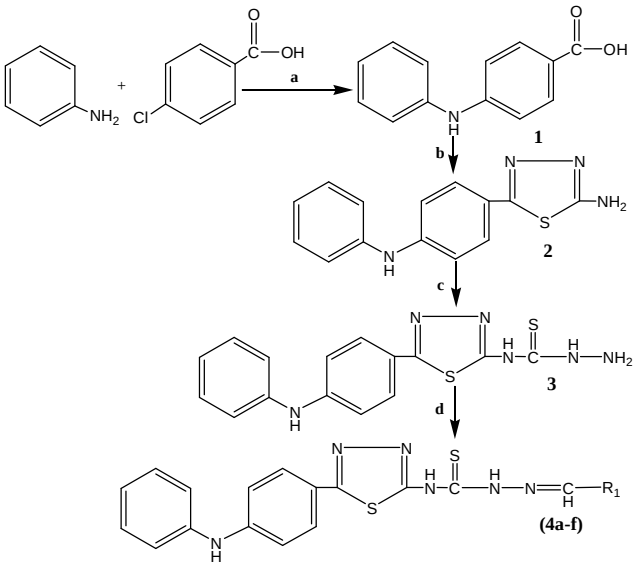
In a dry flat bottom flask 3.42 g. 4-(5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-yl)thiosemicarbazide was taken in 35 ml of ethanol. This solution was added an equimolar quantity of the appropriate cinnamaldehyde in a small quantity of alcohol. Then added few drops of glacial acetic acid, stirring was done 2-4 min. Immediate precipitation occurred and solid was filtered, dried and recrystallized from hot ethanol.

Preparation of 1-((furan-2-yl)methylene)-4-(5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-yl)thiosemicarbazide (4f)

In a dry flat bottom flask 3.42 g. 4-(5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-yl)thiosemicarbazide was taken in 35 ml of ethanol. This solution was added an equimolar quantity of the appropriate furfuraldehyde in a small quantity of alcohol. Then added few drops of glacial acetic acid, stirring was done for 8 min. Immediate precipitation occurred and solid was filtered, dried and recrystallized from hot ethane. The scheme of synthesized compounds was given in Figure 1.

Characterization of the Synthesized Compounds

The 1-methylene-4-(5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-yl)thiosemi- carbazide derivatives (4a-f) were synthesized by the reaction between substituted of 5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-amine and aromatic and heterocycle aldehydes (a-f). All melting points (m.p.) were determined in open capillary method using Jindal melting point apparatus and were uncorrected. The purity of the compounds was routinely checked by thin layer chromatography (TLC) using silica gel G (Merck). The instruments used for spectroscopic data are FTIR: Bruker tensor-27 spectrophotometer (ATR) with diffuse reflectance method. H^1NMR: JEOL GSX-400, 60MHz spectrometer in $CDCl_3$, TMS (tetra methyl



R_1= -C_6H_5, -C_6H_4-OH, p-C_6H_4-Cl, p-C_6H_4-$N(CH_3)_2$, -CH=CH-C_6H_5, -C_4H_3O*
Furan*

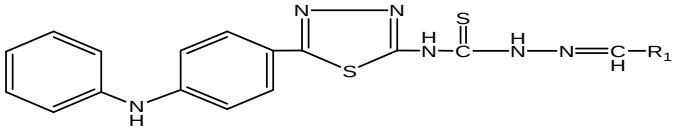
Figure 1: Graphical abstract of synthesized title compounds. (a) Cu, K_2CO_3, Isoamyl alcohol, Reflux 6-7 h. (b) PPA, $NH_2CSNHNH_2$, Cyclization, 1-2 h. (c) NaOH, DMF, CS_2, $NH_2NH_2.H_2O$, 60 °C. (d) Aromatic aldehydes, Few drops CH_3COOH, C_2H_5OH

saline) as an internal standard. H[1]NMR, and IR spectra were consistent with the assigned structure. The results obtained which are shown in Table 1 indicates, 1-methylene-4-(5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-yl)thiosemicarbazide derivatives (4a-f) were synthesized under conventional method. All compounds were conformed to the structures envisaged. Thermodynamics properties, physicochemical properties and constant are given Table 2, 3 and 3D structure of synthesized title compounds are shown fig. 2.

Table 1
Characterization of Synthesized Compounds

Comp. name	*Spectroscopic data*
4a	**IR ATR(cm^{-1})**= 3340(N-H), 304(Ar.C-H), 2910(Ali-C-H), 1576(C=N), 1667 (C-N), 1497(N-N), 104(C=S); **^{1}H-NMR (DMSO-*d*6, δ ppm):** 2.5(s, 2H, NH), 6.6-6.8(m, 9H, CH, Ar-H, diphenylamine), 7.0-7.8(m, 5H, CH, Ar-H, C_6H_5); **Electron absorption spectra (UV)** $\lambda_{max,}$ 296.76(methanol).
4b	**IR ATR(cm^{-1})**= 3390(N-H), 3105(Ar.C-H), 2878 (Ali-C-H), 1560(C=N), 1650 (C-N), 1524(N-N), 1214(C-S); **^{1}H-NMR (DMSO-*d*6, δ ppm):** 2.1(s, 2H, NH), 2.6(s, 1H, Ar-OH), 6.8-6.99(m, 9H,CH, Ar-H, diphenylamine), 7.0-7.8(m,4H,Ar-H,C_6H_4), 8.0-8.7(s,1H,CH, α- to C_6H_4-OH); **Electron absorption spectra (UV)** λ_{max} 328 (methanol).
4c	**IR ATR(cm^{-1})**= 3420 (N-H), 3020(Ar-C-H), 2915(Ali-C-H), 1720(C=N), 1570 (C-N), 1645(Ar-C=C), 1440(N-N), 1210(C-S), 1095(Ar. C-Cl); **^{1}H-NMR (DMSO-*d*6, δ ppm):** 2.5(s, 2H, NH), 2.5-2.8(t, 3H, $N(CH_3)_2$), 6.6-6.8(m, 9H,CH, Ar-H, diphenylamine); **Electron absorption spectra (UV)** λ_{max} 334.6 (methanol).
4d	**IR ATR(cm^{-1})**= 3420(N-H), 3000(Ar-CH), 2950(Ali-C-H), 1540(C=N), 1540 (C-N), 1550(N-N), 1210(C-S), **^{1}H-NMR (DMSO-*d*6, δ ppm):** 2.1(t, 3H, CH_3, Aliph-H, dimethylamine), 2.4(s, 1H, NH), 6.5-6.9(m, 9H,CH, Ar-H, diphenylamine), 7.2-7.4(m, Ar-CH, C_6H_4); **Electron absorption spectra (UV)** λ_{max} 315.8 (methanol).
4e	**IR ATR(cm^{-1})**= 3130(N-H), 3010(Ar-C-H), 2960(Ali-CH) 1660(C=N), 1580(C-N), 1510(Ar- C-C), 1515(N-N); **^{1}H-NMR (DMSO-*d*6, δ ppm):** 2.1(s, 1H, NH), 6.6(s, 1H, CH, Aliph.-H, α- to C_6H_5) 7.0-7.5(m, 9H, CH, Ar-H, diphenylamine); **Electron absorption spectra (UV)** λ_{max} 246.46 (methanol).
4f	**IR ATR(cm^{-1})**= 3240(N-H), 3060(Ar-C-H), 2910(CH_2), 1620(C=N), 1610 (C-N), 1540(Ar-C-C), 1540(N-N), 1486(C-O), 1210(C-S); **^{1}H-NMR (DMSO-*d*6, δ ppm):** 3.3(s, 1H, NH), 5.9(m, 3H, CH, heter.-H,furan) 6.5-6.9(m, 9H,CH, Ar-H, diphenylamine); **Electron absorption spectra (UV)** λ_{max} 326.6 (methanol).

Table 2
Physiochemical Properties of Synthesized Compounds



Com	*R*	*Molecular formula*	*Molecul weight*	*Melting Point(°C)*	*% yield*	*$R_f$value*
4a	$-C_6H_5$	$C_{22}H_{18}N_6S_2$	431	247	75	0.66
4b	*o*-C_6H_4-OH	$C_{22}H_{18}N_6OS_2$	447	237	72	0.61
4c	*p*-C_6H_4-Cl	$C_{22}H_{17}ClN_6S_2$	464.5	230	65	0.76
4d	*p*-C_6H_4-$N(CH_3)_2$	$C_{24}H_{23}N_7S_2$	474	259	82	0.72
4e	$-CH=CH-C_6H_5$	$C_{24}H_{20}N_6S_2$	457	211	80	0.69
4f	$-C_4H_3O$*	$C_{20}H_{16}N_6OS_2$	421	207	78	0.56

Table 3
Physicochemical and Thermodynamic Properties of the Title Compounds

Com.	*Log P*	*CLogP*	*Henry's Law*	*MR[cm3/mol]*	*Critical V [cm3/mol]*	*Heat of Form [kJ/mol]*	*Gibbs Energy [kJ/mol]*
4a	6.88	4.93699	6.3	128.86	715.5	504.84	712.93
4b	6.49	5.01199	6.3	130.68	771.5	463.73	712.6
4c	7.43	5.64999	6.3	133.47	789.5	331.51	617.4
4d	7.16	5.52899	6.3	144.04	775.5	478.33	691.37
4e	6.76	5.42099	6.3	138.91	782.5	512.3	726.3
4f	5.49	4.11299	6.3	121.38	786.5	486.52	711.9

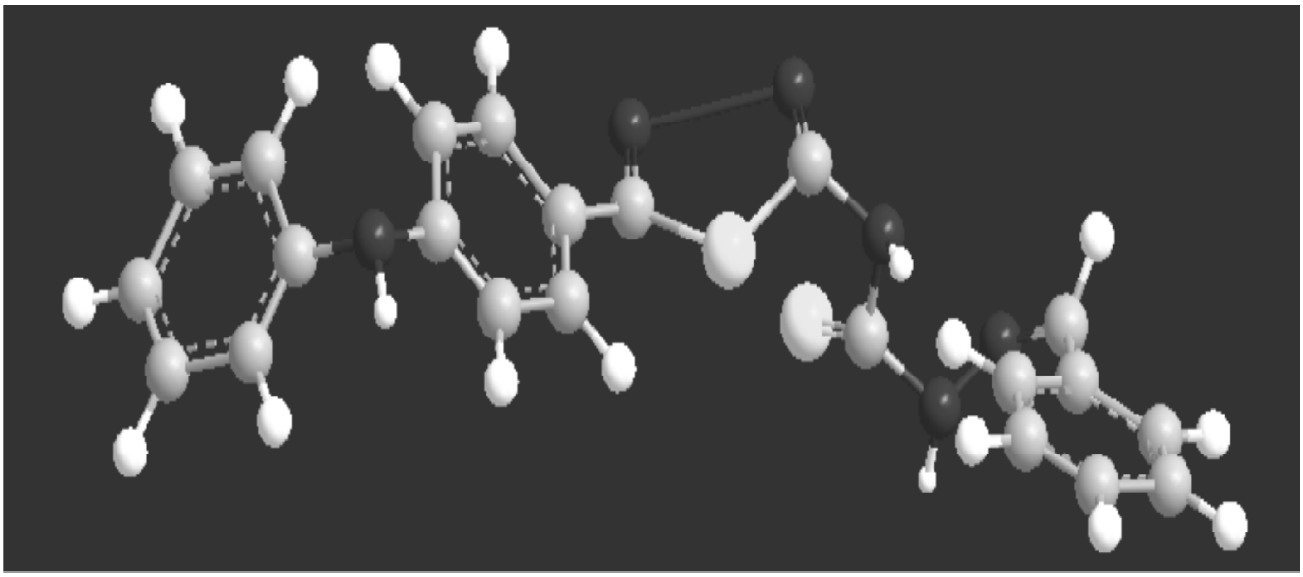


Figure 2: Three Dimension Structure of Title Compound with Energy Minima

BIOLOGICAL EVALUATION

Antimicrobial Activity [20-21]

In an approach to develop of new antimicrobial agents, synthesized 1-methylene-4-(5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-yl)thiosemicarbazide derivatives (4a–f). The *in vitro* antimicrobial activity of the synthesized compounds was screened by cup plate method against two gram positive bacteria viz. *Staphylococcus aureus* & *Bacillus subtilis* and two gram negative bacteria viz. *Escherichia coli, Klebsiella pneumoniae* and two pathogenic fungi *Candida albicans, Aspergillus niger*. The standard antibacterial agent used in the study was Ciprofloxacin, for the antifungal standard drug Fluconazole. Twenty five milliliter of molten nutrient agar [Sabouraud's Dextrose Agar (at pH 6.8)] was poured into pre sterilized Petri-dishes and allowed to solidify at room temperature. Broth cultures of the test microbial were used as inoculums under sterile conditions. Dimethyl formamide (DMF) was used as control and as solvent to prepare the stock solutions of the synthesized compounds. The concentration of the prepared stock solutions was 100µg / ml. Then 250 ìl of the stock solution was poured into each cup, the Petri dishes were incubated at 25 °C± 2 °C for 48 hours and were examined for zone of inhibition (in mm) and % inhibition, exhibited by the test and standard compounds, which is given in Tables 4, 5. The observed results were given in Figure 4.

Table 4
Results of *in vitro* Antibacterial Activity of the Synthesized Compounds 4a-f.

Comp.	*Gram + ve bacteria*				*Gram –ve bacteria*			
	S. aureus		*B. subtilis*		*E. coli*		*K. pneumoniae*	
	ZOI (mm)	*% Inhibition*	*ZOI (mm)*	*% Inhibition*	*ZOI (mm)*	*% Inhibition*	*ZOI (mm)*	*% Inhibition*
4a	05	21.73	06	28.57	12	52.17	15	65.21
4b	03	13.04	08	38.09	08	34.78	15	65.21
4c	12	52.17	06	28.57	14	60.86	15	65.21
4d	06	26.08	06	28.57	08	34.78	11	47.82
4e	08	34.78	12	57.14	10	43.47	13	56.52
4f	06	26.08	06	28.57	16	69.56	09	39.13
Standard (Ciprofloxacin)	23	100.00	21	100.00	23	100.00	23	100.00

Table 5
Results of in vitro Antifungal Activity of the Synthesized Compounds 4a-f.

Comp.	*A. niger*		*C. albicans*	
	Zone of Inhibition (mm)	*% Inhibition*	*Zone of Inhibition (mm)*	*% Inhibition*
4a	10	52.63	04	25.00
4b	12	63.15	06	37.50
4c	07	36.84	06	37.50
4d	13	68.42	17	106.25
4e	06	31.57	10	62.50
4f	09	47.36	16	100.00
Std (Fluco nazole)	19	100.00	16	100.00

RESULT AND DISCUSSION

Antimicrobial Activity

The research work was aimed to synthesized 1-methylene-4-(5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-yl)thiosemicarbazide derivatives (4a-f) by the reaction between 4-(5-(4-(phenylamino) phenyl)-1,3,4-thiadiazol-2-yl)thiosemicarbazide (3) and aromatic aldehydes. The *in vitro* antimicrobial activity of the synthesized compounds was evaluated by cup plate method for bacteria viz. *S. aureus, B. subtilis, E. coli, K. pneumoniae* and fungi *C. albicans, A. niger*. Some compounds exhibited potent pharmacological activities as compare to the standard drugs (Figure 3).

Most of the compounds showed less than moderate activity except the compounds 4c (52.17% inhibition) and 4e (57.14 % inhibition) against bacteria *S. aureus and B. subtilis* respectively. Compounds 4c (60.86% inhibition),

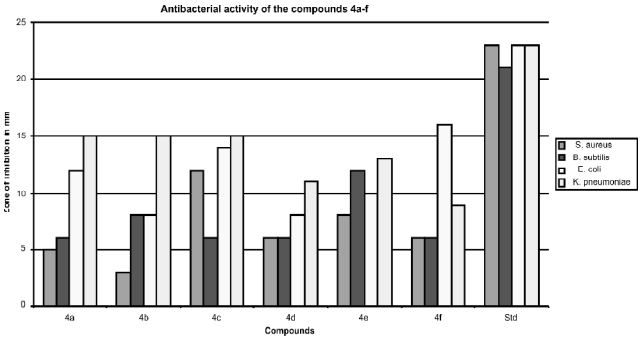


Figure 3: Comparison of the *in vitro* Antibacterial Activity Exhibited by the Test Compounds (4a-f) and Standard Drug Ciprofloxacin

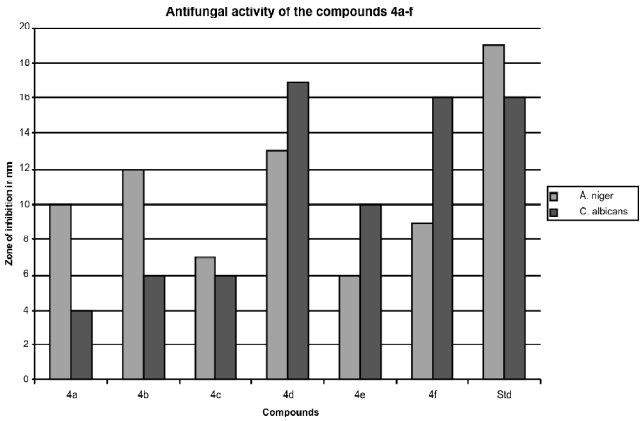


Figure 4: Comparison of the *in vitro* Antifungal Activity Exhibited by the Test Compounds (4a-f) and Standard Drug Fluconazole

4f (69.56% inhibition) and 4a, 4b, 4c (each 65.21% inhibition) showed excellent activity against bacteria *E. coli* and *K. pneumoniae* respectively compare with standard drug Ciprofloxacin. Some of them showed excellent activity, 4b(63.15% inhibition), 4d(68.42% inhibition) and 4e (62.50% inhibition) against fungal *A. niger* and *C. albicans* respectively. Compound 4d (106.25% inhibition) showed highest or more than standard drug and compound 4f (100.00% inhibition) showed equal activity to standard drug fluconazole against fungal *C. albicans*.

On the basis of above observation it was assumed that the presence of halogen on aromatic ring increased lipophilicity in the compound 4c produced moderate and excellent antibacterial activity against *S. aureus, E. coli* and *K. pneumoniae*. More number of hydrocarbon and unsaturation in the compound 4e exhibited moderate activity against *B. subtilis* and *K. pneumoniae*. Unsubstituted aromatic, *o*-hydroxy aromatic ring and *p*-Chloro aromatic ring in the compounds 4a, 4b and 4c showed excellent activity respectively against bacteria *K. pneumoniae*. Hydroxyl and dimethylamine groups on aromatic ring showed excellent antifungal activity for the compounds 4b and 4d against *A. niger*. Two heterocyclic rings in single molecules in compound 4f may enhance this activity equal to standard drug Fluconazole against *C. albicans*. Dimethylamine on para position of aromatic ring showed highest antifungal activity more than standard in compound 4d. Antimicrobial values are given in Tables 4, 5.

SUMMARY AND CONCLUSION

In summary, designed and synthesized a series of 1-methylene-4-(5-(4-(phenylamino)phenyl)-1,3,4-thiadiazol-2-yl)thiosemicarbazide derivatives (4a-f) and characterization of the synthesized compounds was carried out by determining their melting points, R_f value, UV, IR Spectra, ^{1}H-NMR and evaluated for *in-vitro* anti-microbial activities.

Among the synthesized compounds 4a, unsubstitution of phenyl ring showed excellent antibacterial activity against gramme negative bacteria. Substitution of halogen at para position on aromatic ring showed broad spectrum activity for the compound 4c. Compound 4d showed potent antifungal activity more than standard. Compound 4e showed equal potency against fungal strain.

It concluded compounds 4a, 4b, 4c and 4f showed potent inhibition against all the bacterial and fungal strains tested and found compounds 4f and 4d showed equal and more than equal potency comparison with standard. Further, the research on modification of the title compounds to understand the structure activity relationship and the mechanism of inhibition is underway.

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