Notice of the Final Oral Examination
for the Degree of Master of Science

of

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BSc (Nankai University, 2014)

“Microfluidic Synthesis of Drug-Loaded Block Copolymer Nanoparticles and its Effect on Drug Delivery”

Department of Chemistry

Thursday, January 12, 2017
9:30 A.M.
Human and Social Development Building
Room A264

Supervisory Committee:
Dr. Matthew Moffitt, Department of Chemistry, University of Victoria (Supervisor)
Dr. Fraser Hof, Department of Chemistry, UVic (Member)

External Examiner:
Dr. Stephanie Willerth, Department of Mechanical Engineering, UVic

Chair of Oral Examination:
Dr. Conrad Alexandrowicz, Theater Department, UVic

Dr. David Capson, Dean, Faculty of Graduate Studies
Abstract

In this thesis, we used a two-phase gas-liquid segmented microfluidic platform to synthesize drug-loaded block copolymer nanoparticles. In Chapter 2 and 3, the anti-cancer drug 7-ethyl-10-hydroxycamptothecin (SN-38) was physically encapsulated in poly(6-methyl-caprolactone-co-ε-caprolactone)-block-poly(ethylene oxide) (P(MCL-co-CL)-b-PEO) nanoparticles with various drug-to-polymer loading ratios, under different flow conditions. The effects of chemical and flow conditions on the size, morphology, drug loading efficiency, \textit{in vitro} release and (in Chapter 3) cytotoxicity of the nanoparticles were determined. For various loading ratios, the intermediate total flow rate ($Q = 200$ μL/min) produced the smallest nanoparticle sizes and pure spheres. The various nanoparticle preparation conditions showed flow-variable release rates and cytotoxicities against MCF-7 cancer cell line. Specifically, we found that release half times of SN-38 from the nanoparticles showed from $\tau_{1/2} = 0.8$ to 3.3 h as the total flow rate increased from $Q = 50$ to 200 μL/min. We also found that the cytotoxic response of all SN-38 formulations were stronger than that of free SN-38. As well, at short and intermediate incubation time (48 and 72 h), the cytotoxic potency of microfluidic nanoparticles prepared at $Q = 200$ μL/min were slightly higher than nanoparticles prepared using a conventional bulk method, while potencies of microfluidic nanoparticles prepared at higher and lower flow rates were slightly lower than the bulk control. In Chapter 4, in order to pursue even higher shear rate and increased throughput, we investigated the same gas-liquid microfluidic reactor design used in Chapters 2 and 3 but made from silicon/glass, which supported higher internal pressures than PDMS chips used in the earlier chapters. A comparison between the two microfluidic reactor materials at constant liquid flow rate showed that channel material affected both flow behaviour and the resulting nanoparticle morphologies. A new, single-phase microfluidic strategy was also proposed in order to generate high shear, in which variable high and low shear would arise from periodic changes in channel dimensions. Unfortunately, initial attempts to run this microreactor lead to clogging of the more narrow microchannels which will require further improvements in either reactor design or the microfabrication process.