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Synthesis, spectral LFER and antimicrobial activities of some (*E*)-*N′*-(1-(substituted phenyl)ethylidene) benzohydrazides

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About eleven substituted (*E*)-*N′*-(1-(substituted phenyl) ethylidene) benzo- hydrazides have been synthesized. They are characterized by their analytical, ultraviolet, infrared and NMR spectral data. The antibacterial and fungal activities of these hydrazides have been evaluated.

Keywords: (*E*)-*N′*-(1-(substituted phenyl)ethylidene)benzohydrazides, UV, IR and NMR spectra, antibacterial and antifungal activities.

1. INTRODUCTION

Nitrogen containing compounds are synthetically challenging models for a number of therapeutically significant products. Azole derivatives occupies a domain of interest in natural and synthetic chemistry. Diazoles are the central building blocks for synthesizing compound libraries in pharmaceutical and agrochemical industries. The organic and medicinal chemistry consists of design and synthesize molecules that possess potent therapeutic values. The rapid development of resistance to existing antimicrobial drugs generates a serious challenge to the scientific community. It is also interesting to note that the range of bioactivities involved is different substantially from those seems with the benzofused rings [1]. Schiff's bases are considered as a most important group of compounds in medicinal chemistry. The general method for the synthesis of (*E*)-*N*′-(1-(substituted phenyl)ethylidene)benzohydrazides is the reaction of benzo hydrazide with carbonyl compounds such as aldehydes or ketones in solvents like ethanol [2, 3] and so forth. The (*E*)-*N*′-(1-(substituted phenyl)ethylidene)benzohydrazides belong to the Schiff's base family containing azomethine –NHN=CH– protons and they are considered as the important class of compounds for the development of new drugs [4].

Hydrazide-hydrazone derivatives have been claimed to possess interesting bioactive potents such as anti-HIV [5], antimicrobial [6, 7], antidiabetic [8], leishmanicidal [7], antimalarial [8], antimycobacterial [9–12], anticancer [13, 14] anti-inflammatory [15, 16], antiparasitic [17], antiproliferative [18], trypanocidal [19], antitumor [20], analgesic [21], anticonvulsant [22] and antiviral [23] activities. Hence, the development of newer antimycobacterial agents is essential to overcome the rapidly developing drug resistance and side effects with high efficacy. The QSAR and QPR study of spectral data with Hammett equation is interesting to predicting the reactivity on specific functional groups in the aromatic compounds such as carbonyl, vinyl, acetyl, azo, azomethines [24–28].

This study is useful for ground state equilibration behavior of carbonyl and vinyl compounds through infrared spectra [24–28]. The spatial arrangement of vinyl and heterocyclic ring protons were confirmed by proton NMR spectra [29–32]. Recently Rajarajan et al. have studied the spectral correlation study of some (*E*)-1-benzylidene-2-(4-chlorophenyl)hydrazines [33]. Vijayakumar et al. have studied the spectral correlation analysis of some substituted(*E*)-2-benzylidene hydrazine-carbothio amides and observed satisfactory and good correlation coefficients in single and multi-parameter correlations [34].

Within the above view, there is no information available in literature in the past for synthesis, spectral correlation and antimicrobial activities of the titled compounds. Therefore the authors have taken efforts for the synthesis of (*E*)-*N*'-(1-(substituted phenyl)ethylidene)benzohydrazides to study the quantitative structure activity relationships by spectral correlation through Hammett equation with their UV, IR and NMR spectral data. Using Bauer-Kriby [35] disc diffusion method for evaluation of antimicrobial activities of synthesized (*E*)-*N'*-(1-(substituted phenyl)ethylidene)benzohydrazides .

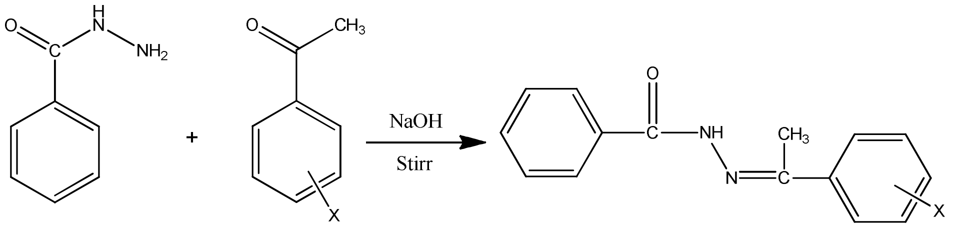
2. EXPERIMENTAL

2.1. Materials and methods

All chemicals used were purchased from Sigma-Aldrich chemical company Bangalore. Melting points of all chalcones have been determined in open glass capillaries on Suntex melting point apparatus and are uncorrected. The Ultra violet spectra of the chalcones synthesized have been recorded using ELICO-double beam BL222 Bio- Spectro-photometer. Infrared spectra (KBr, 4000–400 cm^{-1}) have been recorded on AVATAR-300 Fourier transform spectrophotometer. BRUKER-500MHz NMR spectrometers have been utilized for recording ^{1}H and ^{13}C spectra in $CDCl_3$ solvent using TMS as internal standard. The micro analysis of these hydrazides were performed in Thermofinnigan analyzer.

2.2. General procedure for synthesis of (E)-N'-(1-(substituted phenyl) ethylidene) benzohydrazides

Appropriate mixture of benzhydrazide (100 mmol) and *ortho, meta* and *para* substituted acetophenones (100 mmol) and aqueous solution of sodium hydroxide (20 cm^3 0.5M) with absolute ethanol (20 cm^3) (Scheme 1). The reaction mixture was vigorously stirred at room temperature for 30 minutes [24]. After complete conversion of the ketones as monitored by TLC, the mixture was allowed to stand 20 minutes. The reagents were removed by filtration. The filtrate was washed with distilled water and recrystallized from absolute ethanol, dried well and kept in a desiccator.



X = H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2

Scheme 1.

Table 1. Physical constants of substituted(*E*)-*N'*-(1-phenylethylidene)benzohydrazides

Entry	X	MF	MW	Yield [%]	Mp [°C]	Found (Calcd.) (%)		
						C	H	N
1	H	$C_{15}H_{14}N_2O$	238	90	141–142	75.54 (75.61)	5.90 (5.87)	11.69 (11.76)
2	4-Br	$C_{15}H_{13}BrN_2O$	316	89	146–147	56.78 (56.80)	4.10 (4.13)	8.79 (8.83)
3	4-F	$C_{15}H_{13}FN_2O$	256	91	139–140	70.27 (70.30)	5.08 (5.11)	10.88 (10.93)
4	2-OH	$C_{15}H_{14}N_2O_2$	254	90	134–135	70.88 (70.85)	5.48 (5.55)	10.97 (11.02)
5	3-OH	$C_{15}H_{14}N_2O_2$	254	87	119–120	70.88 (70.85)	5.51 (5.55)	10.98 (11.02)
6	4-OH	$C_{15}H_{14}N_2O_2$	254	96	168–169	70.78 (70.85)	5.50 (5.55)	10.96 (11.02)

cont. Table .1

7	4-I	$C_{15}H_{13}IN_2O$	364	99	182–183	48.98 (49.02)	3.55 (3.60)	7.62 (7.69)
8	4- OCH_3	$C_{16}H_{16}N_2O_2$	268	80	142–143	71.59 (71.62)	(5.96 (6.01)	10.38 (10.44)
9	4-CH_3	$C_{16}H_{16}N_2O$	252	91	138–139	76.19 (76.16)	6.27 (6.39)	11.08 (11.10)
10	3-NO_2	$C_{15}H_{13}N_3O_3$	283	93	108–109	63.54 (63.60)	4.59 (4.63)	14.76 (14.83)
11	4-NO_2	$C_{15}H_{13}N_3O_3$	283	94	136–137	63.52 (63.60)	4.58 (4.63)	14.78 (14.83)

Table 2. The ultraviolet absorption maxima (λ_{max}, nm), infrared absorptions (υ, cm^{-1}) and NMR chemical shifts (δ ppm) spectral data of substituted (*E*)-*N'*-(1-phenylethylidene)benzohydrazide compounds.

Entry	X	UV [nm]	IR ν [cm^{-1}]			^{1}H NMR [δ, ppm]		^{13}H NMR [δ, ppm]		
		λ_{max}	C=O	C=N	N-H	N-H	CH_3	C=O	C=N	CH_3
1	H	245.0	1645.28	1539.20	3452.58	8.966	1.698	163.26	168.72	13.50
2	4-Br	243.0	1651.07	1523.76	3277.06	8.368	1.623	162.84	165.42	12.76
3	4-F	247.0	1645.28	1543.05	3429.43	8.937	1.669	164.75	169.20	14.24
4	2-OH	245.0	1643.35	1537.27	3452.58	8.150	1.551	163.51	168.64	12.90
5	3-OH	216.0	1651.07	1535.34	3298.28	7.770	1.734	161.40	168.75	13.34
6	4-OH	215.0	1662.64	1517.98	3296.35	7.748	1.963	160.86	168.75	12.64
7	4-I	243.0	1664.57	1564.27	3296.35	7.882	1.255	163.64	168.72	14.54
8	4-OCH_3	242.0	1647.21	1529.55	3217.27	8.935	1.640	159.68	166.42	12.54
9	4-CH_3	248.0	1651.07	1521.84	3296.35	9.075	1.275	163.45	168.71	12.30
10	3-NO_2	247.0	1656.85	1519.91	3290.56	9.168	1.720	164.20	168.71	16.40
11	4-NO_2	246.0	1649.14	1523.76	3294.42	9.136	1.669	162.40	168.80	14.04

The synthesized (*E*)-*N'*-(1-(substituted phenyl) ethylidene) benzohydrazides have been characterized by their physical constants, elemental analysis and spectral data. The physical constants, analytical and micro analysis data of these (*E*)-*N'*-(1-(substituted phenyl) ethylidene) benzohydrazides were presented in Table 1. The spectral data of synthesized substituted(*E*)-*N'*-(1-phenylethylidene)benzohydrazides are presented in Table 2.

3. RESULTS AND DISCUSSION

3.1. Spectral linearity

In the present investigation, the spectral linearity of synthesized (*E*)-*N'*-(1-phenylethylidene) benzohydrazides has been studied by evaluating the substituent effects. The spectral data observed for the benzohydrazides, UV λ_{max} (nm), infrared νC=O, νC=N, νN-H, the proton chemical shifts δ(ppm) of N–H, CH_3 and carbon chemical shifts of C=O, C=N and CH_3 have been correlated with various Hammett substituent constants [25, 26, 27, 28].

3.2. UV spectral study

The measured absorption maxima (λ_{max} nm) values of the synthesized (*E*)-*N'*-(1-phenylethylidene)benzohydrazide compounds have been recorded and presented in Table 2. These data are correlated with Hammett substituent constants and *F* and *R* parameters using single and multi-linear regression analysis [25–28]. Hammett equation employed for the correlation analysis, involving the absorption maxima is as shown below in equation (1).

$$\lambda = \rho\sigma + \lambda o \tag{1}$$

where λo is the frequency for the parent member of the series.

From the Table 3, it is evident that the UV absorption maximum (λ_{max} nm) values of all substituted (*E*)-*N'*-(1-phenylethylidene)benzohydrazide compounds, have shown poor correlations (r < 0.900) with Hammett substituent constants and *F* and *R* parameters. This is attributed to the weak polar, inductive, field and resonance effects of substituents unable to predicting the reactivity on the UV absorption through electronic effect of substituents as per the conjugative structure as shown in Figure 1.

Table 3. The results of statistical analysis of ultraviolet absorption maxima ($\lambda_{max,}$ nm), infrared absorptions (v, cm^{-1}) and NMR chemical shifts (δ ppm) of substituted(E)-N'-(1-phenylethylidene)benzohydrazides with Hammett σ, σ^+, σ_I, σ_R and F and R parameters.

Frequency	Const.	R	I	ρ	S	n	Correlated derivatives
λ_{max}	σ	0.844	237.93	14.811	11.46	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.869	239.55	15.046	9.13	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3,3-NO_2, 4-NO_2
	σ_I	0.821	237.29	7.264	12.65	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.838	243.74	17.959	11.78	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.814	236.97	7.271	12.64	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.870	247.46	20.313	9.01	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
νCO	σ	0.805	1651.48	0.880	7.38	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3,4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.811	1651.61	–1.423	7.34	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3,4-CH_3, 3-NO_2, 4-NO_2

cont. Table 3.

	σ_I	0.819	1649.60	5.938	7.24	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH$_3$,4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ_R	0.802	1652.83	5.555	7.23	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH$_3$,4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	F	0.813	1650.38	3.184	7.34	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	R	0.808	1652.10	1.336	7.36	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
νC=N	σ	0.812	1532.91	–4.599	14.19	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ^+	0.805	1532.37	–1.427	14.27	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ_I	0.804	1533.15	–2.393	14.28	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ_R	0.802	1529.86	–11.140	13.96	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	F	0.801	1531.95	1.064	14.29	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	R	0.801	1530.53	–4.774	14.14	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$

cont. Table 3.

νN-H	σ	0.803	335.45	–66.853	79.41	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3,4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.828	3327.83	–39.724	79.98	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3,4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.813	3349.88	–67.246	81.74	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.822	3310.98	–73.335	80.91	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.808	3337.42	–26.483	83.12	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.804	3324.39	–7.845	83.32	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
δN-H	σ	0.900	8.453	0.858	0.51	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.906	8.549	0.689	0.45	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.814	8.462	0.284	0.60	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.905	8.827	1.206	0.51	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2

cont. Table 3.

	F	0.811	8.453	0.275	0.60	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.906	8.911	0.928	0.44	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
δCH_3	σ	0.800	1.617	0.001	0.21	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.801	1.618	–0.061	0.20	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.821	1.549	0.205	0.20	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3,4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.813	1.594	–0.102	0.20	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.822	1.541	0.200	0.21	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.821	1.572	–0.120	0.20	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
δCO	σ	0.821	162.61	0.903	1.56	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.818	162.72	0.491	1.57	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2

cont. Table 3.

	σ_I	0.824	162.20	1.568	1.55	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.821	163.07	1.573	1.54	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.795	162.04	1.796	1.53	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.841	163.29	1.496	1.45	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
δC=N	σ	0.804	168.28	–0.251		1.24 11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.802	168.26	–0.740	1.17	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.802	168.30	–0.144	1.25	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.804	168.30	0.191	1.24	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.805	168.14	0.286	1.24	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.803	168.21	–0.111	1.24	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2

cont. Table 3.

δCH_3	σ	0.907	13.28	2.337	2.59	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.905	13.55	1.067	2.59	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.906	12.40	3.449	2.49	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.905	14.08	2.350	2.25	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.906	12.39	3.092	2.45	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.904	14.02	1.204	2.33	11	H, 4-Br, 4-F, 2-OH, 3-OH, 4-OH, 4-I, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2

r = Correlation co-efficient; ρ = slope; I = Intercept; s = Standard deviation; n = Number of substituents.

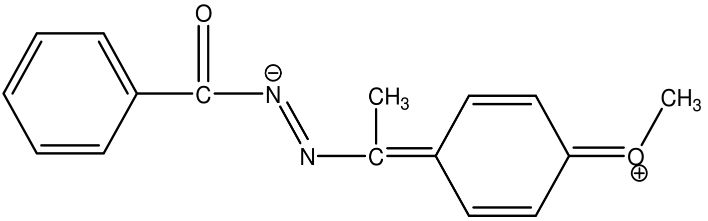


Figure 1. Resonance conjugative structure.

All the correlations have shown positive ρ values. This indicates the operation of normal substituent effects on UV absorption maximum (λ_{max} nm) values of all substituted (*E*)-*N'*-(1-phenylethylidene)benzohydrazide compounds. All single parameter correlations were failed for the UV absorption maximum (λ_{max} nm) values with Hammett constants and *F* and *R* parameter, it is decided to go for multi-regression analysis with Swain-Lupton's [36]. While seeking the multi regression analysis, there is a satisfactory correlations are observed as shown in the following equations (2) and (3).

$$\lambda_{max}\,(\text{nm}) = 242.94\,(\pm 8.475) + 92.067(\pm 17.554)\sigma I + + 17.470(\pm 15.655)\,\sigma_R \tag{2}$$

$$(r = 0.938,\ n = 11,\ P > 90\%)$$

$$\lambda_{max}\,(\text{nm}) = 246.09(\pm 6.409) + 3.394(\pm 12.538)F + + 20.100(\pm 7.149)\,R \tag{3}$$

$$(r = 0.971,\ n = 11,\ P > 95)$$

3.3. IR spectral study

The assigned infrared frequencies (cm^{-1}) of νC=O, νC=N, νN–H of substituted (*E*)-*N'*-(1-phenylethylidene)benzohydrazides are presented in Table 2. The measured infrared frequencies (cm^{-1}) were correlated [25, 26, 27, 28] with Hammett substituent constants and *F* and *R* parameters using single and multi-linear regression analysis. Hammett equation employed for the correlation analysis, involving the absorption maxima is as shown below in equation (4).

$$\upsilon = \rho\sigma + \upsilon_o \tag{4}$$

where υ_o is the frequency for the parent member of the series.

3.3.1. IR Spectral Correlation of υC=O (cm^{-1})

From the Table 3, it is evident that the IR frequency υC=O(cm^{-1}) values of all substituted (*E*)-*N’*-(1-phenylethylidene)benzohydrazide compounds have shown poor correlations ($r < 0.900$) with Hammett substituent constants and *F* and *R* parameters. This is attributed to the weak polar, inductive, field and resonance effects of substituents are incapable for predicting the reactivity on the υC=O(cm^{-1}) through electronic effects of substituents and it is associated with the conjugative structure as shown in Figure 1.

All correlations have shown positive ρ values except σ^+ constant. This indicates that the normal substituent effects operates in all substituted (*E*)-*N’*-(1-phenylethylidene)benzohydrazide compounds.

3.3.2. IR Spectral Correlation of υC=N (cm^{-1})

From the Table 3, it is evident that the IR frequency υC=N(cm^{-1}) values of all substituted (*E*)-*N’*-(1-phenylethylidene)benzohydrazide compounds have shown poor correlations ($r < 0.900$) with Hammett substituent constants and *F* and *R* parameters. This is attributed to the weak polar, inductive, field and resonance effects of substituents for predicting the reactivity on the IR frequency υC=N(cm^{-1}) through resonance as per the conjugative structure as shown in Figure 1.

All the correlations have shown negative ρ values. This indicates the operation of reverse substituent effect with respect to infrared υC=N(cm^{-1}) frequencies of all substituted (*E*)-*N’*-(1-phenylethylidene) benzohydrazide compounds.

3.3.3. IR Spectral Correlation of υN-H (cm^{-1})

From the Table 3, it is evident that the IR υN–H(cm^{-1}) frequencies of all substituted (*E*)-*N’*-(1-phenylethylidene)benzohydrazide compounds have shown poor correlations ($r < 0.900$) with Hammett substituent constants and *F* and *R* parameters. This is attributed to the weak polar, inductive, field and resonance effects of substituents for predicting the reactivity on the IR frequency υN–H(cm^{-1}) through resonance-conjugative structure as shown in Figure 1.

All the correlations have shown negative ρ values. This indicates the operation of reverse substituent effects by the electron donating substituents on IR υN–H(cm^{-1}) frequencies of all substituted (*E*)-*N’*-(1-phenylethylidene)benzohydrazide compounds.

All the single parameter correlations failed for the single parameter correlation of IR υC=O, υC=N and υN–H, (cm^{-1}) frequencies with Hammett constants and *F* and *R* parameters. Then the authors decided to go for multi-regression analysis with Swain-Lupton's [36] parameters. While seeking the multi regression analysis there is a satisfactory correlations have to be found and are shown in the following equations (5) and (10).

$$\nu CO(cm^{-1}) = 1651.05(\pm 5.146) + 4.610(\pm 10.659)\sigma_I + + 4.465(\pm 9.506)\,\sigma_R \tag{5}$$

(r = 0.925, n = 11, P > 90%)

$$\nu CO(cm^{-1}) = 1650.90(\pm 5.238) + 2.962(\pm 10.246)F + + 1.150(\pm 5.842)R \tag{6}$$

(r = 0.912, n = 11, P > 90%)

$$\nu C{=}N(cm^{-1}) = 1529.48(\pm 10.053) + 0.989(\pm 20.823)\sigma_I - - 11.374(\pm 18.571)\,\sigma_R \tag{7}$$

(r = 0.902 n = 11, P > 90%)

$$\nu C{=}N(cm^{-1}) = 1529.72(\pm 10.099) + 2.010(\pm 19.756)F - - 4.900(\pm 11.264)\,R \tag{8}$$

(r = 0.915, n = 11, P > 90%)

$$\nu N\text{-}H(cm^{-1}) = 3329.92(\pm 57.648) - 48.873(\pm 119.402)\sigma_I - - 61.773(\pm 106.491)\,\sigma_R \tag{9}$$

(r = 0.927, n = 11, P > 90%)

$$\nu N\text{-}H(cm^{-1}) = 334.582(\pm 59.372) - 25.275(\pm 116.143)F - - 6.260(\pm 66.223)\,R \tag{10}$$

(r = 0.908, n = 11, P > 90%)

3.4. NMR spectral study

In nuclear magnetic resonance spectra, the proton and the ^{13}C chemical shifts (δ) depends on the electronic environment of the nuclei concerned. The assigned chemical shifts (ppm) have been correlated with reactivity parameters using Hammett equation [25, 26, 27, 28] in the form of

$$\delta = \rho\sigma + \delta_o \tag{10}$$

where δ_o is the frequency for the parent member of the series.

3.4.1. ^{1}H NMR Spectral Correlation

3.4.1.1. ^{1}H NMR Spectral Correlations of N-H (ppm)

From the Table 3, the assigned N-H chemical shifts(δ ppm) values of (*E*)-*N'*-(1-phenylethylidene)benzohydrazide compounds have shown satisfactory correlations with Hammett substituent constants σ (r = 0.900), σ^+ (r = 0.906), σ_R (r = 0.905),), R parameter (r = 0.906). However, (δ ppm)^{1}H NMR values of(*E*)-*N'*-(1-phenylethylidene)benzohydrazide compounds have shown poor correlation (r < 0.900) with Hammett σ_I substituent constant and *F* parameter. The reason for the poor correlation is due to the incapability of weak field and +I and –I effects of substituents are unable to predict the reactivity on the proton chemical shifts (δ, ppm). Also this is associated with the resonance-conjugative structure as shown in Figure 1.

All the correlations have shown positive ρ values. This indicates the operation of normal substituent effects on the proton NMR chemical shifts(δ, ppm) of all substituted (*E*)-*N'*-(1-phenylethylidene)benzohydrazide compounds.

3.4.1.2. ^{1}H NMR Spectral Correlations of CH_3 (ppm)

From the Table 3, the assigned CH_3 proton chemical shifts (δ ppm) values of (*E*)-*N'*-(1-phenylethylidene)benzohydrazide compounds have shown poor correlations (r < 0.900) with Hammett substituent constants and *F* and *R* parameter. This due to the absence of electronic effects such as polar, inductive, field and resonance effects of substituents for predicting the reactivity on the CH_3 proton chemical shifts (δ ppm). The substituents effect of substituents are unable to dominates to the methyl proton chemical shifts(δ, ppm) by more than 4 or more carbon atoms of lengths and it is associated with resonance-conjugative structure as shown in Figure 1.

Some of the correlations have shown negative ρ values. This indicates the operation of reversal substituent effects by electron donating substituents on CH_3 proton chemical shifts(δ ppm) of all substituted (*E*)-*N'*-(1-phenylethylidene)benzohydrazide compounds.

Some of the single parameter correlations analyses have shown poor correlation coefficients with Hammett substituent constants and *F* and *R* parameter, then the authors have decided to go for multi regression analysis with Swain-Lupton's [36] parameters. While seeking the multi-regression analysis, there is a satisfactory correlation coefficients observed and are shown in the following equations (11) and (14).

$$\delta\text{N-H(ppm)} = 8.858(\pm0.368) - 0.080(\pm0.763)\sigma I + \\ + 1.225(\pm0.681)\ \sigma_R \tag{11}$$
$$(r = 0.954,\ n = 11,\ P > 90\%)$$

$$\delta\text{N-H(ppm)} = 8.871(\pm0.320) - 0.097(\pm0.627)\ F + \\ + 0.921(\pm0.357)R \tag{12}$$
$$(r = 0.967,\ n = 11,\ P > 95\%)$$

$$\delta\text{CH}_3\text{(ppm)} = 1.496(\pm0.145) + 0.253(\pm0.301)\sigma I - \\ - 0.162(\pm0.269)\sigma_R \tag{13}$$
$$(r = 0.931,\ n = 11,\ P > 95\%)$$

$$\delta\text{CH}_3\text{(ppm)} = 1.480(\pm0.141) + 0.226(\pm0.277)F - \\ - 0.134(\pm0.157)R \tag{14}$$
$$(r = 0.931,\ n = 11,\ P > 95\%)$$

3.4.2. ^{13}C NMR Spectral Correlation

3.4.2.1. ^{13}C NMR Spectral Correlations of C=O (ppm)

From the Table 3, the assigned ^{13}C NMR chemical shifts (δ ppm) of C=O carbons of (*E*)-*N'*-(1-phenyl ethylidene)benzohydrazide compounds have shown poor correlations (r < 0.900) with Hammett substituent constants and *F* and *R* parameter. This is attributed to the weak and absence of polar, inductive, field and resonance effects of substituents for predicting the reactivity and associated with the resonance-conjugative structure as shown in Figure 1.

All the correlations have shown positive ρ values. This indicates the operation of normal substituent effects with respect to ^{13}C NMR chemical shifts(δ ppm) of C=O carbons of all substituted (*E*)-*N'*-(1-phenylethylidene)benzohydrazide compounds.

3.4.2.2. ^{13}C NMR Spectral Correlations of C=N (ppm)

From the Table 3, the assigned C=N chemical shifts(δ ppm) values of (*E*)-*N'*-(1-phenylethylidene)benzohydrazide compounds have shown poor correlations (r < 0.900) with Hammett substituent constants and *F* and *R* parameter. The reason for the poor correlations was stated earlier and associated with resonance-conjugative structure as shown in Figure 1.

All the correlations have shown negative ρ values. This indicates the operation of reverse substituent effects with respect to ^{13}C NMR chemical shifts(δ ppm) of C=O carbons of all substituted (*E*)-*N'*-(1-phenylethylidene)benzohydrazide compounds.

3.4.2.3. ^{13}CNMRSpectral Correlations of CH_3 (ppm)

From the Table 3, the assigned CH_3 chemical shifts(δ ppm) values of (*E*)-*N'*-(1-phenylethylidene)benzohydrazide compounds have shown satisfactory correlations (r > 0.900) with Hammett substituent constants and *F* and *R* parameter.

All the correlations have shown positive ρ values. This indicates the operation of normal substituent effect with respect to CH_3 chemical shifts(δ ppm) values of all substituted (*E*)-*N'*-(1-phenylethylidene) benzohydrazide compounds.

Some of the single parameter correlations analyses have shown poor correlation coefficients with Hammett substituent constants and *F* and *R* parameter, then it is decided to go for multi-regression analysis with Swain-Lupton's [36] parameters. While seeking the multi-regression analysis, there is a satisfactory correlations have to be found and are shown in the multi-regression equations (14) and (19).

$$\delta C{=}O\ (ppm) = 162.619(\pm 1.093) + 1.183(\pm 2.264)\sigma_I + 1.293(\pm 2.019)\sigma_R \qquad (14)$$
$$(r = 0.932,\ n = 11,\ P > 95\%)$$

$$\delta C{=}O\ (ppm) = 162.681(\pm 1.005) + 1.526(\pm 1.966)F + 1.400(\pm 1.121)\,R \qquad (15)$$
$$(r = 0.942,\ n = 11,\ P > 95\%)$$

$$\delta C{=}N\ (ppm) = 168.384(\pm 0.898) - 0.216(\pm 1.861)\sigma I + 0.242(\pm 1.660)\sigma_R \qquad (16)$$
$$(r = 0.905,\ n = 11,\ P > 95\%)$$

$$\delta C{=}N\ (ppm) = 168.089(\pm 0.891) + 0.311(\pm 1.743)F - 0.131(\pm 0.994)R \qquad (17)$$
$$(r = 0.907,\ n = 11,\ P > 90\%)$$

$$\delta C{=}O\ CH_3\ (ppm) = 12.943(\pm 0.593) + 2.958(\pm 1.228)\sigma I + 1.650(\pm 1.095)\sigma_R \qquad (18)$$
$$(r = 0.975,\ n = 11,\ P > 95\%)$$

$$\delta C{=}O\ CH3\ (ppm) = 12.855(\pm 0.625) + 2.894(\pm 1.223)F + 1.022(\pm 0.697)R \qquad (19)$$
$$(r = 0.972,\ n = 11,\ P > 90\%)$$

3.5. Anti-microbial activities

All the aryl hydrazides possess a wide range of biological activities. These multi-prolonged activities are associated with different substituents and the unsaturation of C=N moiety in between the aryl rings. Hence, it is intended to examine their antimicrobial activities against their respective microbes-bacterial and fungal strains.

3.6. Antibacterial sensitivity assay

Antibacterial sensitivity assay has been performed using disc diffusion technique [30]. In each Petri plate about 0.5 cm^3 of the test bacterial sample has been spreaded uniformly over the solidified Mueller Hinton agar using sterile glass spreader. Then the discs with 5 mm diameter made up of Whatmann No.1 filter paper, impregnated with the solution of the compound have been placed on the medium using sterile forceps. The plates have been incubated for 24 hours at 37°C by keeping the plates upside down to prevent the collection of water droplets over the medium. After 24 hours, the plates have been visually examined and the diameter values of the zone of inhibition were measured. Triplicate results have been recorded by repeating the same procedure.

The antibacterial screening effect of synthesized (*E*)-*N'*-(1-phenylethylidene) benzohydrazide is shown in Figure 2 (Plates 1–26). The antibacterial activities of all the synthesized imines have been studied against four gram positive pathogenic strains *S. Aureus, S. Pyogenes, M. Luteus, B. Substilis and* seven gram negative strains *K. Pneumoniae, S. Typhi, V. Parahaemdyticus, V. Cholerae, K. Oxytoca, P. Mirabilis, S. Paratyphi, E. Coli, P. Aeruginosa.* The disc diffusion technique was followed at a concentration of 250 μg/cm^3 with Ciprofloxacin taken as the standard.

The mm of zone of inhibition is compared using Table 4 and Table 5 is the corresponding clustered column chart is shown in Figure-3. A good antibacterial activity has been possessed by all substituents on the microorganisms in general. The substituents 4-CH_3, 3-$NO_2$and 4-NO_2 have very good activity against all bacterial strains. The parent compound (H), 4-Br, 4-F, 4-OCH_3 and 4-NO_2substituents has equal antibacterial activity with standard Ciprofloxacin against *B.substilis bacterial strains.*

Table 4. Antibacterial activity of substituted(*E*)-*N'*-(1-phenylethylidene)benzohydrazides

Entry	X	Gram +ve Bacteria (Zone of inhibition(mm) values)			
		S.Aureus	*S.Pyogenes*	*M.Luteus*	*B Substilis*
1	H	0	6	0	0
2	4-Br	0	6	0	6
3	4-F	0	8	6	6
4	2-OH	0	6	0	6
5	3-OH	0	0	6	0
6	4-OH	0	6	0	6
7	4-I	6	0	6	6
8	4-OCH_3	6	0	0	0
9	4-CH_3	6	6	6	0
10	3-NO_2	6	0	6	6
11	4-NO_2	6	0	0	0
Standard	Ciprofloxacin	15	14	6	15
Control	DMSO	0	0	0	0

Table 5. Antibacterial activity of substituted(*E*)-*N'*-(1-phenylethylidene)benzohydrazides compounds

Entry	X	Gram -ve Bacteria (Zone of inhibition (mm) values)								
		K.Pneumoniae	*S.Typhi*	*V.Parahaemdyticus*	*V.Cholerae*	*K.Oxytoca*	*P.Mirabilis*	*S.Paratyphi*	*E.Coli*	*P.Aeruginosa*
1	H	6	6	6	6	6	0	0	6	6
2	4-Br	0	6	0	6	6	0	7	6	6
3	4-F	6	0	7	8	6	0	0	6	0
4	2-OH	0	0	0	6	6	0	0	0	0
5	3-OH	6	0	0	6	0	0	6	0	0
6	4-OH	7	6	0	6	0	6	0	0	0
7	4-I	8	0	0	0	0	0	6	0	0
8	4-OCH_3	0	0	0	0	6	6	0	6	0
9	4-CH_3	7	6	7	0	6	0	0	0	6
10	3-NO_2	6	7	6	0	7	0	6	0	6
11	4-NO_2	0	6	6	0	6	0	8	6	6
Standard	Ciprofloxacin	15	13	10	14	8	12	14	6	15
Control	DMSO	0	0	0	0	0	0	0	0	0

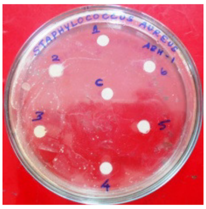
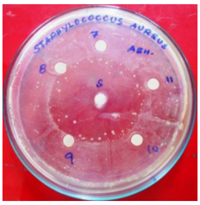


Plate 1



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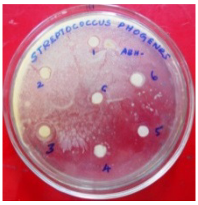

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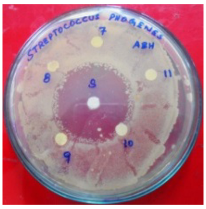

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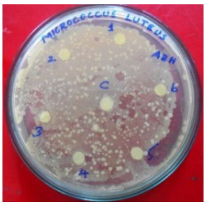

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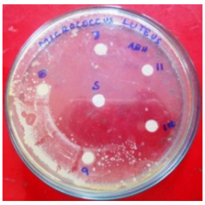


Plate 6

Plate 7

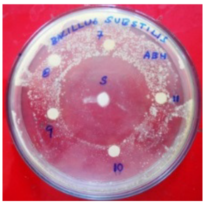
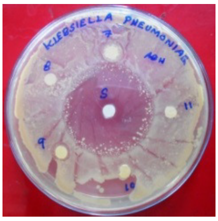


Plate 8

Plate 9



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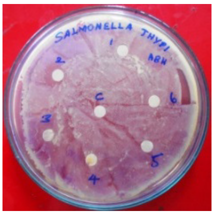
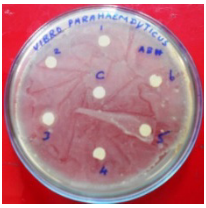


Plate 11

Plate 12



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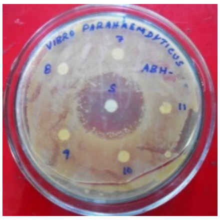

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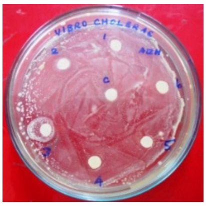

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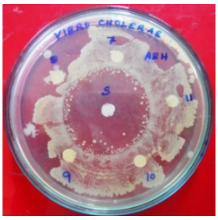
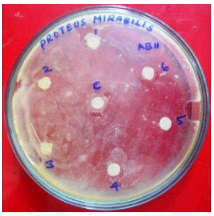


Plate 16

Plate 17

Plate 18



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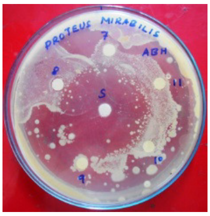

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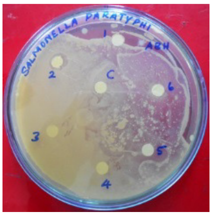
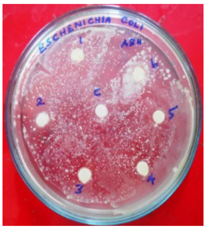


Plate 21

Plate 22



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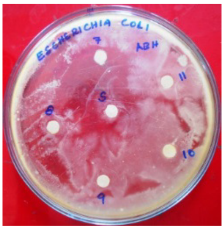

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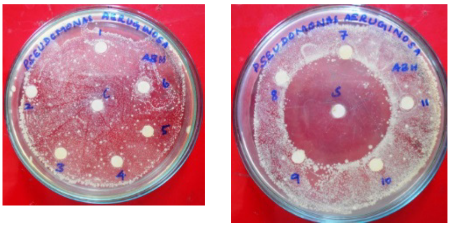

Plate 25 **Plate 26**

Fig. 2. Antibacterial activities of Substituted(*E*)-*N'*-(1-phenylethylidene)benzohydrazides.

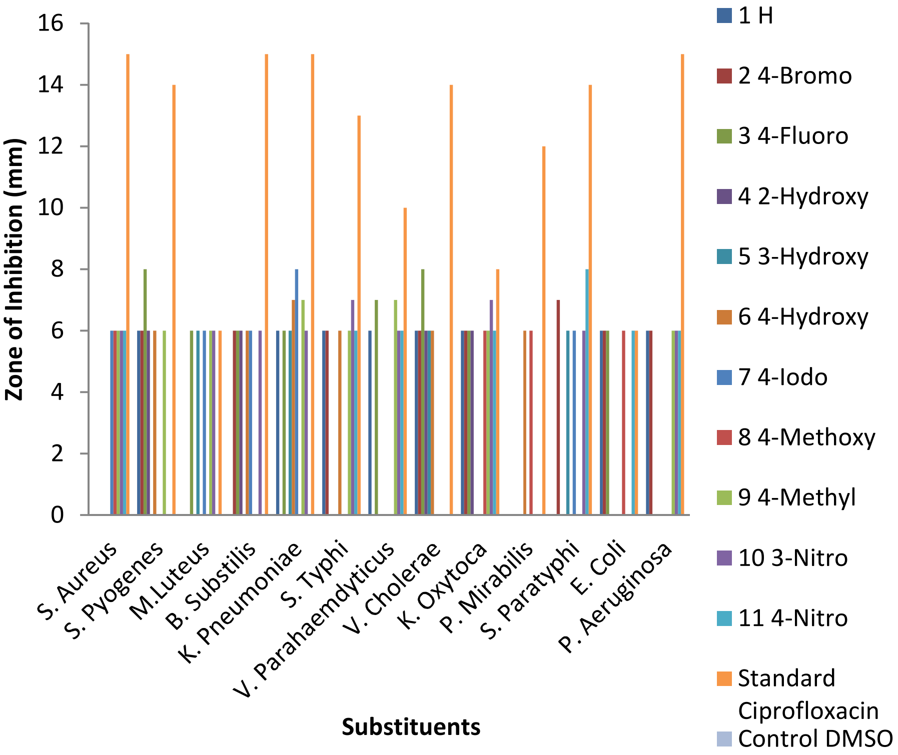

Fig. 3. Antibacterial activities of substituted(*E*)-*N'*-(1-phenylethylidene)benzohydrazide-clustered column chart.

3.7. Antifungal sensitivity assay

Antifungal sensitivity assay has been performed using disc diffusion technique. PDA medium was prepared and sterilized as above. It has been poured (ear bearing heating condition) in the Petri-plate which has been already filled with 1 cm^3 of the fungal species. The fungal activities of all the synthesized (*E*)-*N'*-(1-phenylethylidene)benzohydrazide have been studied against three fungal species *A.niger, M.specie,* and *T.viride.*

The plates have been rotated clockwise and counter clock-wise for uniform spreading of the species. The discs have been impregnated with the test solution. The test solution has been prepared by dissolving 15mg of the imines in 1ml of DMSO solvent. The medium have been allowed to solidify and kept for 24 h. Then the plates have been visually examined and the diameter values of zone of inhibition have been measured. Triplicate results have been recorded by repeating the same procedure. The antifungal activities of substituted (*E*)-*N'*-(1-phenylethylidene)benzohydrazide have been studied and are shown in Figure 4 for Plates (27–32) and the zone of inhibition values of the effect is given in Table 6. The clustered column chart, shown in Figure-5. It reveals that the compounds with 4-Br and 3-NO_2 substituents have moderate antifungal activity against all fungal species namely *A.niger, M.species* and *T.viride.*

Table 6. Antifungal activities of substituted(*E*)-*N'*-(1-phenylethylidene) benzohydrazides

Entry	X	(Zone of inhibition(mm) values)		
		A.niger	*M.species*	*T.viride*
1	H	6	6	0
2	4-Br	7	7	6
3	4-F	7	6	0
4	2-OH	0	0	0
5	3-OH	0	0	0
6	4-OH	6	0	0
7	4-I	0	6	0
8	4-OCH_3	0	6	0
9	4-CH_3	0	6	6
10	3-NO_2	6	7	7
11	4-NO_2	6	6	0
Standard	Ciprofloxacin	8	9	8
Control	DMSO	0	0	0

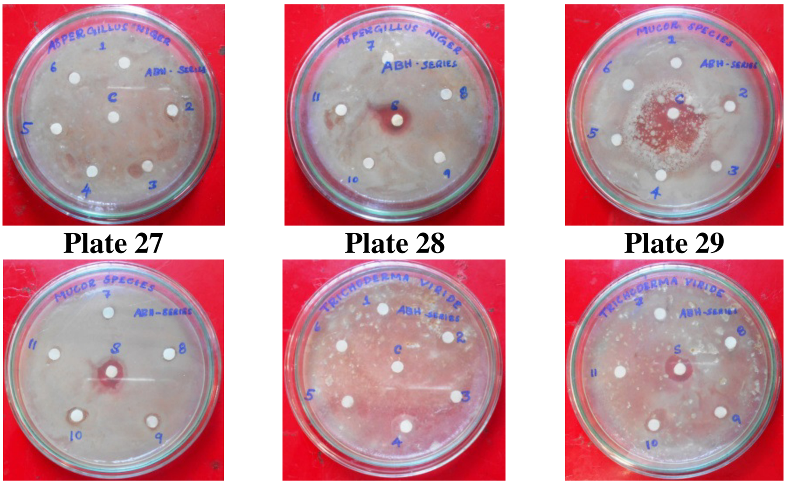

Plate 27 **Plate 28** **Plate 29**

Plate 30 **Plate 31** **Plate 32**

Fig. 4. Antifungal activities of Substituted(*E*)-*N'*-(1-phenylethylidene)benzohydrazides.

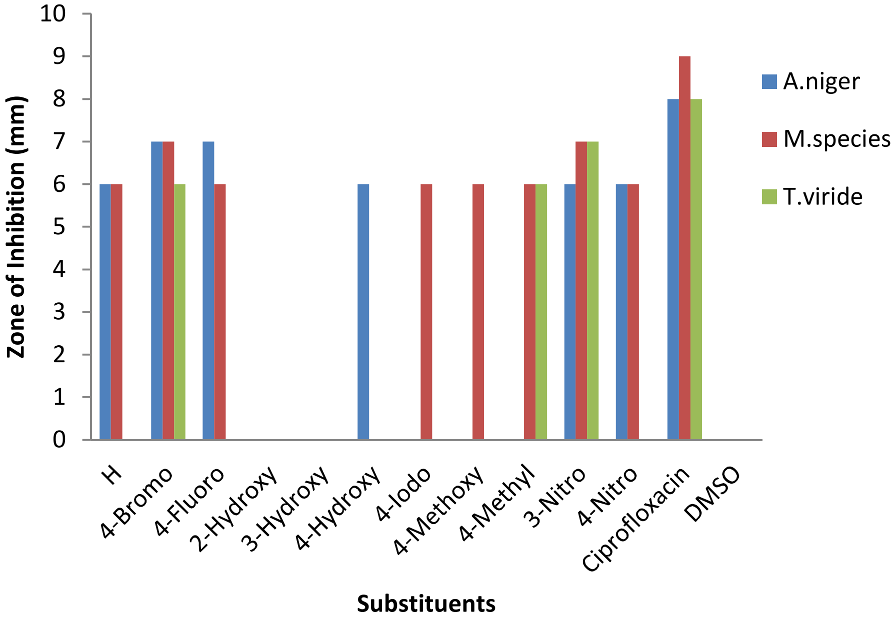

Fig. 5. Antifungal activities of substituted(*E*)-*N'*-(1-phenylethylidene)benzohydrazides-clustered column chart.

4. CONCLUSIONS

A series containing eleven numbers of substituted (*E*)-*N'*-(1-phenylethylidene) benzohydrazide compounds have been synthesized by condensation of benzohydrazide and substituted acetophenones. These synthesized substituted (*E*)-*N'*-(1-phenylethylidene) benzo- hydrazide compounds have been characterized by their physical constants, spectral data. The assigned UV, IR, NMR spectral data of these aryl hydrazides has been correlated with Hammett substituent constants, *F* and *R* parameters. From the results of statistical analyses the effects of substituent on the spectral data have been studied. ^{1}H and ^{13}C NMR spectral correlations produced more number of satisfactory correlations. But UV and IR spectral values give poor correlations with all Hammett substituents constants and Swain-Lupton's parameters. However, all the multi-regression analyses have shown satisfactory correlations. The antimicrobial activities of all synthesized imines have been studied using Bauer-Kirby method. A very good antibacterial and antifungal activity was possessed by halogens, methoxy, methyl and nitro substituents in the hydrazides to the respective microorganisms.

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