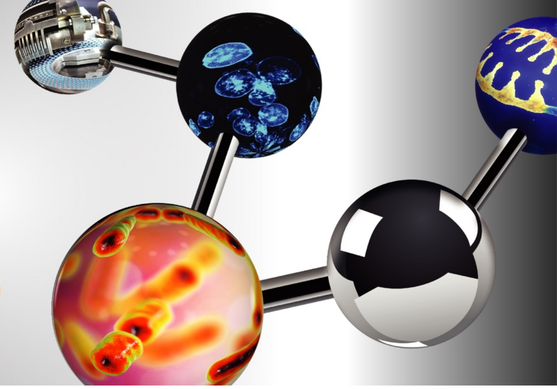
T3136 Effect of Coacervation Processing Parameters on Drug Release from Minocycline Hydrochloride Microspheres

Ruifeng Wang[1], Quanying Bao[1], Yan Wang[2], Bin Qin[2], Josh Lomeo[3], Shawn Zhang[3], Diane J. Burgess[1]

[1]University of Connecticut, School of Pharmacy, Storrs, CT 06269, USA
[2]Office of Research and Standards, Office of Generic Drugs, Center for Drug Evaluation and Research, U.S. Food and Drug Administration, Silver Spring, MD 20993, USA
[3]DigiM Solution LLC, 67 South Bedford Street, Suite 400 West, Burlington, MA 01803 USA

Contact Information: ruifeng.2.wang@uconn.edu; d.burgess@uconn.edu



Purpose

- Commonly used manufacturing methods for poly (lactic-*co*-glycolic acid) (PLGA) microsphere drug products include solvent evaporation, spray drying, and coacervation.
- Minor changes in the manufacturing processes are shown to affect the physicochemical properties (such as particle size, and morphology) and drug release behavior of microspheres[1].
- The objective of this work was to investigate the effect of coacervation processing parameters on PLGA microsphere quality and *in vitro* release characteristics.

Methods

- Minocycline hydrochloride was selected as the model drug. PLGA with similar properties (molecular weight, lactic acid to glycolic acid ratio, and end groups) as in the commercial product Arestin® was used for the formulation preparation.
- Four compositionally equivalent minocycline hydrochloride microsphere formulations were prepared *via* a coacervation method with different processing parameters (**Table 1**). Briefly, the micronized minocycline hydrochloride powder was suspended in PLGA solution and then transferred into a vessel equipped with an overhead stirrer. Coacervation was induced by the addition of silicone oil with different viscosity while stirring. The coacervate dispersion was transferred into a beaker with hardening agent for solidification, followed by washing and vacuum drying prior to final microspheres collection.

Table 1. *Different coacervation processing parameters for four compositionally equivalent minocycline hydrochloride microspheres.*

Stirring speed \ Silicone oil viscosity	350 cSt	1000 cSt
350 rpm	Formulation A	Formulation B
600 rpm	Formulation C	Formulation D

- The physicochemical properties including drug loading, particle size, and morphology of the prepared microspheres were characterized. In addition, the in vitro release testing of the microspheres was conducted using a sample-and-separate method.

Results

1. Physicochemical properties of the prepared microsphere formulations

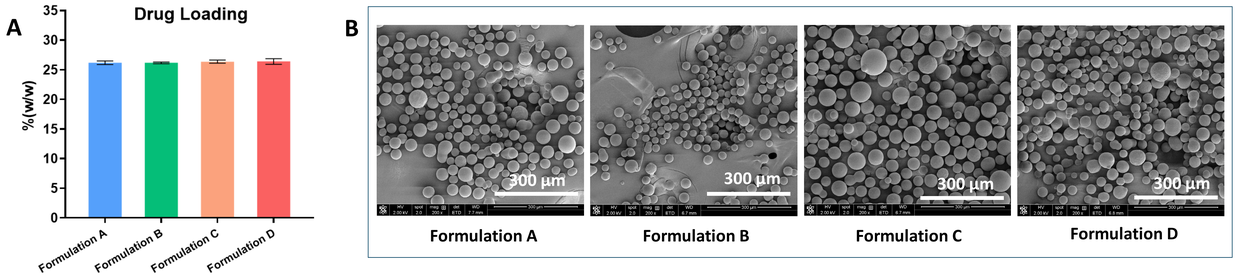


Figure 1. A) *Drug loading;* ***B)*** *Scanning electron microscope images of prepared microsphere formulations.* The experiments were performed in triplicate (n=3) and the data are presented as mean ± standard deviation.

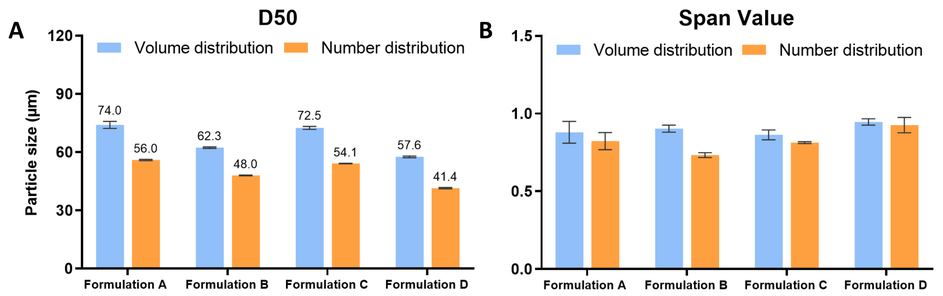


Figure 2. A) *Particle size and* ***B)*** *span values of prepared microsphere formulations.* The experiments were performed in triplicate (n=3) and the data are presented as mean ± standard deviation.

2. *In vitro* release characteristics of the prepared microsphere formulations

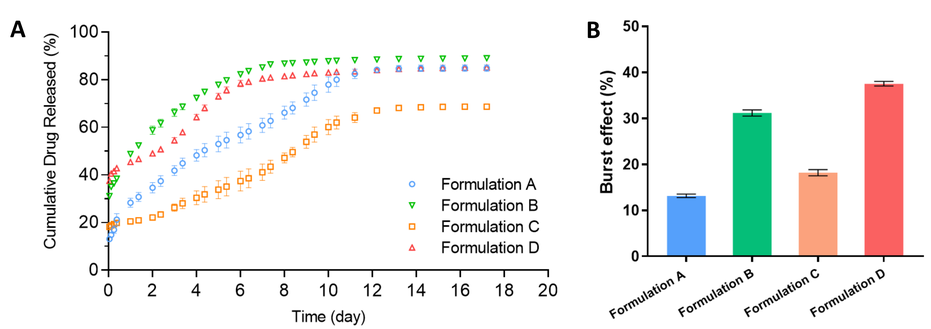


Figure 3. A) *In vitro release profiles and* ***B)*** *burst effect (%) of the prepared microsphere formulations.* The experiments were performed in triplicate (n=3) and the data are presented as mean ± standard deviation.

Conclusions

- Four compositionally equivalent minocycline hydrochloride microspheres were prepared using a coacervation method.
- Physicochemical properties (such as particle size) of the prepared microspheres were determined to be sensitive to minor changes in coacervation processing (such as viscosity of silicone oil and stirring speed), which in turn affected the *in vitro* release characteristics.

Reference

[1] Andhariya, Janki V., et al. *Journal of controlled release,* 255 (2017): 27-35.

Acknowledgments

- The funding for this project was provided by the U.S. Food and Drug Administration through the Contract #75F40119C10157.
- The views expressed in this poster are those of authors and do not reflect the official policies of the U.S. Food and Drug Administration.