Open Label Study to Assess the Safety, Pharmacokinetics (PK) and Pharmacodynamics (PD) of Five Oral Insulin Formulations in Healthy Subjects

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Methods:

Eight healthy male volunteers (mean age 26 years, BMI 24 kg/m²) participated in this 5-period, cross-over study. Subjects were dosed after an overnight fast and each consecutive visit was separated by a 72 to 96 hours washout period. The formulations consisted of 1 capsule containing 8 mg of insulin and 5 different concentration of Oramed’s absorption enhancing agents. Individual blood samples (29 totals) for PK/PD analysis were collected up to 5 hours post-dose. Pharmacodynamic effects were assessed by measuring the effects of the formulation on glucose, insulin and c-peptide.

Results:

Administration of an oral form of insulin in the fasted state demonstrated a significant decrease in c-peptide levels in all formulations (16%-92%) as well as reduction in blood glucose (7%-32%). All of the formulations were well tolerated by the volunteers, and no serious adverse events have been reported. A lead formulation was identified.

Discussion:

Oral delivery of proteins and peptide drugs remains a major challenge because of their unique physico-chemical and biologic properties. Oramed’s proprietary technology has been demonstrated to effectively deliver these molecules in preclinical and early clinical studies. In the current study 5 different formulations were assessed, and all were found to be safe and showed a salutary PD profile. The most apparent effects observed were on c-peptide and glucose. C-peptide co-secreted in equimolar concentration with insulin from the β-cell is not metabolized by the liver and thus reflects accurately the effects of exogenous insulin administration. The pharmacokinetics and pharmacodynamics of this specific enteric coated formulation are characterized by a delayed absorption and onset of action and effect (Figs 3,4).

Conclusions:

The results of this study in healthy volunteers showed that insulin combined with Oramed’s drug delivery enhancers and formulated in a capsule dosage form is absorbed and results in plasma glucose reduction, c-peptide decrease and insulin increase. The PK and PD of the current formulation suggests a potential clinical utility in IGT and early stage T2DM as a supplement to endogenous insulin. Supplementing endogenous insulin is likely to reduce the burden of the “overtaxed” β-cells as suggested by the observed consistent reduction in c-peptide in this study, and allow for β-cell “sparing”.

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