324c Sequestration of Amitriptyline by Liposomes

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Nanoparticles, such as liposomes, can potentially separate compounds from aqueous solutions by either adsorption on the surface or absorption into the particle. Such separations can be important in a variety of applications, such as removal of toxic substances from the blood stream. Liposomes have the ability to sequester drug molecules, and therefore, have the potential to treat drug overdoses by reducing the free drug concentration in the body. We aim to understand how liposomes sequester drugs, determine the effect of pH on drug uptake by liposomes, and quantify the amount of drug liposomes sequester.

We study the separation of amitriptyline, which is a common cause of overdose-related fatalities in the United States, from aqueous solutions by 1,2-dimyristoyl-sn-glycero-3-phosphocholine (DMPC) liposomes as well as liposomes composed of mixtures of DMPC and 1,2-dioleoyl-sn-glycero-3-[phospho-rac-(1-glycerol)] (DOPG). The amount of drug that is sequestered by the liposomes at the solubility limit of the drug is determined through UV spectrophotometry at three different pH values (9, 10.7, and 12) and two different liposome concentrations (9 and 18% liposomes by volume). The results indicate that the amount of drug on the DMPC liposomes is relatively independent of the pH. We determine that at the solubility limit, DMPC liposomes sequester approximately 70 – 100% of the drug present in the solution. We conclude that, for DMPC liposomes, the amount of drug uptake is relatively independent of pH, which is consistent with the fact that DMPC liposomes have no net charge. On assuming monolayer coverage, the area of a drug molecule on the liposome's surface is calculated to be about 25 Å2/molecule, which is considerably small. This suggests that the drug may be adsorbing to the surface of the liposomes in a bilayer configuration with an area per molecule of 50 Å2/molecule . The drug uptake is larger for the charged liposomes that contain DOPG. Results also suggest that the charged liposomes are less tightly packed, and thus, a fraction of the drug enters the bilayer, whereas all of the drug sequesterd by the uncharged DMPC liposomes is adsorbed on the surface.