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OBJECTIVE : To evaluate the feasibility of *in vitro* transport and *in vivo* ocular delivery of PRINT® nanoparticles using EyeGate® II iontophoretic device

PRINT® Nanoparticles

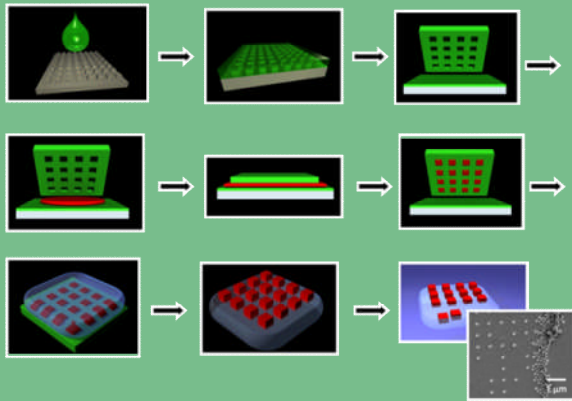


Figure 1. Illustration of PRINT® Process. Wetting of the silicon template with (green) Fluorocur™ material followed by curing to create a mold (top row); Fluorocur™ mold produced with nanoscale features from the template; confining (red) organic liquid to cavities via a wetting process; harvesting organic particles from mold with adhesive layer (bottom left); dissolution of adhesive layer producing free particles (bottom right).

PRINT® particle control over size, shape, and composition

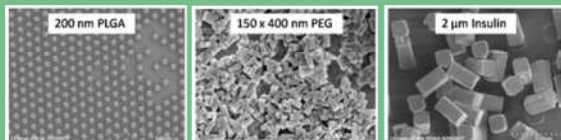


Table 1. PRINT® particle characterization data.

Lot #	PRINT™ FITC-labeled PEG Nanoparticles Master Template: Cylindrical 200 nm x 200 nm	Z-ave (nm)	ζ Potential (mV)
L/EG1(2)	212 ± 6 nm x 155 ± 3 nm	298 ± 2	+47.4 ± 2.3
L/EG2(3)	218 ± 5 nm x 156 ± 4 nm	347 ± 6	-47.9 ± 2.8
L/EG3(A.2)	210 ± 10 nm x 170 ± 7 nm	376 ± 17	+31.0 ± 0.8

Iontophoretic *in vitro* Transport

- Positively charged L/EG1(2) and negatively charged L/EG2(3) nanoparticles were suspended each in Na-citrate buffer at 1 mg/mL.
- Particle suspension was loaded into the donor compartment of an Ussing chamber setup (Figure 2) while the receptor compartment received the particle-free buffer.
- Iontophoretic current of +4 mA for (+) particles and -4 mA for (-) particles was applied for 60 min. Sclera was removed and analyzed by fluorescence microscopy.

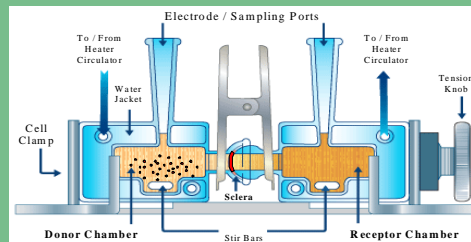


Figure 2. Ussing chamber setup to evaluate *in vitro* transport of PRINT nanoparticles through rabbit scleral explants.

(-) Nanoparticles (+) Nanoparticles

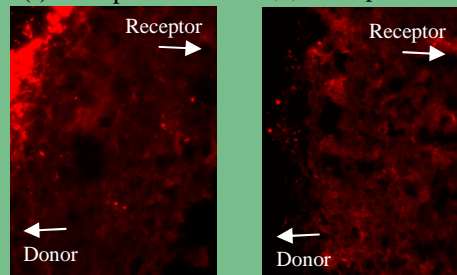


Figure 3. Microscopic images of rabbit sclera after iontophoretic *in vitro* transport.

Iontophoretic *in vivo* Delivery

- New Zealand White rabbits received a single ocular iontophoretic dose (+4 mA for 5 min) using the EyeGate® II device to deliver a 1 mg/mL positively charged L/EG3(A.2) nanoparticle suspension.
- Ocular tissues were harvested and processed for sectioning immediately after treatment.

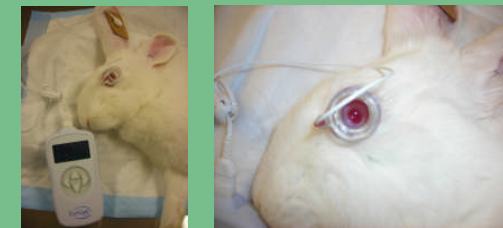


Figure 4. Setup of iontophoretic dosing in New Zealand rabbit eyes with the EyeGate® II device and generator.

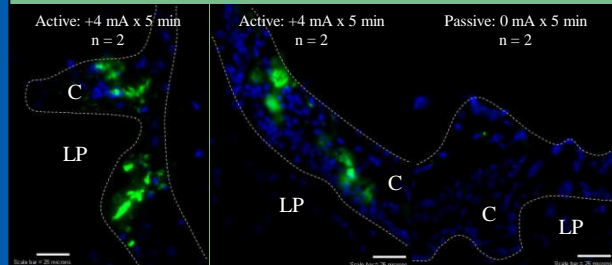


Figure 5. Microscopic images of rabbit Conjunctiva (C) and Lamina Propria (LP) tissues after iontophoretic *in vivo* delivery. Sections were counter-stained with DAPI.

CONCLUSIONS : Iontophoretic delivery of PRINT® nanoparticles was achieved in rabbit ocular tissues by using the EyeGate® II device. Combining PRINT® nanoparticles containing ophthalmic therapeutics with iontophoretic treatment via the EyeGate® technology can create an opportunity to provide sustained drug delivery for a variety of acute and chronic ophthalmic diseases.