



WHAT'S THE BIOBUZZ?

A journal for students by students

How to Re(cyst) a Stoney Problem?

Key Terms

Atomic Force Microscopy (AFM): A magnification tool with excellent resolution using a laser to view objects in nanometers size.

Chemical Synthesis: The formation of a new compound from various substances.

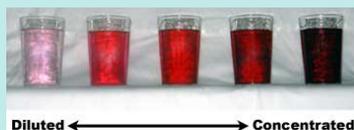
Concentrations: The amount of the substance added.



Low concentration → High Concentration

Crystals: A 3D arrangement of molecules in a regular pattern.

Dilute: Reducing the concentration by exposing it to more fluid.



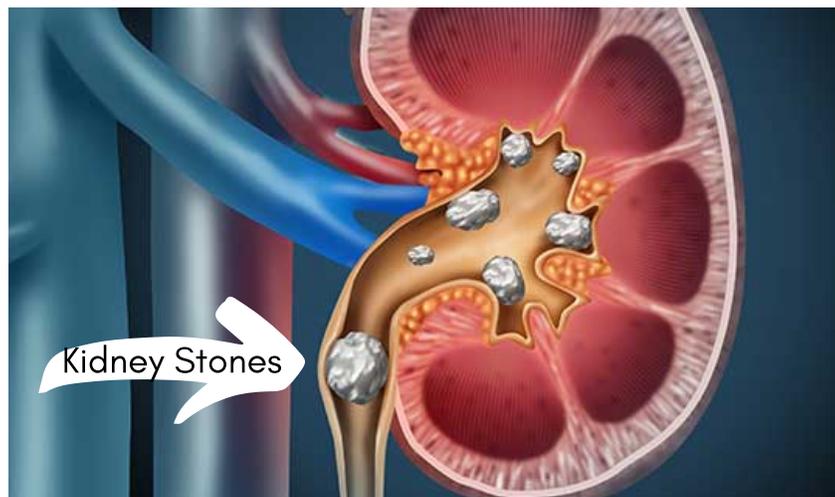
Inhibitor: The prevention of certain biological activities from occurring. In this case, it slows down the growth of crystal build-up.

Kidney Stones: Development of crystallized minerals in the kidney affecting a person's urinary tract.

L-cystine: A chemical compound that when it is build up, it contributes to the formation of kidney stones.

Nanometer (nm): A sheet of paper is about 100,000 nanometers thick!

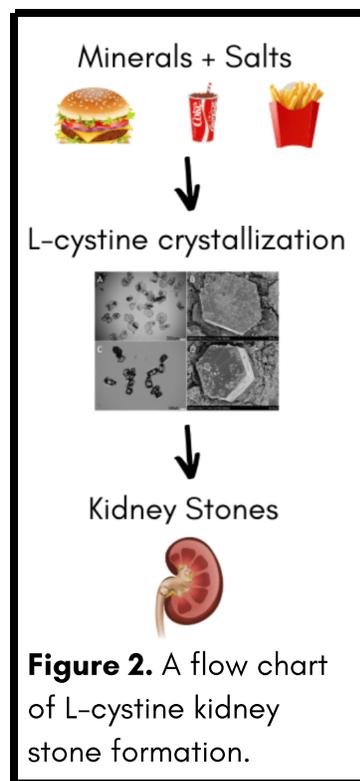
Size layer: The thickness of the new crystal sheet.



HOW DO KIDNEY STONES FORM?

Passing gas is easier than passing a stone!

Eating lots of sodium-rich foods such as those in fast food is harmful to your body. They contain chemicals that when combined with calcium, produces a solid **crystal**. Some individuals have a rare disorder where one molecule accumulates in the urine, forming a sizable solid **kidney stone**.



L-cystine crystallization plays a crucial role in the progress of becoming a kidney stone. The purpose of this lab is to introduce the use of **inhibitors**, L-CDME, and L-CME to prevent the growth of kidney stones.

INTRODUCTION

Kidney stones form when bodily fluids do not **dilute** crystal-forming substances in the urinary tract. A genetic condition of an aggressive form of kidney stones is L-cystine kidney stones. L-cystine kidney stones affect around 20,000 individuals in the U.S. and are likely to cause chronic (long-term) kidney disease. This disorder prevents the reabsorption of L-cystine, resulting in the formation of a large kidney stone compared to "regular" kidney stones.

L-cystine kidney stones exist in a large hexagonal structure. New treatments indicate that using artificial inhibitors, which mimic the shape of L-cystine, reduces the growth of the crystals.

L-CDME and L-CME recognize (binds to) the existing kidney stone crystal. The binding of the inhibitor to the crystal arrests the crystal structure from advancing.

METHODS

In order to study the effectiveness of the inhibitors, scientists used three groups based on a control group and the two inhibitors: L-CME and L-CDME. The scientists observed the effect the inhibitors have when compared to the control treatment. From the **AFM**, we get a collection of measurements of crystal **concentration** and size (**nm**).

Lock and Key Inhibitors



Figure 3. Lock and key analogy of inhibitors.

Think of each key as a different molecule with the same lock specificity but made up of slightly different materials.

- The **green key** provides access to the build-up of more minerals - enhancing the size of the crystal structure.
- The **yellow** performs the opposite effect and limits the number of minerals building up by locking the doorway of possibility.
- The **black** serves as a double lock, reducing even more entrance of minerals.

Step 1
Synthesize the initial L-cystine "mock" kidney stones.

Step 2
Synthesize the inhibitors L-CDME and L-CME.

Step 3
Exposure of the crystal to the inhibitor.

Step 4
Utilize the AFM to determine the measurements of the crystal **size layers**.

Step 5
Form a graphical representation of the AFM data.

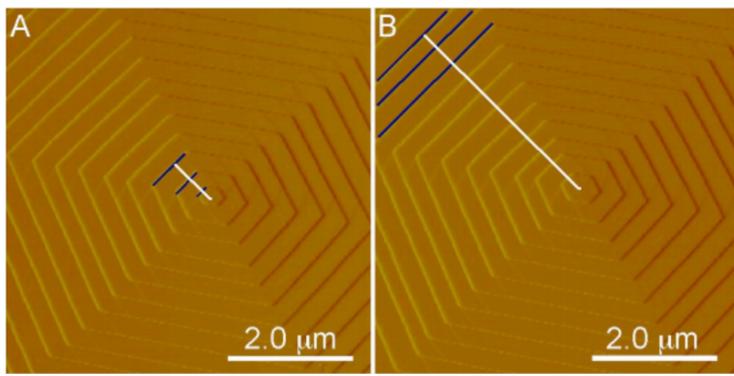


Figure 4. Image obtained from the experiment displaying the measurement of additional crystal layers using AFM.

RESULTS

More substantial growth advancement is unfavorable because it represents a larger "mock" kidney stone causing a painful experience for the individual.

The goal is to minimize the size activity of the L-cystine crystals. Using the AFM, the measurement of the size layer of the crystals was determined and recorded in Figure 6. Based on Figure 6, L-CDME was more successful at slowing the growth than L-CME because of how well it blocks (or locks out) other L-cystine crystals from forming/entering.

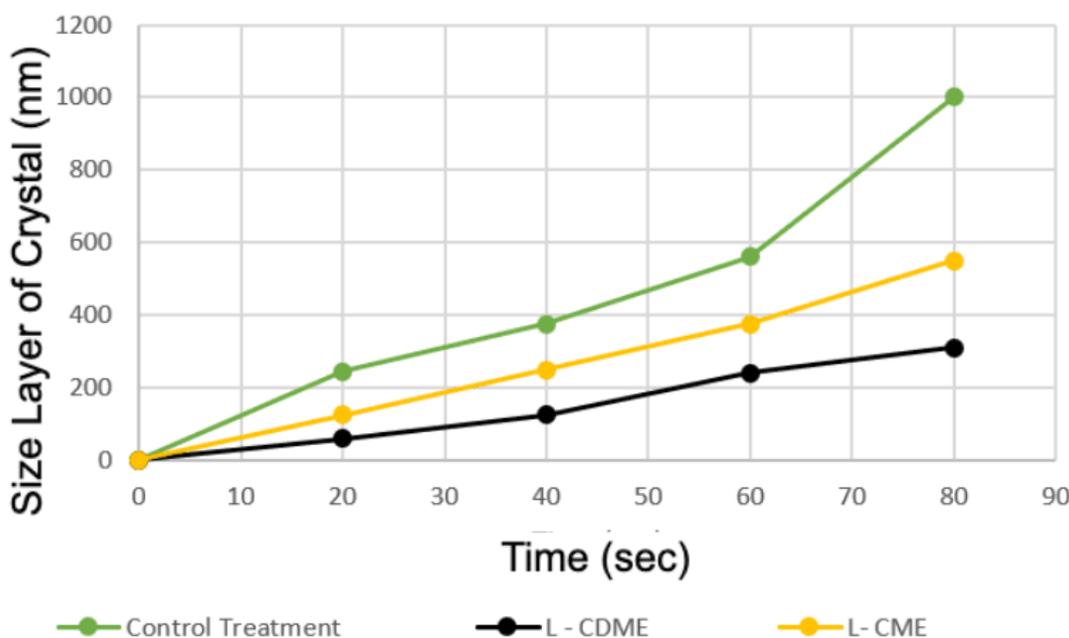


Figure 6: L-CDME and L-CME inhibitors when compared to the control treatment with no amount of inhibitors. The crystals began at 5.6 nm high. Recall we want the crystals to be as close to 0 (x-axis) as possible in which it represents a smaller kidney stone.

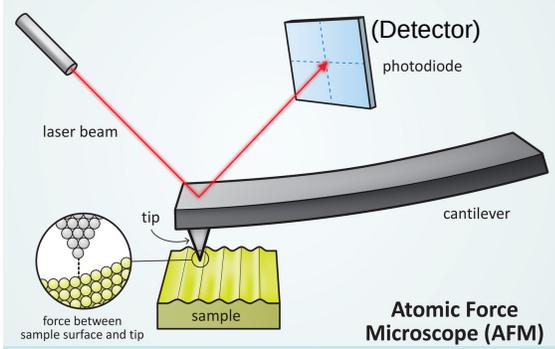


Figure 5. Demonstration of the inner workings of an AFM.

How does AFM work ?

AFM uses a laser beam deflection technique along with a specialized tip and looped lever that measures the surface of the sample. The tip travels over the sample where the detector records its path. As the tip moves, the deflection of the laser is picked up by a light detector creating a graph representation of the sample's surface. In this experiment, this measurement of the crystals layer growth was observed with and without the inhibitors.

AFM resolution is more exceptional as compared to a compound microscope.

DISCUSSION

- Cystine stone disorder range from the size of sand grains to giant pearls!
- Concentration waste from high-sodium diets leads to the formation of crystals.
- In a healthy functioning kidney, crystal contents pass out of the body along with urine quickly.
- The study shows that the use of an inhibitor can reduce L-cystine levels. It seizes the growth of the crystal. Without the inhibitor, the crystal grows into a problematic size. Using AFM measurements, scientists were able to conclude that the inhibitor reduces the crystal growth. In the absence of the inhibitors, the process naturally occurs faster.
- L-CDME is a more effective inhibitor than L-CME because L-CDME has a better chemical lock that binds more readily to the crystal site-preventing further growth.
- The use of a crystal growth inhibitor has potential in reducing the possibility of other drug side effects. However, this study is still in its infancy stage - more studies are necessary.

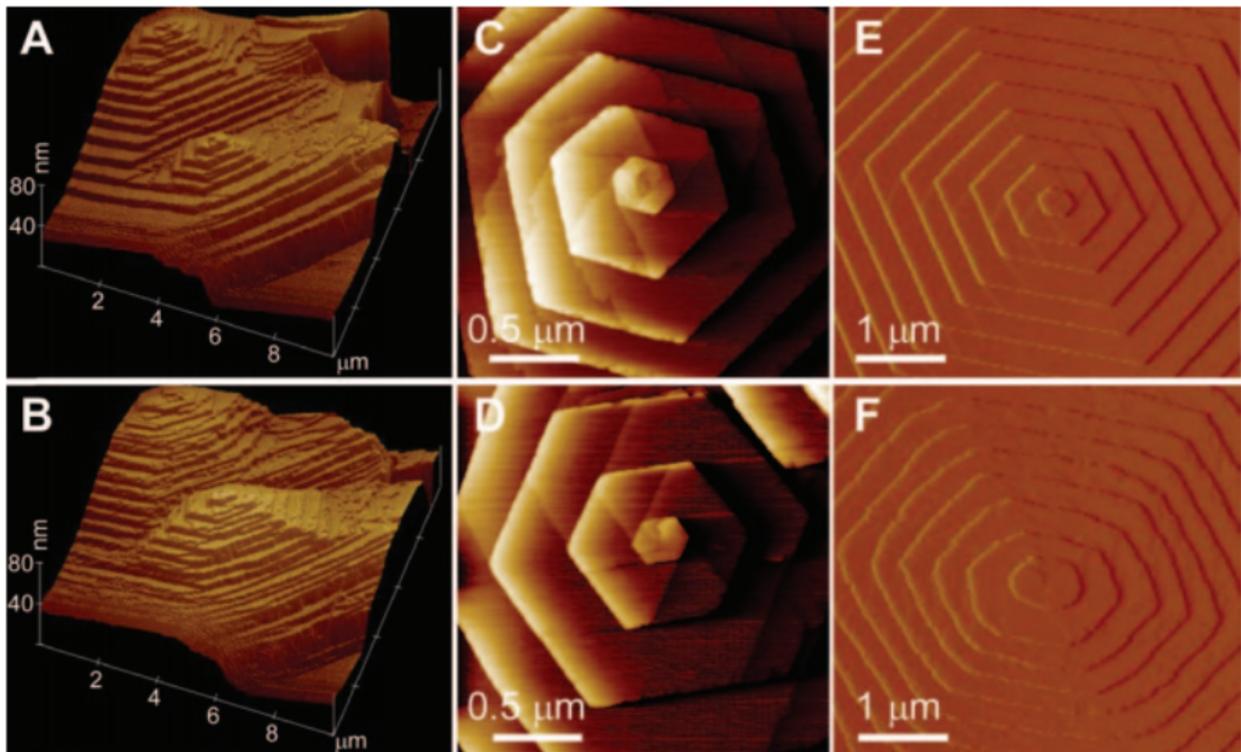


Figure 7. Experimental images of the crystals from the AFM. (**A and B**) Image showing AFM images of the growth L-cystine crystal taken 12 minutes apart. (**C and D**) Image showing the center of the crystal. (**E and F**) Image of crystal over time with the addition of the inhibitor L-CDME.