pharmaceutics

MDPI

Supplementary Materials: Optimized 5-Fluorouridine Prodrug for Co-Loading with Doxorubicin in Clinically Relevant Liposomes

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Table S1. Liposomal dosages in 4T1 animal studies.

	5FURW (mg/kg)	DOX (mg/kg)
$DAFODIL_{R=2.5}$	2.4	1
$DAFODIL_{R=6}$	5.8	1
$DAFODIL_{R=10}$	9.7	1

Table S2. In vitro dose-response parameters of free drug combinations on 4T1 cells. All ratios given are molar ratios.

4T1, 500 cells/well		
Drug/Drug combination	**IC_{50} (μM)**	**Hill Coefficient**
DOX	$0.004 \pm 6.7\times10^{-4}$	0.41 ± 0.025
5FUR-W	0.061 ± 0.007	0.95 ± 0.092
1:5 5FUR-W:DOX	0.016 ± 0.002	0.48 ± 0.029
1:1 5FUR-W:DOX	$0.011 \pm 7.9\times10^{-4}$	0.51 ± 0.019
5:1 5FUR-W:DOX	0.040 ± 0.004	0.038 ± 0.004
5FUR-W_3	0.040 ± 0.006	0.69 ± 0.067
1:5 5FUR-W_3:DOX	0.033 ± 0.003	0.72 ± 0.051
1:1 5FUR-W_3:DOX	$0.004 \pm 5.0\times10^{-4}$	0.43 ± 0.020
5:1 5FUR-W_3:DOX	0.038 ± 0.004	0.59 ± 0.033

Table S3. In vitro dose-response parameters of liposomes on 4T1 and SKOV3 cells.

4T1, 500 cells/well		
Formulation	**IC_{50} (μM)**	**Hill Coefficient**
DOX-L	1.61 ± 0.24	0.67 ± 0.07
5FURW-L	0.094 ± 0.02	0.65 ± 0.08
R=2.5 5FURW-L:DOX-L	0.030 ± 0.003	0.60 ± 0.04
$DAFODIL_{R=2.5}$	0.06 ± 0.007	0.74 ± 0.06
SKOV3, 5000 cells/well		
Formulation	**IC_{50} (μM)**	**Hill Coefficient**
DOX-L	55.16 ± 9.57	0.46 ± 0.05
5FURW-L	22.02 ± 3.90	0.43 ± 0.04
R=2.5 5FURW-L:DOX-L	24.37 ± 5.95	0.42 ± 0.05
$DAFODIL_{R=2.5}$	8.76 ± 1.47	0.56 ± 0.05

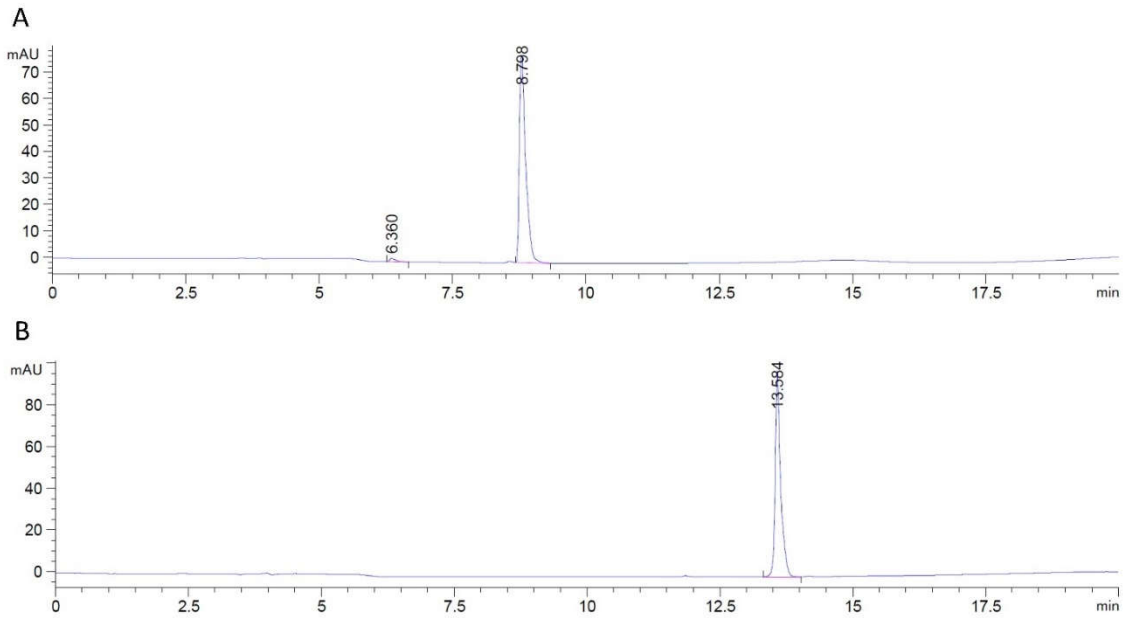

Figure S1. Example HPLC chromatogram of free drugs. **(A)** 5FUR-W3. **(B)** Doxorubicin.

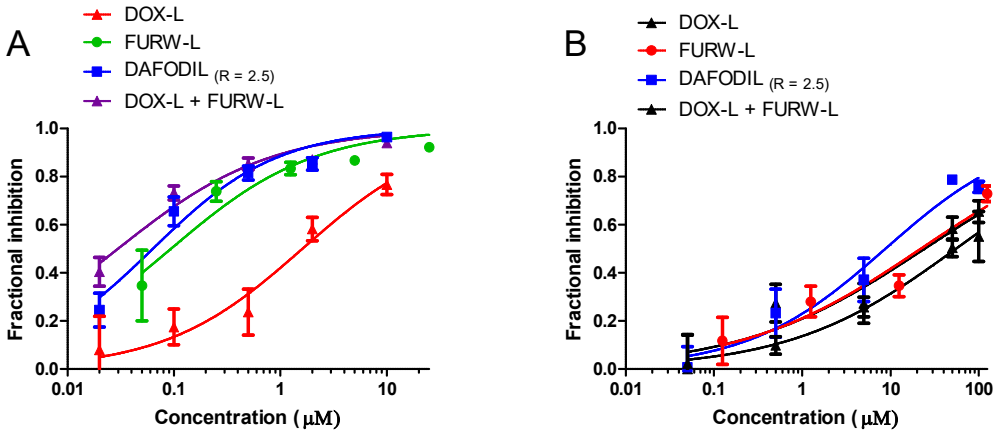

Figure S2. In vitro cellular toxicity of DAFODIL on both **(A)** 4T1 cells (500 cells/well) and **(B)** SKOV3 cells (5000 cells/well).

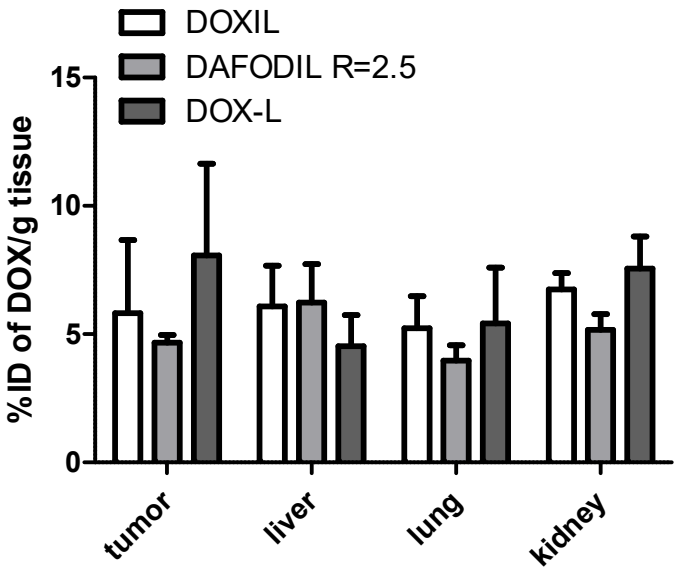

Figure S3. DAFODIL biodistribution is simmilar to commercial generic PEGylated liposomal doxorubicin, as well as DOX-L.

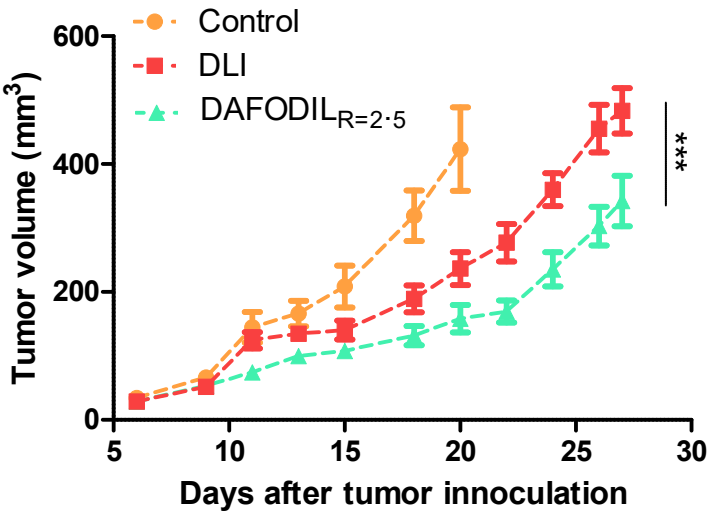

Figure S4. DAFODIL R=2.5 tumor response in comparison to DLI extended to 27 days.