Synthesis and importance of complex diaquo bis (3-Hydroxy-5-hydroxymethyl-2-methoxypyridine-4-carbaldehyde amidoguanidine) copper (II) chloride: [Cu (MPLAG-H) $(H_2O)_2$] Cl_2. $2H_2O$.

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Abstract :-

By mixing the solution of amidoguanidine bicarbonate in HCL with methanolic MPL and refluxing for about an hour yellowish coloured MPLAG is farmed as aligned and appropriate salt $CuCl_2$ are coordinate and form a brown coloured complex [Cu (MPLAG-H) $(H_2O)_2$] Cl_2. $2H_2O$. This paper present the synthesis and importance of complex with Schiff base ligand.

Key Word:- MPLAG, dimmeric copper (II) complex, Amidoguanidine.

Intorduction:-

Diabetes is now a days common disease all over the world. Hypegycemia has been identified as a major risk factor for the development of diabetic complication[1]. Amidoguanidine (AG) has been extensively studied as one of the most promising compound for the treatment of diabetic complecations, because the compound has both advanced glycation inhibitory activity[2] and antioxidant activity[3, 4]. It has been reported that a pyridoxal amidoguanidine Schiff base adduct exhibits advanced glycation inhibitory activity comparable to that of AG while causing no decrease in the liver pyridoxal phosphate content of normal mice [5,6] also PL-AG is more potent than AG in preventing nephropathy in strepotozotocin- induced diabetic mice[7]. These findings suggest that PL-AG is superior to AG for the treatment of diabetic complications because it not only prevents Vitamin B_6 deficiency, but is also better at controlling diabetic nephropathy. The preventive effect of this adduct against diabetic nephropathy is mediated via inhibition of both oxidation and glycation[8] . The inhibition of advanced glycation end products (AGEs) at millimolar concentrations of AGEs inhibitors, used in many in virto studies, results primarily from the copper chelating or antioxidant activity of the AGEs inhibitors, rather than their carbonyl trapping activity[9]. Defining the chelating activity of AGEs inhibitors is essential for understanding the mechanism of action of drugs and possible benefits of chelation therapy in diabetes, as well as for developing more effective clinically useful inhibitors of diabetic complications.

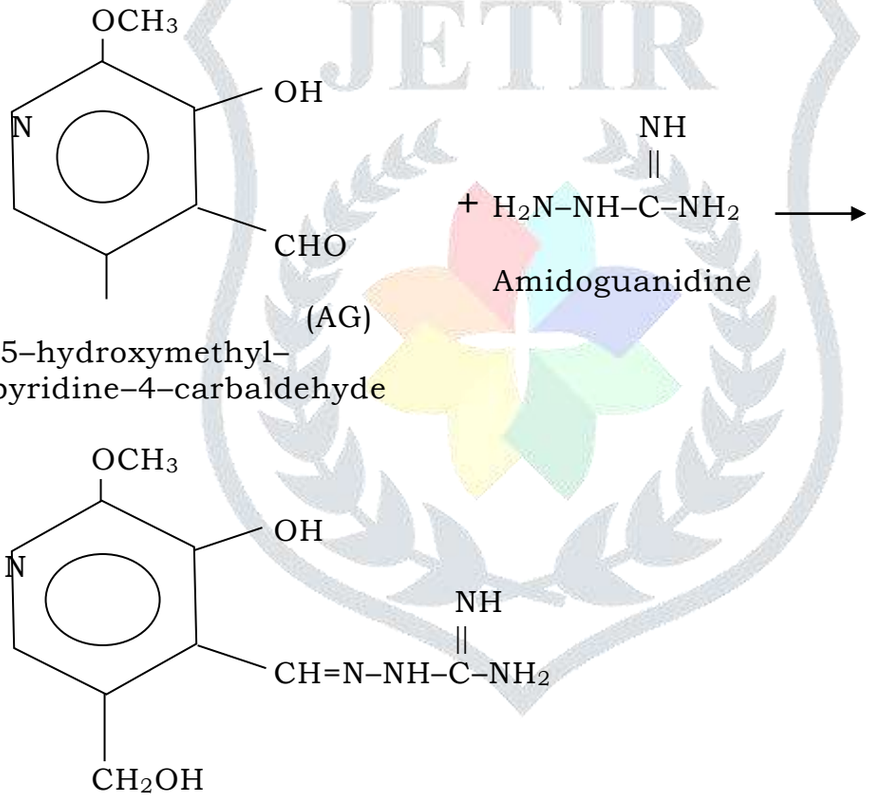
Bearing in mind the biological and medicinal importance of AG and PL-AG adduct and the influence of copper (II) ions on their inhibitory activity, in the present study we attempted to evaluate the chelating ability of PL-AG inhibitor in order to cast more light on the role of copper chelation in the mechanism of action of AGEs inhibitors.

EXPERIMENTAL

`All the chemicals used of research grade chemicals of either B.D.H. Annalar or pure E. Merck quality. Carbon, Hydrogen, Nitrogen analysis were carried form C.D.R.I. Lucknow. The conductivity of the complexes were determined with help of systronics conductivity bridge. The conductivity of complexes were measure in DMF solution. Molar conductivity of complex was calculated by using the formula M = K x 1000 /C were K = conductivity of complex, C = concentration of complex. The magnetic susceptibilities of solid complexes were determined by the Bouy method at room temperature. The magnetic moment data were made available to us by kind courtesy of Patna Science College Laboratory Patna. IR Spectra were taken from Perkin Elmer IR Spectrometer from department of Chemistry I.I.T. New Delhi and by the courtesy of C.D.R.I. Lucknow.

Synthesis of Ligand :-

PREPARATION OF 3-HYDROXY-5-HYDROXYMETHYL-2-METHOXYPYRIDINE-4-CARBALDEHYDE-AMIDOGUANIDINE



3-Hydroxy–5–hydroxymethyl–2–methoxypyridine–4–carbaldehyde amidoguanidine (MPLAG)

Amidoguanidine bicarbonate (0.5 milli mole) was dissolved in HCl, while 3–hydroxy–5–hydroxymethyl–2–methoxypyridine–4–carbaldehyde (MPL) of (1 milli mole) was dissolved in MeOH. Both the solution were mixed together and refluxed for about an hour. On cooling yellowish coloured precipitate appeared. The solid mass filtered and washed thoroughly with water. The crude product was recrystalised from alcohol. mpts. 265^0C.

Analysis : $C_9H_{13}O_3N_5$

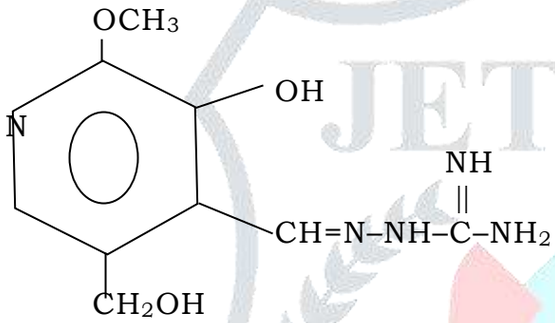
Calculated : C– 45.18, H – 5.44, N – 29.28%

Found : C– 45.12, H – 5.50, N – 29.20%

I.R. Bands of 3-hydroxy-5-hydroxymethyl-2-methoxypyridine-4-carbaldehyde amidoguanidine.

Bands (cm^{-1})	Assignment
3410	ν OH (1 alcohol)
3200	ν N–H_2 stretching
3080	ν O–H (H- bonded) stretching
1585	ν C=N–H stretching
1350	ν C=N stretching

From the study of IR spectra and analysis concluded that the ligand under investigation has following structure :



3-Hydroxy–5–hydroxymethyl–2–methoxypyridine–4–carbaldehyde amidoguanidine (MPL AG)

Synthesis of Complex:-

Diaquo Bis(3–hydroxy–5–hydroxymethyl–2–methoxypyridine–4–carbaldehydeamidoguanidine) Copper(II) chloride:

$[Cu(MPLAG–H)\ (H_2O)_2]_2Cl_2\ 2H_2O$

The alcoholic solution of the ligand (MPLAG) (1 mmole) was mixed with aqueous solution of Copper(II) chloride (0.267 mmole) and heated on water bath for two hours and left to stand for one hour. The brown ppt. separated was filtered and washed with water, MeOH and finally dried.

The compound was analysed chemically

Elemental Analysis :

Calculated

Cu	20.00%
C	34.00%
H	4.00%
N	22.00%

Found

Cu	19.86%
C	33.92%
H	5.02%
N	19.98%

The compounds is insoluble in water. It dissolves fairly in DMF.

The complex is the decomposed to metallic oxide when heated to about 230^0C.

MAGNETIC SUSCEPTIBILITY :

The μ_{eff} value of the complex found to be 1.84 BM.

ELECTRONIC SPECTRA ;

Complex shows one broad band at 32154 and 37878 cm^{-1} which may be assigned to the envelop of $^2E_{1g} \rightarrow {}^2T_{2g}$

I.R. BANDS OF $[Cu(MPLAG–H)(H_2O)_2]_2\ Cl_2.\ 2H_2O$

BANDS POSITION (cm^{-})	ASSIGNMENT
3400	ν N–H stretching
3140	ν O–H stretching
3080	ν N–H stretching
2980	ν aromatic C–H stretching
1670	ν N–H bending
1565	ν C=N stretching
520	ν M–N stretching
440	ν M–O stretching

Result & Discussion:

3-HYDROXY–5–HYDROXYMETHYL–2–METHOXYPYRIDINE–4–CARBALDEHYDEAMIDOGUANIDINE(MPLAG)

The interpretation of I.R. spectra shows the important information regarding the nature of ligand as well as the co-ordination sites through which metal in co-ordinated with ligand.

The band at 3200 cm^{-1} in the ligand assignable to phenolic OH(hydrogen bonded) stretching frequency disappears in the Ni(II), Co(II), Co(III), Fe(II), Fe(III), and Cu(II) complexes showing deprotonation of enolic proton through complexation[10]. The ligand also shows strong bands near 1200 cm^{-1} which may be attributed to the phenolic νCO vibration. A shift of this band to higher frequency (~1300 cm^{-1}) in the complexes indicated chelation of the ligand to metal ion through phenolic oxygen. The presence of a band near 3260 cm^{-1} in Cu(II) and Ni(II) complexes may be due to OH of water molecules associated with the complexes.

This is further justified by the presence of a band around 1600 cm^{-1} as deformation band of water molecules.

The ligand exibit a band near 3420 cm^{-1} which assigned to N-H and N–H_2 stretching[11] does not change appreciably in the complexes indicating non involvement of NH_2 nitrogen atom in chelate formations. Bands at 2460 cm^{-1}, 2200 cm^{-1}, 1900 cm^{-1}, 920, 840 and 780 cm^{-1} are the characteristic bands of the compound which remain unaffected on complex formation.

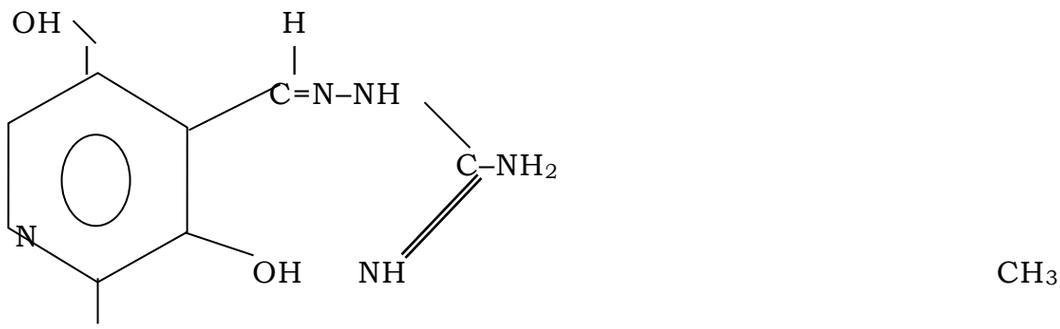
In the case of metal complexes, the most interesting features noted is about doublet band[12] observed in the I.R. spectrum of the ligand near 1620 cm^{-1}. The higher one goes upto 1650 cm^{-1} – 1680 cm^{-1} and probably due to the bending mode of NH_2 group which remain practically unaffected and shows that the –NH_2 Moity does not take part in co-ordination[13]. The other component which is due to C=NH (imine) stretching frequency shifts to the lowers frequencies about (~ 1600 cm^{-1}) in the complexes, indicating the co-ordination of through C=N (in the group). In the cases of Ni(II) and Cu(II) it has been observed that as the reaction is carried out at pH ≥ 9, the band assigned to C=NH group disappears. It suggests that at higher pH co-ordination of Ni(II) and Cu(II) through C=N (imine) group by diprotonation. Martin and co-workers[14] have also reported the same thing.

A sharp band at 1585 cm^{-1} observable in free ligand is assigned to C=N vibration of schief base residue. This band shifts to the lower frequencies in the complexes, which indicates that azomthine Nitrogen of C=N takes part in co-ordination.

The νC–O due to methoxy group appearing in the region 1350 cm^{-1} in the free ligand and νO–H the due to hydroxy methyl group appearing in the region remain unalterd in all the complexes, suggesting non- participation of methoxy group in co-ordination.

Thus, 3–hydroxy–5–hydroxy methye–2–metoxypyridine 4–carbaldehydeamidoguanidine behaves as tridentate ligand co-ordinating through phenolic oxygen, nitrogen atom of C=N of azomethine group and Nitrogen atom of C=NH imine group. It is further confirmed by work of Havorva[15].

It is notworthy that the ligand behaves as monoprotonic for all the metal ions under investigation concept for Nickel(II) and cupper(II) whom complexation is carried out at higher pH (pH = 9). In latter cases ligand behaves like biprotonic involving the deprotonation of C–NH (imine) proton.



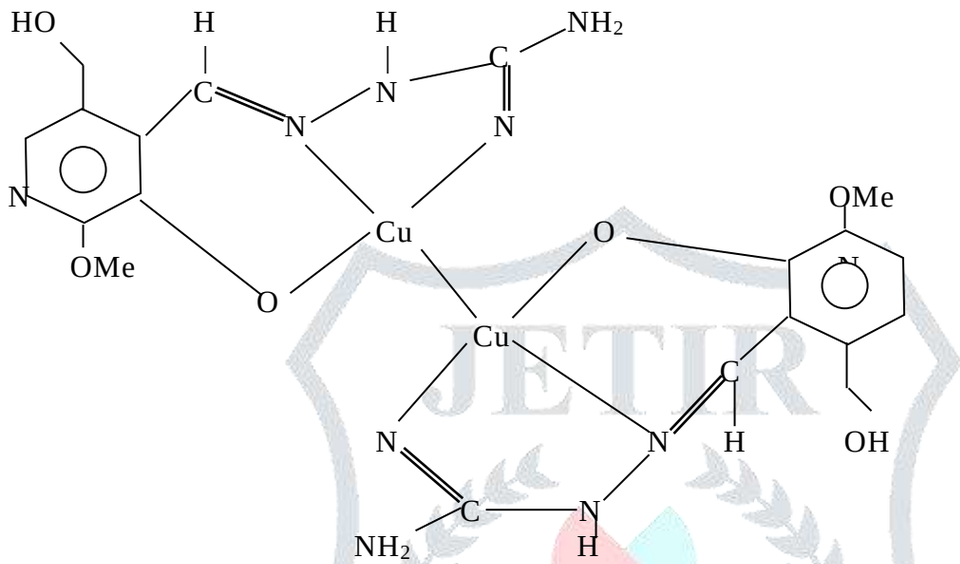
Diaquo Bis(3–hydroxy–5–hydroxymethyl–2–methoxypyridine–4–carbaldehydeamido-guanidine) Copper(II) chloride [Cu(MPLAG–H) $(H_2O)_2]_2$ $Cl_2.2H_2O$.

Visible reflectance spectra of Copper(II) complex, [Cu(MPLSC–H) $(H_2O)_2]_2$ Cl_2. $2H_2O$ [Cu(MPLTSC–H) $(H_2O)_2]_2$ $Cl_2.2H_2O$ and [Cu(MPLAG–H) $(H_2O)_2]_2$ $Cl_2.2H_2O$ show

a broad band in 32154 & 37878 cm^{-1} due to $^2E_{1g} \rightarrow {}^2T_{2g}$ transition and suggest binuclear Cu(II) dimeric structure. The magnetic moment value of these complexes are 1.83 – 1.85 BM.

These complexes are electrolytes, as suggested by their conductance values. Infrared bands for coordinated water molecules are present in I.R. Bands of these complexes.

Therefore we may propose the following structure for these complexes which are consistent with the data obtained from their elemental analysis.



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