

# Carrier in Carrier: DNA-doxorubicin Complex Self-assembled with Amphiphilic Cyclodextrins as Nanosystems for Cancer Therapy <sup>†</sup>

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**Abstract:** The goal of the present work was to characterize the interaction between DNA–Doxorubicin (DNA-Dox) complex and cationic vesicles based on amphiphilic cyclodextrins (ModCBHD) for their application as drug delivery systems. The systems were characterized by dynamic light scattering (DLS), Zeta potential ( $\zeta$ ), circular dichroism (CD), Emission spectroscopy, atomic force microscope (AFM), transmission electron microscopy (TEM), and drug release in two-compartment Franz cells. Fluorescence spectra, CD profile, and  $\zeta$  showed multifaceted interaction pathways between DNA and Dox, with ionic and intercalation interactions, thought of the amino sugar residue and the tetracene ring system of the drug, to form DNA-Dox complexes with a negative surface charge. DNA behaves as a reservoir of Dox, which is slowly released from the complex triggered by the presence of ions in the medium. ModCBHD-DNA-Dox complexes were formed by self-assembling in an aqueous solution without introducing any subsequent steps and exhibited around 160 nm particle size, monodisperse size distribution (PDI 0.250), and spherical shape, which could be an advantage for the enhanced permeability and retention (EPR) effect in cancer therapy. All these results demonstrated that ModCBHD could load the DNA-Dox complex and indicated the potential of the ModCBHD-DNA-Dox systems as nanocarriers to be evaluated in both *in vitro* cancer cell lines and *in vivo* tumor models.

**Keywords:** DNA-doxorubicin complex; amphiphilic cyclodextrins; cancer therapy; drug delivery; vesicles.

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## **Conflicts of Interest**

The authors declare no conflict of interest.