of liposomes. Prepare a solution of a lipid (lecithin) in an organic solvent (acetone, chloroform) in a beaker. Allow the solvent to evaporate, leaving a thin film of the lipid on the walls of the container. Add an aqueous solution of the drug to the beaker and place it in an ultrasonic bath. As the lipid is displaced from the beaker walls, it forms spheres or cylinders, trapping the aqueous solution inside. The liposomes can be collected, sized, and used.

Numerous configurations are possible for liposomes, including spheres and cylinders. Spherical liposomes can be unilamellar (only one layer) or multilamellar (many layers). They are often designated LUV (large unilamellar vesicle), SUV (small unilamellar vesicle), and MLV (multilamellar vesicle). The smaller vesicles, or liposomes, generally range in size from 0.02 to 0.2 mm and the large vesicles from about 0.2 mm to more than 10 mm. The MLVs may have an onion-skin structure of several layers.

The phospholipids composing liposomes are amphipathic, possessing both a hydrophilic or polar head and a hydrophobic or nonpolar tail. This is similar to the hydrophilic–lipophilic balance (HLB) and wedge orientation theories of emulsification. The hydrophobic tail is composed of fatty acids containing generally 10 to 24 carbon atoms, and the polar end may contain phosphoric acid bound to a water-soluble portion; the composition may vary considerably. Lecithin (phosphatidylcholine) is a backbone structure that has been studied extensively. When these phospholipids are exposed to water and line up, they do so in a manner that the fatty acid tails associate together as the lipophilic phase and the polar head groups associate toward the bulk water phase. Depending on the system and the water solubility of the drug, the drug may be in the aqueous compartments (if water soluble) or in the lipophilic bilayers (if oil soluble).

Some liposomes are unique because they can be selectively absorbed by tissues rich in reticuloendothelial cells, such as the liver, spleen, and bone marrow. This can serve as a targeting mechanism, but it also removes liposomes from the circulation rather rapidly. To extend the half-life of liposomes in the body, "stealth liposomes" have been developed by coating the liposomes with materials, such as the polymer polyethylene glycol (PEG), enabling liposomes to evade detection through the components of the body's immune system. This extends their half-life and may also alter their biodistribution.

Advantages of liposomes include the following: (*a*) Liposome-encapsulated drugs are delivered intact to various tissues and cells and can be released when the liposome is destroyed, enabling site-specific and targeted drug delivery. (*b*) Liposomes can be used for both hydrophilic and lipophilic drugs without chemical modification. (*c*) Other tissues and cells of the body are protected from the drug until it is released by the liposomes, decreasing the drug's toxicity. (*d*) The size, charge, and other characteristics can be altered depending on the drug and the intended use of the product.

Disadvantages of liposomes include their tendency to be taken up by cells of the reticuloendothelial system (RES) and the slow release of the drug when the liposomes are taken up by phagocytes through endocytosis, fusion, surface adsorption, or lipid exchange.

Many advances in liposome preparation, including composition, sizing, classification, and enhancing stability, have been made. Stability has been a problem, but stable liposomes can now be prepared. Liposomes have been investigated for a number of years as potential drug delivery systems, and now are on the market.

One product is Abelcet Injection (Enzon). It is a sterile, pyrogen-free suspension for intravenous infusion consisting of amphotericin B complexed with two phospholipids in a 1:1 drug-to-lipid molar ratio. The two phospholipids, L-alpha-dimyristoyl phosphatidyl choline (DMPC) and L-alpha-dimyristoyl phosphatidyl glycerol (DMPG), are present in a 7:3 molar ratio. The product is yellow and opaque with a pH in the range of 5 to 7. The formulation per milliliter is provided as the following (9):

Amphotericin B, USP, 5 mg
DMPC 3.4 mg