

Self-assembled curcumin-PAH nanoplex with enhanced solubility

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2014

Zhang, J. (2014, March). Self-assembled curcumin-PAH nanoplex with enhanced solubility. Presented at Discover URECA @ NTU poster exhibition and competition, Nanyang Technological University, Singapore.

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Self-assembled Curcumin-PAH Nanoplex with Enhanced Solubility

INTRODUCTION

Self-assembled drug-polyelectrolyte complexation is a novel formulation of a nanoscale amorphous drug from its poorly soluble crystalline form, resulting in greater solubility and enhanced bioavailability of the drug. Nanoscale amorphous drug is formed by dispersing the ionised drug particles onto an oppositely charged polyelectrolyte (PE). The drug-PE complex is held together by strong electrostatic interaction.

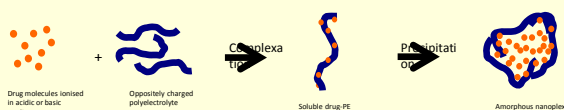


Figure 1. Schematic diagram of nanoplex complexation

Curcumin (CCM) is a substance in turmeric that exhibits anti-inflammatory and chemo-preventive effects. However, research has shown poor absorption of the weakly acidic CCM by the body due to its poor solubility and fast metabolism. Increasing the solubility and prolonging drug release are critical for enhancing its absorption by the body.

Poly(allylamine hydrochloride) (PAH) is a cationic PE. It has several biomedical applications such as cell encapsulation and drug delivery.

This research aims to examine the solubility and duration of drug release of the self-assembled freeze-dried CCM-PE nanoplex.

METHODOLOGY

1. Preparation of CCM Nanoplex

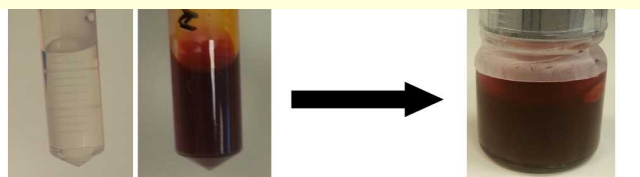


Figure 2a. Mixture of PAH, NaCl, H₂O and acetic acid (left); CCM in potassium hydroxide (right).

Figure 2b. CCM nanoplex in suspension form



Figure 2d. Dried CCM nanoplex (left); Dried CCM nanoplex with hydroxypropyl methylcellulose (HPMC) (right).

Figure 2c. Freeze-dryer

2. Quantification of Supersaturation



15mg of CCM-PAH nanoplex and 30 mg of CCM-PAH nanoplex with hydroxypropyl methylcellulose (HPMC) were dissolved in 8.5mL of 1X phosphate buffered saline (PBS) respectively and incubated at 37°C. 300uL of the each incubated sample was withdrawn and filtered before 200uL of the withdrawn sample was diluted 10 folds with 1X PBS at specific time interval. The drug concentration was then measured to determine dissolution of the nanoplex.

Figure 3. Shaking incubator

RESULTS & DISCUSSION

Supersaturation Profile

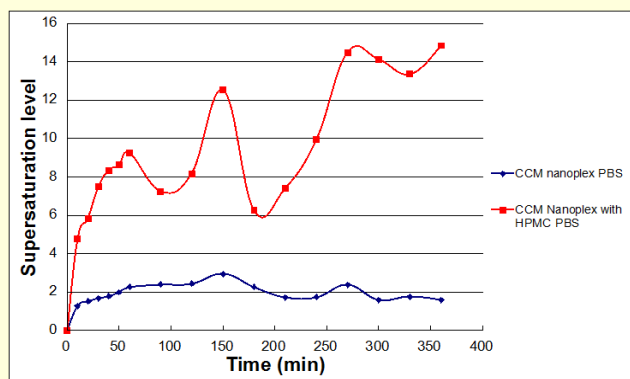


Figure 4. Supersaturation profile of CCM nanoplex in PBS and CCM nanoplex with HPMC in PBS.

CCM Nanoplex in PBS

- Measured apparent solubility is slightly higher than the saturation solubility. The supersaturation level is between 1~3.
- Increased dissolution rate due to the presence of PAH. But rapid precipitation prevent high level of supersaturation from being quantified.

CCM Nanoplex with HPMC in PBS

- The supersaturation level increases to ~9 in 1 h and remains high though the supersaturation level fluctuates after 1 h. High supersaturation level over the next 5 h provides sufficient time for drug absorption.
- HPMC slows precipitation of CCM, allowing high supersaturation level of CCM nanoplex to be determined.

CONCLUSION

- The solubility of CCM is enhanced after complexation with PAH.
- High and prolonged supersaturation level of CCM nanoplex with HPMC provides sufficient time for drug absorption.

Future studies

The explanation for fluctuation of supersaturation level is unknown. More studies need to be done to examine the cause.

ACKNOWLEDGEMENT

I would like to thank my supervisor, Professor Kunn Hadinoto Ong, Dr. Cheow Wean Sin and Ms Kiew Tie Yi for their advice and guidance.

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