Pharmacological characterization of FE 203799, a novel long acting peptide analog of glucagon-like peptide-2 (GLP-2)

Diane M. Hargrove, Sudar Alagarsamy, Steve Qi, Kartik Shinivasan, Glenn Gostin, Regent Laporte, Javier Suarez-Diaz, Kazimierz Wisniewski, Jennifer Hartwig, Hailuo Wisniewski, Mark Liu, Alexander P. Posch, Claudio D. Schteingart, Pierre J. Riviere

Ferring Research Institute Inc., 4245 Sorrento Valley Boulevard, San Diego, CA 9222, USA

1. Introduction

Glucagon-like peptide-2 (GLP-2) is a 33 amino acid peptide derived from posttranslational processing of proglucagon in intestinal L-cells. GLP-2 is released into the circulation following nutrient ingestion and acts at distinct G protein coupled GLP-2 receptors that are primarily expressed in the small intestine and colon in a localized manner. GLP-2 has pronounced biological actions in the intestine and pancreas.

2. Experimental Methods

Peptide Synthesis

Peptides were synthesized by solid phase peptide synthesis and purified by reverse phase HPLC.

In Vitro Receptor Assays

Activity of peptides at the GLP-1 receptor and at the GLP-2 receptor was determined using radioligand binding assays. Compounds were tested in the presence of human GLP-1 or GLP-2 receptor expressed in Chinese Hamster ovarian cells. Each compound was tested at a single concentration (5 nM) in the absence or presence of 50 nM of native ligand (GLP-1 or GLP-2) to determine IC50 or EC50. Results were analyzed using a 3 parameter logistic equation to account for non-saturation at high concentrations.

3. Results

In Vitro Pharmacological Profile

GLP-2 agonists are known to have pronounced intestinotrophic activity. 

Intestinal Growth in Rats

Intestinal growth in rats was measured as a primary pharmacodynamic endpoint. Compounds or vehicle were administered by oral gavage at a single dose or by IV bolus injection and the rats euthanized 96 h after the last dose. Results were analyzed using a modified three-parameter Hill equation.

4. Summary and Conclusions

FE 203799 is a novel long acting peptide analog of GLP-2 with a half-life of 60 h and efficacies (fitted maximum response, %Max) were 41% higher than teduglutide.

5. References
