Modeling and Simulation of Drug Release Through Polymer Matrices

V. Runkana[1], A. Pareek[1], P. Arora[2]

[1]TRDDC, Pune, Maharashtra, India
[2]Indian Institute of Technology Delhi, New Delhi, Delhi, India

Abstract

Limited drug efficacy, undesirable temporal changes in drug concentration and patient non-compliance due to frequent dosing schedule have given impetus to design of controlled drug release systems [1]. Biodegradable polymers due to their favorable and tunable properties and biocompatibility have found widespread use in the field of controlled drug delivery [2]. Exploratory in vitro experiments with controlled drug release formulations have often resulted in various release profiles. Mathematical models that account for phenomena involved in drug release from biodegradable matrices will not only help in understanding the factors influencing the drug release kinetics but also in reducing the number of experiments.

We present a mathematical model, similar to those proposed in the literature previously [3, 4], that includes polymer hydrolysis and degradation kinetics, time dependent pore formation and diffusion of drug. The model utilizes numerical solvers available in COMSOL Multiphysics® to solve the coupled PDEs and its post-processing tools to predict drug release and erosion kinetics of polymer matrices.

The predictions of the model were in accord with experimental studies (see Figure 1). The model correctly predicted different phases observed during drug release studies. It also helped in characterizing the eroding behavior of the polymer matrices (see Figure 2 and 3). A regression model was also developed using the simulated data to estimate conditions needed to obtain desired drug release kinetics.

The mathematical model presented successfully integrates diffusional egress of drug through polymer with its degradation kinetics. Furthermore, it is based on parameters which can be estimated before performing experiments. This will prove helpful in designing controlled drug delivery devices.

Reference

1. Uhrich, Kathryn E., et al., "Polymeric systems for controlled drug release." Chemical reviews 99, no. 11 (1999): 3181-3198.
2. Lisa, Brannon-Peppas. "Polymers in controlled drug delivery." Biomaterials (1997): 1-13.
3. Rothstein, Sam N., et al., "A simple model framework for the prediction of controlled release from bulk eroding polymer matrices." Journal of Materials Chemistry 18, no. 16 (2008): 1873-1880.
4. Rothstein, Sam N., et al., "A unified mathematical model for the prediction of controlled release from surface and bulk eroding polymer matrices." Biomaterials 30, no. 8 (2009): 1657-1664.
5. Cui, Fude, et al., "Preparation and characterization of melittin-loaded poly (DL-lactic acid) or poly (DL-lactic-co-glycolic acid) microspheres made by the double emulsion method." Journal of Controlled Release 107, no. 2 (2005): 310-319

Figures used in the abstract

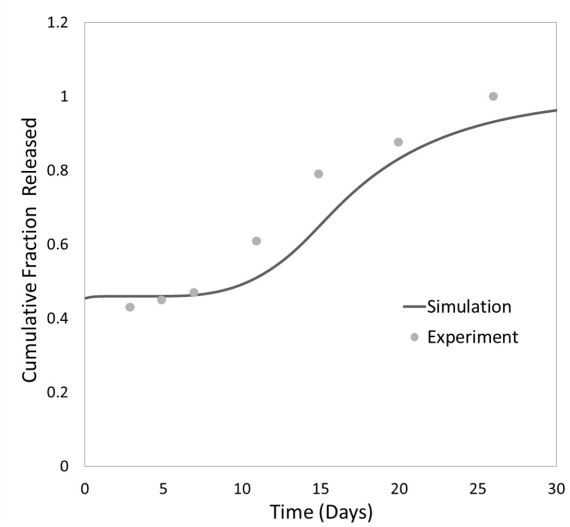

Figure 1: Simulated vs Experimental data for a drug released from PLGA microparticles [5].

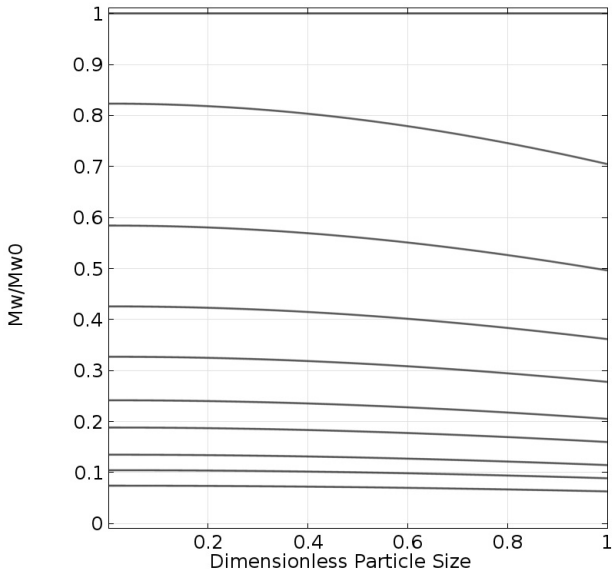

Figure 2: Temporal and Radial variation of Molecular weight of a Polyanhydride particle of size 0.2 mm.

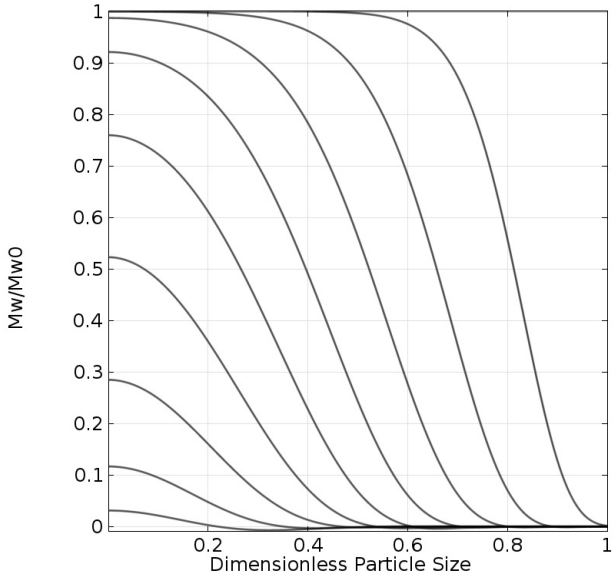

Figure 3: Temporal and Radial variation of Molecular weight of a Polyanhydride particle of size 5 mm.