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HYDRAZONE LINKAGE BASED SCHIFF BASE: SYNTHESIS, CHARACTERIZATION AND THEIR BIOLOGICAL APPLICATIONS

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ABSTRACT

The chemistry of compounds possessing Schiff base moiety and Hydrazone moiety have been an interesting field of research since long time. 1-(4-aminophenyl) ethan-1-one was taken with thiosemicarbazide which gives 2-[1-(4-aminophenyl) ethylidene] hydrazine-1-carbothioamide. Hydrazone linkage containing 2-[1-(4-aminophenyl) ethylidene]hydrazine-1-carbothioamide derivatives are further condensed with'S aromatic aldehyde derivatives which gives a series of newly synthesized Schiff base. Synthesized derivatives of Schiff base are characterized by the physo chemical, physiological and IR. All synthesized compounds are screened for their antibacterial and antifungal activity by using agar well diffusion method. The results revealed that the compound IIA, IIB and IID show excellent activity against *E. coli* and moderate show against *P. aerugenosaand* and *S.aureus.* Compound IIB, IIE and IIF are show excellent against *S.aureus.* All compounds show moderate anti-fungal activity against *A. flavus and A. fumigates* and show excellent against *Candida albicans.*

KEYWORDS: Hydrazone, Azomethine linkages and Biological applications.

INTRODUCTION

Pathogens are micro-organisms that has the potential to cause disease. A few harmful microbes, for example less than 1% of bacteria, viruses and fungus invade our body causing illness and are responsible for the substantial morbidity and mortality.

The chemistry of compounds possessing Schiff base moiety and Hydrazone moiety have been an interesting field of research since long time. Schiff Base Moiety (>C=N-) show various

biological applications such as anti cancer[01], anti tuberculostatic[02], diuretic[03], antibacterial[03], anti fungal[03] and anti inflammatory[04], apart from their role in dye and agrochemical industries.[05] Literature survey exposed that work on Hydrazone moiety ((>C=N-NH_2) have been extensively studied for its spacious rang for biological and clinical applications.[06-07]

Hydrazones have gained much importance due to their diverse biological applications including antibacterial[08], antifungal[08], anti-inflammatory[09], antimutagenic and antioxident activities.[10]

OBJECTIVE

Schiff base moieties are well known for their various physiological and pharmacological activities. On the other hand, Hydrazone moieties have been also found to possess anti cancer, anti tuberculostatic, diuretic, anti bacterial, anti fungal and anti inflammatory properties.[11-12]

Considering all the above facts, it was found that the Hydrazone moiety when introduced with the Schiff base moiety, the compound synthesized may have some remarkable pharmacological and microbiological activity.

MATERIAL AND METHODS

All the chemical reagents and solvents were purchased commercially and used without any further purification. The melting points of compounds were recorded on a hot stage Gallen Kamp melting point apparatus in open capillary and was found uncorrected.

The characterization of synthesized compounds were determined by the ^{1}HNMR, C^{13}NMR, infrared and physical properties.

Method of Synthesis of Schiff base series

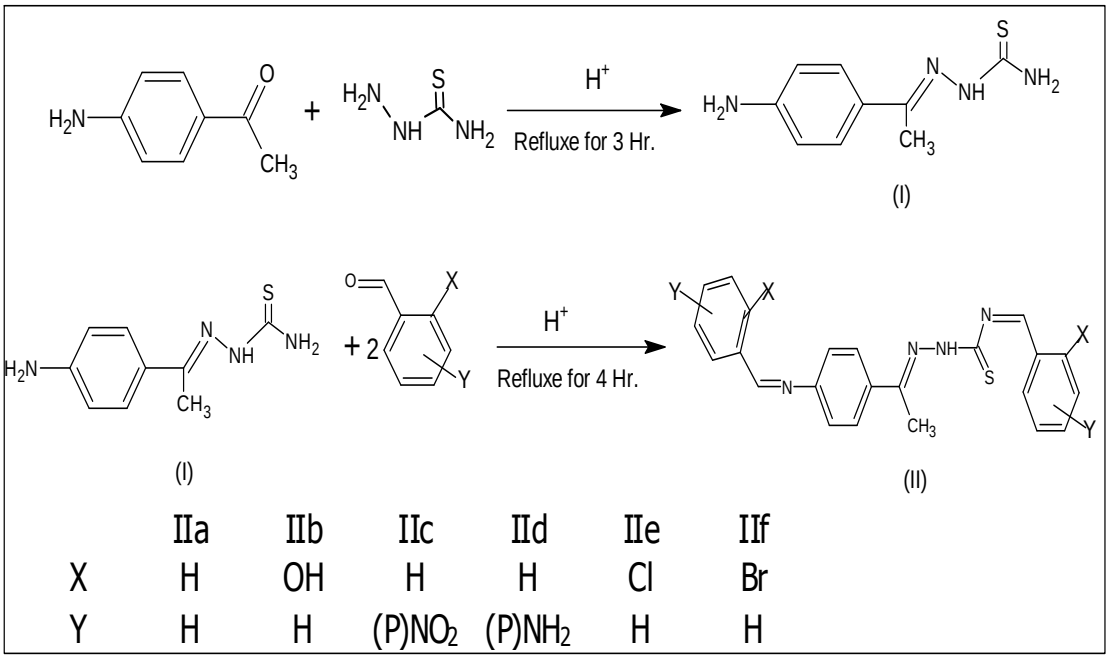
4-aminoacetophenone (0.005 mole, 0.6 gm) and thiosemicarbezide (0.005 mol, 0.37gml) were taken in round bottom flask containing absolute ethanol (15ml). To this mixture, few drops of condensing reagent as glacial acetic acid or concentrated sulfuric acid was added and then refluxed on water bath for 3 hr.

Purity of the reaction was monitored by TLC. The mixture was cooled to room temperature and poured into crushed ice. Product separated was filtered and further crystallized from

ethanol to give a yellow coloured crystalline form of **2-[1-(4-aminophenyl) ethylidene] hydrazine-1-carbothioamide]**.

A series of substituted aldehyde (IIA to IIF) was condensed with **2-[1-(4-aminophenyl) ethylidene] hydrazine-1-carbothioamide]** (2:1 molar ratio) in 1,4-dioxane by adding catalytic amount of glacial acid and placed on water bath for 4 hr. Further ice cubes were added to it. The solid mass was filtered and recrystallized in ethanol.

Synthesis Scheme



	IIa	IIb	IIc	IId	IIe	IIf
X	H	OH	H	H	Cl	Br
Y	H	H	(P)NO_2	(P)NH_2	H	H

RESULTS AND DISCUSSION

All noval synthesized Schiff bases were found to be stable in air at room temperature. They have soluble in Chloroform and DMSO, partially soluble in methanol and ethanol but insoluble in water. The physical properties of all synthesized compounds reported in table (1). The approximate yield recorded was 20-30% and their melting point ranged from 188-212 ^{0}C.

All compounds colour range yellow to muddy and they gave satisfahectory results for IR, H^1NMR and C^{13}NMR.

Table (1): Physical properties of newly synthesized Schiff bases with Hydrazone moiety.

Com Cod	Mole. Formula	Name of Derivatives of Schiff bases	Color	MP (^{o}C)	Yeild (%)
IIA	$C_{23}H_{20}N_4S$	2-{1-[4-(benzylideneamino)phenyl]ethylidene}-*N*-[(*Z*)-phenylmethylidene]hydrazine-1-carbothioamide	Yellow	207	38.28
IIB	$C_{23}H_{20}N_2O_2S$	*N*-[(*Z*)-(2-hydroxyphenyl)methylidene]-2-[1-(4-{[(2-hydroxyphenyl)methylidene]amino}phenyl)ethylidene]hydrazine-1-carbothioamide	Purple	203	26.11
IIC	$C_{23}H_{18}N_6O_4S$	[((4- nitrobenzylidene)methylidene]-2-[1-(4-{[(3-nitrobenzylidene)] }phenyl)ethylidene]hydrazine-1-carbothioamide	Muddy Yellow	211	32.11
IID	$C_{23}H_{22}N_6S$	[((4-aminobenzylidene)methylidene]-2-[1-(4-{[(3-aminobenzylidene)]})]hydrazine-1-carbothioamide	Muddy	198	24.11
IIE	$C_{23}H_{18}N_4SCl_2$	*N*-[(*Z*)-(2-chlorophenyl)methylidene]-2-[1-(4-{[(2-chlorophenyl)methylidene]amino}phenyl)ethylidene]hydrazine-1-carbothioamide	Yellow	192	26.11
IIF	$C_{23}H_{18}N_4SBr_2$	(2*E*)-*N*-[(*Z*)-(2-bromophenyl)methylidene]-2-[1-(4-{[(2-bromophenyl)methylidene]amino}phenyl)ethylidene]hydrazine-1-carbothioamide	Yellow	198	27.24

Infrared spectra of newly synthesized Schiff base with Hydrazone moiety

They are characterized by a azomethine moiety (C=N) at 1609 cm^{-1}, (C=S) at 826 cm^{-1}, (N-H) at 3157 cm^{-1}, (N-N) at 1508 cm^{-1}, (C-H) of the benzene ring at 2927 and (C-H) of -CH_3 at 2800 and few other stretching are mentioned in table (2).

Table (2): Some infrared of newly synthesized Schiff bases with Hydrazone moiety.

S.No	Group	cm^{-1}
	OH	3382
	NO_2	1356
	NH_2	3182
	C-Cl	689
	C-Br	650

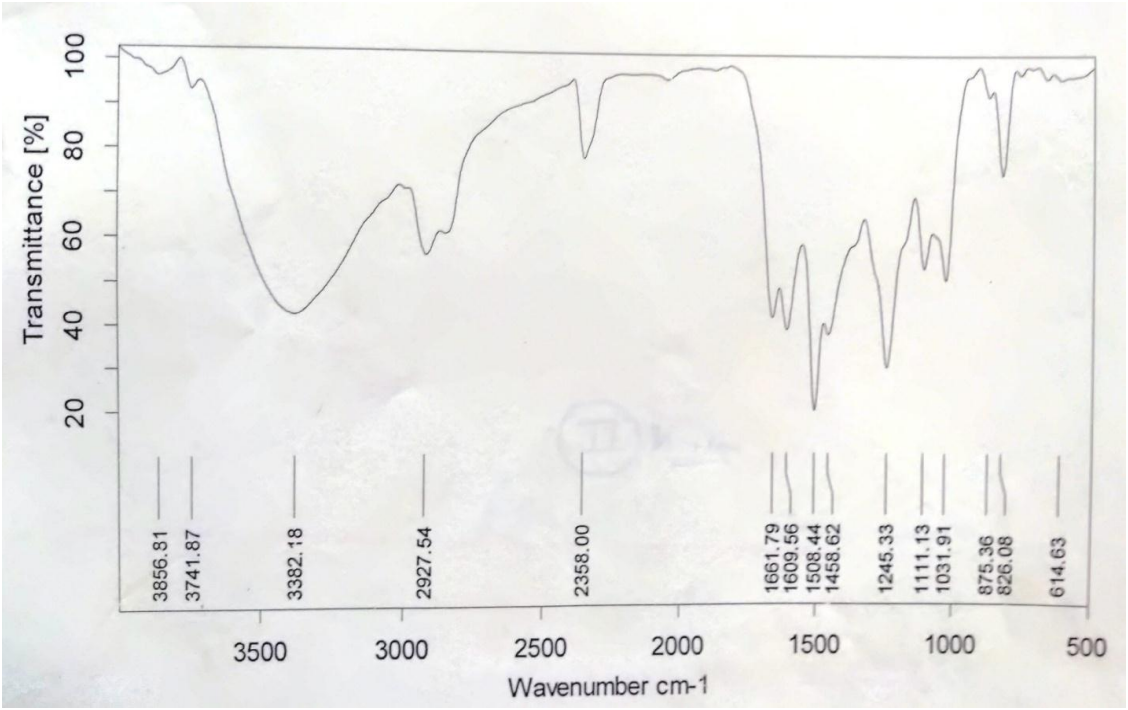


Fig No 1: FTIR spectrum of "*N*-[(2-hydroxyphenyl) methylidene]-2-[1-(4-{[(2-hydroxyphenyl)methylidene]amino}phenyl)ethylidene]hydrazine-1-carbothioamide"

^{1}H-NMR spectrum of newly synthesized Schiff base with hydrazone moiety

The ^{1}H-NMR spectrum of the Schiff base as shown in figure(2), was measured using Chloroform as solvent. Spectral analysis of Schiff base show multiple peaks at δ =7.01-8.25 ppm attributed to the phenyl ring. The single peaks at δ =1.28 ppm and 11.40 ppm due to the CH_3 and N-H groups in the compound respectively. Schiff base H-C=N show single peak at δ=8.74 ppm which is assigned due to the presence of protons of azomethine group.[23,24]. The result are tabulated in table (3).

Table 3: ^{1}H -NMR data of the Schiff base.

S.No	Group	δ (ppm)
01	**CH3** (methyl)	1.28
02	C-H (Phenyl ring)	7.01-8.25
03	C-H (azomethine)	8.74
04	N-H(amine)	11.40
05	O-H	11.02

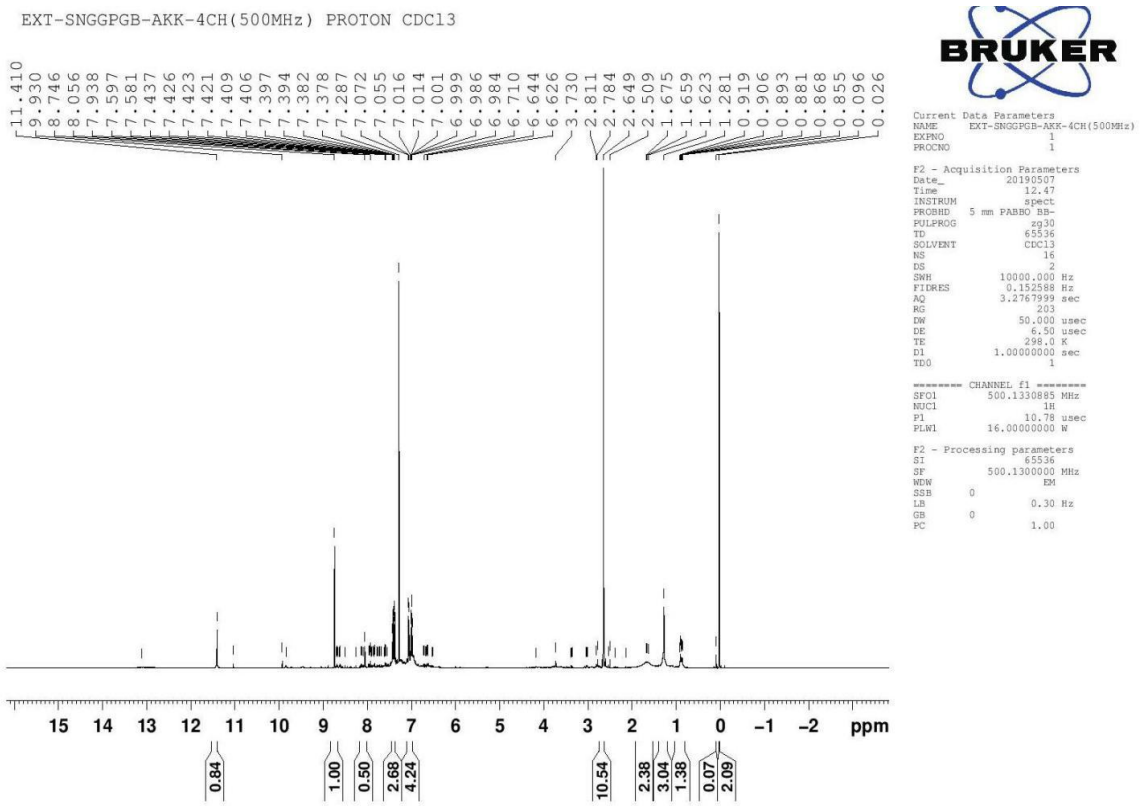


Fig No 2: FTIR spectrum of FTIR spectrum of "2-{1-[4-(benzylideneamino) phenyl] ethylidene}-*N*-[(*Z*)-phenylmethylidene]hydrazine-1-carbothioamide"

BIOLOGICAL STUDIES

Antimicrobial screening was done using disc diffusion test given by Bauer *et al.*, (1966). The filter no. 1 disc of 6mm diameter was impregnated with different concentrations (25%, 50%, 75% and 100%) of IIA, IIB, IIC, IID, IIE and IIF. The disc was placed in the center of pre-inoculated culture plates and incubated for 24 hrs at 37 ºC. After incubation, plates was observed for the sensitivity of the test extract against microorganisms in terms of zone of inhibition (ZOI). The zone of inhibition was measured by using transparent plastic ruler scale.

Table 04: Antimicrobial activity of compound code II(A-F) against pathogens.

Code	Name of Bacteria	Bacterial Culture- Zone of Inhibition concentration in % (mm)				Name of fungal	fungal Culture- Zone of Inhibition concentration in % (mm)			
		25	50	75	100		25	50	75	100
IIA	*S.aureus*	-	-	-	+	*Candida albicans*	-	-	-	+
	P. aerugenosa	-	-	+	+	*A. flavus*	-	+	+	+
	E. coli	+	+	+	+	*A. fumigates*	-	+	+	+
IIB	*S.aureus*	+	+	+	+	*Candida albicans*	+	+	+	+
	P. aerugenosa	-	-	+	+	*A. flavus*	-	+	+	+

	E. coli	+	+	+	+	*A. fumigates*	-	+	+	+
IIC	*S.aureus*	-	+	+	+	*Candida albicans*	+	+	+	+
	P. aerugenosa	+	+	+	+	*A. flavus*	+	+	+	+
	E. coli	-	+	+	+	*A. fumigates*	-	-	+	+
IID	*S.aureus*	-	-	-	+	*Candida albicans*	-	+	+	+
	P. aerugenosa	-	+	+	+	*A. flavus*	-	-	+	+
	E. coli	+	+	+	+	*A. fumigates*	-	-	-	-
IIE	*S.aureus*	+	+	+	+	*Candida albicans*	+	+	+	+
	P. aerugenosa	+	+	+	+	*A. flavus*	-	-	+	+
	E. coli	-	+	+	+	*A. fumigates*	+	+	+	+
IIF	*S.aureus*	+	+	+	+	*Candida albicans*	-	-	+	+
	P. aerugenosa	-	+	+	+	*A. flavus*	-	-	+	+
	E. coli	-	+	+	+	*A. fumigates*	-	+	+	+

CONCLUSION

We have developed the easier and simple synthetic technique of Schiff base related hydrazone moiety containing derivatives and the reactions occurred much secured, under modest condition using reasonable solvents and reagents. The anti-bacterial activity of newly synthesized novel Schiff base with hydrazones moiety were effectively screened against Gram posi-tive *S. aureus* and Gram-negative *P. aeruginosa* and *E. coli* bacterial strains. Compound IIA, IIB and IID show excellent activity against *E. coli and mordent show against P. aerugenosaand and S.aureus.* Compound IIB,IIE and IIF are show excellent against *S.aureus.*

To assess the antifungal activity of synthesized compounds were checked against *Candida albicans, A. flavus* and *A. fumigates.* All compounds show moderate anti-fungal activity against *A. flavus and A. fumigates* and show excellent against *Candida albicans*.

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