Lipid-based Nanocarriers for Oral Delivery of Therapeutic Peptides: Hype or Hope?

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Oral administration of therapeutic peptides is favoured from a patient point of view. To shuttle therapeutic peptides into the systemic circulation, however, oral delivery systems have to address various barriers including the enzymatic, sulfhydryl, mucus and absorption barrier. Among the most promising drug delivery systems are lipid-based nanocarriers such as nanoemulsions, self-emulsifying drug delivery systems, solid lipid nanoparticles, nanostructured lipid carriers, liposomes and micelles. As lipophilicity of therapeutic peptides can be strongly increased by the formation of hydrophobic ion pairs with ionic surfactants, they can be embedded in the lipophilic phase of these carrier systems. Since peptidases and proteases as well as sulfhydryl compounds such as dietary proteins are too hydrophilic to enter this lipophilic phase, incorporated therapeutic peptides are protected towards enzymatic degradation as well as unintended thiol/disulfide exchange reactions. Stability of lipid-based nanocarriers towards lipases can be provided by the use of lipids and surfactants that are not at all or very slowly degraded by these enzymes. Nanocarriers with a size <200 nm and a PEG or zwitterionic surface show also high mucus permeating properties. Having reached the epithelium lipid-based nanocarriers enable paracellular and lymphatic uptake of therapeutic peptides, induce endocytosis or simply fuse with the cellar membrane releasing their payload into the systemic circulation. Evidence for the potential of lipid-based nanocarriers is provided by numerous in vivo studies. Because of these advantages and already available data lipid-based nanocarriers are a powerful tool for oral delivery of therapeutic peptides.

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