



1) What are liposomes?

Liposomes are microscopic vesicular phospholipid (lecithin) membrane-lipid structures dispersed in water. Liposomes can be developed for different purposes ranging from targeting of water soluble compounds to the solubilization of poorly soluble compounds.

The particle size and drug loading must be carefully controlled. Considerable experience and skill in formulating vesicular structures from single (*SUV*) through a few (*oligo-lamellae*) to multiple (*MLV*) are required to make sure the poorly soluble drug is correctly delivered and optimal.

2) Which administration route is our Liposome technology suitable for?

Liposomes are suitable for a variety of administration routes because of their excellent tolerability, ranging from parenteral (particularly intravenous) through to topical, pulmonary and oral. However, liposomes are most useful intravenously because, unlike most surfactants, they are well tolerated across multiple species.

3) Which types of compound are suited to liposomes?

Both water soluble and water insoluble compounds can be delivered. At Phares, we focus on using liposomes to solubilize compounds that are poorly soluble and lipophilic. Such compounds are mainly solubilized within the lipophilic domains between the lipid bilayers.

4) How do liposomes increase bioavailability?

After oral administration, dissolution of the poorly soluble compound is not required before absorption because the drug is solubilized. Liposomal solubilization may increase the solubility of insoluble drugs between one hundred to ten thousand fold depending upon the properties of the insoluble drug.

In the small intestine, liposomes are digested in the presence of bile and enzymes. The solubilized compound is liberated and further solubilized in bile and digested lipids.

For intravenous administration, we design and develop liposomes to disintegrate rapidly in the plasma. After administration in the bloodstream, most drugs spontaneously partition from the liposomes into albumin and lipoproteins.

Drug load is dependent on the type of compound and is related to how a drug fits inside the lipophilic domains- typically the range is between 1 mg/ml to 20 mg/ml for intravenous and between 10 to 100 mg/unit dose for oral forms. The administration forms can be liquids or solid powders, depending on the properties of the compound.

5) Which Phares services use the Liposome technology?

Liposomes can be used during the Survey and Icebreaker services.

Liposomes can be applied in our Speed pre-clinical tox service if the fit between the drug and liposomes is satisfactory.

6) Advantages and disadvantages of liposomes

Advantages

- Precipitation at the injection site and in the blood circulation can be prevented
- Phospholipids are one of the few solubilizers that are well tolerated intravenously

Disadvantages

- More complicated QC is required to monitor the quality of the product
- The pharmacokinetics of highly lipophilic compounds can be modified at extreme lipid to drug ratios
- If formulated incorrectly, drugs can precipitate from the liposomes upon storage

7) Scale-up of liposomes

Scale up of liposomal formulations requires specialist equipment and expertise, particularly for intravenous delivery where particle size and sterility are crucial factors. Conventional liposome formulations can be one of the most complicated colloidal systems to upscale.

8) Phares liposome expertise

We understand how to use liposomes and which compounds are well suited to this approach. Over the years, we have developed specialist liposome analytics (such as transfer assays) and have helped numerous companies with their liposome projects in both pre-clinical and clinical development. Phares pioneered a technology for the large scale production of liposomes using proliposomes. Phares has a comprehensive infrastructure for liposome production suitable for small and large scale manufacture of liposomes.

We are well versed in conventional liposome techniques, but find that most traditional approaches take too long to develop. This is why Phares has developed a variety of smart ways to speed up the testing of NCEs with liposomes. One such example is a proprietary technique called Instant Solubilization, which involves the *in situ* addition of drug in a solvent to well defined liposomes specifically designed for pre-clinical solubilization. This is just one way we can help you fast track the development of your NCE.

9) Liposome products

Benzoporphyrin (Verteporfin®, Novartis) and amphotericin B (Ambisome®, Gilead) are examples of commercial liposome products for solubilization of poorly soluble compounds.

KEY SERVICES:

