Effect of Coacervation Processing Parameters on *In vitro* Drug Release from Minocycline Hydrochloride Microspheres

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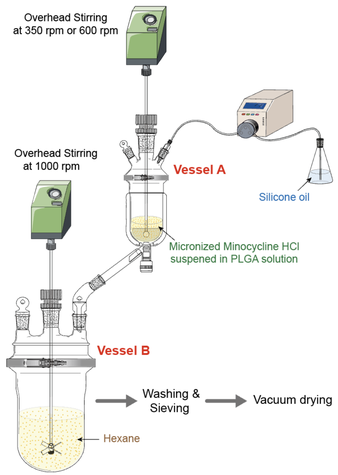
Purpose

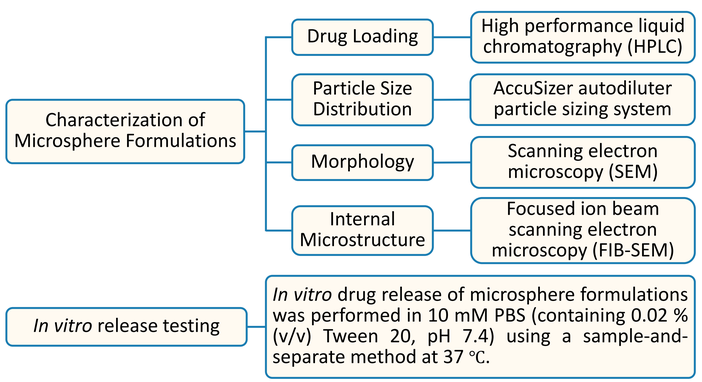
- Minor changes in the manufacturing processes are shown to affect the physicochemical properties (such as particle size, and morphology) as well as the drug release behavior of microspheres[1].
- Minocycline hydrochloride was selected as the model drug. The objective of this work was to investigate the effect of coacervation processing parameters on PLGA microsphere quality and *in vitro* release characteristics.

Methods



- The minocycline hydrochloride microspheres were prepared *via* the coacervation method using a well-designed glass vessel assembly (**Fig. 1**) with different processing parameters, as shown in **Table 1**. Briefly, the micronized minocycline hydrochloride was suspended in PLGA solution and then transferred into the vessel A equipped with an overhead stirrer. Coacervation was induced by the addition of silicone oil with different viscosity while stirring. The coacervate dispersion was then discharged into the vessel B containing hexane for solidification, followed by washing and vacuum drying prior to final microsphere collection.

Figure 1. *Schematic demonstration of the coacervation process. Vessel A was used for the encapsulation step and vessel B was used for the hardening step.*



Results

1. Physicochemical properties of the prepared microsphere formulations

Table 1. *Drug loading of minocycline hydrochloride microspheres prepared with different coacervation processing parameters. DCM: dichloride methane; EA: ethyl acetate*

	Solvent	Stirring rate (rpm)	Silicone oil viscosity (cSt)	Drug Loading (%, w/w)
FA	DCM	350	350	26.18 ± 0.31
FB	DCM	350	1000	26.17 ± 0.14
FC	DCM	600	350	26.37 ± 0.27
FD	DCM	600	1000	26.41 ± 0.47
FE	EA	350	350	27.07 ± 0.66
FF	EA	350	1000	27.63 ± 0.43
FG	EA	600	350	27.39 ± 0.48
FH	EA	600	1000	26.61 ± 0.13

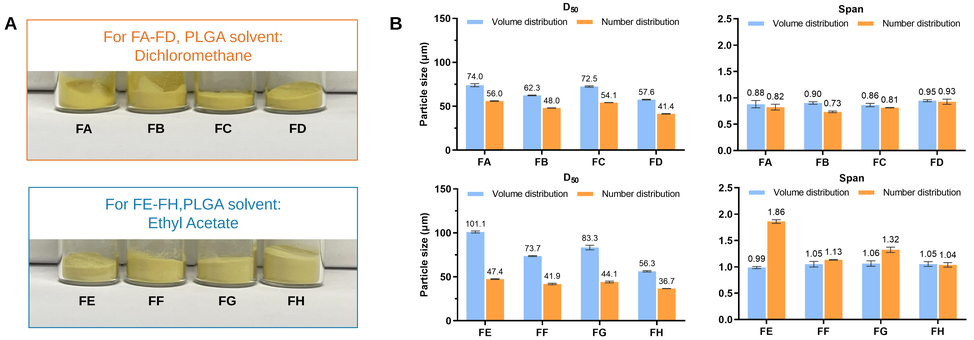


Figure 2. A) *appearance and* ***B)*** *particle size distribution of prepared microsphere formulations.* The experiments were performed in triplicate (n=3) and the data are presented as mean ± standard deviation.

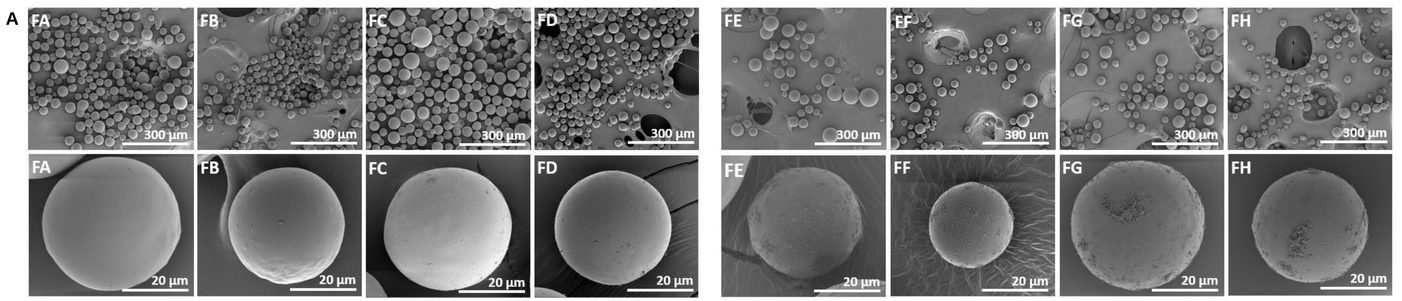


Figure 3. A) *representative SEM images and* ***B)*** *representative illustrations of the prepared microsphere formulations subjected to SEM and FIB-SEM imaging, together with representative SEM images showing the surface morphology and the cross-section of the microspheres.*

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

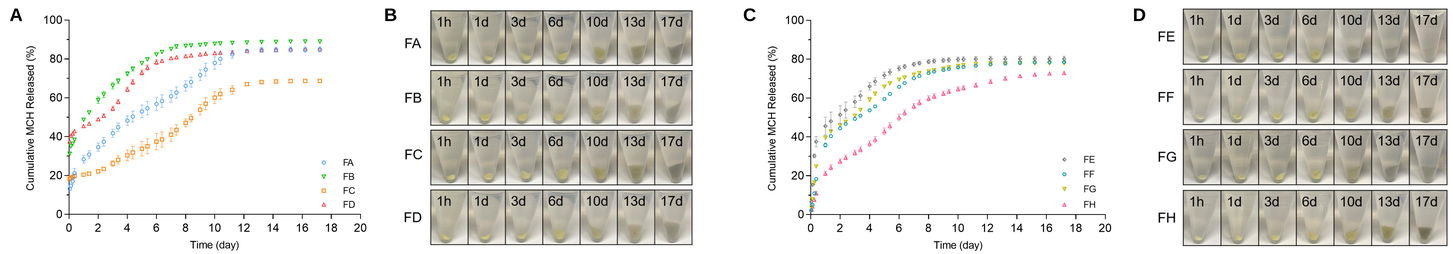


Figure 4. A), C) *In vitro release profiles and* ***B), D)*** *status of microspheres during in vitro release testing of the prepared microsphere formulations.* The experiments were performed in triplicate (n=3) and the data are presented as mean ± standard deviation.

Conclusions

- Eight 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 (*i.e.,* viscosity of silicone oil and stirring speed), and so were the *in vitro* release characteristics.

Acknowledgments

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Reference

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