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Biological Potential of Synthetic Hydrazide Based Schiff Bases

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Abstract

All Schiff bases were synthesized from 4-chloro benzaldehyde and substituted Hydrazide. Antioxidant activities were evaluated of all the Schiff bases. 3a and 3g Schiff bases shows maximum lipoxygenase (Lox) inhibition at 500 µM %, Antioxidant DPPH % at 500 µM, FRAP value and TEAC value. While remaining Schiff bases shows abnormal values for all antioxidant parameters. While Antimicrobial values show that all Schiff bases were inactive against *Staphlococcus aureus* bacteria but few one active against *E. coli* and *Bacillus Subtilis* microbial. Majority of the synthesized product were active against *Typhimusium Salmonella* bacteria and some are active against *Candida albicans* bacteria.

Keywords: Antimicrobial Activity, Antioxidant Assay, FRAP Assay, Lipoxygenase Enzyme Inhibition, *E. coli*, *Bacillus Subtilis*.

Introduction

One of largely used families of organic compounds includes 'Schiff bases' or imines. They are used as artificial intermediates and also in co-ordination chemistry. Schiff bases and their complexes have marked antibacterial activity for *E. coli* and *B. subtilis*. Some pyrazine, and amino acid based 'Schiff bases' also have antibacterial activity.[1-3] Moreover, Schiff bases which are derived from heterocyclic possess antibacterial and anti HIV activity. Many other examples which possess such activity include quinazolinones, toluidinones, benzimidazole, thiazole, glucosamine pyrazolon, hydrozide furforaldiamine, halogenated thiazolidiones indole p-fluorobenzaldehyde.[4] Many hydrazide based preparations like oxadiazolines and pyrozolines showed antitumor activated and anti-oxidant activity by the DPPH method and No scavenging method.[5-7] Therefore the synthesis of hydrazide based Schiff bases is an attractive field in this regard.[8, 9]

For our targeted hydrazide based Schiff bases, first we synthesized esters ($RCOOCH_3$) from substituted aromatic carboxylic acid. For substituted aromatic hydrazides ($RCONHNH_2$), these esters were further reacted with hydrazine hydrate. Finally, these hydrazides condensed with 4-chloro benzaldehyde to get targeted compounds. Structure confirmation was done with the help of Elemental analysis and FTIR spectrum.

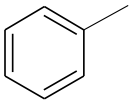
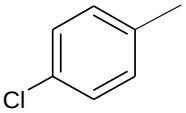
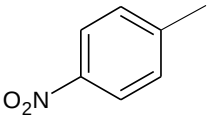
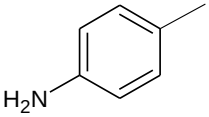
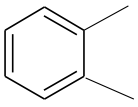
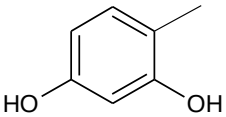
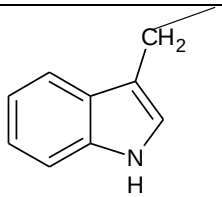
Enzyme inhibition potential, antioxidant activity and antimicrobial activity were tested of all the hydrazide based Schiff bases. Different results were found.

Experimental Work

Production of Substituted Ester

Take 100 mL of dry methanol in round bottom flask then allowed reacting with 10 grams of substituted aromatic carboxylic acid with few mL conc. H_2SO_4. The whole solution mixture was refluxed for 6 hours. Evaporate the solvent then neutralize the concentrated solution mixture with diluted Na_2CO_3 solution. Isolate the pure water by solvent extraction method. Process monitored by TLC. Different esters were synthesized as shown in Table-1.

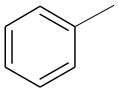
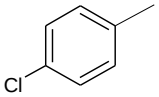
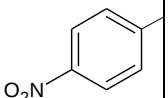
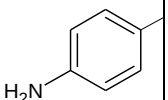
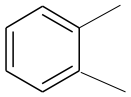
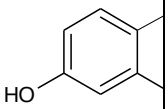
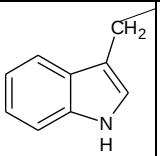
Table- 1

R in Ester	Physical State	Yield
	Colorless liquid	78 %
	White solid	75%
	Yellow solid	71%
	Light pink solid	82 %
	Yellowish liquid	79%
	Light yellow solid	76%
	Brown solid	75%

Production of Substituted Hydrazide

Take methanol round about 20 ml in round bottom flask then added substituted Ester (l mmol). Hydrated hydrazine (2.5 eq) was also added in the above solution mixture. Refluxed the reaction mixture, isolate the product through filtration and finally with crystallization. Different derivatives of hydrazide were synthesized which shown in Table-2.

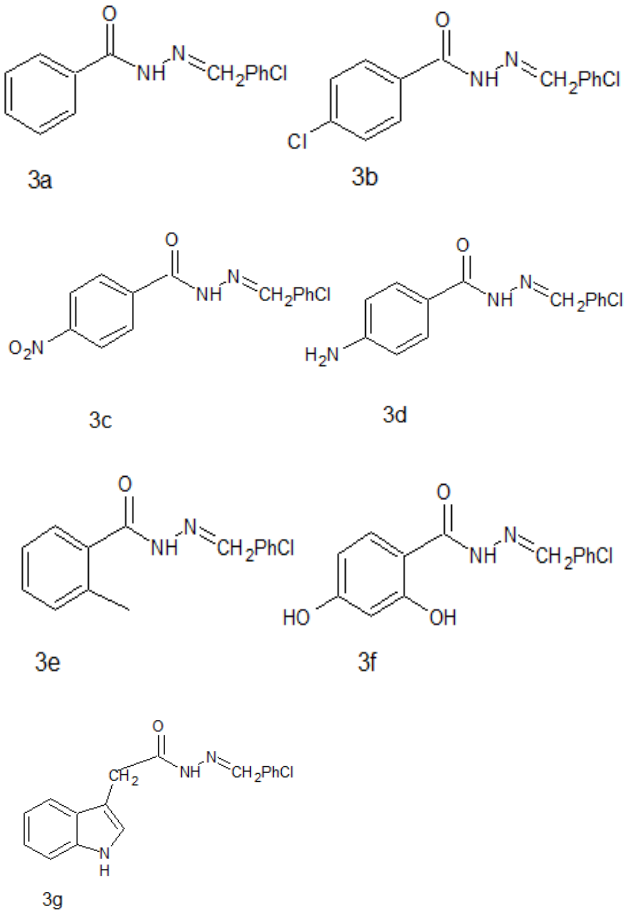
Table- 2

R-Group in Hydrazide	Physical state	Melting Point	Yield
	Flaky needles	113 °C	72 %
	White flaky crystalline powder	163 °C	75 %
	Yellow crystalline powder	210 °C	68 %
	Creamish white crystals	226 °C	65 %
	Yellowish tiny beads	——	66 %
	Yellowish shiny crystalline powder	180 °C	72 %
	Light Brown crystalline powder	122°C	77 %

Production of Hydrazide based Schiff bases

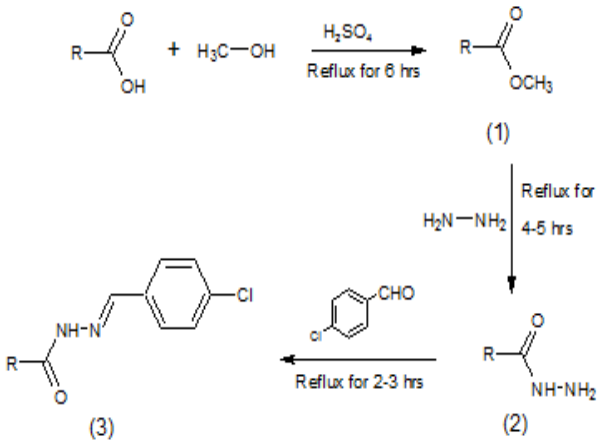
Take equimolar ratio of 4-chloro benzaldehyde and substituted hydrazide in round bottom flask while some amount of dry methanol was added as a solvent. Refluxed

the above solution was for about 2 hours. Upon cooling precipitate of Schiff bases was appeared. Recrystallize the product to obtained good quality product. Different Schiff bases were synthesized which are shown below.



Result and Discussion

General outline to synthesize hydrazide base Schiff bases is shown in Scheme No. 1.



Scheme-1: General Scheme for the synthesis of Hydrazide base Schiff bases

The Analytical Data and yields of all hydrazide base Schiff bases are shown in Table-3

Table- 3

Compound	M.p. °C	Rf Value	% age Yield	IR spectrum	Elemental Analyzer
3a	140	0.51	69	3276 (N–H) Str, 3059 (C–H) Str, 1652 (C=O Str), 1551 (C=N), 1400 (C=C), 1277 (C–N) Str, 824 (C–Cl)	C 64.95% H 4.25% N 10.79% S 0%
3b	175	0.56	71	3287 (N–H) Str, 3065 (C–H) Str, 1663 (C=O), 1600 (C=N), 1543 (C=C), 824 (C–Cl)	C 57.51% H 3.41% N 9.55% S 0 %
3c	247	0.61	74	3084 (N – H Str); 2956 (C – H Str) 1622 (C = 0 Str); 1278 (C – N); 823 {(C –N) NO2}; 1590 (C=N) 1500 (C=C)	C 55.29% H 3.22% 13.6% S 0%

3d	250	0.52	80	3415 (N–H) Str, 2949 (C–H) Str, 1705 (C=O) Str, 1584 (C=N) Str 1487, 1423 (C=C) Str, 1270 (C–N) Str 766 (C–Cl)	C 61.40% H 4.34% N 15.34% S 0 %
3e	340	0.39	63	3460 (N–H) Str, 3019, 2905 (C–H) Str, 1657 (C=O) Str, 1491 (C=C) 1323 (C– N) Str, 1165 (C–O) Str	C 57.31% H 4.45% N 17.82% S 0 %
3f	200	0.43	69	3366 (N–H) Str, 2942 (C–H) Str, 1663 (C=O) , 3624 (O–H), 1549 (C=N), 1400 (C=C), 818 (C–Cl)	C 57.80% H 3.78% N 9.61% S 0 %
3g	216	0.61	72	3388 (N – H Str), 3052 (C – H Str) 1666 C=O,1608 C=N, 1488 C=C, 1088 C-H bend, 741 C-Cl 1202 C-N St	C 65.3% H 4.44% N 13.36% S 0 %

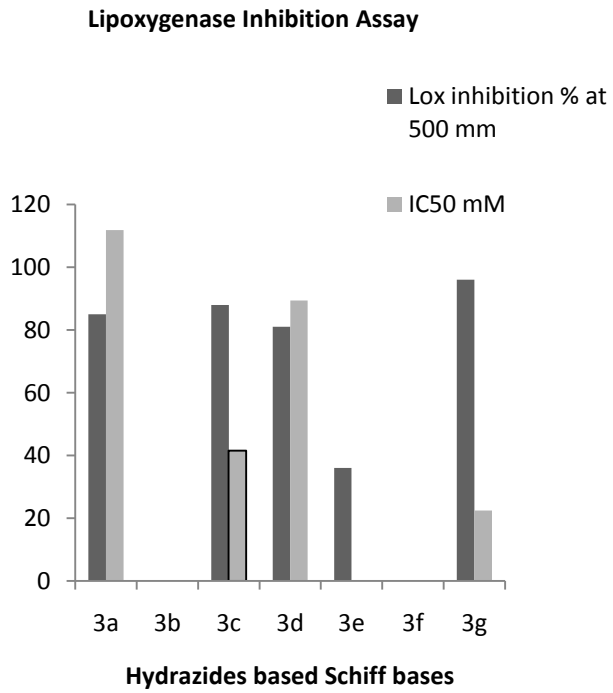
Enzyme Inhibition

Lipoxygenase Inhibition Assay

Lipoxygenase inhibition assay were determined for all hydrazides based Schiff bases. Result shows that 3c hydrazides Schiff base having maximum LOX inhibition % at 500 µm. Results of Lipoxygenase inhibition assay of all the synthesized hydrazide base Schiff bases are shown in Table- 4.

Table- 4

Hydrazides based Schiff Bases	LOX inhibition % at 500 µm	IC_{50} µM
3a	85	111.8
3b	-	-
3c	88	41.6
3d	81	89.4
3e	36	–
3f	–	–
3g	96	22.5



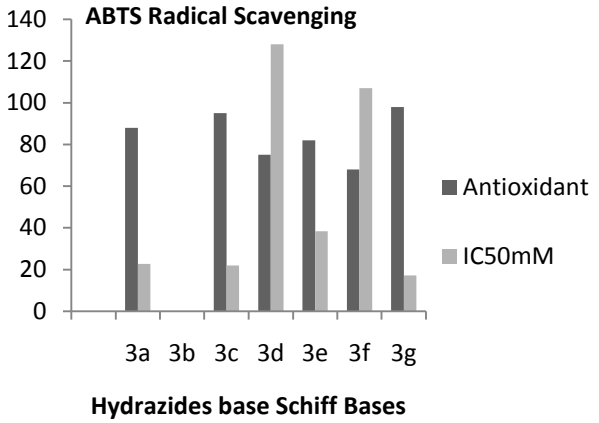
Antioxidant Assay

ABTS Radical Scavenging

Results of ABTS Radical Scavenging assay of all hydrazide based Schiff bases are shown in Table No. 5. ABTS assay results show that 3g hydrazides Schiff base has the uppermost free radical scavenging ability whereas hydrazide Schiff bases of 3a and 3c also have high ABTS value.

Table- 5

Hydrazides based Schiff Bases	Antioxidant DPPH % at 500 μM	IC_{50}μM
3a	88	22.7
3b	-	-
3c	95	21.9
3d	75	128
3e	82	38.4
3f	68	107
3g	98	17.2

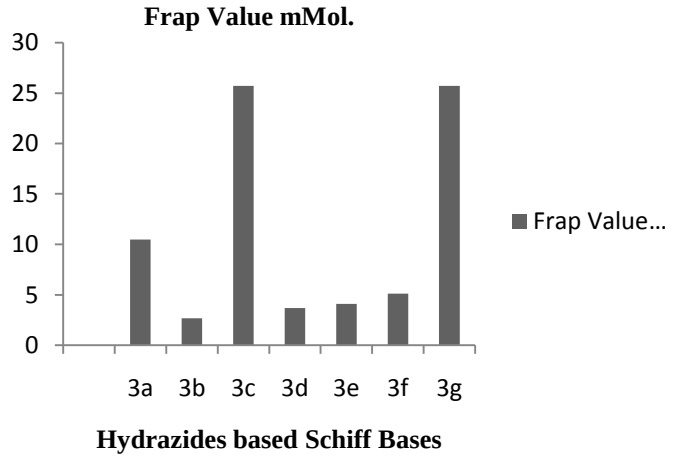


FRAP Assay

Results of FRAP assay of all synthesized Schiff bases are shown in Table No. 6. Frap values shows that Schiff bases of 3c and 3g have equal and maximum FRAP activity. On the other hand 3b Schiff base shows minimum FRAP activity.

Table- 6

Hydrazides based Schiff Bases	Frap Value mMol.
3a	10.48
3b	2.664
3c	25.72
3d	3.696
3e	4.096
3f	5.104
3g	25.72



Antimicrobial Activity Evaluation

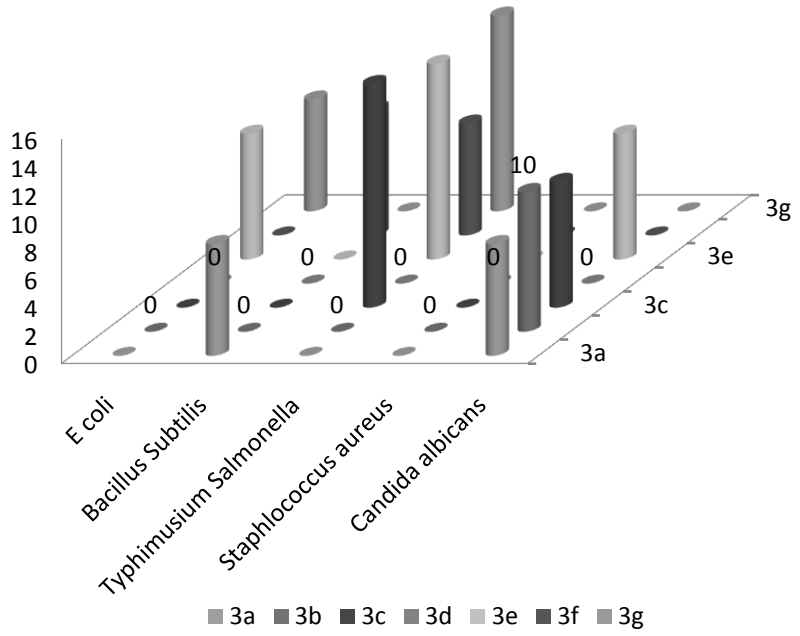
Antimicrobial assay of all Schiff bases are shown in Table- 7. 3d Schiff base show no activity against all bacteria, while remaining Schiff bases shown bacterial activity.

Table- 7

Hydrazides based Schiff Bases	*E. coli*	*Bacillus Subtilis*	*Typhimusium Salmonella*	*Staphlococcus aureus*	*Candida albicans*
3a	Nil	8mm	Nil	Nil	8mm
3b	Nil	Nil	Nil	Nil	10mm
3c	Nil	Nil	16mm	Buk	9mm
3d	Nil	Nil	Nil	Nil	Nil

3e	9mm	Nil	14mm	Nil	9mm
3f	Nil	9mm	8mm	Nil	Nil
3g	8mm	Nil	14mm	Nil	Nil

Antimicrobial Assay of Hydrazide Schiff Baseses



Conclusion

The proposed structure of synthesized hydrazide based Schiff bases were confirmed FTIR data and Elemental Analyzer data. Some Schiff bases show moderate activity against some bacteria while majority of Schiff bases were inactive against antimicrobials.

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