An Acid-Labile System Based on Lipid-Polymer Modified Carbon Nanotubes for Controlled Release and Delivery Applications

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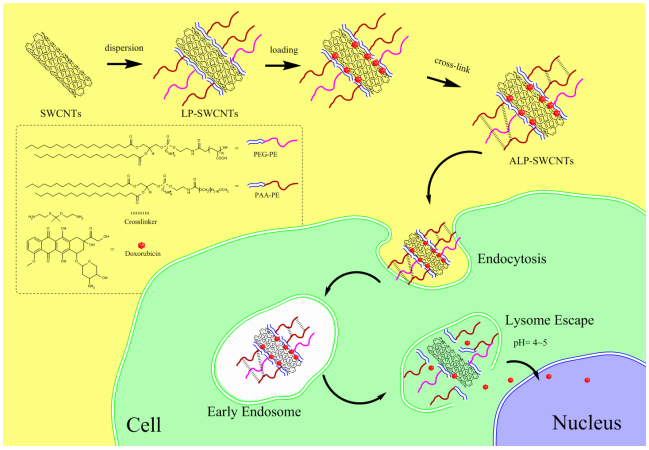
INTRODUCTION

The ability of carbon nanotubes (CNTs) to cross the biological barriers provides a possible way for the drug to be delivered to the cytoplasm and in many cases to the nucleus [1]. Therefore, the CNTs have shown significant advantage in the field of drug delivery [2]. However, the poor dispersion of CNTs has limited their uses. CNTs can be dispersed by chemical modification or physical coating. The physical methods are always preferred since they do not cause any structural change of CNTs.

Herein, the dispersion of CNTs is achieved by the use of lipid-polymer, poly(acrylic acid) modified dioleoylphosphatidylethanolamine (PAA-PE) and 1,2-Distearoyl-*sn*-glycero-3-Phosphoethanolamine-N-[Amino(Polyethylene glycol)2000] (PEG-PE). The PAA-PE is cross-linked by 2,2' -(propane-2,2-diylbis(oxy))diethanamine, an acid-labile cross-linker, which makes the system acid sensitive. Preliminary results showed strong release of Doxorubicin (DOX), an anticancer drug, at acidic condition (pH= 4~5) compared with weak leakage at physiological pH (~7.4).

METHODS



Scheme 1. Schematic representation for the preparation of Lipid-polymer-SWCNTs (LP-SWCNTs). The scheme shows the two LP that were used. After the SWCNTs were dispersed, DOX was loaded and then the sample was cross-linked by an acid labile cross-linker to form (ALP-SWCNTs). The expected pathway of ALP-SWCNTs inside the cell is shown by the arrows.

RESULTS

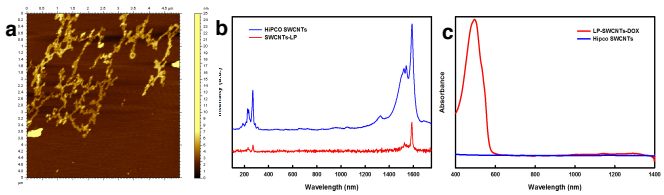


Fig. 1. (a) An atomic force microscopy (AFM) image of the dispersed LP-SWCNTs on a silicon substrate, (b) Raman spectra of HiPCO SWCNTs and the dispersed LP-SWCNTs, and (c) UV-VIS-NIR spectra of solution of the dispersed LP-SWCNTs (blue) before loading DOX and (red) after loading DOX. The peak of DOX can be seen at wavelength 485nm.

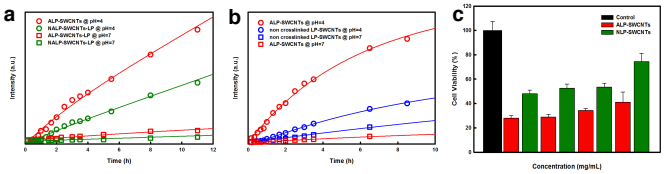


Fig. 2 (a) The release of DOX from ALP-SWCNTs and NALP-SWCNTs at pH 4 and 7 (b) The release of DOX from ALP-SWCNTs and non cross-linked LP-SWCNTs at pH 4 and 7, and (c) MTT assay results showing the cells viability of the control sample (without treatment) (black) and after the treatment by different concentration of ALP-SWCNTs (red) or NALP-SWCNTs (green).

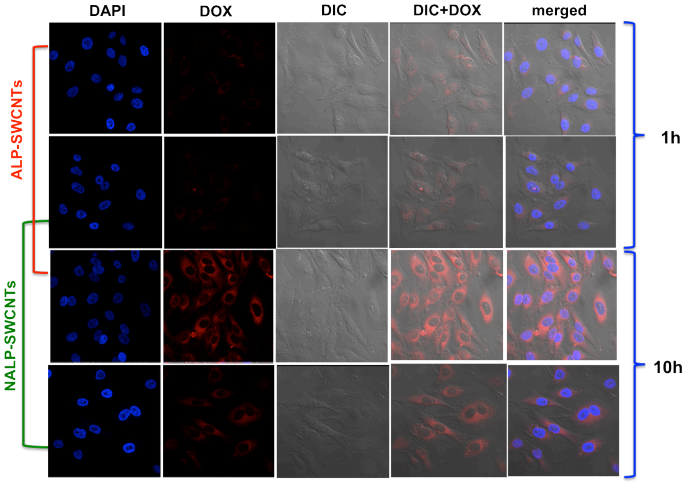


Fig. 3. Confocal laser scanning microscopy (CLSM) images of HeLa cells incubated with ALP-SWCNTs and NALP-SWCNTs for 1h and 10h.

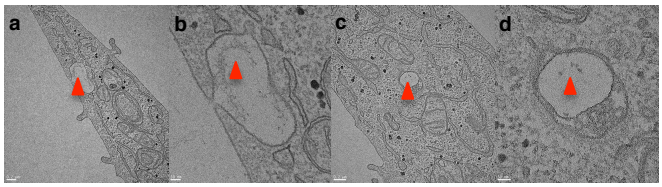


Fig. 4. TEM images of HeLa cells incubated with LP-SWCNTs. The arrows show the LP-SWCNTs inside the endosomes. (b) is an amplified image of (a), and (d) is an amplified image of (c).

CONCLUSION

The acid labile lipid-polymer (ALP-SWCNTs) were prepared successfully and can be used for drug delivery applications.

REFERENCES

[1] F. Liang, B. Chen, A Review on Biomedical Applications of Single-Walled Carbon Nanotubes, Curr. Med. Chem. 17 (2010) 10-24.
[2] A.A. Bhirde, G. Liu, A. Jin, R. Iglesias-Bartolome, A.A. Sousa, R.D. Leapman, J.S. Gutkind, S. Lee, X.Y. Chen, Combining Portable Raman Probes with Nanotubes for Theranostic Applications, Theranostics 1 (2011) 310-321.

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