Evaluation of the Bioactivity of Semaglutide Compounded in SubMagna™ SL HMW using a Cell-Based Assay

SUMMARY: Semaglutide (GLP-1 agonist) induces the production of cAMP upon activation of the GLP-1 receptor. The cAMP Hunter™ bioassay was used to compare this bioactivity of semaglutide released from a compounded formulation using SubMagna™ SL HMW and semaglutide powder dissolved in PBS. The induction of cAMP was comparable with no statistical differences.

Introduction:

There is a growing demand worldwide for glucagon-like peptide (GLP)-1 agonists, a class of medications utilized in the treatment of type 2 diabetes and obesity. Semaglutide, the active ingredient in the injectable medications Ozempic® and Wegovy®, is the most popular GLP-1 agonist and there are often shortages in the marketplace. A compounded formulation of semaglutide for sublingual administration comprising Rybelsus® tablets and SubMagna SL HMW has been developed as an alternative to the injectable medications. An investigational cell-based study was hypothesized to evaluate and compare ligand-receptor activation by semaglutide released from the compounded formulation and semaglutide powder.

Methodology:

The cAMP Hunter™ semaglutide bioassay provides a robust, and highly sensitive, functional, cell-based assay to monitor 3'-5'-cyclic adenosine monophosphate (cAMP) production in cells, as a result of ligand-mediated activation of the GLP-1 receptor. The cyclic AMP is a derivative of adenosine triphosphate (ATP) and it is used for intracellular signaling. In this study, semaglutide was used as the ligand of GLP-1 receptor to evaluate the production of cAMP by the cells (Figure 1).

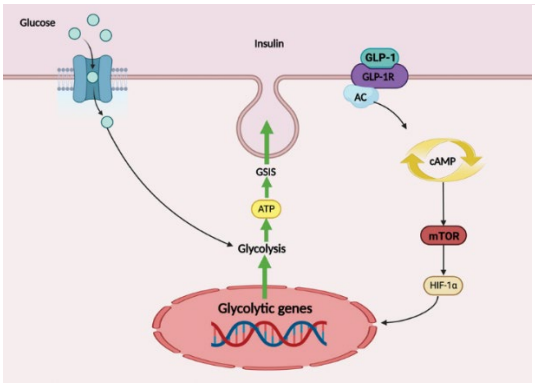

Figure 1. Graphic illustration of GLP-1 (e.g., semaglutide) binding to the receptor GLP-1R and stimulating the production of cAMP.

A bioassay kit was used for its conveniency and ready-to-use format. CHO-K1 GLP1R cells were seeded to each well of 96-well assay plate and incubated at 37° C and 5% CO_2 for 24 hrs before proceeding with the assay.

Serial dilutions from 3 ng/mL to 0.0123 ng/mL with PDB-B2 dilution buffer were made for semaglutide (powder, dissolved in PBS), semaglutide 3 mg/mL (SubMagna SL HMW) compounded, and positive control Exendin-4. The cells were treated with the diluted solutions for 30 min. cAMP antibody and cAMP working solution were added to each well and incubated for 1 hr at room temperature. The relative light units were read using a plate reader

Results and Discussion:

The dose response curve for semaglutide powder and semaglutide released from SubMagna was comparable with no significant statistical differences (*p* value=0.062), as shown in Figure 2. This result implies that Semaglutide (CADP) 3 mg/mL Sublingual Suspension (SubMagna SL HMW) functionally induced cAMP as well as the semaglutide powder.

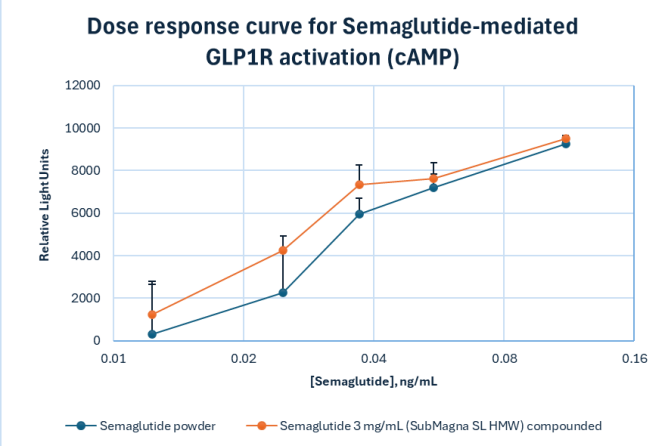

Figure 2. Dose response curve (relative light units) for semaglutide powder and semaglutide 3 mg/mL (SubMagna SL HMW) compounded.

References:

1. Novo Nordisk USA (2023) "Supply Update". Available at: https://www.novonordisk-us.com/supply-update.html (Accessed: October 2, 2024).
2. SubSema (2023) "Understanding Compounded Semaglutide Making and Informed Decision". Available at: https://subsema.com/ (Accessed: October 2, 2024).