PEG-free Drug Formulations: From Polymer Drug Conjugates to Lipid Nanoparticles

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Polyethylene glycol (PEG) is widely used in drug delivery to improve stability and circulation time of drugs. However, it has been associated with immune responses, in particular due to pre-existing anti-PEG antibodies. Those can lead to accelerated drug clearance, reduced therapeutic efficacy, and even hypersensitivity reactions.

A promising class of PEG alternatives are poly(cyclic imino ether) (PCIE) such as poly(2-oxazoline)s (POx) and poly(2-oxazine)s (POz). In particular, poly(2-methyl-2-oxazoline) (PMeOx) and poly(2-ethyl-2-oxazoline) (PEtOx) have received major attention due to their similarity to PEG with respect to their solubility, biocompatibility, and "stealth" behaviour.[1] However, there is a wealth of other water-soluble PCIE variants,[2] which have emerged and attracted attention as shell components of nanoparticles,[3] or hydrogel matrices for applications in drug delivery, tissue engineering and biofabrication.

In this presentation, we will look into the versatility of PCIE and highlight the various options they offer for the design of biocompatible materials. We will focus on our recent efforts in employing these polymers in polymer-drug conjugates,[4] nanorod-drug conjugates,[5-7] and lipid nanoparticles (LNPs).[8] Their interactions with biological entities through variation of size, shape and surface modifications will be discussed.

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