PURDUE UNIVERSITY | Department of Industrial and Physical Pharmacy

Industrial & Physical Pharmacy Seminar

IPPH 69600

Monday, October 3, 2022
3:30 PM in RHPH 164

"Long-term ocular delivery of griseofulvin for therapy of age-related macular degeneration"

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Last Seminar

Age-related macular degeneration (AMD) is one of the leading causes of irreversible vision loss and blindness in elderly population worldwide. Current AMD treatments based on anti-vascular endothelial growth factor therapy are ineffective in a significant fraction of patients. In the quest of alternative targets, ferrochelatase (FECH) was identified as a promising target. FECH is a metalloenzyme and can be inhibited by a known anti-fungal drug griseofulvin (GRF), a microtubule inhibitor. Long-term delivery to the posterior segment of the eye is critical to repurposing GRF for AMD therapy. A long-acting release GRF-eluting poly(lactic-co-glycolic acid) (PLGA) microparticles (MPs) system was developed for intravitreal administration. Particle size distribution (<20 µm), drug loading (>3.5 wt%), and drug release kinetics (>30 days) were identified as critical quality attributes (CQAs) of MP formulation. Magnesium hydroxide [$Mg(OH)_2$] was encapsulated in MPs, varying the amount from 2 to 20 wt% of total mass, to control the release kinetics of GRF. Among the tested GRF MP formulations, the MP containing 2% $Mg(OH)_2$ showed a minimal burst release (~18% of total loaded drug in 1 day) and continuous release (~100% in 38 days) and was considered optimal for 1 month delivery. GRF MPs provided sustained release of bioactive GRF and inhibited proliferation and tube formation of human retinal endothelial cells for a prolonged period compared to the unformulated GRF solution. *In vivo* efficacy of GRF MPs was evaluated in a mouse model of laser-induced choroidal neovascularization (L-CNV). The volume of neovascularization was estimated from in situ optical coherent tomography and confocal images of stained ex vivo choroids. GRF MPs provided a sustained effect in reducing CNV lesion volume. Fluorescein angiography suggests that GRF MPs reduce the severity of lesions. Also, in-situ imaging of fundus and ex-vivo microscopic imaging of retina suggest that GRF MPs do not cause off-target damage in the eyes and are safe for intravitreal administration. These results support that PLGA MPs can prolong the antiangiogenic effect of GRF and interfere with the progression of neovascularization in the eyes. Therefore, the GRF MP formulation may be further optimized for AMD therapy.

Dhawal is a 5th year PhD student in Prof. Yoon Yeo's lab. He received his Master in Pharmaceutics from Institute of Chemical Technology, India. Before joining IPPH, he had been working on formulation development for 4 years at Dr. Reddy's Laboratories.