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pH Initiated Site Specific Drug Release

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Abstract

Studies have shown that unhealthy cells can have more acidic conditions in the cytoplasm. A medical application for this is to target unhealthy cells with vesicles containing a drug and then lyse when exposed to a more acidic environment. To demonstrate acidic pH initiated cell lysing, phenol red was trapped in vesicles with sodium laurate integrated into the DMPC bilayer.

Background

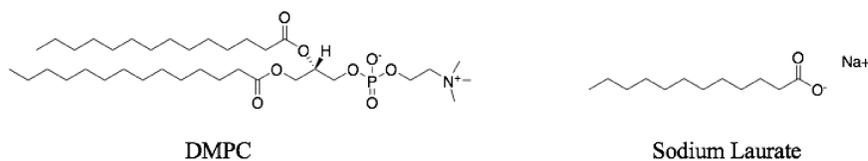


Figure 1: Structural comparison between DMPC and deprotonated sodium laurate.

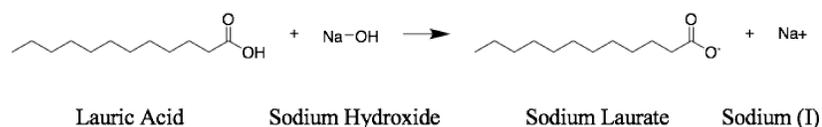


Figure 2: Reaction scheme of the deprotonation of lauric acid to sodium laurate using sodium hydroxide.

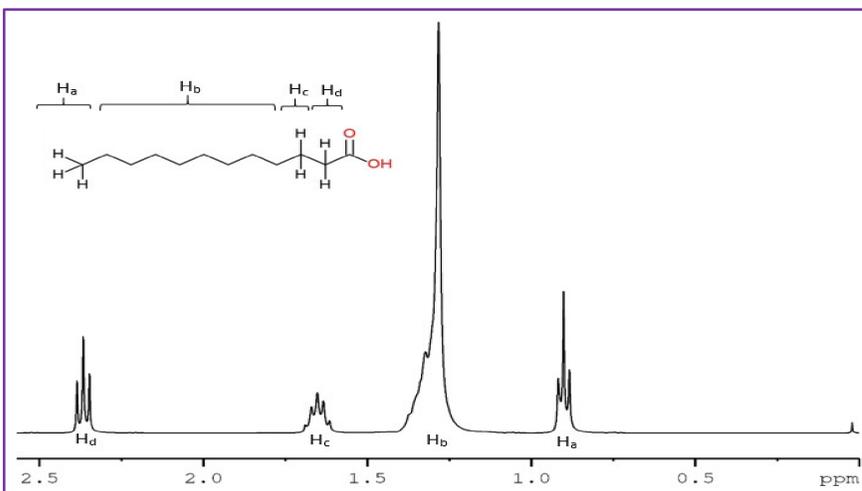


Figure 3: ¹H NMR of lauric acid.

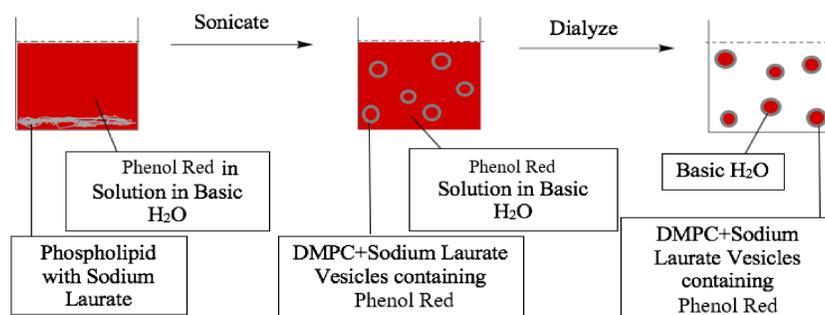


Figure 4: Reaction scheme for the formation of sodium laurate integrated DMPC vesicles containing phenol red.

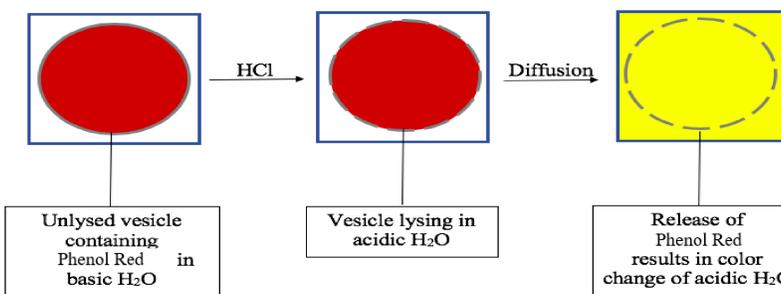


Figure 5: Reaction scheme for the lysing of cells as the solution becomes more acidic.

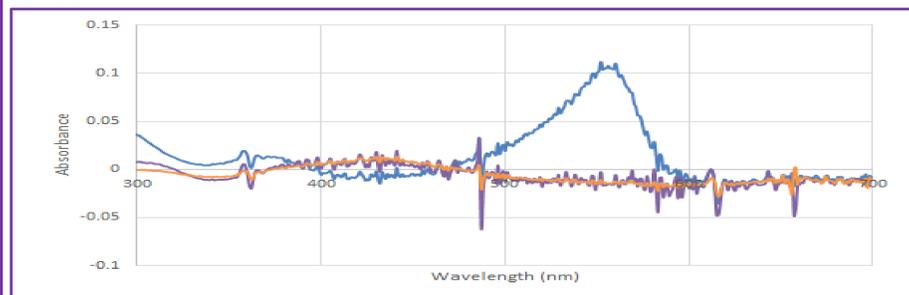


Figure 6: UVvis spectra of a serial titration using phenol red. Absorbances were taken for phenol red in solution at varying levels of pH and are represented by the following graphs: pH 11 (blue), pH 7 (purple), and pH 3 (orange). Absorbance at 540 nm decreases and absorbance at 420 nm increases as solution becomes more acidic.

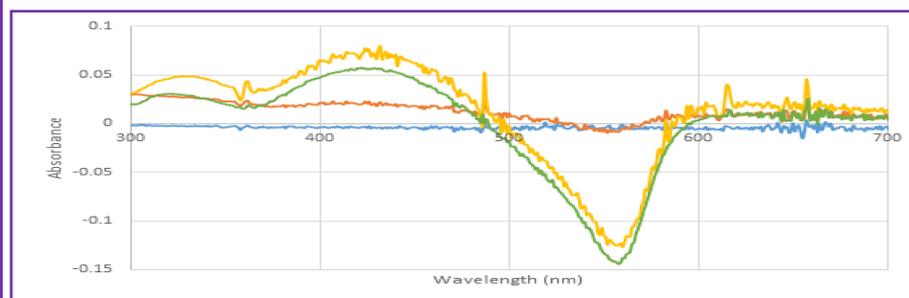


Figure 7: UVvis spectra of DMPC and sodium laurate liposomes containing phenol red under basic conditions treated with 1.0 M HCl. Absorbances were taken at varying levels of pH for phenol red and are represented by the following graphs: pH 11 (blue), pH 10 (orange), pH 7.5 (yellow), and pH 2.5 (green). Absorbance at 540 nm decreases and absorbance at 420 nm increases as solution becomes more acidic.

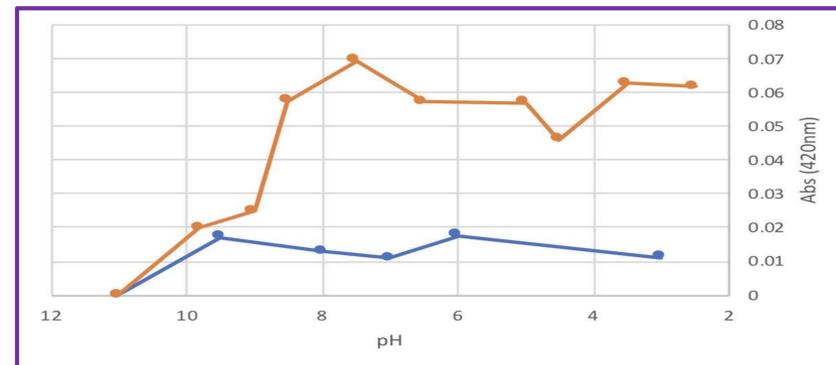


Figure 8: Comparing increases in absorbance at 420 nm from figure 6 (orange) and figure 7 (blue) as pH levels change.

Conclusion

We were unable to demonstrate pH initiated cell lysing in a basic environment. Despite similar trends at 540 and 420 nm in Figures 6 and 7, due to the red color of filtration solution, it is possible that phenol red was still present in solution outside of formed vesicles. If the experiment was successful, we would see a delayed increase in absorbance at 420 when lysing the vesicles. Should the experiment be repeated, vesicle solution must be kept in dialysis bag for a longer time allowing all phenol red that is not captured in the vesicles to escape through the dialysis bag.

Acknowledgments

- Dr. John Rowley
- Carroll College Department of Chemistry and Physics
- Carroll College Department of Biology

References

- 1) Langmuir (2006)_V22_p3498_Formation of Solid-Supported Lipid Bilayers - An Integrated View