

Treatment of Wilson's Disease with Alpha Lipoic Acid

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Abstract: Wilson's disease is the malfunction of the copper removing protein ATP7B. This rare, genetic disease affects the body by accumulating copper in vital organs such as the liver, brain, and eyes. There are currently two drugs on the market for this disease, but they can cost about \$25,000 a month, thus forcing people to weigh the cost and possibly put a price on their life. In this experiment alpha lipoic acid, an antioxidant used as a dietary supplement, was tested under neutral and acidic conditions to see if it could bind with copper and render it insoluble. Two experiments were performed, one with a neutral environment and one with an acidic environment. The results showed that alpha lipoic acid was best at rendering copper insoluble in the neutral environment. With further research and tests in biological systems, alpha lipoic acid could be an effective and inexpensive treatment for Wilson's disease.

Keywords: Alpha Lipoic Acid, Wilson's Disease, ATP7B Protein, UV Visible Spectrophotometer, Liver

Introduction

Wilson's disease is a rare, genetic disease that causes the body to accumulate excess amounts of copper. This disease causes the malfunction of the ATP7B protein, also known as the Wilson's disease protein, which aids in the natural removal of copper from the body (Forbes and Cox 2000). Copper then collects in vital organs such as the brain, eyes, and liver causing damage anywhere from scarring of the liver to organ failure and ultimately death (Ala et al. 2007).

There are currently two types of drugs approved for treating Wilson's disease that have been proven to halt the progression of the disease. The first one is Penicillamine and the second is Trientine which is used in patients who can't take Penicillamine (Walshe 1956). Both of the medicines work in similar ways in that they bind to copper, making it insoluble in the body, and excrete it through the urinary tract. Although these treatments have proven to be effective, the average monthly cost for these drugs is about \$25,000 (Schilsky et al. 2015).

Alpha lipoic acid is an antioxidant that is used as a dietary supplement. It can be taken to help

with HIV, depression, diabetes and many other diseases (Baur et al. 1991; Salazar 2000). It is a coenzyme that is found mostly in nature as its protein form composed of sulfur, carbon, hydrogen, and oxygen (Reed et al. 1953). Studies have shown that because of this compound and its elements, alpha lipoic acid binds well with heavy metals such as copper (Baumgartner et al. 1996). The purpose of this study is to see how alpha lipoic acid reacts with copper in different environments. Through this, collected evidence could be used to test our hypothesis that alpha lipoic acid is a cheap alternative to the pharmaceutical medicines currently used for treating Wilson's disease by binding to the excess copper and rendering it insoluble in the body.

Methods

Stock Solutions

Two stock solutions were made first to be used as the constant environment for the trials. The first stock solution, which was the neutral solution, was made by mixing approximately 100 grams of deionized water with 1 gram of CuCl_2 . The second, which was the acidic solution, was made by first obtaining 1M HCl solution and adding 1 gram of

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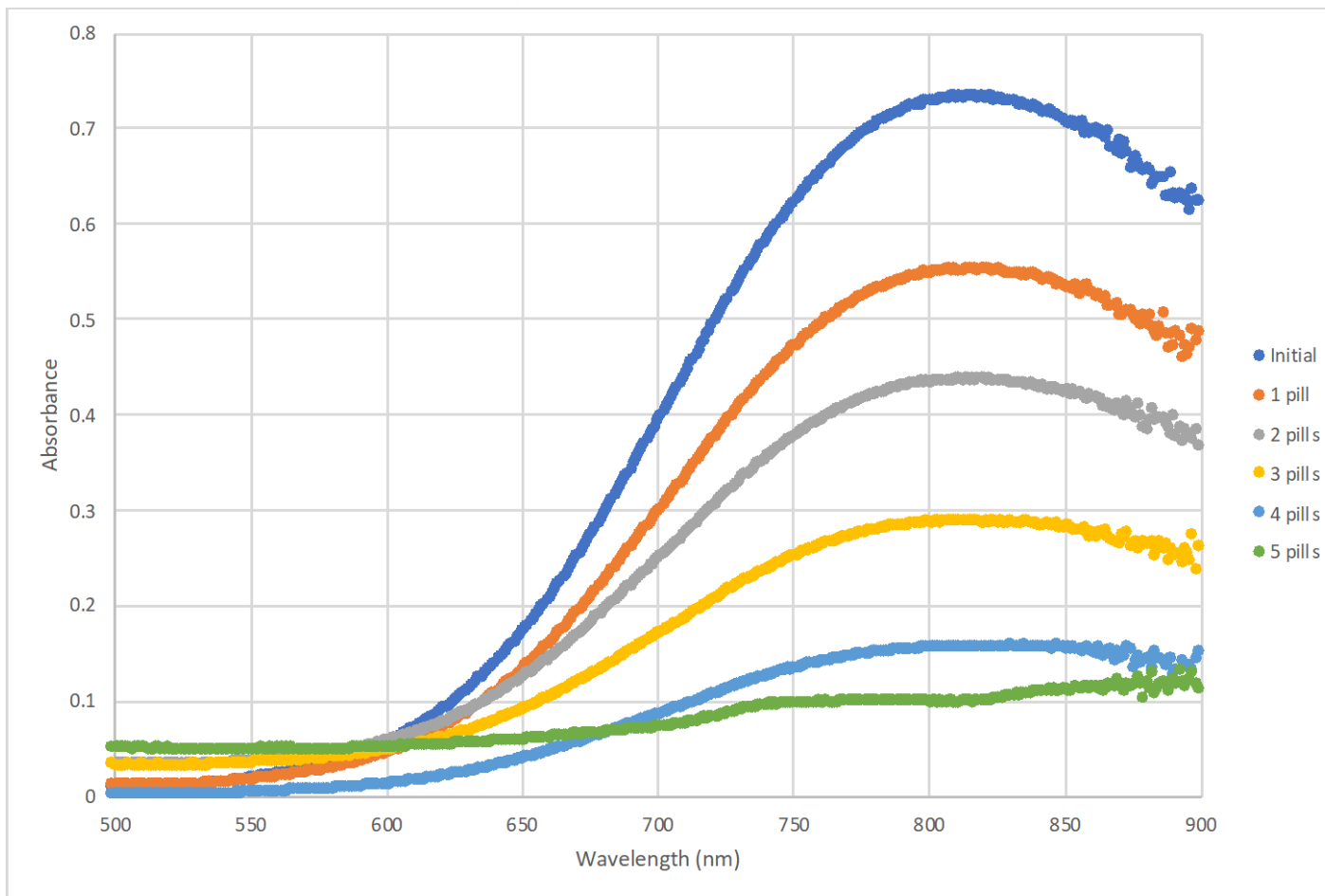


Figure 1: This is the scatterplot that was created by the reading from the UV-visible spectrophotometer of the lipoic acid reaction with the CuCl_2 neutral stock solution for 0 to 5 pills.

CuCl_2 . To obtain the 1M HCl solution, approximately 8.5 grams of HCl were added to 91.5 grams of deionized water. vials of CuCl_2 and an MCP-AES was used to measure the concentration.

Alpha Lipoic Acid Reactions

Five 20mL vials were then filled with 10 grams of the neutral stock solution each. One pill of “Doctor’s Best Science-Based Nutrition Alpha Lipoic Acid 600” was broken open into one vial of the solution. Two, three, four, five pills were broken open into the remaining four vials. These steps were repeated for the acidic stock solution. All 10 vials were then put on a sample rotator for 24 hours, and after, the contents were centrifuged. Once the centrifuge was finished, the remaining solutions were transferred into clean vials. A UV-Visible spectrophotometer was used to measure the absorption of the solutions of the 10

Results

After 24 hours on the sample rotator every vial had formed a precipitate. Analyzing the UV-Visible spectrophotometer readings for the 5 vials of alpha lipoic acid in the neutral stock solution, showed there was a clear trend that as there were more pills added, there was less copper absorbance (Figure 1). As for the readings on the 5 vials in the acidic stock solution, there seemed to be the same amount of absorbance no matter how many pills were added (Figure 2). Since there wasn’t much absorption in the acidic stock solution, the concentrations were only taken for the vials with the neutral stock solution. The MCP-AES measured the concentration of the initial stock solution

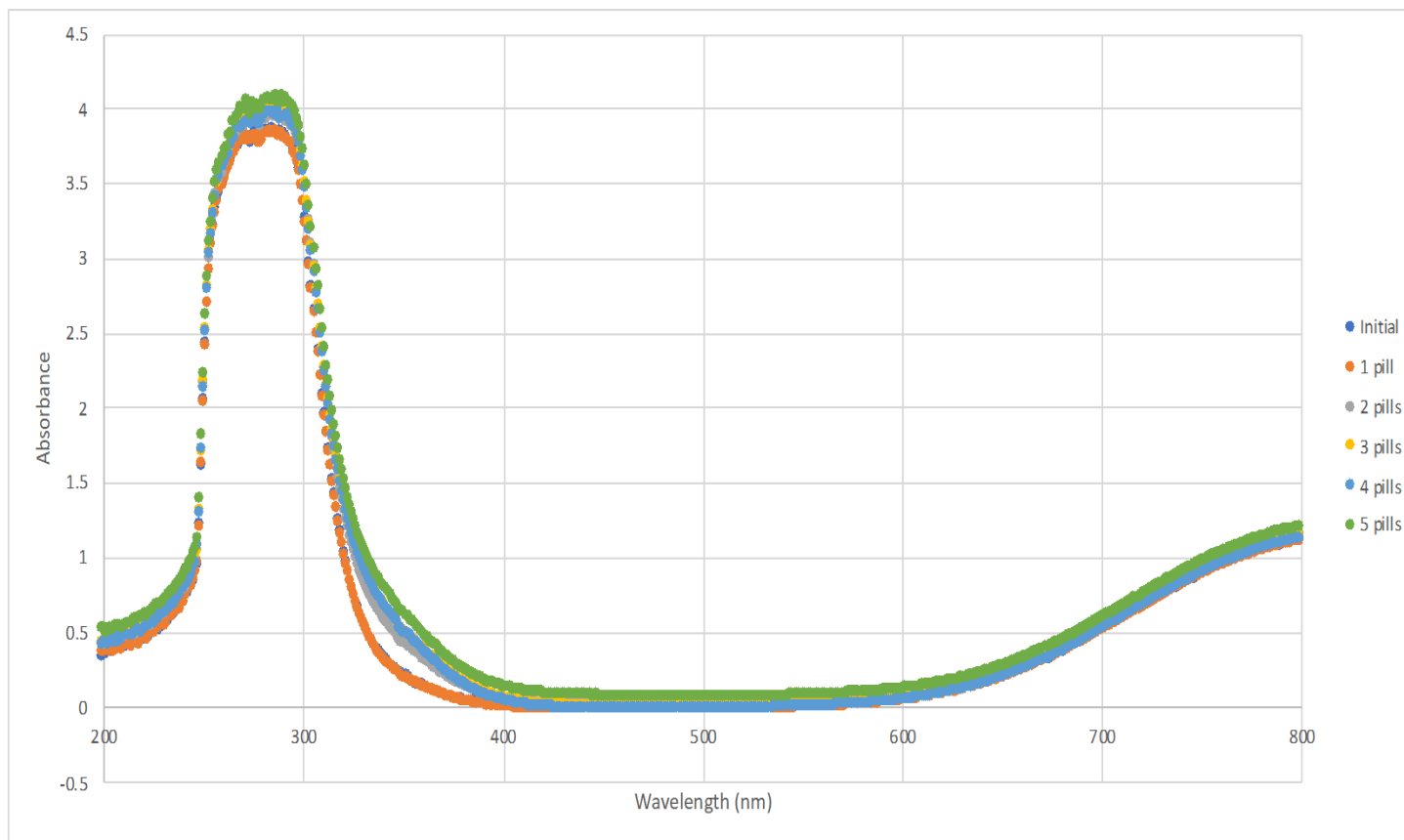


Figure 2: This is the scatterplot that was created by the reading from the UV-visible spectrophotometer of the lipoic acid reaction with the CuCl_2 acidic stock solution for 0 to 5 pills.

with no alpha lipoic acid to be 3045.71 ppm and the concentration of the vial with 5 pills to be 156.1 ppm. This showed that there was a 94.87% decrease of copper from the solution when 5 pills of alpha lipoic acid were added.

Discussion

From the figures we can see that as the amount of alpha lipoic acid increased, the UV-Visible reading for the neutral solution decreased because there was less copper to be absorbed. These results show that alpha lipoic acid is capable of rendering copper insoluble under neutral conditions. When the alpha lipoic acid was mixed with the copper, it combined together to form a chain of an insoluble compound in water (Figure 3). From the readings of the UV-Visible for the acidic solution, it can be concluded that the alpha lipoic acid does not react with copper under acidic conditions. Because of this, alpha lipoic acid

can be applied to the body by working best in the liver. Since the pH of the liver is neutral, alpha lipoic acid is capable of binding with copper and possibly removing it through the hepatic portal, a system of vessels surrounding the liver.

In the future, we would like to take this research and use it in a biological system.

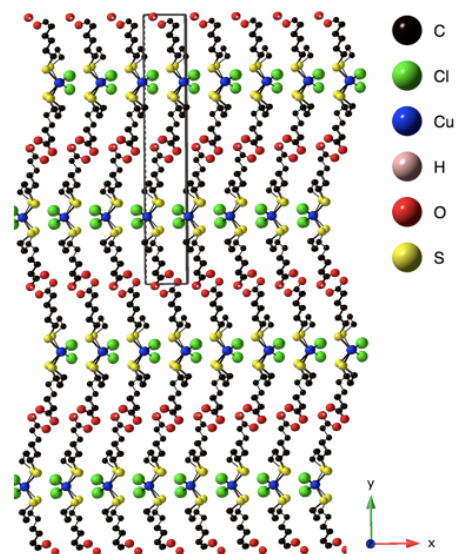


Figure 3: This is the chain that copper makes when it bonds with alpha lipoic acid.

We think it would be best to test in vivo with a rat model. This way we can see how this supplement works in different conditions other than a vial. With further research we believe alpha lipoic acid can be an excellent and inexpensive treatment for Wilson's disease.

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