Anti-Cancer Drug Delivery via DNA-Inspired Janus Base Nanotubes

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Introduction: Musculoskeletal cancers are significant clinical challenges. Because many anti-cancer drugs are hydrophobic, delivery of these molecules is a challenge in clinics. For example, Doxorubicin (DOX) is an anthracycline type of anticancer chemotherapy drug that is insoluble in water, so it's commonly sold in a liposome encapsulated form as Doxil. However, liposomes are likely to be accumulated in liver and lipid materials can cause pro-inflammation reactions, which limit the applications of Doxil. Therefore, we developed a novel biomimetic and biocompatible delivery system for DOX. Janus-Based Nanotubes (JBNTs) are self-assembled and amphiphilic nano-polymers with G^C or A^T DNA base pairs being the basic building blocks. JBNTs have been shown to have low toxicity both *in vitro* and *in vivo* and are designed to incorporate and deliver therapeutic agents such as anticancer drugs, RNAs, small peptides and protein molecules. Compared with traditional drug delivery vehicles, the non-covalent structure of JBNTs are more biocompatible and biodegradable and have low cytotoxicity and low immunogenicity due to their biological nature.

Methods: This study looked at the behavior of DOX loaded into JBNTs at different pH. In ^{1}H NMR characterizations, the drug encapsulation rates were calculated based on the NMR peak integration value differences between the DOX alone and DOX loaded into JBNTs. Incorporation of DOX in JBNTs was also investigated by UV-Vis spectroscopy.

Results: ^{1}H NMR and UV-Vis experiments provided strong evidence for the feasibility of the JBNT-DOX encapsulation. In the UV-Vis spectra, the significant differences observed at 290 nm suggest an interaction between DOX and JBNTs (**Figure 1**, left); as the pH changes, the differences at 290 nm indicate that DOX cannot load into JBNTs at low pH (**Figure 1**, right). In ^{1}H NMR experiments, the drug encapsulation rates were calculated to be 8% and 22% at pH 4.10 and 5.27, respectively (**Table 1**).

Discussion: Based on the results of the characterizations, we could safely conclude that DOX can be successfully loaded into JBNTs under nearly neutral condition, but at low pH DOX cannot load into JBNTs which we suppose there is strong repulsion between DOX and JBNTs because both of them are positively charged. Although the research about JBNTs applied as drug delivery vehicles is still at the beginning stage, the superior advantages of JBNTs make them highly potential to be one of the safest, most stable, most efficient, and most efficacious drug delivery vehicles in the future.

Significance/Clinical Relevance: Delivery of DOX is relevant to the treatment of metastatic soft tissue and bone sarcomas. Moreover, our delivery approach can be used for many different anti-cancer drugs other than DOX.

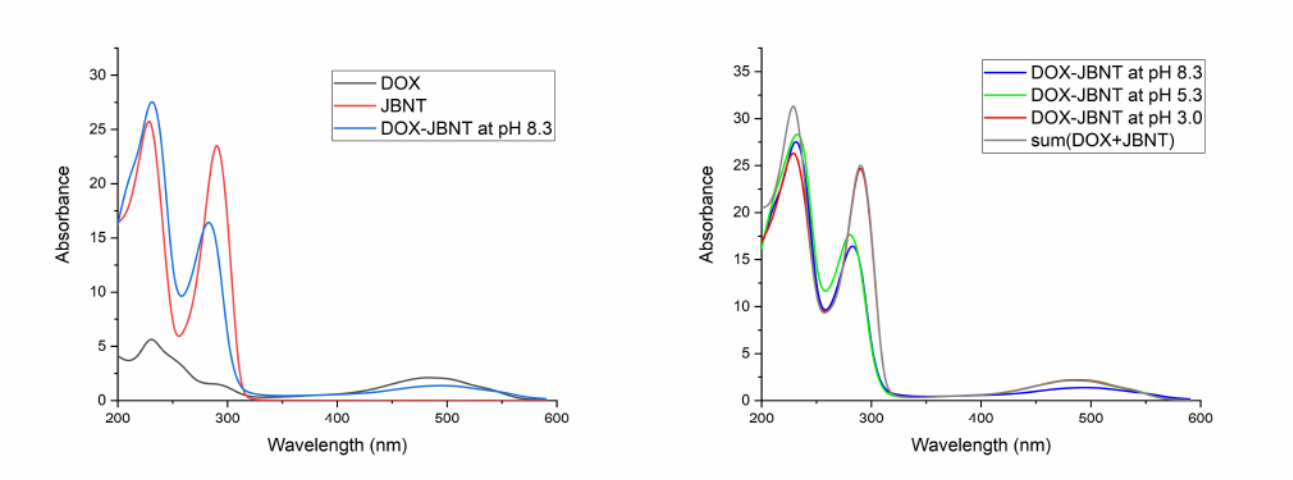

Figure 1. UV-Vis spectra recorded in water (mole ratio: DOX/JBNT=1/25).

Loading time	pH 3.34	pH 4.10	pH 5.27	pH 8.64
30 mins	0	0	6%	–
1 day	0	8%	22%	–

Table 1. DOX incorporation rates calculated using ^{1}H NMR (mole ratio: DOX/JBNT=1/5). DOX incorporation rates at pH 8.64 are not given because part of DOX precipitated due to low solubility.