The Role of Hydroximate Type Siderophore on Cr^{+3} Concentration in Biological System

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Abstract: In iron overload condition a drug desferioxamine mesylate has been used. It is linear trihydroxamic acid, a natural siderophore produced nocardia and streptomyces. The complex formation of Cr^{+3} and Fe^{+3} with salicylhydroxamic were studied potentiometrically at different temperatures. The data were subjected to computer program "BEST". The stability constant values and thermodynamic stabilities were calculated. It was found that salicylhydroxamate forms 1:1 complex at pH 3 and 1:2 complex at pH 4 with Cr^{+3}. The stability constant and thermodynamic abilities are close to Fe^{+3} salicyl hydroxamate complexes.

Key words: Siderophore, hydroximate, Cr^{+3}

Introduction

Chromium is an essential element in the biological systems. It is involved in carbohydrate, lipid and protein metabolism. It has got an important role in serum cholesterol hemostasis (Das, 1990). It has been proposed that chromium forms essential part of the glucose tolerance factor which together with insulin is responsible for controlling the clearance of glucose from the blood stream (Mertz, 1969). Bovine colostrum contain a biologically active low molecular weight chromium binding substance. It contains aspartic acid, glutamic acid, glycine and cysteine (Yamamoto, 1988). The compounds of Cr^{+6} have hepatotoxic, nephrotoxic, mutagenic and carcinogenic effects (Hay lock et al.,1983). Among trace metals iron is a essential nutrient for micro-organic as well as for other organisms because of its varied functions in biological redox processes (Tyfano & Raymond, 1981). Instead of its importance iron could be toxic when in excess. Iron could increase the capacity of transferrin and ferritin. This condition is known as iron overload (Neilands, 1974). There are many natural mechanism for solubilization or removal of iron, for example, the micro-organism utilize a well define iron acquisition strategy which includes the production of low molecular weight chelating agents called siderophores to solubilize and transport ferric ions in aqueous medium (Huges and Poole, 1989). These siderophores have high affinity for and are better chelators for Fe^{+3} than Fe^{+2}. The stability constants for the ferric siderophore complexes are extremely high (Kf = 10^{36} - 10^{55}), with Fe^{+2} it is very low (Kf = 10^{8}) (Biedermen and Schlindr, 1957). For the treatment of iron over load the salicylhydroxamate appear to be more selective as its stability constant for Fe^{+3} complex is several orders of magnitude greater than those for other useful metal ions complexes. Desferrioxamine mesylate a linear trihydroxamic acid natural siderophore produce by nocardia and streptomyces have been used for the treatment of iron overload (Avdeef et al., 1987). In present work we have established the stability constant, thermodynamic stabilities, spectrophotometric studies and potentiometric studies of chromium salicylhydroxamic acid complexes and comparison with iron salicylhydroxamic acid complexes.

Materials and Methods

All reagents were of AR grade. Solutions were made in deionized water (freed from CO_2). For all pH measurement Orion pH meter was used. A 0.05 M solution of potassium hydrogen pthalate with pH 4.01 at 25°C was used to calibrate

Table 1: $\log \beta$ values of Cr^{+3} and Fe^{+3} salicyl Hydroxamic acid at diffirent temperature calculated by best

Cr^{+3}		30°C	35°C	40C	45°C	50°C
Log β	110	8.6	8.8	9.15	9.50	9.95
Log β	210	12.66	12.9	13.20	13.5	13.70
Log β	310	14.49	14.66	14.75	15.10	15.50
Fe^{+3}						
Logβ	110	14.8	15.12	15.52	15.95	16.60
Logβ	210	24.0	24.5	24.75	24.9	25.1
Logβ	310	31.0	31.25	31.7	32.0	32.15

Table 2: Entropy and Enthalpy Values of Cr^{+3} and Fe^{+3} Salicylxydroxamic Acid Complexes

	ΔH	ΔS	ΔH2	ΔS2	ΔH3	ΔS3
Cr^{+3}	11.35	410	8.5	300	5.10	100
Fe^{+3}	11.75	480	8.45	325	5.5	115

Units for $\Delta H = kJ\ MOLE^{-1}$ and Units for $\Delta S = JK^{-1}\ MOLE^{-1}$

the pH meter along with the standard buffer solution made from BDH standard chemicals.

For potentiometric titrations a double walled glass cell was used. The temperature of the cell was kept constant throughout the experiment by circulating water. All the titrations were done at different temperatures i.e. 30°C, 35°C, 40°C, 45°C and 50°C. 20 ml of 0.01M metal ion solution mixed with 20 ml of 0.01M salicyphydroxamic acid solution and titrated with 0.1 M NaOH solution. The change in pH was noted with the small increment (0.05 ml) of base. The solution was stirred with magnetic stirrer constantly (Tufano and Raymond, 1981). For each metal salicylhydroxamic acid solution, these titrations were performed twice to minimize the probable error. For spectrophotometric measurements (Neilands, 1974), spectra were recorded on Shimadzu UV 160 A Spectrophotometer. The absorbance peek of the complex at different pH were scaned.

Results and Discussion

The potentiometric titration data for salicylhydroxamic acid and its Cr^{+3}, Fe^{+3} complexes were analysed by the computer program "BEST". The log β values and thermodynamic stability of Cr^{+3} and Fe^{+3} complexes are shown in Table 1 & 2 the possible mechanism of reaction of metal ion with salicylhydroxamic. It was found that like other hydroxamic acids, salicylhydroxamic acid forms stepwise complexes. One at pH 3 and other at pH 4. Iron and chromium both showed

three stages of complexation. Each resulted into highly stable complexes, the third one is at pH 6 either 1:3 or the ligands may behave as tridentate ligand, i.e. in addition to the bidentate hydroxamate function the -OH attached directly at o-position becomes capable of binding Fe^{+3} [Kazmi et al., 1990]. A chelating agent to be effective in removing a toxic metal from the body, it must satisfy second law of thermodynamic that is the free energy change for the transfer of metal ions from the binding sites to the chelating drug must be negative. To achieve this requirment, stability constant between the toxic metal and chelating drug must be greater than that of the competing ligands with the metal concerned (Jones and Vaugas, 1978).

The ionic radii of Fe^{+3} is very much similar to that of Cu^{+2} (Greenwood & Earnshaw, 1984). Therefore the thermodynamic stability of Fe^{+3} complexes and Cr^{+3} complexes are suprisingly close. From the observed data, it is suggested that for the treatment of iron over load in B thelesemic patients on hydroxamate based drugs Cr^{+3} equilibrium may also be disturbed.

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