Oral bioavailability and drug/carrier particulate systems

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Résumé en anglais	The oral route remains the preferred route of administration to ensure patient satisfaction and compliance. However, new chemical entities may exhibit low bioavailability after oral administration because of poor stability within the gastrointestinal tract, poor solubility in gastrointestinal fluids, low mucosal permeability, and/or extensive first-pass metabolism. Consequently, these new drug substances cannot be further developed using conventional oral formulations. This issue is addressed by an innovative approach based on the entrapment of drug molecules in drug/carrier assembling systems. The carrier materials are lipids, naturally occurring polymers or synthetic polymers, which are considered as nontoxic and biocompatible materials. Drug entrapment is intended to protect drug substances against degradation by gastrointestinal fluids. Fine drug/carrier particle size ensures increased drug dissolution rates. Carriers and particle supramolecular organization can be designed to enhance drug absorption through the intestinal epithelium and lymphatic transport. Promising preclinical results have been obtained with model drugs like paclitaxel, insulin, calcitonin, or cyclosporin. Attention has focused on mucoadhesive carriers like chitosan that favor an intimate and extended contact between drugs and intestinal cells, thus enhancing absorption. Addition of ligands such as lectins improves intestinal drug absorption through specific binding of the carrier to intestinal cell carbohydrates. In conclusion, drug/carrier particulate systems are an attractive and exciting drug delivery strategy for highly potent drug substances unsuitable for oral use. Further evidence will determine whether this approach has marked therapeutic benefits over conventional drug formulations and is compatible with large-scale industrial production and stringent registration requirements. Producing highly effective particulate systems requiring low-complexity manufacturing processes is therefore an ongoing challenge.
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