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Synthesis, Spectral, Electrochemical analysis and Screening for α-Glucosidase inhibition of some complexes of Cobalt (II) and Ethylenediamine

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Abstract

Schiff bases, having amine group and their metal complexes are widely used for industrial purposes and also reveal a wide range of biological applications. This work describes the most promising biological activities. Cobalt metal complexes, the $[Co(en)_3]2NO_3$ has most potent inhibitory activity among three complexes, having 784.12 µg/ml IC_{50} value while $[Co(en)_3]2Cl$ shows mild inhibition i.e. 47.39±0.83 %.

Keywords: Cobalt metal, diabetes mellitus, metallo-therapeutics, cyclic voltameter, α-Glucosidase Inhibition.

Introduction

Diabetes is chronic metabolic and non communicable disease with multiple etiologies, is considered as one of the five leading causes of death in the world. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030[1,2]. Diabetes mellitus clinically are of types (Type I and Type II) and genetically heterogeneous groups of disorders characterized by hyperglycemia. The main cause of Type I diabetes mellitus is autoimmune destruction of β-cells[3,4]. However etiopathogenesis of Diabetes type II is complex in nature but it is believed that due to impaired insulin secretion, resistance of insulin, genetic and environmental factors are responsible for causing this type of diabetes[4-6].

Metallo-therapeutics is an area of growing interest as is evident through the clinical trials that are being conducted worldwide for the usages of metals in therapeutics. Metallotherapy is a new therapeutic strategy to treat diabetes with metal complexes. Coulson and Dandona in 1980 that $ZnCl_2$ stimulate lipogenesis in rat adipocytes similarly to the action of Insulin. Since many metal complexes have been synthesized, also being with different metals with different coordination modes[7,10].

The aim of present work is to synthesize, characterize and observe the electrochemical behavior of cobalt complexes in sodium perchlorate solution to access further α-Glucosidase inhibitory activity of cobalt (II) complex with ethylenediamine.

Material and Methods

Chemicals: Water, $CoSO_4.7H_2O$, $CoCl_2.6H_2O$, Co $(NO_3)_2.6H_2O$, Potassium Bromide, p-nitrophenyl-α-D-glucopyranoside, were purchased from SRL, India and ethylenediamine, sodium perchlorate monohydrate from Alfa Acear, Great Britain. Acarbose, α–glucosidase rat intestinal acetone powder was procured from Sigma Aldrich, USA. All solvent were HPLC grade, chemicals were A.R grade and used further any purification.

Synthesis of Complex: The $[Co\ (L)_3]^{2+}$complex was prepared from three different salts of cobalt and ethylenediamine. 2 mM aqueous solution of metal salts was stirred in a beaker and 6mM of ethylenediamine were added drop by drop. With continuous string, a orange red colored solution were obtained, which were transferred in a petri dish to remove solvent in incubator at 45 °C. After few days a orange red colored complex $[Co\ (en)_3]$ SO_4, $[Co\ (en)_3]$ 2Cl and $[Co\ (en)_3]$ $2NO_3$ (1, 2 and 3respective) solid obtained[11].

Infra Red Spectroscopy: Infrared (IR) spectra were obtained by the KBr method using a Bruker Alfa-T model Fourier transform (FTIR) spectrometer (Bruker Instrument, Germany).The spectrometer was equipped with a Globar IR source, KBr beam splitter, and detector. For each spectrum, 16 scans were obtained with the resolution of 4 cm^{-1}. The obtained IR spectra were processed by means of the program OPUS 7.0.

Cyclic Volta metric: The cyclic voltammetric measurements were carried out with a Metrohm Instrument (Germany) having an electrochemical cell with a three-electrode system. The reference electrode was an Ag/ $AgCl_2$. Platinum wire was used as a working electrode, while a platinum wire electrode used as an auxiliary electrode. The 3 mg of complex were dissolved in 25 ml supporting electrolyte (0.1 M Sodium perchlorate) solution. The volatammogram, peak position and area were calculated using NOVA 1.9 software.

α-Glucosidase Inhibition: α-glucosidase inhibitory activity was performed following the modified method of Pistia Brueggeman and Hollingsworth[12, 13]. In brief, Rat-intestinal acetone powder was dissolved in 4 ml of 50 mM ice cold phosphate buffer and

sonicated for 6 minutes at 4°C. After vortexing for 20 minutes, the suspension was centrifuged (10,000 rpm, 4°C, 30 minutes) and the resulting supernatant was used for the assay. A reaction mixture containing 50 µl of phosphate buffer (50 mM; pH 6.8), 20 µl of rat α-glucosidase (1 U/ml) and 25 µl of sample of varying concentrations was pre-incubated for 5 min at 37°C, and then 25 µl of 3 mM PNPG was added to the mixture as a substrate. After incubation at 37°C for 30 min, enzymatic activity was quantified by measuring the absorbance at 405 nm in a micro titer plate reader (Bio-TEK, USA). Acarbose was used as a positive control and water as negative control. Experiments were done in triplicates. IC_{50} value was quantified using formula, $Y = 24.935\ln(x) - 37.049$, $R^2 = 0.9883$.

The percentage of enzyme inhibition by the sample was calculated by the following formula:

% Inhibition = {[(AC - AS)/AC] ×100}

Where, AC is the absorbance of the control and AS is the absorbance of the tested sample. The concentration of an inhibitor required to inhibit 50% of enzyme activity under the mentioned assay conditions is defined as the IC_{50} value.

Results and Discussion

Infra Red Spectroscopy: In the IR spectrum of compound 1, the characteristic N-H bending vibration is observed as a strong bond at 1584 cm^{-1}, which is a commonly observed fact for chelated ethylenediamine complex. The -NH stretching vibrations are found in the range 3110-3304 cm^{-1}, the -CH stretching vibration 3050 and 2885 cm^{-1} and -CN stretching vibration are found in the range of 1190, 1140, 800 and 590 cm^{-1}. IR spectra of complexes show a peak in the range of 3500-3400 cm^{-1} which denotes presence of -OH group. IR assignments and spectra of the complex 1, 2 and 3 are given in table 1 and figure 1, 2 and 3 respectively[14].

Table-1
Representing IR spectra of Complexes

S.No	Complexes	Group	Bond cm^{-1}
1	$[Co(en)_3]SO_4$	-OH	3500-3400
		-CH (Stretching Vibration)	3099
		-NH (Bending vibration bonded with metal)	1616 (merged)
		-NH (Stretching vibration)	3210
		-CN (Stretching Vibration)	1056
2	$[Co(en)_3]2Cl$	-OH	3500-3400
		-CH (Stretching Vibration)	3089 (merged)
		-NH (Bending vibration bonded with metal)	1584
		-NH (Stretching vibration)	3169
		-CN (Stretching Vibration)	1055
3	$[Co(en)_3]2NO_3$	-OH	3500-3400
		-CH (Stretching Vibration)	3208
		-NH (Bending vibration bonded with metal)	1581
		-NH (Stretching vibration)	3169
		-CN (Stretching Vibration)	1056

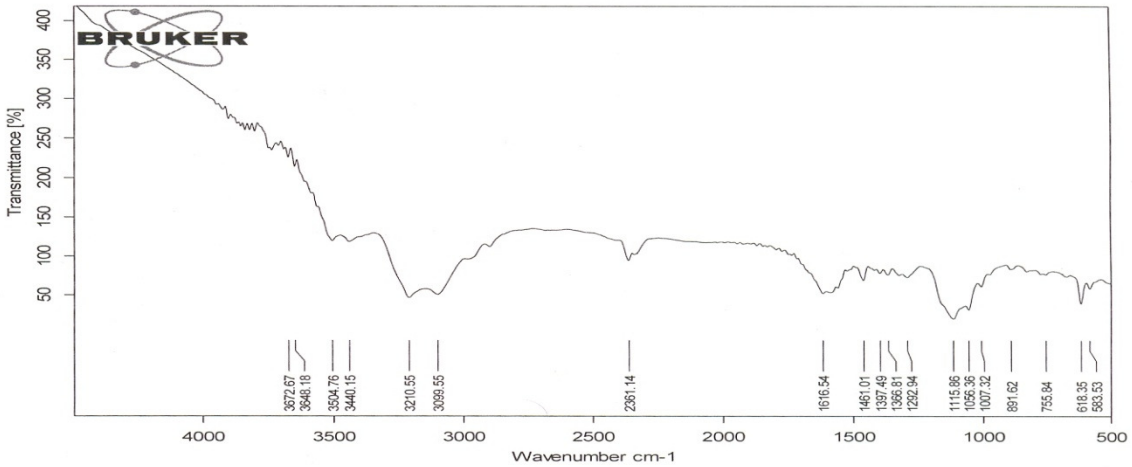

Figure-1
Representing IR Spectra of $[Co\ (en)_3]\ SO_4$

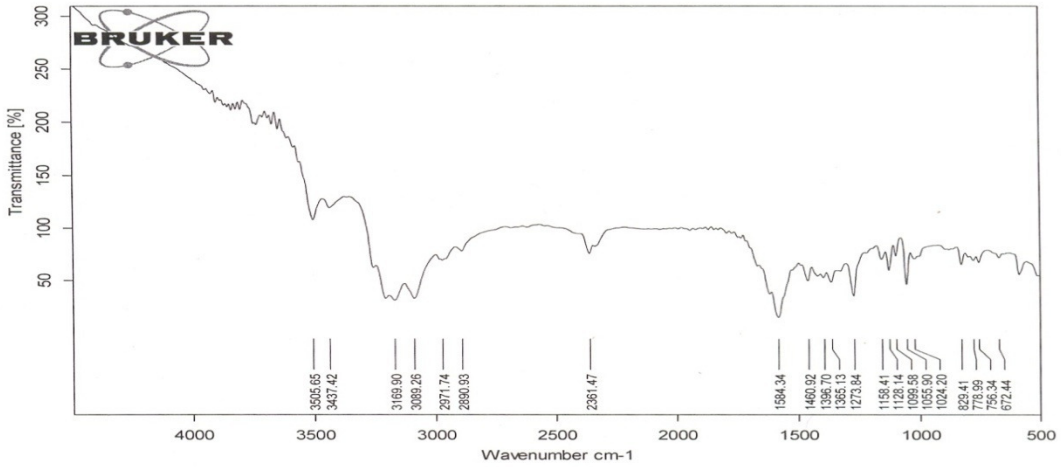

Figure-2
Representing IR Spectra of [Co (en)$_3$] 2Cl

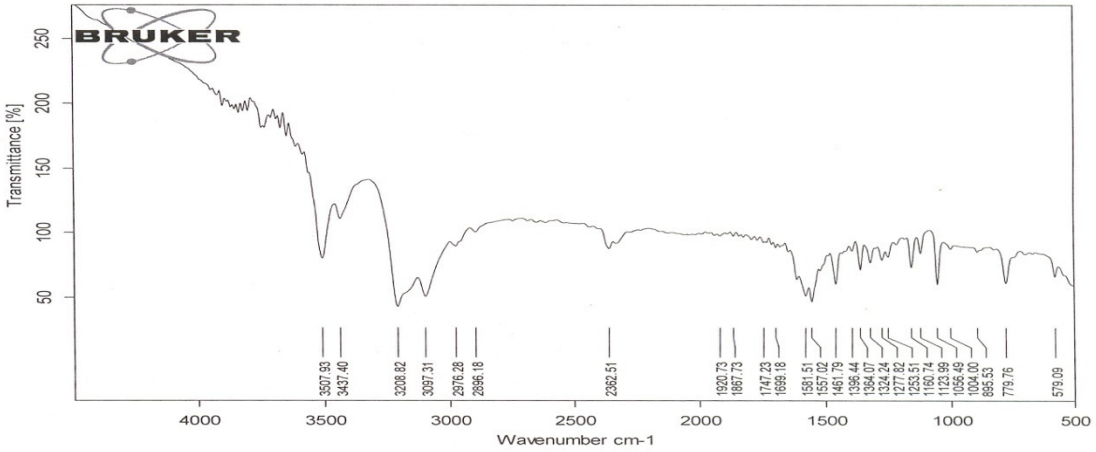

Figure-3
Representing IR Spectra of [Co (en)$_3$] 2NO$_3$

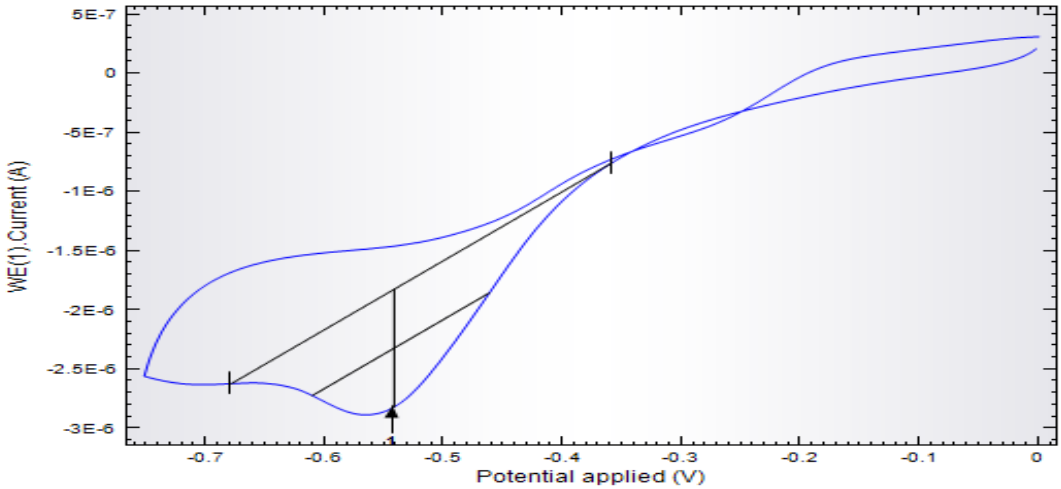

Figure-4
Represents the voltamogram of [Co(en)$_3$]$^{2+}$ system

Figure 4 showes cylic voltamogram (CV) scaned three times cathodically in the potential region 0.00 to -0.750V using Ag/AgCl electrode in 0.1 M $NaClO_4$ solution $[Co(en)_3]^{2+}$ system. In this scan voltamogram showes only single reduction peak at -541.99 mV. Peak width half of complex were 0.14887 and peak (1/2) were 80.138 mV.

α-Glucosidase Inhibition: There are several cobalt (II) complex has been reported to have antidiabetic activity[15,16]. The inhibitory effects of acarbose (positive control), $[Co(en)_3]SO_4$, $[Co(en)_3]_2Cl$, $[Co(en)_3]_2NO_3$ on α-glucosidase activity were concentration dependent. From the result, the apparent IC_{50} values (table 4) of the test compounds with respect to the α-glucosidase activity were estimated (figure 5 and 6). In comparison with acarbose, all test compounds except for $[Co(en)_3]2Cl$ showed mild α-GI effect (table 2 and 3).

Table-2
Represents the Absorbance of Nitrophenol

S.N	Conc. in µg/ml	Acarbose	Error±SD	Conc. of Complexes µg/ml	Complex1	Error±SD	Complex2	Error±SD	Complex3	Error±SD
1	10	0.312	0.001	100	0.344	0.002	0.322	0.002	0.353	0.003
2	20	0.248	0.003	200	0.307	0.002	0.312	0.003	0.293	0.003
3	40	0.167	0.002	400	0.290	0.001	0.265	0.003	0.255	0.002
4	60	0.123	0.003	600	0.241	0.001	0.240	0.002	0.213	0.002
5	80	0.104	0.004	800	0.217	0.003	0.222	0.003	0.192	0.000
6	100	0.098	0.004	1000	0.186	0.002	0.205	0.003	0.168	0.003

Table-3
Represents the % inhibition of α-Glucosidase

S.N	Conc. in µg/ml	Acarbose	Error±SD	Conc. of Complexes µg/ml	Complex1	Error±SD	Complex2	Error±SD	Complex3	Error±SD
1	10	19.96	0.29	100	11.48	0.535	17.22	0.51	9.17	0.65
2	20	36.16	0.64	200	21.08	0.514	19.71	0.65	24.59	0.78
3	40	56.72	0.39	400	25.36	0.392	31.96	0.65	34.53	0.59
4	60	68.03	0.82	600	37.96	0.392	38.22	0.39	45.24	0.44
5	80	73.01	0.92	800	44.22	0.680	42.93	0.68	50.64	0.00
6	100	74.12	0.97	1000	52.18	0.000	47.39	0.83	56.73	0.64

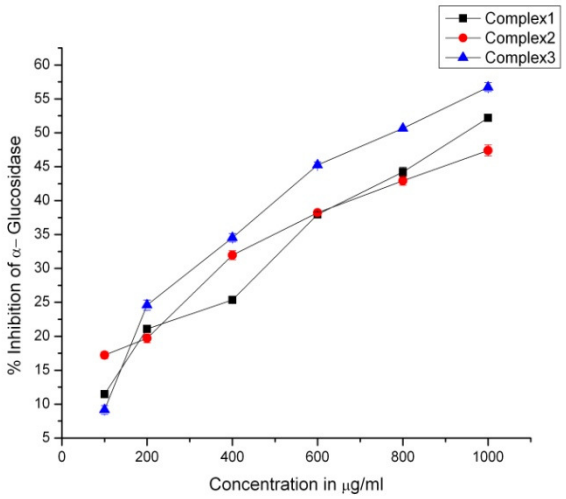

Figure-5
Represents the % Inhibition of α- Glucosidase

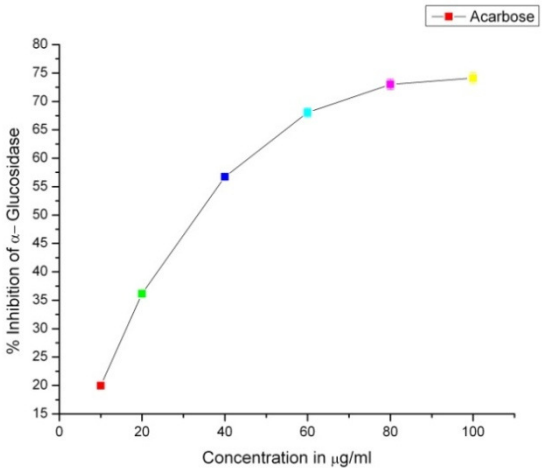

Figure-6
Represents the % Inhibition of α- Glucosidase by Acarbose

Table-4
Represents the IC_{50} Value

S.No	Compounds	IC_{50} Value µg/ml
1	Acarbose	25.60
2	Complex1	927.89
3	Complex2	784.12

Conclusion

The variety and extent of metal ions involvement has been recently appreciated but it has a very long history in toxicology, medicine and pharmacology. For instance, Cr, V, Mn, Cu, Ni, Co, Fe, Zn and Mo among the transition metals are very essential to life. In the present work we have synthesized cobalt complexes with ethylenediamine. The intense peak of IR at 1581 cm^{-1} support the synthesis of cobalt complex and cylic voltamogram represents only reduction peak at -541.99 mV. IC_{50} values represents the $[Co(en)_3]_2NO_3$ have good inhibitory activity among these three complexes

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