University of Victoria | Graduate Studies

Notice of the Final Oral Examination
for the Degree of Doctor of Philosophy

of

AMANDEEP BAINS

BSc (Simon Fraser University, 2012)

"Microfluidic Synthesis of Block Copolymer Nanoparticles for Drug Delivery"

Department of Chemistry

Wednesday, April 20, 2016
2:00 P.M.
Elliott Building
Room 305

Supervisory Committee:
Dr. Matt Moffitt, Department of Chemistry, University of Victoria (Supervisor)
Dr. David Harrington, Department of Chemistry, UVic (Member)
Dr. Dennis Hore, Department of Chemistry, UVic (Member)
Dr. Stephanie Willerth, Department of Mechanical Engineering, UVic (Outside Member)

External Examiner:
Dr. Helen Burt, Department of Research and International, University of British Columbia

Chair of Oral Examination:
Dr. Rustom Bhiladvala, Department of Mechanical Engineering, UVic

Dr. David Capson, Dean, Faculty of Graduate Studies

Abstract

In this dissertation, we studied two-phase microfluidics as a platform for the controlled synthesis of drug delivery polymeric nanoparticles (PNPs). The block copolymer we studied was poly(ε-caprolactone)-*block*-poly(ethylene oxide) (PCL-*b*-PEO). The anticancer drug we studied was paclitaxel (PAX). First, we explored microfluidic control of nanoparticle structure (size, morphology, and core crystallinity) on PCL-*b*-PEO PNPs without loaded PAX. We demonstrated the reproducible variability of PCL-*b*-PEO nanoparticle size and morphology. Microfluidic control of nanoparticle size and morphology was found to arise from the interplay of flow-induced particle coalescence and breakup. Next, we demonstrated the linear dependence of PCL core crystallization on flow-rate. We attributed this dependence of PCL core crystallization on flow-induced crystallization.

We then used our microfluidic device to control PAX-loaded PNP structure and function (small molecule loading efficiency, diffusional release kinetics, and cytotoxicity). At low drug loading ratios ($r < 0.1$), we demonstrated reproducible variability of PAX-loaded PNP size and morphology. With increasing flow rate we were able to manufacture PNPs of high aggregation number. We were also able to reproducibly demonstrate the linear dependence of PCL core crystallinity on flow rate. Furthermore, PAX loading efficiency was dependent on PNP size and morphology. Formulations which consisted of cylindrical and lamellar type morphologies typically had higher PAX loading efficiencies, than formulations which consisted of spherical structures. Next, we studied diffusional PAX release, increasing core crystallinity correlated with slowing diffusional PAX release kinetics.

At high drug loading ratios ($r > 0.1$), we demonstrated reproducible control of PAX-loaded PNP structure and function. PCL core crystallinity was a major factor influencing PNP size and morphology. Samples with high core crystallinity formed PNP structures with low internal curvature. Furthermore, core crystallization had a large influence on PAX loading efficiency; as samples with high PAX loading efficiency correlated with low PCL core crystallinity. With respect to diffusional PAX release, we found that increasing PCL core crystallinity correlated with slowing diffusional PAX release kinetics. Next, we studied the cytotoxicity of our PAX-loaded PNPs using the MCF-7 cancer cell line. Due to the complex nature of the interactions between our PAX-loaded PNPs and the cancer cells, we were not able to elucidate the exact influence of flow rate on PNP cytotoxicity.