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Effect of CAP on the pharmacokinetics of cyclosporin A (CyA) in rats and the mechanism of this food-drug interaction

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Capsaicin (CAP) is the main ingredient responsible for the hot pungent taste of chilli peppers. This study investigated the effect of CAP on the pharmacokinetics of cyclosporin A (CyA) in rats and the mechanism of this food-drug interaction. The results indicated that after 7 days of low or middle dose of CAP (0.3 or 1.0 mg/kg), the blood concentration of CyA was not significantly changed compared with that of vehicle-treated rats, whereas the blood concentration of CyA in high dose group (3.0 mg/kg) was significantly increased. The total clearance (CL/F) of CyA was decreased, and the bioavailability was significantly increased to about 1.44 fold of that in vehicle-treated rats after 7 days of high dose CAP treatment. At this time, the P-gp and CYP3A1/2 in the liver and intestine were decreased at both the mRNA and protein levels. These results demonstrated that chronic ingestion of high doses of CAP will increase the bioavailability of CyA to a significant extent in rats and the food-drug interaction between CAP and CyA appears to be due to modulation of P-gp and CYP3A gene expression by CAP, with differential dose-dependence.

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Enhance oral bioavailability of hydrophobic compounds by using polymeric nanoparticles

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Nearly 40% of all pharmaceutical compounds on the market and 90% of newly developed compounds are hydrophobic, and therefore difficult to deliver and maintain at sufficient bioavailability. The current formulation of many hydrophobic drugs requires toxic solvents and surfactants such as Cremophor and Tween, which often impair drug distribution and are associated with severe side effects. Nanomedicines, which do not require the use of toxic solvents, offer clear advantages. However, in over more than two decades, very few nanomedicines have been successfully developed and approved for clinical use. Those already on the market are either liposome based (such as Doxil® and Myocet®) or a protein-drug complex (such as Abraxane®). Although biodegradable and biocompatible polymers have significant advantages over liposome and protein delivery vehicles, such as better stability and robust molecular structure, polymeric nanoparticles have not been used beyond animal tests. Despite the great effort devoted by many research laboratories to develop nanoformulations for drug delivery, the successful formulations after many empirical trials are usually associated with specific compounds at a particular production scale. Reproducing the formulation at a larger scale using a different compound was not possible. We recently developed a scalable process to generate nanoparticles encapsulating hydrophobic compounds at high drug loading. Moreover, physicochemical properties of the particles (such as surface charge and size distribution), which is essential for improving oral bioavailability of the compounds, can be precisely controlled by a sophisticated combination of mixing and spray drying. Pharmacokinetics study of two hydrophobic compounds (SR13668 and curcumin) in animal models will be demonstrated. The enhanced oral bioavailability of the compounds using polymeric nanoparticles will be presented.

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