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Novel gradient casting method provides high-throughput assessment of blended polyester poly(lactic-*co*-glycolic acid) thin films for parameter optimization

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ABSTRACT

Pure polymer films cannot meet the diverse range of controlled release and material properties demanded for the fabrication of medical implants or other devices. Additives are added to modulate and optimize thin films for the desired qualities. To characterize the property trends that depend on additive concentration, an assay was designed which involved casting a single polyester poly(lactic-*co*-glycolic acid) (PLGA) film that blends a linear gradient of any PLGA-soluble additive desired. Four gradient PLGA films were produced by blending polyethylene glycol or the more hydrophobic polypropylene glycol. The films were made using a custom glass gradient maker in conjunction with a 180 cm film applicator. These films were characterized in terms of thickness, percent additive, total polymer (PLGA + additive), and controlled drug release using drug-like fluorescent molecules such as coumarin 6 (COU) or fluorescein diacetate (FDAc). Material properties of elongation and modulus were also accessed. Linear gradients of additives were readily generated, with phase separation being the limiting factor. Additive concentration had a Pearson's correlation factor (R) of >0.93 with respect to the per cent total release after 30 days for all gradients characterized. Release of COU had a near zero-order release over the same time period, suggesting that coumarin analogs may be suitable for use in PLGA/polyethylene glycol or PLGA/polypropylene glycol matrices, with each having unique material properties while allowing tuneable drug release. The gradient casting method described has considerable potential in offering higher throughput for optimizing film or coating material properties for medical implants or other devices.

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1. Introduction

When engineering polymeric thin films for medical devices, the research and design (R&D) team must optimize numerous parameters. It is rare for a pure polymer to meet all the considerations required for the function of a device.

To develop the thin films for a specific application, the neat polymer must have various additives incorporated into polymer solutions or melts to meet the final design specifications [1]. These additives are used to modify properties such as controlled drug release [2], surface tension [3], mechanical properties [4,5], adhesion [6], etc. These modifications need to be assessed empirically, hence significant resources in labour and materials are often needed. Complicating the assessment is the influence of the parameters on one another. One additive included to improve a specific property may be deleterious to other functions. For example, adding porogens (pore-forming additives) in thin films increases surface area and diffusional drug release as desired. However, the inclusion may drastically change the mechanical properties to an extent where the thin film is no longer suitable for the intended purpose.

At present, optimizing a film with permutations of several additives is a considerable undertaking which may hinder progress in the R&D process. To address this problem, we have successfully developed a novel procedure of thin film casting that produces additive gradients from 0% to 50%. As displayed in Fig. 1, the design of the custom gradient caster allows up to 100 ml of mixed solution to be cast in one session. The casting allows an ascending polymer ratio vs. length, with maximum lengths of 180 cm possible. The method was designed to provide enough material for analysis using the multiple procedures required for characterization, including mechanical testing, controlled drug release, proton nuclear magnetic resonance (^{1}H NMR) analysis, thickness measurements, etc. The advantages of this technique include lower material investment, labour efficiency, and a higher rate of throughput. Moreover, trends dependent on additive concentration in material and film properties are quickly identified.

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