Microfluidic platforms for the synthesis of Chitosan and Glycol Chitosan nanoparticles.

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Abstract

Microfluidics is a multidisciplinary technological field that explores the manipulation of small amounts of fluids in miniaturized systems, allowing the manipulation of single or multiphase flows and promoting new routes to the production of polymer particles. Chitosan is a cationic biopolymer applied in pharmaceutical and medical fields, including drug and gene delivery. When glycosylated, it presents a broader biological applicability due to its solubility in water at all pH conditions. This research explores the synthesis of chitosan and glycol chitosan nanoparticles with polyelectrolyte sodium tripolyphosphate (TPP), using a microfluidic process configuration with a central aqueous stream. The produced nanoparticles were characterized in terms of zeta potential, hydrodynamic diameter and polydispersity index.

Key words:

Microfluidics, chitosan, glycol chitosan.

Introduction

Gene therapy refers to intracellular transfer of therapeutic nucleic acid to modulate cellular functions[1]. Chitosan (CHI) is an excellent biopolymer in drug and gene delivery systems due to its biocompatibility, biodegradability, and low toxicity[2]. As glycol chitosan (GlyCHI) is soluble in water at neutral pH, it presents a broader biological applicability, compared to CHI, which is only soluble in water at acid conditions. One of the most applied methods for obtaining CHI nanoparticles is ionic gelation, based on electrostatic interaction between CHI and anionic polyelectrolytes, such as sodium tripolyphosphate (TPP)[3]. Among the production techniques, microfluidics is characterized by the manipulation of fluids in micrometric scale systems, allowing the production of nanoparticles in reproducible processes[4].

This work analyzed the production of CHI and GlyCHI/TPP nanoparticles using a microfluidic process configuration based on hydrodynamic flow focusing with a central aqueous stream[5] in long design channel (Fig. 1). The effects of CHI/TPP mass ratio ($R_{CHI/TPP}$), final outlet CHI concentration and pH on nanoparticles zeta potential, size and polydispersity index (PDI) were evaluated, using a Zetasizer Nano ZS (Malvern Instruments).

Results and Discussion

The production of CHI/TPP nanoparticles at pH 4 with the final outlet CHI concentration of 0,4 mg.mL^{-1} and $R_{CHI/TPP}$ varying between 2 and 6 was evaluated. However, we were not able to obtain nanoparticles with appropriate sizes and low PDI values, pointing out that optimizations are necessary and different parameters ought to be investigated. On the other hand, GlyCHI/TPP nanoparticles produced at pH 4 and mass ratio ($R_{GlyCHI/TPP}$) of 2 reached better properties for gene delivery, including positive zeta potential, sizes around 150 nm and low PDI (Fig. 2).

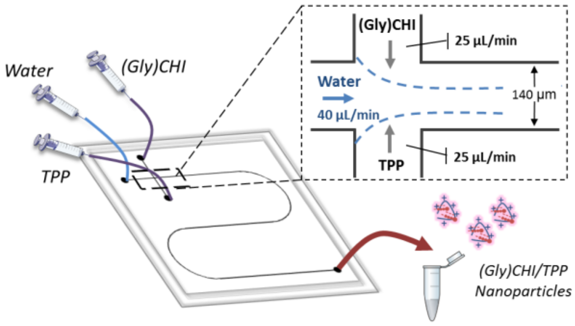

Figure 1. Schematic diagram of the microfluidic device applied for (Gly)CHI/TPP nanoparticles synthesis.

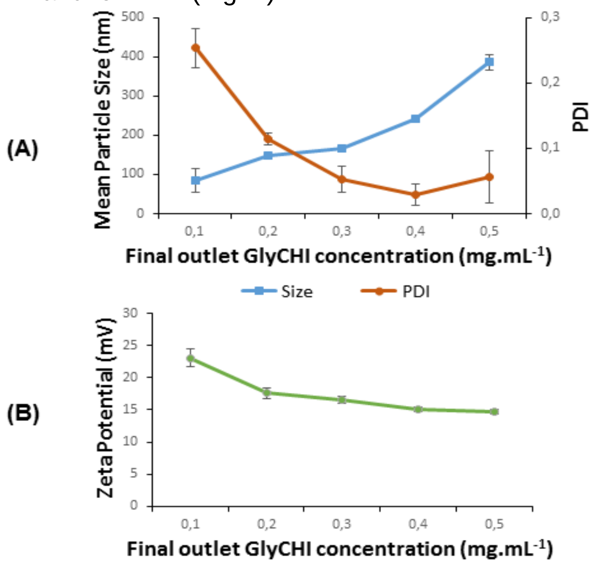

Figure 2. Effects of final outlet GlyCHI concentration on **(A)** particle size (number-weighted), PDI and **(B)** zeta potential for the production of GlyCHI/TPP nanoparticles.

Conclusions

Although further investigations are necessary to successfully achieve CHI/TPP nanoparticles synthesis, the applied microfluidic system allowed the formation of GlyCHI/TPP nanoparticles for different final outlet GlyCHI concentrations with adequate features for gene delivery applications.

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