Comparative assessment of the glucose-lowering effect of multiple oral insulin (ORMD-0801) formulation variants in pigs

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Oral drug delivery platforms are being actively pursued to provide an oral insulin solution to diabetes patients. ORMD-0801, designed using the POD™ technology, has established the indispensability of antiproteolytic support and absorption enhancing factors toward effective passage of orally delivered insulin through the gastrointestinal tract to its site of action. ORMD-0801 has elicited improved glycemic control in type 1 and type 2 diabetes patients and is currently being assessed in large-scale clinical trials. In efforts to further enhance formulation stability and bioperformance, a comparative analysis of the glucose-lowering effects of two surfactant combinations (herein, EC-TA and SW-G), added to the basic oral insulin (ORMD-0801) formulation, was performed following their administration to healthy, fasting pigs (n=3-4). At each session, a single dose of an ORMD-0801 formulation variant, was directly administered to the duodenum, under endoscopic guidance, and blood glucose levels were monitored for the ensuing 150 minutes. All tested formulations, including the surfactant-free variant, induced a significant glucose-lowering effect within 30 min of administration, with C_{min} obtained within 30-90 min of dosing. All but the SW-G formulations led to glucose lows which plateaued for 45-60 min before beginning to return to baseline levels. The overall effect of EC-TA-supplemented formulations on mean blood glucose concentrations, was significantly greater than those supplemented with SW-G, for all tested doses ($p \leq 0.04$). The glucose area under the curve of mean EC-TA-elicited responses was 34% lower than that obtained with the SW-G-supplemented formulation and the surfactant-free formulation. This study demonstrated the primacy of the EC-TA surfactant combination in the tested oral insulin formulation; further studies will be required to evaluate its translation in the clinic.

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