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Adsorption of Anticancer Antibiotic Doxorubicin on Carbon Nanotubes Synthesized by Flame Fragments Deposition Technique

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Abstract: The adsorption of the Doxorubicin drug (DOX) which used as chemotherapy drug called an anthracycline to stop or slow the growth of cancer cell by Oxidized Carbon Nanotubes (O-CNTs) was studied. CNTs were synthesized by Flame Fragments Deposition (FFD) technique. Different concentrations of O-CNTs as a nanocarrier were added to 50 mL of DOX aqueous solution (10 ppm). Each mixture was stirred for ten minutes at 25°C at a pH = 4.8 for different periods of time. The O-CNTs/DOX mixture was isolated by centrifuging for 10 min at a rate of 6000 rpm. The concentrations of DOX in the supernatant liquid were recorded using a UV-Vis spectrophotometer by measuring the absorbance at 480 nm in order to find the ideal dose of CNTs for the drug's optimum adsorption efficiency.

Key words: Anticancer antibiotic, doxorubicin, carbon nanotubes, flame fragments deposition, spectrophotometer, chemotherapy

INTRODUCTION

Doxorubicin ($C_{27}H_{29}NO_{11}$) with a molecular mass 543.52 g/mol is a chemotherapy medication and often used together with other chemotherapy agents to treat breast cancer, bladder cancer, Kapos's sarcoma, lymphoma and acute lymphocytic leukemia.

Drug delivery systems are currently widely studied as they represent an important component of novel therapies free of side effects and oriented toward a precise attack of disease sources. Most investigations are centered around the advancement of new materials or their streamlining. It is difficult to claim that drug transporters, their areas of application and their favorable circumstances and drawbacks have all been considered. Nonetheless, the most developed results including clinical preliminaries, concern liposomes, emulsions, micelles, dendrimers, magnetic nanoparticles or different other nanoparticulate systems (Wong *et al*., 2013). Out of the nanoparticulate frameworks, Carbon Nanotubes (CNTs) are under consideration because of their extraordinary physicochemical properties. They include, but are not limited to, large surface area available for functionalization by various moieties, large inner volume which can accumulate large amounts of small molecule drugs and needle like shape which facilitates penetration of cell membrane. Their disadvantages include insolubility in fluid media and a possible poisonous quality. However, both of these issues can be resolved by substance medicines. However, both these problems can be removed by chemical treatments leading to shortening, purification, and development of hydrophilic functional groups located at the nanotube tips and sidewalls (Pastorin, 2009).

Although, a few investigations accounted for the impact of *in vivo* or *in vitro* antitumor movement and tumor targeting of drug-CNTs complex based on the adsorption but very little is known about the adsorption behavior of anticancer drug on CNTs. To encourage the advancement of CNT-based drug conveyance frameworks, careful investigations into the adsorption and desorption of drugs by CNTs are essential. To improve the adsorption of DOX on MWNTs-PEG, the effect of different factors such as pH, contact time, adsorbent measurement and starting focus on subordinate factors (i.e., entanglement proficiency %) were examined by a two-level, four-factor, full factorial trial plan with Minitab16 programming. The test's strategy was adopted to decrease the number of examinations, time, overall process cost and screened simultaneously a large number of factors to obtain better response Investigation into the adsorption of DOX onto MWNTs will profit by understanding the association component between the adsorbents and is the reason for the foundation of nanoscale medicate conveyance systems (Farahani *et al*., 2016).

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The adsorption of Dissolved Organic Matter (DOM) and toxins by CNTs has been analyzed and tested for systematic and ecological purposes. The adsorption isotherms, adsorption energy and affecting parameters have been researched and improved. For instance, Yang and Xing pointed out that CNTs are likely to adsorb fulvic acid containing more sweet-smelling rings. The adsorption limits could be regulated by the width of CNTs and the natural pH level. The adsorption of methylene blue by CNTs has also been observed (Wang *et al*., 2012). CNTs have a high adsorption limit with respect to methylene blue which is affected by the adsorption temperature and time. In addition, numerous investigations have proven that adsorbed particles can be discharged from CNTs in various conditions. Unlike the widely considered adsorption conduct of DOM and contaminations on CNTs, the adsorption and desorption of drugs by CNTs has received much less consideration. A few pilot studies have detailed the adsorption and arrival of Doxorubicin (DOX), epirubicin and mitoxantrone by CNTs in PBS. Nonetheless, when drug-loaded CNTs enter a biosystem, their practices, i.e., focused adsorption and desorption, become unclear. To encourage the improvement of CNT-based drug delivery frameworks, intensive investigations into the adsorption and desorption of medications by CNTs are crucial (Chen *et al*., 2011).

Next, the adsorption conduct of anticancer drugs by CNTs are considered. Investigating the collaboration between anticancer drugs and CNTs is the reason for the foundation of a transport framework. In particular, carboxylated Carbon Nanotubes (c-CNTs), derivatized with carboxylate compounds, show excellent biocompatibility and can be duplicated and adjusted to encourage their focus on the treatment of tumors. With the increasing use of c-CNTs as an anticancer drug delivery framework, it is important to understand the communication between c-CNTs and anticancer operators and to assess the drug-stacking capacity of c-CNTs (Farahani *et al*., 2016; Wang *et al*., 2012; Chen *et al*., 2011; Kam *et al*., 2005).

MATERIALS AND METHODS

Experimental

The functionalization of carbon nanotubes: Functionalization of CNTs is an important step that can be used in order to introduce some functional groups into the surface and improve its surface properties. The 100 mg of CNTs which was synthesized by using flame fragments deposition technique as described in our previous research (Hammadi *et al*., 2018a, b; Hussein *et al*., 2018; Jassm *et al*., 2017) were suspended in 75 mL of hydrogen peroxide (30 weight %) in a 100 ml round bottom flask equipped with a condenser and the dispersion was heated to 80 at reflux for overnight. The schematic diagrams of the complete the process of functionalization is shown in Fig. 1.

After the reflux, the suspension containing CNTs and hydrogen peroxide was heated to 50°C with irradiation under an (UV) lamp for 5 h to dry the mixture. The oxidation of the CNTs surface is very important to produce the composite. The homogeneous diffusion of O-CNTs takes place in distilled water due to creation hydrogen bonding. The formed functioned O-CNTs was investigated using FTIR.

Adsorption of drug on O-CNTs: Different concentrations of O-CNTs nanocarrier were added to 50 mL of DOX aqueous solution (10 ppm). Each mixture was stirred for 10 min at 25°C at a pH = 4.8 for various periods of time. The mixture of O-CNTs/DOX was isolated by centrifuging for 10 min. At a rate of 6000 rpm. The concentrations of DOX in the supernatant liquid were recorded using UV-Vis spectrophotometer by measuring absorbance at 480 nm and compared with the value of concentrations by using the values indicated in the calibration curve as shown in Fig. 2.

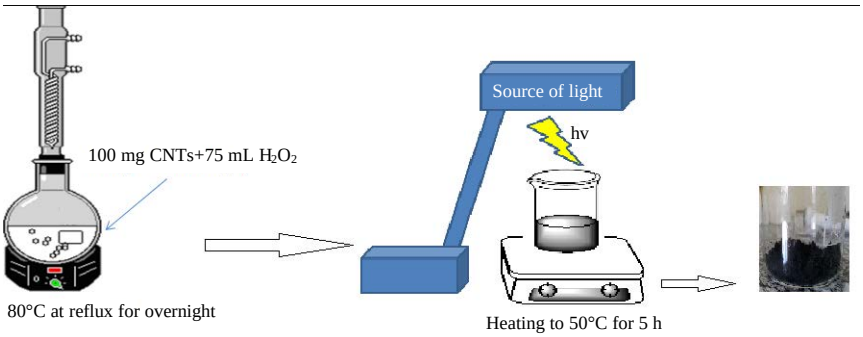

Fig. 1: Schematic diagrams of the complete the process of functionalization

For investigation of the adsorption isotherms, the experiments are carried out by varying the solution temperature and initial DOX concentration. The adsorption percentage (η) and adsorption capacity values at equilibrium and time t (q_e and q_t, mg g^{-1}) were calculated according to Eq. 1-3, respectively:

$$\eta = C_o\text{-}C_e/C_o \times 100\% \quad (1)$$

$$q_e = (C_o\text{-}C_e/m)^*V \quad (2)$$

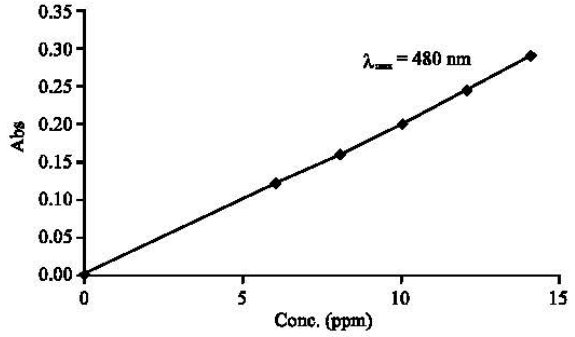

Fig. 2: Calibration curve at 480 nm for different concentrations of doxorubicin drug

$$q_t = (C_o\text{-}C_t/m)^*V \quad (3)$$

Where:

C_o, C_e and C_t (mg L^{-1}) = The DOX Concentrations at initial, equilibrium and time t, correspondingly

V (L) = The solution volume

m (g) = The mass of used nanocarrier

RESULTS AND DISCUSSION

The functionalization of Carbon nanotubes: The chemical oxidation of CNTs is carried out using H_2O_2 with UV in order to obtain the hydrophilic surface structure of oxygen within a certain surface group. This oxidation process with H_2O_2 introduces several functional groups such as -OH (Hydroxyl), -COOH (Carboxyl) and others on the CNT's surface. These surface groups are useful during the interaction and chemical bonding between CNTs and TiO_2. As shown in Fig. 3, the FTIR spectrum of, synthesized CNTs and functionalized CNTs provides sufficient data related to these functional surface groups. Figure 3a shows functionalized CNTs which exhibit strong characteristics as well as a broad band between 3173-3600 cm^{-1} which is attributed to the O-H stretching vibrations in the C-OH groups. The broad band

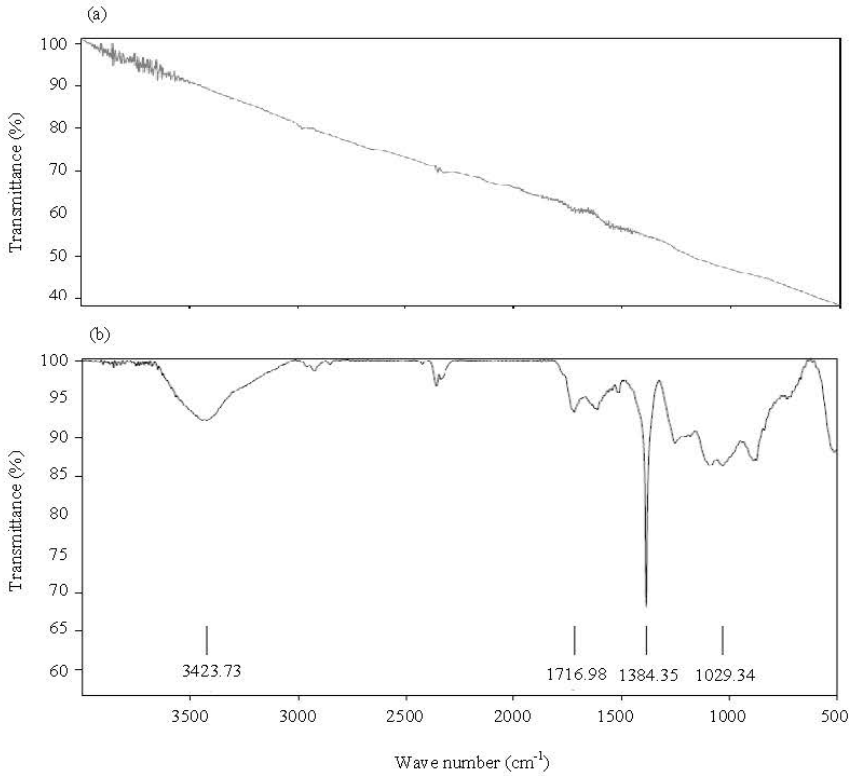

Fig. 3: FTIR spectra for; a)Synthesized CNTs and b) Functionalization of CNTs

between 1766-2017 cm^{-1} on the other hand is caused by the C = O stretching vibrations in the carboxyl, aldehyde and acid anhydride groups.

The adsorption properties of CNTs-DOX: The initial influences of DOX adsorption over O-CNTs are shown in Fig. 4. A pH of 4.8 in an aqueous solution is a rarity among the most essential variables, given its impact on the dynamic destinations of nano-adsorbents and the level of ionization and speciation of the adsorbate. The increasing adsorption productivity along with pH suggests that the surface of functionalized CNTs has a more negative charge. It has been noted that DOX adsorption increases along with increases in the adsorbent doses. Also, the increase in ensnarement productivity with an increase in adsorbent dosage, may be attributed to the accessibility of a large surface area and a more noticeable number of free adsorption sites.

With further increases in adsorbent dosage concentrations, the rate of adsorption does not increase fundamentally. This phenomenon may be due to the fact that both the surface of the adsorbent and the solution concentration of the DOX settle down in order to harmonize with each other. As can be seen in Fig. 4, increasing the O-CNT concentration from 5-50 mg L^{-1} leads to a corresponding increase in the adsorption percentage. These results may be due to the fact that at high CNT concentrations, the ratio of active sites on the surface of the adsorbent to the overall adsorbate (DOX molecules) concentration is relatively high. On the other hand when the O-CNT concentration decreases, the numbers of active adsorption sites are not enough to accommodate drug ions.

Adsorption isotherms: During the batch experiments, the adsorption capacity was measured and the adsorption model was determined. In the first set of experiments, CNTs (5-50 mg/L) were mixed with DOX (10 ppm). The samples were shaken in a thermostat shaker at 6000 rpm for 30 min at 25°C. At the end of both sets of experiments, each sample was centrifuged at 6,000 rpm for 30 min. The absorbance (480 nm) of the supernatant was recorded in order to determine the Concentration of free DOX in the solution in light of the DOX's calibration curve. The equilibrium Concentration (C_e, the concentration of free DOX in the solution after the adsorption attained equilibrium) was also obtained. The equilibrium sorption capacity (q_e, the amount of DOX adsorbed by CNTs after the adsorption attained equilibrium) was calculated by (C_0-C_e)/CNT where C_0 is the initial concentration of DOX and O-CNT is the concentration of O-CNTs. The data meet both the Langmuir and Freundlich Models as shown in Fig. 4 and 5.

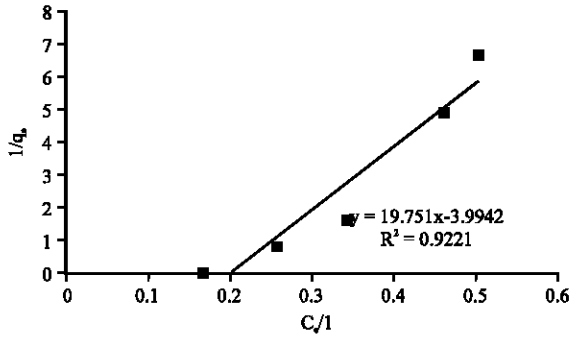

Fig. 4: Linear Langmuir adsorption isotherms for doxorubicin adsorption by CNTs

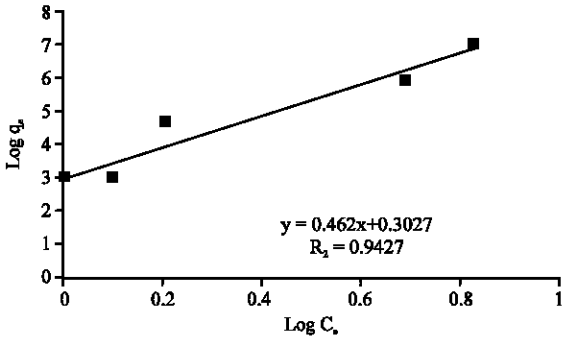

Fig. 5: Linear Freundlich adsorption isotherms for doxorubicin adsorption by CNTs

CONCLUSION

From the obtained results, it can be seen that all of the used doses of CNTs showed good adsorption ability for DOX over CNTs. However, the maximum adsorption efficiency was recorded when using an O-CNT concentration of 50 mg/L. After that, the adsorption efficiency of DOX over CNTs decreased when the CNT concentration was reduced.

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