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## Fenofibrate-Loaded Biodegradable Nanoparticles for the Treatment of Neovascular Age-Related Macular Degeneration

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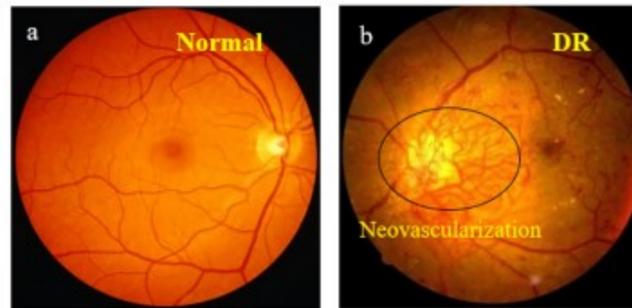
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## BACKGROUND

- Diabetic retinopathy (DR) is the leading cause of blindness in working aged Americans, especially for Hispanics<sup>1</sup>.
- Neovascularization is the most common features of DR. Anti-VEGF drug is the standard treatment method for DR<sup>2</sup>. However, 40% of patients do not respond to it<sup>3</sup>.
- Fenofibrate is a peroxisome proliferator-activated receptor  $\alpha$  (PPAR $\alpha$ ) agonist and has shown therapeutic effects on DR<sup>4</sup>.
- Systemic administration of fenofibrate limits its efficacy due to low ocular bioavailability to the retina<sup>5</sup>.
- Nanomedicine provides sustained drug release to target tissues at effective dosage, which can reduce toxicity, increase efficacy and improve patients compliance<sup>6</sup>.



(Yoshihiko et al. *Annu Rev Ph Sci* 2015)

## PURPOSE

- To construct and fully characterize fenofibrate nanoparticles (Feno-NP) formulations that release fenofibrate over prolonged period of time *in vitro*.
- To evaluate pharmacokinetic and efficacy of the Feno-NP for treating DR *in vivo*.

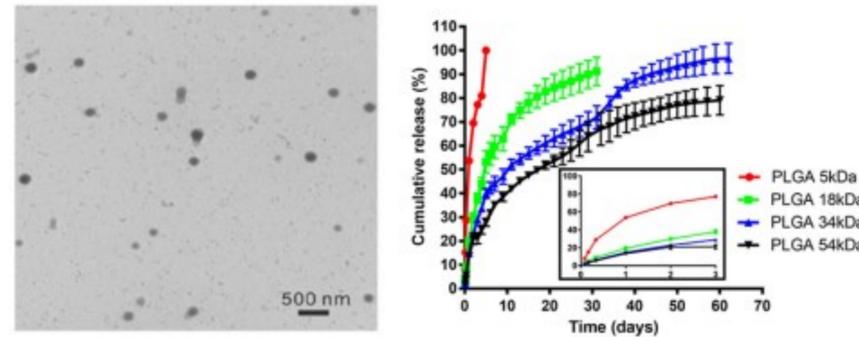
## MATERIALS AND METHODS

- Fenofibrate was encapsulated into poly(lactic-co-glycolic acid) (PLGA) with different molecular weight using an emulsification method.
- Feno-NPs were fully characterized in terms of particle size, morphology, drug loading and *in vitro* drug release profiles.
- 5  $\mu$ l Feno-NPs was administered to rats through intravitreal (IVT) injection. Fenofibric acid concentration in ocular tissues was quantified using LC/MS/MS.
- A single IVT injection of 5  $\mu$ l Feno-NP (30  $\mu$ g Fenofibrate) or blank NP (0.5 mg NP) was given to streptozotocin (STZ) induced diabetic rats. 8 weeks after injection, Feno-NP efficacy on DR was evaluated by retinal vascular leakage, leukostasis, and the expression of VEGF and ICAM-1.

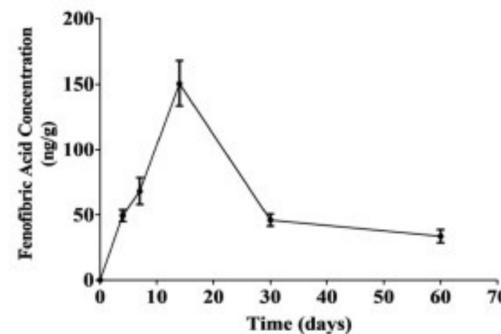
## ACKNOWLEDGEMENTS

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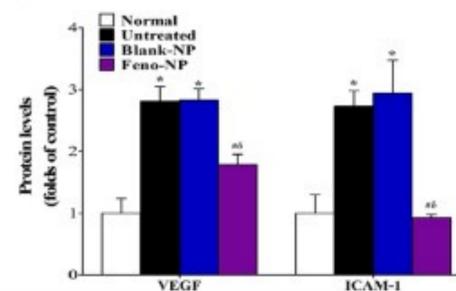
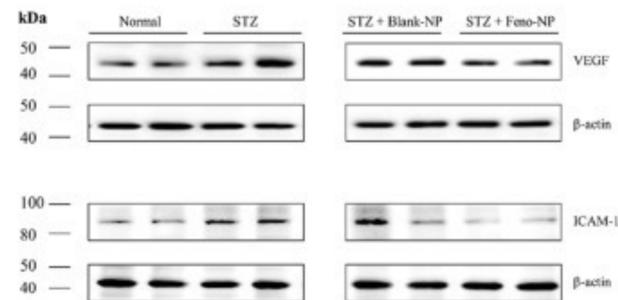
## RESULTS



Fenofibrate PLGA NPs Providing Sustained Drug Release *in vitro*

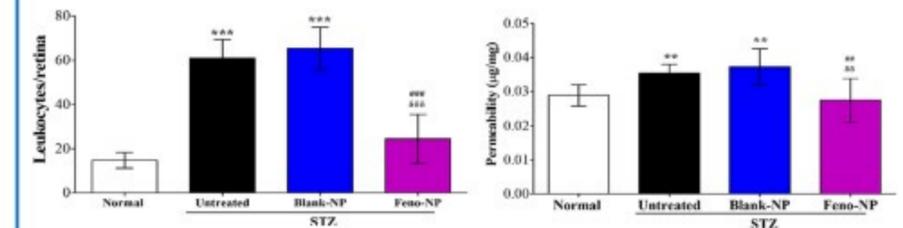
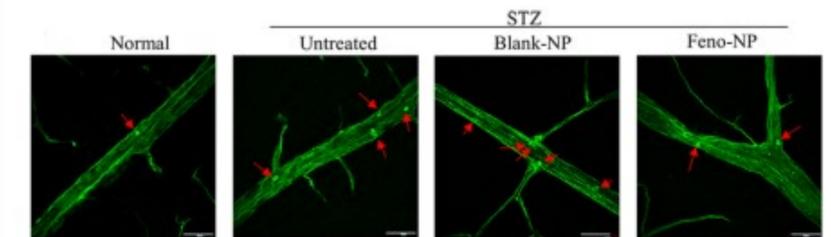
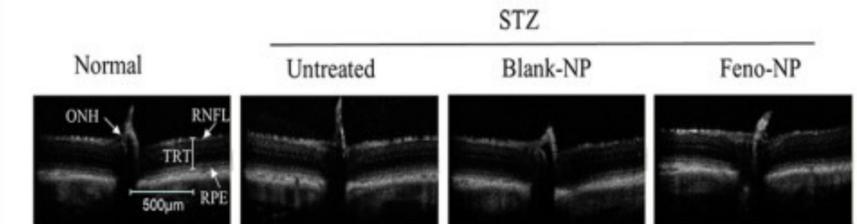


One Single IVT Injection of Feno-NP(34kDa) Provided Sustained Levels of Fenofibric Acid *in vivo*



Feno-NP Attenuate Overexpression of VEGF and ICAM-1 in the Retina of STZ Induced Diabetic Rats 8 Weeks Post Injection

## RESULTS



Single IVT Injection of Feno-NP Attenuates Vascular Leakage and Leukostasis in STZ-Induced Diabetic Rats 8 Weeks Post Injection

## CONCLUSIONS

- Feno-NP made by 34kDa PLGA demonstrated more than 6% drug loading and sustained drug release for more than 2 months *in vitro* and *in vivo*.
- One single IVT injection of Feno-NP (34kDa) reduced diabetic induced retina vascular leakage, leukostasis with long lasting efficacy for at least 8 weeks.
- Feno-NP attenuate overexpression of VEGF and ICAM-1 in the retina of diabetics rats.
- A single IVT injection of Feno-NP displayed promising therapeutic potential for the treatment of DR with sustained drug release.
- The Feno-NP platform is expected to improve DR patients life quality, especially for Latinos.

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