The Effect of Curcumin Encapsulated in Liposomes on MDA-MB-231 Breast Cancer Cells and THP-1 Macrophages, and Their Use as a Possible Drug Delivery System

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Introduction

- Breast cancer is the second most lethal cancer in the United States. This is due in part to triple negative breast cancers (TNBCs), which are those that do not express the three common breast cancer biomarkers
- The goal was to treat MDA-MB-231 breast cancer cells and THP-1 macrophages with curcumin loaded liposomes
- MDA-MB-231 is a TNBC cell line often used in breast cancer research, likely due the hardiness of the cells
- Curcumin has a known cytotoxicity towards and a suppressive effect on the proliferation on MDA-MB-231 cells[1]
- THP-1 is a human macrophage cell line. Macrophages are part of the immune system and protect the body with inflammatory responses, including in tumor environments
- Curcumin has low cytotoxicity towards healthy cells and anti-inflammatory properties, though its effect on THP-1 macrophages is unknown[2]

Methods

- Liposomes were made from phosphatidylcholine lipids and cholesterol. Curcumin liposomes (CL) were prepared with 10 µg curcumin. The solutions were extruded to standardize liposome size to 400 nm
- The following solutions diluted in RPMI were added to MDA-MB-231 and THP-1 cells overnight: 1:10 CL (5% CL), 1:100 CL (0.5% CL), 1:100 unloaded liposomes (0.5% Lip), 1:10 free curcumin (5% Curc), 1:10 DMSO (5% DMSO), and RPMI (Control)
    - DMSO was the negative control since it was known to cause cell death
    - RPMI was the positive control since cells would grow normally in it
- Live-Dead Staining with Trypan Blue Dye determined living cells. Cells were left in the dye for 10-15 minutes and then visualized in sterile PBS

References

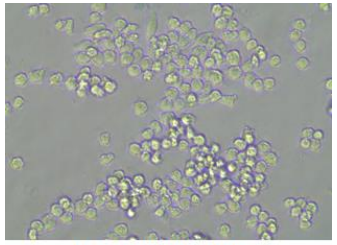
1. Guan, F.; Ding, Y.; Zhang, Y.; Zhou, Y.; Li, M.; Wang, C. Curcumin Suppresses Proliferation and Migration of MDA-MB-231 Breast Cancer Cells through Autophagy-Dependent Akt Degradation. *PLoS One* **2016**, *11* (1).
2. Hewlings, S. J.; Kalman, D. S. Curcumin: A Review of Its' Effects on Human Health. *Foods* **2017**, *6* (10).
3. Chen, C.-H.; Lin, Y.-L.; Liu, Y.-K.; He, P.-J.; Lin, C.-M.; Chiu, Y.-H.; Wu, C.-J.; Cheng, T.-L.; Liu, S.-J.; Liao, K.-W. Liposome-Based Polymer Complex as a Novel Adjuvant: Enhancement of Specific Antibody Production and Isotype Switch. *Int J Nanomedicine* **2012**, *7*, 607–621. https://doi.org/10.2147/IJN.S28097.

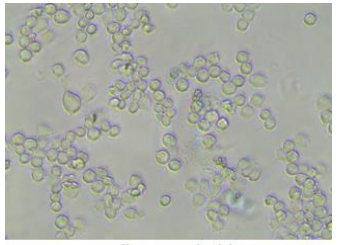
Discussion

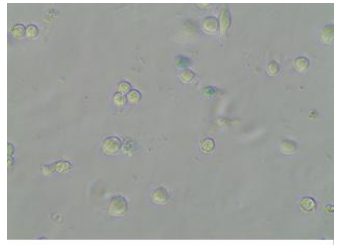
- Liposomes that were loaded with 0.1 µg to 1 µg curcumin had some effect on the survival of the cells
- Due to curcumin's hydrophobic nature, liposomes were used to keep it dissolved within the cellular solution
    - Due to the inconsistency of free curcumin staying within the cellular solution large error bars were seen with 5% Curc. Curcumin was cytotoxic when it did remain within the cellular solution
- Liposomes that were not loaded with curcumin were most likely cytotoxic due to their absorption of "stress" cytokines released by the cells and then re-release of the cytokines back to the cells[3]
    - This creates a cycle of cells releasing stress signals and liposomes repeating them back
- Future tests could determine curcumin liposomes' effect on cellular proliferation (MTT Assay) and THP-1's inflammatory activity (TNF-α ELISA)

Results

- The dosage range of curcumin that affected MDA-MB-231 and THP-1 cells was confirmed both qualitatively and quantitively
- Curcumin causes more MDA-231 cell death than THP-1 cell death. An ideal cancer treatment would kill the cancer cells but not macrophages


Untreated MDA-231 Cells


MDA-231 Cells Treated with 0.1 µg CL


MDA-231 Cells Treated with 1 µg CL