Controlled Release | Targeted Delivery | Solubility Enhancement

LIPID-POLYMER HYBRID NANOPARTICLES
FOR DRUG DELIVERY APPLICATIONS


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Introduction

Since the last decade, there has been a burgeoning interest in the use of nanoparticle-based platforms for drug delivery applications. Nanoparticle-based delivery offers a number of advantages over traditional drug delivery platforms, including the ability to load multiple drugs, attach targeting ligands, enhance drug circulation time, and reduce non-specific drug toxicity. Nanoparticle formulations such as polymeric nanoparticles, liposomes, dendrimers, gold nanoparticles, carbon nanotubes and quantum dots have been widely researched, but only a handful of them have ever reached clinical use.[1]

The inherent advantages of liposomes and polymeric nanoparticles make them the most commonly studied among available drug delivery platforms. For example, liposomes offer excellent biocompatibility,[2] while polymeric nanoparticles possess excellent stability and drug loading capacity.[3] Although the majority of polymeric nanoparticles are still years away from clinical application, researchers have sought to combine the advantages of the two platforms—biocompatibility and high drug loading—by designing hybrids, known as lipid-polymer hybrid nanoparticles (LPNs).[4]

A typical LPN has a core-shell structure, consisting of a polymeric core for loading the cargo, such as small molecule drugs and/or diagnostic molecules, surrounded by a lipid shell for enhanced biocompatibility. The most widely used polymer in the core is poly(lactic-co-glycolic acid) (PLGA) due to its biocompatibility, biodegradability and general drug loading versatility.[5,6] Several lipids, including phosphatidylcholine (PC); 1,2-dilauroyl-*sn*-glycero-3-phosphocholine (DLPC); 1,2-distearoyl-*sn*-glycero-3-phosphoethanolamine (DSPE); cholesterol; myristic acid; stearic acid; and 1,2-dipalmitoyl-*sn*-glycero-3-phosphocholine (DPPC) have been used in the shell, in addition to poly(ethylene glycol) (PEG) lipid conjugates.[5,7]

One-step Synthesis of LPNs

Previously, researchers used various two-step synthesis methods (**Figure 1**), that require the lipid vesicles and polymeric nanoparticle to be separately synthesized before being fused together.[8] This approach gives rise to LPNs with bilayer or multilayer lipid shells. Techniques used to fuse the liposomal shell and the polymeric nanoparticle core together include extrusion, sonication, direct hydration, vortexing, and high-pressure homogenization.

As first demonstrated by Zhang et al., a more convenient one-step synthesis method uses nanoprecipitation and the spontaneous self-assembly of lipid and polymer components (**Figure 1A**), yielding LPNs coated with a lipid monolayer shell.[9] In this method, the polymer and cargo are dissolved in the organic phase (water-miscible organic solvent) and the lipids are dissolved in the aqueous phase. The organic phase is added dropwise to the aqueous phase under continuous stirring, followed by self-assembly at room temperature. To the best of our knowledge, this is the simplest method of synthesizing LPNs currently available.

Alternatively, LPNs can be synthesized using an emulsification technique where the polymer is dissolved in the organic phase (water-immiscible organic solvent) and the lipids are dissolved in the aqueous phase. The solutions are mixed and sonicated to disperse the polymer into droplets and coat the polymers with a layer of lipid. The organic solvent is slowly evaporated under gentle stirring, and the LPNs are then purified for further use.

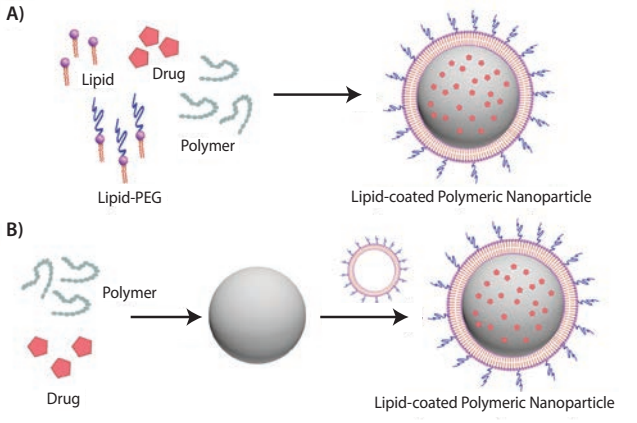

Figure 1. Schematic showing one- and two-step LPN synthesis. **A**) One-step synthesis method. **B**) Two-step synthesis method.