Comparing the *In Vitro* Performance of Cross-linked to Conventional Polyester Microparticles

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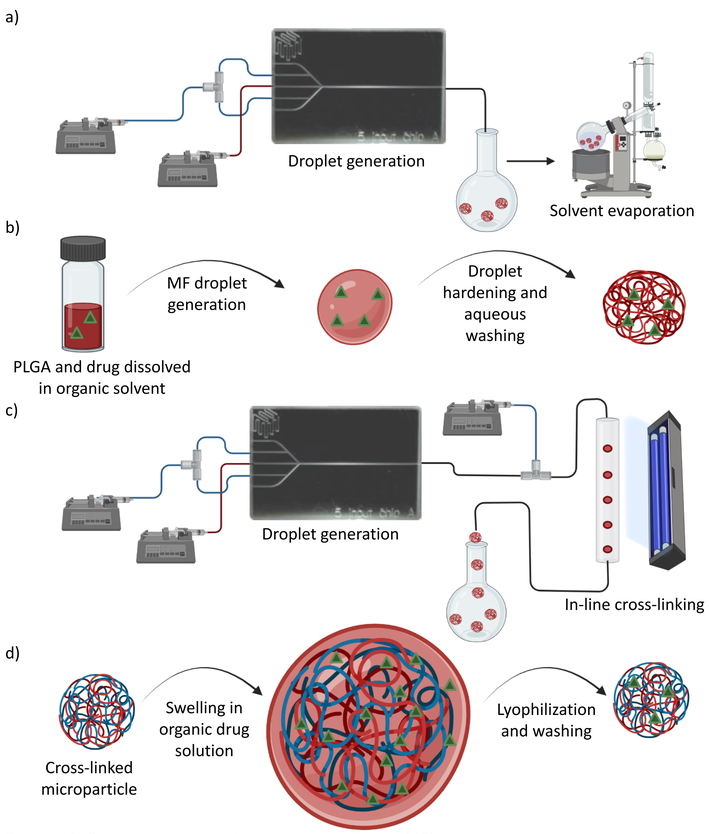
INTRODUCTION

Encapsulation into polymeric microparticles (MPs) has been a successful strategy to achieve the sustained and/or localized release profile required by long-acting injectable drug formulations. With over 30 years in the clinic, the biodegradable polyester poly(lactide-*co*-glycolide) (PLGA) makes up almost all FDA-approved MPs [1]. Despite its success to date, PLGA is not without its limitations. For example, drug-polymer compatibility plays a role in the resulting formulation's performance (i.e., loading and release) [2]. Therefore, no single material is likely to be optimal for the formulation of all drugs. Hence, there is a need to develop novel materials to realize the full potential of long-acting injectables in the clinic. Our lab has previously demonstrated that cross-linked valerolactone-based MPs show high drug loading and sustained release [3]. In this work, cross-linked poly(lactide-*co*-allyl-glycolide) (xMP) MPs are prepared and characterized in terms of morphology, stability, drug loading, and *in vitro* release and compared with conventional PLGA MPs.

METHODS



Scheme 1. Cartoon representation of the microfluidic (MF) setup and fluidic path used to manufacture conventional PLGA microparticles (MP) (a). Cartoon showing the conventional drug loading of MP (b). Cartoon representation of MF setup and fluidic path used to prepare cross-linked microparticles (xMP) (c). Cartoon showing the swelling equilibrium loading of drug into xMP (d).

RESULTS

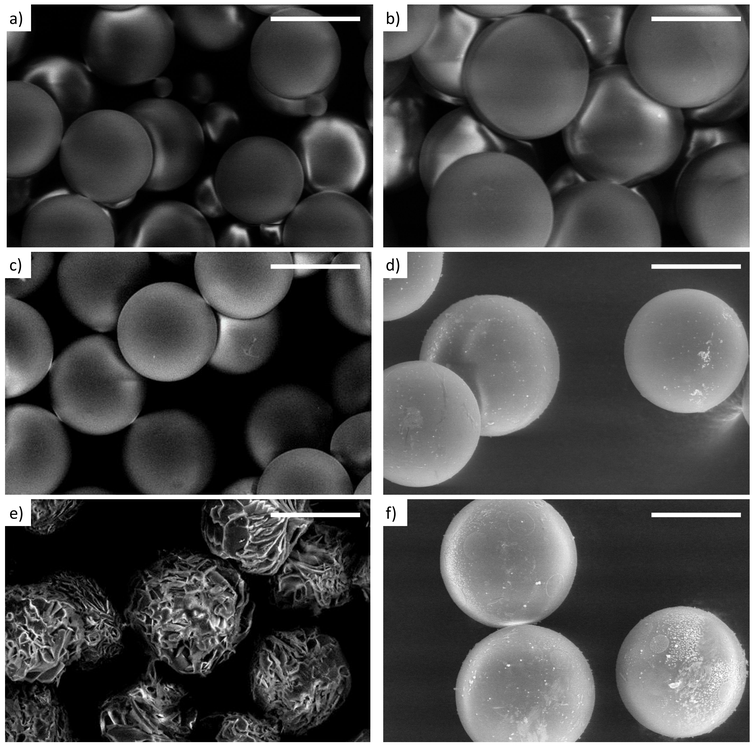


Figure 1. Representative SEM images of prepared microparticle formulations: non-drug loaded PLGA MPs (MP) (a), non-drug loaded cross-linked MPs (xMP) (b), celecoxib (CXB) loaded PLGA MPs at a theoretical loading of 20wt% (CXB20) (c), CXB-loaded crosslinked MPs (xCXB20) at a theoretical loading of 20wt% (d), triamcinolone hexacetonide (TAH) loaded PLGA MPs at a theoretical loading of 20wt% (TAH20) (e), CXB-loaded cross-linked MPs (xCXB60) at a theoretical loading of 60wt% (f). The white scale bars represent 50 µm.

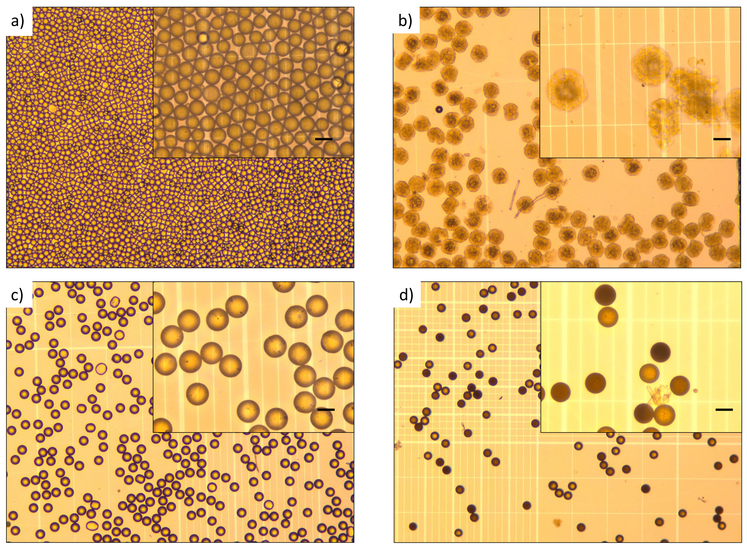


Figure 2. Representative light microscopy image of non-loaded conventional PLGA microparticles (MP) (a). Representative light microscopy image of MP following 16 days under *in vitro* release conditions (b). Representative light microscopy image of non-loaded cross-linked microparticles (xMP) (c). Representative light microscopy image of xMP following 16 days under *in vitro* release conditions (d). The black scale bars represent 50 µm.

RESULTS

	Drug	Theoretical loading (wt%)	Encapsulation efficiency (%)
Conventional	CXB	20	81.8±2.5
	TAH	20	73.8±1.5
Cross-linked	CXB	20	47.4±7.6
	CXB	60	62.9±2.3

Table 1. Tabulated drug-loading results of prepared microparticle formulations. The encapsulation efficiency is calculated by taking the ratio of measured drug loading to the theoretical drug loading. Results are presented as the mean ± standard deviation (n=3).

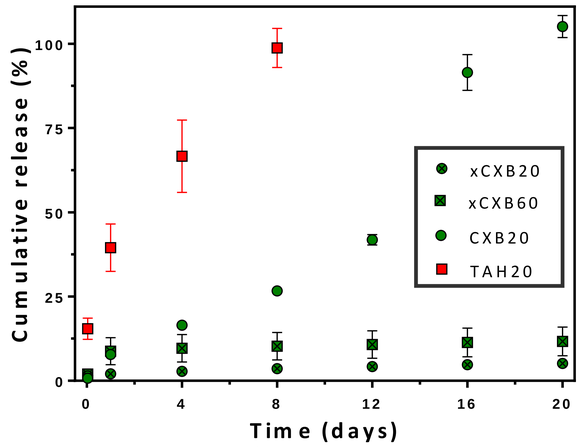


Figure 3. Cumulative *in vitro* release of conventional microparticle formulations loaded with celecoxib (CXB20), triamcinolone hexacetonide (TAH20) at theoretical loading of 20wt%. Cumulative *in vitro* release of cross-linked microparticle formulations loaded with celecoxib at theoretical loading of 20 and 60 wt% (xCXB20 and xCXB60, respectively). Results are presented as the mean ± standard deviation (n=3).

CONCLUSIONS & FUTURE DIRECTIONS

Morphology, loading and *in vitro* release of PLGA MPs was drug-dependent. Cross-linking increased particle stability. Cross-linked particle formation is decoupled from drug loading. Therefore, going forward, it is facile to load a range of drugs (e.g., TAH) into xMP. Additionally, the polymeric matrix could be optimized (i.e., by adjusting the extent and chemistry of cross-linking) to tailor xMP stability.

ACKNOWLEDGEMENTS

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References:

[1] K. Park et al. Journal of Controlled Release. 304 (2019) 125–134 [2] J. Liu et al. Journal of Pharmaceutical Sciences. 93 (2004) 132–143. [3] Z. Bao, et al. Journal of Pharmaceutical Sciences. (2021).