

SUPPLEMENTARY INFORMATION

Molecular dynamics study on the interaction between doxorubicin and hydrophobically modified chitosan oligosaccharide

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Methods:

The synthesis of COS/IMN: COS/IMN was synthesized by a conjugation reaction between amino-groups of COS and carboxyl groups of IMN using 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC) as a coupling agent. In brief, 0.1 g (0.00556 mmol) COS (Mw = 18000) was dissolved in 6 mL doubled distilled water. Meanwhile, 0.0444 g (0.1242 mmol) IMN and 0.1191 g (0.6210 mmol) EDC were dissolved in 6 mL ethanol. Under 25 °C water bath and fast stirring, the IMN/ethanol solution was slowly dropped into the COS aqueous solution. After 53 h, the mixture was transferred into a dialysis bag (MWCO = 7000) and dialyzed against

doubled distilled water for 24 h to remove the unreacted IMN and EDC. The final product was frozen and dried in a vacuum.

The preparation of DOX-loaded COS/IMN nanoparticles: DOX-loaded COS/IMN nanoparticles (NPs) were prepared by a dialysis method as follows. 1 mg of DOX powder was weighed and dissolved into 1 mL DMSO (1 mg/mL). Meanwhile, 10 mg freeze dried COS/IMN powder was weighed and dissolved in 5 mL double distilled water. 1 mL DOX/DMSO (1 mg/mL) was dropped into the COS/IMN water solution according to the fixed feed ratio of drug to polymer (10%, w/w). The available mixture was dispersed by probe-type ultrasonic treatment 40 times (400 w, work 2 s, rest 4) in an ice-bath. The treated solution stirred overnight. Then the solution was transferred into a dialysis bag (MWCO = 7000) and dialyzed against doubled distilled water for 4 h to remove DMSO. The dialyzate was poured out of the dialysis bag and centrifuged at 4000 rpm for 15 min to remove the precipitated particles. The obtained solution of DOX-loaded NPs was frozen and dried to get the lyophilized product.

The characterization of the DOX-loaded nanoparticles: The micelle sizes of the DOX-loaded NPs were measured by dynamic light scattering using a Zetasizer (Malvern zetasizer nano zs90, UK). The encapsulation efficiency (EE) and drug loading rate (DL) were determined by fluorescence spectrophotometer (EX = 468 nm, EM = 566 nm, slit 5 nm, voltage 700 mV). The standard curve equation of DOX: $y = 160464x + 880.15$, $R^2 = 0.9944$.

Results:

The micelle size, encapsulation efficiency (*EE*) and drug loading (*DL*) rate of DOX-loaded NPs were show in Table S1.

Table S1. The micelle size, encapsulation efficiency and drug loading rate of DOX-loaded NPs.

COS _{Mw} /IMN _{theory SD%} ^a	Size ^b (nm)	EE ^c (%)	DL ^d (%)
COS ₁₈₀₀₀ /IMN _{20%}	345.1	81.58±0.86	7.76±0.4

^aMw represents the molecular weight of COS and the theory SD% represents the theory substitution degree of IMN to COS.

^bSize measured by dynamic light scattering using a Zetasizer (Malvern zetasizer nano zs90, UK).

^cDrug encapsulation efficiency of DOX(10%)-loaded COS/IMN NPs measured by Fluorescence.

^dDrug loading capacity of DOX(10%)-loaded COS/IMN NPs measured by Fluorescence spectrophotometer.

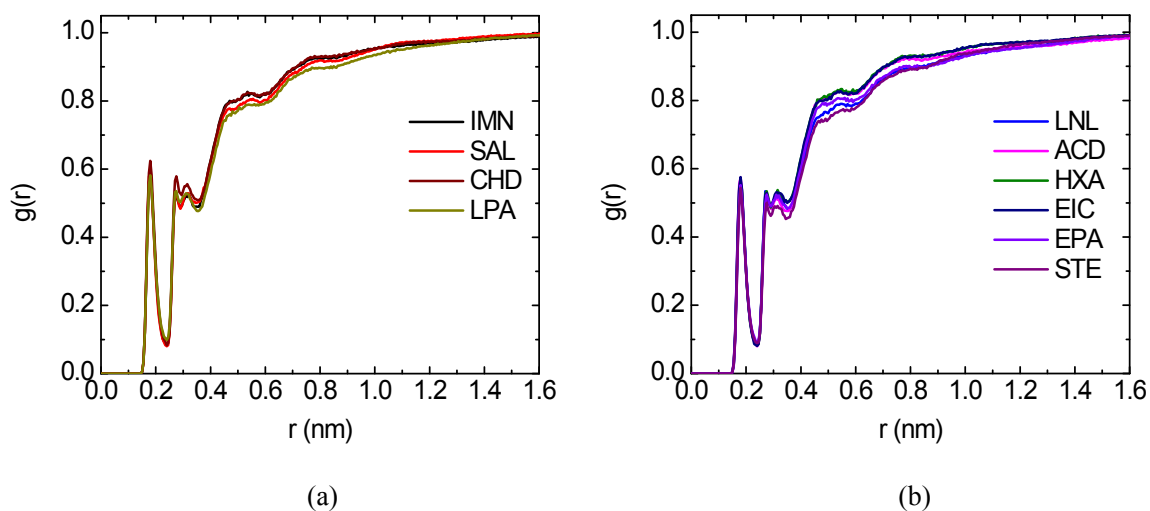


Fig. S1 (a) Radial distribution functions for oxygen (in COS/IMN chain)-oxygen (in water) (black), oxygen (in COS/SAL chain)-oxygen (in water) (red), oxygen (in COS/CHD chain)-oxygen (in water) (wine) and oxygen (in COS/LPA chain)-oxygen (in water) (dark yellow); (b) Radial distribution functions for oxygen (in COS/LNL chain)-oxygen (in water) (blue), oxygen (in COS/ACD chain)-oxygen (in water) (magenta), oxygen (in COS/HXA chain)-oxygen (in water) (olive), oxygen (in COS/EIC chain)-oxygen (in water) (navy), oxygen (in COS/EPA chain)-oxygen (in water) (violet) and oxygen (in COS/STE chain)-oxygen (in water) (purple).

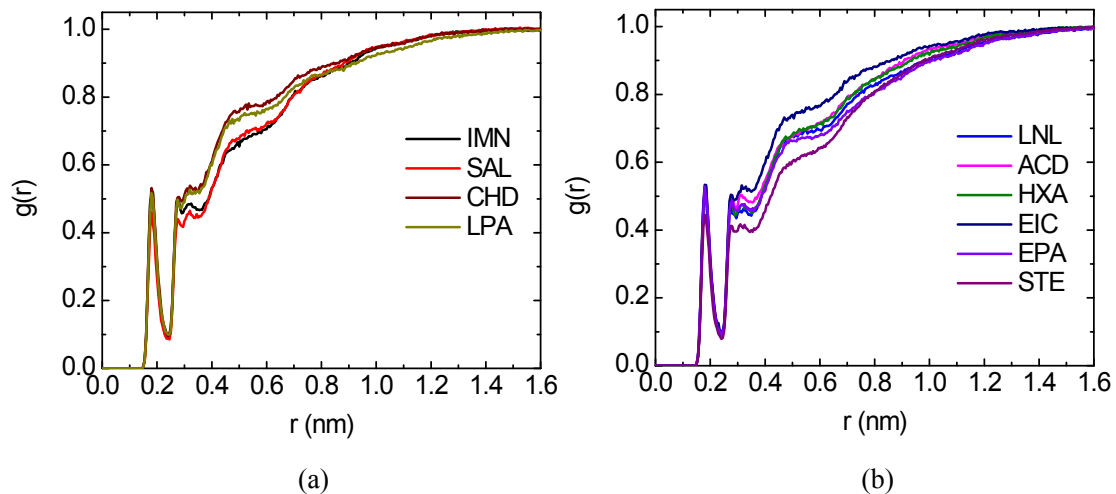


Fig. S2 (a) Radial distribution functions of oxygen (in DOX)-oxygen (in water) in the system of COS/IMN (black), COS/SAL (red), COS/CHD (wine) and COS/LPA (dark yellow); (b) Radial distribution functions of oxygen (in DOX)-oxygen (in water) in the system of COS/LNL (blue), COS/ACD (magenta), COS/HXA (olive), COS/EIC (navy), COS/EPA (violet) and COS/STE (purple).