Understanding Factors Affecting The Size Of Liposomes In Liposomal Drug Delivery

Linh Tran, Zheng Yuan, and Yoonjee Park

Department of Chemical & Environmental Engineering, University of Cincinnati, Cincinnati, OH 45219, USA

Motivation

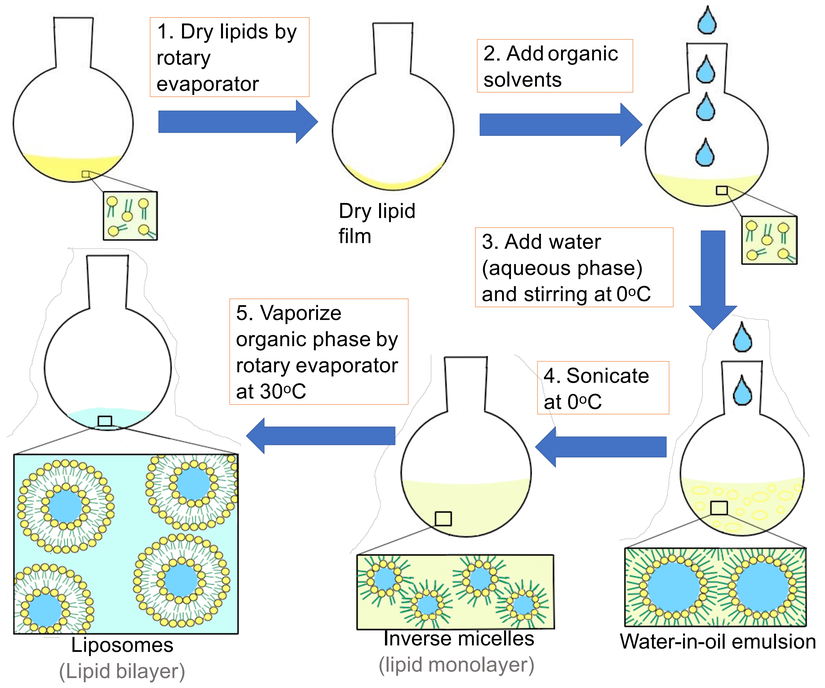
Background

- Liposomes are spherical vesicles having at least one lipid bilayers.
- Liposomal drug delivery is useful in therapeutics due to its benefits
  - Directly target to treatment area
  - Reduce number of injections
- Larger liposomes are favorable in drug delivery because of larger drug capacity and longer time of drug release compared to smaller liposomes.

Hypothesis

- Factors (organic solvents, ratios of aqueous:organic phases, addition of cholesterol) increase the size of inverse micelles (IM), which results in increasing the size of liposome (LIP).

Liposome synthesis via Reverse Phase Evaporation Method



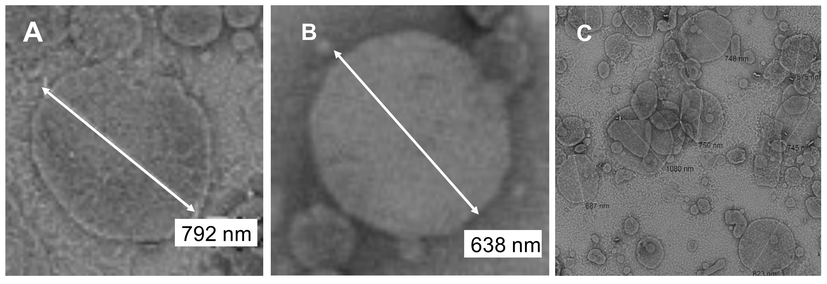
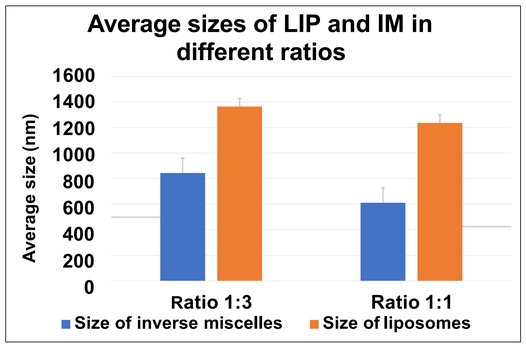


Figure 1: TEM pictures of liposomes. (A) A liposome in magnification of 5000x. (B) A liposome in magnification of 6000x. (C) Liposomes in magnification of 8000x.

Results & Discussion

A. Difference in aqueous:organic ratios



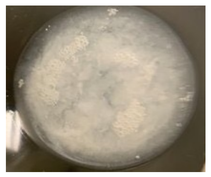
- P-value:
  - IM size = 0.327
  - LIP size = 0.407

⇒ Insignificant effect on IM and LIP size ($p > 0.05$)

Results & Discussion

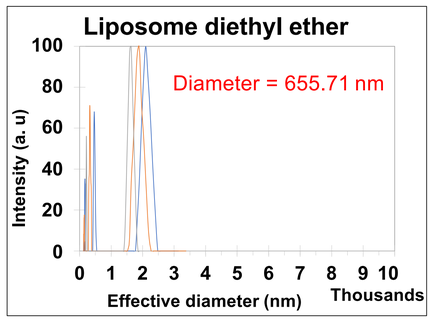
B. Difference in solvents

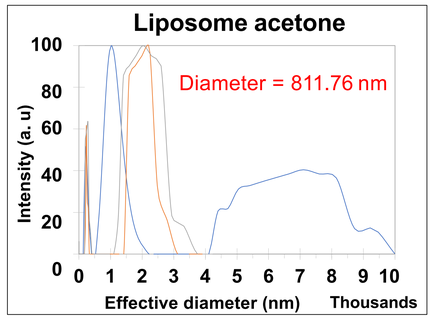
Step 4: Diethyl ether

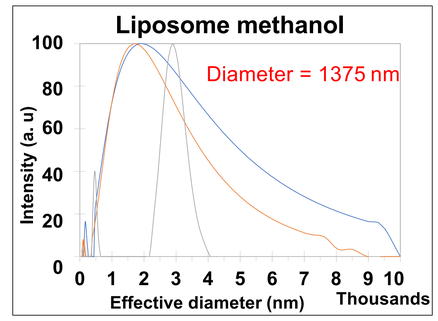


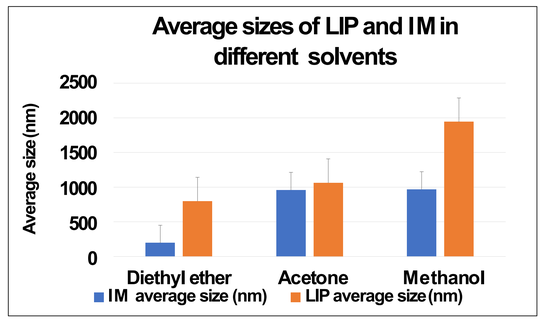
Step 4: Acetone

Step 4: Methanol









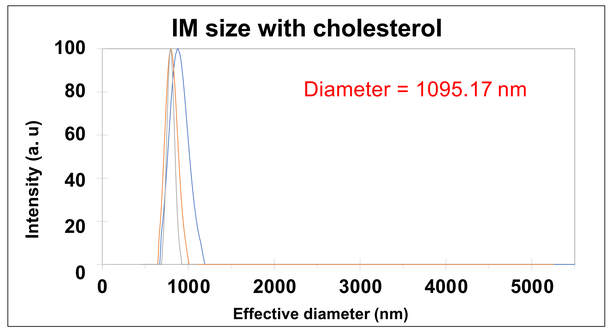
Traits / Solvents	Miscibility of solvent to water at 25°C	Boiling Point (BP)
Diethyl ether	0.0605g/mL	34°C
Acetone	1g/mL	56°C
Methanol	1g/mL	64.7°C

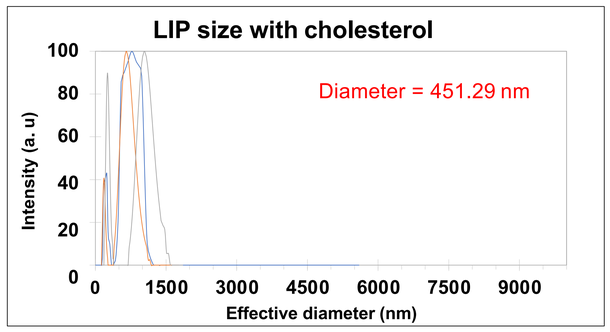
- Miscibility of diethyl ether to lipids is high so lipids clumped together to form small IM.
- Methanol has the highest BP, so it had longer time to form larger LIP.

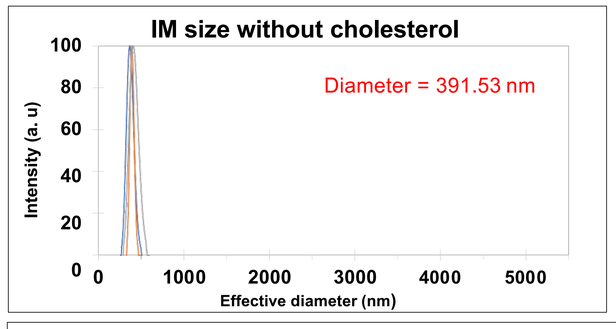
C. Addition of cholesterol (in methanol solvent)

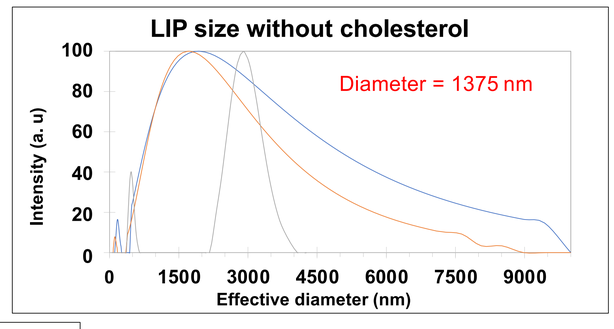
Step 4: Cholesterol

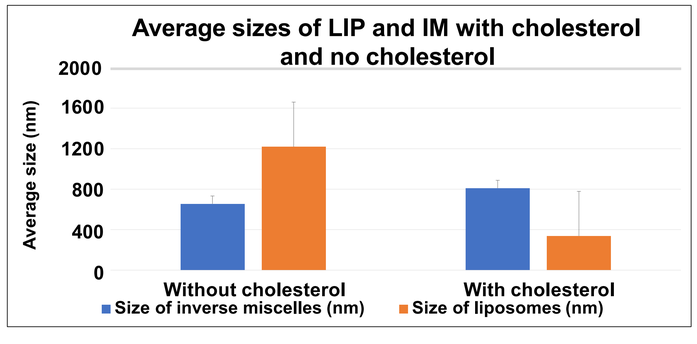
Step 4: No cholesterol











- Without cholesterol: relatively homogeneous solution with no large droplets => smaller IM
- With cholesterol: phase separation occurred with visible droplets => larger IM size

Conclusion

- Solvents with high boiling point and high miscibility to water produce large LIP and have insignificant effect on IM size.
- The increased miscibility of solvents (diethyl ether > acetone≈methanol) to lipids reduces IM size and LIP size.
- Cholesterol significantly affects LIP size and insignificantly affects IM size.
- Difference of ratios insignificantly affect LIP and IM sizes.

ACKNOWLEMENTS: Yoonjee Park, PhD, Zheng Yuan (Department of Chemical & Environment Engineering), Department of Chemistry