Electronic Supplementary Information

Main-Chain Polyacetal Conjugates with HIF-1 Inhibitors: Temperature-Responsive, pH-degradable Drug Delivery Vehicles

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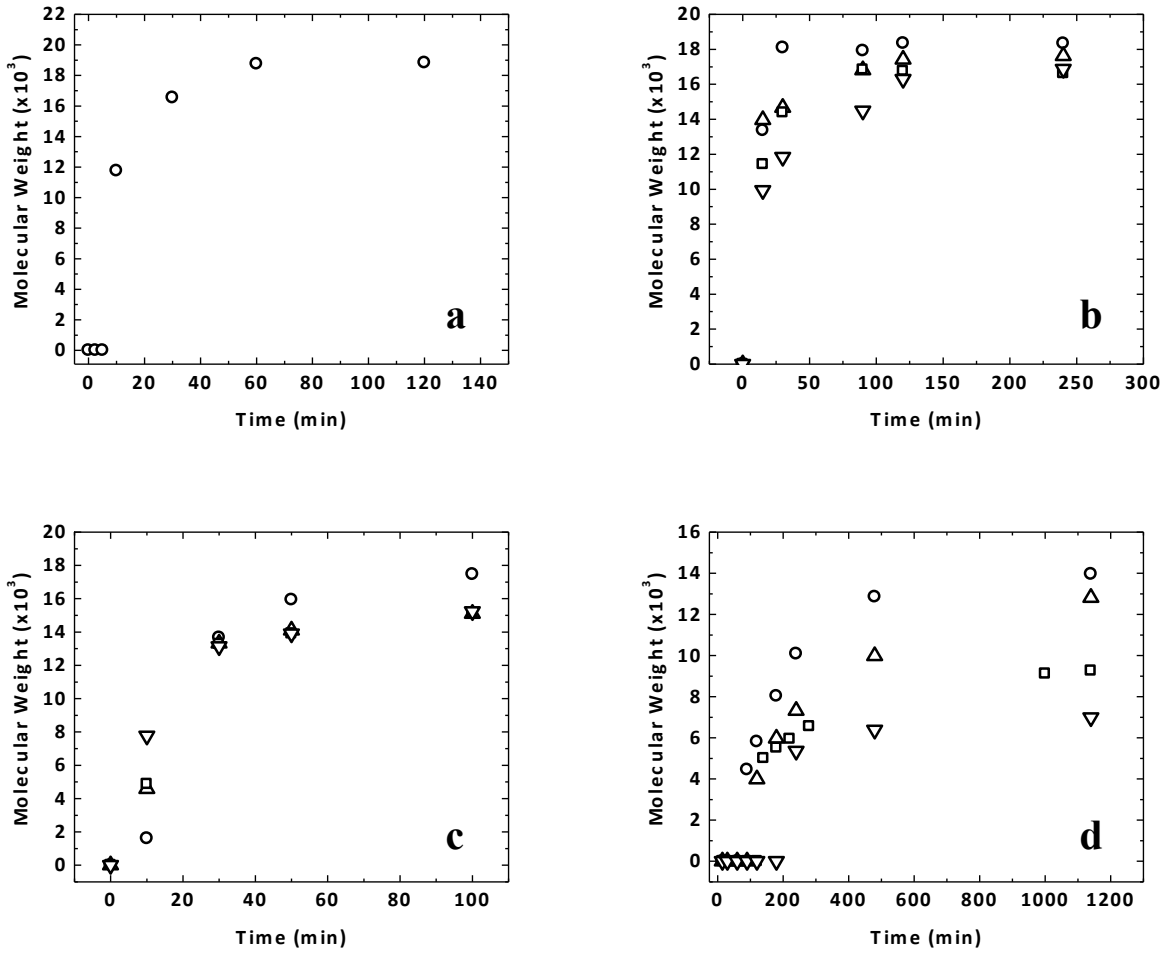
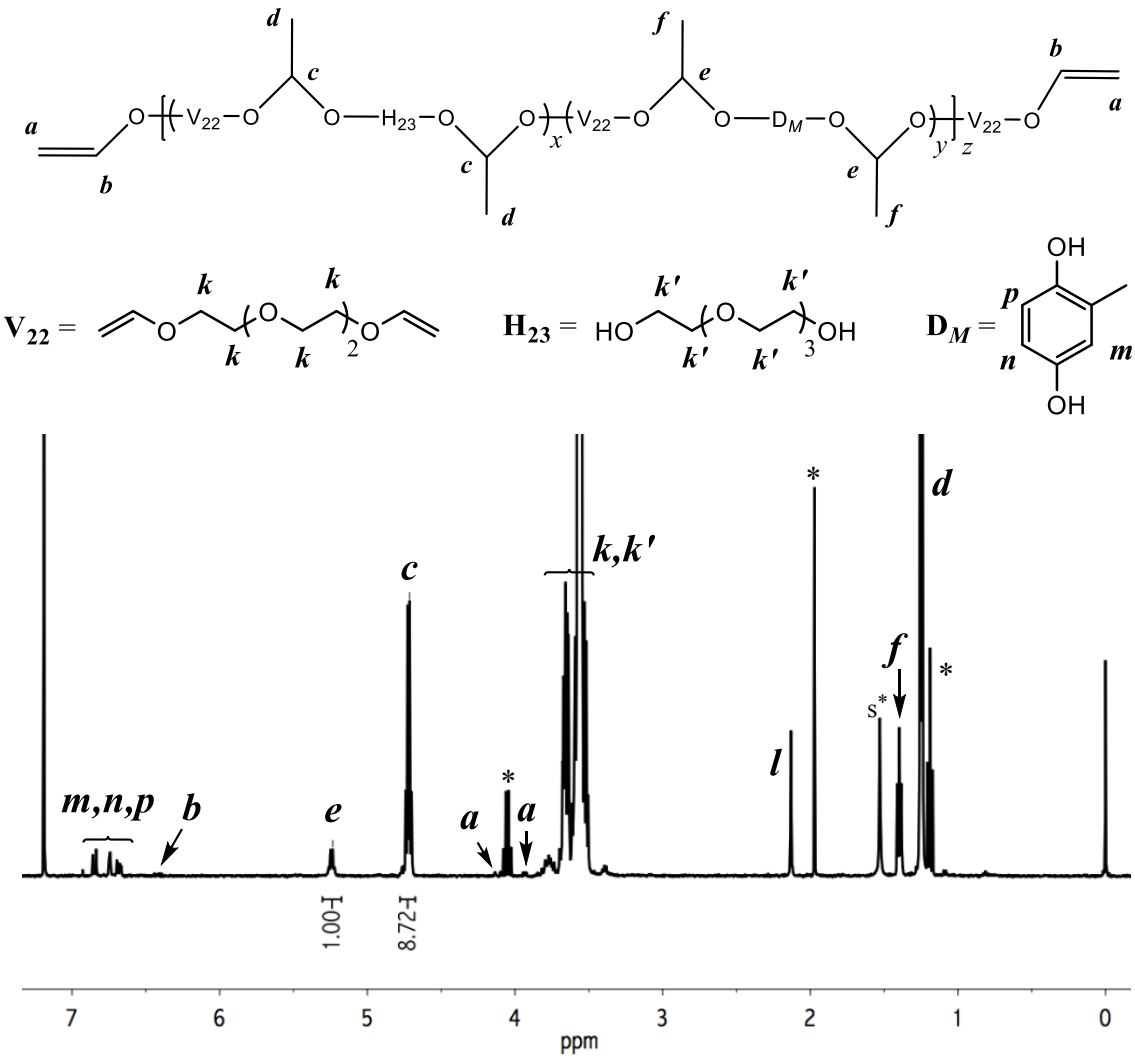


Figure S.1: Polymerization kinetics of (a) PA_{2223} and main-chain PA-drug conjugates prepared from (b) MHQ (c) BIS-A and (d) DES with different drug loading: 5% (circle), 10% (triangle), 15% (square) and 20% (inverted triangle).

S.2a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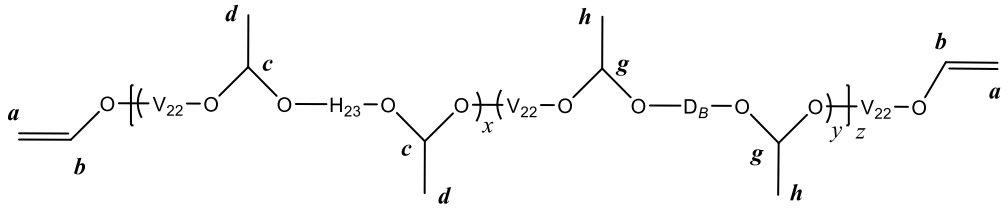
S.2b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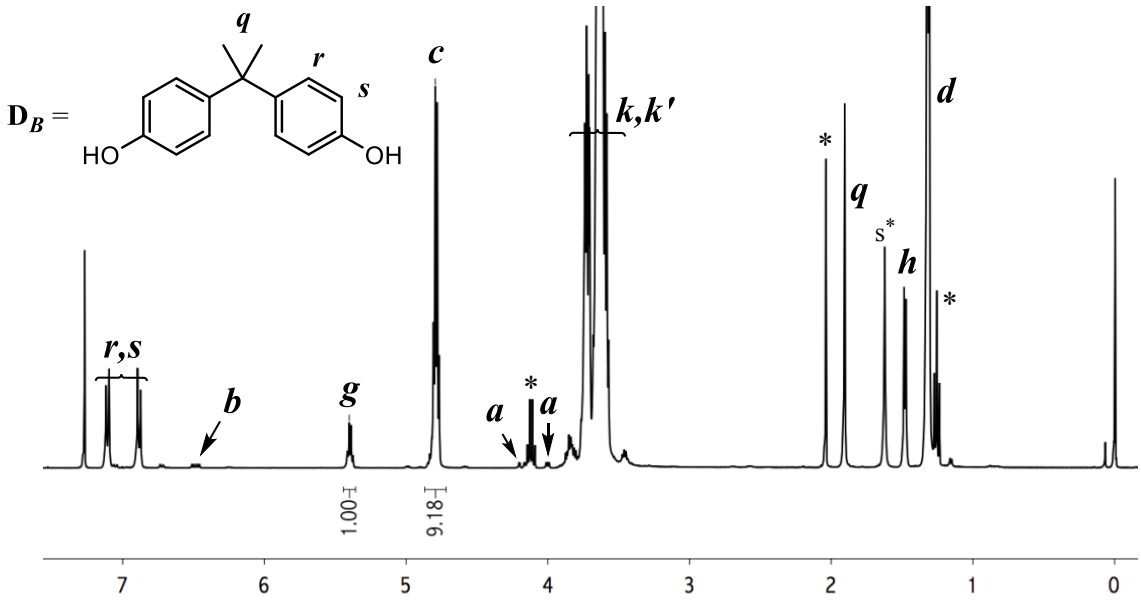
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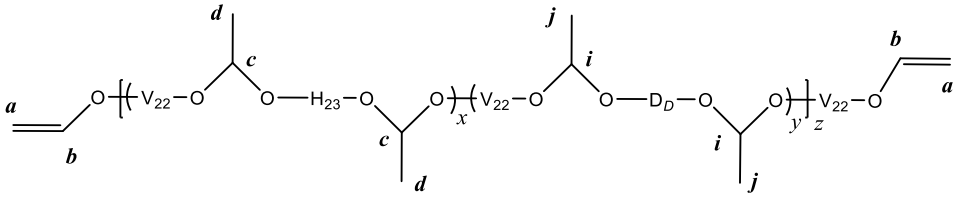
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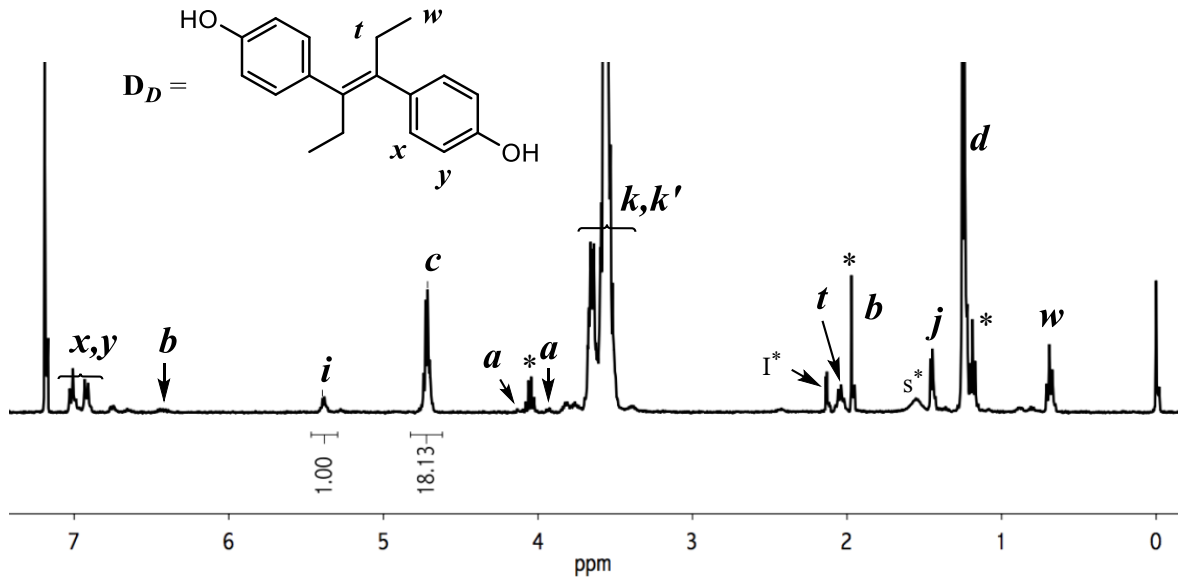
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Figure S.2: ^{1}H NMR ($CDCl_3$, 400 MHz) characterization of polyacetal-based polymer therapeutics: (a) $PA_{2223}D_M10V17.6$ (entry 1, Table 1) (b) $PA_{2223}D_B10V15.1$ (entry 6, Table 1) and (c) $PA_{2223}D_D10V12.9$ (entry 3, Table 1). In the ^{1}H NMR spectrum, "*" comes from the presence of trace amount of ethyl acetate, "s*" from the moisture in $CDCl_3$ and "I*" is unknown to us or from impurity.

Table S.1: Characteristics of PA-DES Conjugates.

Entry	Sample	Drug-diol (D_x)	% of D*x* (p)	% of H_{23}	Mn_{theo} (kDa)[a]	Mn_{expt} (kDa)	Actual % of incorporated DES[b]
S.2	$PA_{2223}D_D5V14.1$	DES	5%	95%	8.20	14.14	2.81
S.3	$PA_{2223}D_D10V12.9$	DES	10%	90%	8.28	12.85	6.26
S.4	$PA_{2223}D_D15V9.3$	DES	15%	85%	8.36	9. 26	12.84
S.5	$PA_{2223}D_D20V6.9$	DES	20%	80%	8.43	6.94	12.77

[a]assuming 100% conversion using the Carothers equation.

[b]calculated GPC area mass fraction of DES conjugated onto the main chain.

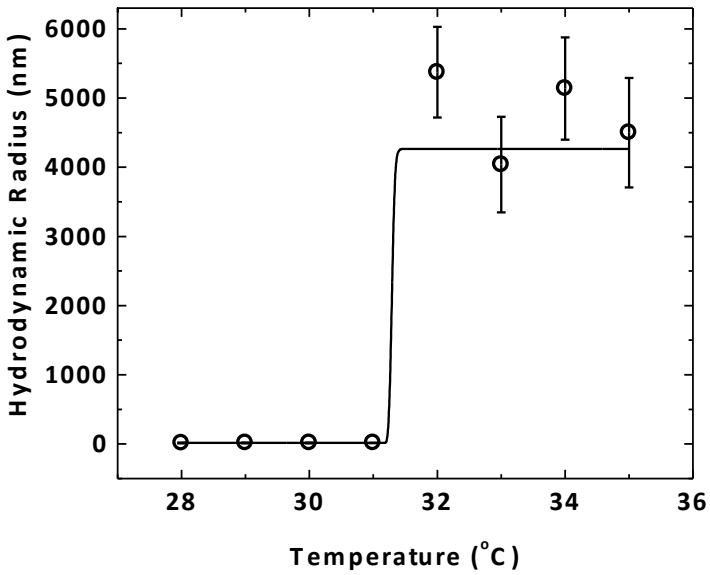

Figure S.3: Temperature dependent dynamic light scattering study of $PA_{2223}D_D20V6.9$ (heating@1 $^0C/min$) in aqueous PBS (0.1 mM). Polymer concentration = $5g.L^{-1}$.

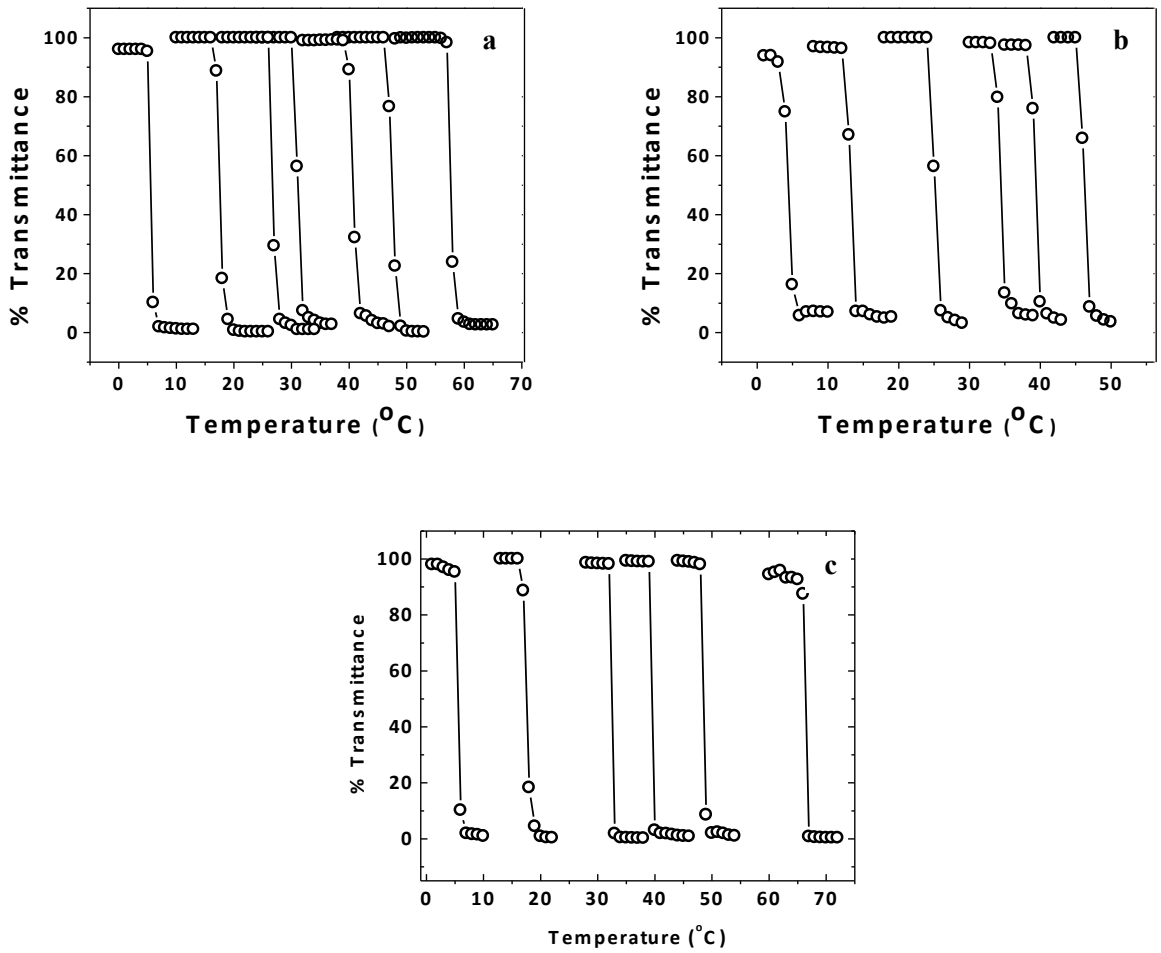

Figure S.4: Temperature induced phase transitions (heating only) for main-chain PA-drug conjugates prepared from (a)MHQ (5, 10, 15, 20, 25, 30 and 40% from right to left), (b) BIS-A (5, 7.5, 10, 15, 20 and 30% from right to left) and (c) DES (5, 10, 15, 20, 30 and 40% from right to left) with increasing drug loading in aqueous PBS (0.1 mM).

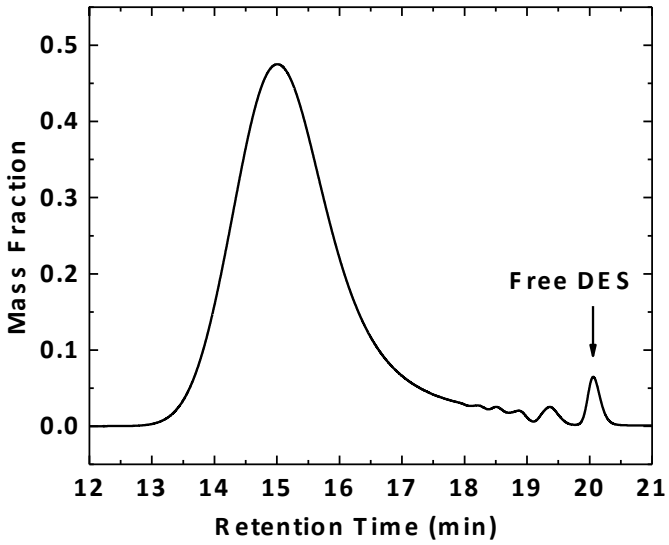

Figure S.5: GPC analysis of DES content for a $PA_{2223}D_D10V12.9$ reaction time (20h). Mass fraction = (area of free DES peak)/(area of main peak)x(total reactant DES added).

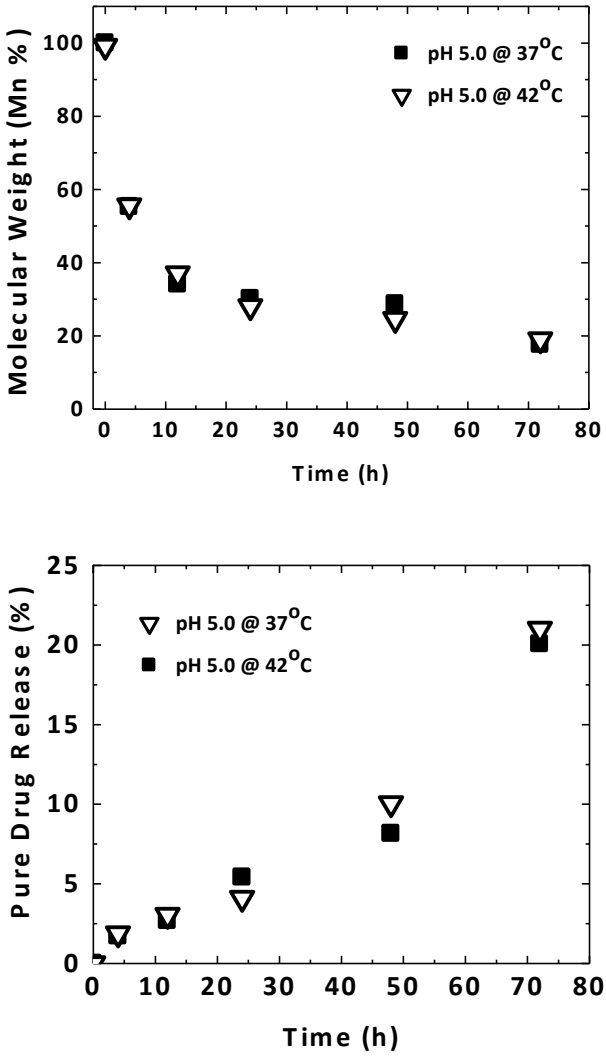

Figure S.6: (a) Comparison of degradation rates of $PA_{2223}D_D15V$ in pH 5 phosphate buffer at 37°C & 42°C, (b) comparison of DES drug release rates from $PA_{2223}D_D15V$ in pH 5 phosphate buffer at 37°C & 42°C