Simulation and Experimental Analysis of Drug Release Rates from Magnetic Nanocomposite Spheres

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Introduction: Breast cancer is the second leading cause of death among female cancer patients. However, if detected early, breast cancer can be treated through surgery followed by post-surgery treatment interventions including radiation therapy, hormone therapy and chemotherapy [1]. One of the major issues in cancer therapy is the toxicity of chemotherapeutic agents, therefore it is desired to target the chemotherapeutic drug to the tumor site instead of circulating it through the body. Nanotechnology has received significant attention in many biomedical applications, such as drug delivery, biosensors, and scaffolding for over 10 years. Nanoparticles can be attached to the small molecules of the drugs and serve as drug carriers to deliver the drug molecules into the area of interest [2]. In this research, polymeric microspheres containing biodegradable poly(D, L-lactide-co-glycolide) (PLGA), magnetic nanoparticles and albumin were incorporated with a cancer therapeutic drug (Cyclophosphamide) and the drug release behavior from PLGA microspheres was studied in-vitro in PBS solution. PLGA is a biodegradable polymer and its rate of degradation has an important role in the drug release mechanism. Figure 1 shows a schematic release mechanism of PLGA microspheres. There is a burst release at the beginning followed by a slow release stage mainly due to diffusion and finally the degradation of the microsphere will cause the second burst release. The experimental release behavior was studied for 72 hours and the second burst release was not observed since PLGA starts degradation in 8 days [3]. The release behavior of drug loaded microspheres was also simulated in COMSOL multi-physics and the results were compared with the experimental data.

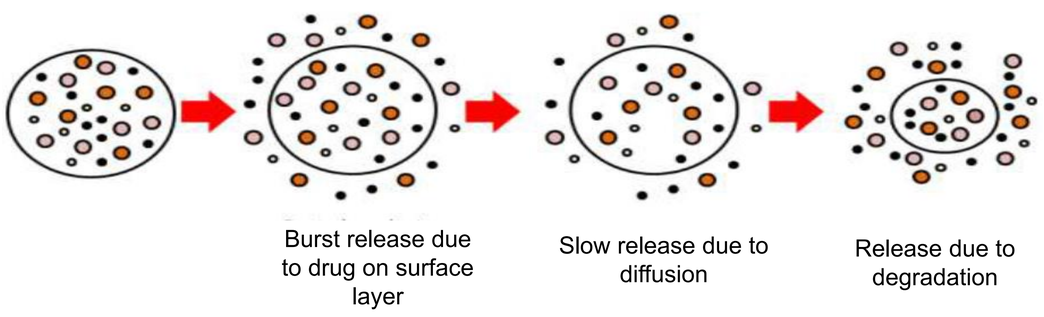

Figure 1. Release mechanism from PLGA microsphere [3]

Computational Methods: This simulation was performed using COMSOL multi-physics.. The drug loaded PLGA microspheres were simulated in a PBS solution medium in a 2D geometry. Fick's law of diffusion was used to simulate the drug release behavior. A time dependent analysis study was done to measure the concentration of the released drug into the medium in a period of 72 hours.

$$\frac{\partial c_i}{\partial t} + \nabla \cdot (-D_i \nabla c_i) + u \cdot \nabla c_i = R_i$$

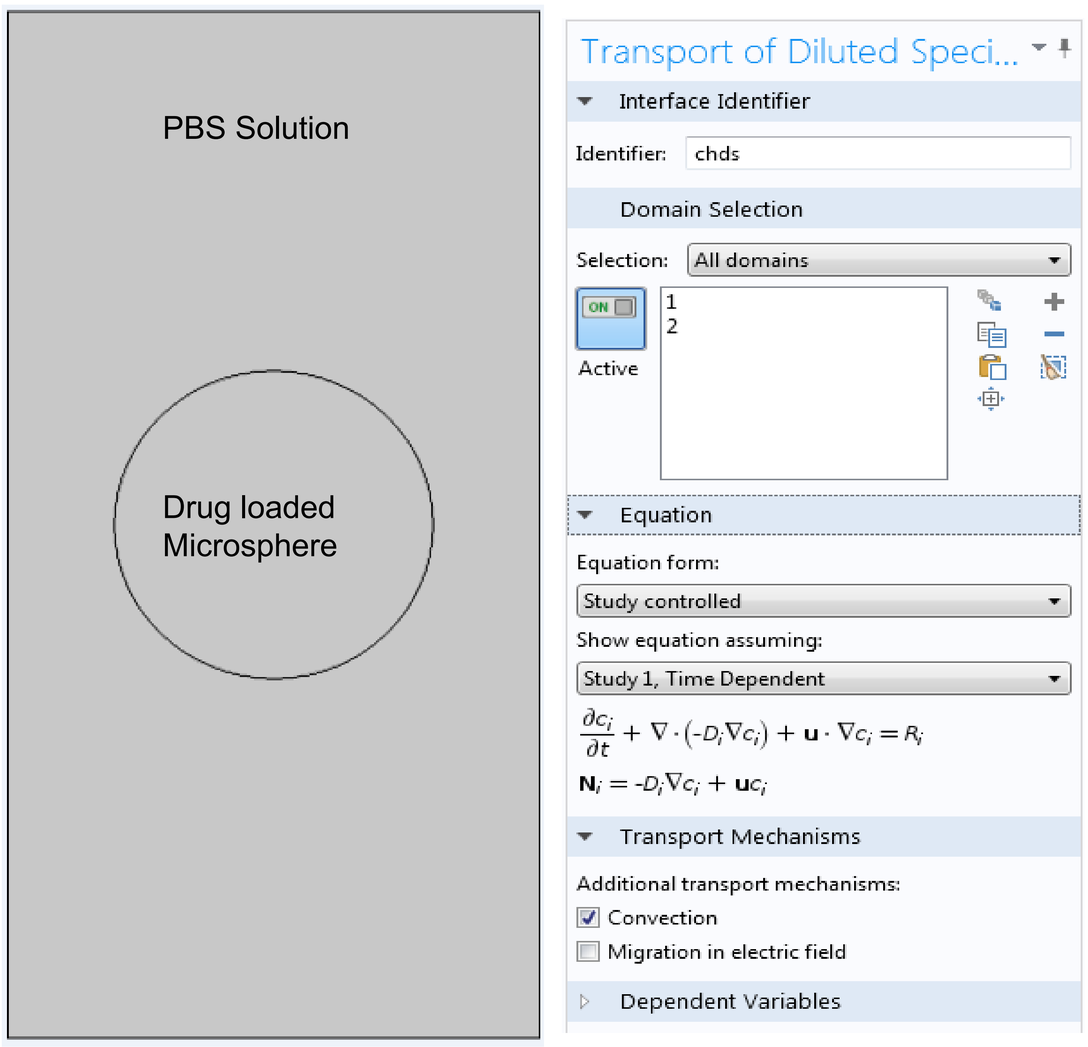

Figure 2. Model Description

Results:

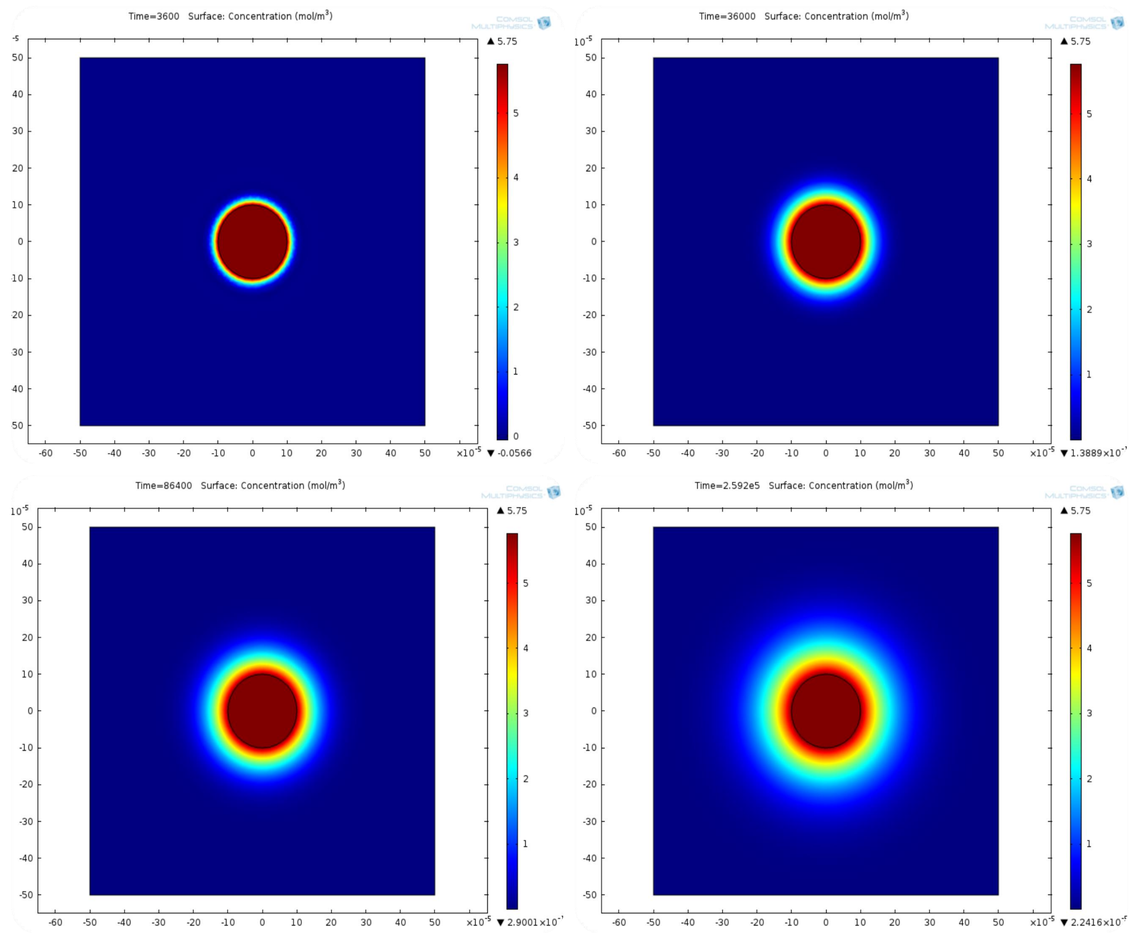

Figure 3. Concentration timeline

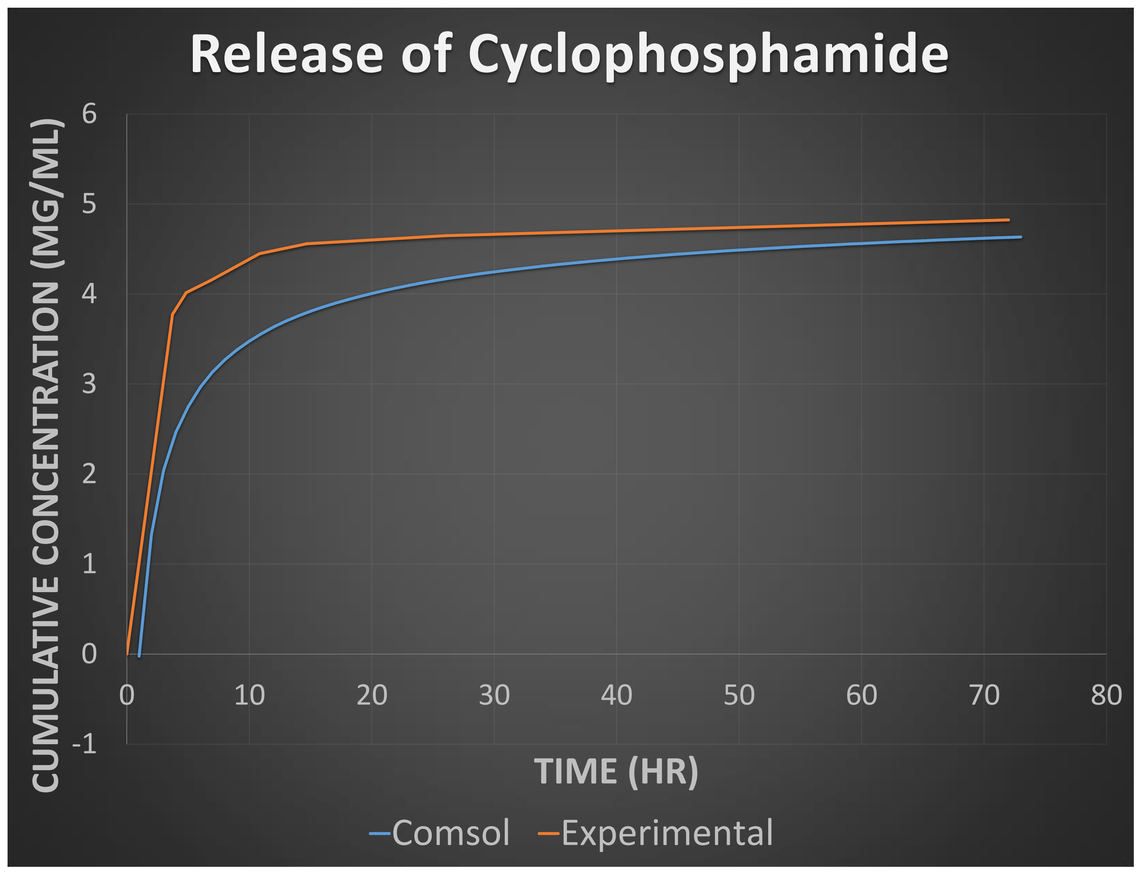

Figure 4. Release profile of cyclophosphamide from PLGA microsphere

Conclusion: In this study the experimental data of in-vitro drug release from PLGA microspheres were simulated in COMSOL multiphysics. The surface concentration analysis was done to measure the released concentration of the drug into the media in a time period of 72 hours. It was observed that the simulation result were in agreement with the experimental data. The first and second stages of the drug release mechanism of PLGA were apparent in the experimental data as well as the simulation results. However the second burst release due to the degradation of PLGA microspheres did not occur in 72 hours.

References:

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3. F. Abedin, "Magnetic and albumin targeted drug delivery for breast cancer treatment," Master of Science Thesis, Department of Mechanical Engineering, Wichita State University, USA, 2011.