

Preparation of paclitaxel-loaded poly(lactic acid)/hydroxyapatite core-shell nanoparticles for drug delivery system carrier

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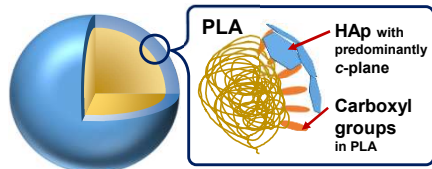
INTRODUCTION

Water insoluble (or fat-soluble) drug

- 1/3 of existing and 40% of newly developed drug
- For administration to patients

Requires dissolve in **ethanol** and **polyoxyethylated castor oil**
↳ Cause serious side-effects¹⁾

(PLA) Poly(lactic acid)/hydroxyapatite core-shell nanoparticle (50-200 nm)²⁾



- #### PLA core
- Biodegradable polymer
 - Load-ability of water insoluble drug
 - Loading capacity (LC) → 250 % of hydrophobic drug³⁾

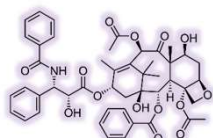
- #### HAP shell
- Excellent biocompatibility
 - pH-sensitivity³⁾ → High solubility in acidic environment (pH of tumor tissue : weakly acidic at 6.5)

- #### Nano-particle (50-200nm)
- Expected to show enhanced permeability and retention (EPR) effect⁴⁾ → Facilitate passive targeting to tumor tissues

Model drug in present work

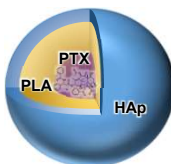
Paclitaxel (PTX)

- Widely used anticancer agent⁵⁾
- Poorly soluble in water



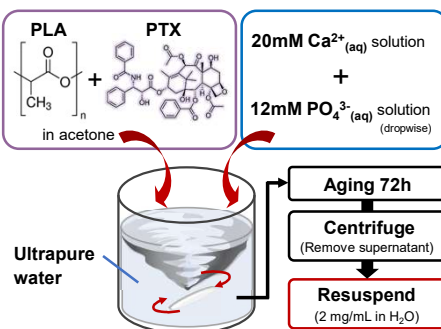
AIM

Preparation of **PTX-loaded PLA/HAP** core-shell nanoparticles and investigation on the **in vitro properties**



METHOD

Preparation of PTX-loaded PLA/HAP core-shell nanoparticles



Sample code	PLA / mg	Ca/P	PTX / mg	PTX wt.% of PLA
PLA@HAP	-	-	-	-
PTX1.0@HAP	20	1.67	0.2	1.0
PTX2.5@HAP	20	1.67	0.5	2.5
PTX5.0@HAP	20	1.67	1.0	5.0

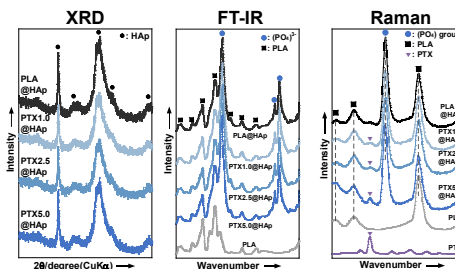
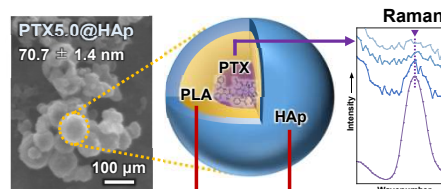
in vitro properties of PTXx@HAP

- Murine breast cancer cells (4T1, ATCC)
- Particle concentration : 20 – 1000 µg/mL
- PTX concentration : 0.05 – 25 µg/mL



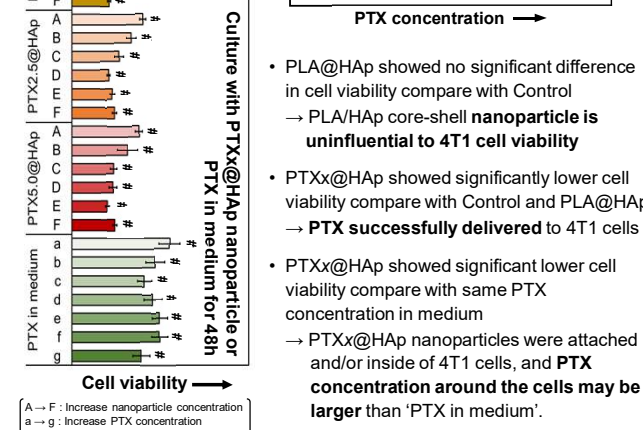
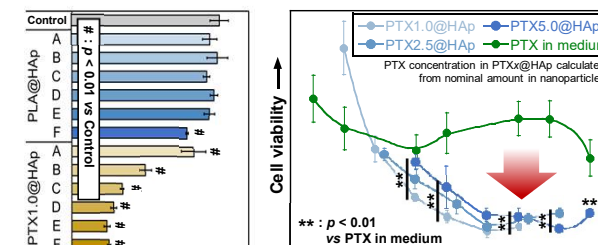
RESULTS

Structure of PTXx@HAP nanoparticles



- PTXx@HAP size was approximately 70 ~ 80 nm → Expected to show the EPR effect
- PLA and HAP was confirmed from XRD, FT-IR, Raman
- Raman peak (▼ : C-C sp³ in PTX) was increased with increasing PTX content in PTXx@HAP

4T1 cell viability culture with PTXx@HAP nanoparticles



- PLA@HAP showed no significant difference in cell viability compare with Control → PLA@HAP core-shell nanoparticle is **uninfluential to 4T1 cell viability**
- PTXx@HAP showed significantly lower cell viability compare with Control and PLA@HAP → **PTX successfully delivered to 4T1 cells**
- PTXx@HAP showed significant lower cell viability compare with same PTX concentration in medium → PTXx@HAP nanoparticles were attached and/or inside of 4T1 cells, and **PTX concentration around the cells may be larger than 'PTX in medium'**.

CONCLUSION

- PTXx@HAP was successfully prepared with **75 nm size** → passive targeting via **EPR effect**
- PTXx@HAP was **cytotoxic against cancer cells** → **pH sensitivity** of the HAP shell

REFERENCES

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Present work in *Royal Society Open Science*.

S. Lee et al., Development of paclitaxel-loaded poly(lactic acid)/hydroxyapatite core-shell nanoparticles as a stimuli-responsive drug delivery system, *R. Soc. Open Sci.* 8: 202030.