Polymersomes via Self-Assembly of Amphiphilic β-Cyclodextrin Centered Tri-arm Star Polymers for Enhanced Oral Bioavailability of Water-Soluble Chemotherapeutics

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Introduction

Oral administration is usually the most preferred route of various drugs because its compliance and convenient. The oral absorption of DOX•HCl, a BCS class III drugs, is extremely poor and the responsible factor has been validated as the limited paracellular transport. We synthesized a novel amphiphilic β-CD-centered tri-arm star polymers ((mPEG-PLA)$_3$-CD)) and prepared DOX•HCl loaded polymersomes. To our knowledge, this is the first time to construct polymersomes for oral delivery of water-soluble chemotherapeutics.

Synthesis Route of (mPEG-PLA)$_3$-CD

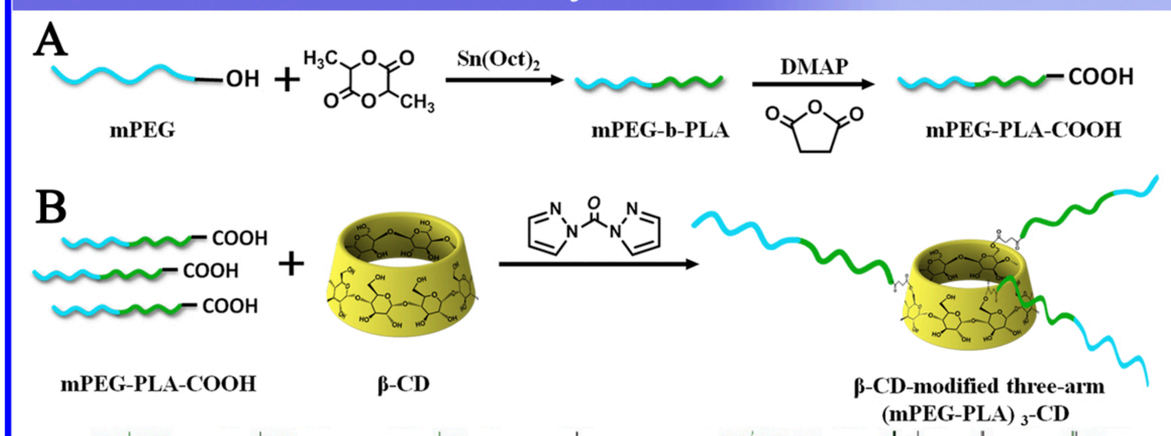


Fig 1. (A) and (B): Synthesis polymer. (C) and (D): ^{1}H NMR of mPEG-PLA and (mPEG-PLA)$_3$-CD.

The structure of polymersome

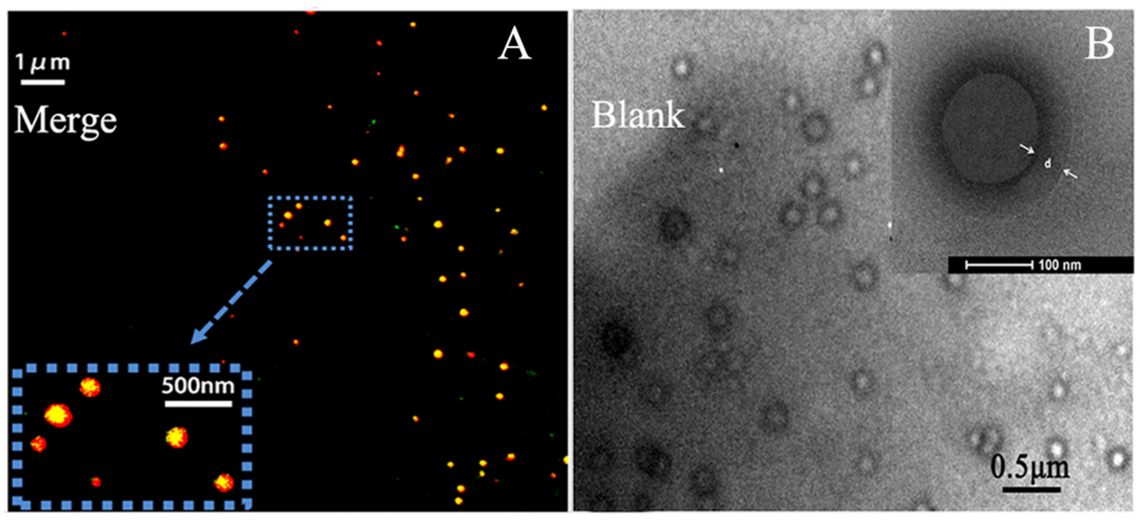


Fig 2. (A) Confocal images of polymersomes. (B) TEM images polymersomes.

Drug loading and release

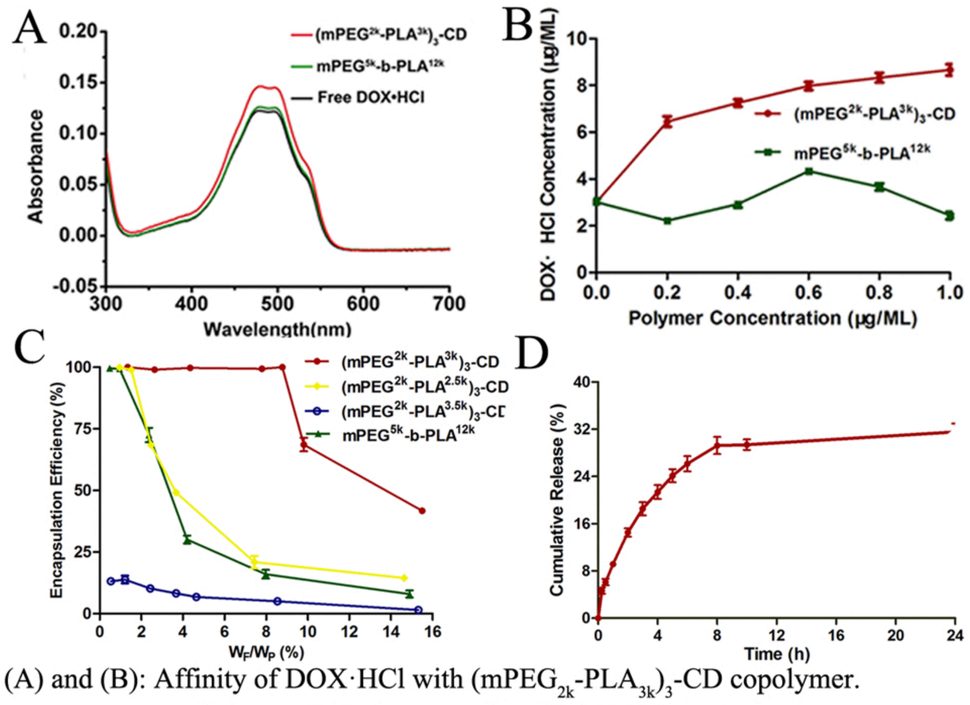
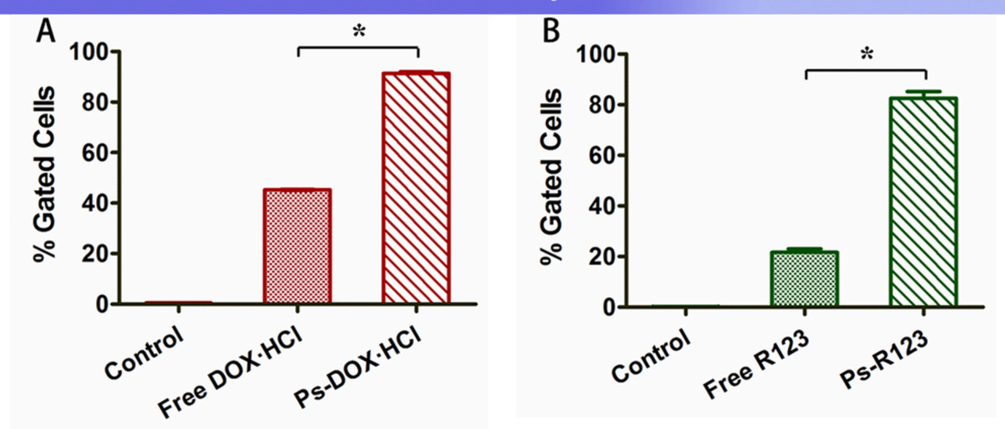


Fig 3. (A) and (B): Affinity of DOX·HCl with (mPEG$_{2k}$-PLA$_{3k}$)$_3$-CD copolymer.
(C) Drug entrapment efficiency (D)Release profile of DOX·HCl-loaded polymersomes at pH 7.4.

Internalization characterization by MDCK cells



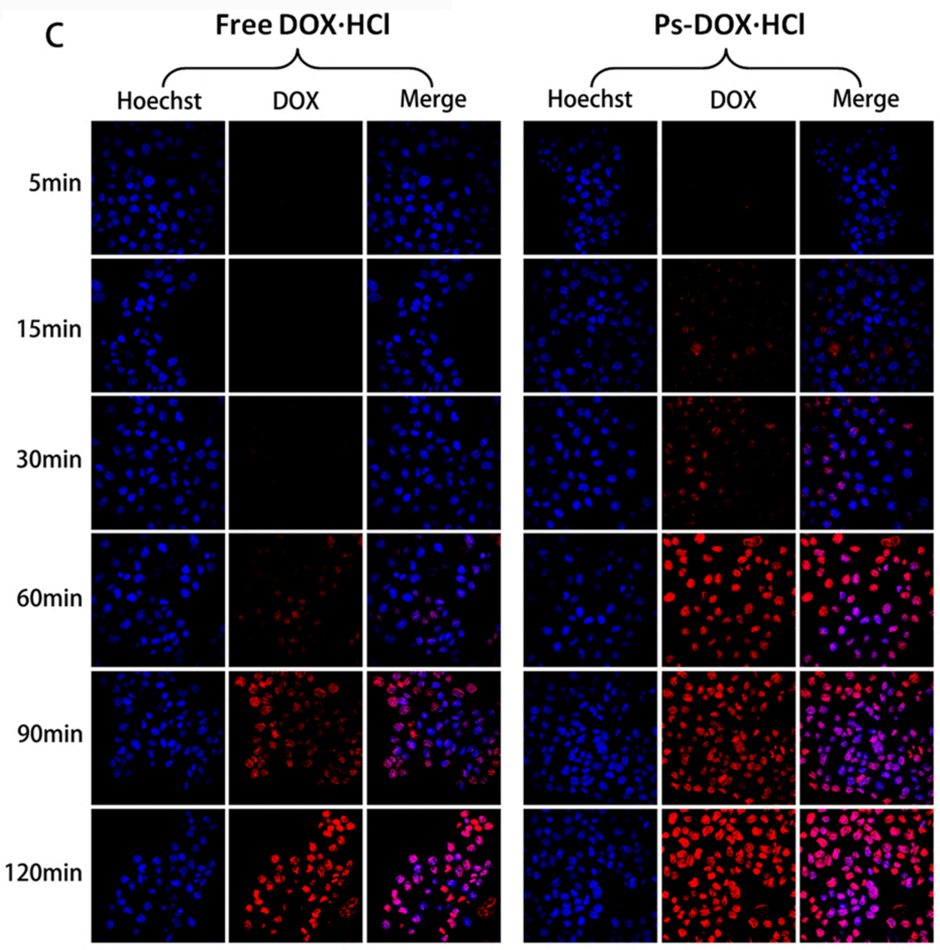


Fig 4. (A) and (B): Cellular uptake by flow cytometry. (C): Cellular uptake by CLSM.

Pharmacokinetic study

Formulation	C_{max} (μg mL^{-1})	$t_{1/2}$ (h)	AUC_{0-8} (μg mL^{-1}h^{-1})
Free DOX·HCl	0.45±0.14	1.35±0.28	1.33±0.14
Ps-DOX·HCl	5.57±1.39	11.10±3.39	9.74±0.17

Table 1. Pharmacokinetic parameters of free DOX•HCl and Ps-DOX•HCl upon single oral administration at the dose of 20 mg kg-1

Conclusions

we successfully constructed a novel DOX•HCl loaded polymersomes self-assembled by β-CD-centered tri-arm star polymer for oral delivery with significantly enhanced bioavailability and antitumor efficacy .

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