Biochaperone Glucagon Exenatide (BC Glu Exe), A Stable Combination Of Glucagon (Glu) And Exenatide (Exe)

Achieved Larger Weight (BW) Loss Than Exe Alone In DIO Mice

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Abstract
Over the last decade, obesity and its associated consequences have become a major health issue worldwide. 1\(^{st}\) Generation Agonists (GLP-1) RA are one of the treatment options currently available, but achieve limited weight loss.

A combination of human glucagon (Glu) and GLP-1 RA is expected to provide a superior body weight (BW) reduction than GLP-1 RA alone. GLP-1 RA acts in the brain to induce satiety while Glu, a tetradecapeptide with an N-terminal biotin-BoSichaperone (BC) proprietary technology allows the stabilization and solubilization of protein drugs. As such, BC enables the combination of Glu and GLP-1 RA.

Methods

Animal Study

Mice were randomly assigned to one of two groups: BC Glu Exe and Exe alone. The BC group was treated with BC Glu Exe for either 2 or 8 weeks. At the end of the treatment period, mice were killed and BWs were measured. Glucagon and exenatide impurity contents were determined using RP-HPLC.

Figure 3: Relative body weight (n=10)

Figure 4: Cumulated food consumption (n=10)

Conclusions

BioChaperone technology enables the combination of glucagon with exenatide, GLP-1 RA.

* BC Glu Exe formulation is clear and colorless solution, essentially free of particle, after storage in vials at 4 \(^\circ\)C for at least 13 months and at 37 \(^\circ\)C for at least 12 weeks.

** Chemical stability after 4 weeks storage at 37 \(^\circ\)C in vials.

*** Both glucagon and exenatide recoveries are around 90%.

**** Glucagon and exenatide impurity contents are 5.4 and 7.8% respectively (Figure 2).

Figure 1: Pictures of solutions containing glucagon (2 mg/mL), glucagon (2 mg/mL) + BC and the combination glucagon (2 mg/mL), exenatide (35 pg/mL) and BC at neutral pH.

Figure 2: Glucagon and exenatide impurity content in BC Glu Exe formulations designed for mice in non-obese or clinical trials.

Animal Study

The treatments were well tolerated in all groups without any clinical finding reported during the study.

Exenatide alone, used as a reference and for 14 days led to a significant 10% decrease in BW compared to vehicle (Saline) (Figure 2). The total food intake in this group was significantly decreased when compared to the vehicle (Figure 4).