

Therapeutic Utility of a Novel Tight Junction Modulating Peptide for Enhancing Intranasal Drug Delivery. SHU-CHIH CHEN, KRISTINE EITING, KUNYUAN CUI, ALEXIS KAYS LEONARD, DANIEL MORRIS, CHING-YUAN LI, KEN FARBER, ANTHONY P. SILENO, MICHAEL E. HOUSTON, JR., PAUL H. JOHNSON, STEVEN C. QUAY, HENRY R. COSTANTINO. Nastech Pharmaceutical Company, Inc., 3450 Monte Villa Parkway, Bothell, Washington.

ABSTRACT: Previously, a novel tight junction modulating (TJM) peptide was described affording a transient, reversible lowering of transepithelial electrical resistance (TER) in an in vitro model of nasal epithelial tissue. In the current report, this peptide has been further evaluated for utility as an excipient in transepithelial drug formulations. Chemical stability was optimal at neutral to acidic pH when stored at or below room temperature, conditions relevant to therapeutic formulations. The TJM peptide was tested in the in vitro tissue model for potential to enhance permeation of a low-molecular weight (LMW) drug, namely the acetylcholinesterase inhibitor galantamine, as well as three peptides, salmon calcitonin, parathyroid hormone 1–34 (PTH1–34), and peptide YY 3–36 (PYY3–36). In all cases, the TJM peptide afforded a dramatic improvement in drug permeation across epithelial tissue. In addition, a formulation containing PYY3–36 and TJM peptide was dosed intranasally in rabbits, resulting in a dramatic increase in bioavailability. The TJM peptide was as or more effective in enhancing PYY3–36 permeation in vivo at a 1000-fold lower molar concentration compared to using LMW enhancers. Based on these in vitro and in vivo data, the novel TJM peptide represents a promising advancement in intranasal formulation development.