

ABSTRACT

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Response to Inhaled GLP-1 is Dependent on Baseline Glucose

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Background and aims: MKC253 is GLP-1 adsorbed to Technosphere[®] microparticles for oral inhalation. This report presents data from two studies: MKC253-001 evaluated the effect of MKC253 under fasting conditions in healthy subjects, and MKC253-002 evaluated MKC253 in subjects with type 2 diabetes.

Material and methods: In MKC253-001, six healthy subjects received GLP-1 1.5 mg. In MKC253-002, 15 subjects with type 2 diabetes received GLP-1 1.5 mg, and five subjects with type 2 diabetes received Technosphere[®] placebo. All subjects were nonsmokers with normal lung function.

Results: In healthy subjects, MKC253 produced a transient decrease in glucose of 0.8 mmol/L. Minimum levels occurred approximately 15 min after inhalation of MKC253. Following the decrease, glucose returned to baseline levels by 1 h. The duration of response was much longer than the half-life of GLP-1 (~2 min). Response to GLP-1 in subjects with type 2 diabetes depended on baseline glucose. Of the 15 subjects in MKC253-002 who received GLP-1, 11 had baseline glucose > 9 mmol/L and four had baseline glucose < 9 mmol/L. Subjects with baseline glucose < 9 mmol/L had a mean maximum decrease of 0.75 mmol/L. The time to reach the minimum was about 0.5 h. Although glucose values recovered, they did not return to baseline levels after 4 h. Subjects with baseline glucose > 9 mmol/L had a 1.2 mmol/L decrease in glucose. The duration of response was longer—the minimum occurred 45 min after inhalation, with no return from the minimum levels. Placebo subjects had no change in glucose over the first 2 h after inhalation.

Conclusion: It has been shown previously that inhalation of MKC253 produces a sharp spike in plasma insulin. This rapid pulse of insulin can produce a long-lasting decline in plasma glucose in fasting subjects with type 2 diabetes.