IOWA STATE UNIVERSITY

Department of Chemistry

Society for Biomaterials- Poster Session
January 8- 10

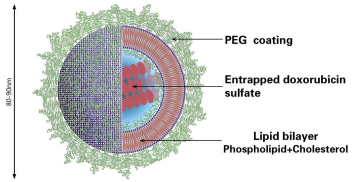
Vittal G. Kamath[1], Tanzeel Ur Rehman[2], Kaitlin M. Bratlie[2,3]

1. Department of Chemistry, Iowa State University
2. Department of Material Science & Engineering, Iowa State University
3. Department of Chemical and Biological Engineering, Iowa State University

Improving selective targeting to macrophage subpopulations through altering the polyethylene glycol composition of liposomes.

Background

- Conventional drugs are often quickly detected by reticuloendothelial system (RES).
- Liposomes are spherical vesicles that consist of one or multiple phospholipid bilayers and can be used to encapsulate these drugs.
- Several liposomes have been approved to selectively target specific tissues in the body as liposomes reduce the toxicity of the encapsulated drug while also improving the efficacy.
- Studies show that liposome PEGylation (the covalent linking of polyethylene glycol (PEG) chains) effectively improves the circulation time of liposomes as it increases the hydrophilicity of the liposome.



Goal

Investigate the effect of DOX loaded PEGylated liposomes on selective targeting to macrophage subpopulations (M0, M1, and M2).

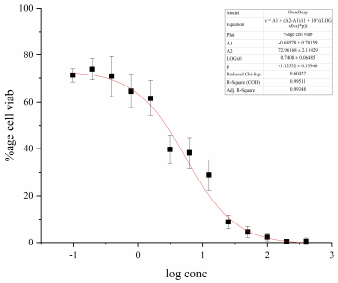
Results

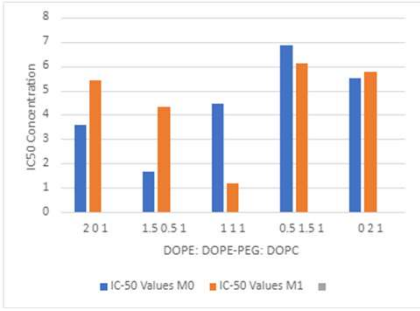
A general trend of increasing IC_{50} concentrations (**Figure 1**) was observed as the composition of PEG increased in the liposomes when delivered to naïve macrophages.

A sigmoidal dose-response curve is used to calculate the IC50 values for each liposome, shown in the equation to the right. Where A_1 is the upper limit of the dose curve, A_2 is the lower limit, p is the steepness of the curve, and x_0 is the IC50 concentration. One of several sigmoidal dose-response curves is shown below in figure below.

$$y = A_2 + \frac{A_1 - A_2}{1 + \left(\frac{x}{x_0}\right)^p}$$

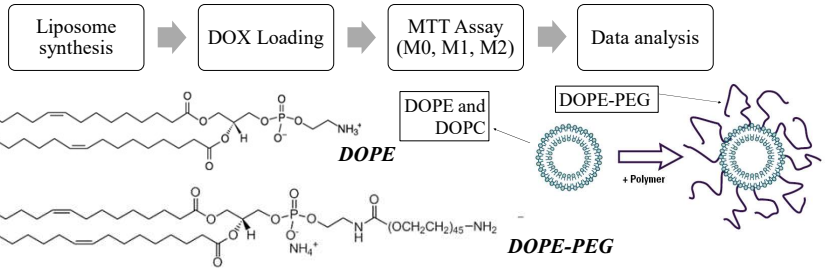
This trend demonstrates a decreased level of toxicity that DOX has with increasing PEG since a higher IC_{50} concentration reflects that more DOX is required for 50% of the cells in the well plate to stay alive and metabolize.





(Figure 1)

Method



The ratios to the right of lipids depict the 5 different liposomes that will be made.

DOPE	DOPE-PEG	DOPC
2	0	1
1.5	0.5	1
1	1	1
0.5	1.5	1
0	2	1

Conclusion and Future works

It is evident that as the PEG content increased in the liposomes, the IC_{50} values increased as well. A liposome with a higher composition of PEG allowed for less naïve macrophages to die when they were exposed to DOX encapsulated liposomes.

Increasing PEG reduced macrophage death

Increasing the PEG composition reduced the cytotoxicity of DOX.

Future Works:

- Can be connected to studies involving targeted drug delivery where drug delivery vehicles are designed to target specific cells only through synthesis of very specific modified liposomes.

References

- Akbarzadeh, Abolfazl, et al. "Liposome: Classification, Preparation, and Applications." 22 Feb. 2013
- [Mohamed, Marwa, et al. "Pegylated Liposomes: Immunological Responses." 26 June 2019
- Zhu Y, Wang F, Zhao Y, et al Pegylated liposomal doxorubicin-related palmar-plantar erythrodysesthesia: a literature review of pharmaceutical and clinical aspects European Journal of Hospital Pharmacy 2021;28:124-128.