Towards sustainable preparation of oral solid dosage form of drug nanoparticles

Jia, Tong

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NANYANG TECHNOLOGICAL UNIVERSITY

URECA
Undergraduate Research Experience on CAMpus

Category: 6 **Student: Jia Tong** **Project ID: SCBE11013**
School of Chemical and Biomedical Engineering

Towards Sustainable Preparation of Oral Solid Dosage Form of Drug Nanoparticles

Introduction

Advanced drug discovery techniques have led to identifications of complex chemical compounds with excellent therapeutic potentials. However, many of these compounds exhibit poor aqueous solubility[1] and lead to incomplete, erratic and slow systemic absorption. To enhance drug solubility as well as bioavailability, formulating the active pharmaceutical ingredients (API) into nano-particles (NPs) has been proven to be simple and effective[2]. To improve flow properties and compaction characteristics within further tablets and capsules manufacturing process (Figure 1), nano-API are adsorbed onto the agglomeration templates to produce hierarchically-ordered micro-granules of the NPs. Many of current nano-API production and micro-granulation techniques, however, possess low energy and mass efficiency due to the harsh operating conditions[3]. A more sustainable manufacturing process of nano-API and micro-granules operated at ambient temperature, pressure, neutral pH, and absent of organic solvent, is studied in this project.

Figure 1. End Products as Tablets and Capsules
Source: flickr.com/photos/amandamarcotte/3761282895

Objectives

Design a sustainable manufacturing process without any organic solvent and high energy input, merely by ionic cross-linking or self-assembly complexation:

1. To prepare CIP nanoplex as the nano-API from drug Ciprofloxacin (CIP) and polyelectrolyte Dextran Sulfate (DXT), with the desired diameter of 300nm;

2. To develop CS/TPP templates as the agglomeration templates from polymer Chitosan (CS) and salt Sodium Tripolyphosphate (TPP).

3. To investigate the adsorption of CIP nanoplex onto the CS/TPP templates. The desired diameter of the drug loaded micro-granules is between 300 µm and 500µm.

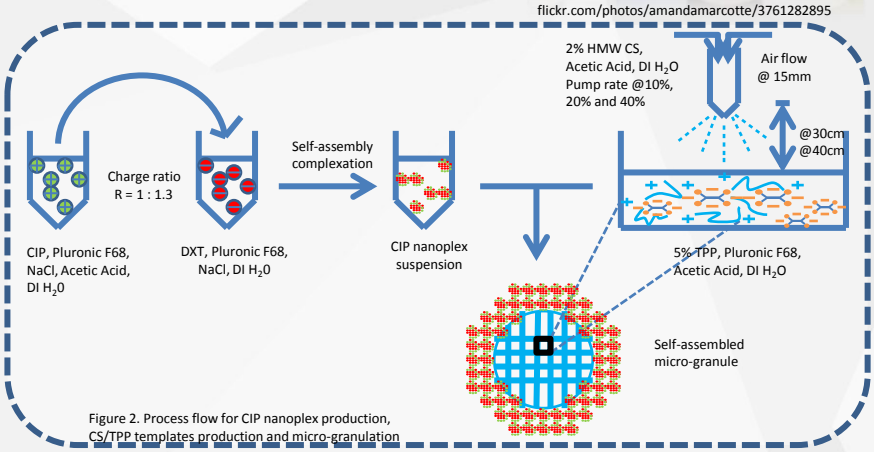

Figure 2. Process flow for CIP nanoplex production, CS/TPP templates production and micro-granulation

Results

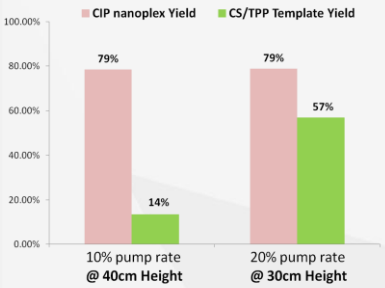

Figure 3. CIP nanoplex yield and CS/TPP template yield at different heights

Pump Rate	CS/TPP Template Diameter	Micro-granules Diameter	Layers of CIP nanoplex
10%	100 µm	142 µm	139
20%	162 µm	183 µm	71
40%	235 µm	on-going	on-going

Table 1. Size comparison of CS/TPP templates and micro-granules at different pump rates . Rough estimation of nano-CIP layers.

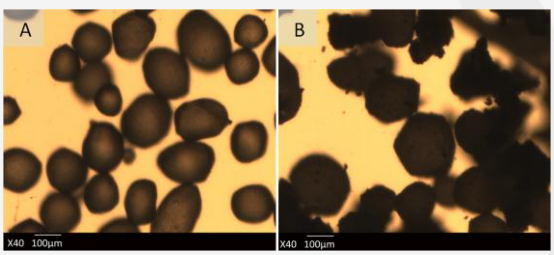

Figure 4. Light Microscope Images (@ 20% pump rate, 30cm)
(A): CS/TPP Templates (B): Drug loaded micro-granules

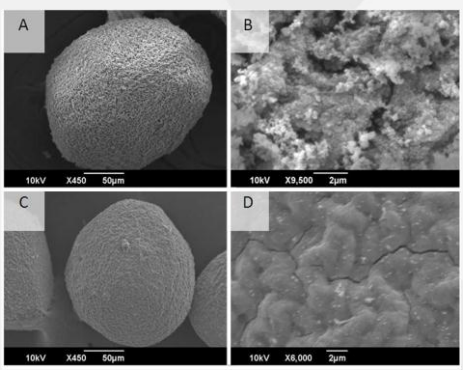

Figure 5. SEM Images (@ 20% pump rate, 30cm)
(A) & (B): Drug loaded Micro-granules and surface morphology
(C) & (D): CS/TPP templates and surface morphology

- The production of CIP nanoplex was relatively stable and the yield maintained constant around 80% (see Figure 3).
- The reduction of distance between nozzle and TPP solution surface from 40cm to 30cm significantly increased the yield of CS/TPP templates from 14% to 57% (see Figure 3).
- CS/TPP template diameter increased to 235µm when pump rate increased to 40% (see Table 1).
- Number of CIP nanoplex layers adsorbed on CS/TPP templates can be roughly estimated to be from 70 to 140 (see Table 1 and Figure 4).
- Distinct difference in morphologies of CS/TPP templates between before and after loading CIP nanoplex could be viewed under Scanning Electron Microscope (SEM) (see Figure 5).

Conclusion and on-going tasks

CS/TPP template can be produced in a green and sustainable method using ionic cross-linking. Ggranulation by simple mixing CIP nanoplex and CS/TPP template is a good method to adsorb NPs.

On-going tasks

1. Pump rate will be increased to increase CS/TPP template diameter to reach desired 300µm.

2. Under the premise to form spherical shape, the height between nozzle and TPP solution will be further reduced to increase CS/TPP templates yield.

3. Different mixing ratios of CIP nanoplex and CS/TPP templates are being tested to determine the maximum drug loading ratio.

Project Title: Towards Sustainable Preparation of Oral Solid Dosage Form of Drug Nanoparticles
Supervisor: Asst Prof Kunn Hadinoto
Co-supervisors: Ms Cheow Wean Sin & Ms Yang Yue