Thermo-Responsive Hemoglobin-Polymer Conjugates with Oxygen-carrying Capacity

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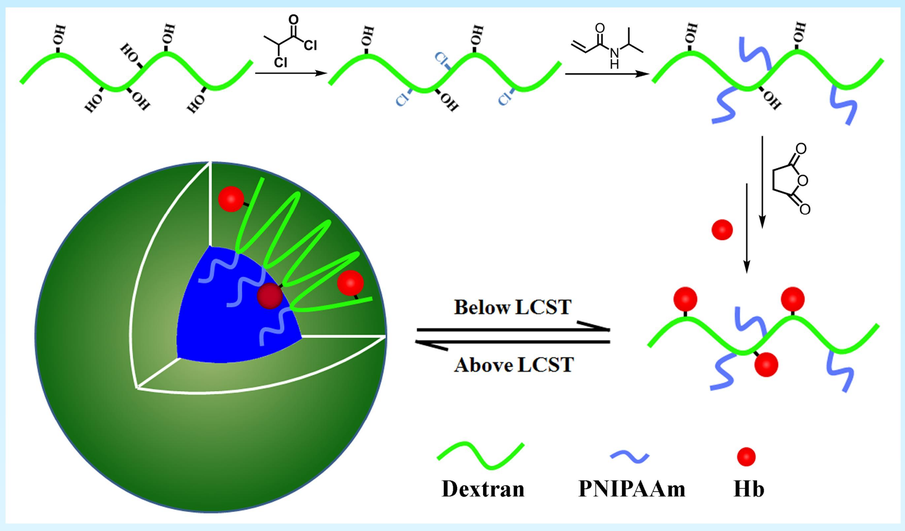
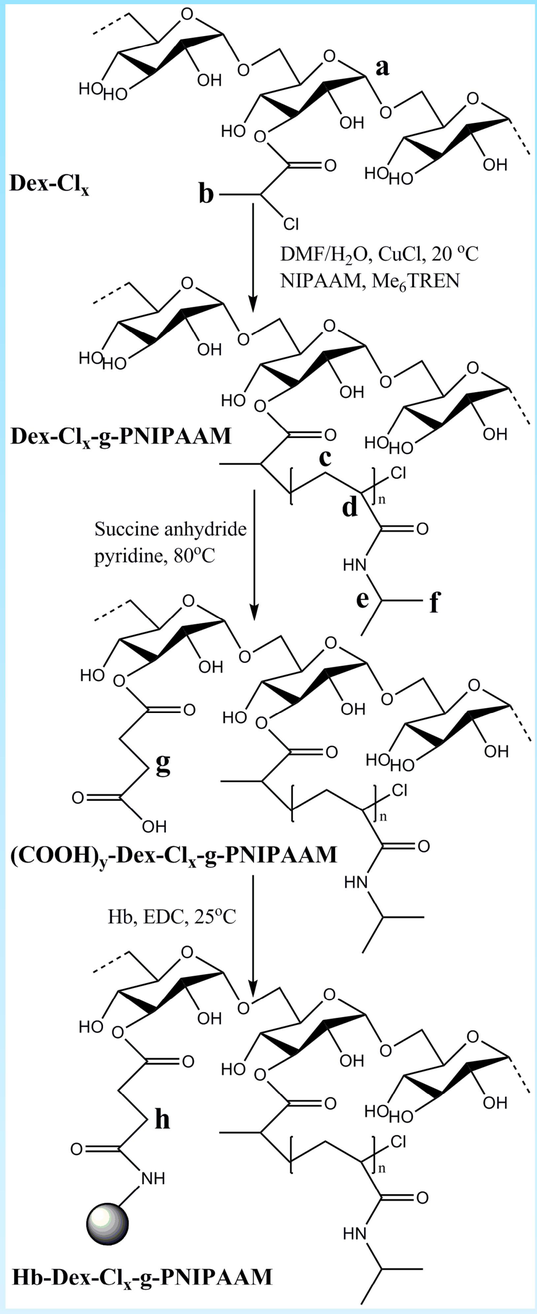
Introduction

The potential toxicity towards human kidneys of hemoglobin (Hb), when used directly, has severely limited its application as a red blood cell substitute and in cancer treatments. In this work, a novel hemoglobin–polymer conjugate was prepared by a reaction between the lysine amino groups of Hb and the carboxyl groups of a copolymer, poly(N-isopropylacrylamide) grafted carboxylated dextran (HOOC-Dex-g-PNIPAAm), which was synthesized by single electron transfer living radical polymerization (SET-LRP) and post-carboxylation. Both the thermo-responsive nature of PNIPAAM and the oxygen-binding capacity of Hb were conferred to the conjugate. Furthermore, we also demonstrated that this conjugate had a unique property to improve the stability of O_2–Hb above LCST, probably due to the thermo-sensitivity of grafted PNIPAAm chains. And the stability of O_2–Hb in the conjugates would increase with the number of PNIPAAm chains.



Synthesis & Characterization



Scheme 1. Synthesis of the conjugate of Hb-Dex-Cl$_x$-g-PNIPAAm

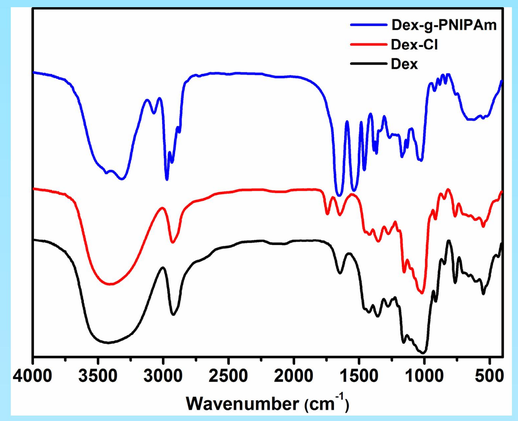


Fig 1. FTIR spectra of Dex, Dex-Cl and Dex-Cl-g-PNIPAAM

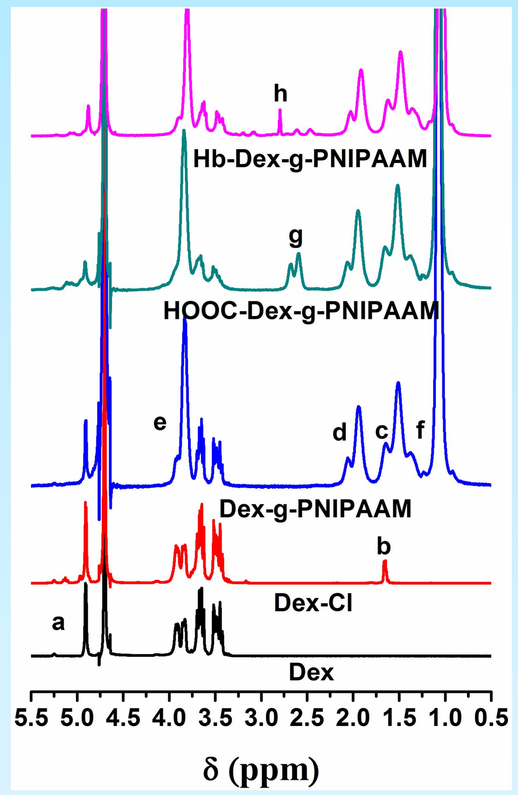


Fig 2. ^{1}H NMR spectra of reaction products in D_2O at 25 °C

Results

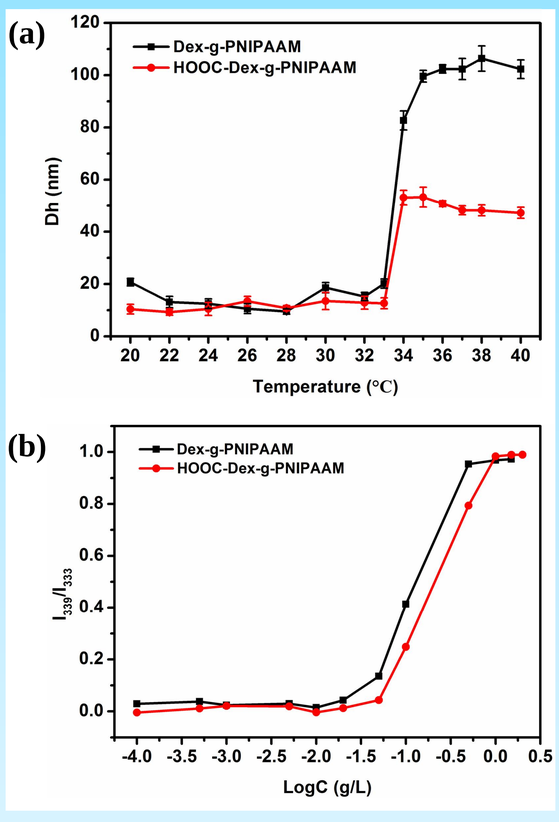


Fig 3. Thermo-responsive properties: (a) LCST obtained by DLS; (b) CMC

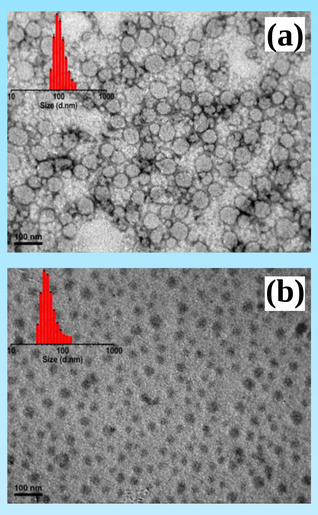


Fig 4. TEM images of (a) Dex-g-PNIPAAm and (b) HOOC-Dex-g-PNIPAAm

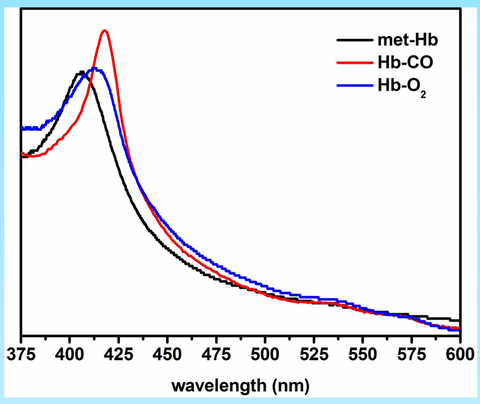


Fig 5. Gas-bindig capacity of Hb-Dex-g-PNIPAAM

Table 1. Stability of the conjugates of Hb-Dex-Cl$_x$-g-PNIPAAm with different number of PNIPAAm chains

Hb-polymer conjugates	$t_{1/2}$ (min)	
	25 °C	37 °C
Hb-Dex-Cl$_{10}$-g-PNIPAAm	55	21
Hb-Dex-Cl$_{22}$-g-PNIPAAm	90	77
Hb-Dex-Cl$_{30}$-g-PNIPAAm	119	107

Conclusions

The conjugate of Hb-Dex-g-PNIPAAm was synthesized and endowed with both the thermo-responsive nature of PNIPA-Am and the oxygen-binding capacity of Hb.

The conjugate of Hb-Dex-g-PNIPAAm could improve the stability of O_2-Hb which increased with the number of PNIPAAm chains, probably due to the thermo-sensitivity of PNIPAAm chains.

Acknowledgements

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