Research Proposal

Cancer Cell Death Surveillance:
A Comparison of the effects of Liposomal Vitamin C and Traditional Vitamin C

Date: December 3, 2022
Principal Investigator: Zaysha Akina-Mahoe

The purpose of this study is to determine if Liposomal Vitamin C at certain doses will kill more cancer cells in a patient compared to traditional liposomal vitamin C. If this is the case, liposomal vitamin C will be a new product given to patients battling cancer and will help patients to live healthier lives.

In the 1970s and 1980s, Mayo Clinic conducted a large clinical study regarding the benefit of vitamin c as a cancer treatment. However, their results showed no correlation with cancer therapy (Reczek and Chandel, 2015). However, more recent studies showed the opposite. One of these studies carried out showed that vitamin c concentrations above 1000 μmol/L were toxic to some cancer cells but not to normal cells. This allowed patients with advanced cancers to have taken vitamin c intravenously and live longer than expected (Padayatty, 2006). Another study conducted by Jihye Yun found that colon cancer cells with growth driven by mutations in the KRAS gene and BRAF gene make excessively large amounts of a protein that aids in the transport of glucose across the cell membrane. This transporter is GLUT1 which also transports the oxidized form of vitamin c, also known as dehydroascorbic acid, into the cell. This depletes cancer cells because it gets rid of the cancer cell's chemical that takes away free radicals against that cancer cell. In conclusion, Jihye Yun found that large doses of vitamin c killed culture colon cancer cells with BRAF and KRAS mutations by raising the exposure of free radicals. These free radicals eventually inactivated the enzyme needed to metabolize glucose, leading to a decrease in the cells' energy production (Kaiser, 2015).

With contradicting results, the use of liposomal vitamin c in cancer treatment should be revisited. Since liposomal vitamin creates a higher bioavailability rate compared to traditional vitamin c, there is a possibility that liposomal vitamin c can be better used in cancer treatment. Oral intake of liposomal vitamin c could produce higher concentrations of vitamin c in the body, leading to toxicity towards cancer cells and possible cancer recovery.

Literature Review

Ascorbic acid, commonly known as Vitamin C, has been widely used in many forms to combat many health-related problems due to its antioxidant effects. Vitamin C is one of the 13 essential vitamins that must be eaten because the human body cannot synthesize it from other substances. There are numerous food sources that you can get vitamin C from. For example, Vitamin C can be obtained from beans, broccoli, cabbage, chili peppers, nori, onions, potatoes, pummelo, squash, etc. Some food sources that include a high concentration of Vitamin C are oranges, guava, lemon, lime, mango, pineapple, raspberries, strawberries, and tangerines. Vitamin C can also be obtained over the counter in liquid and solid forms (Mayo Clinic Staff, 2020).

A significant aspect of vitamin C is that when it is ingested, it can limit the free radicals that are formed in your body. Reactive oxygen species are subsets of free radicals and are normal products of a cell's aerobic metabolic reaction. Reactive oxygen species can be formed endogenously with the help of reactive oxygen species-generating enzymes, or they can be formed from environmental factors such as UV radiation. When antioxidant protection mechanisms cannot keep up with the production of reactive oxidative species these free radicals can disrupt the cell's normal metabolic pathway and structure, which in turn can lead to more free radicals. If this is

the case, extensive cell and tissue damage can build up in the body and lead to a disease like cancer (Attia, 2020).

When it comes to the actual uptake of vitamin C after the body has processed the substance that is carrying the vitamin, not much of it is absorbed. In other words, the body's cells do not take in as much vitamin C as someone eats. This is mainly because vitamin C is soluble in water, so it can leave the body much more easily. However, liposomal vitamin C shows a higher delivery rate to the body's cells. A liposome is a spherical vessel that can range from 0.25 μm to 2.5 μm. It is composed of at least one lipid bilayer. This lipid bilayer allows nutrients, like vitamin C, to reach the body's cells more efficiently because the cell membrane is also composed of a lipid bilayer. This means that taking liposomal Vitamin C will provide more benefits than the traditional intake of Vitamin C (Akbarzadeh et al., 2013).

A study done by PlantaCorp in collaboration with Surya Research Clinic showed that liquid liposomal vitamin c is 12.17 times more bioavailable than non-liposomal vitamin c. However, there comes a point where liposomal vitamin c can hurt at higher doses. At doses around 200 mg vitamin c can be well-absorbed, but at doses above 500mg vitamin c cannot be absorbed as well. The limit of transporters causes this limit in absorption (Krawiec, 2021).

Study Population

I will include adults 18 years and older of either gender who are at any stage of cancer. We will include those who are willing to do the following: abstain from food, coffee, tea, and soft drinks at least 1 hour before arriving at the clinic, abstain from alcohol for at least 12 hours before their clinic visit, and are willing to maintain a consistent exercise and supplement schedule. We will not include participants who have any other major diseases because we do not know the downstream impact our study could have on a person's health. We will not include those taking large amounts of

Vitamin C regularly. Overall, we want to focus on cancer itself and not interfere with other underlying health issues. These participants will then be randomized into 4 groups of 5 people each. This study is deemed ethical as it got approval from the Institutional Review Board (IRB).

Consumable test products

The test product, liposomal vitamin c, will be provided by a significant nutritional company. The liposomal vitamin C is emulsified in bioactive phospholipids that help to deliver vitamin C more efficiently to the body's cells. There are 3 versions of this liposomal vitamin C. One version has 200 mg of vitamin c, another has 400 mg of vitamin c, and another has 500 mg of vitamin c. A placebo with a veggie mix will also be given to a randomized group. All of these test products will be served with rice milk to help the product digest easier.

Clinic Visits

Clinic visits will take place over the course of four weeks. At the beginning of each visit, the participant's height, weight, and temperature will be measured. They will also be asked a few questions about their activities and meals in the past 24 hours. Each visit will be spaced out 1 week apart with 5 visits in total. At the visits, participants will be asked to remain calm and comfortable in their rooms for 1 hour before the first blood draw. After the first blood draw, a test product will be given to them. Then, in 1-hour intervals, 3 more blood draws will be taken.

Blood Draws

For each blood draw, 1 heparin tube, 1 serum separator tube, and 1 EDTA tube will be collected. The heparin tube will be immediately placed in an ice bath after blood collection. The plasma from this tube was harvested and frozen. This sample will be sent to a clinical laboratory where vitamin c levels are tested. The serum separator tube and

EDTA tube will be processed at the lab and aliquoted. The samples will be tested for cancer cell levels, free radical stress, and cytokine levels.

Data collection

Ascorbate levels will be measured by High-Performance Liquid Chromatography (HPLC). Ascorbate radicals will be detected by electron paramagnetic resonance. Cell death will be measured by nuclear staining and propidium iodine.

Data analysis

All data collected will be placed on graphs and measured for significant changes in numbers. Microsoft Excel will serve as the major software to showcase data.

Expectation

I am expecting to find that liposomal vitamin C at increasing doses will help to kill cancer cells at a higher level compared to traditional vitamin C given new information from recent studies. If this is the case, I will conduct more research to see what doses are beneficial for certain stages of cancer.

References

Akbarzadeh, A., Rezaei-Sadabady, R., Davaran, S., Joo, S. W., Zarghami, N., Hanifehpour, Y., Samiei, M., Kouhi, M., & Nejati-Koshki, K. (2013, February 22). *Liposome: Classification, preparation, and applications*. National Library of Medicine. Retrieved October 26, 2022, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3599573/

Attia, M., Essa, E. A., Zaki, R. M., & Elkordy, A. A. (2020, April 25). *An overview of the antioxidant effects of ascorbic acid and alpha lipoic acid (in liposomal forms) as adjuvant in cancer treatment*. National Library of Medicine. Retrieved October 26, 2022, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7278686/

Krawiec, S. (2021, April 7). *PlantaCorp announces results of bioavailability study, assessing performance of liposomal Vitamin C*. Nutritional Outlook. Retrieved October 26, 2022, from https://www.nutritionaloutlook.com/view/plantacorp-announces-results-of-bioavailability-study-assessing-performance-of-liposomal-vitamin-c

Mayo Clinic Staff. (2020, November 17). *Vitamin C*. Mayo Clinic. Retrieved October 26, 2022, from https://www.mayoclinic.org/drugs-supplements-vitamin-c/art-20363932#:~:text=Because%20your%20body%20doesn't,of%20capsules%20and%20chewable%20tablets.

Padayatty, S. J., Riordan, H. D., Hewitt, S. M., Katz, A., Hoffer, L. J., & Levine, M. (2006, March 28). *Intravenously administered vitamin C as cancer therapy: Three cases*. National Library of Medicine. Retrieved October 26, 2022, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1405876/

Reczek, C., & Chandel, N. (2015, December 11). *Revisiting vitamin C and cancer*. Science. Retrieved October 26, 2022, from https://www.science.org/doi/abs/10.1126/science.aad8671?cookieSet=1