International Journal of Pharmaceutical Research and Development (IJPRD)
Platform for Pharmaceutical Researches & Ideas
www.ijprd.com

EVALUATION OF ANTIRADICAL AND PASS PREDICTION BIO ACTIVITIES OF SCHIFF BASES DERIVED FROM 4-AMINOANTIPYRINE

Dr.G. Valli[1]*, M.Mahalakshmi[1]

[1]Department of chemistry, S.F.R College for women, Sivakasi, Tamil Nadu, India.

ABSTRACT

Schiff bases derived from 4-aminoantipyrine plays a vital role in biological and pharmacological activities. Knowing the importance of 4-Aminoantipyrine Schiff bases and their analogues for their wide varieties of bioactivities like analgesic, antiviral, antipyretic, antirheumatic, antimicrobial, anti-inflammatory and CNS activities etc., our present study deals with the synthesis of (E)-4-(4-hydroxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one, (E)-4-(4-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one, (E)-4-(4-hydroxy-3-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one, (E)-4-((2-hydroxynarhthalen-1-yl)methyleneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one, (E)-4-(2-hydroxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one and (E)-1,5-dimethyl-4-(4-nitrobenzylideneamino)-2-phenyl-1H-pyrazol-3(2H)-one derived from 4-aminoanyipyrine with different aldehydes. Antiradical activity and PASS Prediction of bio activities were determined. In-vitro antiradical activities were determined by DPPH, NO and SO radical scavenging methods at a concentration of 100µg/ml .The DPPH radical scavenging activity of (E)-4-(4-hydroxy-3-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one (91.57%) was observed to be closer to the standard ascorbic acid . The NO radical scavenging activity of (E)-4-(4-hydroxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one was found to exhibit 50% activity as that of ascorbic acid . The Super oxide radical scavenging of (E)-4-(4-hydroxy-3-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one (61.74%), (E)-4-(4-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one (61.13%) were shown to be higher than the standard ascorbic acid (52%).

Among the six different schiff bases (E)-4-(4-hydroxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one exhibited the maximum bioactivities like Antipyretic (96.4%), Insulysin inhibitor (94.9%) and Anti-inflammatory (91.9%), E)-4-(4-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one showed Antipyretic (91.4%), Insulysin inhibitor (9419%), CYP2A8 (93.9) and Anti-inflammatory (91.6%), (E)-4-(4-hydroxy-3-

Correspondence to Author

Dr.G. Valli

Associate Professor of Chemistry,
S.F.R College for women, Sivakasi,
Virdhunagar District, Tamilnadu, India

Email: mrs.valliravichandran@gmail.com

methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one exhibited Antipyretic (96.8%) and Insulysin inhibitor (96.2%) and (E)-4-(2-hydroxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one showed Antipyretic (95.9%), Insulysin inhibitor (95.2%) and Anti-inflammatory (91.5%) compared to other bioactivities

KEYWORDS : **:** Antirdaical, PASS, DPPH, 4-aminoantipyrine

INTRODUCTION

Schiff bases are of the most widely used organic compounds used as dyes, catalysts, and intermediates in organic synthesis and as polymer stabilizers. They have been shown to exhibit a broad range of biological activities, including antibacterial[1], antifungal[2], antimalarial[3], , anti-inflammatory[4], antiviral[5]and antipyretic[6-7] properties [8]. 4-aminoantipyrine Schiff bases have a variety of application in biological, clinical, analytical and Pharmacological studies [9-11]. 4-aminoantipyrine has played an important role in Inorganic Chemistry as it forms stable complexes with many transition metal ions. Schiff bases derived from vanillin have been extensively studied due to their synthetic flexibility[12-14], selectivity and sensitivity towards the central metal atom[15]. Antiradicals have been showed to play an important role in protecting humans against many fatal diseases [16]. Antiradical properties play an important role in the alleviation of diabetes and obesity due to oxidation stress [17].

Pass prediction bioactivity for the synthesized Schiff bases using 4-aminoantipyrine were carried out using online software, **PASS.** Pa **(**probability to be active) value estimates the chance that the studied compound is belonging to the sub-class of active compounds resembles the structures of molecules.

EXPERMINTAL WORK

I. MATERIALS AND METHODS

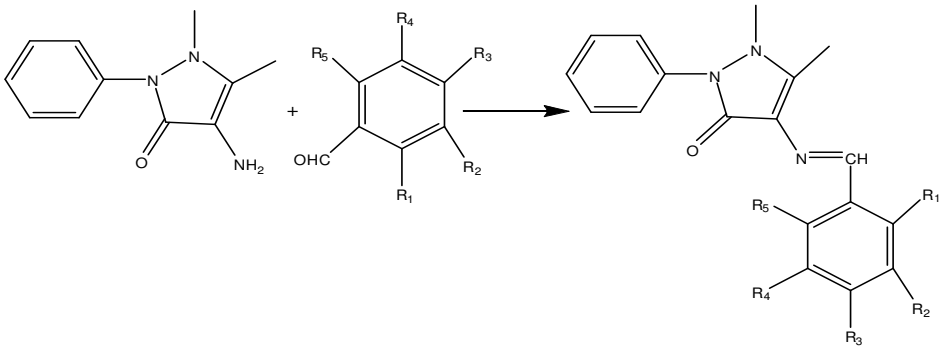
a) Materials

The chemicals such as 4-aminoantipyrine, Salicylaldehyde, Vanillin, Anisaldehyde, 4-nitrobenzaldehyde, 4-hydroxy benzaldehyde and ß-hydroxynapthaldehyde, of E.Merck grade and distilled ethanol were used.

b) Methods

The standard procedures for the preparation of Schiff bases were carried out. An ethanolic solution (5 ml) of 4-amino-1,5-dimethyl-2-phenylpyrazol-3-one (1g, 0.05mmol) (4-aminoantipyrine)was added to an ethanolic solution (5 ml) of substituted benzaldehyde (0.005mmol), and the reaction mixture was placed on microwave oven for 30sec. The progress of the reaction was monitored by TLC.

The precipitates formed were collected by filtration and purified by recrystallization with ethanol. The six different Schiff bases prepared were given in **scheme- I.**



Scheme-I

Table1. 4-aminoantipyrine Schiff bases

Compound no	R1	R2	R3	R4	R5	R6
1a	CHO	H	H	OCH3	H	H
1b	CHO	H	H	OH	H	H
1c	CHO	H	OCH3	OH	H	H
1d	CHO	OH	H	H	H	H
1e	OH	CHO	H	H	H	H
1f	CHO	H	H	NO2	H	H

The melting point and the yield were noted for the above synthesized Schiff bases given in **Table II**

Table II. Yield and Melting point of 4-aminoantipyrine

Compound no	Name of the Schiff bases	M.Pt	Yield
1a	E)-4-(4-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one	90%	161°C
1b	(E)-4-(4-hydroxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one	85%	201°C
1c	(E)-4-(4-hydroxy-3-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one	92%	203°C
1d	(E)-4-((2-hydroxynarhthalen-1-yl)methyleneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one	90%	182°C
1e	(E)-4-(2-hydroxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one	93%	141°C
1f	(E)-1,5-dimethyl-4-(4-nitrobenzylideneamino)-2-phenyl-1H-pyrazol-3(2H)-one	85%	216°C

II. Antiradical activity determination

All the synthesized Schiff bases were tested for their free radical scavenging activities by DPPH, Nitric oxide (NO) and Super oxide (SO) methods. The DPPH (1, 1-Diphenyl -2- picryl-hydrazil) radical scavenging activity was measured by using the method described by Blois.S.

The nitric oxide (NO) radical scavenging activity was measured by using Griess' reagent.

The Superoxide (SO) scavenging radical activity was carried out by using alkaline DMSO method (Henry, 1976). The absorbance of the Schiff bases by above three methods were listed in **Table III.**

Table-III- Antiradical activity of 4-aminoantipyrine Schiff bases

S.No	Compound no	Anti radical scavenging activity (%)		
		DPPH	Nitric oxide	Super oxide
1	**Standard** Ascorbic acid	96.64	32.52	59.82
2	**1a**	91.35	17.40	61.34
3	**1b**	80.43	9.82	51.98
4	**1c**	91.57	7.01	61.74
5	**1d**	79.13	3.96	47.67
6	**1e**	90.89	6.56	61.13
7	**1f**	83.13	4.65	52.08

III. Pass Prediction

The structure of Schiff bases (**1a-1f**) were drawn in **chemdraw ultra11.0** and their structures were saved as mol files **(*.mol).**

The possible bioactivities of 4-aminoantipyrine Schiff bases were predicted using **PASS** software.(V.Poroikov et al, version 1.917) and their highest activities were listed in **Table IV**

Table IV-Pass prediction activities of 4-aminoantipyrine Schiff bases

S.No	Compound no	Name of the activity (%)						
		Antipyretic	**Anti-inflammatory**	**Analgesic**	**CYP2A8**	**Neutrophilic**	**Hypothermic**	**Insulysin inhibitor**
1	**1a**	91.4	91.9	-	93.9	89.5	80.2	91.6
2	**1b**	96.4	91.5	87.2	-	-	-	94.9
3	**1c**	96.8	-	-	-	-	85.0	96.2
4	**1d**	95.4	90.4	83.4	-	-	-	-
5	**1e**	95.9	91.5	85.1	-	-	-	95.5
6	**1f**	90.3	90.0	84.0	-	85.6	-	-

RESULT AND DISCUSSION

A. Antiradical activity

The DPPH radical scavenging effect of (E)-4-(4-hydroxy-3-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one (91.57%) and (E)-4-(4-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one (91.35%) showed approximately closer antiradical activity as that of standard ascorbic acid.

The Nitric oxide radical scavenging effect of the Schiff bases derived from 4-aminoantipyrine were found to exhibit 50% activity as that of standard ascorbic acid.

The Super oxide radical scavenging effect of (E)-4-(4-hydroxy-3-methoxybenzylideneamino) -1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one (61.74%), (E)-4-(4-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one (61.34%) and (E)-4-(4-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one (61.13%) were shown to have higher antiradical activity as that of standard ascorbic acid (59.82%).

B. Pass prediction

All the above synthesized Schiff bases **(1a-1f)** were found to exhibit various activities under PASS prediction like, Anti-inflammatory, analgesic,

Hypothermic, Neurophilic dermatiosis, Antipyretic, Insulysin inhibitor and CYP2A8 activities were observed to be greater than 80% as listed in **Table IV.**

(E)-4-(4-hydroxy-3-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one was found to have highest (i)antipyretic activity (96.8%), (ii) hypothermic activity (85.0%) and (iii) Insulysin inhibitor activity (96.2%) among others Schiff bases.

(E)-4-(4-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one exhibited the following activities as highest among other Schiff bases.

- Anti-inflammatory activity (91.9%)
- CYP2A8 activity (93.9%)
- Neutrophilic dermatiosis activity (89.5%)

CONCLUSION

The antiradical activity determination by DPPH,radical scavenging method of (E)-4-(4-hydroxy-3-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one (92%) was observed to be closer to the standard ascorbic acid. The NO radical scavenging activity of (E)-4-(4-hydroxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one was found to exhibit 50% activity as that of ascorbic acid . The Super oxide radical scavenging of (E)-4-(4-hydroxy-3-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one (61.74%), (E)-4-(4-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one (61.13%) were showed higher activity than the ascorbic acid (52%).

PASS prediction bioactivities of the six Schiff bases of 4-aminoantipyrine showed the following result:

- (E)-4-(4-hydroxy-3-ethoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one exhibited antipyretic(96.8%) and insulysin inhibitor (96.2%) activities.
- (E)-4-(4-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one showed anti-inflammatory activity (91.9%) and antipyretic (91.4%) activities.
- (E)-4-(4-hydroxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one exhibited antipyretic activity (96.4%), Insulysin inhibitor (94.9%) and anti-inflammatory (91.5%) activities

we conclude that (E)-4-(4-hydroxy-3-ethoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one (96.8%) may find its uses as an antioxidant agent in futures.

ACKNOWLEDGEMENT

The authors thank UGC for financial assistant under minor research project.

REFERENCES

1. KN.Venugopal, BS.Jayashree. Indian J Pharm. Sci.2008; 70; 88-91.
2. SN.Pandey, VS.Lakshmi and A.Pandey. Indian J Pharm Sci.2003; 65: 213-222.
3. Y.Li, ZS.Yang, H.Zhang, BJ.Cao and FD Wang, Bioorg and Med Chem. 2003; 11: 4363-4368.
4. G.Valli, P.Mareeswari, K.Ramu, A.Thanga Thirupathi, Research Journal of Pharmacy and Technology, Vol 5(11), Nov.2012, 1457-1460.
5. MS.Karthikeyan, Dasappa Jagadeesh Prasad, K.Boja Poojary Subrahmanya Bhat, Bantwal Shivaram Holla, Bioorg and Med Chem.2006;14:7482-7489.
6. G.Valli, P.Mareeswari, K.Ramu, A.Thanga Thirupathi, International Journal of Pharmaceutical Research and Development, Vol.4(9), Nov 2012, 85-92.
7. G.Valli, P.Mareeswari, K.Ramu, A.Thanga Thirupathi, Journal of Pharmacy Research, Vol.5(6), June 2012, 3453-3455.
8. P. Przybylski, A. Huczynski, K.Pyta., B. Brzezinski, F.Bartl, curr.org.chem 13, 2009, 124-148
9. N.Raman, S.Thalamuthu, J. Dhaveethu Raja, M.A.Neelakandan, Sharmila.J,Banerjee, J.Chilian Chem. Soc., 53 (2008).
10. N.Raman, J.J Raja, J.Joseph., .J.D Raja, J.Chilian Chem. Soc.,52, 2007, 1099.
11. N.Raman, S.Syed Ali Fathimaand, J. Dhaveethu Raja, J. Serbian. chem..Soc 73(11), 2008, 1063-1071

12. Muthukimaran, Spectrochim Acta A Mol Biomol. Spectrosc., 71,628-35 (2008).
13. . Neelakantan.M.A, Rusalraj.F, Dharmaraja.J, Johnsonraja.S, Jeyakumar.T and Pillai.M.S, Spectrochim Acta A Mol. Biomol. Spectrosc., 7, 1599-609 (2008).
14. Wadher.S.J, Int.J. PharmTech Res., 1,1-33 (2009).
15. Ali.M.M, Jesmin,M, Salam.S.M.A, Khanam.J.A, Islam.M.F andIslam.M.N, J. Sci Res , 1(3),641-646 (2009).
16. G.Valli and M.Jeyalakshmi, Asian J. Pharm. Res. 2012: Vol. 2: Issue 4, Pg 153-155.
17. Muhammad Sayed Alam, Jung-Hyun Choi, Bioinorganic and Medicinal Chemistry, 20(2012), 4103-4108.

*****