Evaluation of the Safety and Efficacy of Two Oral Insulin Formulations in Healthy Volunteers

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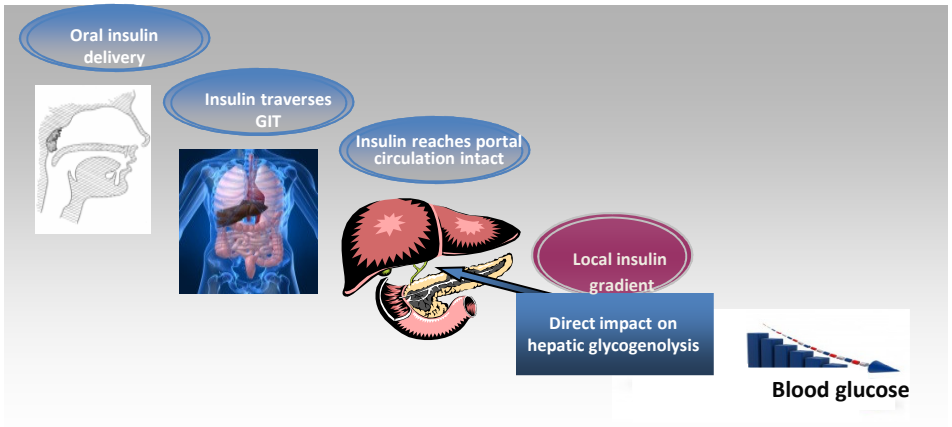
Background

- Oral insulin would revolutionize diabetes care by both encouraging early intervention and by tightening glycemic control.
- However, oral drugs face challenges along the gastrointestinal tract (GIT), which impede their bioavailability and effectiveness.
- Oramed Pharmaceuticals has developed a platform for oral delivery of proteins and peptides. ORMD-0801, Oramed's flagship oral insulin product, has been tested in healthy, Type 1 diabetes mellitus and Type 2 diabetes mellitus populations. In this study, the safety and efficacy of two slightly modified formulation variants were tested among healthy volunteers.
- ORMD0801: Insulin, Protective exipients, absorption enhancer, emulsifier

Methods

STUDY: Single-blind, two-period, single-center
TEST DRUG: F130 and F130GT, two ORMD-0801 formulation variants, each containing 8 mg insulin and only differing in their emulsifier content
PARTICIPANTS: 10 healthy male volunteers, ages 20-45
DESIGN: Fasting volunteers were administered one capsule containing one of the two formulations at each visit and were monitored for five hours thereafter. A blood sample was drawn 15 min before drug administration. Blood samples were then routinely drawn throughout the monitoring session for determination of blood glucose and c-peptide concentrations.

Proposed Mechanism



Results

F130 and F130GT induced similar plasma c-peptide patterns, which gradually decreased over the 5-hour monitoring session (Figure 1A). However, the mean C_{min} value registered after treatment with Formulation F130 significantly lower than that which followed Formulation F130GT treatment (0.12 ng/mL vs. -0.2 ng/mL, respectively; p=0.04). Similar blood glucose concentration profiles were recorded following either treatment (Figure 1B), however, Formulation F130 induced significantly greater glucose reductions, when compared to F130GT, with a two-fold increase in the mean area above the curve (768.3 ± 875.9 (mg/dL)/min versus 1626.4 ± 909.9 (mg/dL)/min; p=0.021).

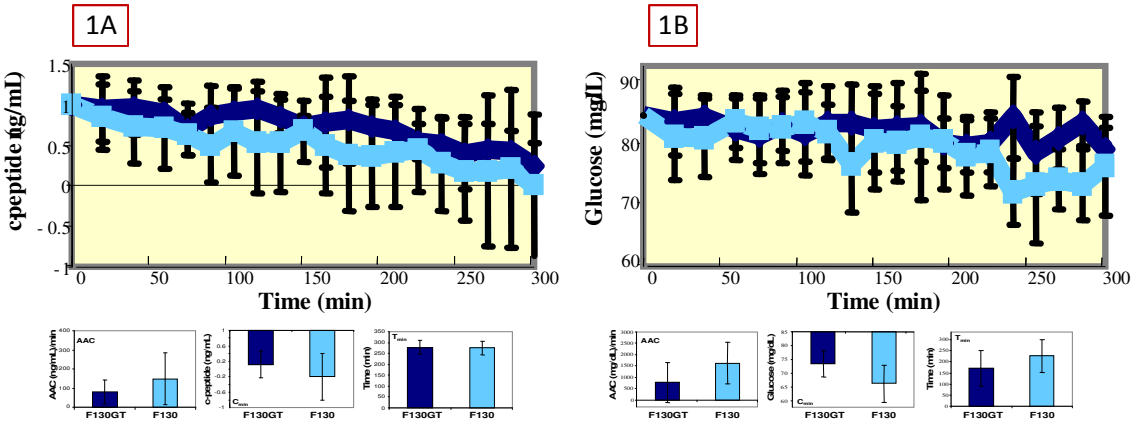


Figure 1. Mean blood marker responses following administration of oral insulin to healthy volunteers. Fasting, healthy subjects were administered a single ORMD-0801 capsule containing 8 mg insulin with varying exipient formulations, at two independent visits to the clinic (F130GT: diamonds; F130: squares). Mean responses (n=10) were graphed as a function of time (min) and mean AAC, Cmin and Tmin values were extrapolated. **A.** Mean c-peptide responses **B.** One-drop glucose tests were routinely performed and mean glucose responses were determined.

- No adverse events were reported throughout the study period.
- Oral insulin formulation F130 was more effective than F130GT.
- The tested emulsifiers and exipient ratios preserved insulin activity upon its oral administration.

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