Evaluation of Iron Chelators for the Prevention of Fenton Chemistry

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Introduction

Intracellular free iron catalyzes hydroxyl radical (•OH) formation from hydrogen peroxide via Fenton-like reactions.

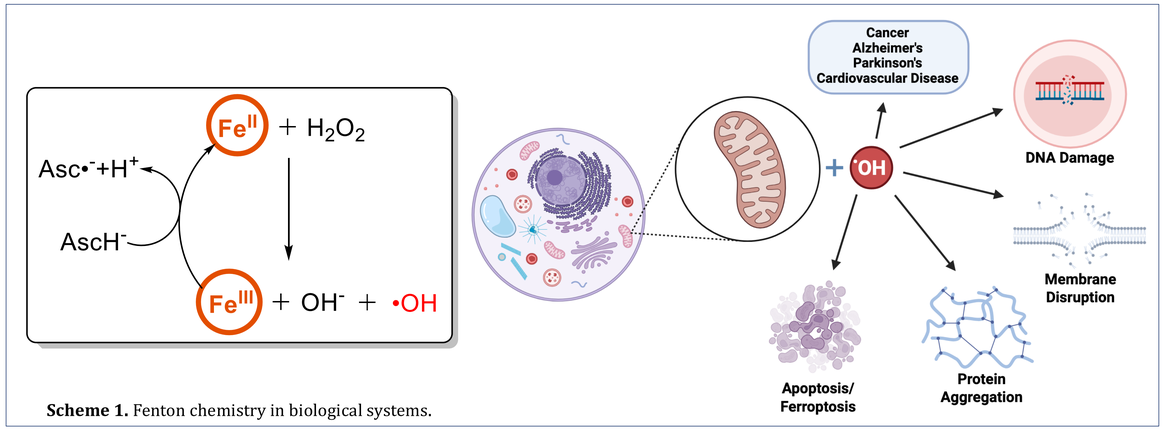
•OH can oxidize biomolecules and disrupt cellular function, contributing to a wide array of diseases.

Iron chelators represent a promising therapeutic avenue for preventing excess •OH production.

Evaluating chelator effectiveness requires reliable assays that approximate intracellular conditions.

Insights gained during synthesis and evaluation help to inform further chelator development in the Planalp Lab.

Background



Scheme 1. Fenton chemistry in biological systems.

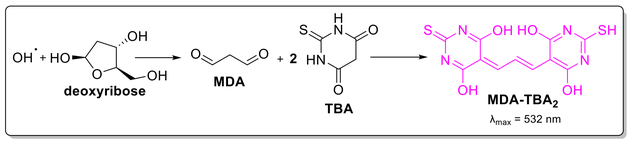
Results

Propox demonstrated significantly greater inhibition of hydroxyl radical production than both OHQ and the EDTA control in the **deoxyribose assay**.

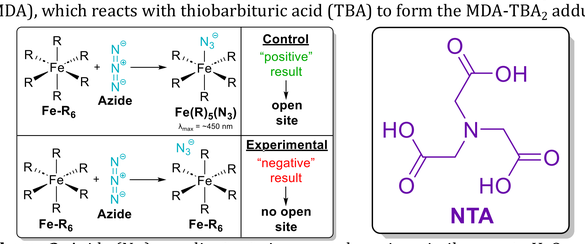
Fe-EDTA and Fe-OHQ show substantial absorbance at 532 nm, while Fe-Propox shows near-zero absorbance, indicating near complete •OH inhibition.

Azide assay validation controls provide strong evidence that the characteristic absorbance increase at ~450 nm reflects coordination of the azide ligand to iron. This validates its use as a method for determining whether a given iron complex contains an open coordination site.

Methodology



Scheme 2. Hydroxyl radicals (•OH) degrade deoxyribose to malondialdehyde (MDA), which reacts with thiobarbituric acid (TBA) to form the MDA-TBA_2 adduct.



Scheme 3. Azide (N_3^-) coordinates to iron complexes in a similar way to H_2O_2, serving as a Fenton-relevant open coordination site probe.

Deoxyribose Assay

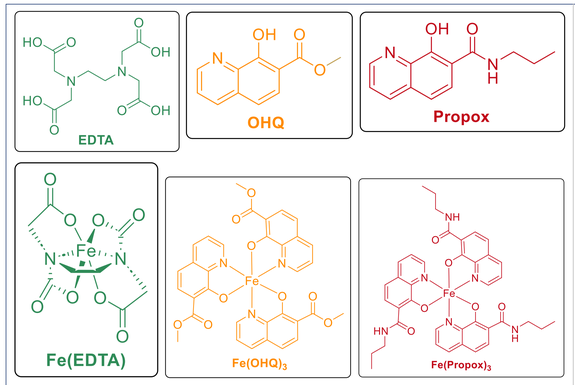


Figure 1. Structures of chelators and iron-chelator complexes.

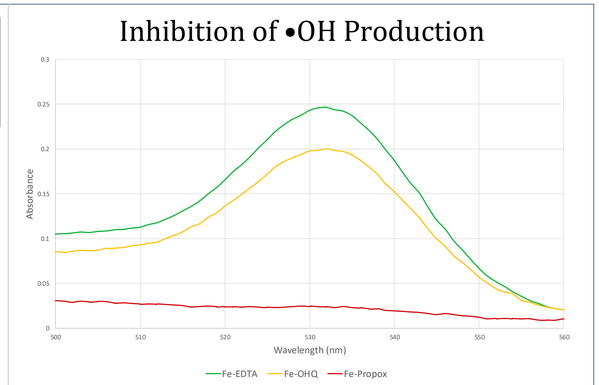


Figure 2. UV-Vis spectra of iron complexes after the deoxyribose assay procedure.

Conclusions

Propox significantly outperforms OHQ and EDTA in the **deoxyribose assay**, showing strong therapeutic potential.

The **azide assay** has been established as a reliable method for determining whether an open coordination site is present on a given iron-chelator complex.

Current **azide assay** results for $Fe(Propox)_3$ are inconclusive due to poor water-solubility.

The Planalp Lab is focused on developing derivative chelators with improved water solubility and greater therapeutic potential.

Data

Deoxyribose assay: absorbance at 532 nm indicates greater •OH production. Lower absorbance = greater chelator function.

Azide assay: strong evidence that the ~450 nm signal arises from azide coordination to iron.

$Fe(Propox)_3$ experimental **azide assay** data is confounded by poor chelator water solubility.

Azide Assay Validation

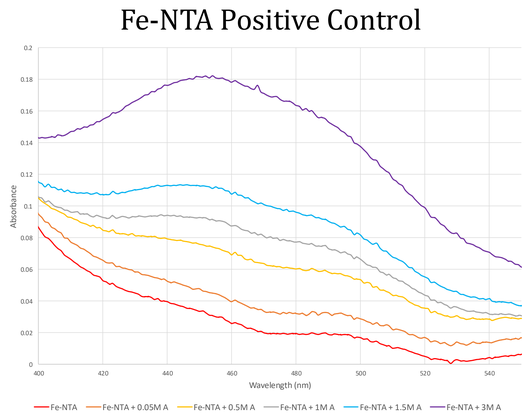


Figure 3. Characteristic absorbance peak at ~450 nm. Abs. @ 532nm is proportional to [Azide] (Legend: A = Azide).

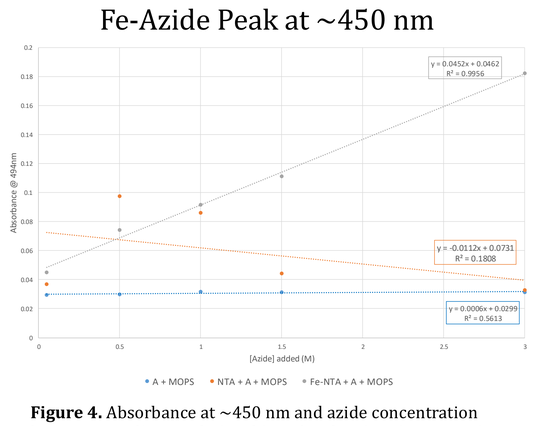


Figure 4. Absorbance at ~450 nm and azide concentration have a strong linear relationship only when iron is present in solution.

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References

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