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Spectral Characterization And In-Vitro Anti-inflammatory Potential Of An EDP Schiff Base.

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ABSTRACT

Heterocyclic Schiff bases always find a versatile use and therefore synthesizing new Schiff bases have become a considerable interest in the chemistry of metal complexes. The new Schiff base have been synthesized using aromatic amine and aromatic aldehyde such as Ethylenediammine and Piperonal in the molar ratio 1:2. The geometry of the newly synthesized complex was predictable using techniques like IR and NMR spectroscopy. Further, anti-inflammatory activity of the synthesized EDP was assesses by various invitro methods. The synthesized Schiffs base EDP showed potent anti-inflammatory activity in a dose dependent manner and the activity is comparable with that of piperonal and Sodium Diclofenac used as standard.

Keywords: Schiff base, Ethylenediammine, NMR, IR, Antiinflammaroty.

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INTRODUCTION

Schiff bases with hetero atoms such as N, O and other donors provide us a variety of active ligand sites which are capable to form metal complexes [1]. Schiff bases of Heterocyclic compounds possess various biological activities such as Antimicrobial activity, Antifungal activity, Antiviral activity, Anti helmintic activity, Anti-tumor activity, cytotoxic and Analgesic activities[2-6]. Schiff bases of chitosan show a very good antioxidant activity. Amino Schiff bases (i.e) Schiff bases derived with amino acids were found to possess an anticancer activity [7]. Schiff bases of hydrogen carboxamide and its metal complexes were reported that it alters a reproductive psychology [8].

Piperonal, an heterocyclic aldehyde with 3,4-methylenedioxy scaffold in its structure is known to possess varied pharmacological properties[9,10]. The novel heterocyclic compounds and their derivatives are continuously explored for pharmacological activity in the field of medicinal chemistry. Hence, with the survey of literature of the Schiff bases, here in we report the synthesis, spectral characterization and anti-inflammatory potential of a newly synthesized Schiff base derived from Ethylenediammine and Piperonal in ethanol medium.

MATERIALS AND METHODS

All the chemicals used were of analytical grade and used as such without purification. All the solvents used in this experiment were purified by standard procedures. Double distilled water were used.

Synthesis of EDP Schiff base

A mixture of Ethylenediammine (0.84g) with Piperonal (1.49g) dissolved in ethanol were taken in the RB flask and refluxed under ice cold conditions for three hours with constant stirring. The white solid substance obtained. It was filtered with distilled water, washed several times and recrystallized from ethanol and dried. The scheme of the reaction is given in Fig 1.

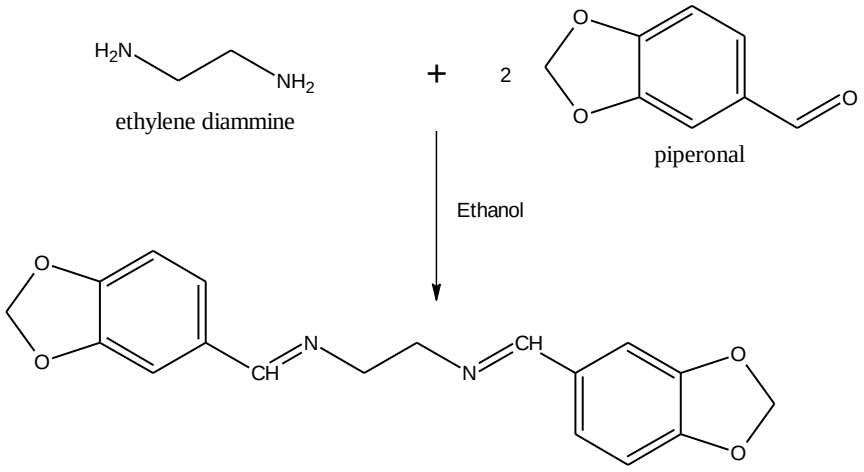

Figure 1: Schematic diagram for synthesis of *N,N'*-Bis-benzo[1,3] dioxol-5-ylmmethylene-ethane-1,2-diamine.

1H-NMR and 13C- NMR spectra were recorded using a Bruker AV 400 MHz spectrometer and chemical shifts are expressed as δ (ppm) with SiMe4 as internal standard when measured in CDCl3 or DMSO-d6. The FT-IR spectra were recorded on a Shimadzu 8201spectrophotometer using KBr and the values are expressed in 4000-400 cm-1.

In vitro anti- inflammatory activity

In vitro Anti-inflammatory activity of piperonal and synthesised schiffs base EDP was assessed using different invitro methods. The activity was compared with Aspirin and Diclofenac which are used as standard

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drug vehicle. The different invitro methods include the determination of activity of test samples against inhibition of Proteinase inhibitory and HRBC membrane stabilization. Concentration in the range of 100-500 µg/ml was fixed for both test samples and standard drug [11].

% of inhibition = (Abs control – Abs sample) X 100 / Abs control

RESULTS AND DISCUSSION

Characterization techniques

The physicochemical parameters such as, molecular weight, melting point and the yield percentage of the newly synthesized EDP Schiff base were reported [Table 1].

Table 1: Physico chemical properties of EDP Schiff base

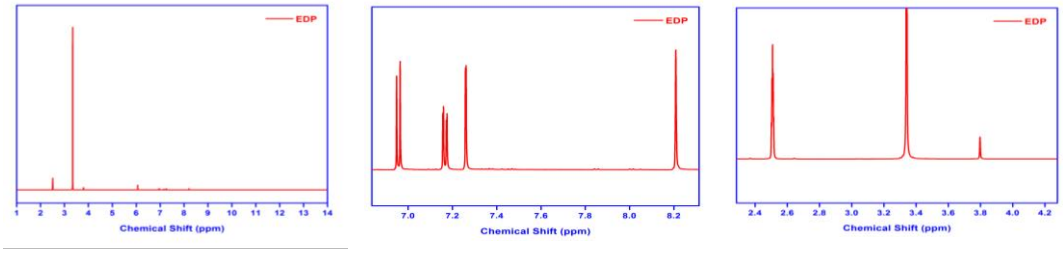
EDP Schiff base	Colour	M.P	Mol. wt	Yield (%)
N,N′-Bis-benzo[1,3]dioxol-5-ylmethylene-ethane-1,2-diamine	White	290	324.3	74

Table 2: NMR Studies

Chemical shift (δ)	Functional group
3.91	Methylene proton of amine group
8.11	R-C=N
5.90	Di oxazole group
6.69, 7.02	Benzene proton

The NMR spectra as given in fig2 and Table2 reveal the proton environment of the newly synthesized Schiff base. The peak signal at δ 3.91 is attributed to the methylene group of amines. The actual peak was at δ 2.91 in ethylenediammine and the increase in this chemical shift shows that the amine group is involved in coordination. The peak at δ 5.90 is attributed to the 1,3dioxazole group and the peaks at δ 6.69 and 7.02 were attributed to the proton of the benzene ring [12,13]. The C=O peak at δ 9.87 in the piperonal compound was disappeared in the newly synthesized Schiff base showing the absence of C=O group in the Schiff base whereas the new peak at δ 8.11strongly gives evidence for R-C=N group which reveals that the coordination at this junction [14,15]. Here each of the NH_2 group of ethylenediammine was coordinated by piperonal molecules.

Figure 2: NMR Spectra of synthesised *N,N*′-Bis-benzo[1,3] dioxol-5-ylmmethylene-ethane-1,2-diamine.



IR Studies

The IR spectra are considered as the basic constructive tool to determine the structure for coordination compounds. The FTIR spectrum of an EDP Schiff base was presented in fig3. It shows strong peak at 3416cm^{-1} which is attributed to N-H stretching of amino compounds [16]. The C-N of amide peak will be present at 1425 cm^{-1} whereas this peak was absent in the new Schiff base indicating that the piperonal C=O was not coordinated with NH_2 group of amines. Here the R-CH group of piperonal was coordinated with each of the NH_2 group of ethylene diamine making a new R-C=N for coordination. This C=N group was seen at 1602

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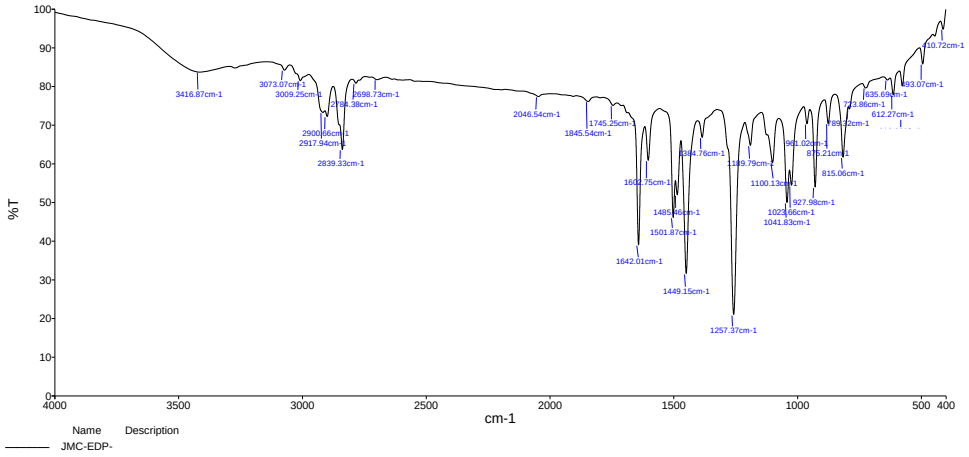
cm^{-1} confirming that the coordination takes place in the synthesized EDP [17,18]. The peaks at 1384, 1480cm^{-1} were assigned for the C-H deformation in substituted aromatic compounds [19].

Figure 3: IR Spectra of synthesised *N,N'*-Bis-benzo[1,3] dioxol-5-ylmmethylene-ethane-1,2-diamine.



Antiinflammatory activity

The antiflammatory activity was assessed by proteinase inhibitory action and HRBC membrane stabilization method [Fig 4 and 5]. The schiffs base conjugate showed increase in activity with increase in concentration and the activity was comparable with that of standard drugs and unconjugated piperonal. The IC 50 values shown by EDP was slighltly higher than the standard when assessed by proteinase inhibitory action whereas the value is lower as shown by HRBC membrane stabilization method. However since the IC 50 values are comparable the schiffs base conjugate has been proved to show potent anti-inflammatory activity [Table 3 and 4].

Table 3: Antiinflammatory activity assessed by proteinase Inhibitory Method

Conc µg/ml	Std OD	Std %	EDP OD	EDP %	Pi OD	Pi %	Control
200	1.285	16.94	1.301	15.90	1.312	15.19	1.547
400	1.145	25.99	1.187	23.27	1.204	22.17	
600	0.797	48.48	0.825	46.67	0.846	45.31	
800	0.562	63.67	0.603	61.02	0.621	59.86	
1000	0.412	73.37	0.482	68.84	0.553	64.25	
IC 50 Values	-	657.261	-	695.523	-	727.295	

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Figure 4: Antiinflammatory activity assessed by proteinase Inhibitory Method

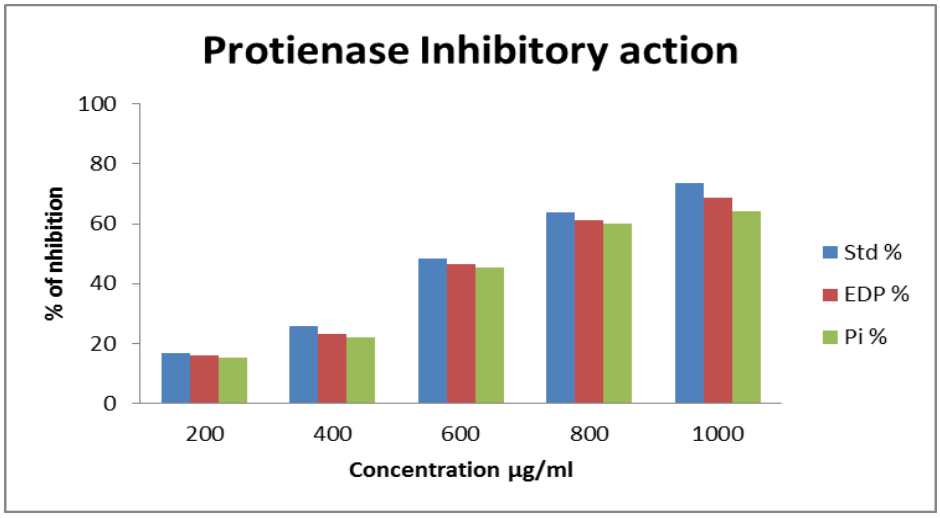
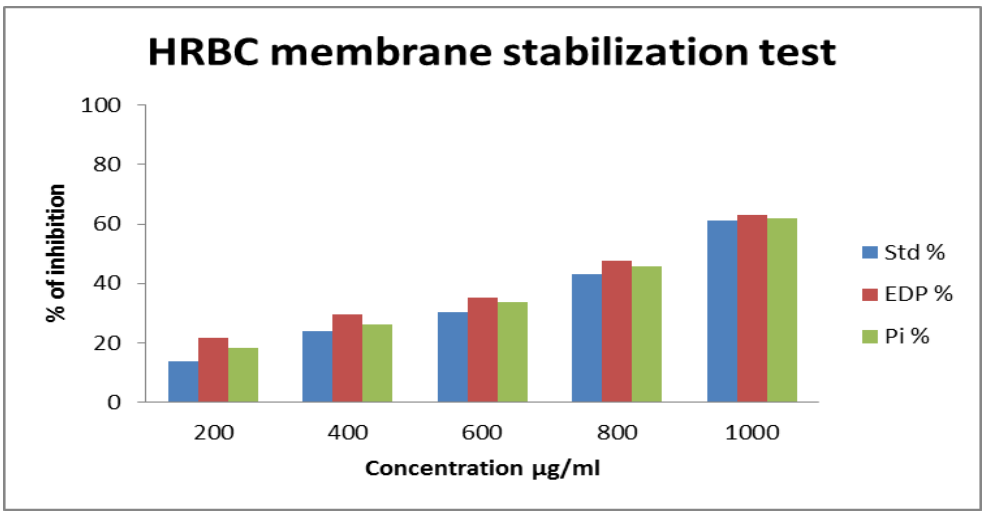


Table 4: Antiinflammatory activity assessed by HRBC membrane stabilization test

Conc µg/ml	Std OD	Std %	EDP OD	EDP %	Pi OD	Pi %	Control
200	2.447	13.69	2.220	21.69	2.312	18.45	2.835
400	2.154	24.02	2.001	29.42	2.072	26.91	
600	1.980	30.16	1.841	35.06	1.882	33.62	
800	1.612	43.14	1.487	47.55	1.543	45.57	
1000	1.101	61.16	1.046	63.10	1.076	62.05	
IC 50 Values	-	872.944	-	810.718	-	839.562	

Figure 5: Antiinflammatory activity assessed by proteinase Inhibitory Method



Novel pyrazoline and benzathiazopines and their derivatives with piperine nucleus has been explored for diverse medicinal properties. Considerable work has been carried out to assess the anti-inflammatory and analgesic activity of pyrazoline derivatives. Their protective role against inflammation is accomplished through inhibition of cycloxygenase and many synthetic compounds have been screened for COX inhibitors [20-24].

CONCLUSION

A new Schiff base has been synthesized with the heterocyclic aromatic compound piperonal and ethylene diamine. Two molecules of piperonal were coordinated with the NH_2 group of amine compounds and the mode of binding was studied by the IR spectroscopy. The proton environment of the Schiff base was identified with the proton NMR spectroscopy. The loss of C=O group has been indicated by the absence of proton NMR signal at δ 9.87. The presence of δ 8.11 in NMR and about 1600cm^{-1} in the IR region clearly depicts the piperonal C-H group is joined with NH_2 group of amine. The potent anti inflammatory activity shown by schiffs base conjugate can be further explored for its pharmacological properties. Hence, further studies were required on in this area for the advancement in applications of many heterocyclics as novel lead molecules to combat against human disease.

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