ND*nano* Undergraduate Research Fellowship (NURF)
2013 Project Summary

Student name: Matthew Kowalski
Faculty mentor name: Prof. Basar Bilgicer
Project title: Engineering carfilzomib-encapsulated nanoparticles

Skills acquired: liposome formation, liposome purification, plate reader analysis, high performance liquid chromatography

Project Summary:

Due to a developed drug resistance, multiple myeloma, a cancer of the blood, currently remains incurable. The Bilgicer lab aims to end this incurability through targeted drug delivery using liposomes. The idea is to form liposomes with therapeutic cancer drug, carfilzomib, encapsulated inside. To create the targeted nature of the system, antibodies specific to the malignant cells will be conjugated to the surface of the liposome, thus allowing the liposomes to selectively attach and deliver drugs to the cancer cells, eliminating drug resistance and minimizing drug toxicity effects. During the summer, I first mastered the process of constructing liposomes, as shown in figure 1 below.

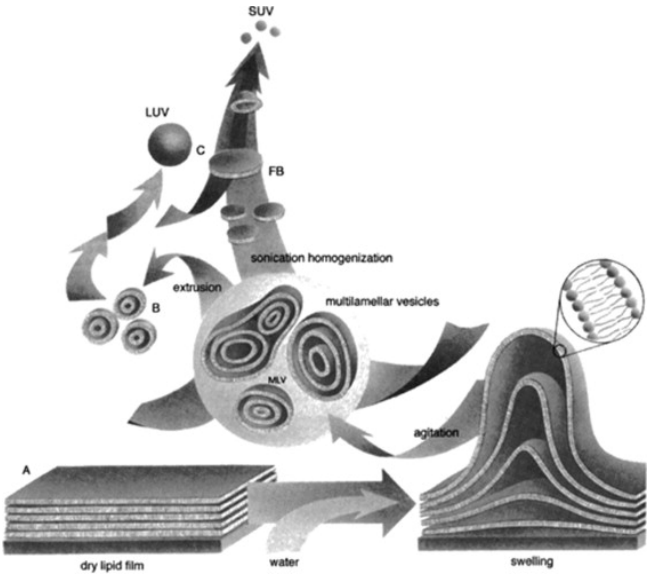

Figure 1. The process starts at the bottom left with drying a lipid fim, continues with hydrating and agitating the film, leading then to extrusion to a particular size. In my work, I finished the process with a purification step. (picture from http://www.sciencedirect.com)

This summer the goal was to pinpoint the liposome composition which achieves the desired carfilzomib loading, since the current composition of liposome cannot encapsulate enough of the drug to make the particles useful. Initially, we tested two different factors: the bulk lipid and the addition of cholesterol. The results showed that the addition of cholesterol reduces the amount of carfilzomib the liposomes hold, as the cholesterol competes with the drug. In changing the bulk lipid, we found some variation in encapsulation, but in general none of the trials were significantly better than the base encapsulation. Moving on, we tested combinations of the six lipids, trying 75:25, 50:50, and 25:75 ratios for each combination of lipids. These trials found that combinations in general performed better than single bulk lipid compositions. This is most likely due to the open spaces created by lipids of varying tail length and structure used together. We then retested the top 3 results to validate the numbers, and found similar results. Future work will involve trials with the top five results to see if we can pinpoint the composition which loads the required amount of carfilzomib.

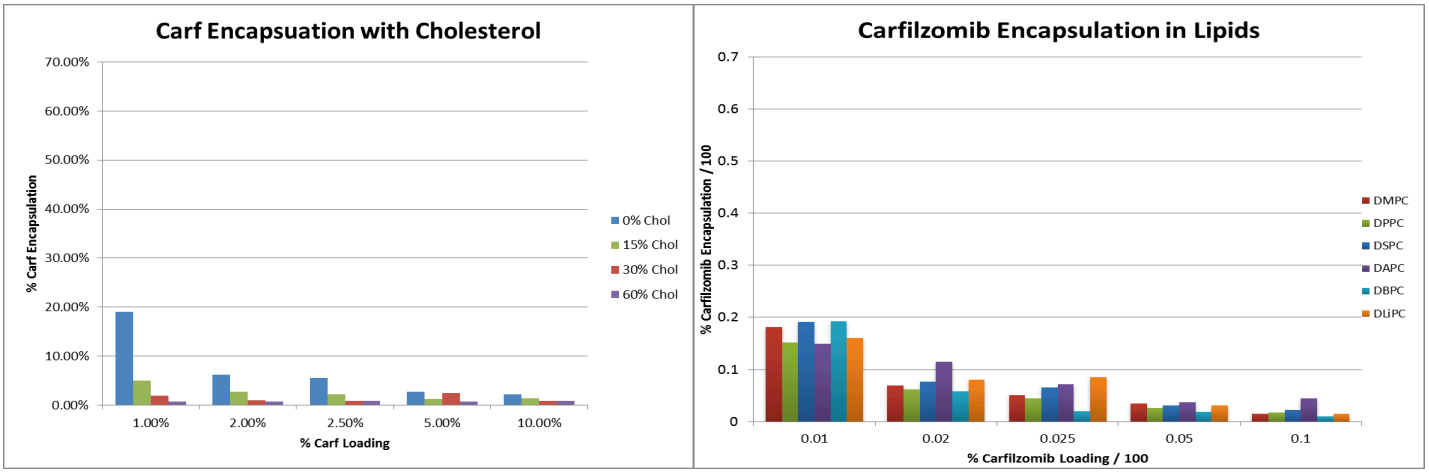

Figure 2. On the left are the results showing that as the amount of cholesterol increases, the amount of carfilzomib (Carf) encapsulated decreases, and that the trend continues with higher percentages of carfilzomib. On the left is the chart that shows the variation of the bulk lipids. There is much increase in encapsulation compared to the base composition.

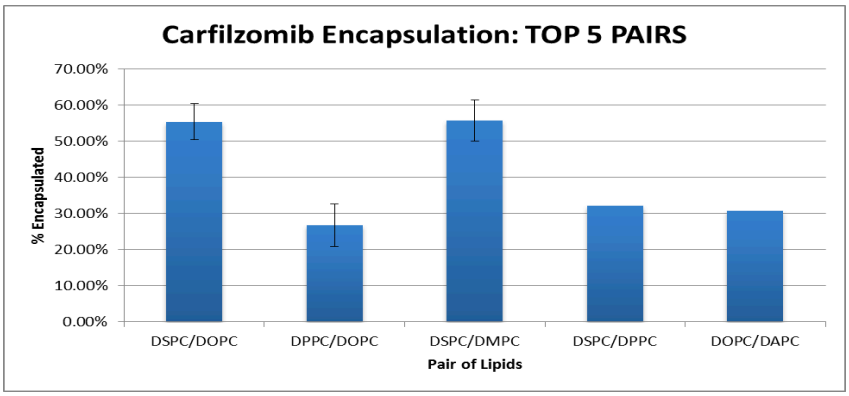

Figure 3. Shown here are the final results from the ratio project, showing much higher encapsulation than the cholesterol trials did. The top three pairs where tested several times, and the error bars show the standard deviation. Each of the ratio trials were tested at 1% carfilzomib only.