

## Supplementary Information

### Effects of Diffusion and Mixing pattern on Microfluidic-Assisted Synthesis of Chitosan/ATP Nanoparticles

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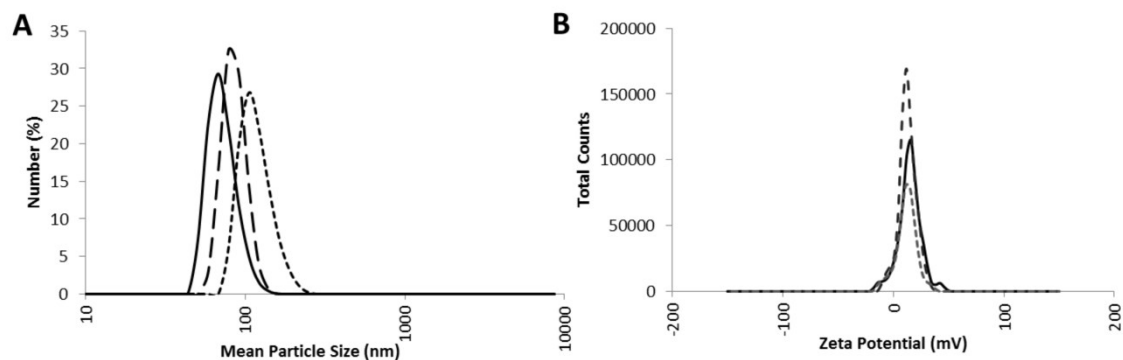
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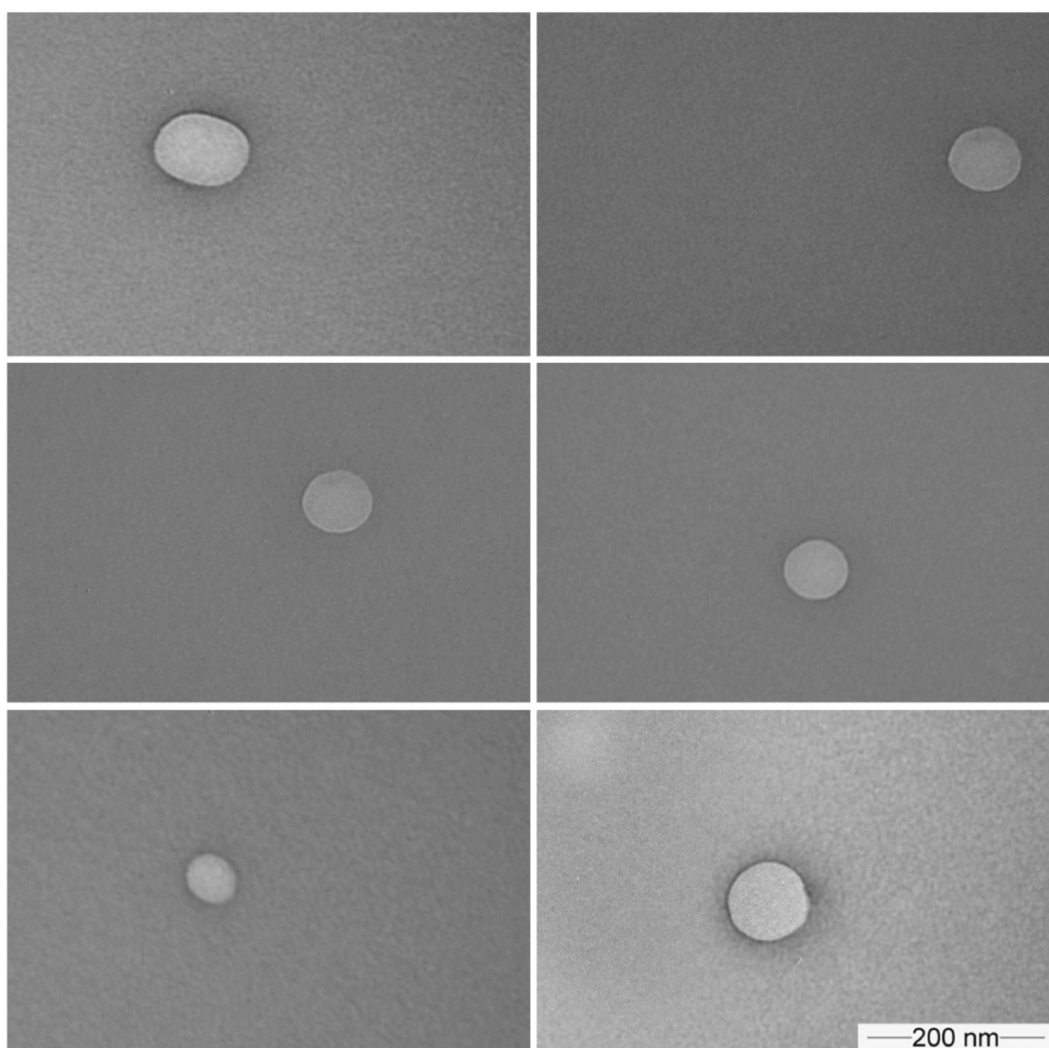
#### Abbreviations

|                                 |   |
|---------------------------------|---|
| ATP                             | Adenosine triphosphate                                  |
| $C_{\text{CHI, ATP}}$           | Inlet Streams Concentrations                            |
| CAS                             | Central Aqueous Stream                                  |
| CHI                             | Chitosan  |
| D-simple                        | Hydrodynamic flow focusing device in Simple Design      |
| D-long                          | Hydrodynamic flow focusing device in Long Design        |
| D-bends                         | Hydrodynamic flow focusing device in Design of Bends    |
| D-barriers                      | Hydrodynamic flow focusing device in Design of Barriers |
| FRR                             | Flow Rate Ratio   |
| PDI                             | Polydispersity index                                    |
| PDMS                            | Polydimethylsiloxane                                    |
| $Q_{\text{T, CHI, ATP, WATER}}$ | Volumetric Flow Rate ( $\mu\text{L}/\text{min}$ )       |
| $R_{\text{CHI/ATP}}$            | CHI/ATP Mass Ratio                                      |
| $V_f$                           | Total Fluid Flow Velocity ( $\text{mm}/\text{s}$ )      |
| $w_0$                           | Width of the microchannel                               |
| $w_f$                           | Width of the focused stream                             |

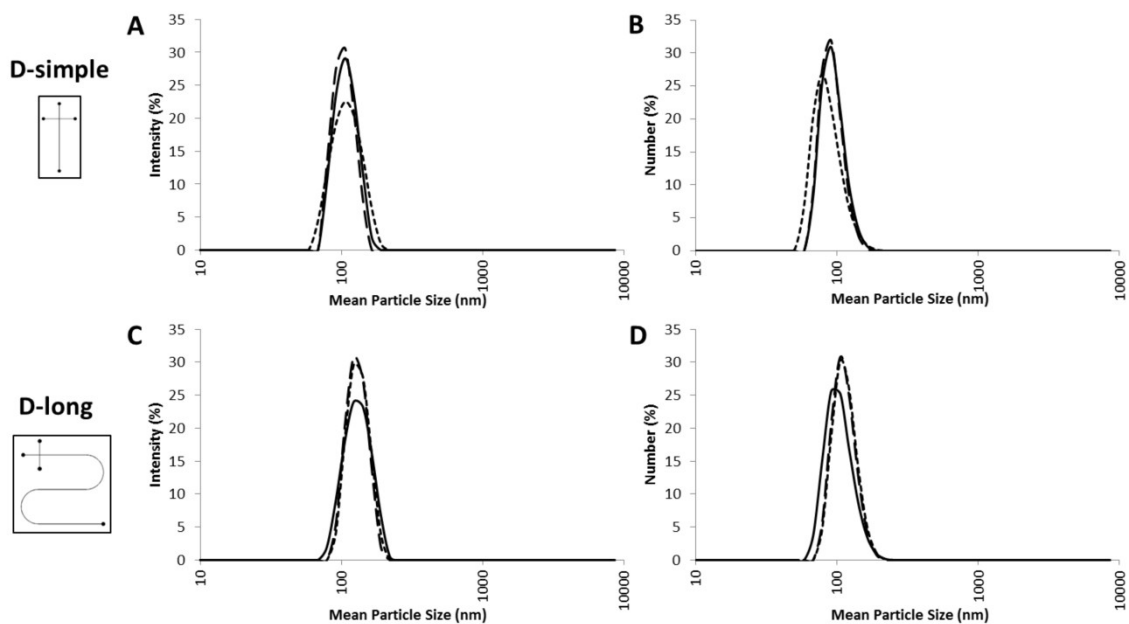
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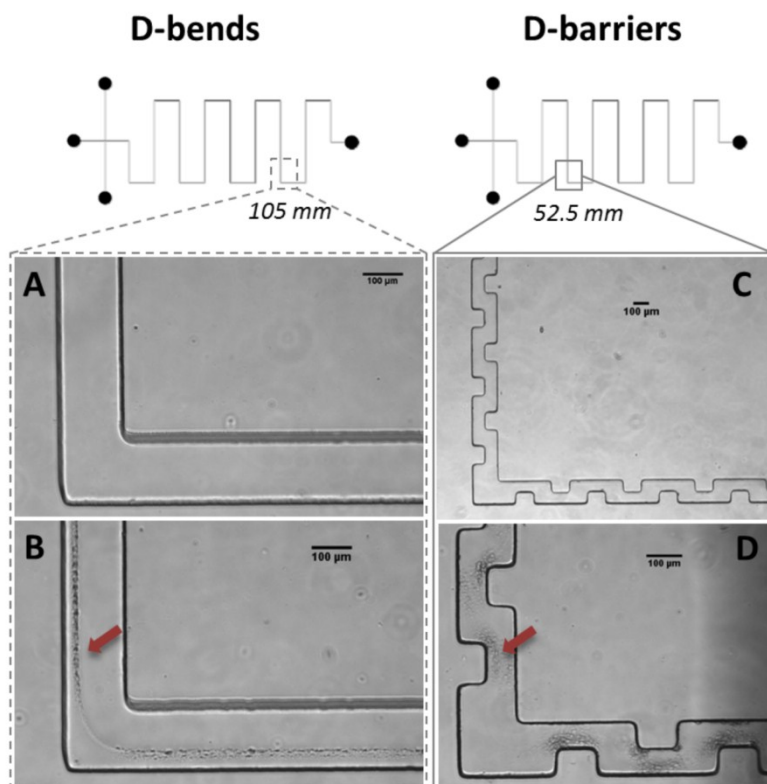
**Fig. S1.** Physicochemical characterization of CHI/ATP nanoparticles produced by conventional bulk synthesis at  $R_{\text{CHI/ATP}}$  of 0.5. The lines represent number-weighted (A) and zeta potential (B) distributions for independent triplicates.



**Fig. S2.** Transmission electron micrographs of CHI/ATP nanoparticles produced by Central Aqueous Stream (CAS) configuration using microfluidic device in Simple Design (D-simple). Production conditions:  $Q_{\text{WATER}}$  of 40  $\mu\text{L}/\text{min}$ ,  $Q_{\text{CHI}} = Q_{\text{ATP}}$  of 25  $\mu\text{L}/\text{min}$ ,  $R_{\text{CHI/ATP}}$  of 0.5 and  $C_{\text{fCHI}}$  of 0.14 mg/mL. The images are representative of three different independent experiments. The bar represents 200 nm.



**Fig. S3.** Intensity and number-weighted size distribution of CHI/ATP nanoparticles synthesized applying the Central Aqueous Stream (CAS) configuration using microfluidic devices in Simple Design (D-simple) (A-B) and Long Design (D-long) (C-D). The lines represent size distributions of CHI/ATP nanoparticles obtained from independent triplicates. Production conditions: FRR of 1.3,  $Q_{\text{WATER}}$  of 40  $\mu\text{L}/\text{min}$ ,  $Q_{\text{CHI}}$  and  $Q_{\text{ATP}}$  of 25  $\mu\text{L}/\text{min}$ ,  $R_{\text{CHI/ATP}}$  of 0.5 and  $C_{\text{fCHI}}$  of 0.14 mg/mL.



**Fig. S4 –** Microstructures (indicated by red arrows) observed during the synthesis of CHI/ATP nanoparticles of  $R_{\text{CHI/ATP}}$  of 1.5 investigated applying Central Aqueous Stream (CAS) process configuration using microfluidic devices in Design of Bends (D-bends) (A-B) and in Design of Barriers (D-barriers) (C-D). Microscopic images taken at different process time points: (A) and (C)  $t = 0$ ; (B) and (D)  $t = 15$  min. Production conditions:  $R_{\text{CHI/ATP}}$  of 1.5, FRR of 1.3,  $Q_{\text{WATER}}$  of 40  $\mu\text{L}/\text{min}$ ,  $Q_{\text{CHI}}$  and  $Q_{\text{ATP}}$  of 25  $\mu\text{L}/\text{min}$ , and  $C_{\text{fCHI}}$  of 0.14 mg/mL.