Development Of Stealth Poly-Ɛ-Caprolactone Nanoparticles For The Delivery Of Bioactive Agents

Ogunwuyi Oluwaseun*, Akala Emmanuel*

* Department of Pharmaceutical Sciences, College of Pharmacy,
Howard University, Washington, DC 20059 eakala@howard.edu

ABSTRACT

Poly-ε-caprolactone belongs to the group of biodegradable polyesters such as poly(lactic acid), polyglycolic acid and poly(lactide-co-glycolide). The use poly-ε-caprolactone cuts across a number of biomedical areas: biomaterials (sutures) and drug delivery. In this study, poly-ε-caprolactone was fabricated into a stealth crosslinked biodegradable nanoparticle by the *in situ* dispersion polymerization method for subsequent use as a delivery system for bioactive agents.

Keywords: polyesters, poly-ε-caprolactone nanoparticles, *in situ* dispersion polymerization, bioactive agents

1 INTRODUCTION

Polyesters have received a lot of attention in recent time. They are the most widely used polymers in biomedical applications because they are biodegradable, biocompatible, non-immunogenic, non-toxic and are approved for use *in vivo* by the Food and Drug Administration (FDA) [1]. The polyesters include poly(lactic acid), poly glycolic acid, poly(lactide-co-glycolide), and poly-ε- caprolactone. Over the years, polyesters have been fabricated into nanoparticles using preformed polymers. In recent time, *in-situ* polymerization technique is being applied to the fabrication of nanoparticles. The technique has a lot advantages such as the opportunity to tether various materials to the nanoparticles and one step synthesis of the nanoparticles [2, 3]. In this study, stealth poly-ε-caprolactone nanoparticles have been fabricated by the *in-situ* dispersion polymerization method. However, prior to the use of the ε-caprolactone as a macromonomer, it was end-functionalized to give it a polymerizable end-group. The nanoparticles were analyzed by scanning electron microscopy and particle size determinations.

2 OBJECTIVES

Our long term goal is to prepare and characterize long-circulating, drug-loaded, biodegradable, crosslinked stealth nanospheres capable of spatial (targeting) and temporal delivery of bioactive agents. The present work seeks to develop conditions for the fabrication of stealth poly-ε-caprolactone nanoparticles suitable for the delivery of bioactive agents.

3 EXPERIMENTAL METHODS

Dispersion of preformed polymers or *in situ* polymerization of monomers are the two main approaches used for the fabrication of polymeric nanoparticles. *In situ* dispersion polymerization was used in this work. The macromonomer used in the fabrication of nanoparticles was synthesized by ring opening polymerization of ε-caprolactone. Molecular weight of the synthesized macromonomer was determined using a Waters 2690 Gel Permeation Chromathography (GPC) with polystyrene standards for calibration and tetrahydrofuran as the mobile phase. Proton NMR (^{1}H-NMR) was also used for molecular weight determination. FT-IR spectrophotometric analysis of the structure of the macromonomer was carried out using a Perkin Elmer Spectrum 100 FT-IR spectrometer. ^{1}H NMR spectrophotometric analysis for the structure of the macromonomer was done using a Bruker AVANCE 400 MHz NMR spectrophotometer. To fabricate nanoparticles, the macromonomer, the stabilizer and the cross-linking agent were dissolved in a suitable solvent system. At appropriate time intervals, the initiators were injected into the system, and polymerization was allowed to continue overnight. The nanoparticles were purified by dynamic dialysis and freeze dried. The surface morphology of the nanoparticles was investigated by Scanning Electron Microscopy (SEM) using the FEI Quanta 200F environmental scanning electron microscope (Figure 1). The average particle size, particle size distribution, and zeta potential were determined by dynamic light scattering using a Zetasizer Nano-ZS (Malvern Instruments, USA) (Figures 2 & 3).

4 RESULTS & DISCUSSION

Increase in the amount of HEMA resulted in a concomitant decrease in the molecular weight of the end-functionlaized macromonomer. The molecular weight of the macromonomer decreased with decrease in the mole ratio of ε-caprolactone : HEMA. The macromonomers were used successfully to fabricate nanoparticles. The choice of the solvent system is very critical in determining the formation and morphology of polycaprolactone nanoparticles. Solvent systems with different polarities and

solubility parameters produced different effects. Particle size distribution studies gave values in the nanometer range, which provides a promise for the development of nanotechnology platform for drug delivery. Zeta potential determinations provided negative values in the range -13 to -36.6. Thus, the pegylated poly-ε- caprolactone-based nanoparticles studied in this work shows promise as drug delivery system capable of carrying the bioactive agents to its site of action [4, 5]. Further work is ongoing to optimize the poly- ε-caprolactone nanoparticle formulations.

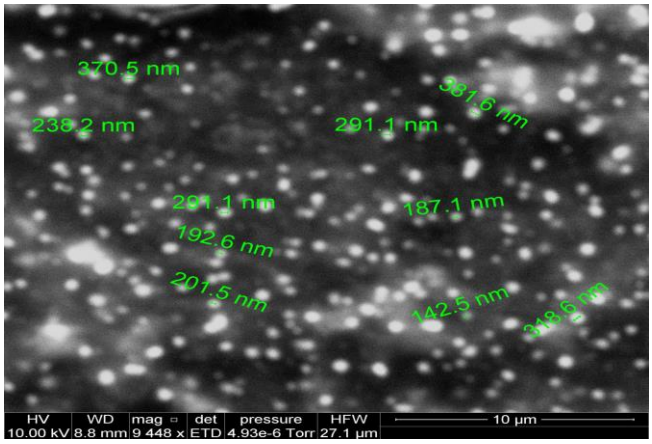

Figure 1: A Typical Scanning Electron Micrograph of Stealth Crosslinked PCL-HEMA Nanoparticles

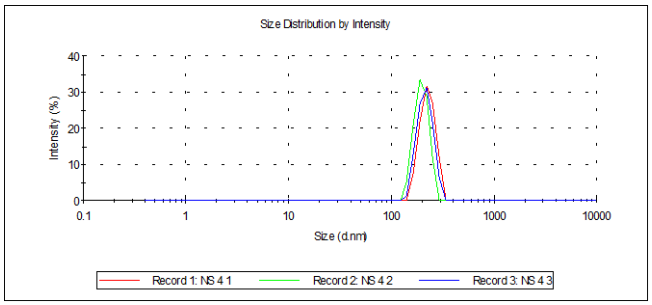

Figure 2: A Typical Particle Size Distribution of Stealth Crosslinked PCL-HEMA Nanoparticles

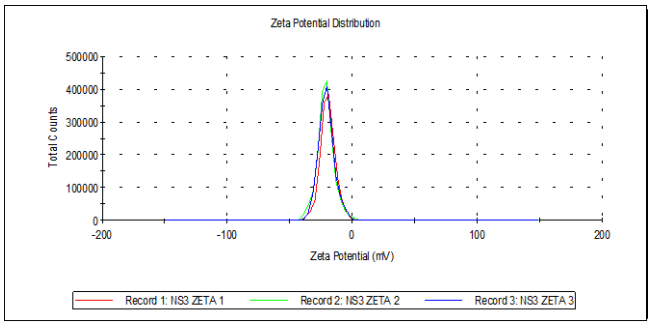

Figure 3: A Typical Zeta Potential of Stealth Crosslinked PCL-HEMA Nanoparticles

5 CONCULSION

Stealth poly-ε-caprolactone nanoparticles have been synthezisized by *in-situ* dispersion polymerization method. Morphology of the nanoparticles has been analyzed by scanning electron microscopy, and particle size distribution and zeta potential have been determined using zetasizer. Further work is ongoing to optimize the nanoparticulate formulations with a view to using the biodegradable nanoparticles for *in-vivo* delivery of bioactive agents.

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