PCCA SubMagna™ SL HMW **TECHNICAL REPORT**

Evaluation of the Absorption of a Sublingual Testosterone Compounded Formulation (SubMagna™ SL HMW) using the EpiOral™ *In Vitro* Tissue Model

SUMMARY: Beyond semaglutide, PCCA SubMagna™ SL HMW accommodates a broad range of active pharmaceutical ingredients (APIs) to be delivered under the tongue (sublingual). In this study, the *in vitro* tissue model suggests that PCCA SubMagna is able to deliver testosterone into and through human oral tissues.

Introduction:

PCCA SubMagna is an anhydrous, sublingual base designed to deliver high molecular weight (HMW) drugs under the tongue. This innovative compounding base also benefits from mucoadhesive properties which increase the contact time of the drugs in the sublingual space.

Beyond semaglutide, PCCA SubMagna accommodates a broad range of active pharmaceutical ingredients (APIs). The purpose of this study was to evaluate the ability of PCCA SubMagna to deliver testosterone through *in vitro* human oral tissues.

Methodology:

The EpiOral tissue (ORL-606), manufactured by MatTek (Ashland, MA), was the model used to evaluate *in vitro* the absorption of the sublingual suspension testosterone 1 mg/0.1 mL in PCCA SubMagna SL HMW (Table 1).

Six tissues were incubated overnight at 37° C and 5% CO_2 for equilibration. The assay medium (Teer-Buffer-GLC buffer) was pre-warmed to 37° C and pipetted into 6-well plates. The tissues were transferred into the plates together with the assay medium. The testosterone compounded formulation was then applied and, following 15 min of elapsed permeation time, the receptor media was collected for analysis. This procedure was repeated for 30 min of total elapsed permeation time.

Rx	
Testosterone USP Micronized (Yam) CIII	1 g
Flavor, Creme DeMenthe	0.4 mL
Base, PCCA SubMagna™ SL HMW	q.s. 100 mL

Table 1. *Testosterone 1 mg/0.1 mL Sublingual Suspension (SubMagna SL HMW): PCCA Formula 15031.*

The quantification of testosterone was performed using Ultra-Performance Liquid Chromatography (UPLC): column Acquity UPLC CSH Phenyl-Hexyl 1.7 um 2.1 x 100 mm; target column temperature of 45.0°C; gradient solvent mixture of water and acetonitrile at a flow rate of 0.5 mL/min.

Results and Discussion:

In this study, the absorption of testosterone into and through the EpiOral tissue model showed a rapid penetration upon application of the sublingual suspension. The permeation flux values for testosterone across EpiOral tissues are: 4.999±0.121 µg/cm^2/hr at 15 min and 5.528±0.0.163 µg/cm^2/hr at 30 min, as displayed in Figure 1.

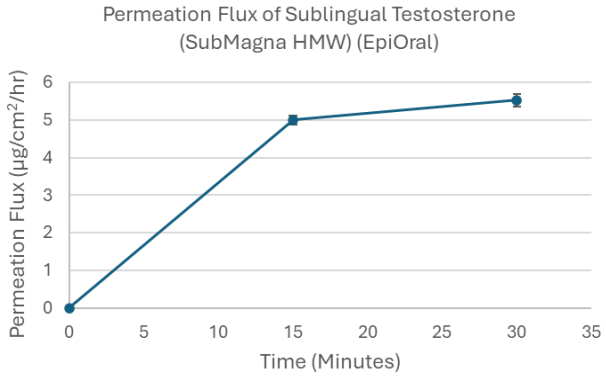

Figure 1. *Permeation flux of the sublingual testosterone compounded formulation over time for 30 minutes.*

Conclusions:

Sublingual formulations offer the potential for improved absorption compared to buccal formulations, such as troches, because the epithelium layer is much thinner under the tongue. The sublingual route is particularly promising for the delivery of hormones. This *in vitro* study demonstrates that PCCA SubMagna SL HMW is able to deliver testosterone into and through human oral tissues, offering compounding pharmacists a key alternative formulation for testosterone.