Chemistry of Contrast Media

Particles and Polymers

Established Particles and Polymers

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Learning Objectives:

- Self-assembly of amphiphilic molecules and aggregate morphology
- Synthetic nanoparticles, natural nanoparticles, hybrid nanoparticles, complex structures
- One-step synthesis methods
- Incorporation of imaging labels and/or nanocrystals
- Surface modification

The nanoparticle platforms that have been investigated most extensively for biomedical purposes are self-assembled nanoparticulate lipid aggregates. Liposomal nanoparticles have thus far been most successful, which has resulted in the FDA approval and clinical application of several liposomal formulations of cytostatic agents. Micelles and micro emulsions are thoroughly investigated for the delivery of hydrophobic compounds, while lipids and other amphiphilic molecules can also function as coating for solid nanoparticles. The relative ease of preparation and functionalization, the possibility to create a variety of lipid aggregate morphologies, and importantly, the ability to combine multiple amphiphilic molecules with different functionalities are the most important reasons for the popularity of lipidic nanoparticles.

In the field of (molecular) imaging lipid-based nanoparticle platforms allow the inclusion of a variety of imaging agents ranging from fluorescent molecules to chelated metals for MRI and nuclear imaging, and nanocrystals, including QDs, FeO and gold. There are several methods to incorporate the aforementioned molecules and materials in lipidic nanoparticles. The most straightforward strategy is to use an amphiphilic version of the molecule of interest. This may be accomplished by conjugating acyl chains to e.g. a fluorescent dye or a metal chelator. In addition, small molecules that are inherently amphiphlic or lipophilic may spontaneously incorporate in lipidic nanoparticles. Amphiphiles tend to nestle and mix with the lipids, whereas lipophilic (or hydrophobic) compounds can be included in the core of micelles and microemulsions. The inclusion of hydrophobic compounds is not limited to small molecules only. Nanocrystals like QDs, capped with hydrophobic ligand, have also been demonstrated to efficiently incorporate in the core of micelles and microemulsions.

In the past decade a variety of multifunctional lipid-based nanoparticles for molecular imaging and targeted therapy have been developed and tested pre-clinically. These nanoparticles differ in size, morphology, multimodal imaging ability, and specificity for biological markers. In this educational the synthesis and characterization of different platforms as well as their application for multimodality (molecular) imaging and targeted therapy will be discussed. Functionalization methods, surface modification and the effect on pharmacokinetics are highlighted. In addition, recent developments in the area of endogenous nanoparticles like lipoproteins and exosomes, modified to carry different diagnostically active materials for multimodality imaging will be discussed. Lastly, some key applications in experimental cancer and cardiovascular disease as well as a pathway for clinical translation will be shown.