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A Novel, Non-Invasive, Self-Administered, Preservative-Free, Sustained Release Product (EySite-NanoM™-TP) for Glaucoma Therapy

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Abstract

One of the leading causes for blindness among the elderly is glaucoma. Among leading standards of care for glaucoma treatment are prostaglandin eye-drops, administered once daily. However, treatment is confounded by lack of patient compliance, inefficient placement of drops and losses of ~90% of the dosage to drainage by the tear duct.

We report the development of a novel, preservative-free, self-administered, Travoprost-containing sustained release, nano-engineered sterile product that can be placed in the conjunctival cul de sac by the patient or caregiver, every 30 days.

EySite-NanoM™-TP is a nano-engineered product that can release at least 1.5 micrograms of drug per day, for 30 days.

Physico-chemical characterization of the product has been presented herein (% encapsulation, % burst, dose uniformity, % hydration, corneal permeability, *in-vitro* release)

Design Attributes and Therapeutic Benefits of EySite-NanoM™-TP

- *Applied to the conjunctival cul de sac (lower lid) using an applicator.*
- *Non-invasive*
- *Self-administered, no clinical intervention*
- *Preservative-free*
- *Flexible drug loading*
- *Flexible, biocompatible*
- *Biodegradable, does not need to be removed*
- *Sustained Release to 30 days*
- *Non-irritating*

Method of Use

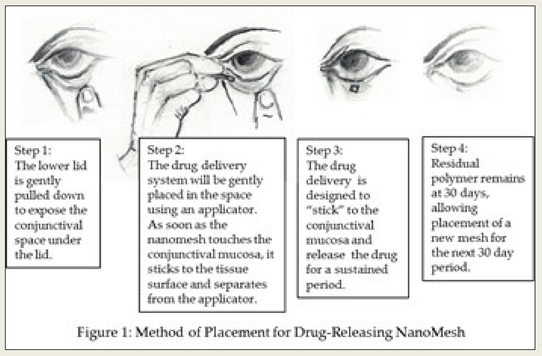


Figure 1: Method of Placement for Drug-Releasing NanoMesh

Materials & Methods

Characterization:

- Imaging: Dry EySite-NanoM-TP was imaged by high resolution scanning electron microscopy.
- Encapsulation (mg/G): 20 mg of the drug product was dissolved in 1mL of acetonitrile. 9mL of HPβD buffer, pH 7.4 was added with light sonication (10 seconds), to precipitate PLGA polymer. 1mL of the slurry was centrifuged (5min; 13200 RPM, 25°C), and the supernatant was removed for HPLC analysis. HPLC analysis was performed on a RP C18 column (Zorbax 300SB, 4.6 mm x 150 mm) and analyzed for drug content at λmax 280 nm.
- *In-Vitro* Burst (%): Approximately 30-35 mgs of the product was placed in a 1 ml Spectrum Float-a-lyzer™ and placed in 40 ml of were reconstituted in HPβD buffer, pH 7.4 and rotated at 37ºC. The sample was analyzed at 1 hour for drug content by HPLC.
- *In-Vitro* Release (%): (20-40 mg) samples were placed in Float-a-lyzer tubes, suspended in 40 g of buffer and rotated at 37ºC. Time point samples were taken over the duration of study and analyzed by HPLC. ES-NanoM samples were analyzed
- Thickness: was measured (n=3) by a Mitutoyo Screw Gauge.
- Stress Degradation Studies: Travoprost-containing EySite-NanoM was subjected to 24 hours of 254 nm UV and hydrogen peroxide solution to ascertain propensity of product to destabilize with light and
- Corneal Permeability: Six fresh bovine calf corneas were obtained from Research 87, LLC and mounted onto 6 Franz diffusion cells, maintained at 37 ºC and the product loaded. The donor chamber contained the product; the receptor chamber was filled with 1% HPCD /Phosphate buffer, pH 7.4. Receptor fluid was sampled at each time-point, pooled and analyzed by HPLC for Travoprost and Travoprost-acid. Concentration of each species was graphed against time in hours. Cornea was also analyzed by extraction of drug, followed by HPLC.

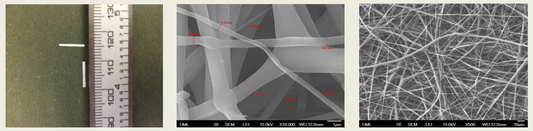
Results

Physico-chemical Characterization

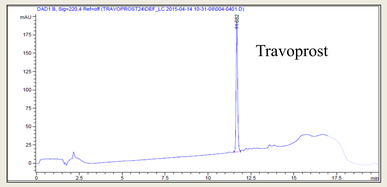
Attributes	Results
Proposed Dimensions of EySite-NanoM-TP	1 mm x 10 mm
Encapsulation (mg/g)	36-39 mg/G
% Burst	2-3%
% Hydration (becomes flexible)	267%

Results

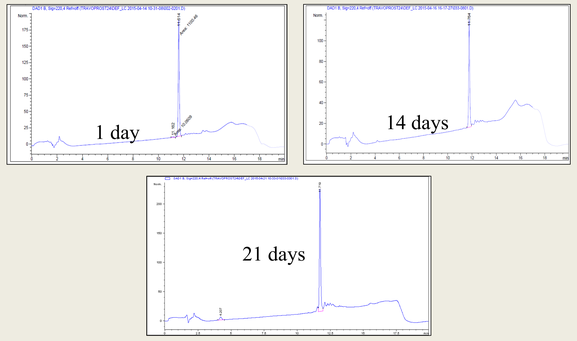
Nanoengineered EySite-NanoM™ is Designed to be Biodegradable, Biocompatible and Adherent to Ocular Mucosa



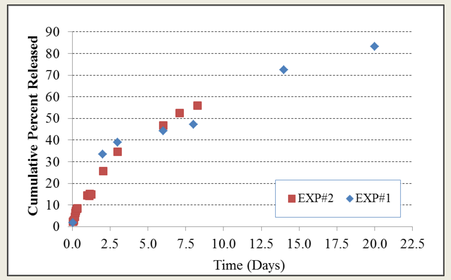
Intact Travoprost is Encapsulated in EySite-NanoM™



Intact Travoprost is Released

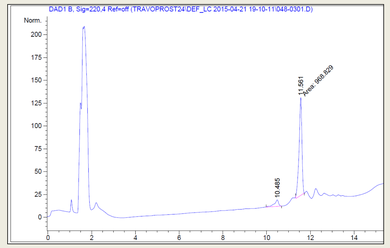


In-Vitro Sustained Release of Travoprost

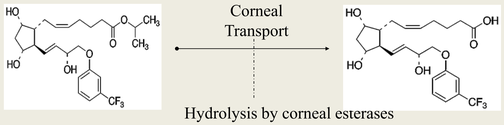


Results

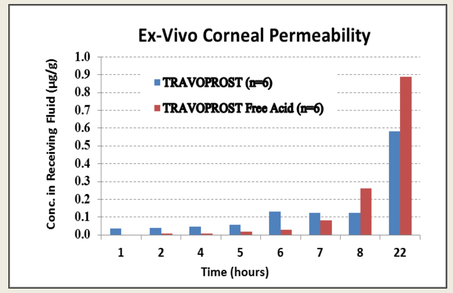
EySite-NanoM™ Can Withstand Photo-oxidative Stress



EySite-NanoM™ Delivers Travoprost through Cornea



Travoprost (pro-drug) **Travoprost Acid (active)**



Concentration of Trav-A at 22 hours = 19.87 µg/g

Concentration of Trav at 22 hours=15.30 µg/g

Conclusions and Future Work

- The feasibility of EySite-NanoM-TP as a sustained release product for Travoprost has been demonstrated.
- Future work will involve optimization of the product for biodegradability, mucoadhesivity, flexibility.
- CMC data will be generated (stability, methods, scale-up, sterilization methods)
- *In-vivo* irritation and pharmacokinetics will be performed.

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