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Linkage of doxycycline onto functionalized multi-walled carbon nanotube and morphological characterization

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ABSTRACT: In this paper functionalized multiwall carbon nanotubes (FMWCNT) were modified using doxycycline, containing reactable nitrogen, which can attach chemically to functionalized MWCNT. The synthesized nano compounds were characterized by Fourier transform infrared spectroscopy (FT-IR) and Raman spectroscopy. These spectrums proved the existence of nitrogen atoms of amide functional groups. The morphology was also determined by scanning electron microscopy (SEM) and Transmission electron microscopy (TEM). Also the SEM and TEM images confirmed the uniformly attachment of doxycycline, onto functionalized MWCNTs.

Keywords: *Doxycycline; Modification; Morphology; Multi-walled carbon nanotubes; Nanotechnology*

INTRODUCTION

Nanotechnology is one of the fastest developing fields in science which have found technological interest to many researchers. Carbon nanotubes (CNTs) which were discovered in 1991 by Sumio Iijima in Japan, caused a revolution in nanotechnology in various fields such as electronic, mechanic, environment, chemistry and pharmacology (Pandurangappa and Kempegowda, 2011). The physical properties, such as porous structures and facile surface functionalization have made the application of the CNTs more attractive as drug delivery vehicles. The poor solubility of carbon nanotubes in organic solvents restricts them to be used as a drug delivery agent into living systems in drug therapy. Hence many modification approaches such as physical, chemical or combined methods have been used for the homogeneous dispersion in common solvents to improve their solubility (Kopaieemalek, *et al.*, 2011). Carbon nanotubes have very wide surface, which is a good position for the functionalization, compared with its length scale in diameter, which is capable of adding different functional groups.

The antimicrobial activity of antibiotics such as doxycycline against microbes is severely limited by poor membrane transport ability. Thus there is a need of delivery vehicles like CNTs that allow localizing and controlling delivery of antibiotics for preventing microbial infections (Ahangari, *et al.*, 2013, Kim and Jones, 2004, Dini, *et al.*, 2003). Multi-walled carbon nanotubes (MWCNTs) have potential roles in delivering pharmacologic agents. (MWCNTs) are more attrac-

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tive than single walled carbon nanotubes because of their relatively low production costs and availability in large quantities.

Biomedical applications for MWNTs are being investigated actively because of their useful combination of size and physicochemical properties (Bianco, *et al.*, 2005, Sedaghat and Mehraji, 2013). The aim of this study is the linkage of doxycycline as a drug containing amino group with functionalized multi-walled carbon nanotubes (FMWCNTs) for the synthesis of nano drug as illustrated in Figs. 1 and 2:

MATERIALS AND METHODS

Materials

Multi-wall carbon nanotube (95% purity, 20-30 nm) were purchased from nanocarbon Co. Thionyl chloride ($SOCl_2$), THF and DMF were purchased from fluka. Deionized water was also used. Fourier transform infra red (FT-IR) spectrum was recorded using KBr tablets on a Perkin Elmer Spectrum-100 FT-IR spectrometer. Raman spectra recorded on Bruker Sentrra-2009 spectrometer. Scanning electron microscope (SEM) was used to study the morphology of the MWCNTs. SEM measurement was carried out on the Hitachi 4160 Electron Microscope.

Surface functionalization of MWCNTs

MWCNTs were refluxed in a mixture of H_2SO_4/ HNO_3 for 30 minutes. Then were filtered with millipore membrane, and were washed by double distilled water. The synthesized MWCNTCOOH were dried and collected as black solid. In another step, carboxylated MWCNTs were stirred in 30 mL of a 20:1 mixture of thionyl chloride ($SOCl_2$) and dimethyl formamide (DMF) at 70°C for 24 hours under reflux conditions. The resulting materials were decanted and the super-

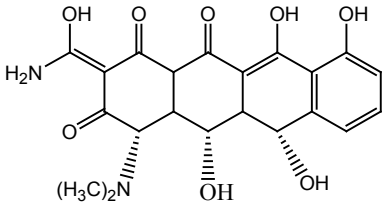


Fig. 1: The structure of doxycycline.

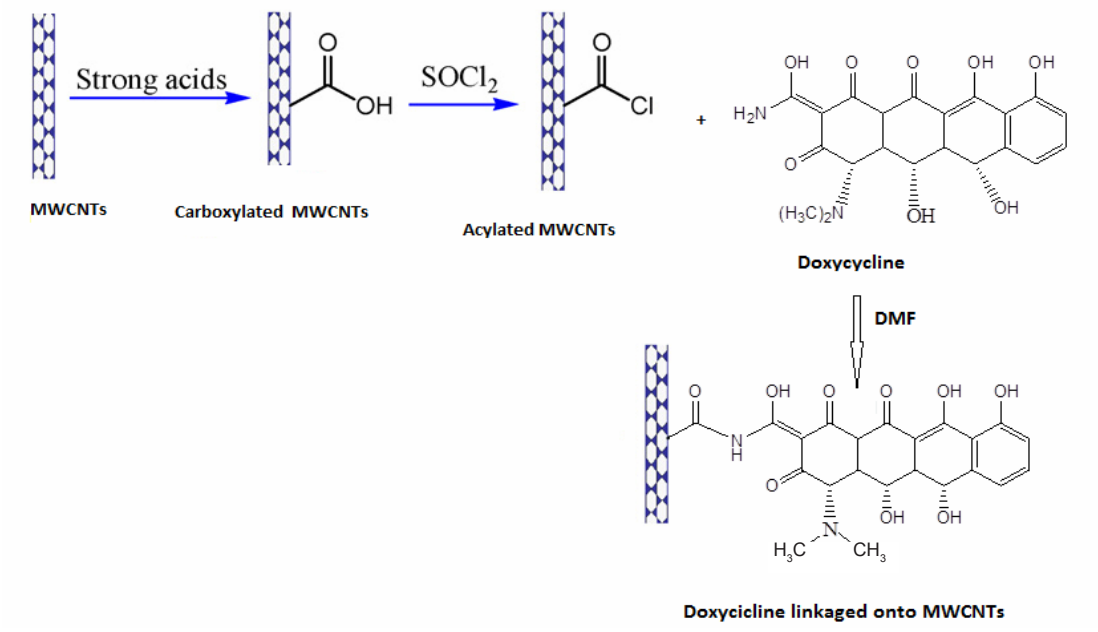


Fig. 2: Strategy for the linkage of doxycycline onto functionalized multi-walled carbon nanotube.

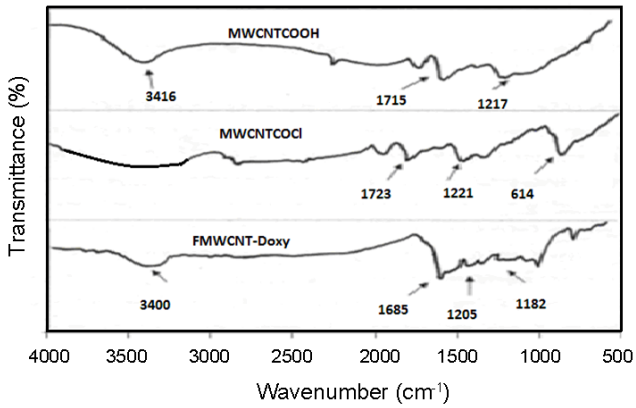


Fig. 3: FT-IR spectra of: MWCNT-COOH, MWCNT-COCl and MWCNT-Doxy.

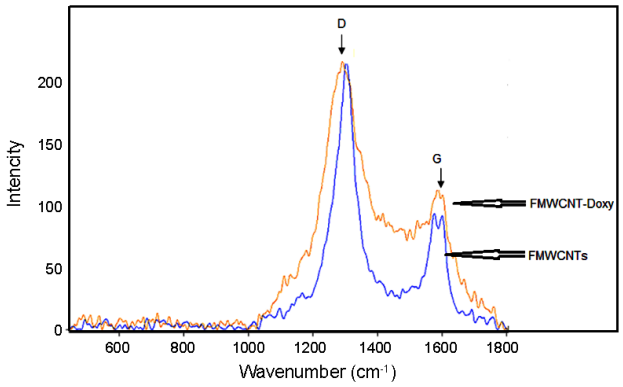


Fig. 4: Raman spectra of MWCNT-COCl and MWCNT-Doxy.

natant were removed. Dry THF was then added and the mixture and then centrifuged. This operation was repeated for 5 times.

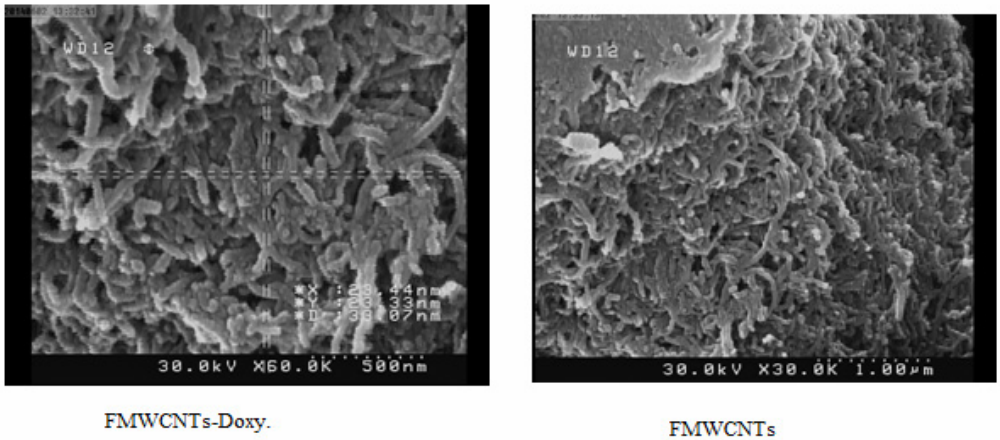
The solid was then filtered on a millipore membrane and washed several times with ethyl alcohol and THF. Subsequently, the black solid was dried at room temperature for 6 hours under vacuum condition as described in our previous work (Sedaghat, 2014).

Linkage of doxycycline onto functionalized multi-walled carbon nanotube 80 mg of previously synthesized MWNT-COCl were mixed with 200 mg of doxycycline and 25 mL of DMF and the reaction mixture were stirred for 72 hours under reflux conditions. The synthesized nano compound was washed thoroughly with ethyl alcohol and THF. Subsequently the black solid was dried at room temperature for 8 hours under vacuum condition (Chen and Hamom, 1998). The synthesized nano compound collected for future evaluations.

RESULTS AND DISCUSSION

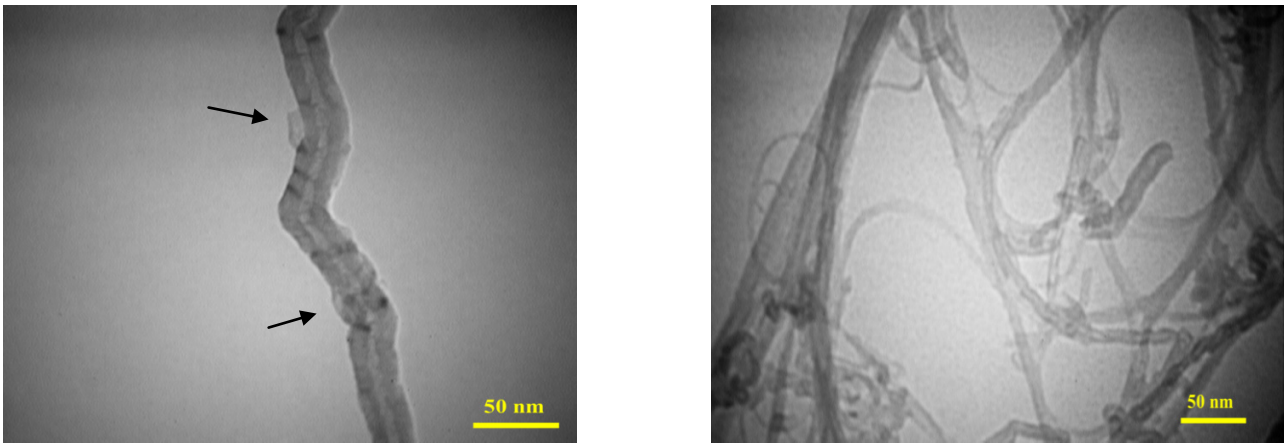
Fig. 3 shows the FT-IR spectra of MWCNTCOOH, MWCNTCOCl and synthesized nano drug respectively. The stretching frequency of OH, C=O and C-O are shown at 3416, 1715 and 1217 cm^{-1}. The peaks who are related to C=O and C-O stretching frequencies are shifted to 1723 and 1221 cm^{-1} because of the negative inductive effect of chlorine atoms and the peak at 614 cm^{-1} can be assigned to the C-CL stretching frequency of COCl groups in MWCNTCOCl. C=O and C-O stretching frequencies are shifted to 1685 and 1205 cm^{-1} due to the formation of amide bond in nono drug and the peak at 1182 cm^{-1} is related to C-N stretching of amide groups, while the peak at 3400 cm^{-1} can be assigned to the N-H stretching frequency for the synthesized nano compound (Tahermansouri, *et al.*, 2013).

Raman spectra of functionalized MWCNTs and nano compound are shown in Fig. 4. As can be seen,



FMWCNTs-Doxy. FMWCNTs

Fig. 5: SEM images of FMWCNT and FMWCNT-doxycycline



FMWCNTs-Doxy FMWCNTs

Fig. 6: TEM image of MWCNT-COCl and MWCNT-Doxy.

the functional reactions slightly influence the "D band" and the "G band" of the samples. The characteristic peaks of MWNT tangential modes, namely the D band at around 1330-1350 cm^{-1} and the G band at around 1560-1580 cm^{-1} are slightly changed because of the strong negative inductive effect, the chlorine atoms are acting as electron withdrawing groups with respect to the nanotubes.

However replacing chlorine atoms by amino functional groups can cause the opposite charge transfer from the lone pair of nitrogen to the nanotubes. These results are obvious evidences for the chemical functionalization and formation of nano compound (FMWCNTs-Doxy).

In Fig. 5, SEM images of the functionalized MWCNTs and nano compound are shown. In the SEM images of MWNT-COOH, it seems that the uniform surfaces of nanotubes are relatively smooth. After functionalization with doxycycline the diameters of the modified MWNTs are slightly increased as compared to that of MWCNT-COOH, the changes in the morphology are clearly shown (Tahermansouri, *et al.*, 2014).

The transmission electron microscopy (TEM) images of the functionalized MWCNTs which are shown in Fig. 6 are the most powerful tool for structure and morphology of MWCNTs. The coating on the nanotubes surface could be observed which might be logically attributed to the doxycycline derivatives functionalities which results the formation of short tubular particles (Entezari, *et al.*, 2013).

CONCLUSIONS

The linkage of doxycycline to the FMWCNTs surface by chemical functionalization is successfully carried out. The modified functionalized MWCNTs obtained were evaluated, using FT-IR, SEM and Raman spectroscopy. SEM and TEM images showed the formation of the FMWCNT-doxycycline and presence of the chemical bonding the matrix. FT-IR results showed the formation of amide in the products. The most important advantage of this method is to optimize the drug delivery.

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