Preparation of Paclitaxel Lipid Nanoparticles from Paclitaxel Conjugates for the Treatment of Breast Cancer

Liang Jia[a, b], Yu Cai[a,b], Timo L.M. ten Hagen[a,b], Mohamadreza Amin[a,b]

a Precision Medicine in Oncology (PrMiO), Department of Pathology, Erasmus MC Cancer Institute, Erasmus MC, Rotterdam, The Netherlands

b Nanomedicine Innovation Center Erasmus (NICE), Erasmus MC, Rotterdam, The Netherlands

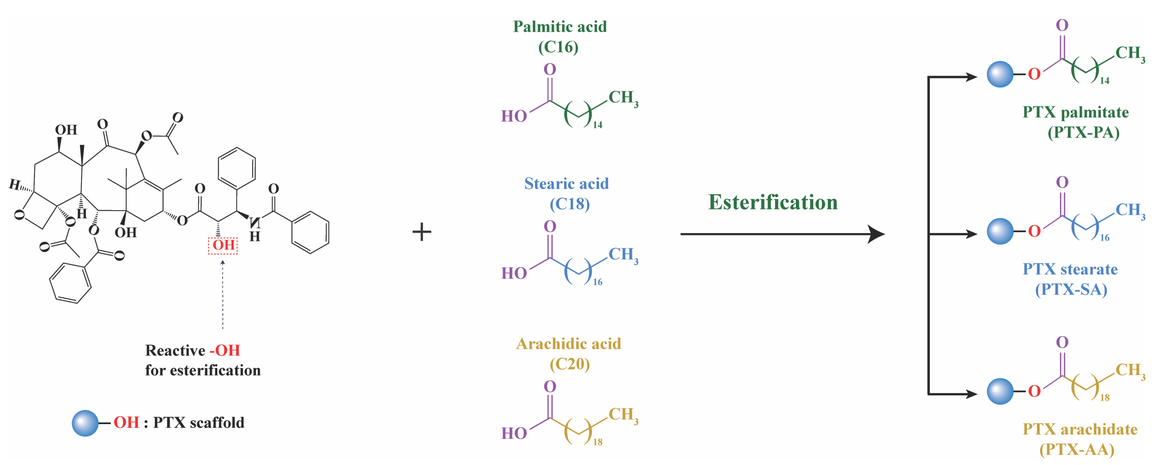
INTRODUCTION

Paclitaxel (PTX) is a broad-spectrum anticancer drug widely used for treating breast, ovarian, lung, and other cancers. Its primary anti-tumor mechanism involves disrupting microtubule dynamics, thereby blocking cell cycle progression and mitosis. However, PTX has extremely low water solubility (~0.03 mg/mL) and cannot be easily ionized to form salts, limiting its formulation options. Although existing PTX-based formulations (e.g., Taxol®, Genexol-PM®, Lipusu®) have made administration of PTX possible, they often suffer from premature drug release and degradation, leading to systemic toxicity. Abraxane®, although effective, poses challenges in terms of complex manufacturing, quality control, and cost.

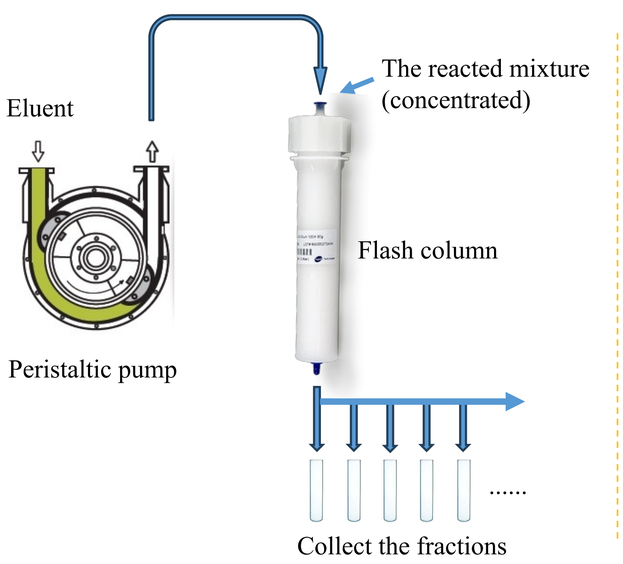
To overcome these limitations, we designed PTX prodrug conjugates with enhanced lipophilicity and modified geometry to facilitate stable encapsulation within lipid nanoparticles (LNP), thereby minimizing premature drug leakage. This approach not only improves colloidal stability but also significantly reduces manufacturing costs.

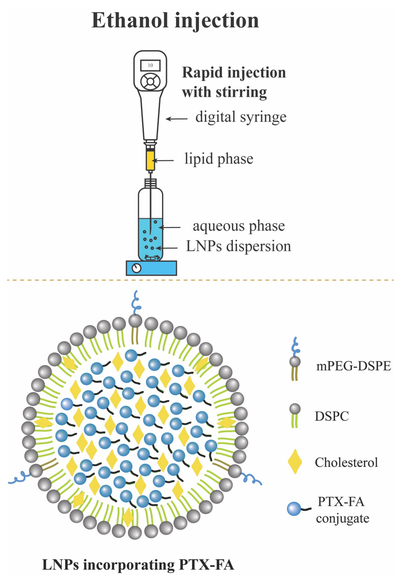
METHODS

1. Synthesize the PTX fatty acid (PTX-FA) conjugates.



2. Characterize the PTX-FAs by, ^{1}H NMR, ESI-MS, and FT-IR.
3. Purify by Flash column (silica) and prepare PTX-FA LNP.

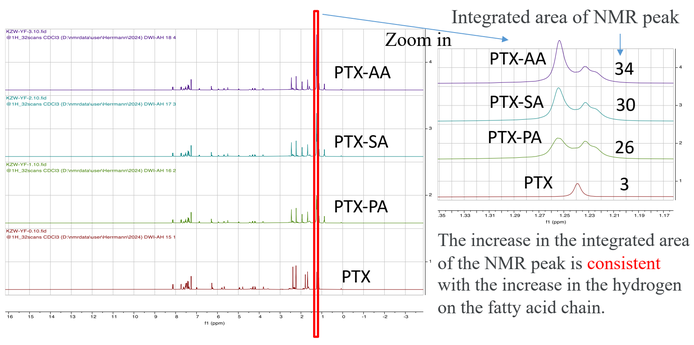




4. Characterize the LNPs by DLS.
5. Cell interactions between MDA-MB-231 cells and LNP.

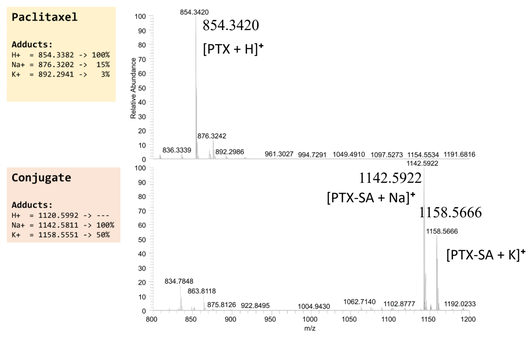
RESULTS

1H NMR spectrum



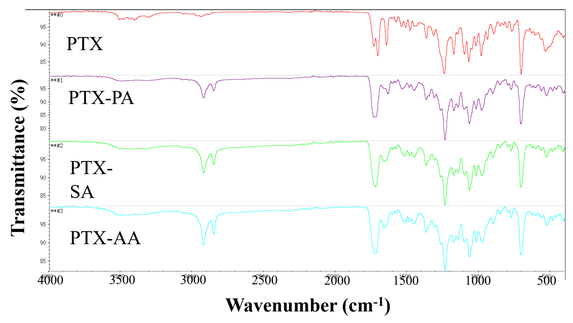
The increase in the integrated area of the NMR peak is consistent with the increase in the hydrogen on the fatty acid chain.

ESI-MS

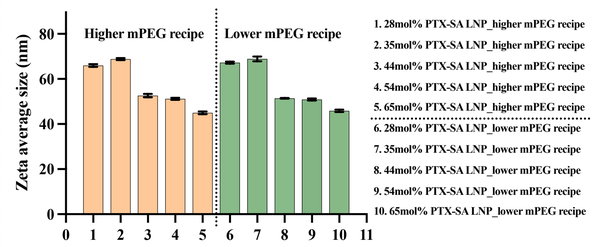


Presenter contact:
Email: l.jia@erasmusmc.nl

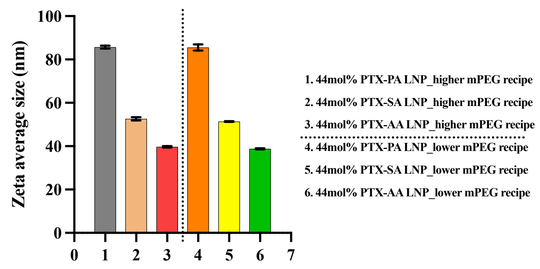
FT-IR



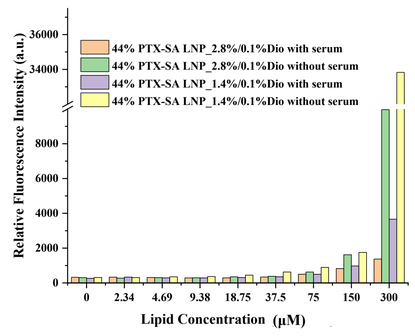
Effect of feeding



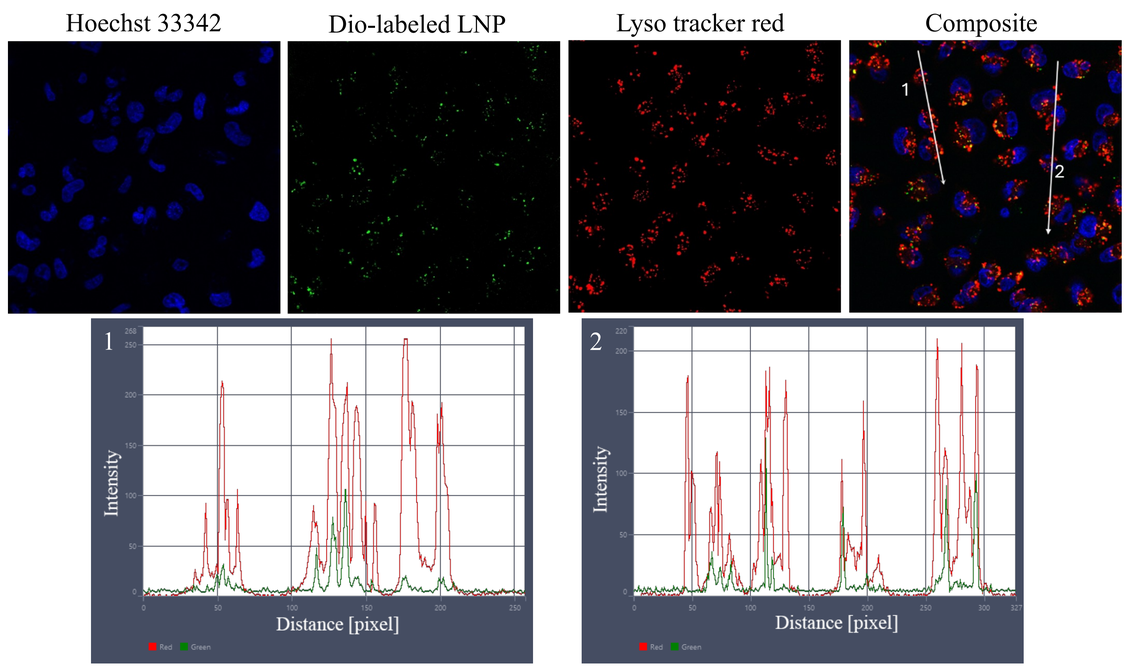
Effect of fatty acid chain



Cell association



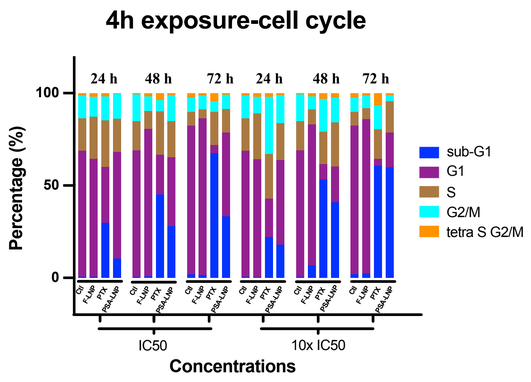
Uptake



IC$_{50}$

Samples	IC$_{50}$ (μM)	R^2	cell type
Free PTX	0.0522	0.9833	MDA-MB-231
44% PTX-PA LNP_1.40%mPEG	4.9	0.9886	
44% PTX-PA LNP_2.82%mPEG	4.95	0.9898	
44% PTX-SA LNP_1.40%mPEG	5.01	0.9902	
44% PTX-SA LNP_2.82%mPEG	4.91	0.9876	
44% PTX-AA LNP_1.40%mPEG	6.81	0.9898	
44% PTX-AA LNP_2.82%mPEG	6.4	0.9806	

Cell cycle



DISCUSSION & LEARNING OBJECTIVES

Discussion

In summary, we successfully synthesized three PTX-FA conjugates and formulated stable, uniformly sized LNPs via ethanol injection. PTX-LNPs demonstrated favorable cellular uptake and potent anti-proliferative effects in breast cancer cells. This prodrug-LNP strategy enhances drug loading, reduces systemic toxicity, and presents strong potential for clinical translation. Furthermore, it offers a versatile platform for improving the delivery of other hydrophobic chemotherapeutics.

Learning Objectives

Learn how chemical modifications and advanced drug formulations can enhance the safety, targeting, and delivery efficiency of anti-tumor therapies by reducing systemic toxicity and improving tumor-specific activation.

ACKNOWLEDGEMENTS

Supervisors:
Timo ten Hagen
Mohamadreza Amin

PrMiO:
A Seynhaeve; T Ojha;
Z Cheng; Y Cai

Pathology:
A Sacchetti

Neurology
C Stingl