COLLEGE OF PHARMACY
PHARMACEUTICAL SCIENCES
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Pharmaceutical Sciences Seminar Series

Wednesday, September 21, 2022
4:00pm
NCRC Building 10 - South Atrium
Zoom Link

"Characterization of core-shell etonogestrel-loaded polymer microparticles prepared by electrospray and optimization of early release kinetics"

Presented by:

Richard Schutzman
PhD Candidate, Pharmaceutical Sciences
University of Michigan

Abstract: Despite its high efficacy and good patient compliance, the only long-acting injectable (LAI) contraceptive currently available in the US, depot medroxyprogesterone acetate (DMPA), is limited by significant side effects and a delayed return to fertility for up to 10 months after its intended duration of action. Coaxial electrospraying was investigated for producing morphologically novel core-shell microparticles (csMPs) prepared from poly(D,L-lactide) (PLA) and related polymers to achieve both elevated drug loading (~50% w/w) and slow and continuous 3-6 month release of the contraceptive hormone—etonogestrel (ENG). Several barriers to development of optimal csMP formulations were identified, including: elevated drug release over the first month of incubation, low product yield, non-spherical geometry, amorphous drug in the core, elevated residual organic solvent, and a lack of *in-vitro-in-vivo* relationships (IVIVCs). System modifications to improve the electrospray Taylor cone such as introduction of a ring electrode increased particle yield from 10-15% to up to 40%. Various methods of exposure with ethanol to the newly formed csMPs were found to increase ENG crystallinity and reduce residual solvents, which in turn led to a decrease in the rapid release during the first month. Increasing ethanol exposure or introduction of a strong surfactant (e.g., Triton X-100) in the aqueous collection vessel created particles with increasing sphericity. The resulting optimized formulations exhibited high load (~50% w/w, >95% encapsulation efficiency), low 1-month release with continuous > 2-month release, very low residual organic solvent, elevated crystalline drug, and spherical core-coat morphology. An IVIVC was developed using Weibull-scaling of *in vitro* and *in vivo* times ($t_{in\ vivo} = At_{in\ vitro}^{k}$) after *in vitro* and *in vivo* testing of eight different disc-shaped csMP formulations over 3 months. Mixed effects modeling of the linearized Weibull time scaling was utilized to analyze individual formulations and compare pre-exponential, A, and exponential terms, k. The IVIVC model based on *in vitro* release explained 81% of absorption variability. Hence, these approaches strongly advance development of csMPs for a 3-6 month long-acting injectable contraceptive. Funding: FHI360 and the Gates Foundation.