

AN EFFICIENT AND EFFIECTIVE HOSPITAL INVENTORY MANAGEMENT SYSTEM USING SUPPLY CHAIN MANAGEMENT

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Abstract

In this research work, we have studied multiple level of supply chain in a hospital considering the distributors, for the need of an effective and efficient inventory management system in the hospital. Our suggested a method comprising of two parts: (1) system designing and optimization; and (2) system monitoring, evaluation, and forecasting. In the first part of this method consist of system designing and optimization approach which consist of a sim-heuristic method where hospital operations and inventory optimization at different levels are considered. As time passed, to observe the relevant system performance measures over time, methods like control-chart are used. When significant deviations occurs in system performance, a re-evaluation of the inventory decision variables factors and/or system operations is conducting for maintain an effective and efficient inventory system. A hierarchical approach is used to determine the amount of evaluation of the system. Experimental results are presented to indicate the effectiveness of this methodology.

Keywords: Metal ligand complex, 5-Fluorouracil, Spectral studies, and Antimicrobial activity.

Introduction

Structural change of 5-Fluorouracil (5-FU), a mono fluorinated result of uracil, has utterly different biological properties than uracil which has substantial biological applications when it forms complexes with metal ions [1]. As the time of its synthesis, 5-FU has been ever more in work alone or in combination with other Cyto toxic drugs and hormones in the medical treatment of solid tumors. It has also been used in the healing of different carcinomas [2]. This is owing to the presence of fluorine atom at the C-5 position which can considerably modify the electronic properties as indicated experimentally by changes in the electronic

spectra [3]. Complexes of amino acids are involved in the exchange and transport mechanism of trace metal ions in the human body. Synthesis and characterization of transition metal complexes of Cu

(II), Ni (II) and Zn (II) with 5-Fluorouracil and some amino acids has been reported [4-7]. The literature reveals that number of drugs have been used to synthesize the complexes by means of many metals with an observation to improve their therapeutic action [8 -11].

In this paper, we report the synthesis, spectral and biological activities of ligand Co (II) complex involving 5-Fluorouracil (5-FU). This study helped in understanding the coordination environment of the ligands around the metal ion and to investigate the antimicrobial activities.

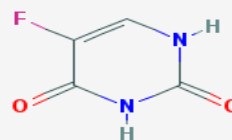


Fig: 1 Structure of 5-Fluorouracil (5-FU).

Molecular formula- [C₄H₃FN₂O₂](#)

Experimental

All the ligands are extra pure Sigma Aldrich, products and they are used without further purification. C, H and N analytical data estimated with the help of elemental analyzer at CDRI Lucknow (U.P.). Metal content of the mixed ligand complexes were estimated gravimetrically by the standard procedure. Molar conductance (1×10^{-3} M)

was measured using an Elico CM 180 conductivity bridge by using 0.01 M KCl solution as calibrant. Magnetic susceptibility measurements were carried out on a Gouy balance at room temperature using mercuric tetra (thio-cyanato) cobaltate (II) as the calibrant. Diamagnetic corrections were applied in compliance with Pascal's constant [12]. Electronic absorption spectra were recorded with a double beam spectrophotometer. Vibrational spectra were recorded on a FTIR (Simadzu, model 8400) spectrometer, in the 400–4000 cm^{-1} range. In vitro antimicrobial activities of 5-Fluorouracil and its Co(II)–5-FU(A) complex in DMSO medium were tested against three Gram-positive pathogenic bacterial strains: *Bacillus subtilis*, *Staphylococcus saprophyticus* and *Staphylococcus aureus*, two Gram-negative bacterial strains: *Escherichia coli* and *Pseudomonas aeruginosa* using Muller Hinton agar nutrient by well diffusion technique [13].

Synthesis of Mixed Ligand Complexes

5-Fluorouracil (0.0132 g, 10 m mol) was dissolved in aqueous (10 ml) solution containing a few drops of concentrated ammonia and stirred. When 5-fluorouracil was completely dissolved, an aqueous (10 ml) solution of metal salt (10 m mol, 0.025 g $\text{Co}(\text{CH}_3\text{COO})_2$) was added slowly and stirred at room temperature. The pH (6.5) of the reaction mixture, adjusted by adding few drops of aqueous Na_2CO_3 solution (0.0104 g, 10 m mol). The resulting solution were reduced to 1/2 of its original volume by water bath and kept overnight. On standing, the mixed ligand complexes were obtained and collected by vacuum filtration, washed several times with cold water, ethanol and anhydrous ether. The mixed ligand complexes were dried in air and stored over anhydrous CaCl_2 at room temperature. The yield of the isolated complexes was found to be 62% (app) [14].

Results and Discussion

1. The elemental analysis and Molar conductance

The analytical data shows, the stoichiometry of Co (II): 5-Fluorouracil is to be 1:2. The observed low molar conductance values (1×10^{-3} M, DMSO solution) at room temperature are reliable with the

non electrolytic nature due to the absence of counter ions in the proposed structure [15].

Empirical Formula of complex- $\text{Co} [\text{C}_4\text{H}_2\text{FO}_2\text{N}_2]_{2.2}\text{H}_2\text{O}$

Color of complex- Bluish white

Yield (%)- 61.9%

Molar conductance- $12.1 (\Omega^{-1} \text{cm}^2 \text{mol}^{-1})$

Table1. Physico-chemical properties

Elemental analysis %

	Co	C	H	F	O	N
found	13.3 9	23.2 7	1.95 2	9.2 5	24.1 7	27.2 1
calculate d	14.4 0	23.4 7	1.95	9.2 9	23.4 7	27.3

Vibrational spectra

The IR spectra provide valuable information on the subject of the nature of functional group attached to the metal ion. The characteristic IR spectral data (KBr pellet, cm^{-1}) with the principal IR frequencies of 5-FU and its complex are given in (Table 2). The presence of coordinated water molecules ν (OH) is confirmed by the rocking, twisting and wagging Vibrational modes at 3101 – 2931 cm^{-1} , 954 – 949 cm^{-1} and 747 – 739 cm^{-1} respectively [16]. ν (M–N) and ν (M–O) bands are tentatively assigned in the region 439–432 cm^{-1} and 551–542 cm^{-1} indicating the complexation of the ligands with transition metal ions [17] respectively.

Table2. IR spectral data (in cm^{-1})

	ν (OH ₂)	ν (C=O)	δ (N-H)	ν (C-F)	ν (M-N)	ν (M-O)
5-Fluorouracil	-	1704, 1685	1513, 1430	1470	-	-
Co(II)-5-FU	3226-2931	1692, 1651	1516, 1407	1472	431	543

From the data, the ligand 5-FU acts as bidentate which form metal chelate all the way through the de protonated N3 and C4 = O of carbonyl oxygen atoms. The magnitude of $\Delta\nu$ value falls in the range 237–252 cm^{-1} suggesting the bidentate coordination in complexation.

Electronic absorption spectra coupled with Magnetic moment value

The spectra suggested octahedral Co (II) ligand complex. The magnetic moment values of these mixed ligand complexes in Bohr Magneton (μ_{eff} (BM) = 2.98) supports the proposed geometry [18].

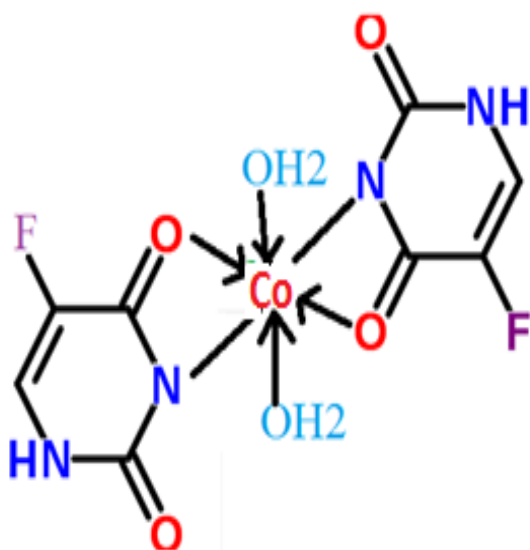


Fig: 2 Structure of 5-Fluorouracil (5-FU)-Co complex.

Molecular formula-Co $[\text{C}_4\text{H}_2\text{FO}_2\text{N}_2]_2 \cdot 2\text{H}_2\text{O}$

Antimicrobial activity

In vitro minimum inhibitory concentration (MIC) values of the ligand complex of Co(II) 5-FU with free ligand (5-FU) were tested against some microorganisms and are summarized in Table 3. Commercially existing standard drugs Ampicillin (antibacterial control) and Nystain (antifungal control) are used as control. The antimicrobial activities of the mixed ligand complex is normally better than the free ligands and the activities depend upon the Co(II) ions i.e., size, charge distribution, shape and redox potential of the metal chelat [19].

The mixed ligand complexes explain moderate activity than the corresponding free ligands and metal salts. From the Table 3, the MIC value of the mixed ligand complex is also confirmed by the liquid dilution route [20] in which the efficacy was also observed at very low concentrations.

Table – 3 .Antimicrobial activity of the free ligand (A) and its complex with Co(II)

Complex	Minimum Inhibitory Concentration values (mg / ml) a			
	Bacillus subtilis	Staphylococcus saphyphiticus	Staphylococcus aureus	Escherichia coli
Control	5.4	4.8	7.2	6.2
5-FU(A)	12.1	14.6	16.6	21.8
Co(II)-5-FU	12.15	14.67	16.5	21.9

The measured MIC values (mg / ml) of the control, ligand complex with free ligands against microorganisms, can be explained on the basis of chelation theory [21-23]. From the MIC values, Co(II) 5-FU(A) complex show moderate activity against all the bacterial strains even than the standard drug. Also the antibacterial activity of complex is due to the presence of electron withdrawing (C5-F) [24]. Also, it was established that the pathogenic Gram positive bacterial strains like *Bacillus subtilis*, *Escherichia coli* strains shows remarkable activities against the free ligand and their complexes.

Pharmacological Studies

In Vitro

The result of *in-vitro* experiments of pure drugs and its complex are shown in Table 4. Perusals of the data it is compared shown that Co (II) 5-FU complex was found to be more effective than pure drug. The complex under study showed an increased inhibition against the **Sarcoma-180 tumor** cell line at all the test concentrations i.e. 1, 10, $\mu\text{m}/\text{ML}$. The increased inhibition activity of complex was $25.58 \pm$

1.13%, $52.06 \pm 1.69\%$ as against 19.98 ± 0.43 , 41.97 ± 0.98 shown by the drug, respectively. The data were statistically significant as at $P < 0.05$.

Table 4: In-Vitro Cytotoxicity of 5-Fluorouracil -Fe complex Against Sarcoma-180 tumor Cell

Compound	Concentration μ M/ml	% inhibition after 8h
5-Fluorouracil	1.0 10	19.98 ± 0.43
		41.97 ± 0.98
Co (II)5-Fluorouracil Complex	1.0 10	25.58 ± 1.13
		52.06 ± 1.68

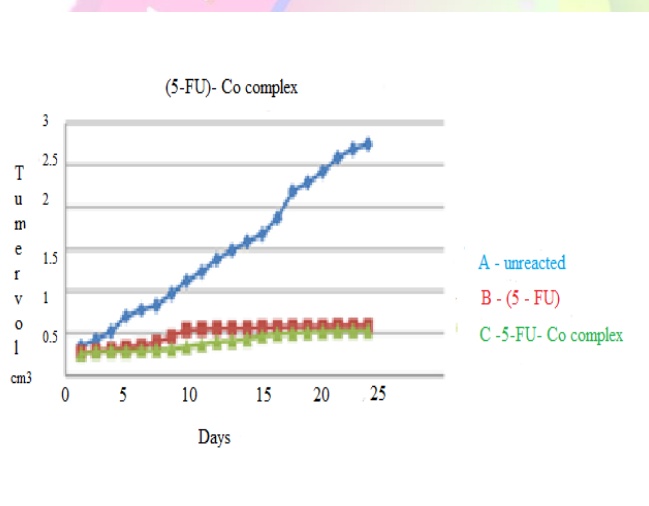


Fig 3: In-Vitro Cyto-toxic activity of 5-Fluorouracil (5-FU) - Co- complex.

Conclusion

The present study explains geometry and nature of the ligand complex which is studied by the electronic absorption spectra. From the spectral studies, the ligand 5-FU (A) and the Co (II) ion via, de protonated N3, C4 = O of carbonyl oxygen atoms forming a stable 4 membered chelate rings. The 5-FU-Co (II) complex under investigation shows octahedral geometry, it is further supported by the magnetic moment. The *in vitro* antimicrobial evaluations show more potent activities for both Co (II) 5-FU & ligand complex [25].

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