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Coumarin based Schiff base: Synthesis and their Antioxidant and Antimicrobial activity

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Abstract: 3-propanoyl-2H-1-benzopyran-2-one was taken with semicarbazide which gives 2-(2-oxo-2H-1-benzopyran-3-carbonyl)hydrazine-1-carboxamide. The prepared Coumarin moiety containing 2-(2-oxo-2H-1-benzopyran-3-carbonyl)hydrazine-1-carboxamide derivatives is further condensed with some aromatic aldehyde derivatives which gives other class of Schiff base.
Synthesized Schiff base are analyzed for their antioxidant and antimicrobial activity. The antioxidant test was done by DPPH and Nitric oxide and antimicrobial activities employed were S. aureus, Pseudomonas, E. coli, Candida albicans, A. flavus, A. fumigates.

Key Words: Azomethine moiety ,antioxidant, antimicrobial activity, Coumarin.

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I. INTRODUCTION

Azomethine linkage (>C=N-) has gained an appreciable attraction to synthesis from an ancient era. Survey of literature exposed that work on Schiff base derivatives have been extensively studied for its spacious rang for biological and clinical applications[01-03].

They have been frequently employed for pharmacological and microbial actives[04]. An Azomethine derivative shows interesting and remarkable biological activities such as anti cancer[05], anti tuberculostatic[06], diuretic[07], anti bacterial[08], anti fungal[09] and anti inflammatory[10] apart from they play an important role in dye and agrochemical industries.

1.1 objectives

Azomethine derivatives are well known for their various physiological and pharmacological activities. On the other hand Coumarin moiety have been also found to possess anti cancer, anti tuberculostatic, diuretic, anti bacterial, anti fungal and anti inflammatory.[11-12]

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

II. MATERIAL AND METHODS

All the chemicals, as well as solvents were purchased commercially and exploited without any further purification. The melting points were recorded on a hot stage Gallen Kamp melting point apparatus in open capillary and was found uncorrected.
Interpretations of compounds were determined by infra red technique and physical properties.

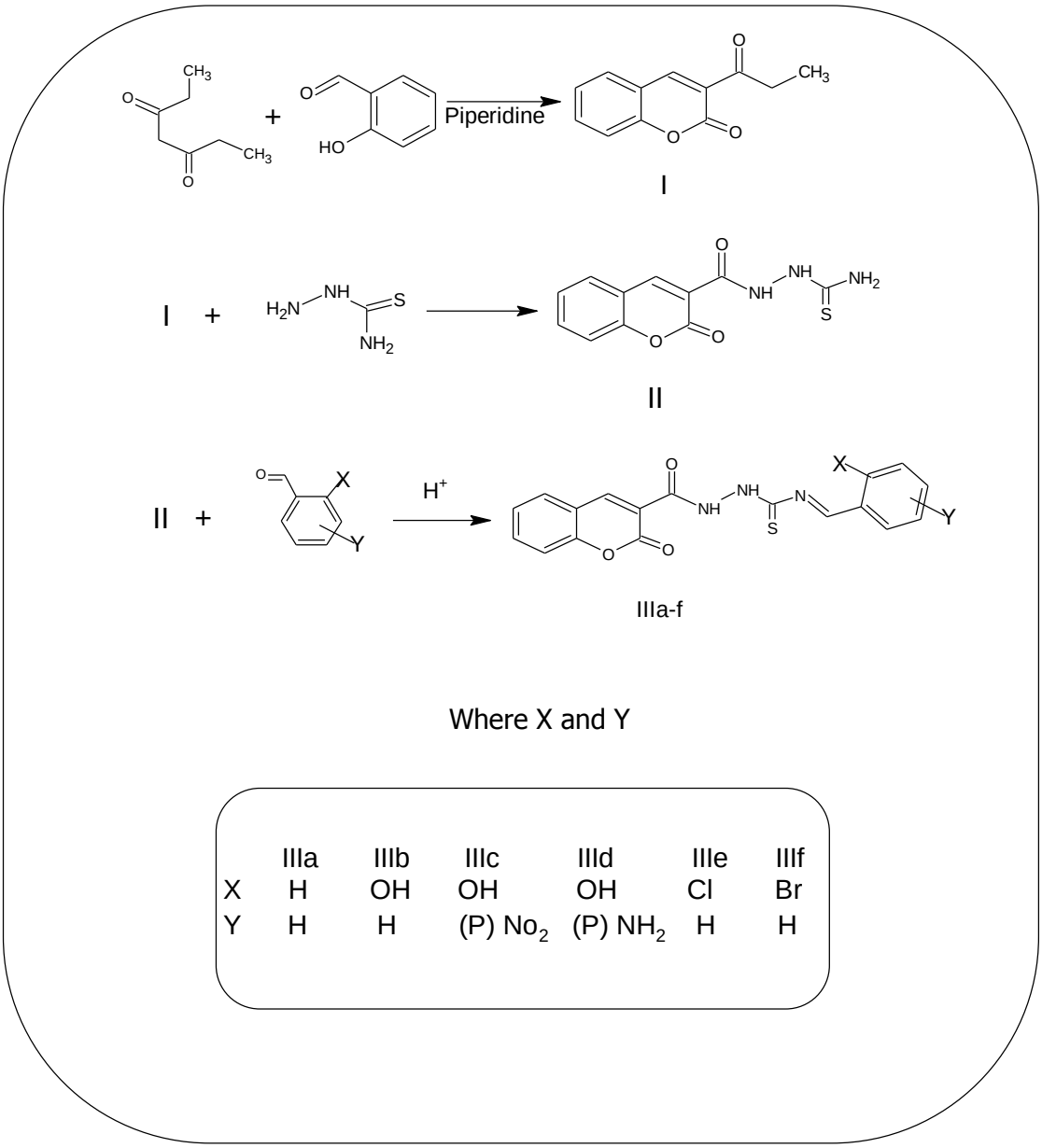
2.1 Synthesis of series of Schiff bases:

Diethyl malonate was reacted with salicylaldehyde in ethanol, refluxed for 6 hr on water bath and allowed to cool at room temperature and filtered. The solid mass obtained is further recrystallized by ethanol giving (I) 3-propanoyl-2*H*-1-benzopyran-2-one.

(I)3-propanoyl-2*H*-1-benzopyran-2-one and semicarbazide are taken in equal mole ration in a round bottom flask in presence of 15 ml ethanol solvent. It is then reflux for 5 hr on water bath and allowed to cool at room temperature. The solid mass thus isolated is and recrystallized by ethanol gives 2-(2-oxo-2*H*-1-benzopyran-3-carbonyl)hydrazine-1-carbothioamide.

A series of substituted aldehyde(IIIa to IIIf) condensed with (II) 2-(2-oxo-2*H*-1-benzopyran-3-carbonyl)hydrazine-1-carbothioamide in the 1,4-dioxane by adding catalytic amount of glacial acid and place on water bath for 3 hr. Further add ice cubes to it, filter the solid mass and recrystallized in ethanol.

Synthesis Scheme



	IIIa	IIIb	IIIc	IIId	IIIe	IIIf
X	H	OH	OH	OH	Cl	Br
Y	H	H	(P) No_2	(P) NH_2	H	H

Physical and IR data of newly synthesized Schiff Bases Code (III a-f)

Code	X	Y	IUPAC Name	Molecular From.	Mole. Wt.	MP (^{O}C)	Color	IR (Cm^{-1})	Yield (%)
IIIa	H	H	2-(2-oxo-2*H*-1-benzopyran-3-carbonyl)-*N*-[phenylmethylidene]hydrazine-1-carbothioamide	$C_{18}H_{13}N_3O_3S$	351.37	207	Black	C=C-H, 2821	21.23
IIIb	OH	H	*N*-[(2-hydroxyphenyl)methylidene]-2-(2-oxo-2*H*-1-benzopyran-3-carbonyl)hydrazine-1-carbothioamide	$C_{18}H_{13}N_3O_4S$	367.37	203	Black	O-H, 3444	26.11
IIIc	O	NO	*N*-[(2-hydroxy-4-	$C_{18}H_{12}N_4O_6S$	412.3	211	Mudd	O-	32.2

	H	$_2$	nitrophenyl)methylidene]-2-(2-oxo-2*H*-1-benzopyran-3-carbonyl)hydrazine-1-carbothioamide		7		y black	H,3443 NO_2,1354	1
IIId	OH	NH_2	*N*-[(4-aminophenyl)methylidene]-2-(2-oxo-2*H*-1-benzopyran-3-carbonyl)hydrazine-1-carbothioamide	$C_{18}H_{14}N_4O_3S$	366.39	198	Muddy yellow	O-H, 3443 NH_2, 3157	19.26
IIIe	Cl	H	*N*-[(2-chlorophenyl)methylidene]-2-(2-oxo-2*H*-1-benzopyran-3-carbonyl)hydrazine-1-carbothioamide	$C_{18}H_{14}N_3O_3SCl$	385.82	192	Yellow	C-Cl, 689	29.11
IIIf	Br	H	*N*-[(*E*)-(2-bromophenyl)methylidene]-2-(2-oxo-2*H*-1-benzopyran-3-carbonyl)hydrazine-1-carbothioamide	$C_{18}H_{14}N_3O_3SBr$	430.27	196	Yellow	C-Br, 645	26.11

2.2 Determination of Antioxidant Activities

2.2.1 DPPH radical scavenging assay

Principle

The free radical scavenging activity of the Schiff bases was measured *in vitro* by 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay described. DPPH• (2,2-diphenyl-1-picrylhydrazyl) with purple color is a stable free radical. Antioxidants (AH) on scavenging the radical species undergoes a color change i.e., purple color of DPPH reduce to yellow (DPPHH), which is the basic principle utilized in this assay.

DPPH inhibition effect (%) = $\frac{AC-AS}{AC} \times 100$

Where

Ac = Absorbance control

As = Absorbance sample

Procedure

DPPH scavenging action was estimated by the spectrophotometer. Stock solution (6 mg in 100 ml methanol) was arranged to such a way that, 1.5 ml of stock solution in 1.5 ml of methanol gave an initial absorbance. Decreasing absorbance in the presence of test sample at various concentrations (10-100 µg/ml) was recorded after 15 minutes. 1.5 ml of DPPH solution was taken and volume was made to 3 ml with methanol and the absorbance was taken promptly at 517 nm. For recording reading of control, 1.5 ml of DPPH and 1.5 ml of the sample of various concentrations were placed in progression of volumetric flasks and the last volume was acclimated to 3 ml with methanol. Three samples were taken and each handled correspondingly. Finally, the mean was taken out and absorbance at zero time for every concentration was recorded as well. Reduction in absorbance of DPPH with the test sample at various concentrations was noted after 15 minutes at 517 nm.

2.2.2 Nitric oxide radical scavenging assay

Principle

Aqueous solution of sodium nitroprusside at physiological pH spontaneously generates nitrite oxide,which interacts with oxygen to produce nitrite ions. These nitrite ions can be measured at 550 nm by spectrophotometer in the presence of Griess reagent.

Procedure

For this quantification, chemical compound was dissolved in distilled water. Sodium nitroprusside (5mM) in standard phosphate buffer saline (0.025m, pH 7.4) was incubated with different concentration (100-400µg/ml) of the compound and tubes were incubated at 29^{o}C for 3 hours. Control experiment without the test compounds, but with an equivalent amount of buffer was conducted in an identical manner. After 3 hours

incubated samples were diluted with 1 ml of Griess reagent. The absorbance of the color developed during diazotization of nitrite with sulphanilamide and its subsequent coupling with Napthylethylenediaminehydro-chloride was observed at 550 nm by spectrophotometer. The same procedure was repeated with ascorbic acid, which was used as standard in comparison to methanol extract. % inhibition was calculated by the formula.

3.3 Formula: % inhibition = [O.D. of control - O.D. of Test/O.D. of control] X 100
Where O.D. of control = Optical Density
O.D. of test = Optical Density

Table:02 DPPH and NO Radical Scavenging activity of Compounds III (a-f) Drug with Reference to Standard Drug.

Conc. (in µl)	**Percentage of Inhibitance**													
	DPPH Radical scavenging activity with reference to Standard Drug							**NO Radical scavenging activity with reference to Standard Drug**						
	Standard (in %)	Compound (in %)						Standard (in %)	Compound (in %)					
		IIIa	IIIb	IIIc	IIId	IIIe	IIIf		IIIa	IIIb	IIIc	IIId	IIIe	IIIf
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
200	89	36	42	38	44	43	42	60	38	40	42	48	46	44
400	91	44	54	52	52	50	53	64	44	46	49	54	52	50
600	94	52	63	61	57	61	60	76	52	52	57	60	59	56
800	95	60	75	68	66	68	67	92	59	60	65	68	66	62
1000	97	66	78	74	76	74	70	96	65	68	73	74	72	69

2.3 Antimicrobial activity

The in vitro antimicrobial activity of compound (Code IIIa-e) done by Agar well diffusion method using by MIC in µg/mt.

Table:03 Antimicrobial activity of compound code III(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
IIIa	*S.aureus*	+	+	+	+	*Candida albicans*	+	+	+	+
	P. aerugenosa	-	+	+	+	*A. flavus*	-	-	+	+
	E. coli	-	-	-	-	*A. fumigates*	-	+	+	+
IIIb	*S.aureus*	+	+	+	+	*Candida albicans*	+	+	+	+
	P. aerugenosa	-	-	+	+	*A. flavus*	-	+	+	+
	E. coli	-	-	+	+	*A. fumigates*	-	-	-	+
IIIc	*S.aureus*	+	+	+	+	*Candida albicans*	+	+	+	+
	P. aerugenosa	-	+	+	+	*A. flavus*	+	+	+	+
	E. coli	+	+	+	+	*A. fumigates*	-	+	+	+
IIId	*S.aureus*	+	+	+	+	*Candida albicans*	+	+	+	+
	P. aerugenosa	-	+	+	+	*A. flavus*	-	-	+	+
	E. coli	-	-	+	+	*A. fumigates*	-	-	-	-
IIIe	*S.aureus*	+	+	+	+	*Candida albicans*	+	+	+	+
	P. aerugenosa	+	+	+	+	*A. flavus*	-	-	+	+
	E. coli	-	+	+	+	*A. fumigates*	+	+	+	+
IIIf	*S.aureus*	+	+	+	+	*Candida albicans*	+	+	+	+
	P. aerugenosa	-	+	+	+	*A. flavus*	-	+	+	+
	E. coli	+	+	+	+	*A. fumigates*	+	+	+	+

III. RESULT AND DISCUSSION

Schiff base synthesized are glazy and needle shaped crystals. Yield recorded was about 30-40 % and their melting point range from 190-210 ^{0}C. They are characterized by a specific Coumarin ring(C=O) at 1737 Cm^{-1}, azomethine moiety (C=N) at 1660 Cm^{-1} , (C=S) at 788 Cm^{-1},(N-H) at 3157 Cm^{-1}, (C=O) at 1703 Cm^{-1} and few other stretching as mentioned in table 01.

Total six organic Schiff bases code III(a-f) were screened for their antibacterial and antifungal effects, and results reveals that all six schiff bases III (a-f) showed an excellent activity against *S.aureus,* and *Candida albicans.* Whereas IIIe were found to be effective against *P. aerugenosa and A. fumigates.* Compound IIIc and IIIf showed good antimicrobial activity against *E. coli* at every concentration.

In order to illuminate the antioxidant capability of the Schiff base, they were tested using radical scavenging assay by DPPH and NO radical methods. The results of free radical scavenging activity of compounds III (a-f) at different concentrations are described in table 02. Among the tested Schiff base compounds, IIId and IIIe have exhibited a good free radical scavenging activity, whereas compound IIIb and IIIc have shown moderate activity.

IV. CONCLUSION

In the present work, a series of new Schiff base compounds III (a-f) were prepared and *in vitro* biological evaluation of complexes against various pathogenic bacterial and fungal species was carried out. Additionally, the compounds exhibited some antioxidant properties due to the presence of their radical scavenging activities. The results of DPPH and NO methods revealed that compounds are capable of donating electron or hydrogen atom and subsequently react with free radicals, or terminate chain reactions in a dose-dependent pattern.

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