Continuous Synthesis of Bio-Inspired Silica using Fluidic Devices

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Highlights

- Bio-inspired silica was synthesized using various continuous fluidic reactors.
- The developed synthesis protocol is rapid and has mild operating conditions.
- The synthesized silica has higher surface areas up to 385 m^2/g.
- Micromixing/ Engulfment model was developed to fit the kinetic data.

1. Introduction

Personalized medicine (PM) is gaining significant attention in recent years as it has the potential to transform healthcare across the globe. Current bulk manufacturing technologies are unsuitable for meeting the needs of PM and there is a need to develop novel continuous distributed manufacturing platforms. Unlike efforts on the manufacturing of active pharmaceutical ingredients (API), on-demand and distributed manufacturing of next-generation excipients and drug delivery systems like silica are not addressed yet. We have recently developed a bio-inspired silica (BIS) synthesis method with a mild & rapid reaction and calcination-free process [1]. In an effort to intensify the synthesis and enable its scale-up, here we are presenting the first steps towards developing a continuous process using different fluidic devices. Based on recent work in our group (Madane & Ranade, 2022 [2]; Yang Yu et al. 2022 [3]), we have selected a fluidic oscillator (FO), vortex diode (VD), and helical coil (HC) in this work. We aim to investigate the influence of mixing and residence time distribution on the silica properties and yield. The results and analysis will provide a sound basis for designing distributed manufacturing of tailored silica particles needed for PM.

2. Experimental Method

Stock solutions of sodium silicate pentahydrate (2.0 M), pentaehtylenehexamine (PEHA) (0.166 M), and HCl (2.0 M) were prepared in DI water. Using these stock solutions, 1 L combined feed solution of silicate (60 mM) and PEHA (10 mM) was prepared. The second feed solution consists of 1 L of HCl solution (0.15 M). In some experiments, feed concentrations were doubled for all reactants. Figure 1A shows the experimental schematic. KNF SIMDOS 10 Diaphragm Metering Pumps were used to dose both the reagents at equal flowrate into the reactor/fluidic device or their combinations (HC, FO, VD, and CSTR). The residence time was 5 min for most of the experiments. A recirculation pump with a flowrate of ~ 1.5 LPM was used in the case of FO and VD. Two steady-state samples were collected separately in a stirred beaker for 30 min each. The first "as synthesized" sample was directly centrifuged, washed, and dried. The second "eluted" sample was treated with hydrochloric acid to achieve pH 2 (PEHA removal step) and then centrifuged, washed, and dried. The synthesized samples were further characterized for measuring their BET surface area, zeta potential, particle size distribution, & SEM.

3. Results and discussion

Initially, batch experiments were performed to understand the synthesis protocol in the literature [1]. Continuous experiments were performed using various reactors viz. HC, FO, VD, and CSTR. The residence time for most of the experiments was 5 min. The steady-state sample was collected after 4-5 residence times. The continuous experiments were operated for at least 15 residence times without any clogging issues at a 30 mM concentration of sodium silicate. The silica product was further characterized by measuring surface area, zeta potential, particle size distribution, and SEM imaging. Surface area. porosity and zeta potential are significant for drug delivery applications. Figure 2 shows the surface area

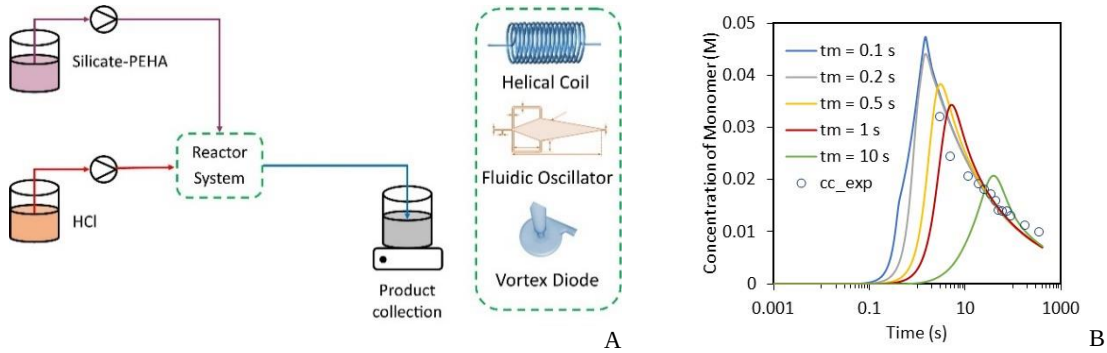

Figure 1. A: Experimental schematic for continuous synthesis of bio-inspired silica, and B: Kinetic data fitted using engulfment model with different mixing time

and zeta potential. These properties strongly depend on the pH (synthesis and work-up) and type of ammine additive used. The yield for continuous experiments is typically in the range of 50-60% with a 30 mM concentration of sodium silicate. Here we are investigating the effect of mixing on the silica properties. The micromixing time can be manipulated by using different fluidic devices and flowrates as discussed before. We have also developed an engulfment model for estimating lumped kinetic parameters (see Figure 1B). Figure 2 shows the surface area and zeta potential of the synthesized silica.

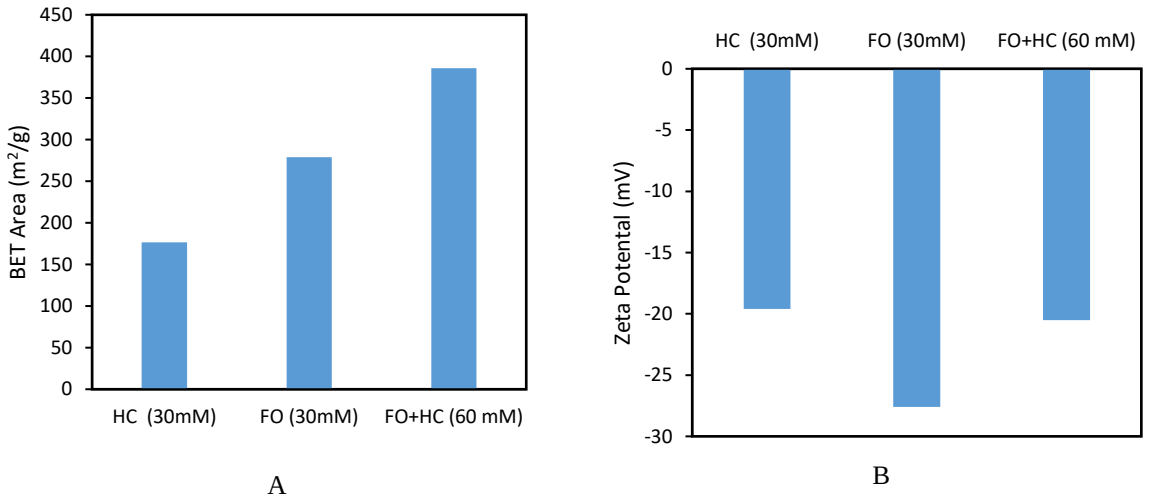

Figure 2. Properties of synthesized silica after acid treatment (pH = 2). A: BET surface area and B: Zeta potential.

4. Conclusions

We have investigated continuous BIS synthesis using different fluidic devices viz. helical coil, fluidic oscillator, vortex diode, CSTR, and their combinations. The silica product was characterized using BET surface area, zeta potential, particle size distribution, and SEM. The surface area and zeta potential of the synthesized silica were in the range of 176 to 385 m^2/g and -19 to -27 mV respectively. We also developed an engulfment model for the fitting kinetic parameter for the bio-inspired silica. Currently, the study of the effect of mixing on particle properties and optimization studies is in progress. The developed results will be used for building a factory in a box for continuous bio-inspired silica synthesis.

References

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