Targeted Delivery of Doxorubicin to Breast Cancer Cells by Multiwalled Carbon Nanotubes Functionalized with Lysine *via* 1,3-Dipolar Cycloaddition and Conjugation with Sugar moieties

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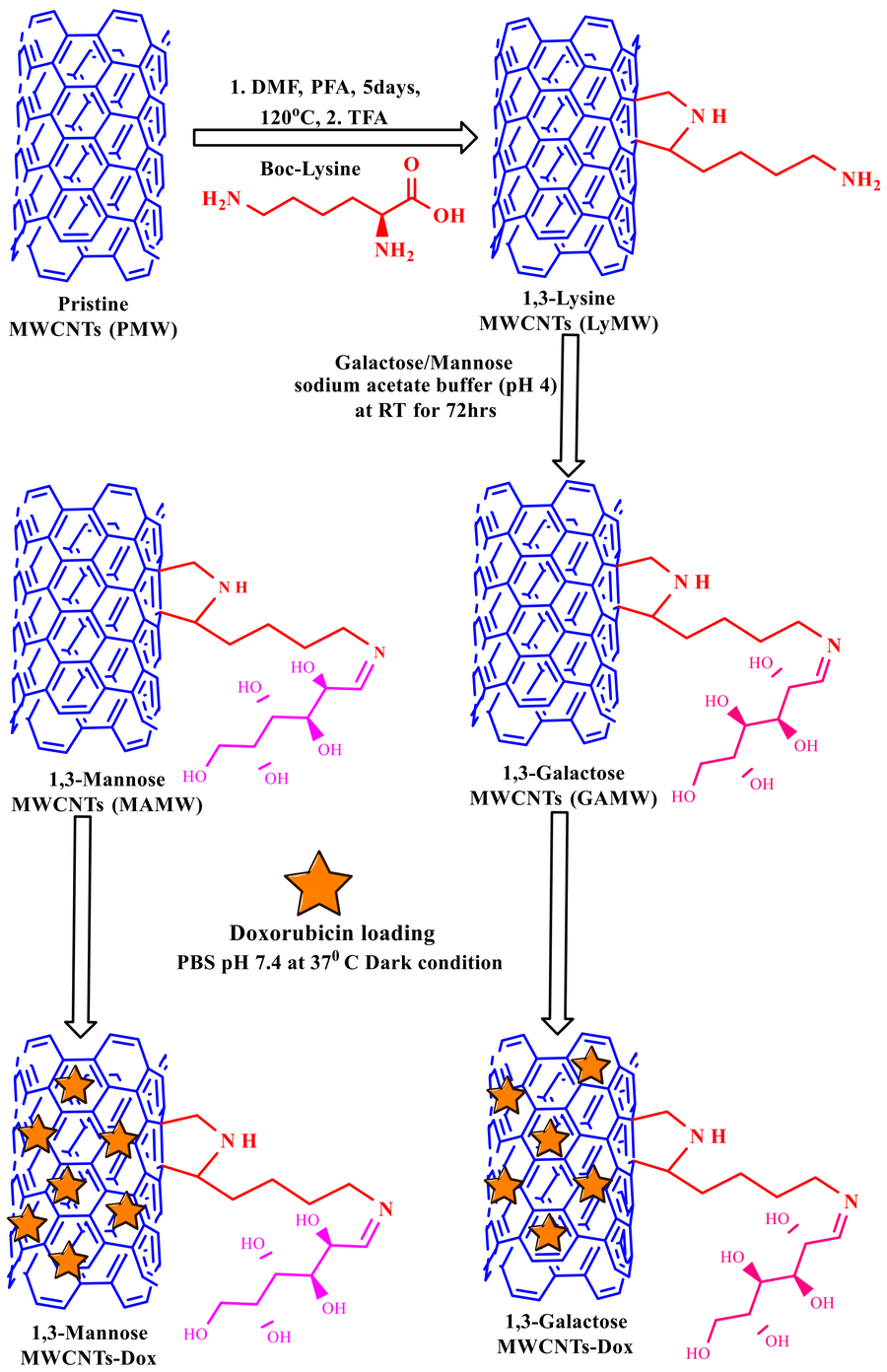
INTRODUCTION

Multiwalled carbon nanotubes (MWCNTs) have shown remarkable growth in recent years due to their multidisciplinary attention and biomedical applications such as drug delivery and imaging because of their distinct physicochemical characteristics. Even though MWCNTs are not used because of low dispersibility in aqueous or non-aqueous medium. Functionalizing MWCNTs is an attractive way to overcome this drawback as well as improve biocompatibility, encapsulation efficiency and promote ligand attachment for targeted drug delivery. However, most functionalization techniques already have reported with hazardous procedures and costly chemicals. The present research employs a simple, economically advantageous method to functionalize MWCNTs with lysine through 1,3-dipolar cycloaddition for enhanced dispersibility and to offer a sugar moieties ligand (galactose/mannose) anchoring ε-amino group for targeted drug delivery to breast cancer (MDA-MB-231 or MCF-7 cells) using Doxorubicin (Dox) as a model drug. Hence, lysine is an essential amino acid, biocompatible, biodegradable, nontoxic and cheaper moiety as well as sugar moieties also cheaper ligands and having high capacity to interact with the lectin receptor which is highly expressed in the breast cancerous cells.

MATERIALS & METHODS

- Synthesis of MWCNTs with lysine by 1,3-dipolar cycloaddition methods then followed with sugar moieties conjugations: Functionalization of MWCNTs were confirmed through IR, NMR.



- MWCNTs water dispersibility study were carried out upto 30days through visualization process.
- Drug Releases were carried out upto 120hrs in pH 5.0 & pH 7.4 through dialysis membrane methods.
- Cell cytotoxicity & Apoptosis was performed in MDA-MB-231 & MCF-7

CONCULSION

Developed MWCNTs formulations was biocompatible and nontoxic, improved the dispersibility in aqueous medium as well as enhanced the % Dox loading efficiency as compared to PMW. Dox release rate also high in acidic environments, it is beneficial for cancer therapy because cancer cell environment is acidic in nature. Dox loaded MWCNTs formulations provided high cytotoxicity as compared to pure Dox, because formulations provided targeted Dox delivery to breast cancer cells.

RESULTS & DISCUSSIONS

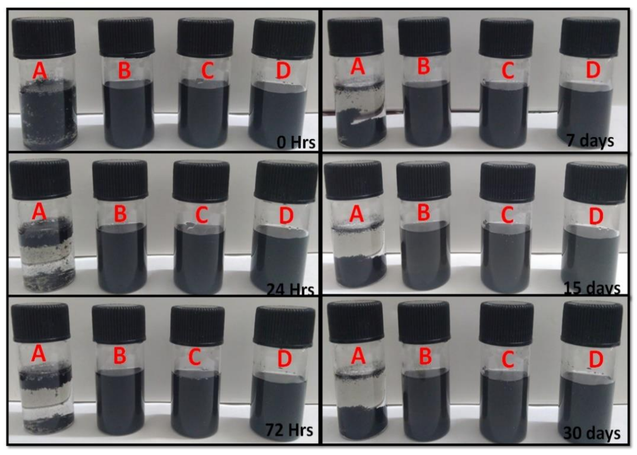


Figure 1: Dispersibility analysis of A (PMW), B (LyMW), C (GAMW), D (MAMW). In this images clearly seen PMW could not be disperse properly in aqueous medium after the 30 min of sonication that indicated the poor dispersibility in aqueous medium but after functionalization of MWCNTs with lysine and galactose/mannose dispersibility was high in aqueous medium without any flocculation and dispersion in aqueous medium was stabile more than 30days.

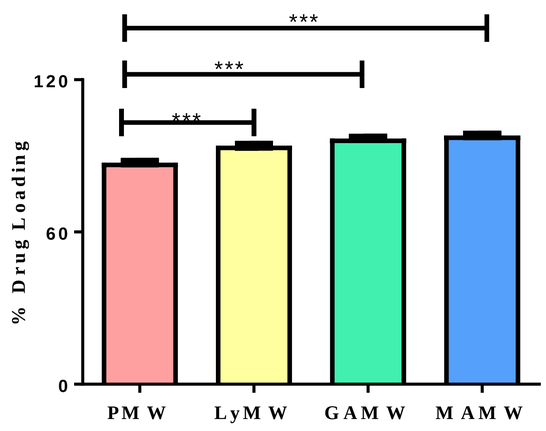


Figure 2: The Dox loading efficiency of PMW was 87.35 ± 2.61 % and after functionalization of MWCNTs Dox loading efficiency also enhanced sightly were: LyMW, GAMW, MAMW as . 94.01 ± 0.32, 96.89 ± 1.58 and 98.07 ± 2.34 respectively, because Dox has an aromatic ring structure, it may interact with the walls of MWCNTs by π-π stacking or hydrophobic interactions.

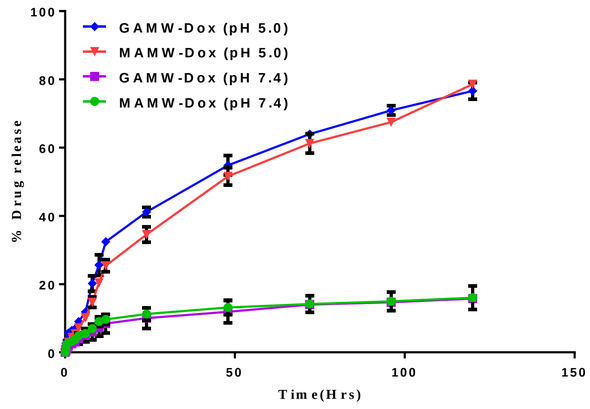


Figure 3: In graph clearly showed that in pH 5.0 Dox was highly released as compared to pH 7.4, because cleavage of bonding and π-π stacking interaction is weaker in acidic environments. Since this pH dependent Dox releases behaviour is beneficial for anticancer therapy. The % cumulative Dox release from GAMW-Dox & MAMW-Dox nanocarrier was founds as >75% release in pH 5.0 & <20% released in pH 7.4 at 120 hrs.

Table 1: Cell cytotoxicity and apoptosis data of Dox and Dox loaded functionalized MWCNTs. In case of both the cells (MDA-MB-231 or MCF-7), GAMW-Dox & MAMW-Dox showed sightly high cell cytotoxicity and apoptosis as compared to pure Dox. But pure GAMW & MAMW formulations shown negligible toxicity, it means pure formulations are biocompatible and nontoxic.

Formulations	% Cell viability		% Apoptosis	
	MDA-MB-231	MCF-7	MDA-MB-231	MCF-7
Control	0	0	0.6±0.01	0.2±0.03
Doxorubicin	2.6±1.01	21±0.09	22.4±0.06	12.76±0.14
1,3-Galactose- MWCNTs-Dox	2.4±0.19	20±0.12	40.1±0.19	27.3±0.28
1,3-Mannose- MWCNTs-Dox	2.2±1.08	18±1.06	49.7±0.22	44.0±0.30
1,3-Galactose- MWCNTs	85±1.18	70±2.09	-	-
1,3-Mannose- MWCNTs	86±0.03	71±1.45	-	-

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