


SYNTHESIS OF VARIOUS PORE-SIZED SILICA NANOPARTICLES AND THE USE OF COMPLEXOMETRIC TITRATION TO QUANTIFY LOADED FE-EDTA.

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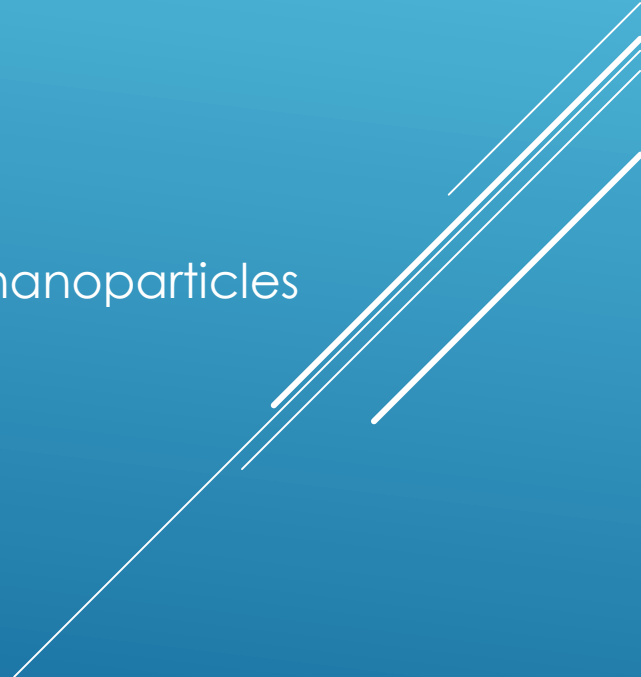
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Presentation Outline

- Project Goals
 - Background information
 - Synthesis
 - Quantification of loading agent concentration
 - Conclusions
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Project Goals

- (Overall): To synthesize mesoporous silica nanoparticles as a possible candidate for CEST imaging as a new possible method for MRI imaging
 - Synthesis of uniform, and pore size controllable particles
 - Determination of quantity of loaded [FeEDTA⁻] within the mesoporous silica nanoparticles
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- A decorative graphic consisting of several parallel white lines of varying lengths, slanted upwards from left to right, located in the bottom right corner of the slide.

MRI

Strengths: High spatial resolution, High temporal resolution, and non-invasive.

Weaknesses: High detection limit, and requires the use of toxic non-renal clearing metals such as Gd^{3+} containing species.

Relevance: A method in which MRI imaging has high resolution and low detection limits, would be of great importance to biomedical imaging technology because of the ability to probe and image diseases in the early stages of development of a diseases many of which occur at receptors where Many constituents are to low in concentration for current MRI imaging methods

Axial MRI - T1 vs. T2

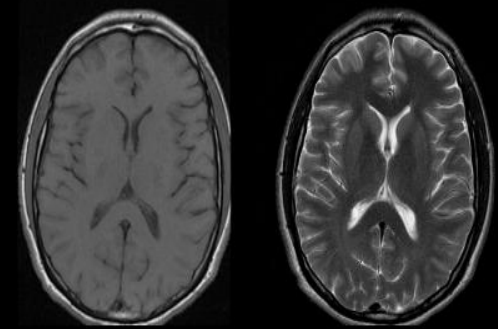


Figure A: MRI contrast images (T_1 and T_2)¹⁵

Chemical Exchange Saturation Transfer (CEST imaging)

Chemical Exchange transfer is alternative nuclear magnetic resonance method that uses the transfer of saturated or spin-state nuclei from a bounded population to a bulk water sample which is considerably higher. The signal intensity is greatly enhanced based on the exchange rate and longevity of the excited spin-state. If the exchange of non excited nuclei continuously exchange with lower concentration of excited nuclei it can attenuate for the weaker signal water making the signal strong enough to produce a readable signal.

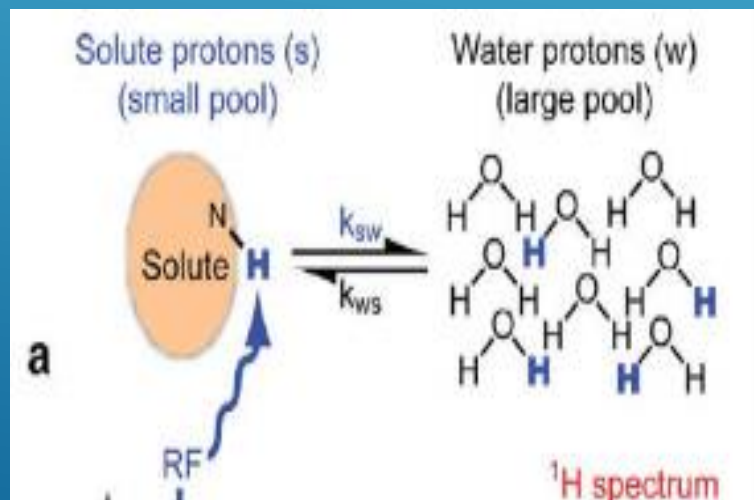


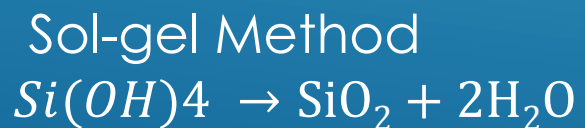
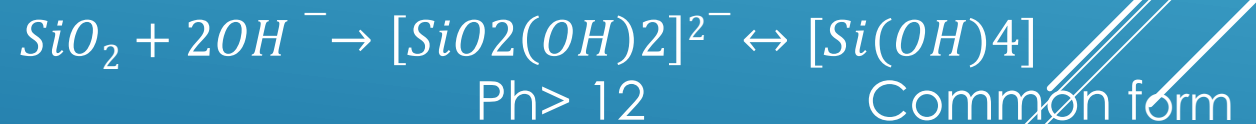
Figure B: Chemical exchange saturation transfer diagram¹⁶

Connecting ideas

- Firstly, the overall aim of this project is to provide a means to improving MRI's main limitation which is a high detection limit which limits MRI from detection of the progression of early onset disease. Additionally, non-toxic renally clearing MRI agents are desired which is a large pitfall of modern MRI imaging.
- It has been suggested in literature that CEST can provide a means of detection at low concentrations due to the continuous exchange of protons causing a water signal attenuation. The use of porous nanoparticles have been explored as CEST agents due to their ability to target specific drug targets and release their payload in a controlled fashion. Porous silica is of especial interest because of its ability to be non-toxic and bio-degradable. Additionally, the parameters that attenuate the water signal within the CEST mechanism are saturated proton exchange rate and longevity of their corresponding excited spin states. () found that a slow exchange rate allowed for the greatest signal attenuation even at low concentrations of the contrast solute.
- Therefore, an exchange agent that could have the exchange purposely slowed could provide an effective CEST imaging agent. Porous silica being proven as a carrier of drugs, has been shown to be able to load and unload materials on precise targets. This ability to carry payloads precisely, unload the payload for interaction, slow the rate of exchange by limiting degrees of freedom and the ability renally cleared make porous silica nanoparticles an excellent candidate to tackle this problem.

Synthesis of mesoporous Silica nanoparticles

Silicon donating species in general have a protective passivating layer of Si-O, and Si-H bonds. In order to remove this layer one must first understand the trends of silicon surface reactivity. Contrary to belief, the bond strength trend doesn't dominate surface bond stability. Electronegativity is the trend to recognize as affecting surface stability and reactivity. Although Si-F by far has the strongest relative bonding energy out of all silicon surface species (Si-F, Si-O, Si-H), a passivating layer of Si-O and Si-H predominate at silicon containing species surfaces. Keeping this in mind, the layer of Silicon oxide (Si-O) can be removed based on its slight dipole based on the electronegative difference amongst silicon and oxygen. The electrophilic Silicon atoms on the surface can be nucleophilically attacked. Overall, keeping this reactivity in mind will allow for manipulation of Silicon donating compounds to be chemically liberated by making advantage of silicon's susceptibility to nucleophilic attack.



Upon exposure to an aqueous basic environment hydroxide ions will nucleophilically attack the silicon atoms which will result in the removal of the oxide layer. The exposed surface can now react with other reactive species. Additionally, to allow formation of orderly shaped particles a surficant (shaping template) will be needed.

A.

NH_4F
CTAB
 H_2O



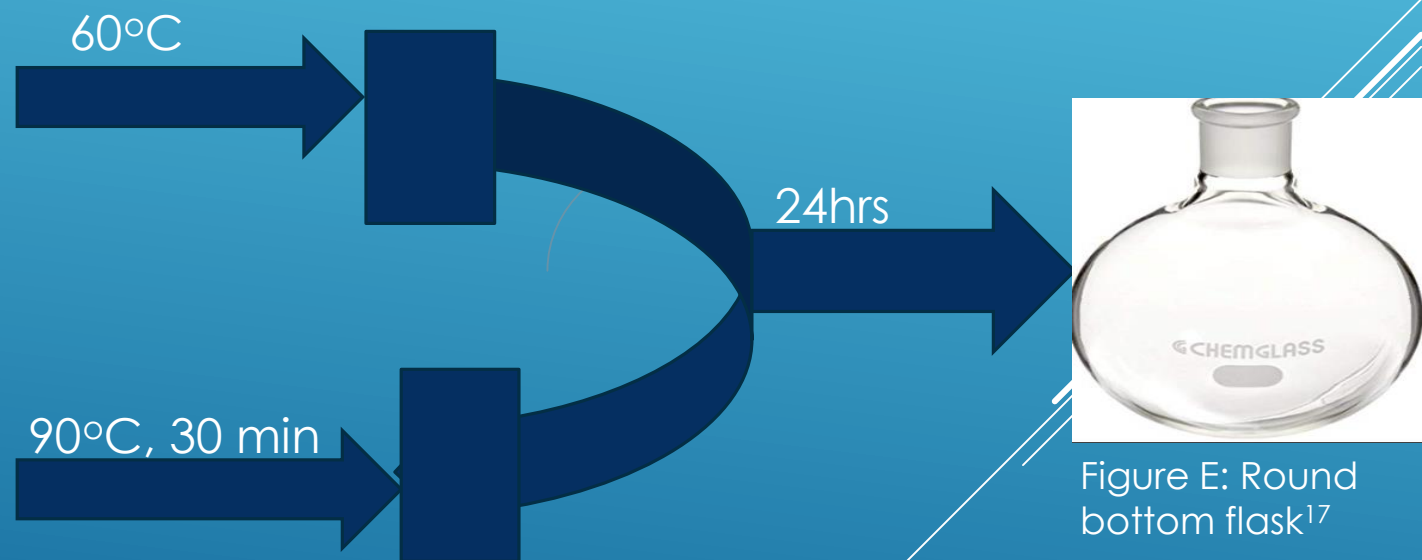
Figure C: Round bottom flask¹⁷

B.

TEA
TEOS
(DIBP, Decane)



Figure D: 50 mL centrifuge tube¹⁸

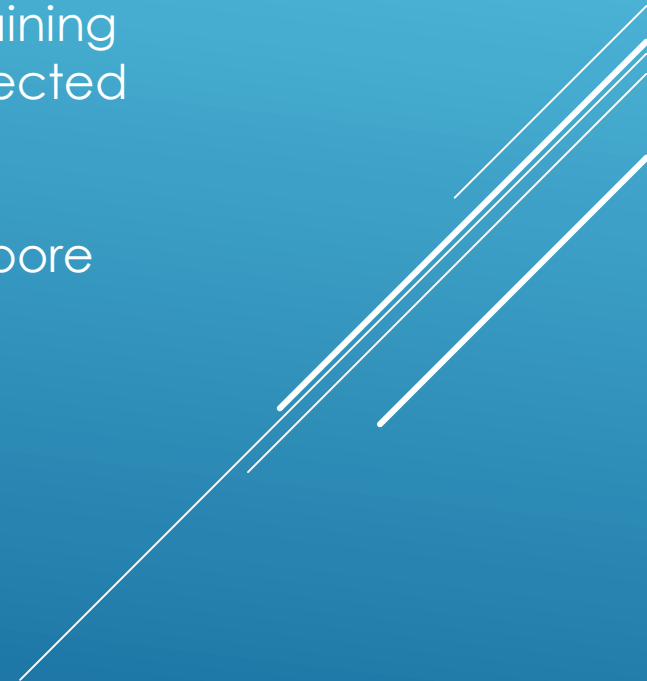


Etching/purification

- The solution in the round bottom flask is transferred to two 50 mL centrifuge tubes which are balanced evenly, and are centrifuged on the Fischer Scientific ultra centrifuge at 12,500 rpm for 1 hour.
- After 1 hour the solution should be clear with a gel-like precipitate. These are the silica nanoparticles.
- A solution of 1:4 EtOH/Hexanes solution is prepared, and the solvent in the bullet tubes are decanted off. The newly created 1:4 solvent is added to the bullet tubes and they silica is dissolved into the solution via sonication.
- Once, the solution is cloudy and no precipitate is present the solutions are centrifuged for .5 hours at 12,500 rpm (x3).
- A 9:1 EtOH/HCl solution is prepared. The final washing solvent is decanted off and the nanoparticle gel-precipitate is dissolved in the EtOH/HCl. The mixture is then put on reflux for 45 min.
- The solution is centrifuged until the precipitate reappears. The solvent is decanted off and the precipitate is dried at 70°C overnight.

UV-VIS SPECTRA

On slide 11 are 10 uv-vis spectra that were used to attempt to create a calibration curve. The purpose of obtaining a calibration curve was to provide a standard, so the solutions could be confirmed as properly prepared dilutions with the commonly expected approximate linear trend of absorbance being dependent on concentration. This would allow one to obtain concentration of the remaining species based on absorbance. Additionally, with the knowledge of the expected absorbances one could determine when the reactant species has been consumed and therefore, would approximately be able to determine the concentration of the products including the concentration of the originally pore loaded species.



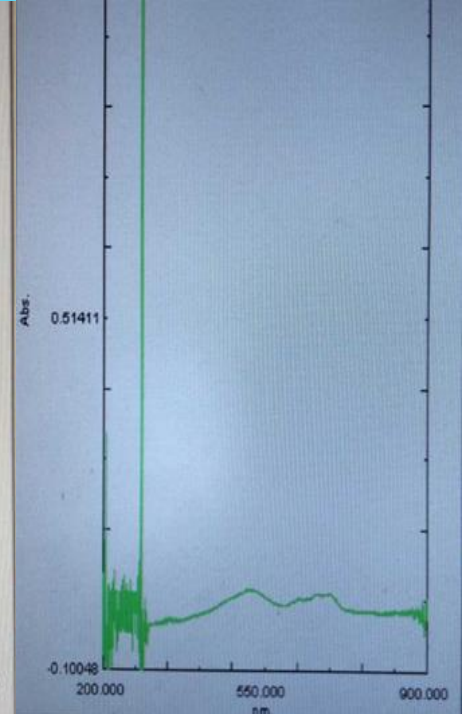
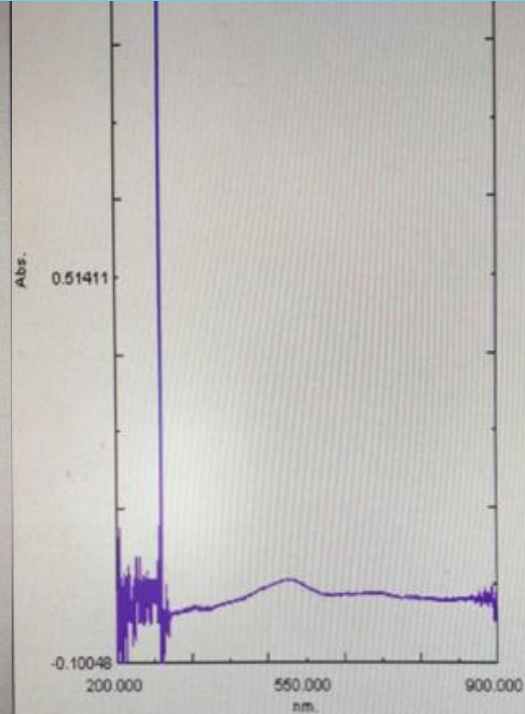
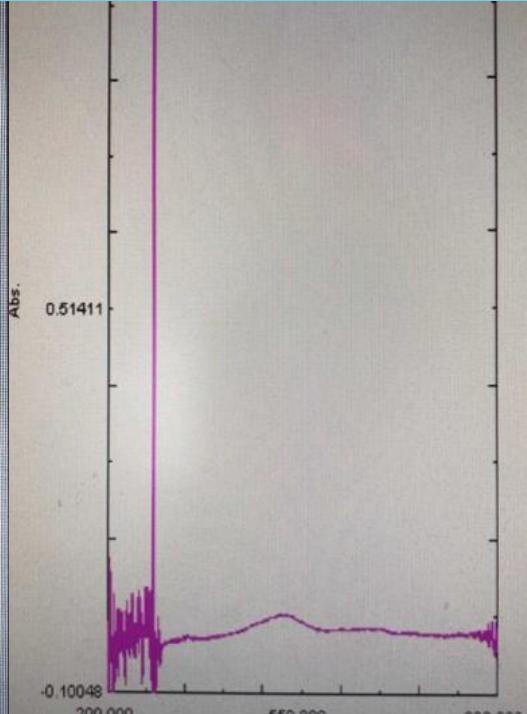
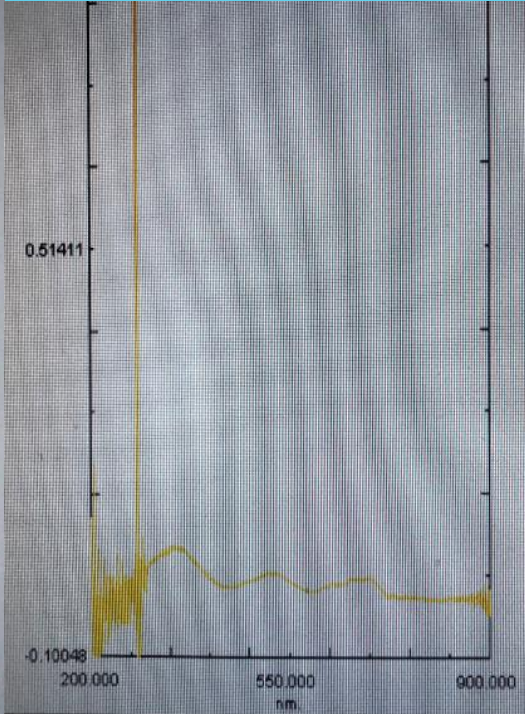
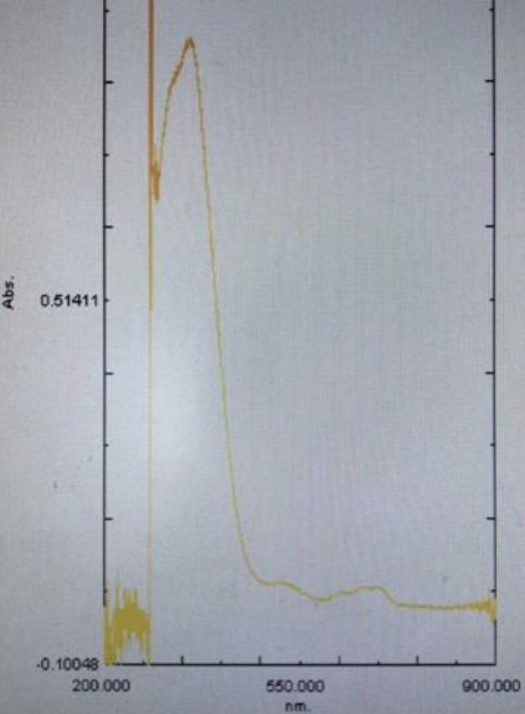


Figure 1: Uv-vis spectra serial dilution 1

Figure 2: Uv-vis spectra serial dilution 2

Figure 3: Uv-vis spectra serial dilution 3

Figure 4: Uv-vis spectra serial dilution 4

Figure 5: Uv-vis spectra serial dilution 5

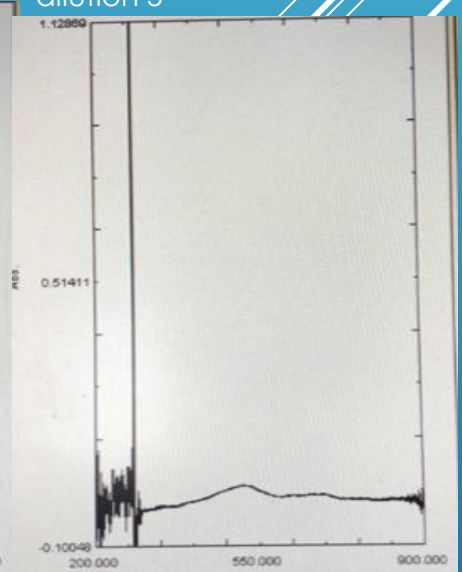
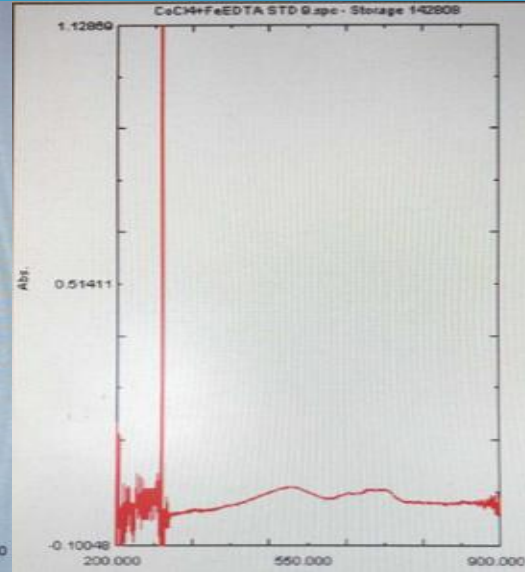
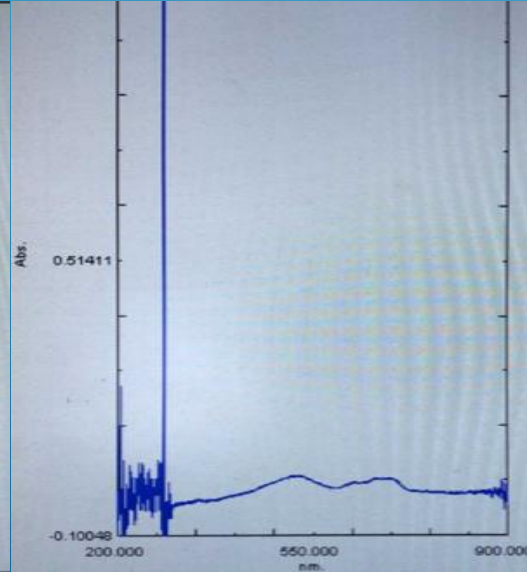
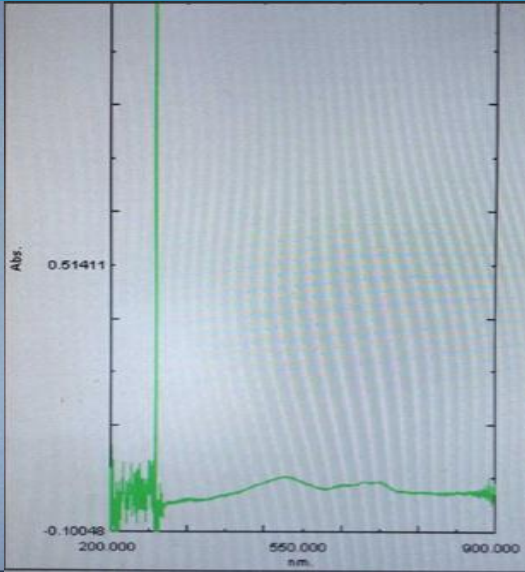
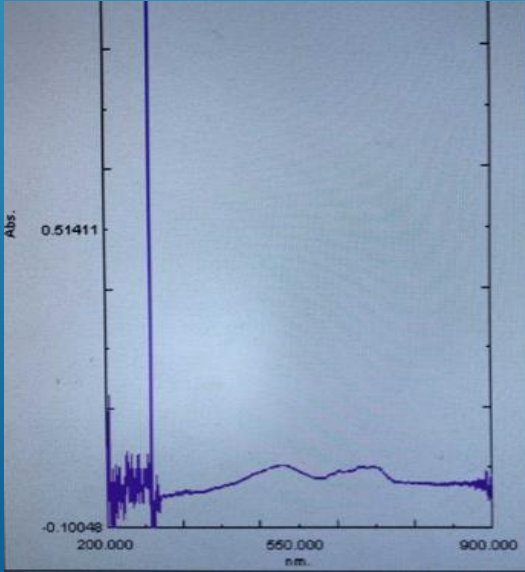


Figure 6: Uv-vis spectra serial dilution 6

Figure 7: Uv-vis spectra serial dilution 7

Figure 8: Uv-vis spectra serial dilution 8

Figure 9: Uv-vis spectra serial dilution 9

Figure 10: Uv-vis spectra serial dilution 10

Table 1: Calibration curve for the interaction of FeEDTA & CoCl₄

Concentration (M) (x)	Absorbance (y)
0.0005	0.0359
0.00005	0.03468
0.000005	0.0313
0.0000005	0.0263
0.00000005	0.03864
0.000000005	0.0304
5E-10	0.02423
5.00E-11	0.02484
5.00E-12	0.03577
5.00E-13	0.02312

Absorbance of FeEDTA + CoCl₄²⁻ mixture at 521 nm

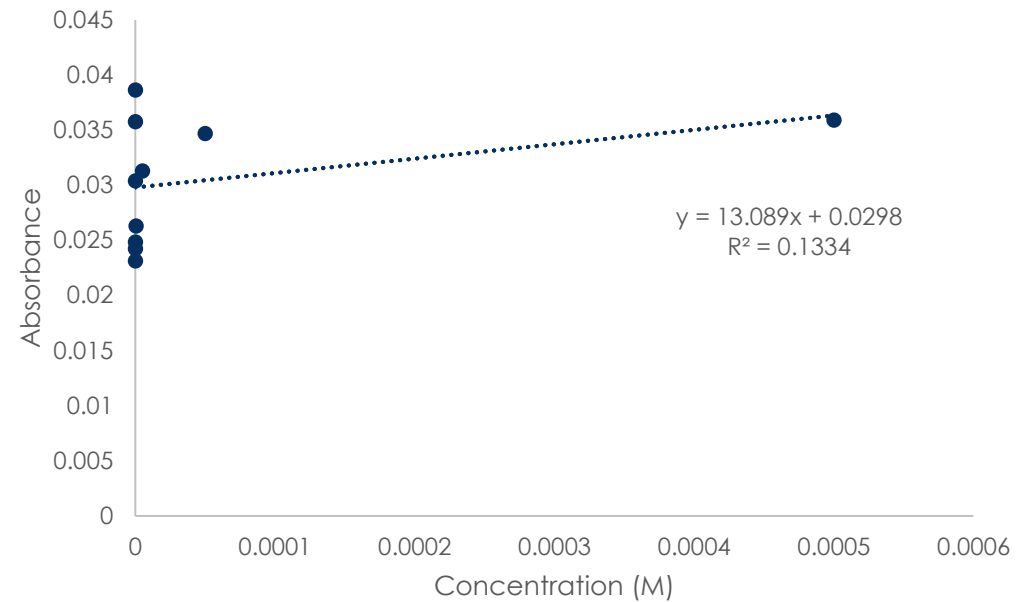


Figure 11: Calibration Curve for the reaction of FeEDTA & CoCl₄

TEM Images of the synthesized mesoporous silica nanoparticles

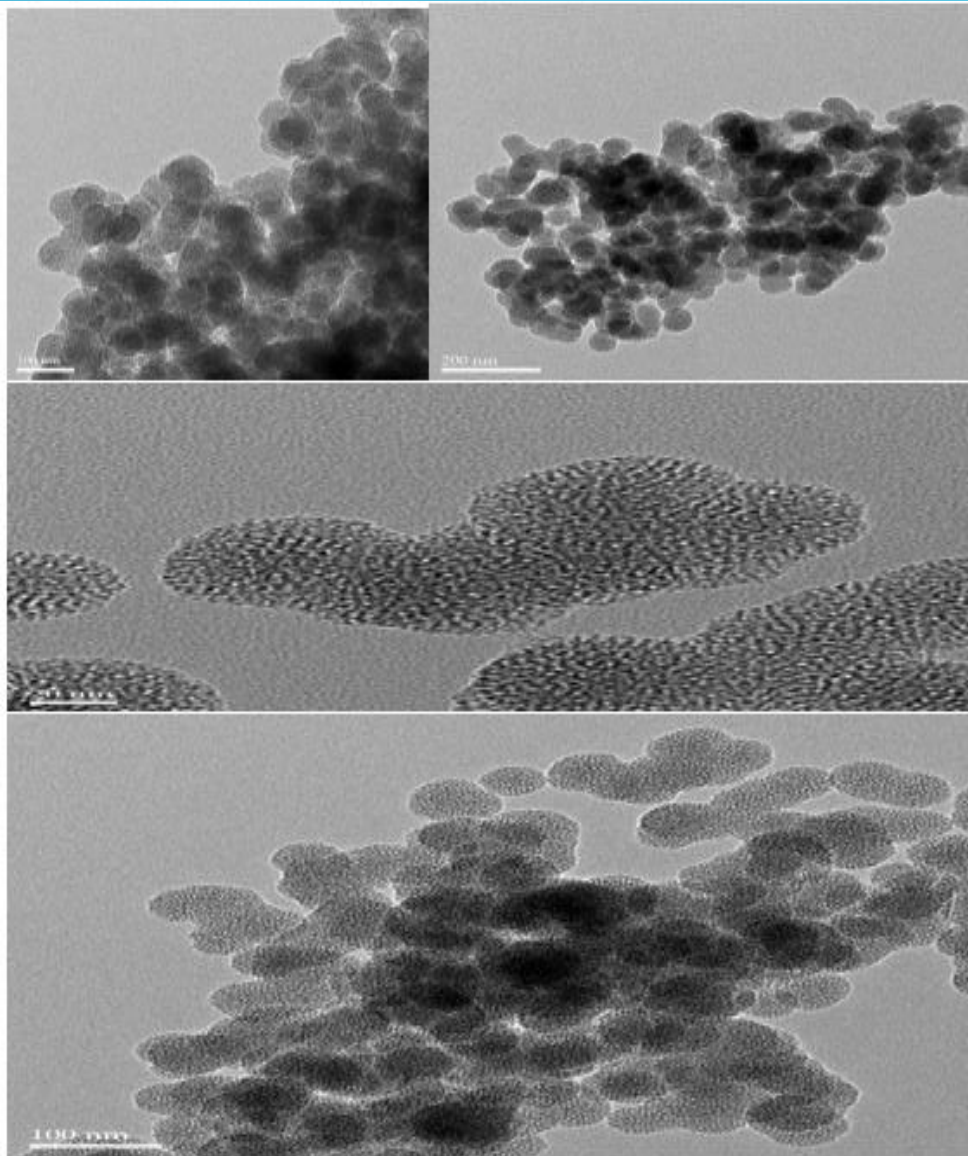


Figure 12: TEM images of unmodified mesoporous silica nanoparticles

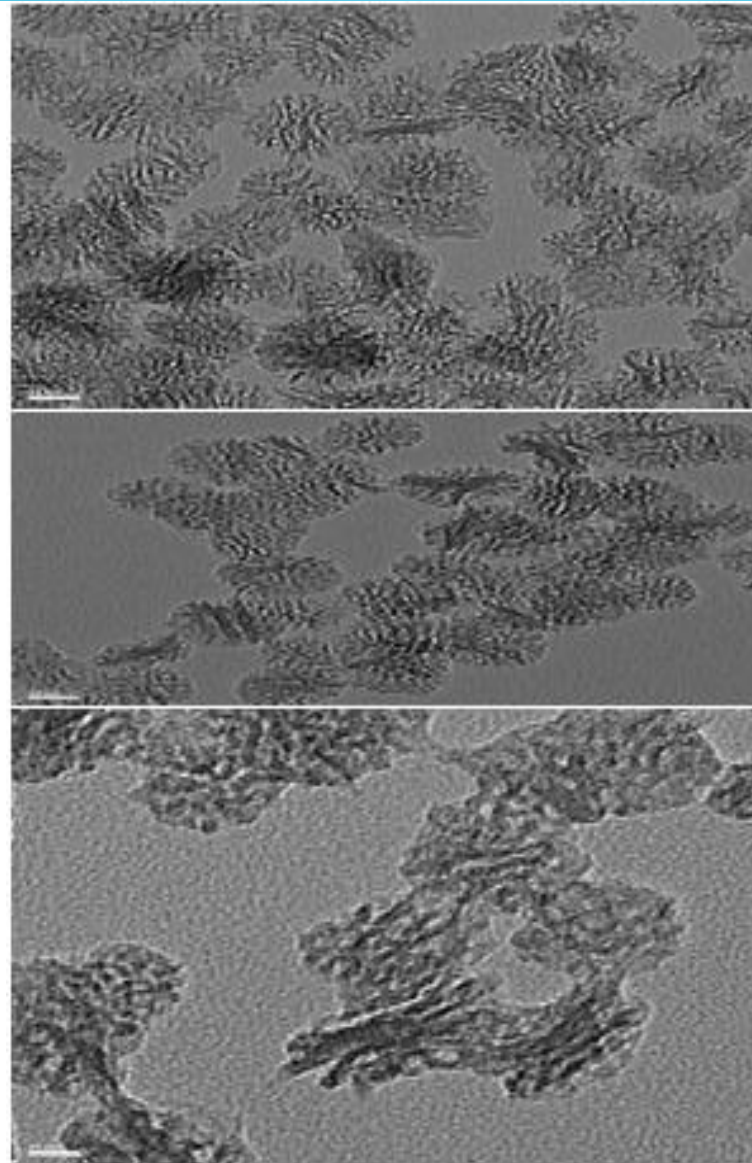


Figure 13: TEM of DIPB modified silica nanoparticles at 10 and 20 nm

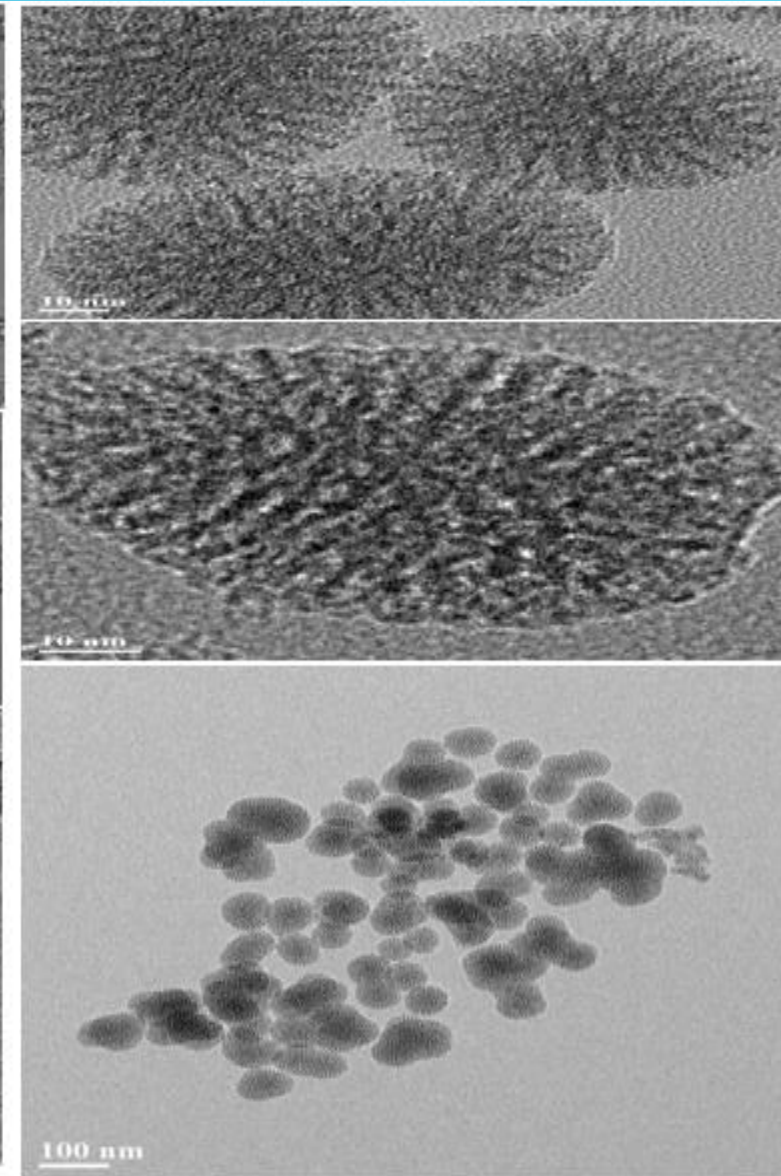


Figure 14: TEM images of Decane modified silica nanoparticles

Conclusions

- Synthesis of various pore sized silica nanoparticles was successful
- The bulking agents were successful at modifying pore size
- The calibration curve was unsuccessful at establishing a linear trend with absorbance and concentration. This was possibly due to poor technique, or interference from $\text{Co}(\text{H}_2\text{O})_6^{2+}$ due to the low concentration of the $[\text{FeEDTA}^-]$ in the titrant.
- Future work will involve obtaining a proper calibration curve in order to obtain the concentration of loaded $[\text{FeEDTA}^-]$ after the emission peak of CoCl_4 has diminished and the expected CoEDTA peak has appeared.

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