

5th World Congress on Bioavailability and Bioequivalence Pharmaceutical R&D Summit

September 29-October 01, 2014 DoubleTree by Hilton Baltimore-BWI Airport, USA

Novel approach to enhance oral bioavailability of drugs with poor permeability

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The epithelial enterocyte barrier of the gastrointestinal (GI) tract limits the absorption of many oral drugs to the systemic circulation. Modulation of intercellular tight junctions has long been considered a potential tool to enhance drug delivery across these biological barriers. However, early modulators (e.g., Ca²⁺ chelators, surfactants, modified fatty acids and esters, and polymers) had unspecific modes of action and insufficient separation between efficacy and toxicity, precluding their clinical use. Recent knowledge regarding the molecular composition and mechanisms regulating tight junctions and adherens junctions has led to a new generation of intercellular junction modulators based on junction protein/peptide mimetics and relevant signaling pathways. E-cadherin peptides (ECPs) represent a class of these new modulators and have shown promise in enhancing small molecule drug delivery across the blood-brain barrier via reversible modulation. Here, the potential of ECPs to enhance oral bioavailability of small molecule drugs that have limited gut absorption was investigated. *In vitro* permeability and *in vivo* pharmacokinetic studies have been performed to demonstrate the feasibility of the ECP-based oral drug delivery approach. Results showed that ECPs substantially increased the permeability of the model drugs, as well as their systemic exposure after oral administration. In conclusion, ECPs-based formulations should be further developed as a vehicle to enhance oral bioavailability of poorly permeable drugs.

Biography

Michael Zhuo Wang completed his PhD in 2003 from Duke University and Postdoctoral studies from University of North Carolina at Chapel Hill School of Pharmacy. He is now an Assistant Professor in the Department of Pharmaceutical Chemistry, University of Kansas. He has published more than 30 papers in reputed journals in the fields of analytical chemistry, drug metabolism, pharmaceuticals and pharmacology.

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