Antibacterial in-habitation zone and instrumental study of Zidovudine as a ligand with nano particles

Dr.Deepa Singh
Department of chemistry, sarojini naidu government girls P.G collage, Bhopal

Abstract- The antibiotic drug 2-amino-1,9-dihydro-9-(2-hydroxyethoxy) methyl)-6H-purin-6-one The IR spectral data on the drug & its Zn (II) complex indicate the co-ordination through nitrogen atom of azid group. The data showed a shift bands of azide group in complex from1634 cm^{-1}1651-cm^{-1}. Hence the tentative structure of the complex has been suggested. The antibiotic activity of the complex has been determine by using paper disc method against herpes simplex viruses (HSV), varicella zoster virus (VZV), Epstein barr virus (EBV), cytomegalovirus (CMV) and human herpes virus 6 (HHV-6). A, etc. Looking at this inhabitation power against the different test pathogens. It presumed that the complex may be more potent at compare to the parent drug. Pharmacological study shows the toxicological or non toxicological study of complex drugs.

Key word – Zidovudine (Zdv), Spectroscopic, Metal complex, Microbial, Pharmacological studies.

INTRODUCTION

Zidovudine (Zdv), 9-[(2-hydroxyethoxy) methyl] guanine, an analogue of 29-deoxyguanosine is an efficient topically active acyclic nucleoside with inhibitory activity towards several herpes viruses, especially HSV-1 and HSV-2. (1) Zidovudine (Zdv)is both the ancestor of and the paradigm for development of many of the purine nucleoside inhibitors. Acyclovir is well known antiviral – a broad spectrum antibiotic – a chemical acyclic analogue of the natural nucleoside 2'-deoxyguanine with antiviral activity "in vitro", against herpes simplex viruses (HSV), varicella zoster virus (VZV), Epstein barr virus (EBV), cytomegalovirus (CMV) and human herpes virus 6 (HHV-6) (2), which is effective against gram positive and gram negative bacteria [3].

Metal chelates have a broad range of medicinal applications. A number of metallic elements play crucial roles in biology and it is clear that many organic compounds used in medicine require metal ions for activation or biotransformation in order to achieve their mode of action.[7](4) Metal ions are often classed as 'toxic' and 'non-toxic', however their biological activity depends very much on speciation and it is now widely accepted that, with carefully controlled co-ordination chemistry, even 'toxic' metals can exhibit therapeutic properties.[8] It is therefore very important to investigate and understand the effects of varying the oxidation state, numbers and geometries of coordinated ligands on the biological properties of metal chelates to design metal – based drugs.. Pharmacological study shows the toxicological or non toxicological study of complex drugs in lung liver and salivary glands

The ligand used was of A.R. grade. It was obtained as a gift from different pharmaceuticals companies. All metal chloride used were also A.R. grade. Stock solutions of Zn (II), Fe (II), Co (II), and were prepared and analyzed by complexometric methods. Conductivity water was used through out the work. The pH of this water was found to be ~ 6.9.

MATERIAL AND METHOD

Preparation of metal complex

To a solution of Zidovudine (Zdv) (2mmol) in methanol (10ml), a s o lu tion of metal chloride salt (2mmol) in methanol (10ml) was added. The mixture was stirred and heated or refluxed at 60 C for 1 hour. The resulting solution was filtered. Precipitate formed for metal- Zidovudine (Zdv) separately complex (8)(5). The filtrate of cobalt, zinc, iron and copper (II) Zdv complexes were subjected to slow evaporation at room temperatu re. Crystals were obtained after three weeks.

The analytical data of the chelates showed 1:1 stoichiometry. The general equation for the formation of the chelate with acyclovir is as shown below.

$M^{2+} + L + H_2O \longrightarrow [M\ L_3]\ H_2O$

$Mg^{2+} + L + H_2O \longrightarrow [Mg\ L]\ H_2O$

Where, L = Conjugated base of Zidovudine (Zdv),

$M^{2+} = Zn^{2+}, Co^{2+}, Fe^{2+}, Cu^{2+}$

Compound & Chelates	-NH 2	>NH	-OH	>C=O	C–O–C	C–O Ether	C–O Alcohol	-CH 2	-C–N	M–N
Zdv	3471, 1573	3302 1541	3522 1715	2927-2854	1346	1106 1048 -	1183	3183	3440	-
Fe- (Zdv)].H 2O	3386	- 1584	3512	2952	412	1183 1048	1720	3121	1346	1109
[Zn- (Zdv) 3] ·3H 2O.2ACV 3	3442 1575	1720	3187 2928-2855	1347	3521	1049	1106	1183	410	3312
[Co(Zdv) 3] ·4 Zdv	1575	3375 3512	2927-2855	1347 412	1720	1106	1183	1049	3187	3441

S.no	Code no.	minimal inhibition concentration			
		E.coli	P.aeruginosa	S.aureus	S.pyogenus
	Compound and chelate	MTCC 443	MTCC 1688	MTCC 96	MTCC 442
1	1 AMPICILLIN (STD. DRUG)	100	100	250	100
2	Zdv	250	250	500	500
3	[Fe- (Zdv)].H 2O	100	100	150	150
4	[Zn (Zdv) 3] ·3H 2O.2 Zdv	250	150	500	500
5	[Co(Zdv) 3] ·4 Zdv	25	100	150	200

Fig- Antibacterial study

RESULT AND DISCUSSION

The IR spectra of the obtained complexes compared with that of Zidovudine . The more relevant feature are : shift to lower frequencies of the strong band at 1718cm-1 which is assigned to the vibration ν [C(6)=O(6)] in free Zdv. This is consistent with the C=O group involved in hydrogen bonds. In some Co-Zidovudine complex, it has been observed that short hydrogen bonds involving O(6) significantly diminish the carbonyl stretching frequency in the IR spectra Fig(1) . The 1634cm-1 band related to $\delta(NH_2)$ is not appreciably shifted for 1,2,4 and 5,although for 3 it is shifted to 1651cm-1, possibly due to the double interaction of the NH2 group present [N(3)···H2N,Cl···H2N]. (b) Splitting of the 1487cm-1band,for δ[C(8)-H]+ν[C(8)-N(7)] and variation, related to the five membered ring, have been observed in the spectra of several structurally known N(7)-metallated complex (9)(5). The far-IRspectra of the complex shown a new band at 312 and 313 cm-1 assigned as essential ν(Co -N).The low frequency band at 332cm-1,found for compound 3,may be attributed to the Co-Cl stretching mode of the terminal chlorides. Table(2) (10),

Antibacterial Activity: Paper disc method (10)(6) was followed for the microbial screening of Co(II) Zidovudine complexes against various pathogenic bacteria's and i..e Gram-positive and Gram- negative bacteria. Staphylococus Aureus, Streptococcus Pyogenes, Escherichia coli and Pseudomonas aeruginosa A sterilized filter paper disc (6mm) were dipped into the complex solutions of 0.01M concentrations. Prior to this, the bacteria and fungi were separately homogenized with nutrient agar and potato dextrose media (at 27-30°C) plated on the sterilized Petri dishes. Dipped filter paper discs were placed on seeded medium. After 24 hour of incubation antimicrobial activities were

The number of replicates in each case of three, percentage inhibition was calculated using the following formula % inhabitation= a-b/a×100

Where a=diameter of inhibition zone for control Zidovudine and b=diameter of inhibition one for complex.

All the synthesized chelates gave incisive activity against different antimicrobial genus in comparison with the ligand as well as the standard drug which indicates that due to chelation the antimicrobial activity of organic counterpart increases. In comparison with the standard drug Ampicillin, chelate of Fe^{2+} gives enhanced activity against Escherichia

coli, while chelate of Zn^{2+} gives equal activity against the same(11)(7).

Similarly in comparison with the same standard drug Ampicillin, the chelates of Fe^{2+} and Zn^{2+} illustrates excellent activity against Staphylococus Aureus, while chelate of Co^{2+} gives equal activity aligned with the same standard drug.

In this progression, when the synthesized chelates were screened in conjunction with Pseudomonas aeruginosa, the chelates of Fe^{2+} and Zn^{2+} bestows identical activity as the standard drug, while the chelate as well as the ligand did not give even equal activity abutting Streptococcus Pyogenes.

But the study revealed interesting changes in antimicrobial activity on chelation including significant activity by some chelates as they compared with the ligand's activity.(12)(8)

The ligand was not sowing even equal activity in comparison with the standard drug, while on chelation it not only give better activity than the standard drug Ampicillin but also donates equal activity as another standard drug Ciprofloxacin (e.g. chelate of Fe^{2+}).

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