Improvement of intestinal absorption of bioactive drugs using functional peptides

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Recent advances of biotechnology have yielded bioactive drugs composed of peptide and protein for the treatment of several diseases. However, these drugs are often administered parenterally because of insufficient oral bioavailability caused by the low permeability through the intestinal mucosa. It is needed for development of oral delivery system for bioactive drugs to bear not only resistibility to enzymatic metabolism but also enhanced permeability through the epithelial membrane. Recently, it has been reported that drugs that are poorly permeable through the cell membrane can be taken up efficiently by diverse cells through conjugating with peptides referred to as cell-penetrating peptides (CPPs) such as HIV-1 Tat peptide and oligoarginine, and application of this functional peptides as intracellular delivery vector are hopeful. Therefore, we have been attempted to develop more efficient intestinal delivery carrier using CPP as tool to improve the oral bioavailability of bioactive drugs. Previously, we have demonstrated that intestinal insulin absorption is enhanced markedly without causing detectable damage in cellular integrity by coadministration of insulin with oligoarginine. In addition, we evaluated the effect of other CPPs on intestinal insulin absorption, and it is suggested that penetratin and pVEC enhanced significantly intestinal insulin absorption. On the other hand, it is thought that a number of pathways were associated with intracellular transduction of CPPs. At present, we evaluate the enhancing mechanisms of intestinal insulin absorption by functional peptides, and strive to develop feasible oral delivery system for bioactive drugs through these studies.