Equilibrium Studies of the Iron Exchange Reaction of Ferrioxamine B with 8-hydroxyquinoline-5-sulfonate

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Introduction

Iron is an essential nutrient for almost all forms of life, however most of the iron in the environment exists in insoluble forms. In order to acquire iron from the environment, many organisms will produce high affinity iron(III) chelators called siderophores. Moreover, once the very stable iron-siderophore complex is formed, it becomes thermodynamically challenging for the iron to be released so that the organism can use it. In order to overcome this challenge, it has been proposed that some organisms may utilize competing ligands to assist in the release of iron through the formation of ternary complexes. These ternary complexes can enhance the release of iron by shifting the reduction potential of the iron complex and facilitating the reduction of iron by physiological reducing agents.[1-3] After reduction the siderophore, which has a much lower binding affinity for iron(II) than iron(III), readily dissociates.

In this study, we will be investigating the ligand exchange reaction between a model siderophore, ferrioxamine B (FeDFB, II) and a model competing ligand, 8-hydroxyquinoline-5-sulfonate (H3QS). Upon deprotonation, 8-hydroxyquinoline-5-sulfonate forms a stable iron(II) complex (FeQ, III) via the aromatic N and hydroxyl (OH) donor atoms. The 8-hydroxyquinoline-5-sulfonate ligand is also biologically relevant as the quinoline functional group is present in flavin mononucleotide, a physiological reductant which has been shown to be capable of reducing ferrioxamine B in vivo,[4] and in the siderophore quinolobactin.[5] In order to study this reaction and determine the stability constants of the products formed, we performed a series of spectrophotometric measurements in which the pH and H2QS ligand concentrations were varied. We also determined the stability constants associated with the H+ + QS– and Fe2+ + QS2– reactions in order to obtain values for these parameters under our experimental conditions. A generalized chemical equation and stability constant expression for the reactions we studied is shown below.

\[
\text{Fe}^{2+} + x \text{DFB}^2+ + y \text{QS}^2– + z \text{H}^+ \rightarrow \text{Fe}_{x} \text{(DFB)}_{y} \text{(QS)}_{z} \text{(H)}_{w} \]

\[
\beta_{\text{FeQS}} = \frac{[\text{Fe}_{x} \text{(DFB)}_{y} \text{(QS)}_{z} \text{(H)}_{w}]}{[\text{Fe}^{2+}]^{x} [\text{DFB}^{2+}]^{y} [\text{QS}^{2–}]^{z} [\text{H}^{+}]^{w}}
\]

Experimental

Spectrophotometric and potentiometric measurements were collected for all reactions studied. Reaction mixtures were allowed to come to equilibrium at 25°C in a thermostated flask. A background electrolyte concentration of 0.1 M NaNO3 was added in order to maintain a constant ionic strength. Absorbance measurements were collected using a Shimadzu UV-1601PC spectrophotometer. The pH was monitored using a general purpose Accumet combination electrode with Ag/AgCl reference and an Oakton pH 1100 meter. The pH meter and electrode were calibrated using the GLERL calibration method.[6] The potentiometric and spectrophotometric data was analyzed using pHAB 2003 software.[7]

Results

Figure 1 shows the absorbance of the species that are present under the conditions of the FeDFB + QS2– reaction series.

- Data in the 425-700 nm range is the useful range for ternary complex analysis.
- Under 425 nm, the absorbance is dominated by the QS ligand species.
- Absorbance in the 525-700 nm range is diagnostic of FeQ2 complexes.

Figure 4 shows a comparison of the fraction of FeDFB+ converted into ternary complex for the QS ligand and previously reported ternary complexes. FeDFB(QS3)2 is clearly has much greater stability than the other ternary complexes at neutral pH values.

Conclusions

- 8-hydroxyquinoline-5-sulfonate (QS) forms a ternary complex with ferrioxamine B (FeDFB) with the stoichiometry of Fe(QS)3.
- At pH 6.0-8.0, the Fe(QS)3(QS) ternary complex is more stable than any of the previous ferrioxamine B ternary complexes reported.

References